Current Studies in Health and Life Science 2024

EDITOR

Prof. Dr. Mehmet ÖZASLAN

ISRES Publishing

Current Studies in Health and Life Sciences

2024

EDITOR

Prof. Dr. Mehmet ÖZASLAN

Current Studies in Health and Life Sciences-2024

Editor

Prof. Dr. Mehmet ÖZASLAN

Language Editors

Lecturer Ceren DOĞAN

Cover Design and Layout

Fatih YAYLA

This book was typeset in 10/12 pt. Times New Roman, Italic, Bold and Bold Italic.

Current Studies in Health and Life Sciences 2024

Published by ISRES Publishing, International Society for Research in Education and Science (ISRES)

Includes bibliographical references and index.

ISBN

978-625-6959-59-0

Date of Issue

October / 2024

Address: Askan Mah. Akinbey Sok. No:5/A Meram/Konya/Türkiye

E-mail

isresoffice@gmail.com

www.isres.org

Current Studies in Health and Life Sciences-2024

PREFACE

Welcome to "Current Studies in Health and Life Sciences 2024." This compilation stands as a testament to the ever-evolving landscape of scientific inquiry, offering a panoramic view of the latest advancements and critical inquiries in the fields that define our understanding of life and well-being. As we navigate the complex terrain of health, and life sciences, this book serves as a comprehensive guide to the forefront of contemporary research.

In the dynamic realm of health and life sciences, the pursuit of knowledge is vigourosly improving year by year. Researchers, scholars, and practitioners continually explore new frontiers, pushing the boundaries of our understanding of the human body, the environment, and the intricate interplay between the two. This book encapsulates the spirit of this intellectual journey, presenting a mosaic of studies that illuminate the multifaceted aspects of our existence.

The book chapters written by different authors within this collection span a diverse range of topics, reflecting the interdisciplinary nature of modern scientific exploration. From cutting-edge medical and dentistry interventions to ecological studies that underscore the delicate balance of our ecosystems, each contribution offers a unique perspective on the challenges and opportunities that define the current state of health and life sciences.

The interconnectedness of health, dentistry and life sciences is a central theme, emphasising that progress in one area often relies on insights from another.

As we embark on this intellectual journey together, let us celebrate the dedication and ingenuity of the researchers who contribute to the collective knowledge of humanity. "Current Studies in Health and Life Sciences 2024" is more than a compilation of selected papers; it is a testament to the indomitable human spirit that drives us to explore the unknown and seek solutions to the complex challenges that shape our world.

May this book inspire curiosity, spark new ideas, and foster a deeper appreciation for the remarkable strides we are making in understanding and enhancing life in all its forms for the readers.

October 2024.

Prof. Dr. Mehmet Ozaslan

Department of Biology, University of Gaziantep, Turkiye

Website: mehmetozaslan.com e-mail: ozaslanmd@gmail.com

Table of Content

Chapter I: Life Science

Chapter II: Dentistry

Chapter III: Animal Sciences

Chapter I:
Life Science

ISRES Publishing

Emerging Infectious Diseases and Their Preventive Measures

Tanveer NASIR

Muhmmad SAFDAR

Salma Bibi

Shafeeq Ur REHMAN

Mehmet OZASLAN

1. Introduction

Infectious diseases are illnesses caused by pathogens such as bacteria, viruses, fungi, or parasites that spread from one person to another. Some examples are the flu (virus), tuberculosis (bacteria), and malaria (parasite) (Verhoef et al., 2019; Zabidi et al., 2023). The landscape of infectious diseases is constantly evolving due to the emergence of new pathogens and the re-emergence of existing controlled infections (Cliff, 2009). From a decade, scientists are trying to monitor these emerging threats, particularly in light of global challenges such as climate change, urbanization, and increased interactions between humans and animals (Myers & Patz, 2009). Recently, the COVID-19 pandemic has demonstrated how quickly infectious diseases can spread worldwide (Baker et al., 2022). Therefore, it is a dire need for rapid surveillance systems and response strategies to combat these threats (Peeri et al., 2020).

It is known that emerging pathogens including novel viruses, bacteria, and parasites, pose significant public health challenges due to their potential for high transmissibility, virulence, and resistance to existing treatments (Levitt et al., 2010). The World Health Organization (WHO) classifies emerging infectious diseases that are newly appeared in a population or already existed in this environment but are rapidly increasing in incidence or geographic range (Dye, 2014). For examples, the emergence of SARS-CoV-2, Zika virus, and antibiotic-resistant strains of bacteria, such as Methicillin-resistant Staphylococcus aureus (MRSA) (Janik et al., 2020). Indeed, pathogens are not only threatening individual health but also impose substantial burdens on healthcare systems and economies (Bloom & Cadarette, 2019).

In addition, the zoonotic diseases are major concern and have a significant impact on human health (Rahman et al., 2020). These diseases can transfer from animals to humans, often facilitated by environmental changes and human behaviors (Weiss & McMichael, 2004). It is also important to consider that many risk factors such as deforestation, intensive agriculture, and climate change are involved and may increase the likelihood of zoonotic spillover events (Tazerji et al., 2022). Some researchers have shown that habitat destruction brings wildlife into closer contact with human populations, and may create opportunities for pathogens to transfer (Plowright et al., 2017). Moreover, global travel and trade accelerate the spread of these pathogens, as evidenced by the rapid international dissemination of COVID-19 (Kuo & Chiu, 2021).

Some other researchers have published in openly-access journals that emphasized the importance of the ecological and evolutionary dynamics of emerging pathogens (Salim et al., 2022). The genetic analysis revealed that how pathogens adapt to new hosts, develop resistance to treatments, and change their virulence profiles (Neckers & Tatu, 2008). Therefore, new insights are critical for informing public health strategies and developing effective vaccines and therapeutics (Meganck & Baric, 2021). Additionally, the interdisciplinary approaches that integrate with microbiology, epidemiology, environmental science, and social sciences are crucial for addressing the multifaceted nature of emerging infectious diseases (Janes et al., 2012). In context with the recent studies indicate that marginalized populations often bear a disproportionate burden of infectious diseases

(Quinn & Kumar, 2014). Therefore, effectively managing these diseases requires a swift response through the implementation of health policies and targeted interventions (Haldane et al., 2021).

2.Evolution of Infectious Disease

The evolution of infectious diseases is a complex and multifactorial process that includes different aspects of genetics, epidemiology, and pathogen-host interactions (Forst, 2010). Advances in genetic sequencing and bioinformatics have significantly enhanced our concepts of the genetics and evolution of infectious diseases (Pybus & Rambaut, 2009). Moreover, this includes the study of microbial genetic data and the evolutionary biology of pathogens, such as viruses, bacteria, and fungi (Tibayrenc & Ayala, 2012). In addition, the co-evolution of hosts and pathogens, the evolution of antibiotic resistance, and the role of genetic variation in pathogenesis and epidemiology (Woolhouse et al., 2002). In another study, scientists focus on the evolutionary mechanisms of bacterial pathogens (Martinez, 2009). For example, Mycobacterium tuberculosis highlighted its interactions with the lung environment and the evolution of drug-resistant strains (Müller et al., 2013). In some similar studies, they conducted analyses on pathogens like Burkholderia pseudomallei and Klebsiella pneumoniae, examining their genetic diversity and the evolutionary arms race between these pathogens and their hosts (Chomkatekaew et al., 2021). Additionally, the evolutionary dynamics of antibiotic resistance and the phenotypic changes are associated with resistance acquisition (Hughes & Andersson, 2017).

The field of molecular evolution of infectious agents includes studies on genomic adaptations and the impact of selective pressures such as antibiotics and host immune responses (Sheppard et al., 2018). Some studies emphasize the importance of genetic elements like genomic islands and plasmids in the evolution and epidemic spread of pathogens (Dobrindt et al., 2004). For instance, the emergence and adaptation of SARS-CoV-2 variants during the COVID-19 pandemic serve as an understanding of pathogen evolution and guide public health responses (Telenti et al., 2022).

The evolution of eukaryotic pathogens, such as malaria parasites, Cryptosporidium, and Giardia were studied (Ortega-Pierres et al., 2009). They explored the interactions between parasites and hosts, the impact of medical interventions on the evolution of drug resistance, and the genetic diversity of these pathogens (Hughes & Andersson, 2015). For instance, Plasmodium vivax provides some insights into genetic diversity and resistance patterns, which are crucial for developing effective control strategies (Arnott et al., 2012).

The interplay between host and pathogen is a critical area, as we can examine how genetic changes in pathogens influence their virulence and the host's susceptibility (Casadevall & Pirofski, 1999). In a study, host-pathogen interactions help identify markers for disease severity and inform the development of diagnostic tools and therapeutic interventions (Lydon et al., 2018). This holistic understanding is essential for predicting disease outcomes and managing infectious disease outbreaks effectively (Wearing et al., 2005). These studies collectively highlight the dynamic nature of infectious disease evolution and the continuous need for advanced research to cope emerging challenges in disease control and prevention (Heesterbeek et al., 2015) as shown in Figure 1.

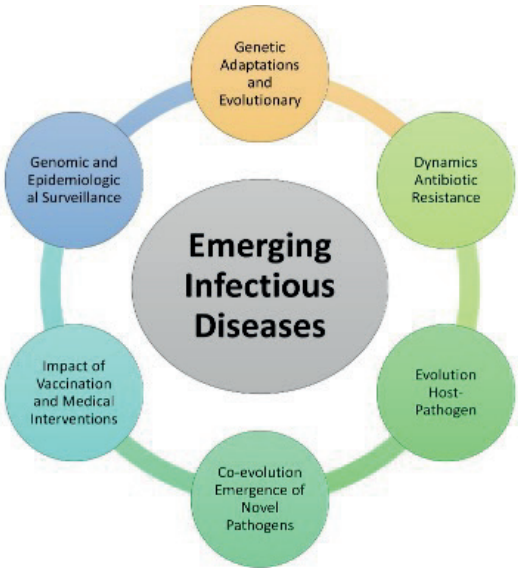


Figure 1. Eveolutionary steps for Emerging Infectous Diseases

3. Global Spread of New Infections

The emergence and re-emergence of infectious diseases are a major public health challenge globally (Church, 2004). New infectious agents are arising from various sources including zoonotic transfers, antibiotic resistance, and changes in human behavior and climate (Vaz□Moreira et al., 2019). The SARS-CoV-2 virus is arised in China and spread worldwide rapidly due to international travel and urban density (Li et al., 2021). Therefore, outbreaks have shown the potential for rapid spread due to human-to-human transmission, particularly in healthcare systems (Herfst et al., 2017). For example, the emergence of Zika virus in the Americas in the 2010s showed changes due to climate and human behavior that affect the distribution of mosquito-borne diseases (Caminade et al., 2019).

It is noted that the spread of new infections is influenced by multiple factors including the increased level of travel and trade that facilitate the rapid movement of people and goods, allowing pathogens to cross borders more easily (Baker et al., 2022). For instance, international air travel played a critical role in the rapid global spread of COVID-19 (Christidis & Christodoulou, 2020). Urban areas play critical role in the outbreaks of these diseases, particularly in low- and middle-income countries because they have higher population densities, poor sanitation, and limited healthcare access (Wilkinson et al., 2020). The WHO has reported that over 55% of the global population now lives in urban areas, a trend projected to rise day by day (Cohen, 2004). In this conditions climate change affect vector populations (e.g., mosquitoes) and lead to the spread of diseases into new geographic areas (Kovats et al., 2001). For example, warmer temperatures have expanded the range of ticks to increase the incidence of Lyme disease in existing unaffected regions (Dantas-Torres, 2015).

The global surveillance systems, such as the Global Outbreak Alert and Response Network (GOARN) is playing a crucial role for early detection and rapid response to outbreaks (Ansell et al., 2012). Vaccines have proven effective in controlling outbreaks. For instance, the rapid development and deployment of COVID-19 vaccines showcased the importance of vaccination in mitigating the impact of new infections (Flanagan et al., 2020). The public education campaigns are critical in promoting preventive measures, such as hygiene practices and vaccination uptake (Weiss et al., 2009). A significant proportion of emerging infections are zoonotic, originating from animals (Bengis et al., 2004). The One Health approach should be emphasized to protect human, animal, and environmental from zoonotic diseases (Erkyihun & Alemayehu, 2022) as shown in Figure 2.

Figure 2. Global Spread of New Infections

4. Ecological Factors in Disease Emergence

Disease emergence is influenced by some complex systems that interplay with different ecological factors such as climate change, deforestation, urbanization, biodiversity loss and global travel and trades between pathogens, hosts, and the environment (McMichael, 2004). These factors are crucial for predicting and management for different infectious diseases (Woolhouse, 2011) as shown in Figure 3. For example, higher biodiversity often leads to a dilution effect, where a greater variety of species reduce the likelihood of transmission of pathogens(Keesing & Ostfeld, 2021). Therefore, diverse ecosystems support a range of hosts, limiting the spread of pathogens that thrive in less diverse system (Dobson, 2004).

Some species act as reservoirs for pathogens that facilitate their transmission to humans such as changes in biodiversity, habitat loss or invasive species alter the dynamics (Crowl et al., 2008). Secondly, the rapid expansion of urban areas that lead to habitat fragmentation and increased contact between wildlife, domestic animals, and humans (Bai et al., 2019). This proximity accelerates the risk of zoonotic diseases. The intensive agriculture disturbs the environments to disease emergence (Mustafa & Makhawi, 2023). For example, monoculture and the use of antibiotics disrupt ecological balance and promote pathogen resistance (Bennett et al., 2012).

There are changes in climate affect the distribution and life cycles of both pathogens and vectors (Gallana et al., 2013). For example, warmer temperatures expand the habitat range for mosquitoes that elevate the risk of diseases like malaria and dengue (Reiter, 2001). Some other factors such as floods and droughts disrupt ecosystems and facilitate disease spread (Semenza et al., 2022). Vectors increase their populations in the grounds, while droughts force wildlife into closer contact with human populations (Sutherst, 2004).

The global wildlife trade introduces pathogens into new environments leading to spillover events (Rush et al., 2021). Therefore, monitoring and regulating this trade are crucial for preventing disease emergence (Tsai et al., 2010). In addition, local cultural practices, such as hunting or consumption of bushmeat increase the risk of zoonotic diseases (Friant et al., 2015). Moreover, public health interventions consider these behaviors to be effective to prevent disease emergence (Raude et al., 2019). Furthermore, surveillance systems that incorporate ecological data can help to predict disease outbreaks (Milinovich et al., 2014).

Figure 3. Ecological Factors in emergence of infectous diseases.

5. Genetic Variations and Disease Evolution

The genetic variations play a vital role in the evolution of diseases i.e influencing susceptibility, progression, and responses to treatments (Rabaneda-Bueno et al., 2021). These variations are linked to genetic diversity that contribute to the emergence and spread of diseases (Davies et al., 2009). Most of genetic variations among individuals influence traits and disease susceptibility. The alterations in the number of copies of a particular gene that affect gene dosage and contribute to complex diseases (Almal & Padh, 2012) as shown in table 1. For example, the larger scale alterations in the genome including inversions and translocations may impact gene function and regulation (Puig et al., 2015). The genetic variations that confer a survival advantage become more prevalent in a population (Perls et al., 2002) . Therefore, certain alleles may provide resistance to these infectious diseases, such as the CCR5-Δ32 allele conferring resistance to HIV (de Silva & Stumpf, 2004). Random changes in allele frequencies can lead to the fixation of harmful mutations, particularly in small populations (Whitlock, 2000). Continuous mutations contribute to the genetic diversity of pathogens, especially viruses like influenza and SARS-CoV-2, exploit for rapid evolution (Telenti et al., 2022).

The study of genetic variations has identified many SNPs associated with increased risk for various cancers (Telenti et al., 2022). It is known that variants in the BRCA1 and BRCA2 genes significantly elevate breast and ovarian cancers (Rebbeck et al., 2015). They have shown that variations in genes related to immune functions (Tsuchiya et al., 2002). For instance, in the Human Leukocyte Antigen (HLA) region are linked to different diseases like rheumatoid arthritis and lupus. In another study, viral pathogens such as HIV and SARS-CoV-2, has demonstrated how genetic mutations can lead to increased transmissibility and resistance to treatments and vaccines. The emergence of antibiotic resistance is often driven by genetic variations within bacterial populations that lead to the spread of resistant strains (Normark & Normark, 2002). The recent studies have shown that certain genetic variations are positively selected in human populations in response to environmental pressures such as the ability to metabolize certain foods or resist diseases that are endemic to specific regions (Hancock et al., 2008).

The genetic variations across different populations help to identify at-risk groups and tailor prevention and treatment strategies (Arnett et al., 2007). The integration of genomic data with clinical information is essential to understand the complex relationships between genetic variations and disease outcomes (West et al., 2006). The advancements in genomics are paving the way for personalized medicine, where treatments can be tailored based on an individual's genetic profile (Ginsburg & Willard, 2009). In addition, ethical considerations regarding genetic privacy, discrimination, and the implications of gene editing technologies like CRISPR must be addressed (Brokowski & Adli, 2019). Finally, these variations are fundamental to understand disease evolution and dynamics. Therefore, continue research in this field is crucial for advancing public health, developing effective treatments, and anticipating future disease outbreaks (Brokowski & Adli, 2019).

Table 1: List of Emerging Infectious Diseases (2000-2024), their Genetic Variations, and Evolutionary Changes.

Sr#	Emerging Infectious Disease	Genetic Variations	Disease Evolution	References
1	Severe Acute Respiratory Syndrome (SARS) (2002-2003)	Mutations in SARS-CoV genome, particularly in the spike (S) protein	Rapid spread to multiple countries, high mortality rate, controlled through public health measures	(Chan-Yeung & Xu, 2003)
2	Middle East Respiratory Syndrome (MERS) (2012-present)	Variations in MERS-CoV spike (S) protein, ORF1a	Zoonotic transmission from camels to humans, ongoing sporadic outbreaks	(Chan-Yeung & Xu, 2003)
3	H1N1 Influenza (Swine Flu) (2009)	Reassortment of H1N1 genes from avian, swine, and human influenza viruses	Pandemic spread, high infectivity but lower mortality compared to other pandemics	(Shu et al., 2011)
4	Ebola Virus Disease (2014-2016, 2018, 2021)	Genetic drift and bottleneck events in EBOV genome	Multiple outbreaks with varying mortality rates, zoonotic transmission	(Organization, 2016)
5	Zika Virus (2015-2016)	Mutations in the prM protein, leading to increased neurovirulence	Rapid spread across the Americas, associated with microcephaly and Guillain-Barré syndrome	(Karwowski et al., 2016)
6	Chikungunya Virus (2004-present)	Mutations in the E1 protein, increasing vector competence in Aedes albopictus	Re-emergence in Asia, Africa, and the Americas, causing large outbreaks	(Pialoux et al., 2007)
7	COVID-19 (SARS-CoV-2) (2019-present)	Numerous genetic variations, including Alpha, Delta, Omicron variants	Global pandemic, with significant waves driven by variants of concern	(Ciotti et al., 2020)
8	Nipah Virus (2001-present)	Variability in G and F glycoproteins among different strains	Periodic outbreaks in South and Southeast Asia, high mortality, zoonotic transmission from bats	(Ciotti et al., 2020)
9	H5N1 Avian Influenza (2004-present)	Mutations in the HA and NA proteins, enabling zoonotic transmission	Sporadic human infections, high mortality, ongoing pandemic potential	(Thomas & Noppenberger, 2007)
10	Monkeypox (mpox) (2022-present)	Genetic variations in Clade II associated with human-to-human transmission	Spread beyond endemic regions in Africa to Europe, the Americas; changing transmission dynamics	(Cholli, 2022)

Sr#	Emerging Infectious Disease	Genetic Variations	Disease Evolution	References
11	Crimean-Congo Hemorrhagic Fever (CCHF) (2000-present)	Genetic diversity among strains, particularly in the S segment of the genome	Increasing cases in endemic regions, zoonotic transmission via ticks	(Nasirian, 2020)
12	Marburg Virus Disease (2005-present)	Variations in the GP gene across different outbreaks	Sporadic outbreaks with high mortality rates, zoonotic transmission from bats	(Control & Prevention, 2009)
13	Severe Fever with Thrombocytopenia Syndrome (SFTS) (2011-present)	Genetic reassortment in the SFTSV genome, including NSs protein	Emerging in East Asia, with a high case-fatality rate, tick-borne transmission	(Sharma & Kamthania, 2021)
14	H7N9 Avian Influenza (2013-present)	Mutations in the HA protein, leading to human infections	Sporadic cases, high mortality in infected individuals, potential for reassortment	(Iuliano, 2017)

6. Antimicrobial Resistance and Re-emerging Infections

The World Health Organization (WHO) has recognized antimicrobial resistance (AMR) as one of the top 10 global public health threats (Salam et al., 2023). The AMR has emerged a critical global health issue that threatening the efficacy of antibiotics and other antimicrobial agents. AMR occurs when microorganisms evolve and develop the ability to resist the effects of drugs that once effectively treated them (Ferri et al., 2017). This phenomenon is impaired because of overuse and misuse of antibiotics that leading to rise in infections that are more difficult to treat (Prestinaci et al., 2015). The spontaneous mutations in bacterial DNA may confer resistance. The resistance genes transferred from bacteria to human beings through plasmids, transposons, and bacteriophages (Lerminiaux & Cameron, 2019). Some invitro studies, bacteria exhibit increased resistance due to reduced penetration of antimicrobials and enhanced metabolic state. The inappropriate prescribing practices in both human and veterinary medicine contribute significantly to AMR (Lerminiaux & Cameron, 2019).

The use of antibiotics in livestock for growth promotion and disease prevention is a major contributor to resistance (Singer et al., 2003). Moreover, inadequate sanitation, hygiene practices, and infection prevention measures in healthcare system facilitate the spread of resistant strains (Endale et al., 2023). Re-emerging infections refer to existed controlled or eradicated infectious diseases that have resurfaced due to various factors, including AMR (Hassan et al., 2024). In addition to multi-drug-resistant (MDR), TB and extensively drug-resistant (XDR) TB have emerged as significant public health challenges (Jain & Mondal, 2008). These factors such as incomplete treatment regimens and the global movement of people contribute to the resurgence of diseases (Weiss & McMichael, 2004). MRSA, once confined to healthcare system is now prevalent in community system (David & Daum, 2010). It is resistant to various commonly used antibiotics, complicating treatment options (Bader et al., 2010). Some viral infections, such as influenza and HIV, have also seen the emergence of resistant strains due to mutations, challenging vaccination and antiviral strategies (Boroumand et al., 2021). AMR is associated to increased morbidity and mortality rates, longer hospital stays, and higher healthcare costs (Dadgostar, 2019).

The economic impact of AMR is another major concern (Dadgostar, 2019). They increased healthcare costs as well as low productivity (Gorasso et al., 2022). It is estimated that AMR cost the

global economy up to $100 trillion by 2050 (Dadgostar, 2019). Therefore, it should be addressed on urgent basis(Kaye et al., 2020) . Some implementing to use effective antibiotic against infectious diseases in healthcare systems to optimize the concentrations of antibiotics to ensure precise prescription and duration (Kaye et al., 2020). The surveillance of antibiotic usage and resistance patterns help to understand the dynamics of AMR and making policy decisions (Tompson et al., 2021). Therefore, it is urgent need for the development of new antibiotics and alternative therapies such as bacteriophages, immunotherapy, and vaccines (Zalewska-Piątek & Piątek, 2021). Secondly, we should educate the healthcare professionals as well as the public about the accurate dose of antibiotics that is essential in curbing AMR (Dhingra et al., 2020). Thirdly, there should be an authority to tackle and quick response to the AMR locally and globally (Baekkeskov et al., 2020).

Table. 2. List of Antimicrobial Resistance Agents, their Associated Genes, Diagnostic Tests, and Re-emerging Infections from 2000-2024.

Sr#	AMR Agent	Associated Genes	Diagnostic Tests	Re-emerging Infections (2000-2024)	References
1	Methicillin-resistant Staphylococcus aureus (MRSA)	mecA, mecC	PCR, culture, PBP2a test	MRSA infections, particularly in community settings	(Lee et al., 2018)
2	Vancomycin-resistant Enterococci (VRE)	vanA, vanB	PCR, culture, E-test	Enterococcal infections	(Tacconelli & Cataldo, 2008)
3	Extended-spectrum β-lactamases (ESBLs) producing Enterobacteriaceae	blaCTX-M, blaSHV, blaTEM	PCR, culture, ESBL test	ESBL-producing Entero(Organization & Initiative, 2010) bacteriaceae infections	(Lawandi et al., 2022)
4	Carbapenem-resistant Enterobacteriaceae (CRE)	KPC, NDM, OXA-48, VIM, IMP	PCR, culture, Carba NP test, multiplex assays	CRE infections	(Lawandi et al., 2022)
5	Multidrug-resistant Mycobacterium tuberculosis (MDR-TB)	katG, inhA, rpoB	GeneXpert MTB/RIF, Line probe assays, culture	Tuberculosis (MDR-TB and XDR-TB)	(Organization & Initiative, 2010)
6	Neisseria gonorrhoeae (resistant to multiple antibiotics)	penA, mtrR, gyrA, parC	NAAT, culture, E-test	Gonorrhea (drug-resistant strains)	(Hook III et al., 2013)
7	Clostridioides difficile (CDI)	tcdA, tcdB	PCR, enzyme immunoassay (EIA), stool culture	Clostridioides difficile infection	(Feuerstadt et al., 2023)
8	Drug-resistant Plasmodium falciparum	pfcrt, pfmdr1, k13	PCR, microscopy, Rapid Diagnostic Tests (RDTs)	Malaria (drug-resistant strains)	(Organization, 2021)
9	Drug-resistant Salmonella typhi (Typhoid fever)	gyrA, parC, blaCTX-M	PCR, culture, Widal test, blood culture	Typhoid fever	(Organization, 2019)

Sr#	AMR Agent	Associated Genes	Diagnostic Tests	Re-emerging Infections (2000-2024)	References
10	Multidrug-resistant Acinetobacter baumannii	OXA-23, OXA-24/40, OXA-58	PCR, culture, MALDI-TOF MS	Acinetobacter infections	(Moss et al., 1988)
11	Candida auris (antifungal resistance)	ERG11, FKS1	PCR, culture, MALDI-TOF MS	Candida auris infections	(Prestel, 2021)
12	Multidrug-resistant Pseudomonas aeruginosa	mexA, mexB, mexC, mexE	PCR, culture, E-test, automated systems (e.g., VITEK)	Pseudomonas infections	(Bodey et al., 1983)
13	Colistin-resistant Enterobacteriaceae (mcr-1 positive)	mcr-1	PCR, culture, broth microdilution	Colistin-resistant infections	(Shenoy et al., 2019)
14	Influenza A (H5N1, H1N1)	NA, HA	RT-PCR, rapid antigen tests, serology	Avian Influenza (H5N1), H1N1 pandemic (2009)	(Control & Prevention, 2010a)
15	Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)	ORF1ab, S, E, N genes	RT-PCR, rapid antigen tests, serology, whole genome sequencing	COVID-19 pandemic (2019-2024)	(Ciotti et al., 2020)
16	Drug-resistant Klebsiella pneumoniae	blaKPC, blaNDM, blaOXA-48	PCR, culture, automated systems (e.g., VITEK)	Klebsiella infections (hospital-acquired)	(Control & Prevention, 2010b)

7. Public Health Responses to Emerging Diseases

The emerging infectious diseases (EIDs) pose significant challenges to global health systems. Recent outbreaks such as COVID-19, Ebola, and Zika virus have great importance to give rapid public health responses (Guilamo-Ramos et al., 2021). The key strategies have to be enpolyed, lessons should be learnt, and the role of technology and community engagement to addresss the EIDs.The effective surveillance systems are crucial for early detection of outbreaks (Schierhout et al., 2017). The integration of human, animal, and environmental health data is known as the One Health approach, have to be emphasized (Rock et al., 2009). In addition, the technologies such as the Global Public Health Intelligence Network (GPHIN) facilitate rapid sharing of data that allow for timely responses to the emerging threats (Amir et al., 2021).

The COVID-19 pandemic demonstrated the potential for expedited vaccine development through platforms like mRNA technology (Szabó et al., 2022).Therefore, collaborative efforts such as COVAX have aim to ensure equitable access to vaccines. The rapid development of therapeutics including antiviral treatments and monoclonal antibodies, has been critical in managing outbreaks (Hotez et al., 2021). The strengthening healthcare systems, particularly in low and middle income countries are essential for effective responses. Therefore, this includes training of healthcare workers to enhance laboratory capacity (Almal & Padh, 2012). These regularly updating emergency plans can help to mitigate the impact of outbreaks. These simulations and trainings are essential for testing response capabilities.

To engaging communities through transparent communication has a major role for building trust (Frerichs et al., 2017). The Public health messages must be culturally sensitive and accessible to ensure compliance with health measures (Resnicow et al., 1999). Therefore, community leaders and stakeholders have to be involved in decision-making that increase public engagement and adherence to health guidelines. Moreover, collaborative efforts among countries, NGOs, and international organizations (e.g., WHO) are critical for coordinated responses. These partnerships facilitate resource sharing and technical assistance. The global research initiatives should be promoted to share findings for best practices to enhance the cumulative response to EIDs (Theobald et al., 2018).

The COVID-19 pandemic highlighted the need for countries to invest in public health infrastructure plans. If nations with pre-existing frameworks for managing outbreaks is far better to control the spread of viruses (Williams et al., 2023). The use of digital health tools, including contact tracing apps and telehealth services, became essential during the pandemic. These technologies helped to mitigate the impact of social distancing measus (Alo et al., 2021). The inequitable distribution of vaccines and resources during the COVID-19 pandemic emphasized the importance of addressing health disparities.Therefore, public health responses must prioritize equity to ensure all populations are protecting, so the world continues to face new health threats (Shadmi et al., 2020).

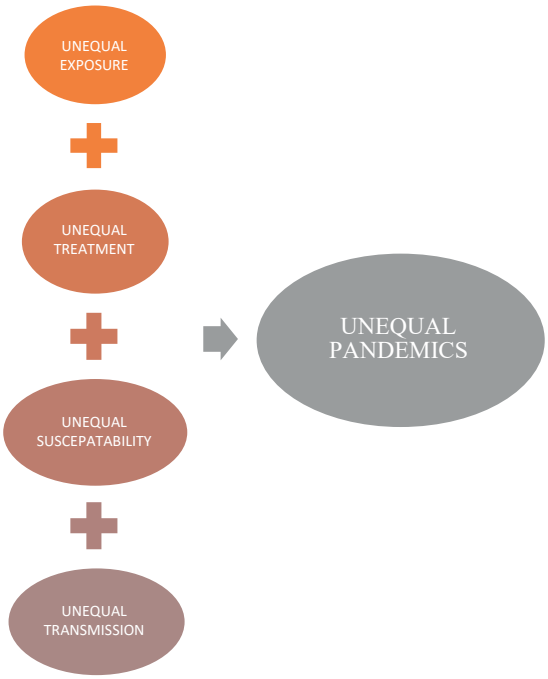


Figure 4. Reasons of Un-equal Pandemics

8. Emerging Diseases Challenges

Emerging infectious diseases (EIDs) pose significant challenges to global health systems due to their complex nature and rapid evolution. Recently some scientists highlighted the importance of timely and accurate diagnosis for effective management and containment of these diseases. One of the primary challenges in diagnosing of EIDs is the vast diversity of pathogens, such as viruses, bacteria, fungi, and parasites (Heesterbeek et al., 2015). Many of these pathogens have unique and often overlapping clinical symptoms that make their differential diagnosis difficult. For instance, the diseases i.e Zika virus and chikungunya can present with similar symptoms that complicate clinical assessment (Álvarez-Argüelles et al., 2019). In some other studies, researchers emphasized the need for advanced diagnostic methods that can quickly identify a range of pathogens like multiplex PCR and multiplex ELISA etc (Panwar et al., 2023).

The rapid mutation rates of different emerging pathogens complicate diagnosis. These pathogens such as influenza and coronaviruses undergo frequent genetic changes that may lead to variations

that evade standard diagnostic tests (Zabidi et al., 2023) . The emergence of new variants render existing assays, ineffective, therefore, it is necessaryto be updated. Moreover, the rise of AMR among bacterial EIDs poses additional challenges (Pennington, 2023). The AMR mechanisms may not be adequately detected by traditional diagnostic methods that lead to inappropriate treatment choices and worse clinical outcomes. (Okeke et al., 2020). Many regions lack the infrastructure, trained personnel, and resources that are required to implement sophisticated diagnostic techniques. As a result, diseases may go undiagnosed or misdiagnosed, leading to ineffective control measures and increased transmission. Point-of-care (POC) tests have shown promise in improving access to diagnostics in remote areas. However, many POC tests are not sensitive or specific enough, and their performance in real-world systems may vary significantly. Moreover, ensuring the reliability and accessibility of these tests are essential for improving diagnostic capabilities in these populations (Boehme et al., 2011).

The ethical implications of diagnosing EIDs, particularly in relation to testing and treatment, may not be overlooked (Tejiokem et al., 2011). The rapid tests may produce false negative or positive results that lead to mismanagement of cases(Simpson et al., 2020). These collaboration among public health organizations, regulatory agencies, and the diagnostic industry are essential to streamline the approval process for new diagnostic tools, ensuring that they are safe, effective, and accessible in a timely manner. The diagnosis of emerging infectious diseases is fraught with challenges that demand a multifaceted approach. Furthermore, improve diagnostic capabilities that is essential to invest in research and development of novel technologies to increase surveillance systems, and to ensure equitable access to diagnostic resources (Adachi et al., 2023).

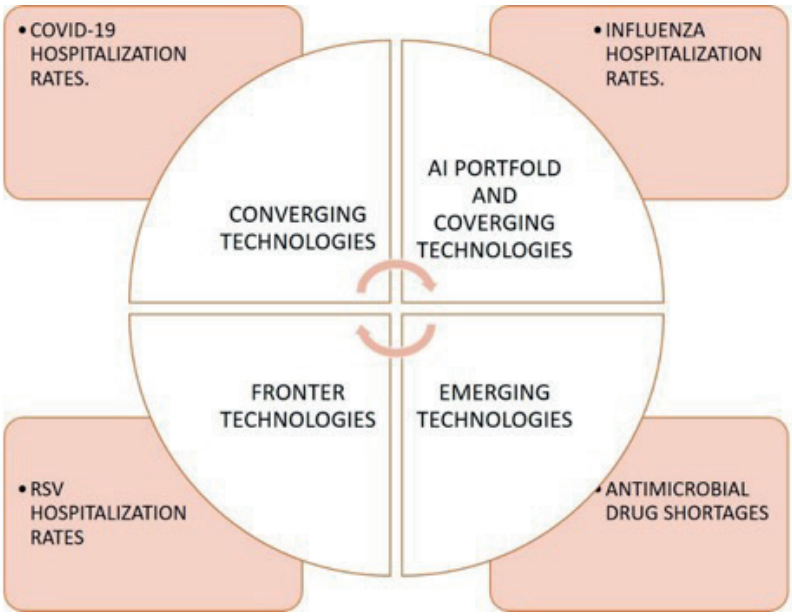


Figure 5. Challenges against Emerging Infectous Diseases

9. Preventative Strategies and Vaccination

Preventative strategies and vaccination efforts play a critical role in public health by reducing the incidence of infectious diseases and controlling outbreaks. For instance, the COVID-19 pandemic has emphasized the importance of these measures, prompting an acceleration in research, development, and implementation of vaccines and public health strategies. The success of mRNA vaccines against COVID-19 has spurred interest in mRNA technology for other diseases. This research leads to develop mRNA vaccines for influenza, Zika virus, and many other diseases. The flexibility of mRNA platforms allows for rapid updates and adaptations in response to emerging variants and pathogens. Moreover, vaccine uncertainty remains a significant barrier to achieving herd immunity. Therefore, recent studies highlighted the need for targeted communication strategies

that address specific concerns among different demographic groups. Therefore, these community leaders and social media effectively can help to build trust in vaccination programs.

Secondly, the global initiatives like COVAX have aim to ensure equitable access to vaccines, particularly in low and middle income countries. Furthermore, recent studies emphasized the importance of collaboration between governments, NGOs, and private sectors to increase distribution networks and address logistical challenges. The achievements of herd immunity through vaccination is essential for controlling outbreaks. The community engagement initiatives, such as educational campaigns and local vaccination drives, have proven effective in increasing vaccination rates. These are involving local healthcare providers may also foster trust and participation. Moreover, increasing surveillance systems are critical for early detection of outbreaks. The use of digital tools and data analytics may help to track disease patterns and vaccination coverage. Therefore, the quick response teams may be mobilized to contain outbreaks that have been seen in recent responses to measles and polio resurgence in certain countries.

Thirdly, some strong public health policies that mandate vaccinations for school entry and certain jobs have demonstrated efficacy in increasing vaccination rates. These policymakers are encouraged to take measures while ensuring exemptions are appropriately managed to protect public health. Furthermore, distribution of vaccines, especially in rural and deprived areas, poses logistical challenges. In addition, cold chain requirements for certain vaccines complicate transportation and storage. In future, efforts must focus to develop some stable formulations and innovative delivery methods, such as microneedle patches. The emergence of new pathogens need a proactive approach to vaccine development. Therefore, research to develop some universal vaccines, such as influenza multi-vaccine, is crucial. Moreover, the collaborations between academic institutions, industry, and governments can expedite the research and development process.

Finally, a multi-faceted approach combining vaccination with other preventative measures (such as hygiene, sanitation, and education) is essential. Those programs that promote comprehensive health education may empower communities to adopt healthier behaviors and improve cummulative public health outcomes. In additionally, recent literature may play a pivotal role to make preventative strategies to protect the public health. While challenges remain, innovative approaches and collaborative efforts offer hope for more effective prevention and control of infectious diseases in the future.

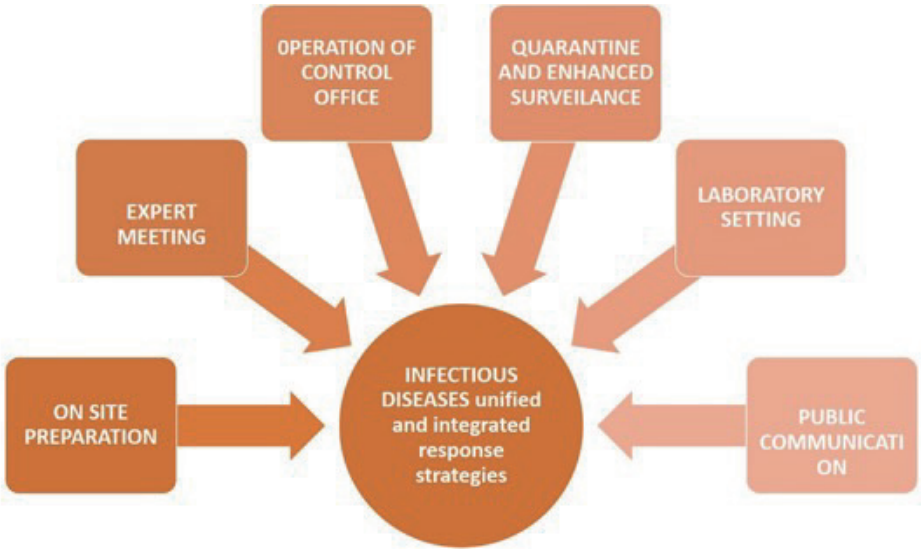


Figure 6. Preventative Strategies and Vaccinations against Infectous Diseases

References

Adachi, T., El-Hattab, A. W., Jain, R., Nogales Crespo, K. A., Quirland Lazo, C. I., Scarpa, M., Summar, M., & Wattanasirichaigoon, D. (2023). Enhancing equitable access to rare disease diagnosis and treatment around the world: a review of evidence, policies, and challenges. International Journal of Environmental Research and Public Health, 20(6), 4732.

Almal, S. H., & Padh, H. (2012). Implications of gene copy-number variation in health and diseases. Journal of human genetics, 57(1), 6-13.

Alo, U. R., Nkwo, F. O., Nweke, H. F., Achi, I. I., & Okemiri, H. A. (2021). Non-pharmaceutical interventions against COVID-19 pandemic: Review of contact tracing and social distancing technologies, protocols, apps, security and open research directions. Sensors, 22(1), 280.

Álvarez-Argüelles, M. E., Alba, S. R., Pérez, M. R., Riveiro, J. A. B., & García, S. M. (2019). Diagnosis and molecular characterization of chikungunya virus infections. Current Topics in Neglected Tropical Diseases, 375-385.

Amir, P. N., Sazali, M. F., Salvaraji, L., Dulajis, N., Rahim, S. S. S. A., & Avoi, R. (2021). Public health informatics in global health surveillance: a review: public health informatics. Borneo Epidemiology Journal, 2(2), 74-88.

Ansell, C., Sondorp, E., & Stevens, R. H. (2012). The promise and challenge of global network governance: the global outbreak alert and response network. Global Governance, 317-337.

Arnett, D. K., Baird, A. E., Barkley, R. A., Basson, C. T., Boerwinkle, E., Ganesh, S. K., Herrington, D. M., Hong, Y., Jaquish, C., & McDermott, D. A. (2007). Relevance of genetics and genomics for prevention and treatment of cardiovascular disease: a scientific statement from the American Heart Association Council on Epidemiology and Prevention, the Stroke Council, and the Functional Genomics and Translational Biology Interdisciplinary Working Group. Circulation, 115(22), 2878-2901.

Arnott, A., Barry, A. E., & Reeder, J. C. (2012). Understanding the population genetics of Plasmodium vivax is essential for malaria control and elimination. Malaria journal, 11, 1-10.

Bader, M. S., Hawboldt, J., & Brooks, A. (2010). Management of complicated urinary tract infections in the era of antimicrobial resistance. Postgraduate medicine, 122(6), 7-15.

Baekkeskov, E., Rubin, O., Munkholm, L., & Zaman, W. (2020). Antimicrobial resistance as a global health crisis. Oxford Research Encyclopedia of Politics, 1-24.

Bai, L., Xiu, C., Feng, X., & Liu, D. (2019). Influence of urbanization on regional habitat quality: a case study of Changchun City. Habitat International, 93, 102042.

Baker, R. E., Mahmud, A. S., Miller, I. F., Rajeev, M., Rasambainarivo, F., Rice, B. L., Takahashi, S., Tatem, A. J., Wagner, C. E., & Wang, L.-F. (2022). Infectious disease in an era of global change. Nature Reviews Microbiology, 20(4), 193-205.

Bengis, R., Leighton, F., Fischer, J., Artois, M., Morner, T., & Tate, C. (2004). The role of wildlife in emerging and re-emerging zoonoses. Revue scientifique et technique-office international des epizooties, 23(2), 497-512.

Bennett, A. J., Bending, G. D., Chandler, D., Hilton, S., & Mills, P. (2012). Meeting the demand for crop production: the challenge of yield decline in crops grown in short rotations. Biological reviews, 87(1), 52-71.

Bloom, D. E., & Cadarette, D. (2019). Infectious disease threats in the twenty-first century: strengthening the global response. Frontiers in immunology, 10, 549.

Bodey, G. P., Bolivar, R., Fainstein, V., & Jadeja, L. (1983). Infections caused by Pseudomonas aeruginosa. Reviews of infectious diseases, 5(2), 279-313.

Boehme, C. C., Nicol, M. P., Nabeta, P., Michael, J. S., Gotuzzo, E., Tahirli, R., Gler, M. T., Blakemore, R., Worodria, W., & Gray, C. (2011). Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicentre implementation study. The Lancet, 377(9776), 1495-1505.

Boroumand, H., Badie, F., Mazaheri, S., Seyedi, Z. S., Nahand, J. S., Nejati, M., Baghi, H. B., Abbasi-Kolli, M., Badehnoosh, B., & Ghandali, M. (2021). Chitosan-based nanoparticles against viral infections. Frontiers in Cellular and Infection Microbiology, 11, 643953.

Brokowski, C., & Adli, M. (2019). CRISPR ethics: moral considerations for applications of a powerful tool. Journal of molecular biology, 431(1), 88-101.

Caminade, C., McIntyre, K. M., & Jones, A. E. (2019). Impact of recent and future climate change on vector□borne diseases. Annals of the New York Academy of Sciences, 1436(1), 157-173.

Casadevall, A., & Pirofski, L.-a. (1999). Host-pathogen interactions: redefining the basic concepts of virulence and pathogenicity. Infection and immunity, 67(8), 3703-3713.

Chan□Yeung, M., & Xu, R. H. (2003). SARS: epidemiology. Respirology, 8, S9-S14.

Cholli, P. A. (2022). Characteristics of patients hospitalized with mpox during the 2022 US outbreak. Morb Mortal Wkly Rep, 71, 1412-1417.

Chomkatekaew, C., Boonklang, P., Sangphukieo, A., & Chewapreecha, C. (2021). An evolutionary arms race between Burkholderia pseudomallei and host immune system: what do we know? Frontiers in microbiology, 11, 612568.

Christidis, P., & Christodoulou, A. (2020). The predictive capacity of air travel patterns during the global spread of the COVID-19 pandemic: risk, uncertainty and randomness. International Journal of Environmental Research and Public Health, 17(10), 3356.

Church, D. L. (2004). Major factors affecting the emergence and re-emergence of infectious diseases. Clinics in Laboratory Medicine, 24(3), 559-586.

Ciotti, M., Ciccozzi, M., Terrinoni, A., Jiang, W.-C., Wang, C.-B., & Bernardini, S. (2020). The COVID-19 pandemic. Critical reviews in clinical laboratory sciences, 57(6), 365-388.

Cliff, A. D. (2009). Infectious diseases: Emergence and re-emergence: a geographical analysis. Oxford University Press.

Cohen, B. (2004). Urban growth in developing countries: a review of current trends and a caution regarding existing forecasts. World development, 32(1), 23-51.

Control, C. f. D., & Prevention. (2009). Imported case of Marburg hemorrhagic fever--Colorado, 2008. MMWR: Morbidity & Mortality Weekly Report, 58(49).

Control, C. f. D., & Prevention. (2010a). Estimates of deaths associated with seasonal influenza--United States, 1976-2007. MMWR: Morbidity & Mortality Weekly Report, 59(33).

Control, C. f. D., & Prevention. (2010b). Update: detection of a verona integron-encoded metallo-beta-lactamase in Klebsiella pneumoniae--United States, 2010. MMWR: Morbidity & Mortality Weekly Report, 59(37).

Crowl, T. A., Crist, T. O., Parmenter, R. R., Belovsky, G., & Lugo, A. E. (2008). The spread of invasive species and infectious disease as drivers of ecosystem change. Frontiers in Ecology and the Environment, 6(5), 238-246.

Dadgostar, P. (2019). Antimicrobial resistance: implications and costs. Infection and Drug Resistance, 3903-3910.

Dantas-Torres, F. (2015). Climate change, biodiversity, ticks and tick-borne diseases: The butterfly effect. International Journal for Parasitology: parasites and wildlife, 4(3), 452-461.

David, M. Z., & Daum, R. S. (2010). Community-associated methicillin-resistant Staphylococcus aureus: epidemiology and clinical consequences of an emerging epidemic. Clinical microbiology reviews, 23(3), 616-687.

Davies, G., Genini, S., Bishop, S., & Giuffra, E. (2009). An assessment of opportunities to dissect host genetic variation in resistance to infectious diseases in livestock. Animal, 3(3), 415-436.

de Silva, E., & Stumpf, M. P. (2004). HIV and the CCR5-Δ32 resistance allele. FEMS microbiology letters, 241(1), 1-12.

Dhingra, S., Rahman, N. A. A., Peile, E., Rahman, M., Sartelli, M., Hassali, M. A., Islam, T., Islam, S., & Haque, M. (2020). Microbial resistance movements: an overview of global public health threats posed by antimicrobial resistance, and how best to counter. Frontiers in Public Health, 8, 535668.

Dobrindt, U., Hochhut, B., Hentschel, U., & Hacker, J. (2004). Genomic islands in pathogenic and environmental microorganisms. Nature Reviews Microbiology, 2(5), 414-424.

Dobson, A. (2004). Population dynamics of pathogens with multiple host species. the american naturalist, 164(S5), S64-S78.

Dye, C. (2014). After 2015: infectious diseases in a new era of health and development. Philosophical Transactions of the Royal Society B: Biological Sciences, 369(1645), 20130426.

Endale, H., Mathewos, M., & Abdeta, D. (2023). Potential causes of spread of antimicrobial resistance and preventive measures in one health perspective-a review. Infection and Drug Resistance, 7515-7545.

Erkyihun, G. A., & Alemayehu, M. B. (2022). One Health approach for the control of zoonotic diseases. Zoonoses, 2(1), 963.

Ferri, M., Ranucci, E., Romagnoli, P., & Giaccone, V. (2017). Antimicrobial resistance: A global emerging threat to public health systems. Critical reviews in food science and nutrition, 57(13), 2857-2876.

Feuerstadt, P., Theriault, N., & Tillotson, G. (2023). The burden of CDI in the United States: a multifactorial challenge. BMC Infectious Diseases, 23(1), 132.

Flanagan, K. L., Best, E., Crawford, N. W., Giles, M., Koirala, A., Macartney, K., Russell, F., Teh, B. W., & Wen, S. C. (2020). Progress and pitfalls in the quest for effective SARS-CoV-2 (COVID-19) vaccines. Frontiers in immunology, 11, 579250.

Forst, C. V. (2010). Host–pathogen systems biology. Infectious disease informatics, 123-147.

Frerichs, L., Kim, M., Dave, G., Cheney, A., Hassmiller Lich, K., Jones, J., Young, T. L., Cene, C. W., Varma, D. S., & Schaal, J. (2017). Stakeholder perspectives on creating and maintaining trust in community–academic research partnerships. Health Education & Behavior, 44(1), 182-191.

Friant, S., Paige, S. B., & Goldberg, T. L. (2015). Drivers of bushmeat hunting and perceptions of zoonoses in Nigerian hunting communities. PLoS neglected tropical diseases, 9(5), e0003792.

Gallana, M., Ryser-Degiorgis, M.-P., Wahli, T., & Segner, H. (2013). Climate change and infectious diseases of wildlife: altered interactions between pathogens, vectors and hosts. Current

Zoology, 59(3), 427-437.

Ginsburg, G. S., & Willard, H. F. (2009). Genomic and personalized medicine: foundations and applications. Translational research, 154(6), 277-287.

Gorasso, V., Moyersoen, I., Van der Heyden, J., De Ridder, K., Vandevijvere, S., Vansteelandt, S., De Smedt, D., & Devleesschauwer, B. (2022). Health care costs and lost productivity costs related to excess weight in Belgium. BMC Public Health, 22(1), 1693.

Guilamo-Ramos, V., Thimm-Kaiser, M., Benzekri, A., Hidalgo, A., Lanier, Y., Tlou, S., López, M. d. L. R., Soletti, A. B., & Hagan, H. (2021). Nurses at the frontline of public health emergency preparedness and response: lessons learned from the HIV/AIDS pandemic and emerging infectious disease outbreaks. The Lancet infectious diseases, 21(10), e326-e333.

Haldane, V., De Foo, C., Abdalla, S. M., Jung, A.-S., Tan, M., Wu, S., Chua, A., Verma, M., Shrestha, P., & Singh, S. (2021). Health systems resilience in managing the COVID-19 pandemic: lessons from 28 countries. Nature medicine, 27(6), 964-980.

Hancock, A. M., Witonsky, D. B., Gordon, A. S., Eshel, G., Pritchard, J. K., Coop, G., & Di Rienzo, A. (2008). Adaptations to climate in candidate genes for common metabolic disorders. PLoS genetics, 4(2), e32.

Hassan, Y., Dar, I. M., Uddin, J. M., Saleem, S., Rather, M. Y., & Waza, A. A. (2024). Tackling Infectious Diseases with Special Reference to India: Need for Multidimensional Approach. Journal of Advances in Medicine and Medical Research, 36(1), 82-92.

Heesterbeek, H., Anderson, R. M., Andreasen, V., Bansal, S., De Angelis, D., Dye, C., Eames, K. T., Edmunds, W. J., Frost, S. D., & Funk, S. (2015). Modeling infectious disease dynamics in the complex landscape of global health. Science, 347(6227), aaa4339.

Herfst, S., Böhringer, M., Karo, B., Lawrence, P., Lewis, N. S., Mina, M. J., Russell, C. J., Steel, J., De Swart, R. L., & Menge, C. (2017). Drivers of airborne human-to-human pathogen transmission. Current opinion in virology, 22, 22-29.

Hook III, E. W., Shafer, W., Deal, C., Kirkcaldy, R. D., & Iskander, J. (2013). CDC Grand Rounds: the growing threat of multidrug-resistant gonorrhea. Morbidity and Mortality Weekly Report, 62(6), 103.

Hotez, P. J., Batista, C., Amor, Y. B., Ergonul, O., Figueroa, J. P., Gilbert, S., Gursel, M., Hassanain, M., Kang, G., & Kaslow, D. C. (2021). Global public health security and justice for vaccines and therapeutics in the COVID-19 pandemic. EClinicalMedicine, 39.

Hughes, D., & Andersson, D. I. (2015). Evolutionary consequences of drug resistance: shared principles across diverse targets and organisms. Nature Reviews Genetics, 16(8), 459-471.

Hughes, D., & Andersson, D. I. (2017). Evolutionary trajectories to antibiotic resistance. Annual review of microbiology, 71(1), 579-596.

Iuliano, A. D. (2017). Increase in human infections with avian influenza A (H7N9) virus during the fifth epidemic—China, October 2016–February 2017. MMWR. Morbidity and mortality weekly report, 66.

Jain, A., & Mondal, R. (2008). Extensively drug-resistant tuberculosis: current challenges and threats. FEMS Immunology & Medical Microbiology, 53(2), 145-150.

Janes, C. R., Corbett, K. K., Jones, J. H., & Trostle, J. (2012). Emerging infectious diseases: the role of social sciences. The Lancet, 380(9857), 1884-1886.

Janik, E., Ceremuga, M., Niemcewicz, M., & Bijak, M. (2020). Dangerous pathogens as a potential problem for public health. Medicina, 56(11), 591.

Karwowski, M. P., Nelson, J. M., Staples, J. E., Fischer, M., Fleming-Dutra, K. E., Villanueva, J., Powers, A. M., Mead, P., Honein, M. A., & Moore, C. A. (2016). Zika virus disease: a CDC update for pediatric health care providers. Pediatrics, 137(5).

Kaye, K., Paprottka, F., Escudero, R., Casabona, G., Montes, J., Fakin, R., Moke, L., Stasch, T., Richter, D., & Benito-Ruiz, J. (2020). Elective, non-urgent procedures and aesthetic surgery in the wake of SARS–COVID-19: considerations regarding safety, feasibility and impact on clinical management. Aesthetic plastic surgery, 44(3), 1014-1042.

Keesing, F., & Ostfeld, R. S. (2021). Dilution effects in disease ecology. Ecology Letters, 24(11), 2490-2505.

Kovats, R., Campbell-Lendrum, D., McMichel, A., Woodward, A., & Cox, J. S. H. (2001). Early effects of climate change: do they include changes in vector-borne disease? Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 356(1411), 1057-1068.

Kuo, P.-F., & Chiu, C.-S. (2021). Airline transportation and arrival time of international disease spread: A case study of Covid-19. PloS one, 16(8), e0256398.

Lawandi, A., Yek, C., & Kadri, S. S. (2022). IDSA guidance and ESCMID guidelines: complementary approaches toward a care standard for MDR Gram-negative infections. Clinical Microbiology and Infection, 28(4), 465-469.

Lee, A. S., De Lencastre, H., Garau, J., Kluytmans, J., Malhotra-Kumar, S., Peschel, A., & Harbarth, S. (2018). Methicillin-resistant Staphylococcus aureus. Nature reviews Disease primers, 4(1), 1-23.

Lerminiaux, N. A., & Cameron, A. D. (2019). Horizontal transfer of antibiotic resistance genes in clinical environments. Canadian journal of microbiology, 65(1), 34-44.

Levitt, A. M., Khan, A. S., & Hughes, J. M. (2010). Emerging and re-emerging pathogens and diseases. Infectious Diseases, 56.

Li, J., Lai, S., Gao, G. F., & Shi, W. (2021). The emergence, genomic diversity and global spread of SARS-CoV-2. Nature, 600(7889), 408-418.

Lydon, E. C., Ko, E. R., & Tsalik, E. L. (2018). The host response as a tool for infectious disease diagnosis and management. Expert review of molecular diagnostics, 18(8), 723-738.

Martinez, J. L. (2009). The role of natural environments in the evolution of resistance traits in pathogenic bacteria. Proceedings of the Royal Society B: Biological Sciences, 276(1667), 2521-2530.

McMichael, A. J. (2004). Environmental and social influences on emerging infectious diseases: past, present and future. Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 359(1447), 1049-1058.

Meganck, R. M., & Baric, R. S. (2021). Developing therapeutic approaches for twenty-first-century emerging infectious viral diseases. Nature medicine, 27(3), 401-410.

Milinovich, G. J., Williams, G. M., Clements, A. C., & Hu, W. (2014). Internet-based surveillance systems for monitoring emerging infectious diseases. The Lancet infectious diseases, 14(2), 160-168.

Moss, C. W., Wallace, P. L., Hollis, D., & Weaver, R. E. (1988). Cultural and chemical characterization of CDC groups EO-2, M-5, and M-6, Moraxella (Moraxella) species, Oligella

urethralis, Acinetobacter species, and Psychrobacter immobilis. Journal of clinical microbiology, 26(3), 484-492.

Müller, B., Borrell, S., Rose, G., & Gagneux, S. (2013). The heterogeneous evolution of multidrug-resistant Mycobacterium tuberculosis. Trends in Genetics, 29(3), 160-169.

Mustafa, M., & Makhawi, A. (2023). Risk Factors in the Era of Emerging Infectious Diseases: Challenges and Strategies.

Myers, S. S., & Patz, J. A. (2009). Emerging threats to human health from global environmental change. Annual review of environment and resources, 34(1), 223-252.

Nasirian, H. (2020). New aspects about Crimean-Congo hemorrhagic fever (CCHF) cases and associated fatality trends: A global systematic review and meta-analysis. Comparative immunology, microbiology and infectious diseases, 69, 101429.

Neckers, L., & Tatu, U. (2008). Molecular chaperones in pathogen virulence: emerging new targets for therapy. Cell host & microbe, 4(6), 519-527.

Normark, B. H., & Normark, S. (2002). Evolution and spread of antibiotic resistance. Journal of internal medicine, 252(2), 91-106.

Okeke, I. N., Feasey, N., Parkhill, J., Turner, P., Limmathurotsakul, D., Georgiou, P., Holmes, A., & Peacock, S. J. (2020). Leapfrogging laboratories: the promise and pitfalls of high-tech solutions for antimicrobial resistance surveillance in low-income settings. BMJ global health, 5(12), e003622.

Organization, W. H. (2016). WHO: Ebola situation report.

Organization, W. H. (2019). Typhoid vaccines: WHO position paper, March 2018–Recommendations. Vaccine, 37(2), 214-216.

Organization, W. H. (2021). WHO malaria terminology.

Organization, W. H., & Initiative, S. T. (2010). Treatment of tuberculosis: guidelines. World Health Organization.

Ortega-Pierres, G., Smith, H. V., Cacciò, S. M., & Thompson, R. A. (2009). New tools provide further insights into Giardia and Cryptosporidium biology. Trends in parasitology, 25(9), 410-416.

Panwar, S., Duggirala, K. S., Yadav, P., Debnath, N., Yadav, A. K., & Kumar, A. (2023). Advanced diagnostic methods for identification of bacterial foodborne pathogens: Contemporary and upcoming challenges. Critical Reviews in Biotechnology, 43(7), 982-1000.

Peeri, N. C., Shrestha, N., Rahman, M. S., Zaki, R., Tan, Z., Bibi, S., Baghbanzadeh, M., Aghamohammadi, N., Zhang, W., & Haque, U. (2020). The SARS, MERS and novel coronavirus (COVID-19) epidemics, the newest and biggest global health threats: what lessons have we learned? International journal of epidemiology, 49(3), 717-726.

Pennington, E. (2023). A Bioinformatic Pipeline for the Detection of Drug Resistant Mutations for Bacterial and Viral Pathogens. The George Washington University.

Perls, T., Kunkel, L. M., & Puca, A. A. (2002). The genetics of exceptional human longevity. Journal of the American Geriatrics Society, 50(2), 359-368.

Pialoux, G., Gaüzère, B.-A., Jauréguiberry, S., & Strobel, M. (2007). Chikungunya, an epidemic arbovirosis. The Lancet infectious diseases, 7(5), 319-327.

Plowright, R. K., Parrish, C. R., McCallum, H., Hudson, P. J., Ko, A. I., Graham, A. L., & Lloyd-Smith, J. O. (2017). Pathways to zoonotic spillover. Nature Reviews Microbiology, 15(8),

502-510.

Prestel, C. (2021). Candida auris outbreak in a COVID-19 specialty care unit—Florida, July–August 2020. MMWR. Morbidity and mortality weekly report, 70.

Prestinaci, F., Pezzotti, P., & Pantosti, A. (2015). Antimicrobial resistance: a global multifaceted phenomenon. Pathogens and global health, 109(7), 309-318.

Puig, M., Casillas, S., Villatoro, S., & Cáceres, M. (2015). Human inversions and their functional consequences. Briefings in functional genomics, 14(5), 369-379.

Pybus, O. G., & Rambaut, A. (2009). Evolutionary analysis of the dynamics of viral infectious disease. Nature Reviews Genetics, 10(8), 540-550.

Quinn, S. C., & Kumar, S. (2014). Health inequalities and infectious disease epidemics: a challenge for global health security. Biosecurity and bioterrorism: biodefense strategy, practice, and science, 12(5), 263-273.

Rabaneda-Bueno, R., Mena-Montes, B., Torres-Castro, S., Torres-Carrillo, N., & Torres-Carrillo, N. M. (2021). Advances in genetics and epigenetic alterations in Alzheimer's disease: a notion for therapeutic treatment. Genes, 12(12), 1959.

Rahman, M. T., Sobur, M. A., Islam, M. S., Ievy, S., Hossain, M. J., El Zowalaty, M. E., Rahman, A. T., & Ashour, H. M. (2020). Zoonotic diseases: etiology, impact, and control. Microorganisms, 8(9), 1405.

Raude, J., McColl, K., Flamand, C., & Apostolidis, T. (2019). Understanding health behaviour changes in response to outbreaks: Findings from a longitudinal study of a large epidemic of mosquito-borne disease. Social science & medicine, 230, 184-193.

Rebbeck, T. R., Mitra, N., Wan, F., Sinilnikova, O. M., Healey, S., McGuffog, L., Mazoyer, S., Chenevix-Trench, G., Easton, D. F., & Antoniou, A. C. (2015). Association of type and location of BRCA1 and BRCA2 mutations with risk of breast and ovarian cancer. Jama, 313(13), 1347-1361.

Reiter, P. (2001). Climate change and mosquito-borne disease. Environmental health perspectives, 109(suppl 1), 141-161.

Resnicow, K., Baranowski, T., Ahluwalia, J. S., & Braithwaite, R. L. (1999). Cultural sensitivity in public health: defined and demystified. Ethnicity & disease, 9(1), 10-21.

Rock, M., Buntain, B. J., Hatfield, J. M., & Hallgrímsson, B. (2009). Animal–human connections,"one health," and the syndemic approach to prevention. Social science & medicine, 68(6), 991-995.

Rush, E. R., Dale, E., & Aguirre, A. A. (2021). Illegal wildlife trade and emerging infectious diseases: pervasive impacts to species, ecosystems and human health. Animals, 11(6), 1821.

Salam, M. A., Al-Amin, M. Y., Salam, M. T., Pawar, J. S., Akhter, N., Rabaan, A. A., & Alqumber, M. A. (2023). Antimicrobial resistance: a growing serious threat for global public health. Healthcare,

Salim, J. A., Saraiva, A. M., Zermoglio, P. F., Agostini, K., Wolowski, M., Drucker, D. P., Soares, F. M., Bergamo, P. J., Varassin, I. G., & Freitas, L. (2022). Data standardization of plant–pollinator interactions. GigaScience, 11, giac043.

Schierhout, G., Gleeson, L., Craig, A., & Wettenhall, I. (2017). Evaluating a decade of Australia's efforts to combat pandemics and emerging infectious diseases in Asia and the Pacific 2006-2015: are health systems stronger? Evaluating a decade of Australia's efforts to combat

pandemics and emerging infectious diseases in Asia and the Pacific 2006-2015.

Semenza, J. C., Rocklöv, J., & Ebi, K. L. (2022). Climate change and cascading risks from infectious disease. Infectious diseases and therapy, 11(4), 1371-1390.

Shadmi, E., Chen, Y., Dourado, I., Faran-Perach, I., Furler, J., Hangoma, P., Hanvoravongchai, P., Obando, C., Petrosyan, V., & Rao, K. D. (2020). Health equity and COVID-19: global perspectives. International journal for equity in health, 19, 1-16.

Sharma, D., & Kamthania, M. (2021). A new emerging pandemic of severe fever with thrombocytopenia syndrome (SFTS). Virusdisease, 32(2), 220-227.

Shenoy, E. S., Pierce, V. M., Walters, M. S., Moulton-Meissner, H., Lawsin, A., Lonsway, D., Shugart, A., McAllister, G., Halpin, A. L., & Zambrano-Gonzalez, A. (2019). Transmission of mobile colistin resistance (mcr-1) by duodenoscope. Clinical Infectious Diseases, 68(8), 1327-1334.

Sheppard, S. K., Guttman, D. S., & Fitzgerald, J. R. (2018). Population genomics of bacterial host adaptation. Nature Reviews Genetics, 19(9), 549-565.

Shu, B., Wu, K.-H., Emery, S., Villanueva, J., Johnson, R., Guthrie, E., Berman, L., Warnes, C., Barnes, N., & Klimov, A. (2011). Design and performance of the CDC real-time reverse transcriptase PCR swine flu panel for detection of 2009 A (H1N1) pandemic influenza virus. Journal of clinical microbiology, 49(7), 2614-2619.

Simpson, S., Kaufmann, M. C., Glozman, V., & Chakrabarti, A. (2020). Disease X: accelerating the development of medical countermeasures for the next pandemic. The Lancet infectious diseases, 20(5), e108-e115.

Singer, R. S., Finch, R., Wegener, H. C., Bywater, R., Walters, J., & Lipsitch, M. (2003). Antibiotic resistance—the interplay between antibiotic use in animals and human beings. The Lancet infectious diseases, 3(1), 47-51.

Sutherst, R. W. (2004). Global change and human vulnerability to vector-borne diseases. Clinical microbiology reviews, 17(1), 136-173.

Szabó, G. T., Mahiny, A. J., & Vlatkovic, I. (2022). COVID-19 mRNA vaccines: Platforms and current developments. Molecular Therapy, 30(5), 1850-1868.

Tacconelli, E., & Cataldo, M. A. (2008). Vancomycin-resistant enterococci (VRE): transmission and control. International journal of antimicrobial agents, 31(2), 99-106.

Tazerji, S. S., Nardini, R., Safdar, M., Shehata, A. A., & Duarte, P. M. (2022). An overview of anthropogenic actions as drivers for emerging and re-emerging zoonotic diseases. Pathogens, 11(11), 1376.

Tejiokem, M. C., Faye, A., Penda, I. C., Guemkam, G., Ateba Ndongo, F., Chewa, G., Rekacewicz, C., Rousset, D., Kfutwah, A., & Boisier, P. (2011). Feasibility of early infant diagnosis of HIV in resource-limited settings: the ANRS 12140-PEDIACAM study in Cameroon. PloS one, 6(7), e21840.

Telenti, A., Hodcroft, E. B., & Robertson, D. L. (2022). The evolution and biology of SARS-CoV-2 variants. Cold Spring Harbor perspectives in medicine, 12(5), a041390.

Theobald, S., Brandes, N., Gyapong, M., El-Saharty, S., Proctor, E., Diaz, T., Wanji, S., Elloker, S., Raven, J., & Elsey, H. (2018). Implementation research: new imperatives and opportunities in global health. The Lancet, 392(10160), 2214-2228.

Thomas, J. K., & Noppenberger, J. (2007). Avian influenza: a review. American Journal of

Health-System Pharmacy, 64(2), 149-165.

Tibayrenc, M., & Ayala, F. J. (2012). Reproductive clonality of pathogens: a perspective on pathogenic viruses, bacteria, fungi, and parasitic protozoa. Proceedings of the National Academy of Sciences, 109(48), E3305-E3313.

Tompson, A., Manderson, L., & Chandler, C. (2021). Understanding antibiotic use: practices, structures and networks. JAC-antimicrobial resistance, 3(4), dlab150.

Tsai, P., Scott, K. A., González, M. C., Pappaioanou, M., & Keusch, G. T. (2010). Sustaining global surveillance and response to emerging zoonotic diseases.

Tsuchiya, N., Ohashi, J., & Tokunaga, K. (2002). Variations in immune response genes and their associations with multifactorial immune disorders. Immunological reviews, 190(1), 169-181.

Vaz-Moreira, I., Ferreira, C., Nunes, O. C., & Manaia, C. M. (2019). Sources of Antibiotic resistance: zoonotic, human, environment. Antibiotic drug resistance, 211-238.

Verhoef, J., van Kessel, K., & Snippe, H. (2019). Immune response in human pathology: infections caused by bacteria, viruses, fungi, and parasites. Nijkamp and Parnham's Principles of Immunopharmacology, 165-178.

Wearing, H. J., Rohani, P., & Keeling, M. J. (2005). Appropriate models for the management of infectious diseases. PLoS medicine, 2(7), e174.

Weiss, R. A., & McMichael, A. J. (2004). Social and environmental risk factors in the emergence of infectious diseases. Nature medicine, 10(Suppl 12), S70-S76.

Weiss, W. M., Winch, P. J., & Burnham, G. (2009). Factors associated with missed vaccination during mass immunization campaigns. Journal of health, population, and nutrition, 27(3), 358.

West, M., Ginsburg, G. S., Huang, A. T., & Nevins, J. R. (2006). Embracing the complexity of genomic data for personalized medicine. Genome research, 16(5), 559-566.

Whitlock, M. C. (2000). Fixation of new alleles and the extinction of small populations: drift load, beneficial alleles, and sexual selection. Evolution, 54(6), 1855-1861.

Wilkinson, A., Ali, H., Bedford, J., Boonyabancha, S., Connolly, C., Conteh, A., Dean, L., Decorte, F., Dercon, B., & Dias, S. (2020). Local response in health emergencies: key considerations for addressing the COVID-19 pandemic in informal urban settlements. Environment and urbanization, 095624782092284.

Williams, B. A., Jones, C. H., Welch, V., & True, J. M. (2023). Outlook of pandemic preparedness in a post-COVID-19 world. npj Vaccines, 8(1), 178.

Woolhouse, M. (2011). How to make predictions about future infectious disease risks. Philosophical Transactions of the Royal Society B: Biological Sciences, 366(1573), 2045-2054.

Woolhouse, M. E., Webster, J. P., Domingo, E., Charlesworth, B., & Levin, B. R. (2002). Biological and biomedical implications of the co-evolution of pathogens and their hosts. Nature genetics, 32(4), 569-577.

Zabidi, N. Z., Liew, H. L., Farouk, I. A., Puniyamurti, A., Yip, A. J. W., Wijesinghe, V. N., Low, Z. Y., Tang, J. W., Chow, V. T., & Lal, S. K. (2023). Evolution of SARS-CoV-2 variants: implications on immune escape, vaccination, therapeutic and diagnostic strategies. Viruses, 15(4), 944.

Zalewska-Piątek, B., & Piątek, R. (2021). Bacteriophages as potential tools for use in antimicrobial therapy and vaccine development. Pharmaceuticals, 14(4), 331.

About The Authors

Mr. Tanveer Nasir is currently pursuing a BS in Biotechnology at the Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His primary areas of interest include Biotechnology, Molecular Biology, and Genetics. He has contributed three book chapters published in international journals, showcasing his growing expertise in these fields.

Email: tanveernasir408@gmail.com ORCID: 0009-0008-7232-1053

Mr. Abdul Rehman received his graduate degree in Applied Microbiology from Cholistan University of Veterinary and Animal Sciences, Bahawalpur, Pakistan. He has completed his internship at the renowned National Institute of Health Pakistan, where he worked on various microbiological studies. Mr. Abdul has written a thesis based on his work during this internship. He has also authored several research and review articles and contributed a chapter on Foot and Mouth Disease in animals and livestock, which is set to be published soon. His research interests encompass viral immune evasion, antimicrobial resistance, and diagnostic advancements.

E-mail: jami.abdrehman@gmail.com, ORCID: 0009-0000-7588-0127

Dr. Muhammad SAFDAR earned his PhD in molecular biology and genetics from Gaziantep University, Turkey. He is a lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 68 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

E-mail: msafdar@cuvas.edu.pk , ORCID: 0000 0002 3720 2090

Prof. Dr. Mehmet ÖZASLAN received his PhD in 1995 Institute of Natural Sciences at Cukurova University, Turkiye. He is a Professor in Molecular Biology and Genetics. His research interests are included Cancer Genetics, Molecular Virology, Molecular Genetics, Microbiology, and Genetic mutations etc. He has published more than 200 research articles in national and international well reputed journals. He also has written many book chapters as well as edited books. He is an editor and editor in chief of many well reputed national and international journals.

E-mail: ozaslanmd@gantep.edu.tr, ORCID: 0000 0001 9380 4902

Miss. Salma Bibi, received her BS degree in Animal Scienes (4 Years) from Cholistan University of Veterinary and Animal Sciences, Bahawalpur, Pakistan. Her main areas of interest is Animal Genetics, Breeding and Reproduction. She have written 8 book chapters in international journals.

Email: salmamalik6809129@gmail.com ORCID: 0009-0003-0798-9886

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as “Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone”. His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

To Cite This Chapter

Nasir, T et al., (2024). Emerging Infectious Diseases and their Preventive Measures. In Current Studies in Health and Life Sciences 2024 (pp.1-21). ISRES Publishing.

Exploring The gut-Brain Axis: How Microbiome Affects Mental Health

Muhammad IBRAHIM

Ukasha TAHIR

Aqsa HAMEED

Maria NAZIR

Adeeba KIRAN

Shafeeq Ur REHMAN

Mehmet OZASLAN

1. Introduction

There exists the concept of the gut-brain axis, a relation that is considered to be intricate since the alimentary canal and the brain are involved. Therefore, its investigation in the sphere of mental health has been further developed. The bidirectional communication system (Figure 1) through neural, hormonal, and immunological signals, referred to as the gut-brain axis, ensures continuous two-way communication between the gastrointestinal tract (GI) and central nervous system (CNS) (Montagnani et al., 2023). This dialogue remains active throughout life and impacts nearly all of the body's physiological and psychological functions, such as digestion, metabolism, immune response, mood, and cognition (Jugran, 2024). The enteric nervous system is the second brain a combination of neurons that exists in the muscular layers of the gastrointestinal tract. This suborder controls peristalsis, secretion, and blood flow in GIT and can be regulated by the non-central nervous system (Pencheva et al., 2015).

However, the enteric nervous system (ENS) is also in consistent conversation with the CNS through the vagus nerve, which is mostly engaged in transmitting messages from the stomach to the head. The human gastrointestinal tract is abode to trillions of microorganisms that are familiar as the gut microbiome and hence act as a moderator in the gut-brain axis (Massaquoi, 2022). These microorganisms release several neuroactive substances like serotonin, dopamine, and gamma-aminobutyric acid (GABA) that, in a way, influence the brain and behavior (Wiley et al., 2021). Moreover, gut microbial communities are known to be closely associated with the immune system during life development and become the chief actor of immune-regulating and stress modulation through the HPA axis during adulthood (Stadler, 2018). The concept of the gut-brain axis is not that novel in scientific circles. This was only when disturbing sensations were identified as butterflies in the stomach gut feeling corresponded to the outlook of the first civilizations where proper functioning of the stomach was perceived necessary for the well-being of the spirit. However, it was at the dawn of the twentieth century that realistic research was focused on the link between gut bacteria, behavior, and the brain (Logan et al., 2016). The human microbiome, a complex, diverse community of microorganisms inhabiting the human body, is considered a novel immune effector and a compelling factor in the occurrence of both health and diseases (Anwar et al., 2019). These bacteria and other single-celled microorganisms that live in humans' digestive systems are mostly involved in metabolism, digestion, immune regulation, and pathogen defense mechanisms. The gut microbiome is not an inactive organ composed of bacteria that waits for an opportunity to invade the host's tissues it communicates with them through a complex method of the gut-brain axis. It influences the functioning of the body and behaviors in humans. Dysbiosis can be defined as alterations in the composition or the function of microbiota. It is linked to various diseases, including inflammatory bowel diseases, obesity, type-2 diabetes mellitus, cardiovascular diseases, Parkinson's disease, multiple sclerosis, and others (Kurowska et al., 2023).

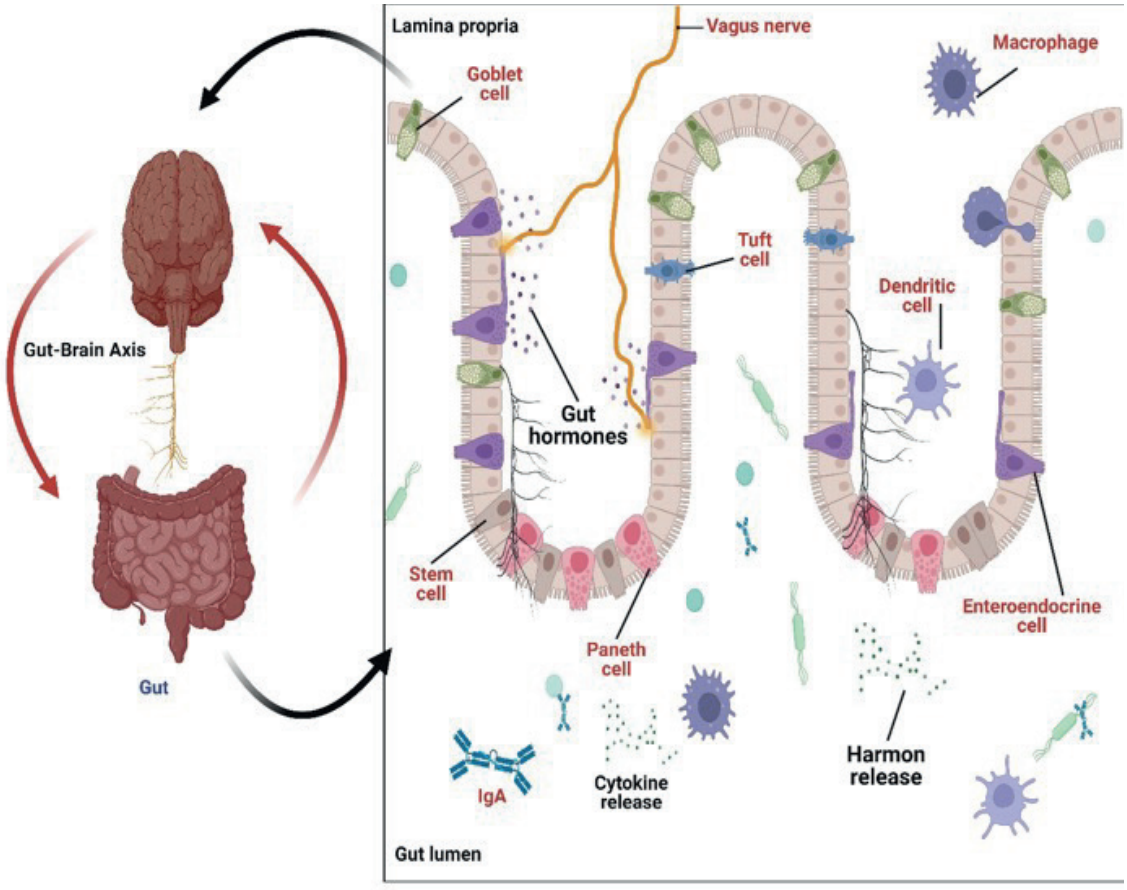


Figure 1. The Gut-Brain Axis: Unveiling the Bidirectional Communication Pathways Between the Gut and Brain

2. Anatomy and Physiology of the Gut-Brain Axis

The Gut-Brain axis can be explained as a very long bidirectional neuroscience line connecting CNS and ENS placed in the digestive system tract. These are the neural, hormonal, and immunological connections whereby all these are involved in bidirectional communication to ensure that at any one time, there is unrestricted flow of information between the gut and the brain (Kazempour, 2022).

2.1 Structure of the Gut-Brain Axis

Gut (Gastrointestinal Tract): Alimentary canal or gastrointestinal tract a long muscular tube from the mouth to the anus itself is the primary organ for the digestion and absorption of foods as well as the excretion of waste products (Maynard & Downes, 2019). But is not just an organ with the tasks of digestion in the limited sense of the term. Coated within the walls of the gastrointestinal tract is the enteric mammalian forebrain like, composed of neurons, neurotransmitters, and glial cells, known as the enteric nervous system (ENS). Also known as the intestinal brain, ENS has evolved and possesses most of the architectural features that can function independently of the CNS. Among these include motor function, secretion, blood flow, and immune responses of the mucosa in the gastrointestinal tract (You et al., 2021).

Brain: Some stimuli from body organs, such as the gut go to the head or the headquarters of the body organ system, which is the brain (Swanson, 2012). It is transported through various networks to the brain, and it is relayed through the vagus nerve, which, in effect, establishes most of the cross-talk between the gut and the brain. Such signs can influence the mood control regions within the brain: the hypothalamus, amygdala, and the prefrontal cortex (Bao & Swaab, 2019).

Communication Pathways

1. Neural Pathways: The vagus nerve, which is the tenth cranial nerve, is the longest in the human body and has bidirectional communication between the gut and the brain (Rangon & Niezgoda, 2022). Sensing in the gut concerns the functional state of the gut, its nutrient status, as well as the reported levels of microbial metabolites, all of which are conveyed to the brain via efferent fibers within the vagal nerve. Efferent fibers transmit information to the latter parts of the body and figure in the motility and secretion of the gut as well as its immune response (Bernardazzi et al., 2016).

2. Hormonal Pathways: These include peptide YY, coicotensin releasing factor and cholecystokinin, and glucagon-like peptide-1 that aids in controlling appetite, satiety, and glucose levels. These gut hormones also act directly on the brain regions the centers for mood regulation, the reward pathways of the brain, and the stress pathway. Conversely, hormones produced by the brain will affect the movements, health, and immune system response of the gut through cortisol, as observed (Makris et al., 2021).

3. Immune Pathways: Based on the congruent distribution of immune cells with the microbes, a definite gut arrangement is made as a premier immunological organ. Available findings prove that microbiota is involved in the formation and maintenance of immunity (Maranduba et al., 2015). However, it should be pointed out that any deviation in the balance of the gut microbial population provokes an immune response, which affects the state of both the gut and the brain. Molecules produced by immune cells are cytokines that are chondroitin and can cross the blood-brain barrier, influencing the brain, which is related to mood disorders and neuroinflammation (Liberman et al., 2019). Therefore, more must be understood about the variety of this relationship to explicate the link between gut microbiota and the mind's condition. Once this relationship is understood, it leads to the implication of treatment methods that will enhance the functioning of this particular axis, improving the methods of treating mental illnesses.

2.2 Key Components and Their Functions

Enteric Nervous System (ENS): The ENS, also referred to as the second brain, is a widespread connection of nerve cells, glial cells located in the submucosa and muscular layers of the gut ranging from the esophagus to rectum (El Munshid, 2000). This Little Brain, a roughly 500 million neuron formation, is quite similar to the neurons located in the spinal cord and is entirely separate from CNS (Sem). The ENS is responsible for a wide array of crucial functions that ensure the smooth operation of the gastrointestinal system: The ENS is in charge of numerous significant functions of the proper functioning of the gastrointestinal tract:

1. Motility: The ENS synchronizes the attenuation and contraction of the muscular layers of the gastrointestinal tract to push food along the tract (peristalsis) and mix it with the digestive juices (segmentation). This rhythmic movement is essential in digestion and the absorption of substances in the GI tracts (Tobias & Sadiq, 2019).

2. Secretion: It regulates the secretion of powerful acids, enzymes, mucus, and other substances that aid in the digestion of foods and the protection of the GI tracts. Other functions include secreting gastric acid, with the aid of parietal cells in the stomach for protein digestion or secreting bicarbonate ions from ducts in the small intestine to neutralize the acids from the stomach (HERE'S).

3. Blood Flow: It assisted in the control of blood flow to the gut, thus participating in oxygen and nutrient delivery to the tissue as well as the elimination process of waste products by using the ENS (Muto, 1988). This regulation is necessary for the health's sake of the gastrointestinal system and the metabolic anticipation of digestion.

4. Immune Response: The ENS interacts with different cells and substances of the intestinal immune system, which consists of definite cells and substances that are involved in the immune response against pathogens and the regulation of the function of the intestine (Giuffrè et al., 2020). It can thus modulate firsthand the synthesis of pro-inflammatory cytokines, the infiltration of immune cells, and the barrier function of the mucosa of the intestinal tract (Yin et al., 2018).

Vagus Nerve: In this subhead, one can develop what is referred to as the 10th cranial nerve, commonly known as the vagus nerve, which connects the gut to the brain in two ways based on its function. It has also been described as the two-way communicative nerve because it sends or transmits signals to or from the body; hence, it has an afferent nerve, which is the sensory function, and an efferent nerve, which is the motor function (Banerjee et al., 2023).

1. Afferent Fibers: These fibers notify the brain about the gut condition and get feedback that it is stretched or has changed its portfolio of chemicals or microbial products (Lipski, 2020). This implies that the head has to control many activities that are considered innate in any human being, for example, hunger and fullness, feelings, and stress.

2. Efferent Fibers: information between the brain and the gut regarding movement, secretion, and immunity (Dinan & Cryan, 2017). The vagus nerve is important in triggering the work of the parasympathetic system referred to as the 'rest and digest'.

Neurotransmitters and Hormones: This molecular communication path from the gut to the brain utilizes many chemicals inherent in the body, including neurotransmitters and hormones (Fatima-Shad, 2024).

1. Neurotransmitters: It generates a vast number of neurotransmitters (Table 1) which are serotonin, dopamine, GABA, non-epinephrine, and acetylcholine involved with mood, emotion, cognition, and the regulation of the stomach (Kuma, 2019).

Table 1: Neurotransmitters and Hormones Involved in Gut-Brain Communication

Neurotransmitter and Hormone	**Source (Gut/Brain)**	**Effects on Gut**	**Effects on Brain**	**References**
Serotonin	Gut (95%)	Motility, secretion	Mood regulation, sleep, appetite	(Fatima-Shad, 2024)
Dopamine	Gut/Brain	Motility	Reward, motivation, motor control	(García-Cabrerizo et al., 2021)
GABA (Gamma-aminobutyric acid)	Gut/Brain	Inhibits nerve activity	Reduces anxiety, promotes relaxation	(Mazzoli & Pessione, 2016)
Norepinephrine	Brain	Inhibits gut function	Arousal, stress response, vigilance	(Bonaz et al., 2012)
Cortisol	Brain	Alters gut permeability	Stress response, metabolism, immune function	(Brzozowski et al., 2016)
Ghrelin	Gut	Stimulates appetite	Reward, motivation, learning	(García-Cabrerizo et al., 2021)
Leptin	Gut	Suppresses appetite	Energy balance, metabolism	(Bauer et al., 2016)
Peptide YY	Gut	Inhibits appetite	Satiety	(Pizarroso et al., 2021)

2. Hormones: This organ secretes several hormones that are involved in appetite, satiety, energy status, and glucose regulation, and they are ghrelin, leptin, peptide YY, and cholecystokinin (Geary, 2004). It can also signal the brain to affect the mood, the brain reward system, and the stress system. Instead, stress hormones produced in the brain, for example, cortisol, influence the function and permeability of the gastrointestinal tract as well as the immune system alternative relationship between the gastrointestinal tract and the brain known as the gut-brain axis.

2.3 Interaction Between Gut Microbiota and the Brain

Fears of microbes exist in the global population's human gastrointestinal tracts, and the one that is particularly relevant to the Gut-brain axis is called the Gut microbiome.

Microbial Composition and Diversity: Previous studies have shown that many of the factors inside an individual's microbiome concerns include diet, genetics, and other features of the environment. Probiotics thus acknowledge the value of the different types of favorable gut bacteria as crucially viable to the gut as well as the overall well-being of an individual (Binns, 2013). However, glycome shift or other forms of dysbiosis in the friendly bacteria are out-competed or suppressed, and the pathogenic bacteria that overgrow frank impact the operations of the gut-brain axis and other health issues, including mental health (Mills et al., 2019).

Mechanisms of Communication

1. Metabolites: They also produce metabolites, which are short-chain fatty acids, tryptophan metabolites, and the neurotransmitters GABA and serotonin. These metabolites can enter circulation and penetrate the blood/brain barrier, and this allows them to have a direct effect on the brain and the animal's behavior (Banks, 2019).

2. Immune System: They state that these microorganisms in the gut affect the immune system and, by extension, the brain functions (Sherman et al., 2015). The smaller intestine bacteria can synthesize cytokines that are inflammatory burdens that affect mood and the brain apart from neuroinflammation.

3. Vagus Nerve: It also has the function of the line by which the body of the organism and the brain information, as well as the signal from the gut microbiota, are transmitted (Hooks et al., 2019) mention that the unpredictable aspect of the communications between digestive microbiota and the brain is perceived through vagal afferent neurons, which control moods, emotions, and cognition.

3. Microbiome and Mental Health

3.1 Microbial profile and Mental health

Anxiety: As for anxious patients, especially those with high cortisol levels, it is possible to use probiotics, but they are not a universal remedy and can have several side effects recalling the connection between the current literature and the gut microbiome and anxiety one can hardly explain that these two are the only means that are linked but have an extremely extensive interaction. Some studies about the correlation between anxiety disorders and the bacterial population in the gut indicate that the patients are comparatively much more deprived of diversity and display certain distinct shifts in the features (Mitrea et al., 2022). Numerous experiments with rats have shown that GM can be changed with probiotics or FMT by decreasing the anxious phenotypes (Vasiliu, 2023b).

Depression: It also mentioned that gut microbiota is before the severity of depression and its parts and drivers. It has been postulated several times that there is a difference in the gastrointestinal microbiota between depressed and normal persons, and it has been noted that slightly there is a correlation between bacterial species and depression. As stated in some articles, constipation is said to be industrialized, and the administration of probiotics or FMT may enhance depressive-like

phenotypes in animals (Gao et al., 2023).

Autism Spectrum Disorders (ASD): For the mentioned disturbances in the composition of the resident microorganisms of the gut the development of ASD is presumed. Some of the researchers stated that there was a change in the proportions of the gastrointestinal microbiome profile in ASD children compared to children without the disorder. In the same regard, defining that SCFA can induce the alteration of microbiota by diet and probiotics can help some behavioral symptoms of ASD (Mintál et al., 2022).

Other Neuropsychiatric Conditions: However, the effects of gut microbiome reach other systems that are involved in disorders to the nervous system as well. It has also been established that Schizophrenia and Bipolar disorder patients also present changed gut microbiota patterns of the same type as was identified in the depression group, obsessive-compulsive disorder, and post-traumatic stress disorder (Offor et al., 2021). There is no information regarding how these activities are affected by the gut microbiome. Still, it is posited that it has the potential to modulate neuroinflammation, generate neurotransmitters, and give feedback to stress, which are relevant in these states.

3.2 Investigations and Research Conducted

Animal Studies: Mice have, therefore, been useful in addressing issues to do with the interaction of the gut microbiota and psychological functions as systems. Animal studies in rats reveal that if mice devoid of bacteria are elevated in a germ-free environment, they have behavioral alterations, such as higher levels of anxiety and inability to survive with stressors properly than the normal gut bacteria. However, this type of manipulation may not always be possible. However, anxiety-like signs could be transmitted by having stressed and anxious mice's gut microbiota transferred to germ-free mice (Yixin, 2019).

Human Clinical Trials: As mentioned, most of the earlier research on the gut-brain axis has been carried out in animals. However, several latest clinical trials in humans exist. These have focused on the effects of probiotics, prebiotics, and diet on the mental health of different populations (Sivamaruthi et al., 2019). For example, a meta-RCT systematic examination was conducted about control trials of probiotics, and it was found that probiotics could have a small effect on reducing depressive symptoms. However, there is still some necessity to define specific randomized strains of probiotics and their doses and the administration period in certain types of mental disorders.

Correlation vs. Causation: According to numerous studies, there is an association between the changes in the strains of the excavated bacterial population and various forms of mental illnesses; however, one should not confuse correlation and causation (Khan, 2015). The reader needs to be told that many of the things explored at the moment are comparative, which means that the studied things can only show some associations but not history. Therefore, considering the interest and the outcomes presented in the present research signifying the role of the gut microbiome in mental health, additional studies are called to identify how much the changes in gut microbiota help to develop a mental disease. In RCTs, individuals are randomly assigned to microbiome-targeted interventions such as probiotics, prebiotics, or diet modifications regarding the composition of mental health outcomes, and these are done over time (Peckmezian et al., 2022). Attempts for such an approach persist, and the results will reveal lots of information on the prospective prospects of tuning the gut microbiota to boost mental health.

3.3 Mechanisms of Action

There are now indications of its implication in mental health through mediating the following mechanisms in the brain and behavior (Figure 2). Information concerning these processes is crucial

in devising the right interventions that could, in one way or another, have a positive impact on the population's mental health.

Inflammation and Immune Response: Gut microbiota impacts the immune system since it is the police of the bacterial movement in the gut. Gut dysbiosis results in the alteration of the microbiota population in the gut and results in locally as well as systematically sustained low-grade inflammation (Vetrani et al., 2022). This inflammation can begin to activate the immune cells and set off a cascade of activation of the production of pro-inflammatory cytokines that can even penetrate the blood-brain sort of thing and, therefore, disrupt normal brain functions. Neuroinflammation is believed to be one of the pathophysiologic mechanisms of multiple mental disorders, including depressive and anxious disorders and schizophrenia (P. G. Almeida et al., 2020).

Neurotransmitter Production: The gut bacteria have been observed to directly produce or else regulate the production of many neuroactive substances, including neurotransmitters that are associated with brain operations and mood alteration (Gupta et al., 2024). For example, some of these gut bacteria produce gamma-aminobutyric acid or GABA, which is the major anti-anxiety neurotransmitter in the brain. Other bacteria influence the synthesis of serotonin, which is a neurotransmitter associated with mood, appetite, and sleep patterns (LaGreca et al., 2021). Hence, any variations to the composition of microbiota should have implications on the synthesis and operation of these neurotransmitters and, therefore, impact mental disease.

Stress Response and HPA Axis: The concept is that the gut microbiome controls the stress regulation system of the body, the HPA axis. Stress impacts the content of gut microbiota, and as such, the changes in homeostasis affecting the microbiota impact the HPA axis stress response (Zhang et al., 2023). This dysregulation can lead to the development of certain mental illnesses, such as depression and other anxiety-related disorders, given that stress is usually related to them. New studies present the above connection between the gut microbiota and mental health as rather intricate. Scientists proved that some alterations in the makeup of people's gut bacteria influence certain diseases, including anxiety, depression, and autism spectrum disorders (C. Almeida et al., 2020). Hence, results obtained from different animal investigations and human clinical trials confirm this relationship; however, most of them are correlational. Among the processes that are fostered in this relationship are immune alteration of the immune system, secretion of neurotransmitters, and stress-responsive system. More efforts are needed to translate the findings on the connection between gut microbiota and mental health into practice and identify which areas require intervention (Swann et al., 2020).

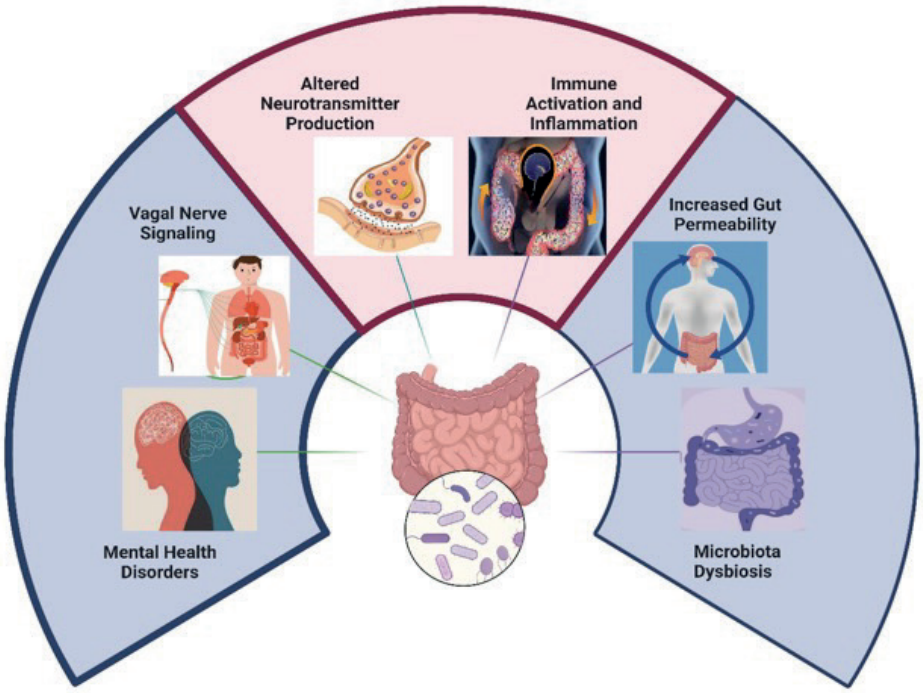


Figure 2. Hypothesized Mechanisms of Gut Microbiota Influence on Mental Health

4. Mechanisms of Microbiome-Gut-Brain Interaction

Collectively referred to as the second brain, the gut microbiome has been established in the current literature as an influential player in regulating the brain and behavior with a focus on the gut-brain axis. This interactive communication system involves a two-way linkage between the aforementioned gut microbes and CNS (Figure 3). It is thanks to such knowledge of the nature of this interaction that one can explain the role of the specific part of the gut microbiome regarding the state of mind and develop new therapeutic approaches.

Neurotransmitter Production: It also notes that the gut microbiome is involved in synthesizing and regulating some of the brain and mood-related neurotransmitters. It is further illustrated that gut bacteria can create neurotransmitters on their own: for instance, gamma-aminobutyric acid (GABA), which is regarded as being one of the major inhibitory transmitters within the brain and relates to depression of neuronal excitation, and lethargy. It has been established that some kinds of Lactobacillus and Bifidobacterium can produce GABA and, hence, manage anxiety action in animal models (Lalonde & Strazielle, 2022). Also, gut microbes are involved in influencing serotonin since it is synthesized in the gut, and is among the mood, appetite, and sleep regulators known as neurotransmitters. Also, tryptophan, a precursor of serotonin, and the metabolites that the gut bacteria produce directly affect serotonin receptors in the brain and can also be regulated by the gut bacteria (Legan et al., 2022). The composition and performance of the gut microbiome can thus be used to influence the content of neurotransmitters, which may lead to poor mental health.

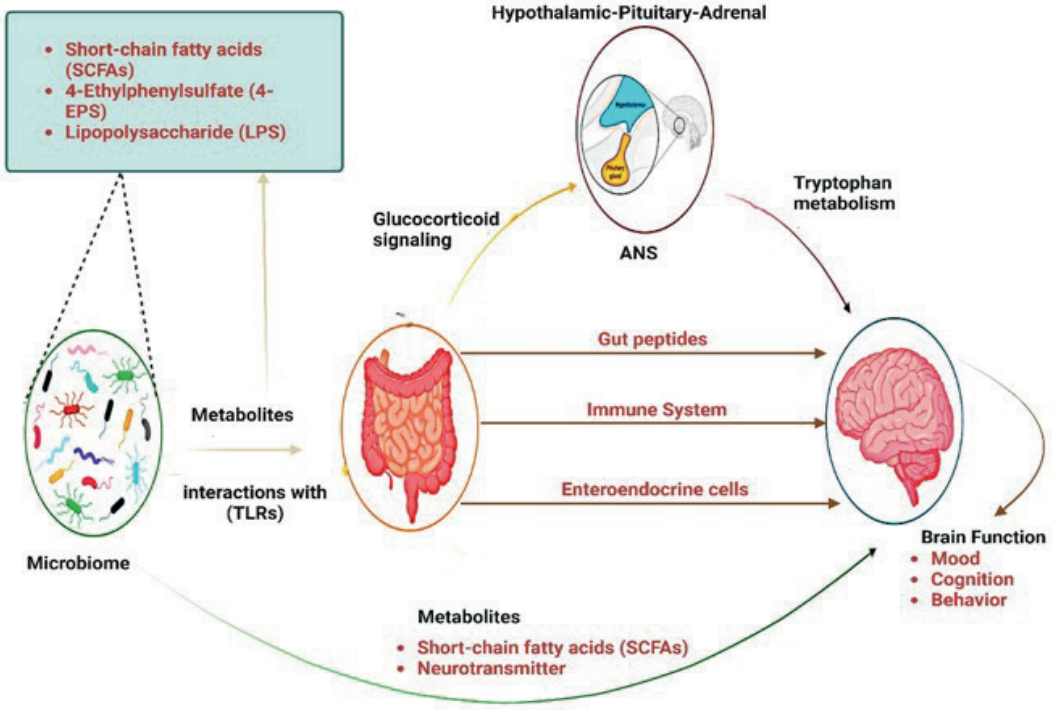


Figure 3. Mechanisms of Microbiome-Gut-Brain Interaction

Short-Chain Fatty Acids (SCFAs) and Inflammation: Butyrate, propionate, and Acetate are referred to as the short-chain fatty acids acting as end products of dietary fibers by gut bacteria (Vinelli et al., 2022). Consequently, SCFAs have more than one role in the gut, including regulation of the integrity of the intestinal barrier, innate immunity, and as an energy substrate for colonocytes. However, besides the regional modulatory effects seen here in the gut region, SCFAs can affect the brain according to the following points. It can cross the blood-brain barrier without restriction and intervene directly with the receptors on neurons and glial cells, hence interfering with neuronal functionality and synaptic plasticity (Zhao et al., 2021). SCFAs have also been described to regulate inflammation as they inhibit the onset of pro-inflammatory signals and enhance the production of anti-inflammatory compounds. Specifically, such an effect can be exerted in the brain, which suggests that it may influence the processes of neuroinflammation and neuroplasticity that occur in connection with various mental disorders (Halaris, 2018).

Immune System Modulation: The construction and familiarization with the immune system rely to a major extent on the gut microbiome (Kuehnast et al., 2022). Many bacteria in the commensal microbiota interact with the immune cells located in the GALT and modulate immune tolerance and the balance of pro-inflammatory and anti-inflammatory reactions. Because dysbiosis pertains to the change in the balance of gut microbiota, any immune response that occurs because of this condition can raise low-grade inflammation locally in the gut and systemically throughout the body (Mundula et al., 2022). It can lead to neuro-inflammation, where there is activation of first responders in the brain, and there is an established connection between inflammation and other psychological afflictions such as depression, anxiety, and schizophrenia, to mention but a few. Furthermore, it is well documented that gut microbes are associated with cytokines, and cytokines are signal proteins that are very imperative in immunity and play a role in regulating the brain and behavior (Caputi et al., 2021).

Endocrine Signaling: The gut microbial communities involve an interaction with the endocrine system, which consists of glands that release hormones to regulate the various operations in the body (Forsythe, 2013). It has been found that the microbiome can change the production rates and release of various hormones, among which is cortisol, which is the main stress hormone. Thus, it has been proposed that stress will manifest an effect on microbiota and that dysbiosis in reciprocation will act on the hypothalamic pituitary adrenal (HPA) axis (Sharma et al., 2022). which is the body's stress response system, leading to hyper-hyperstress, which makes the affected person prone to mental stress to ill-health. Lactobacillus and Bifidobacterium, for instance, have been discovered to reduce cortisol stress hormone and restrain stress-induced behaviors in animal studies in addition to apparently both sexes (Wang, 2018). This is a sign that there is a potential that changing the balance of bacteria in the gut could help in eradicating or at least controlling stress and all the schemes that are bound to affect the mental health of an individual.

5. Factors Influencing the Gut Microbiome

Therefore, the actual combination of microorganisms of gut microbiota regarding bacteria, archaea, fungi, and viruses is thought to be in a constant dynamic state and open that develops under the impact of numerous factors. These attributes include diet, drugs, exercise schedule, and other features of the topic's environment. Some of the factors of interest include. Hence, it is crucial to understand how these factors work in gut microbiome applications in the construct of developing personalized approaches that may improve gut and, by association, mental health.

Table 2: Impact of Dietary Patterns on Gut Microbiome Composition

Dietary Pattern	Effect on Gut Microbiome	References
High-Fiber	Increased diversity, beneficial bacteria (Bifidobacterium, Lactobacillus), SCFAs	(Piccioni et al., 2023)
High-Fat/Sugar	Decreased diversity, harmful bacteria (Bilophila Wadsworth), SCFAs	(Berding & Donovan, 2020)
Plant-Based	Increased beneficial bacteria, decreased harmful bacteria	(Sheflin et al., 2017)
Mediterranean Diet	Diverse, balanced microbiome	(Merra et al., 2020)
Western Diet	Reduced diversity, harmful bacteria	(Zhang et al., 2020)

5.1 Diet and Nutrition

An individual's diet is a key factor of gut microbiota its composition as well as function. For instance, the type of foods that we take contains nutrients (Table 2) entering into our body microenvironments and trillions of microbial passengers in our intestines. These feeding habits are presumed to define the level of complexity in the bacterial strains regarding the batch size with the metabolic parameters and hosts (San Roman & Wagner, 2018).

Probiotics and Prebiotics:

1. Probiotics: They are microorganisms capable of producing a specific function in the body of the host. Each time the consumer takes a particular quality of the microorganisms, the host benefits by experiencing a boost in health. Probiotics can be incorporated in the solid or liquid part of foods that are likely to have passed through some fermentation stage, which includes Yogurt, Kefir, Sauerkraut, and kimchi, and can be taken as nutritional supplements. Certain types of probiotics from the Lactobacillus and Bifidobacterium genera for bettering mental health owing to the management of the gut-brain axis (Sabit et al., 2023). Some of these probiotics also influence the synthesis of neurotransmitters, immunity, and actions against inflammation, leading to psychological health.

2. Prebiotics: Prebiotics can, therefore, be described as food products whose constituents cannot be assimilated, and this brings out the activity and growth of friendly bacteria in the large

intestines (Włodarczyk & Śliżewska, 2021). These fibers nourish the good bacteria as the bad ones do and also give them a better environment to triumph over the latter. Many prebiotic sources are present in foods such as onion, garlic, bananas, salads, asparagus, and wholesome grains. Prebiotics operate by the principle of, and this is the idea that only the positive bacteria are required to restore the balance of the gut microbiome, thus the state of the gut, as well as the moods since they are partners in the stomach (Appanna & Appanna, 2018).

3. Dietary Patterns and Their Impact: It can be distinguished that the researchers did not observe the influence of specific dietary components on the overall microbial population balance but noted the dependency of the location of certain microbes in the gut on the total diet. Plant food, which is rich in fiber and phytochemicals, constitutes a major part of the diet and has a role to play in populating the human gut with healthy bacteria (Sudheer et al., 2022). This is so because fiber varies, and complex carbohydrates get fermented in the presence of specific bacteria, thus producing SCFAs and other useful metabolites that promote the healthy state of the gut and brain. However, a poor diet characterized by taking processed foods high in sugar and unhealthy fats will differentiate the current effect on the microbiome. Thus where microbial diversity is bound to shrink, the gram-negative bacteria have a higher propensity to be inflammatory (Escobar□Salom et al., 2022).

5.2 Antibiotics and Medications

The human gut is known to be a host or a dwelling place for trillions of microorganisms, which are usually referred to as the human microbiota, which plays crucial roles in human health, disregarding the mental health aspect. However, such a balance can change with the assistance of several factors, with the aid of antibiotics and some medications.

Effects of Antibiotics on Gut Flora: Role of Antibiotics on the Experiments on Gut Flora

According to this reasoning, while bacterial infections can be cleared up by antibiotics, the price one pays for this victory is that antibiotics are hostile to the symbiotic flora of the human gastrointestinal tract. However, distinguishing between the pathogenic and the symbiotic bacteria is almost impossible most of the time (Martinson et al., 2020). As a result, antibiotic use can have profound and lasting consequences for the gut microbiome; consequently, the process of antibiotic treatment influences the composition of the gut microbiota, and that effect is quite long-term.

1. Reduced Diversity: Each antibiotic decreases the number of members in the communities living in people's guts, starting with pathogenic germs, which were expected, and continuing with so valuable participants in the digestion process and immune response (Schmidt, 2009). This loss of diversity may offset some of the protective mechanisms of stress and proliferation of vulnerability that keeps the host susceptible to being infected by other diseases.

2. Altered Composition: The primary concern here is that administering antibiotics alters the balance of GM; some types of bacteria decrease in number while others increase (Jiménez-Avalos et al., 2021). This may lead to disruption of the healthy bacterial community, Dysbiosis, which may present or worsen many pathogens' health states, which are inflammatory bowel diseases, obesity, and metabolic disorders.

3. Increased Pathogen Colonization: An example of pathogens that exploit such a break in the maturity of the community include Clostridium difficile, which colonizes the gut and causes infections due to disruption by antibiotics (Rosa et al., 2018). Clostridium difficile infection (CDI) which ranges from mild diarrhea to severe colitis, is a major observed con in patients who were hospitalized and had a history of using broad-spectrum antibiotics.

4. Long-Term Consequences: In similar regards, there is evidence of how antibiotics affect the population of the microbiota in the human gut as having a persistent even after they have ceased to be administered (Kokou et al., 2020). Abnormal changes in the composition of bacterial microflora in the intestine persist for months or even for several years after taking antibiotics and their consequences, including obesity, autoimmune diseases, allergies, and neurodevelopmental disorders.

Role of Psychobiotics

Because antibiotics trigger negative effects on the composition of gut microbiota, much attention is paid to the application of psychobiotics to reduce the negative influence on the mental condition. Probiotics are defined as the live microbial nutrients that cause a positive effect on the host's condition while psychobiotics appear to have a positive influence on the mental health of the host in the considered gut-brain axis (Ağagündüz et al., 2023). Certain Lactobacillus and Bifidobacterium species may have the potential to be classified as psychobiotics and positive effects on anxiety and depression were recorded in clinical studies (Ross, 2023). These beneficial bacteria can modulate the gut-brain axis through various mechanisms, including Such beneficial bacterial can influence the gut-brain axis in several ways;

1. Neurotransmitter Production: Psychobiotics may influence the synthesis processes and added activity of other neurotransmitters like GABA and serotonin, agents that have a big role in dictating a person's feelings (Lachmansingh et al., 2023).

2. Immune Modulation: They may enhance tight junctions and decrease the inflammation as well as immune responses that, in general, contribute to the modulation of brain and mental health (Holzer et al., 2017).

3. Stress Response: As for the improvement of the physiological aspect, regarding the psychobiotics' influence on stress as manifested by cortisol decrease and regulation of the HPA axis, the focus flexibility levels are increased, and anxiety levels are moderated (Hernandez Barrueta, 2022). Thus, it can be concluded that the strategies of using psychobiotics in addition to antibiotics or as a single treatment for patients with mental disorders can be viewed as one of the promising fields for further research. However, these studies need to define the combinations of strains, dosages, and time courses of psychobiotic interventions that can be of therapeutic value to the conditions and patients related to these mental health disorders (Vasiliu, 2023a).

5.3 Lifestyle Factors

Diet is the acknowledged and the most influential factor affecting gut microbiota and its functionality; however, some aspects of a person's lifestyle can also noticeably influence gut microbiota. These include:

Stress: In this case, stress has an impact on the nervous system and hormonal changes, leading to changes in the movement of the gut, secretion, and permeability of the lining thus exposing the gut to inflammations and infections (Oroian et al., 2021). Also, stress can activate the HPA axis and further hormones such as cortisol, which can also remove the gut microbiotas and intensify mental illnesses.

Physical Activity: Motor activity influences the number and density of the beneficial bacteria in the gut; it has been shown that relaxation time physical activity has a positive impact on the density of microbes and the health of the gut (Resende et al., 2021). The movement enhances the motion of the intestines hence improving the composition of the gut microbiome through lessening inflammation while also enhancing the barrier strength. Moreover, exercise assists in the inhibition of stress levels and a myriad of other things that influence the mood thereby creating the bridging of the gut and the brain link.

Sleep Patterns: As illustrated in the literature, sleep plays a crucial role in the health of not only any particular organ but the general health of one's body including the gut. Sleep also has an impact on the gut microbiota and its subsequent functionality; this is because either reduced or disrupted sleep leads to the same outcomes (Han et al., 2022). Individuals who do not sleep can have several health complications due to a changed intestinal barrier, boosted inflammation, and altered balance of the microbiota, which interferes with metabolism and mental well-being.

6. Therapeutic Applications and Directions for Research

A relatively new field of science concerns the relationship between the gut and the brain, where several therapeutic approaches regarding the suppression of mental illnesses have been discovered. Refers to the possible interventions that may be helpful now and those that are currently being tested, proposed to change the focus of mental health disorders.

6.1 Possible Treatments and Action Plan

1. Probiotics and Prebiotics

Probiotics: These live microorganisms, when ingested in adequate quantity, will have positive effects on the host's health (Marco et al., 2020). Some of these probiotics, especially of the Lactobacillus and Bifidobacterium species, have been useful in reducing signs of anxiety, depression, and stress in experimentations. These mechanisms include the influence on the synthesis of neurotransmitters, the strengthening of the gut barrier, and the control of immune response and inflammation (Sharkey & Savidge, 2014).

Prebiotics: Prebiotics are defined as non-hydrolyzable food ingredients that stimulate the growth and activity of beneficial gut bacteria (Garcia-Alonso et al., 2023). It works as a prebiotic that spurs the fermentation by the gut bacteria, resulting in the formation of SCFAs and other beneficial physiologic metabolites for the gut and brain. Inulin, fructooligosaccharides (FOS), and galactooligosaccharides (GOS) are among the most familiar prebiotics inherent in foods such as onions, garlic, bananas, asparagus, and whole grains. The findings from earlier studies practiced in prebiotics revealed that it positively influences mood, stress levels, and cognitive performance (Karbownik et al., 2022).

2. Dietary Interventions

It is essential to distinguish eating habits that have a critical impact on the gut's microbial composition and, therefore, mental health. Various plant matters, for instance, fruits, vegetables, whole grains, legumes, nuts, and seeds, have been linked to better gut flora and a lesser prevalence of mental illnesses (Shanmugam et al., 2022). These foods produce elaborate baskets of fibers and slowly digestible carbohydrates that are prebiotically metabolized by beneficial gut bacteria. This results in the nourishing production of SCFAS and other beneficial metabolites that promote gut and brain health. On the other hand, the customary diet comprising processed foods, sugars, and unfavorable fats in the Western world deteriorates the gut microbiota. It leads to dysbiosis, which is connected to elevated susceptibility to mental disorders (Choi et al., 2020). Like the Mediterranean diet, a balanced and colorful diet that can favorably affect the composition of gut microbiota has been reported to enhance mood and decrease depressive symptoms.

3. Fecal Microbiota Transplantation (FMT)

FMT directly transfers fecal material from a donor into the patient's gastrointestinal tract. For these reasons, people with dysbiosis or those with a particular disease state can have the typical flora recovered in the gut (Bhutiani et al., 2018). FMT has been quite successful in treating multiple relapses of C. difficile infection, and modern research indicates that it may also be useful in managing other diseases, such as inflammatory bowel disease, irritable bowel syndrome, and certain mental disorders. FMT for mental health is a relatively new area under research, and thus,

several studies have documented the amelioration of symptoms of depression, anxiety, and autism spectrum disorder (ASD) (Goo et al., 2020). However, prospective trials must be done to define the level of its sustainable effectiveness for treating mental disorders and the best practices of FMT's application.

6.2 Targeted Strategies in Diseases Related to the Gut-Brain Axis

Precise medicine solutions are applied to GBA, targeting strategies for a person's microbiome and specific disease features. This therapeutic strategy is intended to maximize the potential therapeutic benefit and the least amount of harm from the medications due to the complex interactions between the gut microbiome and the brain, as well as take into consideration the patient's characteristics.

Microbiome Profiling

Metagenomics, the most commonly used holistic approach in personalized therapies in this setting, is the detailed analysis of a human body's microbiome. This can be done using, for instance, 16S rRNA sequencing, metagenomic sequencing, and metabolomic profiling (Han et al., 2020). The above techniques give a clear and detailed depiction of the subsets of microbiota, the items within the subsets, and the functionalities needed to understand dysbiosis that may lead to symptoms of mental disorders.

1. 16S rRNA Sequencing: This technique focuses especially on the 16S rRNA gene sequence of bacteria and allows the identification and determination of the number of bacteria in that sample. It offers information on the bacterial occurrence of gut flora and enables the comparison of the stomach content of the normal and those of the mentally ill (Hooks et al., 2019).

2. Metagenomic Sequencing: This approach is slightly different from the previous one as it includes DNA sequencing of the entire microbial content that was applied to a microbial sample. This provides a clearer picture of the gut microbiome in addition to bacteria, viruses, fungi, and other microorganisms (Pérez, 2021). Some of the basic and advanced properties of the human gut microbiome are as follows: Metagenomic sequencing can help stratify the gut microbiome's metabolic pathways, virulence factors, and antibiotic resistance in the human body.

3. Metabolomic Profiling: This technique estimates the concentrations of metabolites derived from gut bacterial activity and illuminates how the host influences them (Silpe & Balskus, 2020). Using metabolomic analysis, it is possible to define the biomarkers that connect with particular mental disorders and, thus, adjust therapy and treatment.

Customized Treatment Plans

It is possible to design treatment regimens given the microbiome's profile and other characteristics of an individual, clinical symptoms, and other factors influencing the dysbiosis of gut microbiota and mental health. These treatment plans may involve a combination of These treatment plans may involve a combination of:

1. Probiotics and Prebiotics: It is possible to have some specific effects of certain probiotic strains, including Lactobacillus and Bifidobacterium species, on mental health as supported by clinical studies (Dey & Mookherjee, 2021). These probiotics can thus be used to repopulate the gut with helpful bacteria strains or at least attempt to control the communication between the gut and the brain. Probiotics that feed health-promoting bacteria are also recommended and can be prescribed to the patient to supply additional prebiotics, which will help promote the ideal growth and action of such bacteria (Ranjha et al., 2021).

2. Dietary Interventions: Dietary diets also play a role in determining the complex gut microbiota. Sweeping the concept of microbiome-specific interventions relating to diet can involve a set of specific recommendations for developing beneficial bacteria in the gut and reducing

inflammation levels (Juritsch, 2023). These measures may comprise elevating the consumption of fiber-containing foods, foods that undergo fermentation, and nutrients that are believed to enhance the health of the intestinal lining.

3. Fecal Microbiota Transplantation (FMT): The use of FMT is considered for patients with severe dysbiosis or severe mental illness that has not responded to other forms of treatment. The procedure entails the process where the fecal matter of a healthy individual is placed in the recipient's gut to enhance a healthy bacterial flora (Ademe, 2020). FMT for mental health is a relatively new research area however, it has been observed that some studies carried out in this background show positive trends in the treatment of depression, anxiety, and autism spectrum disorder.

6.3 Future Research Directions

The gut-brain axis and its connection to mental health are unexplored and progressively developing research areas. Therefore, future research directions can provide an even deeper understanding of this reciprocal interaction and offer new avenues of therapy and treatment of mental health disorders.

Emerging Technologies and Methodologies

1. Multi-omics Approaches: The use of genomics, transcriptomics, proteomics, and metabolomics will enhance our understanding of gut microbiota, host, and gene-environment interactions in contributing to mental health (Hayes et al., 2020). This particular approach will help define new biomarkers, therapeutic targets, and personalized treatments for patients.

2. Advanced Bioinformatics and Machine Learning: The internship work in this case will involve various analyses using multi-omics data. Thus, bioinformatics tools and intricate machine learning algorithms in analysis will be central to this project. These tools will allow investigators and clinicians to understand regularly the correlations and cause-and-effect relationships between the microbiome and the subject's health, particularly their mental health (Lange et al., 2020).

3. Organoid Models and Humanized Mice: Organoid models are three-dimensional primary cell cultures that establish the structure and functioning of an organ, and humanized mice, which are mice engrafted with human gut microbiota, bring out the gut-brain axis in more physiological settings (Boylin et al., 2024). Such models can enable the comprehension of how gut bacteria influence the host and evaluate the efficiency of the reported treatments.

Long-Term Studies and Clinical Trials

1. Longitudinal Studies: However, to obtain a more profound understanding of how the gut microbiome would affect the mental health parameter's occurrences, elaborate on the needed cohort studies that would look at the state of the above parameter at different time points. Such studies can indicate time shifts in the participants' GI macrobiotic metagenomics and functionality, address the initiating stimuli levels of the condition, and evaluate the interventions' efficacy for the sustainment of mental health (Al Tarraf, 2021).

2. Large-Scale Clinical Trials: Well-controlled trials with large cohorts are required to assess the outcomes of administering microbiome-related products, namely probiotics, prebiotics, diet changes, and Fecal Microbiota Transplant (FMT), for core mental health disorders (Lum, 2023). Suctrials should also recruit people from various ethnic backgrounds to generalize results and uncover variations in response to treatment across different groups.

3. Mechanistic Studies: Several research works have highlighted the interconnection between the gut microbiota and mental health; however, the processes involved are not well explored. Future investigations should concentrate on how gut bacteria directly affect the brain and behavior in more detail, especially regarding neurotransmitter, cytokine, and metabolite levels (Ignatova, 2019).

4. Personalized Medicine Approaches: Precision medicine is an appropriate trend in developing gut microbiome interventions, hence a call for more personalization in approaches (De Filippis et al., 2018). This includes defining personal microbial signatures, selecting therapy based on the patient's characteristics, and assessing therapeutic outcomes using objective markers. Through these future research directions, it is possible to realize the full potential of the gut-brain axis for transforming the future of mental health. Understanding how the gut microbiome and the brain interact will create new treatment approaches for mental disorders, positively affecting the treatment process and patients' quality of life.

7. Conclusion

Different, more recent discoveries, such as the gut-brain axis and the communication network between the microbiome in the gut and the central nervous system, have proven significant to this aspect of human health. This complex interplay affects, among other things, mood, nutrient absorption, and learning capabilities, and its dysregulation is associated with a plethora of mental ailments. Understanding how gut microbiota interacts with the brain is noteworthy; this involves neurotransmitters, short-chain fatty acids, microbe-derived tokens, cytokines, and endocrine signaling. Such understanding has given rise to a novel therapy that seeks to address the microbiome in the gut to enhance patients' mental well-being. Clinical trials and in vitro studies have shown the effectiveness of probiotics, prebiotics, diets, and FMT in improving symptoms of anxiety, depression, and related issues. Microbiome profiling for tailoring individualized treatment programs also seems more effective and responsive to patients' needs in selecting the most appropriate treatment methods. Despite the growing interest, knowledge concerning the so-called gut-brain axis is still rather limited. There is a lot of potential for future work to investigate this intricate association, and new technologies like single-cell sequencing and better bioinformatics tools help in this endeavor. More large-scale and long-term investigations and clinical trials are necessary to prove and confirm the causal benefits of microbiome-based therapies and determine the exact place of such approaches in treating mental diseases. Therefore, the gut-brain axis concept offers a revolutionary standpoint in understanding the causes and cures for psychological disorders. These findings revealed the vast potential of staking a direct claim on the human body's gut-master microbiome to create unique, long-lasting, and more productive treatment mechanisms for many mental health issues that impact millions globally.

References

Ademe, M. (2020). Benefits of fecal microbiota transplantation: a comprehensive review. The Journal of Infection in Developing Countries, 14(10), 1074-1080.

Ağagündüz, D., Çelik, E., Cemali, Ö., Bingöl, F. G., Özenir, Ç., Özoğul, F., & Capasso, R. (2023). Probiotics, live biotherapeutic products (LBPs), and gut-brain axis related psychological conditions: implications for research and dietetics. Probiotics and Antimicrobial Proteins, 15(4), 1014-1031.

Al Tarraf, A. (2021). Impact of polyphenols and feeding rhythms on the immunomodulation properties of the probiotic bacteria in the gastro-intestinal tract Université Bourgogne Franche-Comté].

Almeida, C., Oliveira, R., Soares, R., & Barata, P. (2020). Influence of gut microbiota dysbiosis on brain function: a systematic review. Porto biomedical journal, 5(2), 1.

Almeida, P. G., Nani, J. V., Oses, J. P., Brietzke, E., & Hayashi, M. A. (2020). Neuroinflammation and glial cell activation in mental disorders. Brain, Behavior, & Immunity-Health, 2, 100034.

Anwar, H., Irfan, S., Hussain, G., Faisal, M. N., Muzaffar, H., Mustafa, I., Mukhtar, I., Malik, S., & Ullah, M. I. (2019). Gut microbiome: A new organ system in body. Parasitol Microbiol Res,

1, 17-21.

Appanna, V. D., & Appanna, V. D. (2018). Dysbiosis, probiotics, and prebiotics: in diseases and health. Human microbes-The power within: Health, healing and beyond, 81-122.

Banerjee, D., Das, P. K., & Mukherjee, J. (2023). Nervous System. In Textbook of Veterinary Physiology (pp. 265-293). Springer.

Banks, W. A. (2019). The blood–brain barrier as an endocrine tissue. Nature Reviews Endocrinology, 15(8), 444-455.

Bao, A.-M., & Swaab, D. F. (2019). The human hypothalamus in mood disorders: the HPA axis in the center. IBRO reports, 6, 45-53.

Bauer, P. V., Hamr, S. C., & Duca, F. A. (2016). Regulation of energy balance by a gut–brain axis and involvement of the gut microbiota. Cellular and Molecular Life Sciences, 73, 737-755.

Berding, K., & Donovan, S. M. (2020). Dietary patterns impact temporal dynamics of fecal microbiota composition in children with autism spectrum disorder. Frontiers in Nutrition, 6, 193.

Bernardazzi, C., Pêgo, B., & de Souza, H. S. P. (2016). Neuroimmunomodulation in the gut: focus on inflammatory bowel disease. Mediators of inflammation, 2016(1), 1363818.

Bhutiani, N., Schucht, J., Miller, K., & McClave, S. A. (2018). Technical aspects of fecal microbial transplantation (FMT). Current gastroenterology reports, 20, 1-6.

Binns, N. (2013). Probiotics, prebiotics and the gut microbiota.

Bonaz, B., Pellissier, S., Sinniger, V., Clarençon, D., Peinnequin, A., & Canini, F. (2012). The irritable bowel syndrome: how stress can affect the amygdala activity and the brain-gut axis. The amygdala-A discrete multitasking manager.

Boylin, K., Aquino, G. V., Purdon, M., Abedi, K., Kasendra, M., & Barrile, R. (2024). Basic models to advanced systems: harnessing the power of organoids-based microphysiological models of the human brain. Biofabrication, 16(3), 032007.

Brzozowski, B., Mazur-Bialy, A., Pajdo, R., Kwiecien, S., Bilski, J., Zwolinska-Wcislo, M., Mach, T., & Brzozowski, T. (2016). Mechanisms by which stress affects the experimental and clinical inflammatory bowel disease (IBD): role of brain-gut axis. Current Neuropharmacology, 14(8), 892-900.

Caputi, V., Popov, J., Giron, M. C., & O'Mahony, S. (2021). Gut microbiota as a mediator of host neuro-immune interactions: implications in neuroinflammatory disorders. Microbes and the Mind, 32, 40-57.

Choi, T.-Y., Choi, Y. P., & Koo, J. W. (2020). Mental disorders linked to crosstalk between the gut microbiome and the brain. Experimental Neurobiology, 29(6), 403.

De Filippis, F., Vitaglione, P., Cuomo, R., Berni Canani, R., & Ercolini, D. (2018). Dietary interventions to modulate the gut microbiome—how far away are we from precision medicine. Inflammatory Bowel Diseases, 24(10), 2142-2154.

Dey, G., & Mookherjee, S. (2021). Probiotics-targeting new milestones from gut health to mental health. FEMS Microbiology Letters, 368(15), fnab096.

Dinan, T. G., & Cryan, J. F. (2017). Microbes, immunity, and behavior: psychoneuroimmunology meets the microbiome. Neuropsychopharmacology, 42(1), 178-192.

El Munshid, H. A. (2000). The brain of the gut. Saudi Journal of Gastroenterology, 6(1), 18-26.

Escobar-Salom, M., Torrens, G., Jordana-Lluch, E., Oliver, A., & Juan, C. (2022). Mammals' humoral immune proteins and peptides targeting the bacterial envelope: from natural protection to therapeutic applications against multidrug-resistant Gram-negatives. Biological Reviews, 97(3), 1005-1037.

Fatima-Shad, K. (2024). Serotonin-Neurotransmitter and Hormone of Brain, Bowels and Blood: Neurotransmitter and Hormone of Brain, Bowels and Blood. BoD–Books on Demand.

Forsythe, P. (2013). Gut microbes as modulators of the neuro-immuno-endocrine system. PharmaNutrition, 1(4), 115-122.

Gao, J., Zhao, L., Cheng, Y., Lei, W., Wang, Y., Liu, X., Zheng, N., Shao, L., Chen, X., & Sun, Y. (2023). Probiotics for the treatment of depression and its comorbidities: A systemic review. Frontiers in cellular and infection microbiology, 13, 1167116.

Garcia-Alonso, A., Sanchez-Paniagua Lopez, M., Manzanares-Palenzuela, C. L., Redondo-Cuenca, A., & López-Ruíz, B. (2023). Edible plant by-products as source of polyphenols: Prebiotic effect and analytical methods. Critical reviews in food science and nutrition, 63(31), 10814-10835.

García-Cabrerizo, R., Carbia, C., O´ Riordan, K. J., Schellekens, H., & Cryan, J. F. (2021). Microbiota-gut-brain axis as a regulator of reward processes. Journal of neurochemistry, 157(5), 1495-1524.

Geary, N. (2004). Endocrine controls of eating: CCK, leptin, and ghrelin. Physiology & behavior, 81(5), 719-733.

Giuffrè, M., Moretti, R., Campisciano, G., da Silveira, A. B. M., Monda, V. M., Comar, M., Di Bella, S., Antonello, R. M., Luzzati, R., & Crocè, L. S. (2020). You talking to me? Says the enteric nervous system (ENS) to the microbe. How intestinal microbes interact with the ENS. Journal of Clinical Medicine, 9(11), 3705.

Goo, N., Bae, H. J., Park, K., Kim, J., Jeong, Y., Cai, M., Cho, K., Jung, S. Y., Kim, D.-H., & Ryu, J. H. (2020). The effect of fecal microbiota transplantation on autistic-like behaviors in Fmr1 KO mice. Life sciences, 262, 118497.

Gupta, S., Dinesh, S., & Sharma, S. (2024). Bridging the Mind and Gut: Uncovering the Intricacies of Neurotransmitters, Neuropeptides, and their Influence on Neuropsychiatric Disorders. Central Nervous System Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Central Nervous System Agents), 24(1), 2-21.

Halaris, A. (2018). Neuroinflammation and neurotoxicity contribute to neuroprogression in neurological and psychiatric disorders. Future Neurology, 13(2), 59-69.

Han, D., Gao, P., Li, R., Tan, P., Xie, J., Zhang, R., & Li, J. (2020). Multicenter assessment of microbial community profiling using 16S rRNA gene sequencing and shotgun metagenomic sequencing. Journal of Advanced Research, 26, 111-121.

Han, M., Yuan, S., & Zhang, J. (2022). The interplay between sleep and gut microbiota. Brain research bulletin, 180, 131-146.

Hayes, C. L., Peters, B. J., & Foster, J. A. (2020). Microbes and mental health: Can the microbiome help explain clinical heterogeneity in psychiatry? Frontiers in Neuroendocrinology, 58, 100849.

HERE'S, W. Y. H. B. Digestion and Absorption.

Hernandez-Barrueta, T. (2022). Psychobiotics, a special type of probiotics, and their potential molecular mechanisms to ameliorate symptoms of stress and anxiety. Molecular Mechanisms of

Functional Food, 28-56.

Holzer, P., Farzi, A., Hassan, A. M., Zenz, G., Jačan, A., & Reichmann, F. (2017). Visceral inflammation and immune activation stress the brain. Frontiers in immunology, 8, 1613.

Hooks, K. B., Konsman, J. P., & O'Malley, M. A. (2019). Microbiota-gut-brain research: a critical analysis. Behavioral and Brain Sciences, 42, e60.

Ignatova, V. (2019). Influence of gut microbiota on behavior and its disturbances. Behavioral Neuroscience, 17-43.

Jiménez-Avalos, J. A., Arrevillaga-Boni, G., González-López, L., García-Carvajal, Z. Y., & González-Avila, M. (2021). Classical methods and perspectives for manipulating the human gut microbial ecosystem. Critical reviews in food science and nutrition, 61(2), 234-258.

Jugran, D. (2024). The Healing Mindset: Understanding Psychology of Wellness: The Synthesis: Unleashing the power of Body & Mindset. Shashwat Publication.

Juritsch, A. F. (2023). Utilizing Human Microbiota Associated Mice to Understand the Gut Microbiome-Dependent Effects of Dietary Fiber from Sorghum on Experimental Intestinal Inflammation.

Karbownik, M. S., Mokros, Ł., Dobielska, M., Kowalczyk, M., & Kowalczyk, E. (2022). Association between consumption of fermented food and food-derived prebiotics with cognitive performance, depressive, and anxiety symptoms in psychiatrically healthy medical students under psychological stress: a prospective cohort study. Frontiers in Nutrition, 9, 850249.

Kazempour, A. (2022). Large Association of GI Tract Microbial Community with Immune and Nervous Systems. In Immunology of the GI Tract-Recent Advances. IntechOpen.

Khan, S. (2015). Health and disease according to Darwinian evolution. Shahriar Khan.

Kokou, F., Sasson, G., Mizrahi, I., & Cnaani, A. (2020). Antibiotic effect and microbiome persistence vary along the European seabass gut. Scientific reports, 10(1), 10003.

Kuehnast, T., Abbott, C., Pausan, M. R., Pearce, D. A., Moissl-Eichinger, C., & Mahnert, A. (2022). The crewed journey to Mars and its implications for the human microbiome. Microbiome, 10(1), 26.

Kuma, S. S. (2019). Clinical Study on the Effectiveness of Jatipatri Ksheerapaka in Anidra (Primary Insomnia) Rajiv Gandhi University of Health Sciences (India)].

Kurowska, A., Ziemichód, W., Herbet, M., & Piątkowska-Chmiel, I. (2023). The role of diet as a modulator of the inflammatory process in the neurological diseases. Nutrients, 15(6), 1436.

Lachmansingh, D. A., Lavelle, A., Cryan, J. F., & Clarke, G. (2023). Microbiota-Gut-Brain Axis and Antidepressant Treatment. In. Springer.

LaGreca, M., Hutchinson, D. R., & Skehan, L. (2021). The microbiome and neurotransmitter activity. The Journal of Science and Medicine, 3(2).

Lalonde, R., & Strazielle, C. (2022). Probiotic effects on anxiety-like behavior in animal models. Reviews in the Neurosciences, 33(6), 691-701.

Lange, K. W., Lange, K. M., Nakamura, Y., & Kanaya, S. (2020). Is there a role of gut microbiota in mental health? Journal of Food Bioactives, 9.

Legan, T. B., Lavoie, B., & Mawe, G. M. (2022). Direct and indirect mechanisms by which the gut microbiota influence host serotonin systems. Neurogastroenterology & Motility, 34(10),

e14346.

Liberman, A. C., Trias, E., da Silva Chagas, L., Trindade, P., dos Santos Pereira, M., Refojo, D., Hedin-Pereira, C., & Serfaty, C. A. (2019). Neuroimmune and inflammatory signals in complex disorders of the central nervous system. Neuroimmunomodulation, 25(5-6), 246-270.

Lipski, E. (2020). The GUT-immune system. Integrative and Functional Medical Nutrition Therapy: Principles and Practices, 367-377.

Logan, A. C., Jacka, F. N., Craig, J. M., & Prescott, S. L. (2016). The microbiome and mental health: looking back, moving forward with lessons from allergic diseases. Clinical Psychopharmacology and Neuroscience, 14(2), 131.

Lum, G. R. T. (2023). Effects of clinical ketogenic diet therapy for pediatric epilepsy on the gut microbiota and seizure resistance. University of California, Los Angeles.

Makris, A. P., Karianaki, M., Tsamis, K. I., & Paschou, S. A. (2021). The role of the gut-brain axis in depression: endocrine, neural, and immune pathways. Hormones, 20(1), 1-12.

Maranduba, C. M. d. C., De Castro, S. B. R., Souza, G. T. d., Rossato, C., da Guia, F. C., Valente, M. A. S., Rettore, J. V. P., Maranduba, C. P., Souza, C. M. d., & Carmo, A. M. R. d. (2015). Intestinal microbiota as modulators of the immune system and neuroimmune system: impact on the host health and homeostasis. Journal of immunology research, 2015(1), 931574.

Marco, M. L., Hill, C., Hutkins, R., Slavin, J., Tancredi, D. J., Merenstein, D., & Sanders, M. E. (2020). Should there be a recommended daily intake of microbes? The Journal of Nutrition, 150(12), 3061-3067.

Martinson, V. G., Gawryluk, R. M., Gowen, B. E., Curtis, C. I., Jaenike, J., & Perlman, S. J. (2020). Multiple origins of obligate nematode and insect symbionts by a clade of bacteria closely related to plant pathogens. Proceedings of the National Academy of Sciences, 117(50), 31979-31986.

Massaquoi, M. S. (2022). Cell Specific Responses to Microbiota Play Global Roles in Host Development & Homeostasis University of Oregon].

Maynard, R. L., & Downes, N. (2019). Alimentary canal or gastrointestinal tract. Anatomy and Histology of the Laboratory Rat in Toxicology and Biomedical Research, 147-158.

Mazzoli, R., & Pessione, E. (2016). The neuro-endocrinological role of microbial glutamate and GABA signaling. Frontiers in microbiology, 7, 1934.

Merra, G., Noce, A., Marrone, G., Cintoni, M., Tarsitano, M. G., Capacci, A., & De Lorenzo, A. (2020). Influence of mediterranean diet on human gut microbiota. Nutrients, 13(1), 7.

Mills, S., Stanton, C., Lane, J. A., Smith, G. J., & Ross, R. P. (2019). Precision nutrition and the microbiome, part I: current state of the science. Nutrients, 11(4), 923.

Mintál, K., Tóth, A., Hormay, E., Kovács, A., László, K., Bufa, A., Marosvölgyi, T., Kocsis, B., Varga, A., & Vizvári, Z. (2022). Novel probiotic treatment of autism spectrum disorder associated social behavioral symptoms in two rodent models. Scientific reports, 12(1), 5399.

Mitrea, L., Nemeş, S.-A., Szabo, K., Teleky, B.-E., & Vodnar, D.-C. (2022). Guts imbalance imbalances the brain: a review of gut microbiota association with neurological and psychiatric disorders. Frontiers in medicine, 9, 813204.

Montagnani, M., Bottalico, L., Potenza, M. A., Charitos, I. A., Topi, S., Colella, M., & Santacroce, L. (2023). The crosstalk between gut microbiota and nervous system: a bidirectional interaction between microorganisms and metabolome. International journal of molecular sciences,

24(12), 10322.

Mundula, T., Russo, E., Curini, L., Giudici, F., Piccioni, A., Franceschi, F., & Amedei, A. (2022). Chronic systemic low-grade inflammation and modern lifestyle: The dark role of gut microbiota on related diseases with a focus on COVID-19 pandemic. Current medicinal chemistry, 29(33), 5370-5396.

Muto, T. (1988). Digestion and absorption. Tokyo: Daiichishuppan Co., Ltd, 228.

Offor, S. J., Orish, C. N., Frazzoli, C., & Orisakwe, O. E. (2021). Augmenting clinical interventions in psychiatric disorders: systematic review and update on nutrition. Frontiers in psychiatry, 12, 565583.

Oroian, B. A., Ciobica, A., Timofte, D., Stefanescu, C., & Serban, I. L. (2021). New Metabolic, Digestive, and Oxidative Stress-Related Manifestations Associated with Posttraumatic Stress Disorder. Oxidative Medicine and Cellular Longevity, 2021(1), 5599265.

Peckmezian, T., Garcia-Larsen, V., Wilkins, K., Mosli, R. H., BinDhim, N. F., John, G. K., Yasir, M., Azhar, E. I., Mullin, G. E., & Alqahtani, S. A. (2022). Microbiome-targeted therapies as an adjunct to traditional weight loss interventions: A systematic review and meta-analysis. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 3777-3798.

Pencheva, M., Darmonska, P., Aleksandrov, A., & Milkov, D. (2015). BM SPERM ANALYSIS OF MEN WITH A HISTORY OF INFERTILITY. Folia Medica, 57, 1.

Pérez, J. C. (2021). Fungi of the human gut microbiota: Roles and significance. International Journal of Medical Microbiology, 311(3), 151490.

Piccioni, A., Covino, M., Candelli, M., Ojetti, V., Capacci, A., Gasbarrini, A., Franceschi, F., & Merra, G. (2023). How do diet patterns, single foods, prebiotics and probiotics impact gut microbiota? Microbiology Research, 14(1), 390-408.

Pizarroso, N. A., Fuciños, P., Gonçalves, C., Pastrana, L., & Amado, I. R. (2021). A review on the role of food-derived bioactive molecules and the microbiota–gut–brain axis in satiety regulation. Nutrients, 13(2), 632.

Rangon, C.-M., & Niezgoda, A. (2022). Understanding the pivotal role of the vagus nerve in Health from pandemics. Bioengineering, 9(8), 352.

Ranjha, M. M. A. N., Shafique, B., Batool, M., Kowalczewski, P. Ł., Shehzad, Q., Usman, M., Manzoor, M. F., Zahra, S. M., Yaqub, S., & Aadil, R. M. (2021). Nutritional and health potential of probiotics: a review. Applied sciences, 11(23), 11204.

Resende, A. S., Leite, G. S., & Lancha Junior, A. H. (2021). Changes in the gut bacteria composition of healthy men with the same nutritional profile undergoing 10-week aerobic exercise training: a randomized controlled trial. Nutrients, 13(8), 2839.

Rosa, R., Donskey, C. J., & Munoz-Price, L. S. (2018). The intersection between colonization resistance, antimicrobial stewardship, and Clostridium difficile. Current infectious disease reports, 20, 1-6.

Ross, K. (2023). Psychobiotics: Are they the future intervention for managing depression and anxiety? A literature review. Explore, 19(5), 669-680.

Sabit, H., Kassab, A., Alaa, D., Mohamed, S., Abdel-Ghany, S., Mansy, M., Said, O. A., Khalifa, M. A., Hafiz, H., & Abushady, A. M. (2023). The effect of probiotic supplementation on the gut–brain axis in psychiatric patients. Current Issues in Molecular Biology, 45(5), 4080-4099.

San Roman, M., & Wagner, A. (2018). An enormous potential for niche construction through bacterial cross-feeding in a homogeneous environment. PLoS computational biology, 14(7), e1006340.

Schmidt, M. A. (2009). Beyond antibiotics: Strategies for living in a world of emerging infections and antibiotic-resistant bacteria. North Atlantic Books.

Sem, I. UNIVERSITY OF C SCHOOL OF DISTANC.

Shanmugam, H., Ganguly, S., & Priya, B. (2022). Plant food bioactives and its effects on gut microbiota profile modulation for better brain health and functioning in Autism Spectrum Disorder individuals: A review. Food frontiers, 3(1), 124-141.

Sharkey, K. A., & Savidge, T. C. (2014). Role of enteric neurotransmission in host defense and protection of the gastrointestinal tract. Autonomic Neuroscience, 181, 94-106.

Sharma, A., Singh, A. K., Kumar, V., & Prakash, H. (2022). Interferon and HPA Axis: Impact on Neuroimmunological Perturbations. In Basic and Clinical Aspects of Interferon Gamma. IntechOpen.

Sheflin, A. M., Melby, C. L., Carbonero, F., & Weir, T. L. (2017). Linking dietary patterns with gut microbial composition and function. Gut microbes, 8(2), 113-129.

Sherman, M. P., Zaghouani, H., & Niklas, V. (2015). Gut microbiota, the immune system, and diet influence the neonatal gut–brain axis. Pediatric research, 77(1), 127-135.

Silpe, J. E., & Balskus, E. P. (2020). Deciphering human microbiota–host chemical interactions. ACS Central Science, 7(1), 20-29.

Sivamaruthi, B. S., Prasanth, M. I., Kesika, P., & Chaiyasut, C. (2019). Probiotics in human mental health and diseases-A minireview. Tropical Journal of Pharmaceutical Research, 18(4), 889-895.

Stadler, C. (2018). NUTRITIONAL DETERMINANTS IN THE DEVELOPMENTAL PROGRAMMING OF AUTOIMMUNE DISEASES–FACTS AND HYPOTHESES.

Sudheer, S., Gangwar, P., Usmani, Z., Sharma, M., Sharma, V. K., Sana, S. S., Almeida, F., Dubey, N. K., Singh, D. P., & Dilbaghi, N. (2022). Shaping the gut microbiota by bioactive phytochemicals: An emerging approach for the prevention and treatment of human diseases. Biochimie, 193, 38-63.

Swann, J., Rajilic-Stojanovic, M., Salonen, A., Sakwinska, O., Gill, C., Meynier, A., Fança-Berthon, P., Schelkle, B., Segata, N., & Shortt, C. (2020). Considerations for the design and conduct of human gut microbiota intervention studies relating to foods. European journal of nutrition, 59, 3347-3368.

Swanson, L. W. (2012). Brain architecture: understanding the basic plan. Oxford University Press, USA.

Tobias, A., & Sadiq, N. M. (2019). Physiology, gastrointestinal nervous control.

Vasiliu, O. (2023a). The current state of research for psychobiotics use in the management of psychiatric disorders–A systematic literature review. Frontiers in psychiatry, 14, 1074736.

Vasiliu, O. (2023b). Is fecal microbiota transplantation a useful therapeutic intervention for psychiatric disorders? A narrative review of clinical and preclinical evidence. Current Medical Research and Opinion, 39(1), 161-177.

Vetrani, C., Di Nisio, A., Paschou, S. A., Barrea, L., Muscogiuri, G., Graziadio, C., Savastano, S., Colao, A., Obesity Programs of Nutrition, E., Research, & Group, A. (2022). From gut microbiota through low-grade inflammation to obesity: key players and potential targets. Nutrients, 14(10), 2103.

Vinelli, V., Biscotti, P., Martini, D., Del Bo', C., Marino, M., Meroño, T., Nikoloudaki, O., Calabrese, F. M., Turroni, S., & Taverniti, V. (2022). Effects of dietary fibers on short-chain fatty acids and gut microbiota composition in healthy adults: a systematic review. Nutrients, 14(13), 2559.

Wang, H. (2018). Effects of probiotics on central nervous system functions in humans Universität Tübingen].

Wiley, N. C., Cryan, J. F., Dinan, T. G., Ross, R. P., & Stanton, C. (2021). Production of psychoactive metabolites by gut bacteria. Microbes and the Mind, 32, 74-99.

Włodarczyk, M., & Śliżewska, K. (2021). Obesity as the 21st Century's major disease: The role of probiotics and prebiotics in prevention and treatment. Food Bioscience, 42, 101115.

Yin, M., Yan, X., Weng, W., Yang, Y., Gao, R., Liu, M., Pan, C., Zhu, Q., Li, H., & Wei, Q. (2018). Micro integral membrane protein (MIMP), a newly discovered anti-inflammatory protein of Lactobacillus plantarum, enhances the gut barrier and modulates microbiota and inflammatory cytokines. Cellular Physiology and Biochemistry, 45(2), 474-490.

Yixin, X. (2019). Absence of Gut Microbiota Causes Stress-Induced Anxiety via Amygdala Hyperexcitability in Mice National University of Singapore (Singapore)].

You, X.-y., Zhang, H.-y., Han, X., Wang, F., Zhuang, P.-w., & Zhang, Y.-j. (2021). Intestinal mucosal barrier is regulated by intestinal tract neuro-immune interplay. Frontiers in Pharmacology, 12, 659716.

Zhang, H., Wang, Z., Wang, G., Song, X., Qian, Y., Liao, Z., Sui, L., Ai, L., & Xia, Y. (2023). Understanding the connection between gut homeostasis and psychological stress. The Journal of Nutrition, 153(4), 924-939.

Zhang, Q.-S., Tian, F.-W., Zhao, J.-X., Zhang, H., Zhai, Q.-X., & Chen, W. (2020). The influence of dietary patterns on gut microbiome and its consequences for nonalcoholic fatty liver disease. Trends in Food Science & Technology, 96, 135-144.

Zhao, M., Jiang, X.-F., Zhang, H.-Q., Sun, J.-H., Pei, H., Ma, L.-N., Cao, Y., & Li, H. (2021). Interactions between glial cells and the blood-brain barrier and their role in Alzheimer's disease. Ageing research reviews, 72, 101483.

About The Authors

Muhammad Ibrahim received his MPhil in 2024 from Gomal University DIKHAN, Pakistan. His research interests include natural product isolation, identification, and their biological assessments. He has also written book chapters.

Email: michemist6835@gmail.com ORCID:0009-0009-8560-9272

Ukasha Tahir completed her MPhil in 2023 from the School of Biological Sciences, University of the Punjab, Lahore. She also worked as a research fellow in a research project for one year entitled "Effect of cytochrome b5 on the half-life of human recombinant interferons". She also worked as a development fellow in a project " Development of computer-controlled fermenters and production of bioproducts and biochemicals" at PCSIR Laboratories Complex, Lahore. Her research interests include Biochemistry, enzymology, protein chemistry, immunology, animal handling, molecular cloning, protein expression and purification. Her two papers are accepted in well-reputed journals. She also has written book chapters.

Email: ukashatahir123@gmail.com ORCID: 0009-0003-0209-8785

Aqsa Hameed has completed her MPhil degree in Biochemistry from Bahauddin Zakariya University, Multan. She is a researcher specializing in neurobiochemistry, with a keen interest in animal behavior and the evaluation of various compounds on brain health. Aqsa has submitted one research paper as the first author, which is currently under review.

Email aqsahameed13@gmail.com ORCID 0009-0003-7968-2197

Maria Nazir is an MPhil Scholar of Microbiology at the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur, Pakistan. She is involved in a National Research Program for Universities (NRPU) Project, with research interests in Molecular Characterization. She has submitted abstracts to various conferences and authored and coauthored of several book chapters. Her research focuses on the isolation and Molecular characterization of Corynebacterium pseudotuberculosis and their applications in promoting animal health. Her interested research criteria are based on genetics, molecular biology, and bioinformatics.

Email: nazirmaria545@gmail.com ORCID 0009-0004-6714-6212

Ms. Adeeba Kiran holds an MS in Clinical Psychology with a strong focus on neuropsychology, cognition, and the complex dynamics between brain function and behavior. Her research interests revolve around understanding the neural mechanisms that drive cognitive processes and behavior patterns. She has contributed to the field through the publication of a research article and had the opportunity to present her findings at a international research conference. Additionally, her role as a research assistant has provided her with valuable experience in conducting rigorous studies and exploring innovative approaches.

Email ID: adeebakiran444@gmail.com ORCID ID: 0009-0001-4342-2479

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as “Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone”. His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

Prof. Dr. Mehmet ÖZASLAN received his PhD in 1995 Institute of Natural Sciences at Cukurova University, Turkiye. He is a Professor in Molecular Biology and Genetics. His research interests are included Cancer Genetics, Molecular Virology, Molecular Genetics, Microbiology, and Genetic mutations etc. He has published more than 200 research articles in national and international well reputed journals. He also has written many book chapters as well as edited books. He is an editor and editor-in-chief of many well-reputed national and international journals.

E-mail: ozaslanmd@gantep.edu.tr, ORCID: 0000 0001 9380 4902

To Cite This Chapter

IBRAHIM M et al., (2024). Exploring the gut-brain axis: how microbiome affects mental health In Current Studies in Health and Life Sciences 2024 (pp.23-45). ISRES Publishing.

Microbial Threats: Global Health Governance in The Age of Superbugs

Maria NAZIR

Rohina ARIF

Jawad ASLAM

Shafeeq Ur REHMAN

Muhammad MUDASSAIR

Muhammad SAFDAR

Mehmet OZASLAN

1. Introduction

When it comes to the chronicle of man, there was no greater advancement in how man fought off diseases than the use of antibiotics. Such 'wonder drugs,' which were considered the tonic for diseases, changed the history of medical sciences and raised the bar of health indices (Davies, 2013). However, the narrative of triumph has taken a disquieting turn as a new threat looms large on the horizon the increasing cases of substances that are resistant to antibiotics, such as antimicrobial resistance (AMR), commonly referred to as "superbugs. Exclusion of the elements other than Superbugs and AMR Other than implying the Superbugs and AMR, the above terms refer to those bacteria that have been deemed highly resistant to antibiotics. In other words, antimicrobial resistance can also be described as the microorganisms' ability to not be neutralized by the antimicrobial agents that are claimed to either eliminate the microorganisms or inhibit their multiplication. This is a progressive process however, the uptake and abuse of antimicrobials have triggered the occurrence of this event at an unusually fast rate (Christaki et al., 2020).

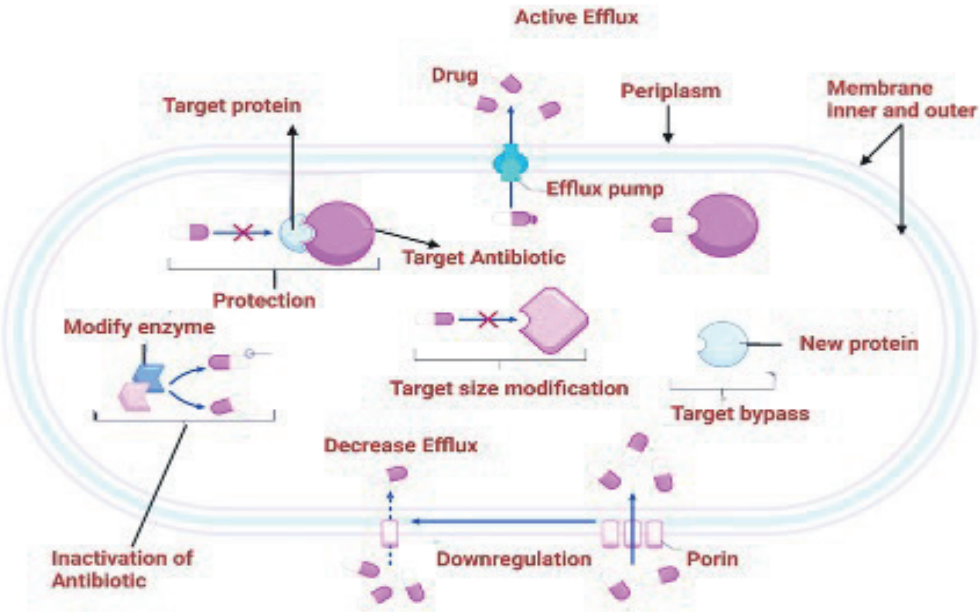


Figure 1. Mechanisms of Antimicrobial Resistance

Superbugs are the fearsome offspring of this resistance, types of microorganisms that factor in the ability to resist more than one type of antimicrobial agent, making them almost inflammable. The methicillin-resistant Staphylococcus aureus (MRSA), Carbapenem-resistant Enterobacterales (CRE), and vancomycin Resistant Enterococci (VRE) are among the well-known superbugs all have distinct weapons in their arsenals of resistance. These resistance mechanisms (Figure 1) include the elimination of drugs by enzymatic activity, modifications to the targets of drugs as well as through efflux pumps that eject antibiotics out of the bacterial cell (Farhat et al., 2020). This leads to the evolution of what has come to be referred to as superbugs Since the genetic resistance can be mutated or transferred from one microorganism to another.

A Global Threat by Superbugs

The scale and reach of AMR and superbugs do not remain limited to hospitals and clinics but affect everyone. This not only turns into an issue but is categorized as a great threat to health security in the world that has rolled back the years of progress in eradicating diseases. AMR is recognized as one of the main challenges for world health. On the economic side, the picture is no different, with estimates pointing to an aggregate figure of 100 trillion USD in terms of foregone output by the same year (Dasgupta, 2021). The effect is deep-seated in that easily curable diseases turn into a nightmare, thus prolonging patients' stay in healthcare facilities, escalating the cost of treating the patients in addition to record high mortality rates. The emergence of AMR is worrisome due to its increased risk in LMICs, characterized by poor healthcare accessibility, poor sanitation, and inadequate or almost non-existent stewardship programs (Kpokiri, 2019). In these contexts, AMR drives the incidence of other communicable diseases such as TB, malaria, and HIV/AIDS, while greed widens existing socioeconomic imbalances (Michaud et al., 2024). Global health governance is an important topic that must not be neglected, especially given today's complex systems worldwide. Due to the globalization of AMR, there is a need to address the issue collaboratively and holistically (Aijaz et al., 2023). There is an urgent need to scale up international health diplomacy to prevent the rise of superbugs and protect people's health domestically and globally. This includes surveillance and monitoring, infection prevention and control, continuing antimicrobial stewardship, research and development, new antibiotics and other therapies, and social-financial-ecological actions across borders. Intensive antimicrobial usage and the emergence of superbugs have turned global health governance into a science, politics, economics, and moral issue. It entails achieving consensus with heterogeneous players, including governments, international organizations, healthcare professionals, pharmaceutical firms, and civil society (Walser, 1997). The details regarding the nature of threats posed by superbugs, the state of global health, the current system of governance of such pathogens, and the measures needed to fight this terrorizing threat shall be explored in the subsequent chapters. Utilizing past interventions' difficulties as the primary knowledge, we will reveal the challenges on the way to a sophisticated system of governance and create a blueprint of humanity's roadmap in the context of the current and future microbial threats. The path that we are about to follow can hardly be called predictable, yet the world's state today leaves no space for hesitation and calls for immediate, concerted action to safeguard the currently existing, as well as future, generations' health.

2. Understanding Superbugs

These superbugs are not strictly new species of microbes but mutated strains that can withstand almost all forms of antibiotics being used in the modern world and rank amongst the most fearsome opponents in the ongoing war against infections. This acquired resistance, perfectly normal in evolution, has been made several-fold worse due to the widespread misuse and overuse of antibiotics in humans, animals, and feedstock (Ram et al., 2020). The implications of this phenomenon give rise to dire effects, which are witnessed by the fact that superbug infections necessarily prolong an individual's sickness, raise costs drastically, and can even be fatal. To grip the threat from superbugs, it is necessary to look deeper into the strategies that the organisms use to escape the impact of the drugs. One such mechanism is enzymatic degradation, which entails using enzymes by bacteria capable of degrading the antibiotics before they exhibit their antimicrobial action.

One of the best examples can be narrowed down to the synthesis of beta-lactamases, enzymes that neutralize penicillin and other related antibiotics to the bacteria hence becoming ineffective (Fatima et al., 2021). The other is an example of target alteration; here, the bacteria change the structure of the antibiotic's target within the cell to ensure that the antibiotic cannot bind and exert its inhibitory or killing effect. An example of this mechanism is MRSA, which has had a change in its penicillin-binding protein to that which makes it resistant to methicillin and another beta-lactam category of antibiotics (Kırmusaoğlu, 2017). Efflux pumps in the cell membrane of bacteria such as Pseudomonas aeruginosa expel the antibiotics from their cellular structure before the antibiotic can affect the bacteria (Iman Islamieh et al., 2018). This mechanism enables bacteria to keep sub-lethal concentrations of antibiotics within the cell, thus surviving the drug exposure. Some of the strategies used by bacterial pathogens to exhibit resistance include reduced permeability involved with Gram-negative bacteria and carbapenem-resistant Enterobacteriaceae (CRE). These organisms modify their outer membranes in such a way that the penetration of antibiotics through the cell is limited and is, therefore, unable to get to the target site. This intrinsic resistance, accompanied by other resistance mechanisms, makes CRE infection rather difficult to combat. The superbug market is inhabited by a large number of resistant agents, which are characterized by specific resistance patterns and related diseases (Doron & Broom, 2019). Together, the most common is MRSA causing skin and soft tissue, and bloodstream infection. CRE is a group of bacteria that comes next to facility-acquired or healthcare-associated infections that are very difficult to manage. VRE is responsible for urinary tract, bloodstream, and wound infections; and MDRPA, which is a universal pathogen in hospitalized patients, especially immunocompromised (Fontanot et al., 2024). The appearance and dissemination of these and other resistant pathogens threaten the same audience, testifying to the importance of fighting AMR. This has a very important implication in understanding the right strategies for tackling these superbugs with resistance and in sustaining the effectiveness of the current and newly promoted antibiotics.

3. Antibiotic Resistance

The Rise of Antimicrobial Resistance

This world is not turning into a more customary place. There is conflict going on here and there, let's say even diseases, hunger, and natural disasters. Antibiotics were discovered in the early 20th century, starting with Alexander Fleming in 1928, and introduced new paradigms to medical curing (Lalchhandama, 2021). Where infectious diseases used to wipe out a significant percentage of the entire population, they were now controlled, and life expectancy rocketed. But the excitement of having antibiotics was short-lived because, within a few decades, we had faced a new challenge antibiotic resistance. Antibiotics and other antiseptic substances, together with many others, have catalyzed the escalating instances of antimicrobial resistance or AMR as it is commonly known today (Domínguez & Meza-Rodriguez, 2019).

Historical perspective on the usage of antibiotics and antibiotic resistance

Thus, the story of antibiotics and resistance is a narrative of scientific discovery, social advances, and biological evolution (Table 1). Antibiotic discovery took off in the mid-twentieth century and was characterized by the generation of diverse classes of molecules. Nevertheless, this period also witnessed the birth of the resistance issue, with information indicating that penicillin-resistant S. aureus was first reported in the 1940s (Basset et al., 2011).

Table 1: Evolution of Antibiotic Discovery and Rise of Antimicrobial Resistance (AMR)

Year	Milestone	Significance	References
1928	Discovery of penicillin by Fleming	Revolutionized medicine marked the beginning of the antibiotic era.	(Haider, 2023)
1940s	Widespread use of penicillin	Demonstrated the life-saving potential of antibiotics.	(Lobanovska & Pilla, 2017)
1950s-1960s	"Golden Age" of antibiotic discovery	Numerous new antibiotics were introduced, expanding the arsenal against bacterial infections.	(Fairley)
1960s-1970s	Emergence of penicillin-resistant S. aureus	First documented antibiotic resistance, highlighting bacterial adaptability.	(Pal et al., 2017)
1980s-1990s	Increasing reports of multi-drug-resistant bacteria (e.g., MRSA)	Raised alarm about AMR and the need for new solutions.	(ALSAAD & ZAFER, 2023)
2000s-present	Emergence of extensively drug-resistant (XDR) and pan-drug-resistant (PDR) bacteria	Signaled a critical juncture in the AMR crisis, with virtually untreatable bacteria.	(Peraman et al., 2021)
2015	declares AMR a global health emergency	Underscored the urgency of the crisis and the need for a coordinated global response.	(Aijaz et al., 2023)

This earliest form of resistance only established that bacteria are capable of developing certain changes in reaction to certain selective factors. Subsequent years and decades have shown constant oscillation of new antibiotics with the appearance of resistant strains to these drugs. It has been witnessed since the 1980s that the rate at which new resistance species evolved was far higher than the discovery of new antibiotics, suggesting that the world was heading toward a problem (Selvarajan et al., 2022). The causes for this type of crisis are also complex and based on human actions and structural problems.

Cause of the Emergence of AMR

1. Overuse and Misuse of Antibiotics: The misuse, over-prescription, and over-consumption of antibiotics, whether to humans or animals, is one of the leading causes of AMR. It involves the administration of antibiotics to patients with viral infections, starting with broader spectrum antibiotics instead of going for the more specific ones, or stopping antibiotic therapy midway in a course, which grants rise to resistant bacteria (Justham, 2014). The fact that antibiotics are bought over the counter in some countries with no prescription from a qualified medical practitioner worsens the situation.

2. Agricultural Practices: Another factor that can be attributed to AMR is the liberal use of antibiotics in animal farming, especially in growth promoter diets for livestock. Essential antibiotics that are administered or used in feeding animals have the potential to develop resistance, which could spread to humans through the food chain or direct contact (Kumar et al., 2020). This underlines the necessity to implement the "One Health" concept that deals with the connections between human health, animal health, and the environment.

3. Lack of New Antibiotics: The discovery of new antibiotics has been reported in the past decades for several reasons. New antibiotic development is expensive, antibiotics face long development cycles, antibiotics' profitability is relatively low compared to other drugs, and finally, there are regulatory barriers (Monnier et al., 2019). This has left us with scanty solutions for infections arising from resistant bacteria without adequate treatment. Antimicrobial resistance is potentially

one of the most pressing global issues of the century, and its development is intricate and diverse. It poses serious risks to overpowering advancements made in medicine and public health in the past fifty years and has strong upsetting implications for vulnerable groups in low and middle-income countries (Chilemya, 2016). Combating this crisis involves several preventive strategies, which include the appropriate use of antibiotics, infection prevention and control measures, a search for new antibiotics, and fighting social, economic, and ecological forces that lead to AMR (Figure 2). The consequences cross everyone's threshold, yet the risks cannot wait; we need a joint response that can protect ourselves and all subsequent generations.

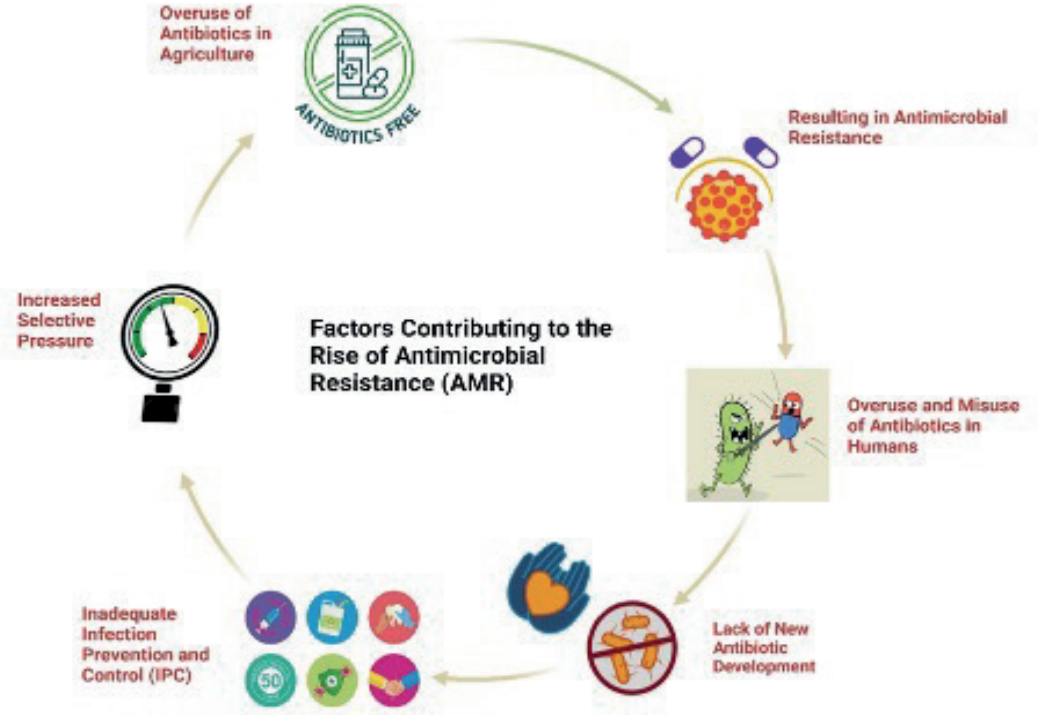


Figure 2. Factors Contributing to the Rise of Antimicrobial Resistance (AMR)

4. Impact of Superbugs on Global Health

Such trends characterize today's global healthcare environment as the growth of AMR and the emergence of superbugs. These antibiotic-resistant microbes are not only a health issue but an extended multifaceted issue that affects the global public health, economy, and healthcare system with the potentiality to act as a potential ground to roll back the several years battle against infectious diseases (Table 2).

Table 2: Impact of Superbugs on Global Health

Area Affected	Consequences	Examples	References
Public Health	Increased illness, and death, especially in vulnerable groups.	1.27 million deaths globally in 2019	(Hamrefors, 2014)
Medical Care	Disrupted surgeries, transplants, and chemotherapy.	Increased risk of infections & and delays in treatment	(Mohammed et al., 2020)
Economy	Trillions of dollars are lost globally due to healthcare costs, lost work, etc.	Up to $100 trillion loss by 2050	(Cordeiro & Wood, 2023)
Hospitals	Strained resources, longer patient stays, difficulty controlling infections.	Overcrowding, increased antibiotic use.	(Hijazi et al., 2019)

Public Health Implications: Superbugs also become a menace to the rate of Morbidity and Mortality, especially to more vulnerable groups of people, including seniors, underage children, and other candidates with compromised immunity. Those infections are often more severe, complicated, and deadly; they require longer curing and are less sensitive to standard antibiotics. Thus, superbug infection affects LMICs much more than the developed world; the reasons include poor access to healthcare, poor hygiene, and misuse of antibiotics (Greco et al., 2022). In addition, superbugs are a threat to public health since they affect people individually. These resistant infections can cause episodic outbreaks in healthcare facilities and society in general, thus posing a high risk to the health and well-being of everyone. These outbreaks can strain healthcare facilities and other services, besides leading to panicky feelings and fear within the populace (Apisarnthanarak et al., 2021).

Economic Burden: The economic ramifications of AMR and superbugs are massive and quite complex. For instance, a report on AMR sponsored by the UK government put the economic loss figure at $100 trillion if no measures are taken to address the threat in the subsequent three and half decades (Rush & Davies, 2016). This staggering figure includes direct health care costs or the costs of prolonged hospital stays, of treatments sourced with last resort antibiotics and additional diagnostic tests, for instance, indirect costs such as lost productivity due to diseases and disability, tourism decreases, and trade restrictions, among others. The economic effect is immensely severe in LMICs that suffer from inadequate resources in healthcare facilities to combat superbugs. In such environments, AMR has the potential of putting already vulnerable communities in the category of the poor, leading to a vicious cycle where disease leads to poverty, and poverty leads to diseases (Hartwig & Segura Kliesow, 2020).

Impact on Healthcare Systems: Global healthcare systems are severely challenged by superbugs. The management of resistant infections is much more invasive and expensive, including the use of last-line antibiotics, which are generally more toxic and less potent than first-line antibiotics (Surya Prakash et al., 2023). Moreover, patients sustaining infections that are resistant to the used means stay longer in the hospital, hence exerting more pressure on the limited resources and are likely to develop other infections acquired from the hospital environment. The subsequent rise in cases of superbug infections also implies the need to incorporate the use of isolation measures as part of infection prevention and control measures, alongside increased hygiene practices (Mitra et al., 2022). These measures are useful in reducing the occurrence of patients with resistant pathogens in the healthcare facility but lead to additional resource challenges and disrupt the regular functioning of the healthcare system.

Case Studies of Outbreaks and Their Consequences: Superbug infection outbreaks have been frequent, thus making AMR a Global health challenge that has had numerous ECIs. Carbapenem-resistant Klebsiella pneumoniae emerged at a New Delhi hospital, killing many patients and spreading to other countries, confirming AMR as a global problem (Das, 2023). This outbreak illustrated the issues of controlling resistant pathogens in hospitals and healthcare facilities and the ability of such a pathogen to quickly spread globally. These are commonly linked to contaminated medical instruments and substandard infection control measures that, therefore, call for intensified measures in the right prevention of infections. All these case studies and many more clearly depict the need to act on the AMR crisis. It shows the possibility of superbugs and their effect on producing diseases and fatalities, affecting the health care systems and the overall economic impacts. This global issue is multi-faceted and requires interdisciplinary research, policy, practice, and education-based solutions internationally (Riekki & Mämmelä, 2021). In conclusion, human beings can fight the menace of superbugs if only they heed the quest of medical practitioners to work hand in hand without compromising future generations' health.

5. Global Health Governance Framework

AMR and the superbugs in the offing require intensive and organized control hence the need for a global health governance system. It entails a system of important organizations, stakeholders, and international relationships created by AMR and requires solving. The following are some of the key players in this global effort:

Key Organizations and Stakeholders

1. World Health Organization (WHO): By being the World Health Organisation, WHO continues to assume a central role in the global management of AMR. They include technical support, establishing international policies, and directing surveillance alongside offering support for policies on the right use of antibiotics and the fight against AMR. The member countries of the WHO at the moment have endorsed the Global Action Plan for AMR. In response, the organization assists countries in the process of creating their national action plans concerning AMR (Hein et al., 2022).

2. Centers for Disease Control and Prevention (CDC): AMR surveillance and research is conducted by some of the best national public health institutions, including the CDC in the USA. It monitors resistance to antimicrobial products, offers assistance to practitioners, and drives measures for the proper use of antibiotics and controlling infections. CDC of the USA has the National Action Plan for Combating Antibiotic-Resistant Bacteria that contains strategies for the control and handling of AR in the United States of America (Bristol, 2020).

3. Global Antibiotic Research and Development Partnership (GARDP): Double, GARDP is an international non-profit making organization that only focuses on new antibiotics or the next best thing. It is geared towards responding to diseases of high demand that affect all populations with those with chronic illnesses and neglected populations. GARDP's work involves engaging with academic institutions, pharma players, and other partners to make new antibiotics for patients in need and foster the innovation of new ones (Segers, 2017). Combating superbugs can only be done in a coordinated manner. Together with the stakeholders and NGO partners, it is possible to design and promote meaningful approaches for countering the threats that come with AMR and maintaining the health of the population (Mudenda et al., 2023).

International Agreements and Policies: A Whole Effort to Address AMR

It is also appropriate to note that many organizations and nations have signed and developed various treaties and policies due to the AMR crisis's overarching and international nature (Figure 3). These agreements are a sort of plan that would facilitate collective movement so that there is a symphony across countries and sectors regarding preventing the emergence of superbugs. Among these strategies, two main strategies include the WHO Global Action Plan on Antimicrobial Resistance (GAP-AMR) and the One Health strategy. This plan is well known by the full name of the Global Action Plan on Antimicrobial Resistance or GAP-AMR.

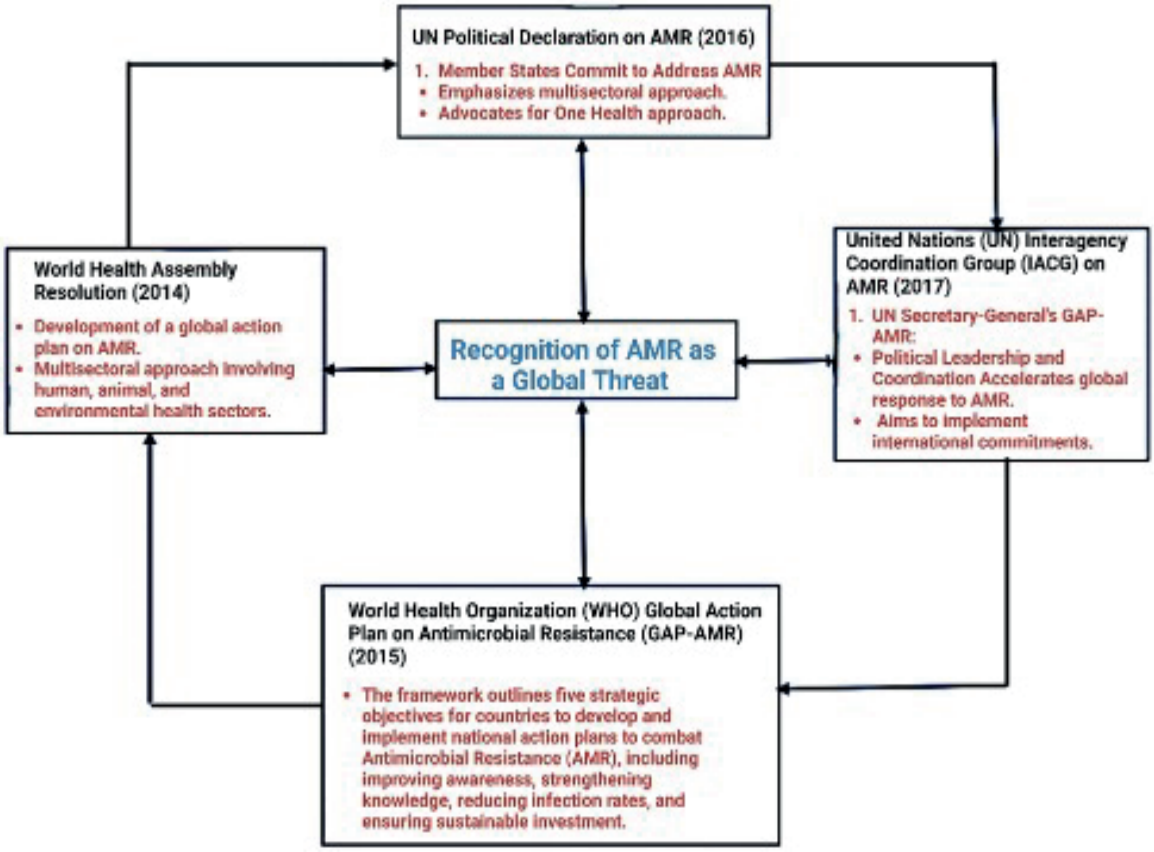


Figure 3. International Agreements and Policies for Combating Antimicrobial Resistance

1. Improve awareness and understanding of AMR: This includes investing in the general public's education, human resources in health care facilities, and the effectiveness or inefficiency of laboratories. Other institutions are involved in research on the emergence of new and spread-resistant pathogens by extending knowledge to the public on how the general population can take antibiotics through public awareness and healthcare education (Arafa, 2019).

2. Strengthen knowledge through surveillance and research: This includes funding research to understand various factors that make bacteria resistant, and improved methods for early identification of such resistant bacteria. New drugs forms of treatment for resistant bacteria, and preliminary assessment of control measures for AMR are used (Sekyere & Asante, 2018).

3. Reduce the incidence of infection: This pertains to strengthening the measures relating to Infection prevention and control in healthcare facilities wards and communities (Alhumaid et al., 2021). Hence, it underlines the need to observe hand washing, vaccinations, safe water and sanitation practices, and proper waste handling to reduce the likelihood of acquiring an infection and the ability of pathogens to develop resistance.

4. Optimize the use of antimicrobial medicines: This involves support of the APR programs that will ensure that antibiotics are not administered carelessly but where necessary. It entails developing a set of protocols for the use of antibiotics, reporting on the use of the drugs, and giving feedback to the concerned practitioners to enable them to enhance their practices (Hulscher & Prins, 2017).

5. Ensure sustainable investment in countering AMR: This entails investment in research and development of new antibiotics and other effective treatments. This enhancement of healthcare facilities to increase infection prevention and control, and increased cross-country cooperation

to address the existing social, economic, and ecological factors that favor AMR (Shrestha et al., 2022). The GAP-AMR works as a blueprint for countries to devise and execute national action plans that will help combat AMR (Moloney-Omar, 2022). It promotes cooperation at the cross-sector level, being aware of the fact that AMR is not and cannot be viewed solely in the categories of health but rather as a social, economic, and even environmental problem. The GAP-AMR has been adopted by many countries and international organizations, proving that the problem has received international-level attention.

One Health Approach

The one health concept is among the core tenets of global AMR management. That is why it appreciates the One Health concept that asserts that human, animal, and environmental health must be treated together with close cooperation among the sectors as a way of combating multifaceted issues like AMR (Humboldt-Dachroeden & Mantovani, 2021). This is why the One Health concept recognizes that the misuse of antibiotics in any of the three sectors can breed resistant bacteria and that solutions have to be as well. It focuses on the implementation of one health approach, which entails the use of multiple strategies based on the interaction of human health, veterinary medicine, agriculture, and the environment (Binot et al., 2015). This entails raising awareness on the rational administration of antibiotics in humans and animals, enhancing infection control measures in hospitals and industries rearing animals, and checking for traces of antibiotic residues in food, water, and soil, among other aspects that may lead to the spread of resistant bacteria. One Health is not just a theoretical model because it has been applied to fight AMR in distinct zones. For example, in Denmark, the One Health program, for one year, has drastically cut the rate of antibiotics employed across people's and animal health sectors without compromising animals' well-being or food security (Aarestrup, 2015). There are Global Action Plans and policies, namely GAP-AMR and One Health, that are vital in combating AMR. These are a basis for coordinated operations, give directions to national and regional actions, and advocate for combined approaches to address this issue. However, the effectiveness of these programs lies in political will, sufficient funding, and proper coordination of various structures.

6. Strategies for Combating Superbugs

The growing threat of AMR and superbugs requires society to employ reactive and preventive strategies that can shoulder the increasing responsibility of protecting and delivering healthcare. This section delves into two crucial strategies: surveillance and monitoring and antimicrobial stewardship programs. Further, the discovery of the best ways of infection control measures, researching the development of new antibiotics, and other treatment therapies and innovations in the medical field.

Surveillance and Monitoring Systems: Good surveillance and monitoring systems act as the regulators and detectors of the world in combating AMR. They give basic information regarding the distribution and trends of antibiotic resistance in various regions and pathogens, thus notifying quick identification of any novel threats and subsequent responsive measures. Such systems are usually accompanied by documenting antibiotic prescribing practices, resistance patterns of bacteria to the drugs, and the emergence of antibiotic-resistant infections in humans and animals. These data are instrumental in defining the prevalence and complexity of the AMR issue, outlining the populations and facilities at higher risk, and assessing the efficiency of mitigations (Mudenda et al., 2023).

Global Antimicrobial Resistance Surveillance System (GLASS): GLASS is a coordinated system of the WHO for the collection, analysis, comparison, and sharing of national-level AMR. They concentrate on priority pathogens causing frequent human diseases and report on the tendencies in antimicrobial resistance and antibiotic intakes (Endale et al., 2023). The information from GLASS is useful for showing the increasing threat of AMR worldwide and was used to direct the necessary actions on the national and international levels. The work published by GLASS recently exhibited

that there had been a high rise in the level of resistance of the E. coli and Klebsiella pneumoniae isolates from the bloodstream infection to third-generation cephalosporins and fluoroquinolones (Saeed et al., 2021).

National Surveillance Systems: In this regard, most countries today have developed local surveillance systems to monitor AMR nationally. Most of the above systems encompass partnerships between public health organizations, laboratories or facilities, and physicians. On one hand, they gather information on antibiotic resistance rates in bacteria obtained from clinical samples, and on the other information on antibiotic consumption in healthcare facilities and the population. In the United States, NHSN has been established for surf for HAI, including the one caused by antibiotic-resistant bacteria, for infection prevention and control (Ananda et al., 2022).

Integrated Surveillance Systems: One Health concept will also refer to the surveillance systems that mobilize information concerning antibiotic resistance across the three interfaces. It provides the chance to get the systemic picture of the redeployment of resistant bacteria and the steps that eliminate the root cause of AMR in all the sectors if done in the following way. For instance, this is seen in the case of antibiotics administered to animals for evaluation of the effect of the production of agricultural products on AMR (Törneke et al., 2015).

Antimicrobial Stewardship Programs: Thus, ASP has been defined as one of the serious strategies for dealing with the increasing trends of AMR. Stewardship interventions seek to enhance the proper prescription of antibiotic medication, decrease unnecessary prescriptions, and ensure that clients receive the correct antibiotic at the correct dose for the appropriate duration (Bankar et al., 2022). ASPs are mainly integrated into the healthcare context; however, they can also be employed in the community and veterinary medicine.

Core Elements of ASPs

1. Leadership Commitment: Judging from the analysis, there is a general agreement that LSC is critical to the effectiveness of ASPs. These comprise the formation of a multidisciplinary steering committee to manage the program, resource provision, and sustained support for ASP activities (Divecha et al.).

2. Accountability: There should be clear reporting authorities, and the accountability of that particular ASP should be clear, with the roles and responsibilities of the distinct individuals. This assists in checking whether the program is being achieved as planned and whether there is regular progress (O'Shea, 2005).

3. Drug Expertise: ASPs need access to drug knowledge to make decisions about the choice of an antibiotic, its dosage, and regimen duration. This may include pharmacists, specialists in infectious diseases, and other practitioners who have a professional interest in the practice of antimicrobial therapy (Ernst et al., 2009).

4. Actionable Recommendations: The ASPs are supposed to offer implementation advice to healthcare providers involving state-of-the-art research findings and local resistance profiles. These guidelines may encompass the type of antibiotics that should be used, the frequency of administering them, and the length of treatment (Elliott et al., 2004).

5. Education and Feedback: Training and education are also components of ASPs. Educational interventions need to be implemented focusing on healthcare practitioners regarding antimicrobial stewardship principles, current guidelines, and local resistance patterns. Prescribing reviews for staff members should be conducted frequently to reveal potential problem areas in the practice (Carter et al., 2021).

6. Tracking and Reporting: ASPs should periodically evaluate and report on the use of antibiotics and resistance data to assess the outcomes of measures and define further directions for

enhancing practice. This data can also help inform intervention and policy in the field of public health (Pezzani et al., 2020).

Infection Prevention and Control Measures

Infection prevention and control (IPC) is acknowledged as one of the key approaches to stopping the emergence of superbugs and lessening their effects. These plans are aimed at termination of further transmission of infection, decreasing HAI contraction, and protecting the exposed people (Percival et al., 2014). IPC strategies encompass a wide range of interventions, including IPC can be described with the help of several approaches and measures that can be grouped as follows:

1. Hand Hygiene: IPC begins with hand washing, which is among the most effective and costless techniques for combating contaminants. Every worker in healthcare, clients, and visitors should wash their hands with water and soap or use alcohol-based hand rub, before and after contact with a patient, object device, or equipment (Swan & McDonald, 2020). Having substantiated it the adherence to hand washing protocols can be of considerable assistance in the fight against HAIs and the promotion of non-resistance to antibiotics.

2. Personal Protective Equipment (PPE): Gloves and gowns, masks, and the protection of eyes are essential since they are barriers to pathogenic organisms to both, workers and patients. Depending on the pathogen or the probability of the pathogen circulating in the community or from the patient to the caregiver, a typical form of PPE involves (Harland, 2020). The measures involving personal protective equipment include proper wearing or putting on and removing or taking off. Governments, international organizations, and private foundations are funding activities that aim at directing resources to identify and develop new antibiotics, especially with the evolving multidrug-resistant pathogens. Such steps include offering crumbs for research grants, providing tax credits for working on antibiotic production, and increasing the ease of regulatory processes (van Hamelen).

Alternative Therapies and Innovations

Other approaches that are currently under active investigation, include the identification of new sources of antibiotics and other therapies for the superbugs. These include:

1. Phage Therapy: Almost all of the phages are bacteria that can kill bacteria that have affected a human being. The process that entails the application of phages to eliminate particular bacterial diseases is known as phage therapy. It has been used to some extent in treating infections caused by multidrug-resistant bacteria, though more research is required to standardize the approach and its outcomes (Nørgaard et al., 2019). Clinical trials have already been carried out to assess the prospect of phage therapy against different infections such as Pseudomonas aeruginosa and Staphylococcus aureus.

2. Monoclonal Antibodies: These are small manufactured proteins for inhibitory uses in bacterial cell physiology: either immobilizing the bacteria or occupying its destruction by the immune system. These therapies are under consideration for use in infections by drug-resistant bacteria (MacNair et al., 2024). For instance, a monoclonal antibody against the PcrV protein of Pseudomonas aeruginosa is another promising candidate observed only in preclinical essays and now in clinical practice.

3. Vaccines: Vaccination is a strategy that assists in controlling the spread of communicable diseases. The discovery of immunizations against bacterial agents could help decrease the reliance on antibiotic-dependent diseases. Several vaccines developed against bacterial pathogens are in the pipeline, including vaccines against S. aureus and Klebsiella pneumonia (Mba et al., 2023). Thus, the development of vaccines for bacterial pathogens is difficult; however, if achieved, that would decrease antibiotic consumption and slow down the development of resistance.

7. Challenges in Global Health Governance

The strategy for world and ex-communication of antimicrobial resistance and superbugs has complex and intertwining threats and obstacles, which make governance difficult and slow progress toward long-lasting cures. All these challenges are systematic and complex; hence, their solutions demand multi-sectoral and multi-disciplinary efforts.

Coordinating International Efforts: The Fragmented Landscape describes the attempts at creating such a space by progressive, ambitious, and creative individuals from around the Western world. Therefore, the threat of AMR is global, which means that solutions must be sought at the international level. It is a very complex system where the interaction between many players, namely governments, international organizations such as WHO, FAO, OIE, NGOs, projects, and a profit-driven sector, are involved with different interests and goals (Kiriti Nganga & Mugo, 2018). It results in overlapping of activities, the objectives and goals of the different agencies may collide, and there are no concerted efforts, as observed in the handling of COVID-19 by different countries and international organizations (Lee, 2021). Also, specific legislation, priorities, and available assets can differ from one country to another, thus raising obstacles to cooperation. For instance, differences in the rules regarding the use of antibiotics, infection monitoring and reporting systems, and infection control measures complicate the ability to draw comparisons and share data on the global AMR problem and progress in addressing it (Kirchhelle et al., 2020).

Funding and Resource Allocation: Growing the combating of AMR thus needs capital-intensive investment in research and development of new antibiotics and other treatments, the implementation of surveillance and monitoring networks, the strengthening of IPC programs, and public health education. However, there is a huge disappointment concerning the available and necessary resources (Gill & Prowse, 2012). The funding shortage is even more challenging given that the development of antibiotics is not as profitable as other forms of pharmaceutical research, cutting off private funding. Low- and middle-income countries (LMICs) are in greatest need of resources to address AMR since the latter is most prevalent in these regions, however, the resource availability is significantly limited (Sartelli et al., 2020). Such a situation forms a negative feedback system because confusion in LMICs to combat AMR due to resource constraints merely fuels the propagation of resistant pathogens and more global strain. The World Bank, in their study, pointed out that the impact of the AMR could be a cut of up to 5% of the GDP in LMICs by the year 2050 (Dolamulla, 2021). Due to the insufficiency of resources to invest in health care in LMIC, they cannot support surveillance systems, infection control measures, and public health education hence, they are cages more by AMR.

Political and Economic Barriers: Several challenges affect the process of global health governance due to political and economic factors. Governments may not act in the best interest of people's health, preferencing immediate economic benefits, so policies could encourage the misuse of antibiotics in meat production or hamper the creation of new antibiotics. For example, feeding livestock with antibiotics as growth enhancers is still rampant in some countries although it is agreed to be compounding the issue of AMR (Ahmed et al., 2024). This is due to economic factors that compel farmers to produce food with high yields for the market, and the ramifications that befall consumers' health in the long run are infinitesimal. In addition, profits instead of saving people's lives can become the focus of large pharmaceutical corporations, which may affect agendas and strategies, including delays in bringing new antibiotics to the market due to the desire to gain more profits. This is apparent in the few acutely needed new antibiotics due to the rising risk of AMR (Chandra et al., 2021). New antibiotics are not being created effectively due to the current economic structure because it is unprofitable to develop a drug.

Cultural and Behavioral Factors: The New Perspectives

This chapter also shows that principles and behavior are major factors of AMR. Many of

the principles used antibiotics for illnesses as simple as headaches, or colds, which has introduced the wrong prescription and wrong use of the antibiotics. This, in combination with the growing practice of antibiotics without a prescription, further worsens the situation (Dyar et al., 2016). Across most nations, the consumption of antibiotics without proper prescription from professional health care practitioners has become the new tradition in others due to reasons such as; inaccessible health care, poverty, and lack of understanding of the right use of antibiotics. In other situations, the patients may not even finish their antibiotics as prescribed; this may be attributed to ignorance or inability to afford the drugs, thus adding to the development of resistance (Sachdev et al., 2022). This is especially detrimental in LMICs, in which the patients may not be able to seek the services of a healthcare professional to follow up on the patient's treatment progress or may be financially unable to complete the course of antibiotics. To alter such a strong-rooted culture, it is essential to launch long-term and specific health promotional activities that help inform the public about the threats of AMR and the irrational use of antibiotics. It also requires solving fundamental social issues such as poverty, lack of health care access, and sanitation, which in turn are the precursors of the resistant pathogen agents. Research evidence indicates that efforts directed towards changing the doctor's and public knowledge can lead to a considerable decrease in the use of antibiotics (Awad & Aboud, 2015). But, as you're probably aware, converting culture and modifying behavioral patterns isn't a quick and easy task and would still need the exertion of lots of time, money, and resources. Altogether, it is clear that the obstacles to global health governance are huge but by no means insurmountable. Thus, by recognizing these threats and efforts to overcome them, combining financial resources, improving coordination, and overcoming political and sociocultural factors, the fight against AMR and the health of future generations might be strengthened.

8. Opportunities for strengthening the structure of global health governance

Thus, despite the comprehensible obstacles in the global health governance settings that have emerged in response to AMR, the issues are far from irreversible. There are quite a few scenarios that depict how these frameworks can be enforced and improved to pave the way for enhanced global cooperation that would help to avert the emergence of superbugs altogether.

Enhancing Surveillance and Reporting Systems: Among these interfaces, the one considered the most significant point of intervention in efforts to improve the framework of global health governance is the systems of surveillance and reporting. The surveillance systems must be strong and all-encompassing to detect antibiotic-resistant bacteria, trends of antibiotic usage, and the efficacy of the implemented strategies (Rajput, 2023). The effectiveness of extensions in the coverage and the range of such programs, such as Global Surveillance of Antimicrobial Resistance (GLASS), would inspire accurate measurement of the actual burden. Science and specimen increase of whole-genome sequencing and other molecular tools can improve the timeliness and precision in categorizing pathogens and their resistance profiles (Trotter et al., 2019). In addition, possible threats and the international dissemination of pathogens with increased resistance must be elucidated based on global cooperation in the sharing and analysis of data. Successful multifaceted systems for collecting and improving international cooperation include the Global Antimicrobial Resistance Surveillance System (GLASS), founded by the WHO, and the European Antimicrobial Resistance Surveillance Network (EARS-Net) (Malania et al., 2021).

Promoting Global Cooperation and Collaboration: It upholds that the AMR crisis involves more than a nation's issue and, therefore, requires multilateral effort to tackle the issues involved. International organizations, such as WHO, FAO, and OIE, are critical in directing global relations and standards setting, besides offering advisory on issues affecting countries (Kouba). However, for them to be effective, members of the international community must be willing participants in the facing initiatives. Strengthening global cooperation involves several key strategies:

1. Political Commitment: This requires political commitment from senior political leaders in governments to enable them to mobilize resources and policies and implement effective interventions.

This includes pushing for global frameworks such as the Global Action Plan on AMR and for AMR to be incorporated in-country health and development blueprints (Bhatia, 2021).

2. Capacity Building: OTA capacities in LMICs must be enhanced, especially in surveillance, infection prevention, and antimicrobial stewardship. Hence, an approach to this is through sensitization, administrative support, and financing from the World Bank, the United Nations, and other developed countries (Fox & Brown, 1998).

3. Public-Private Partnerships: It risks polarizing multi-sectoral implementation of strategies on how the public-private partnership through the former party shall address AMR. It can be done by the pharmaceutical companies sharing their work and knowledge in the development of new antibiotics, while on the other hand, governments and international organizations can promote the funding and support the regulation of new antibiotics (Årdal et al., 2016).

4. Civil Society Engagement: Partnering with civil society organizations, such as patient associations, professional associations, and CBOs, is essential for the intended program since it fosters awareness of AMR and develops policies for the right use of antibiotics (September). Through enhancing international collaboration and partnership, there is a need to share knowledge, information, and expertise in combating AMR since it threatens mankind. Thus, the necessary approach is multifaceted and integrated, where a thousand points of light amplify each other's efforts to counter the burden of AMR for the benefit of all.

Genomic Surveillance: Next-generation sequencing of bacterial genomes is transforming AMR surveillance globally, with WGS being the most utilized method. WGS facilitates quick identification of pathogens and their resistance genes that can help in tracking the flow and spread of outbreaks, new developing resistance mechanisms, and, in turn, making recommendations as far as public health is concerned (Organization, 2018). Over the world, programs such as the Global Microbial Identifier (GMI) are using WGS to generate the Global Microbial Genome Catalogue, which enables exposure of information and coordination on new diseases among researchers and health experts (Trees et al., 2015).

Rapid Diagnostics: Rapid diagnostic tests (RDTs) that distinguish the causative organism and its level of sensitivity to antibiotics are needed to avoid irrational antibiotic utilization. Innovations in molecular diagnostics include PCR and various isothermal amplification formats, which have paved the way to highly sensitive and specific RDTs for various pathogens, including MDR organisms (Kaprou et al., 2021).

Artificial Intelligence (AI): Information gathered on AMR surveillance can be used by AI and machine learning to handle big data through pattern recognition and the ability to foresee the creation of new resistance mechanisms (Ali et al., 2023). AI can also be used to promote healthcare providers' decision-making to identify needs and choose the best antibiotics that can be administered in the right combination.

Vaccine Development: Modern vaccines, like mRNA vaccines and recombinant protein vaccines, present different prospects for controlling contagious diseases that antibiotic-resistant bacteria may cause. Although it is difficult to develop a vaccine against bacterial pathogens, successful vaccines could dramatically decrease antibiotic use and thus curb resistance (Khalid & Poh, 2023).

Community Engagement and Public Education: 'Empowering' people and 'communities'

Awareness about AMR, a positive attitude toward responsible antibiotic use, and a desire to change one's behavior requires communication strategies and community engagement. Public health-promoting messages enhance individual knowledge on matters related to health, remind people to consult a medical practitioner in cases of an ailment and reduce the rate of antibiotic overuse (Anjuli, 2019). Many methods of communication can be used for targeted stakeholders; these are mass

media, social media, learning institutions, and NGOs. It is essential to provide messages that are adapted to cultural and social settings (Waters & Lo, 2012). Community engagement methodologies are stakeholders' collaboration with LMIC leaders, health professionals, and CBOs for information sharing concerning AMR. Participatory workshops and or peer education, for instance, are efficient in behavior change and capacity development of communities to handle AMR proactively (Lambraki et al., 2021). Applying technologically advanced solutions and working with communities, it is possible to advance the concept of global health governance and create better conditions for global health preparedness to fight the dangers of the AMR threat. These interventions, along with timely identification through necessary surveillance systems, proper antimicrobial stewardship program, and strong infection prevention and control measures give a holistic approach to combat superbugs, to protect the current and future generations' health.

9. Effective Governing: Case Studies

However, the global fight against AMR is not entirely devoid of success. The following national and regional programs have also shown effective ways towards good governance and have been inspirational in inspiring newer ideas to counter this problem. The causes of rum have also demonstrated that national and regional programs can underpin efficient governance.

Denmark: AMR has been alarming globally in the last decades, and Denmark has been at the forefront of fighting this menace (Majumder et al., 2020). One Health approach of working at the human-animal interface, high standards of animal welfare and food safety have been achieved in the country without compromising the diminished rate of antibiotic usage in both the human and animal health sectors. This has been done via appropriate legislation and measures on the management of antibiotics, surveillance, monitoring, and education targeting diverse groups and members of the population (Wall, 2019).

Netherlands: The Netherlands has also achieved major shifts in decreasing the use of antibiotics, which involve antimicrobial stewardship in hospitals and primary care, limitations on giving antibiotics to agriculture, and public campaigns (Allerberger et al., 2009). As a consequence of these measures, the consumption of antibiotics and the growth of resistance have been reduced not only for people but also for animals.

Kerala, India: AMR surveillance and control interventions in Kerala state of India is one of the best practice models of CBIs as seen in previous literature. As part of the program, CLWAs have to first engage the community in raising awareness of AMR, the appropriate use of antibiotics for treating infections, and prescribing and reporting of AMR-related infections (Diskin, 2021). It has built onto the awareness created about AMR apart from advocating for community participation in the prevention and control of AMR.

Innovations in Policy and Practice: Feasible New Directions for Change

Innovations of policies and practices that are recognized today to curb AMR have started to trickle in in the recent past. These include:

1. Antibiotic Incentives: Governments and international organizations are assessing an innovative financing option correctly termed pull incentives for developing new antibiotics. These incentives involve providing financial incentives in terms of the revenues controlled by pharmaceutical corporations to value the creation and commercialization of new antibiotics (Dutescu & Hillier, 2021).

2. Diagnostics and Decision Support: New diagnostic tools, point-of-care tests, and Whole-Genome Sequencing are under development to facilitate quicker and correct identification of pathogens that are resistant to a particular antibiotic and, thus, the right decisions regarding treating the disease. Machine learning strategies are also proposed to recommend the best antibiotic

regimens for therapy (Wang et al., 2024).

3. Alternative Therapies: Studies are being conducted for the development of non-antibiotics as these are defined as phage therapy, monoclonal antibodies, and vaccines (Ozma et al., 2023). These therapies encompass potential solutions for infections caused by multidrug-resistant bacteria and may well be an important element in lowering the dependence on antibiotics.

10. Future Directions and Recommendations: Toward a World After Antibiotics

As AMR emerges as the world's greatest problem, it is crucial to envision a future free from superbugs and start preparing right now. These include risk identification and assessment and the formation of sustainable and fairly strong health systems, the delivery of a package of measures and interventions.

Emerging Trends and Future Threats

Some of the emerging trends include more frequent identification of resistance mechanisms and pathogens periodically. The future threats include AMR is an evolving discipline as the world changes continuously in different ways. Some of the emerging trends and future threats include: The future threats and emerging trends includes the following;

1. The Rise of Pan-Resistant Bacteria: This development entails the production of bacteria that are resistant to all existing types of antibiotics. These pathogens are a nuisance to human health since they cause untreatable infections characterized by high mortality rates (Khabbaz et al., 2015).

2. The Spread of AMR in LMICs: Currently, the impact of AMR is most acutely felt in developing nations, or LMICs, mainly because of the inclination toward substandard healthcare infrastructures, poor sanitation, and the utilization of antibiotics for some treatment sessions. AMR is a critical threat to the health of people living in LMICs, and if left unchecked, it will eventually spread to affect the world's population (Otaigbe & Elikwu, 2023).

3. The Impact of Climate Change on AMR: Climate change could aggravate the AMR scenario because it alters the distribution and methods of transmission of pathogens, increases the vulnerability to infections, and provides appropriate environmental factors in the development of antibiotic-resistant bacteria (Allel, 2021).

Importance of Sustainable and Resilient Health Systems

Access to strong and efficient health systems is, therefore, a critical aspect when planning to confront the AMR problem. This encompasses improving health facilities, providing measures to prevent and control infections, increasing the capacity to monitor and report infectious diseases and diseases of public health importance, and providing health to all. Thus, it has been stated that well-functioning health systems can identify and manage episodes of ARIs, treat patients properly, and conduct preventive efforts to control the development of AMR (Costa et al., 2021).

Implementation Strategies for Policies by Global Health Leaders

To address the complex challenges posed by AMR, global health leaders must prioritize the following policy recommendations: So, to overcome the numerous challenges presented by AMR, the international health officers have the following policies to adopt:

1. Invest in Research and Development: There is also the need to foster research where they shall develop new antibiotics, other therapies, and better diagnostics tests. This involves backing both the need to extend edging knowledge on the tactics of resistance as well as efforts to improve its practical application (Hale, 2008).

2. Strengthen Surveillance and Monitoring Systems: Improving detections and assessments at local, regional, and global levels is critical for mapping more resistant pathogens, recognizing vulnerable groups and spaces, and appraising prevention measures (Palaniyandi et al., 2017).

3. Promote Antimicrobial Stewardship: Commissioning and enhancing the ASP in all healthcare facilities is important for the effective use of antibiotics and the avoidance of unnecessary prescriptions, with exemplary measures to counter resistance (Emberger et al., 2018).

4. Improve Infection Prevention and Control: To combat the issue, policies to improve IPC and practices to eliminate the spread of resistant pathogens within HCWs, facilities, and communities should be implemented. These measures cover awareness creation of practices such as hand washing, vaccination, safe water and sanitation handling, and proper waste disposal (Nahimana et al., 2017).

5. Foster Global Collaboration: AMR affects all countries worldwide, so strategies must be used to reach people worldwide. Enhancing regional interoperation and cooperation is valuable for information exchange, resources, policies, and programs, as well as for learning from other countries experiences and how they tackled the problem (Boekholt & Thuriaux, 1999). With these policy recommendations in place, global health leaders can map out a course toward a future where AMR poses no more risks to the two kinds of security. Nevertheless, despite being quite a difficult task, it is crucial for the benefit of current and future generations.

11. Conclusion

Training germs that are resistant to medicines, the concept of AMR, and the existence of superbugs are undoubtedly a headache of the future for the whole world of every health sector. Very often, dynamic and coordinated changes in biological, social, economic, and political aspects create a multilayered context of human rights issues that cannot afford to wait long-term, not to mention individual action. The consequences of doing nothing are severe, possibly eradicating up to a hundred years of achievements in the medical field and widening the inequality gap in the healthcare system. In this extremely comprehensive collection of microbial threats, which are now greatly worsened by the new generation of superbugs, the solutions to the AMR issue have been described in this work. We have mentioned how exactly these sticky bacteria and other microorganisms are in a position to counteract or, at the very least, withstand the effects of antibiotics, what may be the reason for the incapability of those small enemies to be influenced, and how devastating superbugs can be to everyone around the world's health care system, economy, and people. The institutions, the agreements, the policies of the G7, and the other additional layers of the international regulation of health governance offer order to action. However, it is being practiced with some difficulties, such as Inadequate and fragmented coordination, poor funding for programs and services, conflicting interests, and cultural differences, among others. However, at the same time, the potential for future developments and strengthening of the governance of global health is still very vast. Thus, surveillance and reporting events should be enhanced, countries' cooperation should be better performed, technology growth should be introduced, and community engagement should be advanced to strengthen the world for the future. Therefore, Danish, Dutch, and the experience of the Indian state of Kerala illustrate what is possible at the national and regional levels, based on which further steps should be taken. It proves that by employing a series of practices in various sectors, such as proper antibiotic usage, infection prevention and control, and raising and creating awareness, one could fight AMR. Hence, the positive or negative outcome of all such attempts to predict and influence the global health of future hits and misses depends on the appropriate resolution of the AMR issue. The current situation of AMR involves the effects of climate change and the development of pan-resistant bacteria, to mention but a few. Thus, it is high time for the top priority to concerted and take rapid action to strengthen and expand health-system research and development financing. Lastly, it can be affirmed that the fight against superbugs is all about time. This war engulfs them on international, multidisciplinary, and multisectoral levels.

The stakes are high, but the potential rewards are even greater: future, where people are no longer dying from communicable diseases or where modern medicine is still a perfect way of eradicating diseases, diseases, and illnesses, are effectively tackled without any impact on people's earnings and where every individual in the world can get good and effective health care services. This is a future that the world's population will cheer for if it is being sought and carried out at the present.

References

Aarestrup, F. M. (2015). The livestock reservoir for antimicrobial resistance: a personal view on changing patterns of risks, effects of interventions and the way forward. Philosophical Transactions of the Royal Society B: Biological Sciences, 370(1670), 20140085.

Ahmed, S. K., Hussein, S., Qurbani, K., Ibrahim, R. H., Fareeq, A., Mahmood, K. A., & Mohamed, M. G. (2024). Antimicrobial resistance: impacts, challenges, and future prospects. Journal of Medicine, Surgery, and Public Health, 2, 100081.

Aijaz, M., Ahmad, M., Ansari, M. A., & Ahmad, S. (2023). Antimicrobial Resistance in a Globalized World: Current Challenges and Future Perspectives. International Journal of Pharmaceutical Drug Design, 1(1), 7-22.

Alhumaid, S., Al Mutair, A., Al Alawi, Z., Alsuliman, M., Ahmed, G. Y., Rabaan, A. A., Al-Tawfiq, J. A., & Al-Omari, A. (2021). Knowledge of infection prevention and control among healthcare workers and factors influencing compliance: a systematic review. Antimicrobial Resistance & Infection Control, 10(1), 86.

Ali, T., Ahmed, S., & Aslam, M. (2023). Artificial intelligence for antimicrobial resistance prediction: challenges and opportunities towards practical implementation. Antibiotics, 12(3), 523.

Allel, K. (2021). Exploring the Relationship between Climate Change and Antimicrobial-resistant Bacteria: To What Extent Does This Present a Current and Long-term Threat to Population Health? International Journal of Climate Change: Impacts & Responses, 13(1).

Allerberger, F., Gareis, R., Jindrák, V., & Struelens, M. J. (2009). Antibiotic stewardship implementation in the EU: the way forward. Expert Review of Anti-infective Therapy, 7(10), 1175-1183.

ALSAAD, M. M., & ZAFER, M. (2023). Antibiotic Resistance in Microorganisms–Current Status. Quorum Quenching: A Chemical Biological Approach for Microbial Biofilm Mitigation and Drug Development(22), 175.

Ananda, T., Modi, A., Chakraborty, I., Managuli, V., Mukhopadhyay, C., & Mazumder, N. (2022). Nosocomial infections and role of nanotechnology. Bioengineering, 9(2), 51.

Anjuli, B. (2019). Communicating Antibiotic Resistance to the Public: How effective was Public Health England's 2018 'Keep Antibiotics Working' campaign TV advertisement at increasing public understanding of antibiotic resistance and motivating a change in antibiotic seeking behaviours? In: Malmö universitet/Kultur och samhälle.

Apisarnthanarak, A., Siripraparat, C., Apisarnthanarak, P., Ullman, M., Saengaram, P., Leeprechanon, N., & Weber, D. J. (2021). Patients' anxiety, fear, and panic related to coronavirus disease 2019 (COVID-19) and confidence in hospital infection control policy in outpatient departments: A survey from four Thai hospitals. infection control & hospital epidemiology, 42(10), 1288-1290.

Arafa, M. (2019). Factors influencing emergence and spread of antibiotic resistance in Egypt using a one health approach.

Årdal, C., Outterson, K., Hoffman, S. J., Ghafur, A., Sharland, M., Ranganathan, N., Smith, R., Zorzet, A., Cohn, J., & Pittet, D. (2016). International cooperation to improve access to and sustain effectiveness of antimicrobials. The lancet, 387(10015), 296-307.

Awad, A. I., & Aboud, E. A. (2015). Knowledge, attitude and practice towards antibiotic use among the public in Kuwait. PloS one, 10(2), e0117910.

Bankar, N. J., Ugemuge, S., Ambad, R. S., Hawale, D. V., & Timilsina, D. R. (2022). Implementation of antimicrobial stewardship in the healthcare setting. Cureus, 14(7).

Basset, P., Feil, E. J., Zanetti, G., & Blanc, D. S. (2011). The evolution and dynamics of methicillin-resistant Staphylococcus aureus. In Genetics and Evolution of Infectious Disease (pp. 669-688). Elsevier.

Bhatia, R. (2021). National Framework for One Health. Food & Agriculture Org.

Binot, A., Duboz, R., Promburom, P., Phimpraphai, W., Cappelle, J., Lajaunie, C., Goutard, F. L., Pinyopummintr, T., Figuié, M., & Roger, F. L. (2015). A framework to promote collective action within the One Health community of practice: using participatory modelling to enable interdisciplinary, cross-sectoral and multi-level integration. One Health, 1, 44-48.

Boekholt, P., & Thuriaux, B. (1999). Public policies to facilitate clusters: background, rationale and policy practices in international perspective. Boosting innovation: the cluster approach, 381-412.

Bristol, N. (2020). The US Government and Antimicrobial Resistance. JSTOR.

Carter, M., Chapman, S., & Watson, M. C. (2021). Multiplicity and complexity: a qualitative exploration of influences on prescribing in UK general practice. BMJ open, 11(1), e041460.

Chandra, P., Mk, U., Ke, V., Mukhopadhyay, C., U, D. A., & V, R. (2021). Antimicrobial resistance and the post antibiotic era: better late than never effort. Expert opinion on drug safety, 20(11), 1375-1390.

Chilemya, M. S. (2016). Mental health services in Zambia; past, present and future.

Christaki, E., Marcou, M., & Tofarides, A. (2020). Antimicrobial resistance in bacteria: mechanisms, evolution, and persistence. Journal of molecular evolution, 88(1), 26-40.

Cordeiro, J., & Wood, D. (2023). How Much Does It Cost? In The Death of Death: The Scientific Possibility of Physical Immortality and its Moral Defense (pp. 97-127). Springer.

Costa, A. L., Privitera, G. P., Tulli, G., & Toccafondi, G. (2021). Infection prevention and control. Textbook of patient safety and clinical risk management, 99-116.

Das, S. (2023). The crisis of carbapenemase-mediated carbapenem resistance across the human–animal–environmental interface in India. Infectious Diseases Now, 53(1), 104628.

Dasgupta, S. P. (2021). The economics of biodiversity the Dasgupta review abridged version.

Davies, J. (2013). Cracked: Why psychiatry is doing more harm than good. Icon Books Ltd.

Diskin, M. G. (2021). ONE HEALTH: Awareness to Action Antimicrobial and Anthelmintic Resistance Conference.

Divecha, C., Tullu, M., & Karande, S. Challenges in implementing an Antimicrobial Stewardship Program (ASP) in developing countries. In (pp. 10.4103): Medknow.

Dolamulla, S. S. (2021). Reconsidering middle-Income country approaches to a global antimicrobial resistance (AMR) problem: A case study of Sri Lanka University of York].

Domínguez, D. C., & Meza-Rodriguez, S. M. (2019). Development of antimicrobial resistance: Future challenges. In Pharmaceuticals and Personal Care Products: Waste Management and Treatment Technology (pp. 383-408). Elsevier.

Doron, A., & Broom, A. (2019). The spectre of superbugs: waste, structural violence and antimicrobial resistance in India. Worldwide Waste, 2(1), 7-7.

Dutescu, I. A., & Hillier, S. A. (2021). Encouraging the development of new antibiotics: are financial incentives the right way forward? A systematic review and case study. Infection and Drug Resistance, 415-434.

Dyar, O. J., Obua, C., Chandy, S., Xiao, Y., Stålsby Lundborg, C., & Pulcini, C. (2016). Using antibiotics responsibly: are we there yet? Future microbiology, 11(8), 1057-1071.

Elliott, T., Foweraker, J., Gould, F., Perry, J., & Sandoe, J. (2004). Guidelines for the antibiotic treatment of endocarditis in adults: report of the Working Party of the British Society for Antimicrobial Chemotherapy. Journal of Antimicrobial Chemotherapy, 54(6), 971-981.

Emberger, J., Tassone, D., Stevens, M. P., & Markley, J. D. (2018). The current state of antimicrobial stewardship: challenges, successes, and future directions. Current infectious disease reports, 20, 1-12.

Endale, H., Mathewos, M., & Abdeta, D. (2023). Potential causes of spread of antimicrobial resistance and preventive measures in one health perspective-a review. Infection and Drug Resistance, 7515-7545.

Ernst, E. J., Klepser, M. E., Bosso, J. A., Rybak, M. J., Hermsen, E. D., Segarra-Newnham, M., & Drew, R. H. (2009). Recommendations for Training and Certification for Pharmacists Practicing, Mentoring, and Educating in Infectious Diseases Pharmacotherapy: Joint Opinion of the Society of Infectious Diseases Pharmacists and the Infectious Diseases Practice and Research Network of the American College of Clinical Pharmacy. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 29(4), 482-488.

Fairley, C. CAE. ethics, 6, 1Z2.

Farhat, N., Ali, A., Bonomo, R. A., & Khan, A. U. (2020). Efflux pumps as interventions to control infection caused by drug-resistance bacteria. Drug Discovery Today, 25(12), 2307-2316.

Fatima, H., Goel, N., Sinha, R., & Khare, S. K. (2021). Recent strategies for inhibiting multidrug-resistant and β-lactamase producing bacteria: A review. Colloids and Surfaces B: Biointerfaces, 205, 111901.

Fontanot, A., Ellinger, I., Unger, W. W., & Hays, J. P. (2024). A Comprehensive Review of Recent Research into the Effects of Antimicrobial Peptides on Biofilms—January 2020 to September 2023. Antibiotics, 13(4), 343.

Fox, J. A., & Brown, L. D. (1998). The struggle for accountability: The World Bank, NGOs, and grassroots movements. MIT press.

Gill, D., & Prowse, V. (2012). A structural analysis of disappointment aversion in a real effort competition. American Economic Review, 102(1), 469-503.

Greco, S., Putans, R., & Springe, L. (2022). Antimicrobial and antibiotic resistance in developing countries: Health economics, global governance, and sustainable development goals. In Antimicrobial Resistance (pp. 113-140). CRC Press.

Haider, R. (2023). Penicillin and the Antibiotics Revolution Global History. Asian Journal of Pharmaceutical Research, 13(1), 55-62.

Hale, C. R. (2008). Engaging contradictions: Theory, politics, and methods of activist scholarship. Univ of California Press.

Hamrefors, V. (2014). Cardiovascular Risk Genes in Prevention and Treatment Response.

Harland, D. (2020). INFECTION CONTROL: UNDERSTANDING DISEASES, EPIDEMIOLOGY, AND PATHOGEN TRANSMISSION.

Hartwig, R., & Segura Kliesow, P. (2020). Antimicrobial Resistance between Lack of Access and Excess.

Hein, W., Aglanu, L. M., Mensah-Sekyere, M., Harant, A., Brinkel, J., Lamshöft, M., Lorenz, E., Eibach, D., & Amuasi, J. (2022). Fighting antimicrobial resistance: development and implementation of the Ghanaian national action plan (2017–2021). Antibiotics, 11(5), 613.

Hijazi, K., Joshi, C., & Gould, I. M. (2019). Challenges and opportunities for antimicrobial stewardship in resource-rich and resource-limited countries. Expert Review of Anti-infective Therapy, 17(8), 621-634.

Hulscher, M., & Prins, J. (2017). Antibiotic stewardship: does it work in hospital practice? A review of the evidence base. Clinical microbiology and infection, 23(11), 799-805.

Humboldt-Dachroeden, S., & Mantovani, A. (2021). Assessing environmental factors within the one health approach. Medicina, 57(3), 240.

Iman Islamieh, D., Afshar, D., Yousefi, M., & Esmaeili, D. (2018). Efflux pump inhibitors derived from natural sources as novel antibacterial agents against Pseudomonas aeruginosa: a review. International Journal of Medical Reviews, 5(3), 94-105.

Justham, D. (2014). A study of nursing practices used in the management of infection in hospitals, 1929-1948. The University of Manchester (United Kingdom).

Kaprou, G. D., Bergšpica, I., Alexa, E. A., Alvarez-Ordóñez, A., & Prieto, M. (2021). Rapid methods for antimicrobial resistance diagnostics. Antibiotics, 10(2), 209.

Khabbaz, R., Bell, B. P., Schuchat, A., Ostroff, S. M., Moseley, R., Levitt, A., & Hughes, J. M. (2015). Emerging and reemerging infectious disease threats. Mandell, Douglas, and Bennett's principles and practice of infectious diseases, 158.

Khalid, K., & Poh, C. L. (2023). The promising potential of reverse vaccinology-based next-generation vaccine development over conventional vaccines against antibiotic-resistant bacteria. Vaccines, 11(7), 1264.

Kirchhelle, C., Atkinson, P., Broom, A., Chuengsatiansup, K., Ferreira, J. P., Fortané, N., Frost, I., Gradmann, C., Hinchliffe, S., & Hoffman, S. J. (2020). Setting the standard: multidisciplinary hallmarks for structural, equitable and tracked antibiotic policy. BMJ Global Health, 5(9), e003091.

Kiriti Nganga, T., & Mugo, M. G. (2018). Impact of economic regimes on food systems in Kenya.

Kırmusaoğlu, S. (2017). MRSA and MSSA: The mechanism of methicillin resistance and the influence of methicillin resistance on biofilm phenotype of Staphylococcus aureus. The Rise of Virulence and Antibiotic Resistance in Staphylococcus aureus; Enany, S., Ed, 25-41.

Kouba, V. Critical analysis of the OIE Code for international trade facilitating irreparable globalization of animal infections.

Kpokiri, E. E. (2019). Optimizing antibiotic prescribing in Nigerian hospitals UCL (University College London)].

Kumar, S. B., Arnipalli, S. R., & Ziouzenkova, O. (2020). Antibiotics in food chain: The consequences for antibiotic resistance. Antibiotics, 9(10), 688.

Lalchhandama, K. (2021). History of penicillin. WikiJournal of Medicine, 8(1), 1-16.

Lambraki, I. A., Majowicz, S. E., Parmley, E. J., Wernli, D., Léger, A., Graells, T., Cousins, M., Harbarth, S., Carson, C., & Henriksson, P. (2021). Building social-ecological system resilience to tackle antimicrobial resistance across the one health spectrum: protocol for a mixed methods study. JMIR Research Protocols, 10(6), e24378.

Lee, J. (2021). Fragmented before a Global Menace: WHO, COVID-19 and the Fragmentation of International Law. Hong Kong LJ, 51, 169.

Lobanovska, M., & Pilla, G. (2017). Focus: drug development: Penicillin's discovery and antibiotic resistance: lessons for the future? The Yale journal of biology and medicine, 90(1), 135.

MacNair, C. R., Rutherford, S. T., & Tan, M.-W. (2024). Alternative therapeutic strategies to treat antibiotic-resistant pathogens. Nature Reviews Microbiology, 22(5), 262-275.

Majumder, M. A. A., Rahman, S., Cohall, D., Bharatha, A., Singh, K., Haque, M., & Gittens-St Hilaire, M. (2020). Antimicrobial stewardship: fighting antimicrobial resistance and protecting global public health. Infection and Drug Resistance, 4713-4738.

Malania, L., Wagenaar, I., Karatuna, O., Andrasevic, A. T., Tsereteli, D., Baidauri, M., Imnadze, P., Nahrgang, S., & Ruesen, C. (2021). Setting up laboratory-based antimicrobial resistance surveillance in low-and middle-income countries: lessons learned from Georgia. Clinical microbiology and infection, 27(10), 1409-1413.

Mba, I. E., Sharndama, H. C., Anyaegbunam, Z. K. G., Anekpo, C. C., Amadi, B. C., Morumda, D., Doowuese, Y., Ihezuo, U. J., Chukwukelu, J. U., & Okeke, O. P. (2023). Vaccine development for bacterial pathogens: Advances, challenges and prospects. Tropical Medicine & International Health, 28(4), 275-299.

Michaud, A., Stawicki, S. P., Izurieta, R., & Iyer-Raniga, U. (2024). Global Health Security: Contemporary Considerations and Developments. BoD–Books on Demand.

Mitra, S., Sultana, S. A., Prova, S. R., Uddin, T. M., Islam, F., Das, R., Nainu, F., Sartini, S., Chidambaram, K., & Alhumaydhi, F. A. (2022). Investigating forthcoming strategies to tackle deadly superbugs: current status and future vision. Expert Review of Anti-infective Therapy, 20(10), 1309-1332.

Mohammed, A. H., Blebil, A., Dujaili, J., & Rasool-Hassan, B. A. (2020). The risk and impact of COVID-19 pandemic on immunosuppressed patients: cancer, HIV, and solid organ transplant recipients. AIDS reviews, 22(3), 151-157.

Moloney-Omar, K. (2022). Analysis of the progress of antimicrobial resistance management in the pacific island countries and territories through the development and implementation of national action plans.

Monnier, A. A., Schouten, J., Tebano, G., Zanichelli, V., Huttner, B. D., Pulcini, C., Årdal, C., Harbarth, S., Hulscher, M. E., & Gyssens, I. C. (2019). Ensuring antibiotic development, equitable availability, and responsible use of effective antibiotics: recommendations for multisectoral action. Clinical Infectious Diseases, 68(11), 1952-1959.

Mudenda, S., Chabalenge, B., Daka, V., Mfune, R. L., Salachi, K. I., Mohamed, S., Mufwambi, W., Kasanga, M., & Matafwali, S. K. (2023). Global strategies to combat antimicrobial resistance: a one health perspective. Pharmacology & Pharmacy, 14(8), 271-328.

Nahimana, M.-R., Ngoc, C. T., Olu, O., Nyamusore, J., Isiaka, A., Ndahindwa, V., Dassanayake, L., & Rusanganwa, A. (2017). Knowledge, attitude and practice of hygiene and sanitation in a Burundian refugee camp: implications for control of a Salmonella typhi outbreak. Pan African Medical Journal, 28(1).

Nørgaard, S. M., Jensen, C. S., Aalestrup, J., Vandenbroucke-Grauls, C. M., De Boer, M. G., & Pedersen, A. B. (2019). Choice of therapeutic interventions and outcomes for the treatment of infections caused by multidrug-resistant gram-negative pathogens: a systematic review. Antimicrobial Resistance & Infection Control, 8, 1-13.

O'Shea, M. R. (2005). From standards to success: A guide for school leaders. ASCD.

Organization, W. H. (2018). Whole genome sequencing for foodborne disease surveillance: landscape paper.

Otaigbe, I. I., & Elikwu, C. J. (2023). Drivers of inappropriate antibiotic use in low-and middle-income countries. JAC-Antimicrobial Resistance, 5(3), dlad062.

Ozma, M. A., Moaddab, S. R., Hosseini, H., Khodadadi, E., Ghotaslou, R., Asgharzadeh, M., Abbasi, A., Kamounah, F. S., Aghebati Maleki, L., & Ganbarov, K. (2023). A critical review of novel antibiotic resistance prevention approaches with a focus on postbiotics. Critical reviews in food science and nutrition, 1-19.

Pal, C., Asiani, K., Arya, S., Rensing, C., Stekel, D. J., Larsson, D. J., & Hobman, J. L. (2017). Metal resistance and its association with antibiotic resistance. Advances in microbial physiology, 70, 261-313.

Palaniyandi, M., Anand, P., & Pavendar, T. (2017). Environmental risk factors in relation to occurrence of vector borne disease epidemics: Remote sensing and GIS for rapid assessment, picturesque, and monitoring towards sustainable health. International Journal of Mosquito Research, 4(3), 09-20.

Peraman, R., Sure, S. K., Dusthackeer, V. A., Chilamakuru, N. B., Yiragamreddy, P. R., Pokuri, C., Kutagulla, V. K., & Chinni, S. (2021). Insights on recent approaches in drug discovery strategies and untapped drug targets against drug resistance. Future Journal of Pharmaceutical Sciences, 7, 1-25.

Percival, S. L., Williams, D., Cooper, T., & Randle, J. (2014). Biofilms in infection prevention and control: a healthcare handbook. Academic Press.

Pezzani, M. D., Mazzaferri, F., Compri, M., Galia, L., Mutters, N. T., Kahlmeter, G., Zaoutis, T. E., Schwaber, M. J., Rodríguez-Baño, J., & Harbarth, S. (2020). Linking antimicrobial resistance surveillance to antibiotic policy in healthcare settings: the COMBACTE-Magnet EPI-Net COACH project. Journal of Antimicrobial Chemotherapy, 75(Supplement_2), ii2-ii19.

Rajput, A. (2023). Examining the Implementation and Effectiveness of Antibiotic Stewardship Programs in Healthcare Settings to Prevent Antibiotic Resistance and Promote Prudent Antibiotic Use. Knowledgeable Research: A Multidisciplinary Journal, 1(11), 11-24.

Ram, S., Panidepu, H., Cheernam, V., & Tyagi, R. (2020). Pharmaceutical metabolites and their by-products in hospital wastewater. In Current Developments in Biotechnology and Bioengineering (pp. 43-78). Elsevier.

Riekki, J., & Mämmelä, A. (2021). Research and education towards smart and sustainable world. Ieee Access, 9, 53156-53177.

Rush, M., & Davies, S. C. (2016). Combating antimicrobial resistance: building consensus

for global action. Pathways to global health: case studies in global health diplomacy, 2, 89-118.

Sachdev, C., Anjankar, A., & Agrawal, J. (2022). Self-medication with antibiotics: an element increasing resistance. Cureus, 14(10).

Saeed, D. K., Farooqi, J., Shakoor, S., & Hasan, R. (2021). Antimicrobial resistance among GLASS priority pathogens from Pakistan: 2006–2018. BMC infectious diseases, 21, 1-16.

Sartelli, M., C. Hardcastle, T., Catena, F., Chichom-Mefire, A., Coccolini, F., Dhingra, S., Haque, M., Hodonou, A., Iskandar, K., & Labricciosa, F. M. (2020). Antibiotic use in low and middle-income countries and the challenges of antimicrobial resistance in surgery. Antibiotics, 9(8), 497.

Segers, J.-P. (2017). The interplay of regional systems of innovation, strategic alliances and open innovation.

Sekyere, J. O., & Asante, J. (2018). Emerging mechanisms of antimicrobial resistance in bacteria and fungi: advances in the era of genomics. Future microbiology, 13(2), 241-262.

Selvarajan, R., Obize, C., Sibanda, T., Abia, A. L. K., & Long, H. (2022). Evolution and emergence of antibiotic resistance in given ecosystems: possible strategies for addressing the challenge of antibiotic resistance. Antibiotics, 12(1), 28.

September, H. The AMR Challenge.

Shrestha, P., He, S., & Legido-Quigley, H. (2022). Antimicrobial resistance research collaborations in Asia: challenges and opportunities to equitable partnerships. Antibiotics, 11(6), 755.

Surya Prakash, D., Gupta, I., Singhal, S., Pal, D., & Munawar, T. M. (2023). Antibiotic Resistance in Pathogens–a Global Concern.

Swan, J., & McDonald, M. (2020). Infection Control Training for New York State Healthcare Professionals.

Törneke, K., Torren-Edo, J., Grave, K., & Mackay, D. (2015). The management of risk arising from the use of antimicrobial agents in veterinary medicine in EU/EEA countries–a review. Journal of Veterinary Pharmacology and Therapeutics, 38(6), 519-528.

Trees, E., Rota, P. A., MacCannell, D., & Gerner-Smidt, P. (2015). Molecular epidemiology. Manual of clinical microbiology, 131-160.

Trotter, A. J., Aydin, A., Strinden, M. J., & O'grady, J. (2019). Recent and emerging technologies for the rapid diagnosis of infection and antimicrobial resistance. Current opinion in microbiology, 51, 39-45.

van Hamelen, E. Pharma Food.

Wall, S. (2019). Prevention of antibiotic resistance–an epidemiological scoping review to identify research categories and knowledge gaps. Global Health Action, 12(sup1), 1756191.

Walser, B. L. (1997). Shared Technical Decisionmaking and the Disaggregation of Sovereignty: International Regulatory Policy, Expert Communities, and the Multinational Pharmaceutical Industry. Tul. L. Rev., 72, 1597.

Wang, Y., Liu, A., Yang, J., Wang, L., Xiong, N., Cheng, Y., & Wu, Q. (2024). Clinical knowledge-guided deep reinforcement learning for sepsis antibiotic dosing recommendations. Artificial Intelligence in Medicine, 150, 102811.

Waters, R. D., & Lo, K. D. (2012). Exploring the impact of culture in the social media

sphere: A content analysis of nonprofit organizations' use of Facebook. Journal of intercultural communication research, 41(3), 297-319.

About The Authors

Maria Nazir is an MPhil Scholar of Microbiology at the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur, Pakistan. She is involved in a National Research Program for Universities (NRPU) Project, with research interests in Molecular Characterization. She has submitted abstracts to various conferences and authored and coauthored of several book chapters. Her research focuses on the isolation and Molecular characterization of Corynebacterium pseudotuberculosis and their applications in promoting animal health. Her interested research criteria are based on genetics, molecular biology, and bioinformatics.

Email: nazirmaria545@gmail.com ORCID 0009-0004-6714-6212

Rohina Arif is a dedicated educator and researcher with a strong academic background in biotechnology. She completed her MPhil in Biotechnology from Quaid-i-Azam University, Islamabad, Pakistan, and is currently pursuing a Master's in Research (MRes) in Molecular Microbiology at Nottingham Trent University, UK. Rohina has served as a Visiting Lecturer at Fatima Jinnah Women's University, Rawalpindi, Pakistan, her teaching and research experience span various domains, including molecular biology, and biotechnology.

Email: rohinaarif11@gmail.com ORCID Id 0009-0001-5623-8080

Jawad Aslam, doing PhD in Microbiology from Kohat University of Science and Technology Kohat. His research interests include Antibiotic resistance, nanoparticles, and biocontrol. He published one research paper in an HEC-recognized journal and one in a non-HEC-recognised journal.

Email: jawadaslam744@gmail.com ORCID ID: 0009-0003-3775-8691

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as "Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone". His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

Muhammad Mudussair Khan received his bachelor in 2023 from Cholistan university of veterinary and animal science bhawalpur , Pakistan. He is MPhil microbiology scholar at the Islamia University of Bahawalpur, Pakistan. His research interests include predictive breeding models, Genetic selection, Genomics, reproductive biotechnology and selection and judging of animals for beauty attributes. . He also has written book chapters.

Email: muhammadmudussairkhan@gmail.com ORCID:0009-0005-9491-2442

Dr. Muhammad SAFDAR earned his PhD in Molecular Biology and Genetics from Gaziantep University, Turkey. He is Lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 70 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

E-mail: msafdar@cuvas.edu.pk ORCID: 0000 0002 3720 2090

Prof. Dr. Mehmet ÖZASLAN received his PhD in 1995 Institute of Natural Sciences at Cukurova University, Turkiye. He is a Professor in Molecular Biology and Genetics. His research interests are included Cancer Genetics, Molecular Virology, Molecular Genetics, Microbiology, and Genetic mutations etc. He has published more than 200 research articles in national and international well reputed journals. He also has written many book chapters as well as edited books. He is an editor and editor-in-chief of many well-reputed national and international journals.

E-mail: ozaslanmd@gantep.edu.tr, ORCID: 0000 0001 9380 4902

To Cite This Chapter

NAZIR M et al., (2024). Microbial threats: global health governance in the age of superbugs In Current Studies in Health and Life Sciences 2024 (pp.48-72). ISRES Publishing.

Nanotechnology in Microbiology: Bridging Tiny Worlds for Big Impact

Sundas ASHRAF

Maria NAZIR

Muhammad Haris KHAN

Iqra FAZIL

Atif AHMED

Minahal FATIMA

Muhammad SAFDAR

Yasmeen JUNEJO

1. Introduction

Application of items at the scale of 1-100 nanometers or atomic level is called nanotechnology, and it has become the next big thing in science and technology (Sen et al., 1999). From the above developments that these scholars put forward as having benefited from this nanotechnological revolution, it is evident that many fields have benefited, and microbiology is among the beneficiaries. However, blending what might seem to be organized fields to several people is the development of a new opportunity to regulate and direct the great possibilities of microorganisms. These microbial organisms constitute the land. This emerging interest results from realizing the applicability of nanotechnology as a tool that can solve some critical challenges in health care, environment conservation, and industrial biotechnology (Biswas et al., 2023). Therefore, the emphasized synergy of these components revolves around the special characteristics that nanomaterials depict (Figure 1). These particles have a high surface area to volume and are, therefore, rather reactive and good as catalysts. Besides, the size-dependent optical, electronic, and magnetic characteristics enable them to interact with microbial cells and biomolecules selectively (Das & Marsili, 2011). In this way, nanomaterials are versatile for microbiology and its connected branches, such as diagnostics, treatment, environmental applications, and bioprocessing. Nanotechnology is also proving to have a revolutionary influence in diagnostics, especially in the aspect of the identification of pathogens. These include gold nanoparticles and quantum dots, which can be functionalized with specific antibodies or nucleic acid dots that only bind to target microbes (Syed & Bokhari, 2011). Above all, it assists in diagnosing pathogens swiftly and precisely and implementing correct therapy in the diseases associated with infectious sickness. These artifacts are also quickly transforming the sight of antimicrobial solutions. The emergence of resistant bacterial strains threatens global health, thus the need to develop more antimicrobial compounds. Silver nanoparticles and metal oxide nanoparticles are also good antimicrobial agents due to their capability to eradicate different types of microorganisms and how these nanoparticles differ from the bacterial resistance factors (Balderrama-González et al., 2021). Further, the nanoparticles can be produced to liberate antimicrobial particles at the action's site, making the drug more efficient and minimizing the damage to the other parts of the body. Of the given fields, nanotechnology was the most promising and offers cutting-edge solutions to problems in environmental microbiology, notably in bioremediation and pollution sensing. Some useful nanoparticles are iron oxide nanoparticles and carbon nanotubes, which can be used to adsorb with the ability to decrease contaminants in the given environment, heavy metals, and organic compounds (Liosis et al., 2021).

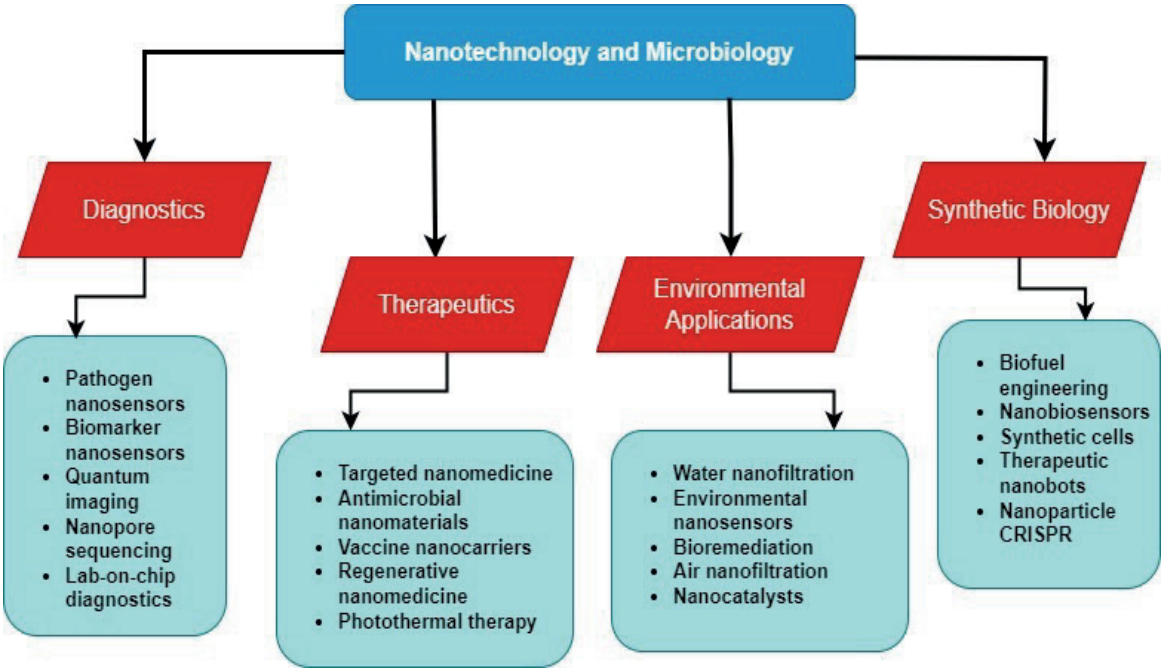


Figure 1. Convergence of Nanotechnology and Microbiology

Equally, it can be used to have a mechanical touch and feel of toxic microbes in water and soil, thus checking the environment's health status in real-time. To the mentioned applications, it is worth adding that nanotechnology is changing industrial biotechnology. At the same time, particles need to increase the efficiency of fermentation processes, new biofuel development, and the synthesis of valuable biomolecules (Manikandan et al., 2022). Considering that with the improvement of technology, it becomes possible to regulate microorganism activity at the nanotechnology level, the opportunities to build the value added, sustainable, and eco-friendly Bioprocesses are opening up. However, these smaller and finer techniques pose certain restrictions once combined with microbiology. Therefore, due to possible toxic effects and harm to the environment of nanomaterials, their great application potential leads to focusing on them and studying and testing them (Aschberger et al., 2011). Other important questions that have to do with the how of nanotechnology in microbiology and which also entail ethical considerations must be addressed. The relationship between nanotechnology and microbiology can be quite complex, and, in this regard, the author will continue with further elucidation of this relationship in this chapter. Therefore, delving into topics of basic tenets, usages, and ramifications of this discipline will help the works elucidate the potential of nanotechnology in changing the perception and utilization of microorganisms. This is an exciting journey directed towards innovating the solutions to potentially life-altering problems in health, ecology, and biotech to build a much-improved world for humanity.

2. Fundamental Concepts

Nanotechnology, which is the manipulation and creation of materials at the nanostructure or atomic level between 1 and 100 nm, is associated with a novel period of innovation (Nasrollahzadeh et al., 2019). Indeed, all scientific disciplines feel this nanotechnological revolution; microbiology is one of the major receivers. It is, in fact, the exponent of the growth rate of research and development at the intersection of nanotechnology and microbiology over the years. With the prospect of nanotechnology, scientists have decided to find valuable solutions to important appeals in health care, ecology, and industry bioengineering (León-Silva et al., 2018).

Table 1: Nanomaterials in Microbiology

Nanomaterial Type	Properties	Applications in Microbiology	References
Metal oxide nanoparticles (e.g., gold, silver)	Reduce size, optical properties, bactericidal properties	Drug delivery, biosensors, imaging, diagnostics, anti-bacterial films	(Sharma et al., 2021)
Polymeric nanoparticles (e.g., PLGA, Chitosan)	Biocompatibility, biodegradability, controlled release	Drug delivery, gene delivery, tissue engineering, Vaccine delivery	(Han et al., 2018)
Lipid-Based Nanoparticle include liposomes, micelles	Biocompatibility relates to the versatility of encapsulating hydrophilic and hydrophobic molecules	Used in drug delivery, gene delivery, vaccines, imaging, and more.	(Campora & Ghersi, 2022)
Carbon Nanotubes	High strength, electrical conductivity, thermal conductivity	Biosensors, tissue engineering, drug delivery, imaging	(A Stout, 2015)
Quantum Dots	Size-tunable fluorescence, high photostability	Cellular imaging, diagnostics, biosensors	(Pandey & Bodas, 2020)
Dendrimers	Branched structure, high surface area, multivalent binding	Drug delivery, gene delivery, diagnostics, imaging	(Sherje et al., 2018)
Magnetic Nanoparticles	Magnetic properties, biocompatibility	Cell separation, magnetic hyperthermia, drug targeting, imaging	(Shabatina et al., 2020)

At this synergy, the properties of the nanomaterials that are the subject of the present work are rooted. Because of the high reactivity and provocative catalytic behaviors; their size-dependent optical-electronic-magnetic nature can modulate interaction with microbial cells and biomolecules. The enumerated characteristics position nanomaterials as multifunctional tools for various applications in microbiology (Table 1) they include diagnostic, therapeutic, environmental, and bioprocessing classes (Babaniyi et al., 2023). In diagnostics, nanotechnology has greatly revolutionized the way diagnostic activities occur and, in more detail, the identification of pathogens. For instance, gold nanoparticles and quantum dots can be functionalized with specific antibodies or nucleic acids to ensure that they trap and identify target microorganisms. This technique is known as nanoparticle-based biosensing and can help in fast diploma identification of pathogens; hence, early treatment measures can be instituted for cases of infectious diseases. For instance, a novel gold nanoparticle-based assay has been synthesized to quickly identify the bacterial pathogens Escherichia coli and Staphylococcus aureus (Hegde et al., 2022).

It also slowly extends this definition toward modifying the theater of an adversarial relationship with antimicrobial agents. The aggression of antibiotic-resistant bacteria is one of the leading threats in the world today, and hence, there is a need to invent new sources of antimicrobial agents. Silver nanoparticles, zinc, titania nanoparticles, and liposomal nanoparticles were other recognized nanoparticles that demonstrated to have broad-spectrum antibacterial activity, and the mode of action is not linked to resistance mechanism in the microbial cells (Mozafari et al., 2021). In particular, it has the following effects on bacterial cell membranes and intracellular functions, such as the silver nanoparticles. Besides, nanoparticles can be developed so that the free radicals of antimicrobial agents discharge exclusively at the site of infection, offering immense curative benefits without exposing the patient to severe side effects (Khorsandi et al., 2021). In the sub-branch of environmental microbiology, nanotechnology entails relevant techniques in bioremediation and pollutant identification. Some of the nanoparticles used for the absorption and decontamination of pollutants in the environment, heavy metals, pesticide sprays, and organic chemicals include Iron oxide nanoparticles, Titanium dioxide nanoparticles, and Carbon nanotubes. In addition,

nanosensors can also be employed to analyze water and soil pollution by dangerous microbes to control the state of the environment in real-time (Chakraborty et al., 2021).

Besides this application, nanotechnology is also rapidly transforming industrial biotechnology. Certain benefits relate to nanoparticles enhancing fermentation processes through enzyme or whole-cell immobilization, enhancing the process yield and solidity. In addition, the nanoparticles can also be used to enhance the activity of the enzymes in the conversion process of bio biomass to biofuels, that is, biodiesel and bioethanol (Mumtaz et al., 2022). Still, this review is in the position to admit the following: nanotechnology use in microbiology has flaws. The existence of toxicities and potential hazards for the environment create issues that require acknowledgment and security tests. Two kinds of issues are frequently found in the ethical implications of nanotechnology in microbiology: the biosafety of nanotechnology and justice issues like risks associated with the technology and fair distribution of the same technology (Kimbrell, 2009). The current chapter start with an extensive discussion on the analysis of primary and secondary aspects of the connection between nanotechnology and microbiology. By studying the categories of nanotechnology concerning its fundamentals and the kinds, one can learn about the advantages of applying this innovation and its impact on perceiving and engaging microorganisms. This path will lead to discovering new strategies for solving concrete everyday challenges in healthcare, ecology, biotechnology, and other topics to establish a superior quality of life for the people.

3. Nanomaterials and Their Properties

The branch of engineering that deals with manipulation and designing material at a size scale of 1-100 nanometers is called nanotechnology and is slowly creeping into almost all branches of science, including microbiology. This fusion of what might initially seem like related fields is paving the way for unexplored possibilities of the phenomenon of controlling microorganisms. These complex microscopic structures fascinate the biosphere's complexities (Skalka, 2018). Activities on nanotechnology in microbiology, reveal the vast available potential of nanotechnology in surviving key problems in healthcare, environment, and industrial biology.

Table 2: Nanomaterials Properties and Applications

Property	Description	Example	Application	Reference
Optical	Different colors or transparency compared to bulk form.	Gold nanoparticles	Diagnostics, imaging, sensors	(Sharifi et al., 2019)
Mechanical	Stronger, harder, or more ductile than bulk form.	Carbon nanotubes	Structural materials, composites	(Kumar et al., 2020)
Electrical	Enhanced conductivity or become insulators.	Quantum dots	Electronics, solar cells	(Kramer & Sargent, 2014)
Magnetic	Unique magnetic properties not seen in bulk form.	Iron oxide nanoparticles	Data storage, medical imaging	(Maldonado-Camargo et al., 2017)
Chemical	Enhanced reactivity due to high surface area.	Titanium dioxide nanoparticles	Catalysis, self-cleaning surfaces	(Khataee & Mansoori, 2011)
Thermal	Enhanced thermal conductivity.	Graphene	Heat dissipation in electronics	(Renteria et al., 2014)

Due to these and other characteristics, nanomaterials are valuable in carrying out many processes in microbiology (Table 2). In diagnostics, nanomaterial-based biosensors, conjugated with specific antibodies or nucleic acid sequences, also help in the rapid and accurate detection of the pathogen load and infection rates, resulting in early intervention in cases of infectious diseases (Markandan et al., 2022). For example, gold nanoparticle-based assays have been synthesized to detect bacterial

pathogens such as E. coli and S. aureus. Nanotechnology is also transforming antiseptic treatments by providing new strategies against the increased problem of antibiotic-resistant bacteria (Khan & Rasool, 2023). Some of the nanoparticles used in the treatment of infection are silver nanoparticles, metal oxide nanoparticles, for instance, zinc and titanium oxide, and liposomal nanoparticles, and these nanoparticles can destroy the pathogens mostly without regard to existing resistance mechanisms. In environmental microbiology, the field of biodegradation, nanotechnology has much to present and effectively address the pollution challenge. It is well demonstrated that pollutants, including heavy metals, pesticides, and organic contaminants, can be adsorbed and degraded with the use of nanoparticles such as iron oxide nanoparticles, titanium dioxide nanoparticles, and carbon nanotubes. The same can be used to monitor the presence of toxic bioagents in water and soil, indicating the environmental condition in real time (Eltzov et al., 2009).

In addition, nanotechnology is revolutionizing industrial biotechnology as follows: Fermentation can also benefit from nanoparticles where enzymes or entire cells can be immobilized, resulting in improved productivity and stability. On the same note, nanoparticles, like biodiesel and bioethanol, can be employed to increase the efficiency of biofuel production by intensifying the enzymatic reactions involved in biomass conversion (Awogbemi & Von Kallon, 2024). Thus, despite the impressive number of successes in introducing nanotechnology to microbiology, certain difficulties are involved in this process. Due to their toxicity and the effects that they can have on the environment, the use of nanomaterials involves issues that should not be taken lightly. Before implementing nanotechnology, they must undergo the toughest safety tests. Some issues that fall under the ethical considerations include the biosafety of nanotechnology in microbiology, the distribution of nanotechnology innovation and impacts, and possible negative externalities (Tanji, 2009). To this end, and as the next chapter, this research will conduct a holistic analysis of the interaction between nanotechnology and microbiology by defining the basics, exploring its versatility, considering the impacts of nanotechnology, and showcasing how it has revolutionized the knowledge and use of microorganisms to solve problems in health, environment, and biotechnology.

3.1 Nanomaterials Types

Metallic Nanoparticles (Silver, Gold)

Metallic nanoparticles, such as silver (AgNPs) and gold (AuNPs), have received considerable attention in microbiology due to their unique characteristics and functionality (Bamal et al., 2021). The materials forming these particles differ in size, shape, and how NPs interact with microbial cells and biomolecules (Table 3).

Table 3: Metallic Nanoparticles Properties and Applications

Property	**Gold Nanoparticles (AuNPs)**	**Silver Nanoparticles (AgNPs)**	**References**
Size (nm)	1-100	1-100	(Ujica et al., 2020)
Shapes	Spheres, rods, cubes, etc.	Spheres, rods, cubes, wires	(Capek & Capek, 2017)
Color	Red to purple	Yellow to brown	(Adebayo et al., 2019)
Biocompatibility	High	Moderate	(Shanmugasundaram et al., 2017)
Antimicrobial Activity	Lower	High	(Patil & Kim, 2017)
Mechanisms	Photothermal, drug delivery	Membrane disruption, ROS, intracellular interactions	(Mikhailova, 2021)

Property	Gold Nanoparticles (AuNPs)	Silver Nanoparticles (AgNPs)	References
Applications	Drug delivery, imaging, diagnostics, photothermal therapy	Antimicrobial coatings, wound dressings, water purification, drug delivery, biosensors	(Jayakumar et al., 2023)

AgNPs are known for their strong antics, which makes them fit through in fighting infections and minimizing microbial build-up. The antimicrobial mechanism of AgNPs is multifaceted and involves several key processes: membrane disruption, formation of ROS, and interaction with cellular components.

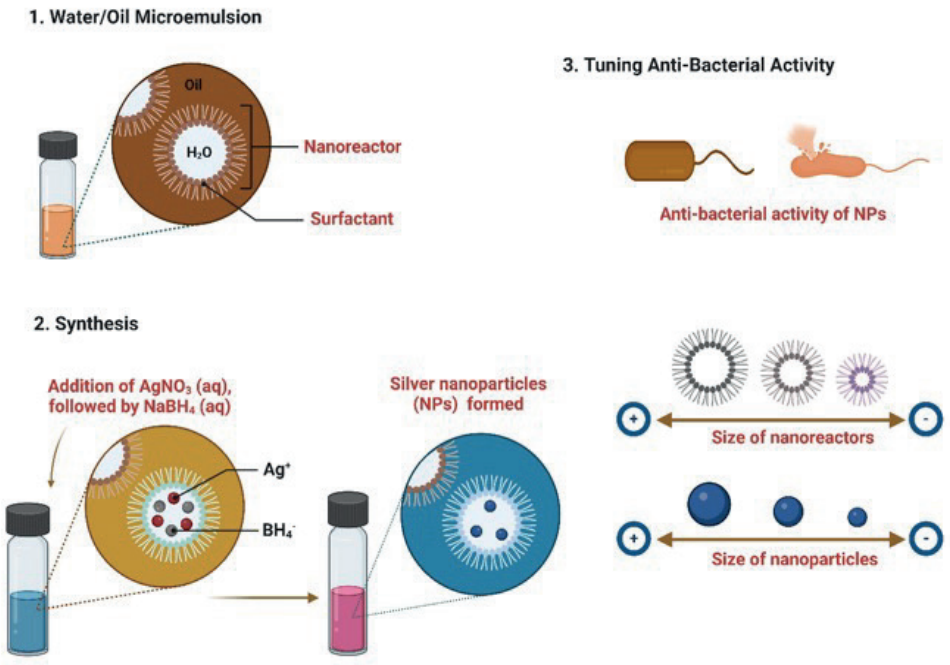


Figure 2. Antimicrobial Mechanism of Silver Nanoparticles

Studies have shown that AgNPs possess integral antibacterial effects against myriad bacterial strains, both, Gram-positive as well as negative, besides fungi and viruses (Leong et al., 2023). This wide-spectrum action and the fact that they can counteract antibiotic resistance mechanisms in parts make AgNPs ideal candidates for the newer generation antimicrobials (Figure 2). On the other hand, the information on the toxicity of AgNPs towards human cells and the environment remains a major concern when using the item. By size, shape, surface charge, and the dose of AgNPs, it is understood that the toxicity and biocompatibility quotient could be altered (Makama, 2016). Thus, monitoring those factors is crucial to creating sound AgNP-based antimicrobial treatments. AuNPs have specific optical characteristics; they disclose intense absorption and light scattering in the visible and near-IR regions because of localized surface plasmon resonance (LSPR) (Long & Jing, 2014). This fact proves valuable for AuNPs employed in microbiology as biosensors, imaging agents, and photothermal therapies. Biosensors developed with AuNP utilize LSPR to reveal the existence of target biomolecules like antibodies, DNA, or enzymes. The specific interaction of target molecules with the surface of the AuNPs can affect the LSPR signal, which can be easily detected using UV-vis spectroscopy. This approach allows for the selective identification of pathogens, biomarkers, and other molecules and the use of assay methods. AuNPs are also employed in microbial imaging because of their biocompatibility and amenability for ready functionalization with targeting moieties (Alim et al., 2018). As AuNPs are conjugated with antibodies or peptides,

scientists can identify individual microbial cells or formations within dense tissue. Moreover, AuNPs are ideal candidates in photothermal therapy, a novel cancer treatment technique. When exposed to near-infrared light, the AuNPs effectively phagocytize the light energy, which in turn produces heat and thereby causes localized increases in the temperature and selective killing of cancer cells (Shen et al., 2020). This strategy can also be applied to the antimicrobial use of AuNPs designed to eliminate pathogenic bacteria after exposure to light.

3. 2 Diamond-like carbon and Its Composites (Graphene, Carbon nanotubes)

Graphene and carbon nanotubes (CNTs) have some microbiological uses because of their nature being carbon-based nanomaterials. Graphene, strictly speaking, is a one-atom-thick layer of carbon crystallites wherein carbon atoms are hexagonal lattices and the material is mechanically extremely inflexible, electrically and thermally conductive (Gupta & Gupta, 2018). Such factors make graphene suitable for applications that include biosensing, the delivery of drugs, and tissue engineering. Graphene oxide (GO), a graphene derivative, could be of special significance in microbial applications due to its large surface area, the availability of functional groups, and its biocompatibility.

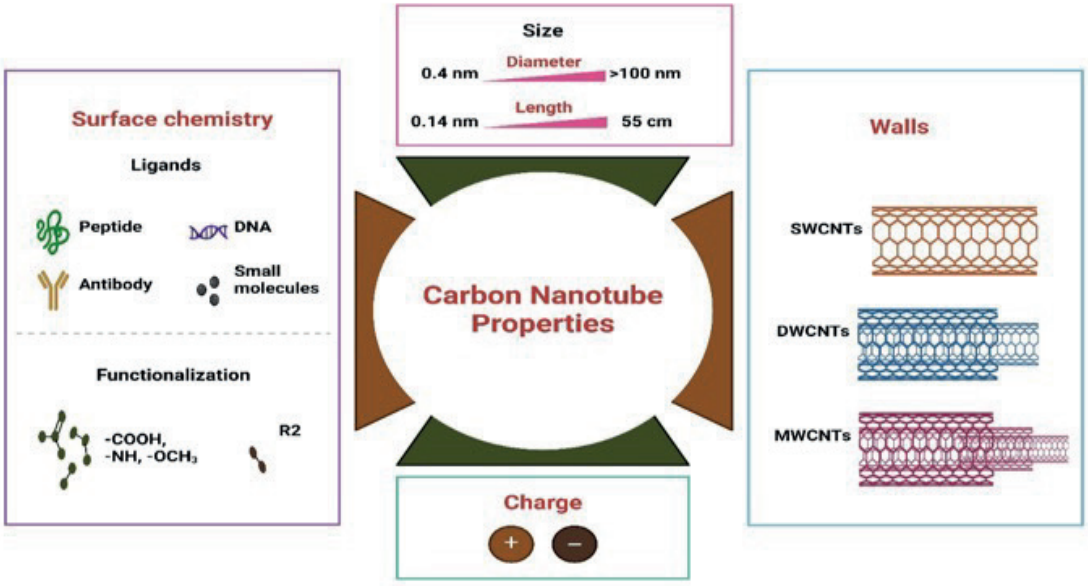


Figure 3. Description of Graphene and Carbon Nanotubes

Among all the nanomaterials that have the probability of being the next generation nanomaterials, the CNTs are cylindrical structures that are made from wrapped-up layers of graphene; they have high tensile strength, electrical conductivity, and thermal stability (Thakur & Thakur, 2018). In this regard, CNTs can be broadly categorized into two categories depending on the number of layers of graphene namely Single-Walled Carbon Nanotubes (SWCNTs) and Multi-Walled Carbon Nanotubes (MWCNTs) (Figure 3). It seems that bactericidal properties were widely investigated among SWCNTs and MWCNTs for the desired properties of cell membrane damage in bacteria and yeast, oxidative stress, and DNA damage. Also, CNTs have been used to support enzymes and whole cells for catalytic action and biodegradation (Maksimova, 2019).

3. 3 Polymeric Nanoparticles

Polymeric nanoparticles are more defined nanomaterials that researchers in the microbiology field get attracted to because of their characteristics like bio-inert, biodegradable, and can encapsulate diversified drug and diagnostic agents with different functions (Ling, 2018). NPs can be obtained from natural and synthetic polymers polysaccharides natural alginates, polylactic acid PLA, polyglycolic acid PGA, chitosan, and synthetic nylon (Smola-Dmochowska et al., 2023). The size,

shape, surface charge, and functionality of NPs can be designed to mediate appropriate interactions with microbial cells and tissue (Figure 4).

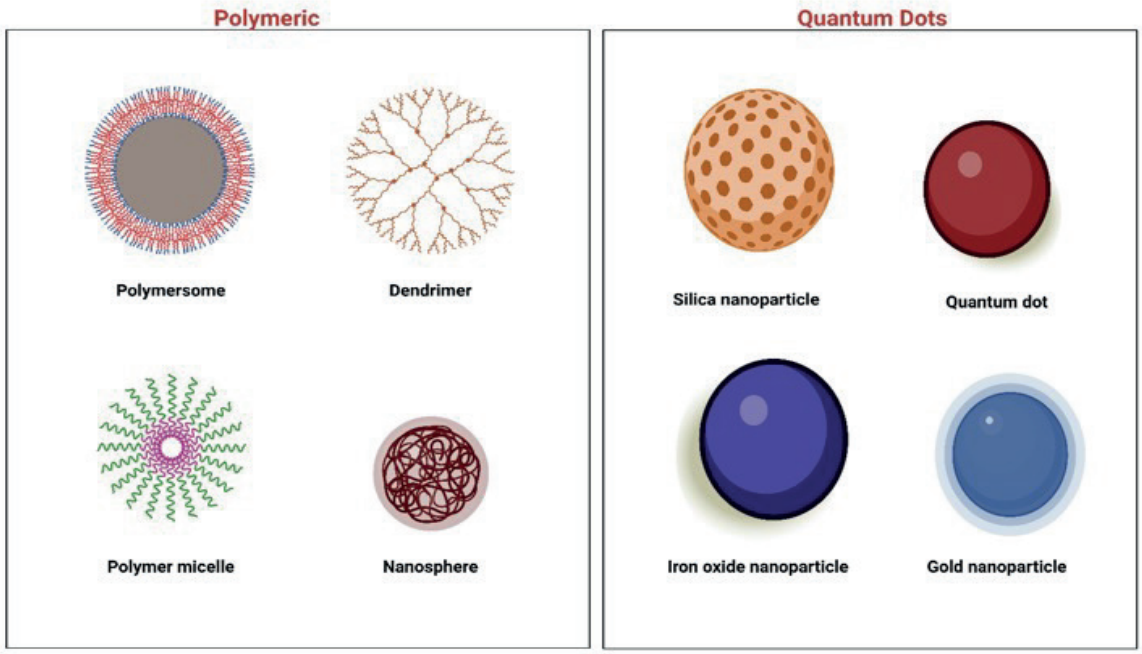


Figure 4. Configuration and shapes of polymeric and Quantum dots nanoparticles

In drug delivery, NPs can help shield the therapeutic agents from degradative processes, increase the solubility of the intended therapeutic agents, increase their bioavailability, and deliver them to the specific sites of infection in the body (Salouti & Ahangari, 2014). For instance, NPs conjugated with antibiotics could facilitate the eradication of intracellular bacterial pathogens emphasized by tuberculosis and listeriosis. In diagnostics, NPs can be functionalized as fluorescent labels or contrast agents to visualize microbial cells and tissue in living organisms (Ruedas-Rama et al., 2012). Moreover, NPs can also be affected by pH or temperature to trigger the release of the encapsulated drug or imaging agents to the right site.

3. 4 Quantum Dots (QDs)

These are classified as nanoscale semiconductor particles called Quantum Dots (QDs). They exhibit optical and electronic behavior because of the quantum size effect (Coto-García et al., 2011). QDs are fluorescent nanocrystals with size-tunable emission properties and high Quantum Yield and Photostability, and they are thus highly useful in multiplex detection in bio-imaging and biosensing (Figure 4). QDs have been used in microbiology to stain and track the movement of microbial cells about other cells and substrates and to study the processes that occur within the microbial cells (Abdel-Salam et al., 2020). For instance, QDs in the form of antibody conjugates have been employed to visualize the migration and accumulation of pathogenic bacteria in the host tissues. QDs can also be included in the biosensors to identify particular microbial biomarkers or toxins (Zhu et al., 2014). For the diagnosis of infectious diseases, QD-based biosensors are tested due to their high sensitivity and multiplexing characteristics.

4. Applications of Nanotechnology in Microbial Detection

The interdisciplinary nature of nanotechnology and microbiology has led to the new and improved detection of microorganisms through touchy, brisk, and particular nanosensors and biosensors (ALBERT, 2023). These analytical instruments' sophistications take advantage of nanomaterials' properties to enhance one or the other feature of the detection and determination of microbial biomolecules, toxins, and whole-body cells, respectively.

Nanosensors and Biosensors

Deployment of the biological receptor with a transducer forms nanosensors and biosensors to measure the target analytes. Concerning the identification of the microbiology discovery, the biological recognition element could be an enzyme, antibody, or nucleic acid, as well as an intact cell with selective reactivity with the target microorganism or the parts of the microbial cell. The signal between the biological entities is converted into an electrical, optical, or electrochemical signal (Liu et al., 2017). As a result of the developments in this area, devices or inventions in nanosensors or biosensors are referred to as nanosensors and biosensors because nanomaterials with better attributes have been included in the devices. For example, gold and silver nanoparticles can be introduced in designing optical biosensors under the influence of LSPR. LSPR is ascribed to the plasmon resonance of the confined electrons on the surface of the nanoparticles, which causes oscillation in interaction with light, enhancing the intensities of electromagnetic fields. This improved field can increase the sensitivity of optical biosensors by detecting the smallest possible target analytes (Zanchetta et al., 2017). Magnetic nanoparticles can also be included in the biosensors to separate and pre-concentrate the targeted microorganisms, reducing the detection limit. Conjugation of magnetic nanoparticles is possible using antibodies or nucleic acids, which can interact with the target microorganism with high specificity and affinity. Further application of a magnetic field to collect the bound microbes from the sample matrix is also possible (Dester & Alocilja, 2022). It has been used to diagnose various pathogens: bacteria, viruses, and parasites are among the microorganisms that can harm the inhabitants. Other categories of nanomaterials applied in the biosensors are carbon nanotubes, CNTs, and graphene due to their high electrical conductivity and large surface area for the mass ratio Such nanomaterials can be used to make electrodes from electrochemical biosensors, mainly, they produce electrical signals, which vary in response to target analytes, interacting with biosensing interface. For instance, CNT-based electrochemical sensors have been used in the detection of bacterial toxins such as botulinum neurotoxin and; staphylococcal enterotoxin B and as noted by Wang and others (Wu et al., 2016). The integration of nanomaterials has especially impacted performance indicators like sensitivity, specificity, and the rate at which microbial detection is done in nanosensors and biosensors. For instance, there is the biosensor line of devices that design nanomaterials for assessing bacterial pathogens in foods as well as in water including Escherichia coli and Salmonella enterica (Ajayi et al., 2022). These biosensors can test pathogens within minutes, while traditional clinical testing can take hours or even days to test them. Also, nanomaterial-based biosensors can be integrated to identify many pathogens simultaneously, thus increasing the chances of testing large samples for various pathogens (Bhardwaj et al., 2021). Such multiplexing capacity is useful in clinical diagnosis, where it is necessary to identify the microorganism as quickly as possible.

Pathogen Detection

Therefore, discovering the pathogen is also important, as is creating competent and effective diagnostic procedures. The various methods have been empowered by nanotechnology, where the properties of nanomaterials are subsequently used to enhance the velocity or, respectively, the sensitivity and selectivity of pathogen identification.

1. Nanoparticle-based immunoassays: These assays involve the use/of nanoparticles conjugated to antibodies for recognition of specific antigens on the external surface of the pathogenic microorganisms. The mechanism of color change, observable or the generation of some signal that can be quantified in terms of fluorescence intensity or absorbance, happens due to the nanoparticles tagging the target antigens (Chen, 2008). An approach similar to that described above was used previously to identify several bacteria and viruses, including S. aureus, Salmonella, and the influenza virus.

2. Nucleic acid-based assays: These assays use nanoparticles to increase and detect the sequences of pathogenic microorganisms' nucleic acids. One example is nanoparticle-PCR, which

utilizes nanoparticles to enhance standard PCR in terms of efficiency and effectiveness in amplifying sample material. Nanoparticle-lateral flow assay, which assists in accurately diagnosing patients' pathogens in different non-laboratory settings (Khaliq et al., 2012).

3. Nanopore sequencing: This is one of the new technologies that entails letting the DNA or RNA samples pass through the channels measured in nanometers, thus offering fast and simple sequencing of microbial specimens (Figure 5). PCR-free defensive and isolate identification from contaminated samples are among the significant areas in which nanopore sequencing can bring significant change. The ability to identify pathogens and track the epidemics of infectious diseases can also not be overlooked (Morse, 2012). Such methods of pathogen identification have shifted the time required to diagnose the illness and even propound a course of action. This is specifically important in managing acute infection since the distinction between life and death may hinge on the timeliness of the patient's treatment. Also, these tests have higher sensitivity depending on their type and specificity, thereby aiding in early detection of illnesses and effective treatment procedures or regimens leading to a more improved patient's condition.

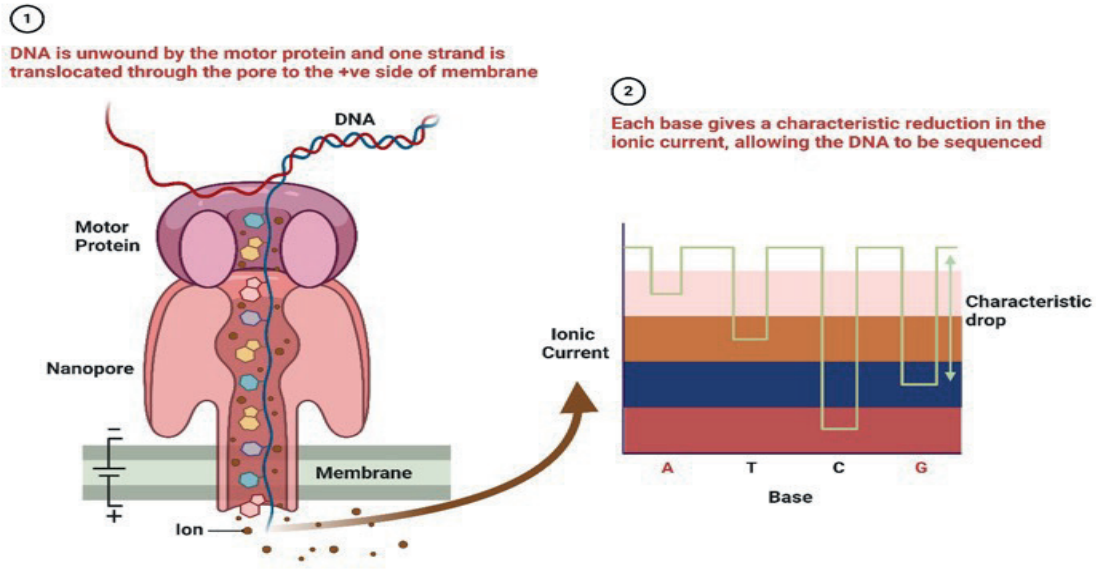


Figure 5. Nanopore Sequencing

5. Nanotechnology in Antimicrobial Strategies

5. 1 Mechanism of Action:

Thus, it is possible to state that nanoparticles can possess several antimicrobial activities, which means that all mentioned mechanisms act in concert to prevent the impressive bactericidal or bacteriostatic effects. These mechanisms can be broadly categorized into the following (Figure 6).

Membrane disruption: This is among the ways that nanoparticles negatively impact the bacteria's cell membrane to eliminate the microorganisms. Since nanoparticles have a very large surface area, they can easily interact with the lipid bilayer of the cell and the membrane proteins; doing so modifies the cell permeability, and the contents of the cell spill out, and the cell dies (Gurtovenko et al., 2010). It can be stated that the action of this mechanism is most effective for gram-negative bacteria because the outer membrane of such bacteria is not as thick as in the case of 'gram-positive' microbes, which are surrounded only by relatively thick peptidoglycan walls.

Generation of reactive oxygen species (ROS): Amongst other nanoparticles like metal/Metal

oxide NPs, possess a characteristic of generating ROS when interacting with cell constituents or on light incidence. ROS are highly reactive and include superoxide anions, hydrogen peroxide, and hydroxyl radicals, of which the necessity of deletion includes DNA, proteins, and lipids, leading to oxidative stress and cell death (Madkour, 2019). The generation of ROS is also said to be one of the reasons why AgNPs possess some degree of antimicrobial activity (Huang et al., 2021).

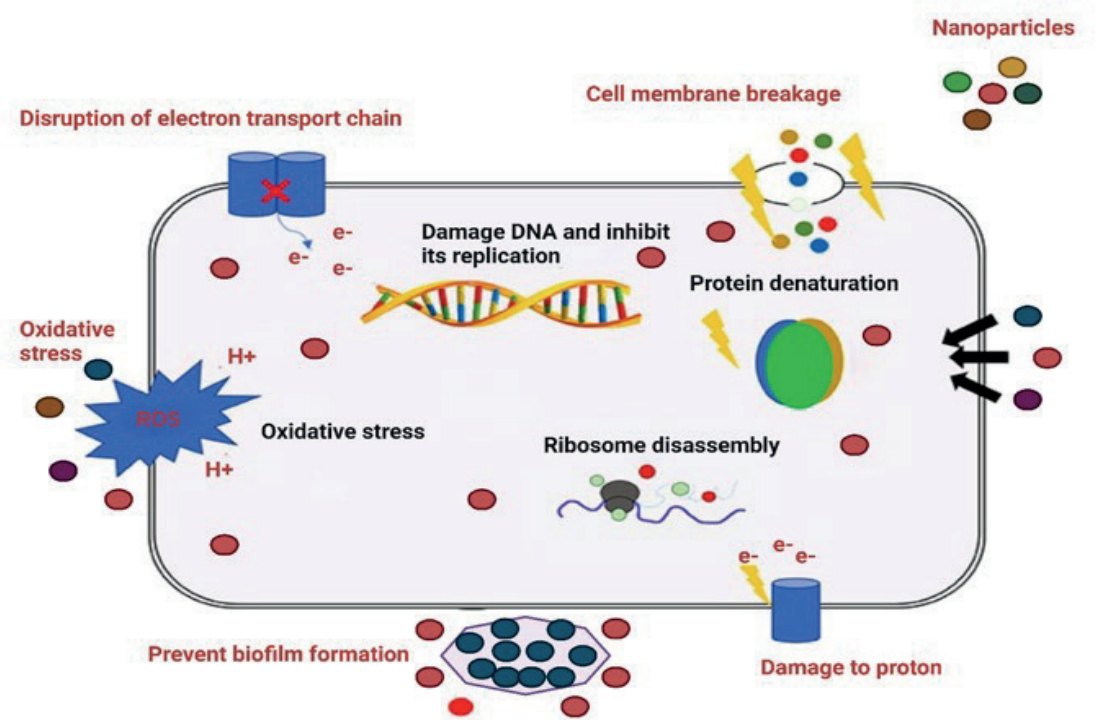


Figure 6. Modes of action of antimicrobials incorporating nanoparticles on the example of membrane disruption

Release of metal ions: Some types of nanoparticles like silver, copper, and zinc-based nanoparticles on coming in direct contact with microbial cells release their metal ions. Such metal ions like DNA, ribosomes, and other cellular proteins, and this chelation alters normal cellular functions and ultimately triggers cell death. For example, the silver ions emanating from the surface of the AgNPs can interact with thiol groups of proteins and thus impede their efficiency besides encouraging the development of oxidative stress (Marchioni et al., 2018).

Modulation of signal transduction pathways: In part, nanoparticles may affect bacterial signal transduction concerning quorum sensing, biofilm formation, and the expression of signs of virulence (Holban et al., 2016). Cell signaling can be described as a way through which bacteria can communicate and react to various activities, such as the synthesis of virulence factors and biofilms. Therefore, by affecting quorum sensing, nanoparticles reduce the pathogenicity of bacteria and the ability to infect the host (Ivanova et al., 2018).

Physical damage: Sometimes, nanoparticles can come into direct contact with bacterial cells through abrasion, affecting them through methods such as disruption of cell membranes (Rawashdeh & Haik, 2009). For example, it has been postulated that pointed-tipped carbon nanotubes penetrate bacterial cells and cause them to rupture. In some cases, the many process depressions improve on each other to create a superbly synergistic antimicrobial contender. This multiple-pod strategy also increases the effectiveness of the antimicrobials based on nanoparticles. It prevents the emergence of resistance in contrast with the traditionally used antibiotics that target a specific cellular process (Murugaiyan et al., 2022). All these facts suggest that by learning different forms of nanoparticle action, one can achieve effective and non-dangerous forms of antimicrobial treatments that are crucial due to the continuous emergence of antibiotic resistance.

5. 2 Technologies and progression towards the use of antimicrobials such as nanoparticles

In this regard, however, it is necessary to emphasize that nanoparticle antimicrobial action depends on several sequential and closely related activities that make this approach rather promising, given the future growth of antibiotic resistance. From these and other postsynaptic activities, NBAs are more effective than conventional antibiotics because NBAs work on multiple targets. The Molecular Action of NBAs. Such an approach can attack bacteria in several areas, making it very hard for the bacteria to develop resistance (Barros Alvarez, 2018). Studies of NBAs continue to this date and have several other possible approaches, which is why the construction of NBAs is a progressive and unexhausted trend. One of the strategies includes the conjugation of nanoparticles with already-established antimicrobial agents. The opportunity to functionalize nanoparticles by antibiotics, antimicrobial peptides, or other bioactive molecules enlarges the antimicrobial activity and effects of a specific substance (Urban et al., 2012). Besides, this functionalization increases the efficacy of delivering antimicrobial agents to the site of inflammation and minimizes the toxic impacts of such devices on the host cells. For instance, vancomycin-conjugated silver nanoparticles have been reported to produce enhanced efficacy against vancomycin-resistant enterococci (Abdelaziz et al., 2022). Among the other strategies, is the creation of novel nanocomposites with co-antimicrobial activity. Combinations of one type of NP with another type of NPs in regular antibiotics should produce major synergistic effects where the improvement is actually beyond the inclusions of the two constituents (building blocks). The same concept has been used better with silver nanoparticles and with different antibiotics, and the progression moves to an efficient form against multidrug-resistant bacteria (Brar et al., 2023). This is achieved as another strategy through the intention of haptenizing the targeted nanoparticles for the right deliverance to the required site of infection with the targeted haptenization and concentration. As mentioned earlier, many functional nanoparticles are capable of capturing bacteria when conjugated with specific targeting ligands such as antibodies, aptamers, or other molecules able to bind to bacterial cell surface markers (Davodabadi et al., 2023). This approach may raise the therapeutic ratio of antimicrobial agents and minimize the side effects by concentrating more of the drug on the area of interest.

5. 3 Addressing Antibiotic Resistance

Nanotechnology has the potential to play a crucial role in overcoming the global crisis of antibiotic resistance through several mechanisms: nanotechnology is currently in a position to offer a great solution to the global problem of resistance to antibiotics through the following ways:

Development of NBAs with novel mechanisms of action: NBAs can impact multiple cell functions. for instance, disruption of the cell membrane, generation of ROS, and formation of damaged proteins, which are conditions that bacteria cannot easily transform themselves to handle. Such an attacking feature is considerably different from the traditional antibiotics, which encompass only one form of cellular action and hence can easily be resisted (Konwar et al., 2022). The fact that the activity is ternary compounded by the ability to inhibit multiple targets simultaneously which in a way reduces the selective pressure for the development of resistance to these new antimicrobials and therefore gives more time for resistance to these new antibiotics.

Synergistic effects with conventional antibiotics: It was discovered that the improvement of the nanoparticles with conventional antibiotics was effective in increasing the efficacy of treatment processes and reducing antibiotic resistance in some instances (Fatima et al., 2021). The nanoparticles can disrupt the bacterial cell wall, and as a result, the antibiotics either penetrate the bacterial cells more easily or the nanoparticles can block the efflux pore through which the bacteria expel the antibiotics. Such synergistic effects include one or different kinds of nanoparticles and antibiotics, which in turn support the view of using nanoparticles to overcome multidrug-resistant infections (León-Buitimea et al., 2022).

Targeted delivery of antibiotics to bacterial cells: Nanoparticles can be used for encapsulation and Targeted delivery of antibiotics into bacterial cells, forcing them to bypass the efflux pump and enzymatic degradation mechanisms, which are putting much action on the drug (Dey et al., 2022). This may enhance the antibiotics' impact and decrease the side effects, mostly arising from the scant damage to the host's healthy cells.

Prevention of biofilm formation: Biofilms, on the other hand, are architecture of microorganisms closely adherent to a surface with a sheath of slimy material that is called EPS biofilm matrix. Microorganisms routinely develop biofilms, and they are difficult to eradicate by regular antimicrobials, although the EPS matrix that develops around the microorganisms constitutes a tangible and physiological barrier (Loots, 2016). These, in turn, may influence bacterial adhesion, bacterial motility, and EPS synthesis and therefore improves, the bacteria's resistance to antibiotics (Uruén et al., 2020). Also, nanoparticles can easily penetrate the biofilm matrix, and the antimicrobial agents can be released directly to the bacteria, enhancing their capacity to combat biofilms-associated diseases. In sum, this entry provides a three-point plan for dealing with the problem of antibiotic resistance in line with nanotechnology. Since nanotechnology can develop NBAs with novel mechanisms of action, increase the effectiveness of the currently used antibiotics, introduce antimicrobial agents into the focus of infection, and prevent bacterial adhesion to surfaces and biofilm formation, such a technology could be very effective in fighting this world issue.

6. Enhancing Microbial Production and Technology

6. 1 Utilizing the Nanotechnology in Fermentation Processes

Techniques for fermentations that employ the metabolic action of microorganisms in the synthesis of demand products are widely used in several industries like pharmaceutical, food, and bioenergy industries, among others. New developments have established that integrating nanotechnology in the fermentation processes is now an excellent method for developing the microbial production process and the functionality of bioreactor systems (Table 4).

Improving Microbial Production Yields

The size of nanoparticles could be used to increase microorganisms' growth rate and yield in fermentation processes in the following manners. The studied method refers to the category known as ‘‘attached’’ methods, which involves the adherence of enzymes or entire cells on nanoparticle carriers (Thomsen & Klok, 2021). It has been pointed out that immobilization allows the stabilization of enzymes, surpassing the environment's stability and ensuring multiple uses of enzymes. The resistance to the environment's harshest conditions increased access of the enzymes to substrates resulting in improvement of both the rate of reactions and the yields. For example, magnetic nanoparticles with definite ligands have been used successfully for enzymes like lipase, which are used in the biodiesel production process, and cellulase, which are used to break down the biomass for producing biofuel (Rai et al., 2017).

Table 4: Comparison of Traditional and Nanotechnology enhanced Fermentation Processes (Ukkund et al., 2022)

Feature	Traditional Fermentation	Nanotechnology-Enhanced Fermentation
Contamination control	Limited to sterilization and aseptic techniques	Enhanced contamination prevention through nanomaterial coatings and sensors
Process monitoring and control	Often relies on offline sampling and analysis	Real-time monitoring and precise control through nanosensors
Nutrient delivery	It may be inefficient and lead to fluctuations	Controlled and targeted nutrient delivery through nanoparticles
Product recovery	It may involve complex and time-consuming steps	Simplified and efficient product recovery using magnetic nanoparticles
Overall efficiency and productivity	Can be limited by various factors (e.g., contamination, suboptimal conditions)	Improved efficiency and productivity due to enhanced control, targeted delivery, and contamination prevention

Besides immobilization, nanoparticles can also be used as a way of transferring nutrients and growth factors to microorganisms, hence enhancing their rate of growth and metabolism. For instance, iron oxide nanoparticles have been applied for the introduction of iron a microelement, to microalgae, and as a result, their growth rate and lipid content were enhanced, which is essential for their future use in biofuels (Aratboni et al., 2023). Similar to the above, nanoparticles with nitrogen-containing compounds have been evidenced to enhance the growth and the nitrogenase activity of the nitrogen-fixing bacteria, which forms the keystone in the conversion of atmospheric nitrogen into a form soluble in agricultural production. Furthermore, the nanoparticles can be engineered to affect the gene expression of the microorganisms in providing more of the wanted compound. This help can be achieved through delivery vectors that can bring in the specific genes of interest into a cell or nanoparticles for silencing or activating specific metabolic genes (Khurana et al., 2010). For instance, gold nanoparticles conjugated with CRISPR-Cas9 plasmids were recently employed to transfect those plasmids into yeast cells to precisely edit the latter's genome for beneficial biomolecule generation (Feng et al., 2022).

Enhancing Bioreactor Efficiency

Nanotechnology can also be equally applied to improving the performances of bioreactors that are used in the performance of fermentation processes. However, it can be seen that there is a dire need for improvement in the area of biofilm formation and contamination. Bacteria or any other microorganisms that have developed a biofilm covered in an extracellular polymeric substance threaten the Bioreactor production and the quality of the product (Muffler et al., 2014). Concerning the coatings applied to the bioreactor, it would be possible to employ silver nanoparticles and zinc oxide nanoparticles with antimicrobial activity to design surfaces that cannot encourage microbes to adhere and form the biofilm. This concept has been reported to work well in the actualization of decreasing contamination rates as well as increasing the yields of the final product in many bioprocesses. Besides contamination, nanoparticles can also be used for controlling the key parameters in the bioreactors, such as pH, temperature, and dissolved oxygen concentration (Yavari-Bafghi et al., 2022). For instance, the use of nanoparticles coated with pH-sensitive dye can be used in optical sensors to identify the change in pH during fermentation (Oun et al., 2023). This real-time monitoring aids in regulating various features, including temperature and pressure, required for the described controlled growth of the microorganisms. Similarly, the temperature and dissolved oxygen content can also be monitored by using the nanoparticles, and based on the feedback, the process can be enhanced. The delivery systems using nanoparticles also help introduce different compounds like inducers or inhibitors at some necessary time and required place in the bioreactor. This can be used to manage the cooperation and operations of the microorganisms in a way that

makes them metabolize in the wanted manner, which would give an easier synthesis of the wanted products and a decrease in the formation of unwanted products. For instance, enzyme inhibitors have acted as a tool for viewing how the inhibition of some metabolic pathways affects yeast for ethanol production through the use of nanoparticles (Shahbaz et al., 2022).

6. 2 Industrial and Utilization of the Environment

Bioremediation with Nanotechnology

Bioremediation, which is the process where microorganisms or their enzymes break down pollutants, has also been well-received as a better option and economical (Ullah et al., 2023). Here, the potential of the new directions and prospects for the further enhancement and development of bioremediation technologies based on nanomaterials is assessed, as well as the opportunities for the expansion of the sphere of using microorganisms for the above-mentioned tasks. Several types of nanomaterials have been reported to be effective and promising for bioremediation applications those nanomaterials are Iron oxide nanoparticles (IONPS), titanium dioxide nanoparticles (TiO2 NPs), and carbon nanotubes (CNTs) (Patel et al., 2020). These nanomaterials have a larger surface area and high reactivity through which they can adsorb other contaminants; heavy metals, pesticides, and even organic pollutants. For instance, IONPs were tested in removing arsenic from the groundwater due to their highly adsorptive nature, and they are also good redox-active materials (Kalita & Baruah, 2020). More specifically, while TiO2 NPs are photocatalytic active, this means that the material can oxidize or degrade an organic contaminant upon exposure to light. Because CNTs have a large surface and a special category of electronically active carbon materials, CNTs can capture and degrade various pollutants such as heavy metals and organic dyes (Abbo et al., 2021). Moreover, since the nanoparticles are 'smaller,' they can access regions that might not be accessible to larger particles or microorganisms, or simple pathogens like the soil pore or the water well (Kumar et al., 2012). The above penetration enhancement can translate into enhanced efficiency and effectiveness of the bioremediation processes by fold. Moreover, the nanomaterials can also act as carriers which provide greater efficiency for microorganisms in bioremediation. For instance, nutrients and electron donors can be brought to the contaminated sites in the form of nanosized particles that will provoke the effective functioning and growth of the microorganisms that will ensure the biodegradation process (Fouad et al., 2022). Nanotechnology does guarantee a new technique of bioremediation is formulated. Consequently, enzymes or the entire intact cells can be fixed to the nanoparticles for the degradation of pollutants. The given approach will prove useful in fine-tuning the parameters and selectivity of bioremediation processes and avoiding the side reactions and effects on the environment. For example, the use of laccase functionalized nanoparticles has been applied for the biodegradation of phenolic effluents originating from pulp and paper industries (Moreno et al., 2020).

Application of the Produced Catalysts in Biosynthesis of Bioenergy

The application of nanotechnology in the creation and synthesis of multiple significant bioenergy and biomolecules in the novel generation is gradually increasing. In bioenergy, nanoparticles are used to enhance the yield of biofuels such as biodiesel and bioethanol (Pandey, 2022). For example, MnO2 and Au NPs can improve the reusability of cellulases and lipases that are utilized for conveying biomass through stability, a factor that directly affects biofuel generation. On the same note, it can transport nutrients and growth factors for the microorganisms used in biofuel production, like microalgae and yeast, required to boost their growth and metabolism (Azarpour et al., 2022). This can speak to a higher biomass yield as well as contribute to the yield of more biofuels. Plant-derived biosynthesis process, nanoparticles are used in the synthesis of various biomolecules, such as pharmaceuticals, Nutraceuticals, and industrial chemicals. Microorganisms can be genetically modified using nanoparticles by using genes or enzymes to express recombinant protein or to somehow affect the metabolic activities of the microorganisms (Gholami-Shabani et al., 2016). For example, nanoparticles have been used in transferring into bacteria genes that produce

insulin at large scale since it is a wanted protein. Besides, they can use nanoparticles to immobilize enzymes that are used in biosynthetic processes so that they can be reused, and exhausted pathways can generate more yields. For instance, when synthesizing new semisynthetic penicillins, magnetic nanoparticles have been used to immobilize penicillin acylase, and the enzymes get stabilized hence enhancing the production of antibiotics (Lv et al., 2024).

7. Microbial Interaction and Ecology

Microorganisms are present in almost all environments and thus play a major role in many ecosystems as far as nutrient cycling, decomposition, and biogeochemical cycling processes are concerned (Maier, 2015). However, several aspects of the nanoparticles' interaction with microbes remain unknown, and studying the impact of nanoparticles on these communities is crucial for assessing the possible consequences of nanotechnology for ecosystems and for devising practical and sustainable approaches to nanoparticles and nanotechnology use.

Effects of Nanoparticles on the Natural and Designed World

Various particles can be released in the natural environment through water effluents and through precipitating from the atmosphere apart from being washed from the agricultural land (Sharma, 1994). After nanoparticles are released into the environment, they can Influence microorganisms in various ways. It can adhere directly to the outer or cell surface of microbial cells, it can be endocytosis or any other associated mechanism that can be Phagocytosis, or it may attach to EPS, which is the extra-cellular polymeric substance excreted by microbes (Jaseera & Abdulla, 2021). This can be; the behavior of microbial communities can be enhanced or hampered by these interactions depending on the type of nanoparticle used, the concentration of the nanoparticle used, and the existing environmental conditions. Sometimes it was recorded that the nanoparticles can promote the growth and activities of microorganisms. This could promote the growth of good microorganisms, for instance, nitrogen-fixing bacteria and algae, which are vital in the provision of soil fertility and first-order productivity. Concerning the enzymatic processes, it must also be noted that nanoparticles can also promote the increased synthesis of extracellular enzymes, which facilitate the biodegradation of the large macromolecules of the organic matter (Zhang et al., 2019). For instance, the iron oxide nanoparticles have agonistically demonstrated appreciable enhancement in the ligninolytic enzyme production from the white-rot fungi capable of degrading the lignin, a complex polymer found in plant cell walls. However, these nanoparticles have the following effects on microbial consortia. The toxicity of nanoparticles to microorganisms depends on the particle's chemical composition, size, shape, and charge, where these particles alter the microorganism's growth, normal processes of metabolism, and even destruction of the cell (Hegde et al., 2016). The general toxicity of nanoparticles is yet to be established but it can be ascertained that they can manifest toxicity in several ways towards certain microorganisms based on the specific nanoparticle in existence. Such effects can present themselves in the form of oxidative stress, alteration of the surface of the molecules, mutation or breakage of the DNA and proteins, and alteration of the cell signaling, thus compromising the function of the cell (Bansal & Kaushal, 2014). For instance, silver NP (AgNPs) have been reported to cause damage to bacterial cell membranes and damaged cells by oxidative stress, leading to cell death. Titanium dioxide nanoparticles (TiO2 NPs) are reported to have photosensitizing properties that result in cell toxicity because of the generation of ROS that react with DNA and other cellular molecules (Lagopati et al., 2021).

Particles of such size might also change the versatility and concentration of microbes, which worsens the community process and the services that the microbial community renders (Schrad et al., 2022). Such facts have represented that nanoparticles are effective in inhibiting certain bacterial strains and also support the growth of other bacterial strains by affecting the structure and functionality of such bacterial communities. This then can result in other effects on other processes that occur in an ecosystem, relating to nutrient cycling and decomposition- a concern to the healthy functioning of an ecosystem. Silver nanoparticles, when applied to the soil, could

alter the entire microbial composition in the soil and noted a decrease in beneficial nitrogen-fixing bacteria and an increase in the pathogenic denitrifying bacteria hence causing nitrogen loss from the soil (Kalwani et al., 2022).

8. Investigations of Interactions of Microbes with the Aid of Nanotechnology

Anything related to the analysis of the interference between nanomaterials and microorganisms is quite a challenging task; that is why the study involves microbiologists, nanotechnologists, and ecologists. Several techniques are used to study these interactions, including Several methods can be employed to analyze these interactions, and they include;

Culture-based methods: Such techniques include culturing microorganisms in the nutrient media extracted from soil, water, or any other sample with/without nanoparticles to determine their capacity to grow, remain viable, and be metabolically active (Khalil et al., 2016). This could also provide useful information on the immediate effect of nanoparticles on some select microbial species.

Molecular techniques: Such methodology includes Polymerase Chain Reaction (PCR) and metagenomics, which can be used to estimate and describe the abundance and composition of microorganisms in samples and assess the impact of nanoparticles on microbes' density and resourcefulness in ecosystems (Crossette, 2021). Metagenomics especially enables one to signify all the genetic data of a microbial assemblage primarily via functional genomics studies.

Imaging techniques: For instance, electron microscopy and fluorescence microscopy in which the researchers can record the physical contact between the nanoparticles and the microbial cells and follow as well as detect the occurrence and movements of nanoparticles within the microbial microcosm (Wu et al., 2017). About the structures of nanoparticles and the way they invade the microbial cells, there is electron microscopic data; Tracking the intracellular and tissue mobility of nanoparticles can be done by using fluorescence microscopy.

Omics techniques: Some of the prominent areas of omics that can be applied for M-N interactions are genomics, transcriptomics, proteomics, and metabolomics which examines the molecular behavior of microbes exposed to nanoparticles (Pal et al., 2022). These techniques are useful as they could assist in the determination of how nanoparticles affect microbial cells as well as the response these cells give to the interaction. With such strategies, the researcher will be informed of the various ways through which nanotechnology influences microbial ecology. Similar data are vital when analyzing threats linked with nanomaterials and identifying potential applications of nanomaterials' unique properties in environmental and industrial contexts.

9. Future Prospects and Innovations

The new perspective in a scientific field like microbiology can be nanotechnology, which, according to the prognosis, will develop in the following years and enter spheres such as healthcare, environmental science, and industrial biotechnology. Several areas can be proven in the future and are favorable for applying the aforementioned technique.

Personalized Medicine and Diagnostics: Nanotechnology is now heading the new world of doctors, wherein the medicine to be administered is chosen based on the patient's genes and molecular values (Shanmugam, 2019). Thus, nanotechnology-based diagnostics can enable the identification of etiological agents and their genomes along with the susceptibility profile to the existing antivirals/antibiotics. Molecular epidemiology can help in designing and even patient-specific treatment for the particular strain of the microbe causing the infection. For example, a still emerging fast technology of nanopore sequencing is thought to be capable of diagnosing pathogens on the spot in real time. The clinicians can decide on the right approach to treatment, and this again can result in a reduction of improper uses of broad-spectrum antibiotics (Om et al., 2016). More so, the drug-delivering systems developed through this nanotechnology can be programmed to

deliver drugs at specific schemata, thus diminishing the side aspect and enhancing the efficiency of the drug in the process. Ligands may be attached to the nanoparticles to locate and home in on the body's infected cells or tissues and deliver the drugs to these cells only (Steinmetz, 2010).

Smart Antimicrobials and Therapeutics: At the present moment, there are many approaches to creating efficient antimicrobials, and the next generation of smart antimicrobials that agents like pH or temperature can activate is regarded as the direction of the future regarding the control of infectious diseases. These nanomaterials can release or deliver antimicrobial agents once it has come across the target pathogen; this disposal eases the problem of resistance to antimicrobial agents as well as the negative impact on beneficial microorganisms (Singh et al., 2018). This strategy may enable us to acquire more yield from the existing list of antibiotics and simultaneously restrain the emergence of new types of resistance. Besides, nanotechnology-applied therapies such as photothermal therapy, in which nanoparticles are used to absorb the light energy and convert it into heat to ensure the destruction of bacteria (Du et al., 2023) immunotherapy which is a form of therapy that uses the immune system to combat microbial infections More strategies in the management of microbial infections that are resistant to conventional antibiotic usage include:

Nanobots for Precision Medicine: The concept of introducing miniature active transport agents or small robots that perform particular work in the organism known as nanobots is gradually unfolding in the field of medicine (Zhao et al., 2022). About bottom-up nanobots, disease identification and treatment such as bacterial, viral, and fungal infections can be conducted in a manner that includes drug delivery to the immune system, elimination of pathogens from the bloodstream, and tissue healing. Nanobots are still in the rudimentary stage currently, but the usage of nanobots in the advancement of medical technologies appears to have a fairly broad element (Amato, 2013) the capacity to regulate drugs and surrender them to tissue and cells without impacting the disparate other parts of the physique. For instance, current scientists have developed nanobots that can bring down cancerous tissues; thus, nanobots may also be programmed to get rid of pathogenic bacteria and viruses.

Sustainable Bioprocesses and Biomanufacturing: The enhancement of life essentials, including biofuels, bioplastics, pharmaceuticals, as well as other biomolecules, is achievable using nanoparticles. Nanomaterials used in the bioreactor have the advantages of high mass transfer rates, low fouling, and the stability of biocatalysts. In addition, nanotechnology can help in the creation of new types of biomanufacturing systems: cell-free, using synthetic cells or cells with altered genes (Qaiser et al., 2023).

Environmental Monitoring and Remediation: The facilities that can be offered by nanotechnology-based sensors for environmental conditions in real-time cannot be overemphasized (Maynard, 2007). For instance, nanosensors can detect many analytes, including heavy metals, pesticides, toxins, and pathogenic microbes in water, soil, and air. This makes it easier to institute early warning mechanisms concerning contamination of the environment and normally intervenes in this matter on time. On a similar note, nanotechnology applied in the bioremediation process, that is, the utilization of nanoparticles and or the enhancement of the activities of the bioremediation microorganisms to combat pollution, has been pointed to as one that has the potential to restore the polluted environment (Benjamin et al., 2019). Nutrient and electron donors can also be introduced into the contaminated site using nanoparticles where microorganisms that are used for the bioremediation process are also made to grow (Ramezani et al., 2021).

Synthetic Biology and Nanobiohybrids: Nanotechnology with Synthetic Biology is opening new opportunities to build new biological systems with better characteristics than the current systems (Le Feuvre & Scrutton, 2018). While incorporating synthetic biology tools and nanomaterials, scientists are in a position to design and develop nanohybrids with new functions, including photosynthesis, the manufacture of biofuels, and even self-recovering materials. For instance, researchers have developed an artificial photosynthesis system that uses nanotechnologies

to utilize light energy and store the energy as chemical energy (Kathpalia & Verma, 2021). It involves the capability of developing electricity out of such systems by probably displacing the fossil fuel systems. Thus, it can be concluded that the future of nanotechnology in microbiology is quite bright. It is pervaded with great potential in various fields, and if implemented, it will bring a hugely significant and positive change to many aspects of human life, including social, medical, environmental, and industrial.

10. Conclusion

Nanotechnology and microbiology revolutionized the study and control of microorganisms, leading to improvements in microbial detection, anti-microbial designs, and biomanufacturing. Nanotechnology has been applied in healthcare, environmental management, and industrial biotechnology, with ultramodern and selective nanosensors and biosensors enhancing pathogen identification and accelerating disease detection. Advances in nanotechnology also address antibiotic resistance by combining antibiotics with nanoparticle-based antimicrobials (NBAs), which can be managed for multiple target sites, posing a threat to bacterial resistance. They can also be used with known antibiotics to widen the spectrum and or to act behind the bacterial factors of resistance. Morphological and mechanical characteristics of NBAs also contribute towards augmenting the therapeutic outcome by promoting the utility of the targeted drug delivery systems on nanoparticles in such a way that extends the effect of the antimicrobial agents only to the involved tissues and organs and thus minimizes the overall impact on the rest of the body tissues and organs as well as reduce their required dosage. Other areas where nanotechnology is offering much help are Bioremediation techniques, pollution control, and monitoring. Nanoiron oxide, titanium dioxide, and carbon nanotubes are some of the nanomaterials well known for the adsorption and degradation of environmental pollutants, including heavy metals, pesticides, and organic pollutants. Likewise; nanosensors have been employed in establishing the presence of prospective poisonous microorganisms and toxins in water and soil, continuously checking the quality of the environment and providing ways for managers to prevent occurrences of pollution when these are suspected. When modeling the relationships between biotechnology and nanotechnology, one of the fields of application is the improvement of industrial bioprocesses. Nanocarriers, a type of support material, are used to immobilize enzymes and whole cells, which improves their stability and reusability, improving the production of vital bioproducts such as biofuels, enzymes, and pharmaceuticals. The fouling and mass transfer rates are again improving the process and efficiency of bioprocesses by using nanotechnology-assisted bioreactors. It is specifically in the field of microbiology that the future has appeared bright in the employment of nanotechnology, given the numerous possibilities that could be imparted to society concerning health, the surrounding environment, and the whole industry. Today's academic studies in the field of P4 medicine, on smart antimicrobials, nanobots, and precision medicine together with synthetic biology, quell a breakthrough in the future novelty therapeutics, diagnostics, and green bioprocesses. But that requires moving forward with the proper precaution as well as the safety of human beings alongside safety in the use of nanotechnology carrying out safety measures on top of the proper ethical use of the technology. Thus, the hybridization of nanotechnology and microbiology is the key to upgrading science and technology. Thus, as we continue unveiling the face of microbes at the nano-scale, we expect many opportunities to improve human health and preserve the environment and wait in anticipation of a sustainable future. Thus, in walking the path that continues in front of us, we have numerous opposite scenarios in the future, and the union of nanotechnology and microbiology is the key to a better future.

References

A Stout, D. (2015). Recent advancements in carbon nanofiber and carbon nanotube applications in drug delivery and tissue engineering. Current Pharmaceutical Design, 21(15), 2037-2044.

Abbo, H. S., Gupta, K. C., Khaligh, N. G., & Titinchi, S. J. (2021). Carbon nanomaterials for wastewater treatment. ChemBioEng reviews, 8(5), 463-489.

Abdel-Salam, M., Omran, B., Whitehead, K., & Baek, K.-H. (2020). Superior properties and biomedical applications of microorganism-derived fluorescent quantum dots. Molecules, 25(19), 4486.

Abdelaziz, M. M., Hefnawy, A., Anter, A., Abdellatif, M. M., Khalil, M. A., & Khalil, I. A. (2022). Silica-coated magnetic nanoparticles for vancomycin conjugation. ACS omega, 7(34), 30161-30170.

Adebayo, A. E., Oke, A. M., Lateef, A., Oyatokun, A. A., Abisoye, O. D., Adiji, I. P., Fagbenro, D. O., Amusan, T. V., Badmus, J., & Asafa, T. (2019). Biosynthesis of silver, gold and silver–gold alloy nanoparticles using Persea americana fruit peel aqueous extract for their biomedical properties. Nanotechnology for Environmental Engineering, 4, 1-15.

Ajayi, R. F., Barry, S., Nkuna, M., Ndou, N., Rakgotho, T., Nqunqa, S., Ngema, N., Thipe, V., & Muluadzi, T. (2022). Nanoparticles in biosensor development for the detection of pathogenic bacteria in water. In Emerging freshwater pollutants (pp. 331-358). Elsevier.

ALBERT, H. M. (2023). Nanotechnology: Physicochemical and Green Synthesis, Characterizations and Applications. Perfect Writer Publishing.

Alim, S., Vejayan, J., Yusoff, M. M., & Kafi, A. (2018). Recent uses of carbon nanotubes & gold nanoparticles in electrochemistry with application in biosensing: A review. Biosensors and Bioelectronics, 121, 125-136.

Amato, P. (2013). Swarm-intelligence strategy for diagnosis of endogenous diseases by nanobots.

Aratboni, H. A., Rafiei, N., Allaf, M. M., Abedini, S., Rasheed, R. N., Seif, A., Barati, B., Wang, S., & Morones-Ramírez, J. R. (2023). Nanotechnology: an outstanding tool for increasing and better exploitation of microalgae valuable compounds. Algal Research, 71, 103019.

Aschberger, K., Micheletti, C., Sokull-Klüttgen, B., & Christensen, F. M. (2011). Analysis of currently available data for characterising the risk of engineered nanomaterials to the environment and human health—lessons learned from four case studies. Environment international, 37(6), 1143-1156.

Awogbemi, O., & Von Kallon, D. V. (2024). Recent advances in the application of nanomaterials for improved biodiesel, biogas, biohydrogen, and bioethanol production. Fuel, 358, 130261.

Azarpour, A., Zendehboudi, S., Mohammadzadeh, O., Rajabzadeh, A. R., & Chatzis, I. (2022). A review on microalgal biomass and biodiesel production through Co-cultivation strategy. Energy Conversion and Management, 267, 115757.

Babaniyi, B. R., Ogundele, O. D., Thompson, S. O., & Aransiola, S. A. (2023). Microbial Nanomaterial Synthesis: Types and Applications. In Microbial Processes for Synthesizing Nanomaterials (pp. 3-28). Springer.

Balderrama-González, A.-S., Piñón-Castillo, H.-A., Ramírez-Valdespino, C.-A., Landeros-Martínez, L.-L., Orrantia-Borunda, E., & Esparza-Ponce, H.-E. (2021). Antimicrobial resistance and inorganic nanoparticles. International journal of molecular sciences, 22(23), 12890.

Bamal, D., Singh, A., Chaudhary, G., Kumar, M., Singh, M., Rani, N., Mundlia, P., & Sehrawat, A. R. (2021). Silver nanoparticles biosynthesis, characterization, antimicrobial activities, applications, cytotoxicity and safety issues: An updated review. Nanomaterials, 11(8), 2086.

Bansal, M., & Kaushal, N. (2014). Oxidative stress mechanisms and their modulation (Vol. 9). Springer.

Barros Alvarez, X. (2018). Aminoacyl-tRNA Synthetases as Targets for Structure Guided Drug Design (SGDD) Against Pathogenic Protozoa and Bacteria

Benjamin, S. R., Lima, F. D., Florean, E. O. P. T., & Guedes, M. I. F. (2019). Current trends in nanotechnology for bioremediation. International Journal of Environment and Pollution, 66(1-3), 19-40.

Bhardwaj, S. K., Bhardwaj, N., Kumar, V., Bhatt, D., Azzouz, A., Bhaumik, J., Kim, K.-H., & Deep, A. (2021). Recent progress in nanomaterial-based sensing of airborne viral and bacterial pathogens. Environment international, 146, 106183.

Biswas, P., Polash, S. A., Dey, D., Kaium, M. A., Mahmud, A. R., Yasmin, F., Baral, S. K., Islam, M. A., Rahaman, T. I., & Abdullah, A. (2023). Advanced implications of nanotechnology in disease control and environmental perspectives. Biomedicine & Pharmacotherapy, 158, 114172.

Brar, B., Marwaha, S., Poonia, A. K., Koul, B., Kajla, S., & Rajput, V. D. (2023). Nanotechnology: a contemporary therapeutic approach in combating infections from multidrug-resistant bacteria. Archives of Microbiology, 205(2), 62.

Campora, S., & Ghersi, G. (2022). Recent developments and applications of smart nanoparticles in biomedicine. Nanotechnology Reviews, 11(1), 2595-2631.

Capek, I., & Capek, I. (2017). Noble metal nanoparticles. Noble Metal Nanoparticles: Preparation, Composite Nanostructures, Biodecoration and Collective Properties, 125-210.

Chakraborty, U., Kaur, G., & Chaudhary, G. R. (2021). Development of environmental nanosensors for detection monitoring and assessment. New frontiers of nanomaterials in environmental science, 91-143.

Chen, W. (2008). Nanoparticle fluorescence based technology for biological applications. Journal of nanoscience and nanotechnology, 8(3), 1019-1051.

Coto-García, A. M., Sotelo-González, E., Fernández-Argüelles, M. T., Pereiro, R., Costa-Fernández, J. M., & Sanz-Medel, A. (2011). Nanoparticles as fluorescent labels for optical imaging and sensing in genomics and proteomics. Analytical and bioanalytical chemistry, 399, 29-42.

Crossette, E. (2021). Microbial Diversity and Antimicrobial Resistance in Land Applied Manure

Das, S. K., & Marsili, E. (2011). Bioinspired metal nanoparticle: synthesis, properties and application. Croacia: InTech.

Davodabadi, F., Mirinejad, S., Fathi-Karkan, S., Majidpour, M., Ajalli, N., Sheervalilou, R., Sargazi, S., Rozmus, D., Rahdar, A., & Diez-Pascual, A. M. (2023). Aptamer-functionalized quantum dots as theranostic nanotools against cancer and bacterial infections: a comprehensive overview of recent trends. Biotechnology Progress, 39(5), e3366.

Dester, E., & Alocilja, E. (2022). Current methods for extraction and concentration of foodborne bacteria with glycan-coated magnetic nanoparticles: A review. Biosensors, 12(2), 112.

Dey, N., Kamatchi, C., Vickram, A., Anbarasu, K., Thanigaivel, S., Palanivelu, J., Pugazhendhi, A., & Ponnusamy, V. K. (2022). Role of nanomaterials in deactivating multiple drug resistance efflux pumps–A review. Environmental research, 204, 111968.

Du, Y., Zhou, J., He, F., Zang, P., Gong, H., Liu, C., & Yang, P. (2023). A bright future: advanced nanotechnology-assisted microwave therapy. Nano Today, 52, 101963.

Eltzov, E., Marks, R. S., Voost, S., Wullings, B. A., & Heringa, M. B. (2009). Flow-through real time bacterial biosensor for toxic compounds in water. Sensors and Actuators B: Chemical,

142(1), 11-18.

Fatima, F., Siddiqui, S., & Khan, W. A. (2021). Nanoparticles as novel emerging therapeutic antibacterial agents in the antibiotics resistant era. Biological Trace Element Research, 199(7), 2552-2564.

Feng, S., Wang, Z., Li, A., Xie, X., Liu, J., Li, S., Li, Y., Wang, B., Hu, L., & Yang, L. (2022). Strategies for high-efficiency mutation using the CRISPR/Cas system. Frontiers in Cell and Developmental Biology, 9, 803252.

Fouad, F. A., Youssef, D. G., Shahat, F. M., & Abd El-Ghany, M. N. (2022). Role of microorganisms in biodegradation of pollutants. In Handbook of biodegradable materials (pp. 1-40). Springer.

Gholami-Shabani, M., Shams-Ghahfarokhi, M., Gholami-Shabani, Z., & Razzaghi-Abyaneh, M. (2016). Microbial enzymes: current features and potential applications in nanobiotechnology. Advances and applications through fungal nanobiotechnology, 91-127.

Gupta, T., & Gupta, T. (2018). Graphene. Carbon: The Black, the Gray and the Transparent, 197-228.

Gurtovenko, A. A., Anwar, J., & Vattulainen, I. (2010). Defect-mediated trafficking across cell membranes: insights from in silico modeling. Chemical Reviews, 110(10), 6077-6103.

Han, J., Zhao, D., Li, D., Wang, X., Jin, Z., & Zhao, K. (2018). Polymer-based nanomaterials and applications for vaccines and drugs. Polymers, 10(1), 31.

Hegde, K., Brar, S. K., Verma, M., & Surampalli, R. Y. (2016). Current understandings of toxicity, risks and regulations of engineered nanoparticles with respect to environmental microorganisms. Nanotechnology for Environmental Engineering, 1, 1-12.

Hegde, M., Pai, P., Shetty, M. G., & Babitha, K. S. (2022). Gold nanoparticle based biosensors for rapid pathogen detection: A review. Environmental Nanotechnology, Monitoring & Management, 18, 100756.

Holban, A. M., Gestal, M. C., & Grumezescu, A. M. (2016). Control of biofilm-associated infections by signaling molecules and nanoparticles. International journal of pharmaceutics, 510(2), 409-418.

Huang, M., Ye, K., Hu, T., Liu, K., You, M., Wang, L., & Qin, H. (2021). Silver nanoparticles attenuate the antimicrobial activity of the innate immune system by inhibiting neutrophil-mediated phagocytosis and reactive oxygen species production. International journal of nanomedicine, 1345-1360.

Ivanova, A., Ivanova, K., & Tzanov, T. (2018). Inhibition of quorum-sensing: A new paradigm in controlling bacterial virulence and biofilm formation. biotechnological applications of quorum sensing inhibitors, 3-21.

Jaseera, K., & Abdulla, T. (2021). Microbial EPS as Immunomodulatory Agents. Microbial Exopolysaccharides as Novel and Significant Biomaterials, 235-264.

Jayakumar, A., Mathew, S., Radoor, S., Kim, J. T., Rhim, J.-W., & Siengchin, S. (2023). Recent advances in two-dimensional nanomaterials: Properties, antimicrobial, and drug delivery application of nanocomposites. Materials Today Chemistry, 30, 101492.

Kalita, E., & Baruah, J. (2020). Environmental remediation. In Colloidal metal oxide nanoparticles (pp. 525-576). Elsevier.

Kalwani, M., Chakdar, H., Srivastava, A., Pabbi, S., & Shukla, P. (2022). Effects of nanofertilizers on soil and plant-associated microbial communities: Emerging trends and perspectives. Chemosphere, 287, 132107.

Kathpalia, R., & Verma, A. K. (2021). Bio-inspired nanoparticles for artificial photosynthesis. Materials Today: Proceedings, 45, 3825-3832.

Khalil, N., El-Sheshtawy, H., & Aman, D. (2016). Elimination of different heavy metals in contaminated soil using indigenous microorganisms and nanoparticle in the El-Rahawy village, Egypt. Egypt. J. Mater. Environ. Sci, 7, 2603-2616.

Khaliq, A., Kafafy, R., Salleh, H. M., & Faris, W. F. (2012). Enhancing the efficiency of polymerase chain reaction using graphene nanoflakes. Nanotechnology, 23(45), 455106.

Khan, R. T., & Rasool, S. (2023). Nanotechnology: A new strategy to combat bacterial infections and antibiotic resistant bacteria. In Nanotechnology and Human Health (pp. 167-190). Elsevier.

Khataee, A., & Mansoori, G. A. (2011). Nanostructured titanium dioxide materials: properties, preparation and applications. World scientific.

Khorsandi, K., Hosseinzadeh, R., Sadat Esfahani, H., Keyvani-Ghamsari, S., & Ur Rahman, S. (2021). Nanomaterials as drug delivery systems with antibacterial properties: current trends and future priorities. Expert Review of Anti-infective Therapy, 19(10), 1299-1323.

Khurana, B., K Goyal, A., Budhiraja, A., Arora, D., & P Vyas, S. (2010). siRNA delivery using nanocarriers-an efficient tool for gene silencing. Current gene therapy, 10(2), 139-155.

Kimbrell, G. A. (2009). Governance of nanotechnology and nanomaterials: principles, regulation, and renegotiating the social contract. Journal of Law, Medicine & Ethics, 37(4), 706-723.

Konwar, A. N., Hazarika, S. N., Bharadwaj, P., & Thakur, D. (2022). Emerging non-traditional approaches to combat antibiotic resistance. Current microbiology, 79(11), 330.

Kramer, I. J., & Sargent, E. H. (2014). The architecture of colloidal quantum dot solar cells: materials to devices. Chemical Reviews, 114(1), 863-882.

Kumar, A., Sharma, K., & Dixit, A. R. (2020). Carbon nanotube-and graphene-reinforced multiphase polymeric composites: review on their properties and applications. Journal of Materials Science, 55(7), 2682-2724.

Kumar, R., Rawat, K. S., & Mishra, A. K. (2012). Nanoparticles in the soil environment and their behaviour: An overview. Journal of Applied and Natural Science, 4(2), 310-324.

Lagopati, N., Evangelou, K., Falaras, P., Tsilibary, E.-P. C., Vasileiou, P. V., Havaki, S., Angelopoulou, A., Pavlatou, E. A., & Gorgoulis, V. G. (2021). Nanomedicine: Photo-activated nanostructured titanium dioxide, as a promising anticancer agent. Pharmacology & therapeutics, 222, 107795.

Le Feuvre, R. A., & Scrutton, N. S. (2018). A living foundry for synthetic biological materials: a synthetic biology roadmap to new advanced materials. Synthetic and Systems Biotechnology, 3(2), 105-112.

León-Buitimea, A., Garza-Cárdenas, C. R., Román-García, M. F., Ramírez-Díaz, C. A., Ulloa-Ramírez, M., & Morones-Ramírez, J. R. (2022). Nanomaterials-based combinatorial therapy as a strategy to combat antibiotic resistance. Antibiotics, 11(6), 794.

León-Silva, S., Fernández-Luqueño, F., & López-Valdez, F. (2018). Engineered nanoparticles: are they an inestimable achievement or a health and environmental concern? Agricultural

nanobiotechnology: Modern agriculture for a sustainable future, 183-212.

Leong, C. Y., Wahab, R. A., Lee, S. L., Ponnusamy, V. K., & Chen, Y.-H. (2023). Current perspectives of metal-based nanomaterials as photocatalytic antimicrobial agents and their therapeutic modes of action: A review. Environmental research, 227, 115578.

Ling, K. (2018). ENGINEERING THERAPEUTIC AVRA NANOPARTICLES WITH ENHANCED UPTAKE AND INTRACELLULAR DELIVERY WITH APPLICATIONS IN INFLAMMATORY BOWEL DISEASE Georgia Institute of Technology].

Liosis, C., Papadopoulou, A., Karvelas, E., Karakasidis, T. E., & Sarris, I. E. (2021). Heavy metal adsorption using magnetic nanoparticles for water purification: A critical review. Materials, 14(24), 7500.

Liu, Y., Li, J., Tschirhart, T., Terrell, J. L., Kim, E., Tsao, C. Y., Kelly, D. L., Bentley, W. E., & Payne, G. F. (2017). Connecting biology to electronics: Molecular communication via redox modality. Advanced healthcare materials, 6(24), 1700789.

Long, Y.-T., & Jing, C. (2014). Localized surface plasmon resonance based nanobiosensors. Springer.

Loots, R. (2016). Biofilms as multifunctional surface coatings and adaptive systems: a biomimetic approach Stellenbosch: Stellenbosch University].

Lv, Z., Wang, Z., Wu, S., & Yu, X. (2024). Enhanced catalytic performance of penicillin G acylase by covalent immobilization onto functionally-modified magnetic Ni0. 4Cu0. 5Zn0. 1Fe2O4 nanoparticles. PloS one, 19(1), e0297149.

Madkour, L. H. (2019). Function of reactive oxygen species (ROS) inside the living organisms and sources of oxidants. Pharm. Sci. Anal. Res. J, 2, 180023.

Maier, R. M. (2015). Biogeochemical cycling. In Environmental microbiology (pp. 339-373). Elsevier.

Makama, S. L. (2016). An in vitro–in vivo integrated approach for hazard and risk assessment of silver nanoparticles for soil organisms Wageningen University and Research].

Maksimova, Y. G. (2019). Microorganisms and carbon nanotubes: interaction and applications. Applied biochemistry and microbiology, 55, 1-12.

Maldonado-Camargo, L., Unni, M., & Rinaldi, C. (2017). Magnetic characterization of iron oxide nanoparticles for biomedical applications. Biomedical Nanotechnology: Methods and Protocols, 47-71.

Manikandan, S., Subbaiya, R., Biruntha, M., Krishnan, R. Y., Muthusamy, G., & Karmegam, N. (2022). Recent development patterns, utilization and prospective of biofuel production: Emerging nanotechnological intervention for environmental sustainability–A review. Fuel, 314, 122757.

Marchioni, M., Jouneau, P.-H., Chevallet, M., Michaud-Soret, I., & Deniaud, A. (2018). Silver nanoparticle fate in mammals: Bridging in vitro and in vivo studies. Coordination Chemistry Reviews, 364, 118-136.

Markandan, K., Tiong, Y. W., Sankaran, R., Subramanian, S., Markandan, U. D., Chaudhary, V., Numan, A., Khalid, M., & Walvekar, R. (2022). Emergence of infectious diseases and role of advanced nanomaterials in point-of-care diagnostics: a review. Biotechnology and Genetic Engineering Reviews, 1-89.

Maynard, A. D. (2007). Nanotechnologies: overview and issues. Nanotechnology–Toxicological

Issues and Environmental Safety and Environmental Safety, 1-14.

Mikhailova, E. O. (2021). Gold nanoparticles: Biosynthesis and potential of biomedical application. Journal of Functional Biomaterials, 12(4), 70.

Moreno, A. D., Ibarra, D., Eugenio, M. E., & Tomás-Pejó, E. (2020). Laccases as versatile enzymes: from industrial uses to novel applications. Journal of Chemical Technology & Biotechnology, 95(3), 481-494.

Morse, S. S. (2012). Public health surveillance and infectious disease detection. Biosecurity and bioterrorism: biodefense strategy, practice, and science, 10(1), 6-16.

Mozafari, M., Torkaman, S., Karamouzian, F. M., Rasti, B., & Baral, B. (2021). Antimicrobial applications of nanoliposome encapsulated silver nanoparticles: A potential strategy to overcome bacterial resistance. Current Nanoscience, 17(1), 26-40.

Muffler, K., Lakatos, M., Schlegel, C., Strieth, D., Kuhne, S., & Ulber, R. (2014). Application of biofilm bioreactors in white biotechnology. Productive biofilms, 123-161.

Mumtaz, M., Baqar, Z., Hussain, N., Bilal, M., Azam, H. M. H., & Iqbal, H. M. (2022). Application of nanomaterials for enhanced production of biodiesel, biooil, biogas, bioethanol, and biohydrogen via lignocellulosic biomass transformation. Fuel, 315, 122840.

Murugaiyan, J., Kumar, P. A., Rao, G. S., Iskandar, K., Hawser, S., Hays, J. P., Mohsen, Y., Adukkadukkam, S., Awuah, W. A., & Jose, R. A. M. (2022). Progress in alternative strategies to combat antimicrobial resistance: Focus on antibiotics. Antibiotics, 11(2), 200.

Nasrollahzadeh, M., Sajadi, S. M., Sajjadi, M., & Issaabadi, Z. (2019). An introduction to nanotechnology. In Interface science and technology (Vol. 28, pp. 1-27). Elsevier.

Om, C., Daily, F., Vlieghe, E., McLaughlin, J. C., & McLaws, M.-L. (2016). "If it'sa broad spectrum, it can shoot better": inappropriate antibiotic prescribing in Cambodia. Antimicrobial Resistance & Infection Control, 5, 1-8.

Oun, A. A., Roy, S., Shin, G. H., Yoo, S., & Kim, J. T. (2023). pH-sensitive smart indicators based on cellulose and different natural pigments for tracing kimchi ripening stages. International journal of biological macromolecules, 242, 124905.

Pal, S., Jana, A., Mondal, K. C., & Halder, S. K. (2022). Omics Approach to Understanding Microbial Diversity. In Biotechnological Advances for Microbiology, Molecular Biology, and Nanotechnology (pp. 25-38). Apple Academic Press.

Pandey, M. D. (2022). Perspective of nanomaterials for sustainable biofuel and bioenergy production. Materials Letters, 313, 131686.

Pandey, S., & Bodas, D. (2020). High-quality quantum dots for multiplexed bioimaging: A critical review. Advances in Colloid and Interface Science, 278, 102137.

Patel, H. K., Kalaria, R. K., & Khimani, M. R. (2020). Nanotechnology: a promising tool for bioremediation. Removal of toxic pollutants through microbiological and tertiary treatment, 515-547.

Patil, M. P., & Kim, G.-D. (2017). Eco-friendly approach for nanoparticles synthesis and mechanism behind antibacterial activity of silver and anticancer activity of gold nanoparticles. Applied microbiology and biotechnology, 101, 79-92.

Qaiser, H., Uzair, M., Arshad, A., Khattak, J. Z. K., & Bashir, S. (2023). Cell-Free Synthetic Biology: The Novel Approach Towards the Biotechnological Applications. In Applications of Synthetic Biology in Health, Energy, and Environment (pp. 22-41). IGI Global.

Rai, M., Ingle, A. P., Gaikwad, S., Dussán, K. J., & da Silva, S. S. (2017). Role of nanoparticles in enzymatic hydrolysis of lignocellulose in ethanol. Nanotechnology for bioenergy and biofuel production, 153-171.

Ramezani, M., Rad, F. A., Ghahari, S., Ghahari, S., & Ramezani, M. (2021). Nano-bioremediation application for environment contamination by microorganism. Microbial Rejuvenation of Polluted Environment: Volume 2, 349-378.

Rawashdeh, R., & Haik, Y. (2009). Antibacterial mechanisms of metallic nanoparticles: a review. Dynamic biochemistry, process biotechnology and molecular biology, 3(2), 12-20.

Renteria, J. D., Nika, D. L., & Balandin, A. A. (2014). Graphene thermal properties: applications in thermal management and energy storage. Applied sciences, 4(4), 525-547.

Ruedas-Rama, M. J., Walters, J. D., Orte, A., & Hall, E. A. (2012). Fluorescent nanoparticles for intracellular sensing: a review. Analytica chimica acta, 751, 1-23.

Salouti, M., & Ahangari, A. (2014). Nanoparticle based drug delivery systems for treatment of infectious diseases (Vol. 552). InTech London, UK.

Schrad, N., Pensky, J., Gorski, G., Beganskas, S., Fisher, A. T., & Saltikov, C. (2022). Soil characteristics and redox properties of infiltrating water are determinants of microbial communities at managed aquifer recharge sites. FEMS Microbiology Ecology, 98(12), fiac130.

Sen, S., Banerjee, A., & Acharjee, A. (1999). Nanotechnology: Shaping the world atom by atom. Nstc/Ct.

Shabatina, T. I., Vernaya, O. I., Shabatin, V. P., & Melnikov, M. Y. (2020). Magnetic nanoparticles for biomedical purposes: Modern trends and prospects. Magnetochemistry, 6(3), 30.

Shahbaz, A., Hussain, N., Saleem, M. Z., Saeed, M. U., Bilal, M., & Iqbal, H. M. (2022). Nanoparticles as stimulants for efficient generation of biofuels and renewables. Fuel, 319, 123724.

Shanmugam, S. (2019). Nanotechnology. MJP Publisher.

Shanmugasundaram, T., Radhakrishnan, M., Gopikrishnan, V., Kadirvelu, K., & Balagurunathan, R. (2017). Biocompatible silver, gold and silver/gold alloy nanoparticles for enhanced cancer therapy: in vitro and in vivo perspectives. Nanoscale, 9(43), 16773-16790.

Sharifi, M., Attar, F., Saboury, A. A., Akhtari, K., Hooshmand, N., Hasan, A., El-Sayed, M. A., & Falahati, M. (2019). Plasmonic gold nanoparticles: Optical manipulation, imaging, drug delivery and therapy. Journal of Controlled Release, 311, 170-189.

Sharma, B. (1994). Water pollution. Krishna Prakashan Media.

Sharma, P. K., Dorlikar, S., Rawat, P., Malik, V., Vats, N., Sharma, M., Rhyee, J. S., & Kaushik, A. K. (2021). Nanotechnology and its application: a review. Nanotechnology in cancer management, 1-33.

Shen, Y., Xia, Y., Yang, E., Ye, Z., Ding, Y., Tu, J., Zhang, Y., & Xu, P. (2020). A polyoxyethylene sorbitan oleate modified hollow gold nanoparticle system to escape macrophage phagocytosis designed for triple combination lung cancer therapy via LDL-R mediated endocytosis. Drug Delivery, 27(1), 1342-1359.

Sherje, A. P., Jadhav, M., Dravyakar, B. R., & Kadam, D. (2018). Dendrimers: A versatile nanocarrier for drug delivery and targeting. International journal of pharmaceutics, 548(1), 707-720.

Singh, P., Garg, A., Pandit, S., Mokkapati, V., & Mijakovic, I. (2018). Antimicrobial effects of biogenic nanoparticles. Nanomaterials, 8(12), 1009.

Skalka, A. M. (2018). Discovering retroviruses: beacons in the biosphere. Harvard University Press.

Smola-Dmochowska, A., Lewicka, K., Macyk, A., Rychter, P., Pamuła, E., & Dobrzyński, P. (2023). Biodegradable polymers and polymer composites with antibacterial properties. International journal of molecular sciences, 24(8), 7473.

Steinmetz, N. F. (2010). Viral nanoparticles as platforms for next-generation therapeutics and imaging devices. Nanomedicine: Nanotechnology, Biology and Medicine, 6(5), 634-641.

Syed, M. A., & Bokhari, S. (2011). Gold nanoparticle based microbial detection and identification. Journal of biomedical nanotechnology, 7(2), 229-237.

Tanji, T. (2009). Oversight policy in synthetic biology.

Thakur, V. K., & Thakur, M. K. (2018). Chemical functionalization of carbon nanomaterials. CRC Press Warentown (NJ.

Thomsen, T., & Klok, H.-A. (2021). Chemical cell surface modification and analysis of nanoparticle-modified living cells. ACS Applied Bio Materials, 4(3), 2293-2306.

Ujica, M. A., Paltinean, G. A., Mocanu, A., & Tomoaia-Cotisel, M. (2020). Silver and gold nanoparticles: challenges and perspectives. Acad. Rom. Sci. Ann.-Ser. Biol. Sci, 9, 97-139.

Ukkund, S. J., Alke, B., Taqui, S. N., & Syed, U. T. (2022). Role of microbial nanotechnology in energy devices. In Handbook of Microbial Nanotechnology (pp. 517-547). Elsevier.

Ullah, N. M., Bashir, K., Ali, Q., Amin, M. U., Yilmaz, S., & Amin, F. U. (2023). An Overview of Bioremediation: An Ecofriendly Approach for Heavy Metals Removal.

Urban, P., Jose Valle-Delgado, J., Moles, E., Marques, J., Diez, C., & Fernandez-Busquets, X. (2012). Nanotools for the delivery of antimicrobial peptides. Current Drug Targets, 13(9), 1158-1172.

Uruén, C., Chopo-Escuin, G., Tommassen, J., Mainar-Jaime, R. C., & Arenas, J. (2020). Biofilms as promoters of bacterial antibiotic resistance and tolerance. Antibiotics, 10(1), 3.

Wu, F., Harper, B. J., & Harper, S. L. (2017). Differential dissolution and toxicity of surface functionalized silver nanoparticles in small-scale microcosms: Impacts of community complexity. Environmental Science: Nano, 4(2), 359-372.

Wu, S., Duan, N., Gu, H., Hao, L., Ye, H., Gong, W., & Wang, Z. (2016). A Review of the Methods for Detection of Staphylococcus aureus Enterotoxins. Toxins, 8(7), 176.

Yavari-Bafghi, M., Shavandi, M., Dastgheib, S. M. M., & Amoozegar, M. A. (2022). Simultaneous application of CaO2 nanoparticles and microbial consortium in Small Bioreactor Chambers (SBCs) for phenol removal from groundwater. Process Safety and Environmental Protection, 160, 465-477.

Zanchetta, G., Lanfranco, R., Giavazzi, F., Bellini, T., & Buscaglia, M. (2017). Emerging applications of label-free optical biosensors. Nanophotonics, 6(4), 627-645.

Zhang, L., Zhu, Y., Zhang, J., Zeng, G., Dong, H., Cao, W., Fang, W., Cheng, Y., Wang, Y., & Ning, Q. (2019). Impacts of iron oxide nanoparticles on organic matter degradation and microbial enzyme activities during agricultural waste composting. Waste Management, 95, 289-297.

Zhao, S., Sun, D., Zhang, J., Lu, H., Wang, Y., Xiong, R., & Grattan, K. (2022). Actuation and biomedical development of micro-/nanorobots–A review. Materials Today Nano, 18, 100223.

Zhu, K., Dietrich, R., Didier, A., Doyscher, D., & Märtlbauer, E. (2014). Recent developments

in antibody-based assays for the detection of bacterial toxins. Toxins, 6(4), 1325-1348.

About The Authors

Sundas Ashraf received her Bachelor degree in 2023 from Cholistan university of veterinary and Animal Sciences, Bahawalpur, Pakistan and is currently pursuing Her M.phil from University of Agriculture Faisalabad, Pakistan. Her Research interest Include, Epidemiology, public Health, Nanotechnology and Food safety.

Email: sundasashraf2001@gmail.com ORCID:0009-0002-8109-1209

Maria Nazir is an MPhil Scholar of Microbiology at the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur, Pakistan. She is involved in a National Research Program for Universities (NRPU) Project, with research interests in Molecular Characterization. She has submitted abstracts to various conferences and authored and coauthored of several book chapters. Her research focuses on the isolation and Molecular characterization of Corynebacterium pseudotuberculosis and their applications in promoting animal health. Her interested research criteria are based on genetics, molecular biology, and bioinformatics.

Email: nazirmaria545@gmail.com ORCID 0009-0004-6714-6212

Muhammad Haris Khan received his MPhil in biochemistry in 2022 from the University of Veterinary and Animal Sciences, Lahore Pakistan. He is a Researcher of Biochemistry, Molecular Biology, and Genetics at the University of Veterinary and Animal Sciences, Lahore Pakistan. His research interests include predictive breeding models, Genetic selection, biochemistry, and molecular Biology.

Email: muhammadhariskhan92@gmail.com ORCID: 0009-0002-4778-0828

Miss Iqra Fazil completed her MPhil in Microbiology in 2024 from Khyber Medical University Peshawar. Her research interests include biosafety and biosecurity, animal model handling, infectious disease, genetic disease, genomics, and molecular diagnosis.

Email: iqrafaziluop@gmail.com ORCID:0009-0009-3545-7055

Mr. Atif Ahmed received his M. Phil. 2023 from CEMB, University of the Punjab l, Lahore. His research includes microbiology, molecular biology, and proteomics. He has published one research article in an international journal.

Email: atif.ahmed@cemb.edu.pk ORCID: 0000-0001-9571-1304

Minahal Fatima and She is doing M.Phil in Zoology, Wildlife and Fisheries from University of Agriculture, Fasilabad, Pakistan. Her research interest includes fish survival via changing the environmental factor. Not only the fish survive it also counts the progeny's survival. She has only one paper in International Journal and 12 Chapters in national and international Journals.

Email: fatimaabdulhameed08@gmail.com ORCID: 0009-0003-4387-6854

Dr. Muhammad SAFDAR earned his PhD in Molecular Biology and Genetics from Gaziantep University, Turkey. He is Lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 70 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

E-mail: msafdar@cuvas.edu.pk ORCID: 0000 0002 3720 2090

To Cite This Chapter

ASHRAF S et al., (2024). Nanotechnology in microbiology: bridging tiny worlds for big impacts. In Current Studies in Health and Life Sciences 2024 (pp.74-101). ISRES Publishing.

Revolutionizing Chronic Disease Management with Precision Medicine and Navigating

Maria NAZIR

Hameer Khan KHASKHELI

Nighat BATOOL

Rumaisa NAWAL

Minal HUSSAIN

Danish RIAZ

Shafeeq Ur Rehman

Muhammad SAFDAR

1. Introduction

Chronic disease is recognized as an illness that takes a long time to develop and never has a short duration of occurrence they are dangerous to the global community's health (Who & Consultation, 2003). This rank includes a broad spectrum of diseases like Cardiovascular diseases, Cancers, Diabetes, Chronic respiratory disorders, Mental illnesses, etc. Chronic diseases have become common about 71% of all deaths are attributed to chronic diseases. First of all, they are accompanied by a high level of mortality and non-trivial rates of morbidity, and second, they cause inexpressible pain and significant material losses for people, families, healthcare facilities, and states (Fitzgerald et al., 2020). Chronic disease management refers to an extensive procedure. The conventional ways of approaching ideas, as well as ways of handling and managing a problem, have not been effective; whereby one has to wait for indications that a problem exists and apply standard means to many patients regardless of their differences. In such cases, these methods fail to consider the biophysical social environmental, and behavioral factors linked to chronic illnesses. This may result in patients experiencing difficulties in their quest to receive therapies and interventions that are more appropriate to their clinical condition based on other factors in the patient's case (Reichenberg & Seligman, 2016). They are exposed to suboptimal medicine, having to dig deeper into their pockets to pay for their treatment, and ultimately have a low quality of life. To counter these restrictions, the philosophy of Precision Medicine is saliently emerging as what is believed to be a brighter future in managing conditions (Duncan et al., 2021). However, when referring to the concept, precision medicine stems from the premise that people are not the same and hence, are genetically different from other individuals, have a unique history regarding their exposure to several factors, and have unique lifestyles (Figure 1). Therefore, the integration of genomics, proteomics, metabolomics, and other data analysis technologies for precision medicine enables suitable interventions that meet each person's needs (Singh et al., 2023). The provided approach can be viewed as the approach to change the formation of disease prevention, early diagnosis, further diagnostics, and management, and thus, it is possible to promote the healthcare system as well as enhance patient results.

Thus, precision medicine cannot be implemented in a way that will be effective without reconstructing the environment through which health care is currently delivered. It means a shift from the linear model of public health interventions to individualized medicine in the setting of the massive amount of information arising from the implementation of technologies in Medicine (Clim et al., 2019). This definition entails utilizing clinical data, genomics, wearable applications, and other data for a patient's health to create a patient picture. Therefore, the utilization of this information can be immensely advantageous as it helps the respective authorities in medicine supply

the appropriate centers with far superior treatment strategies (Moon et al., 2011).

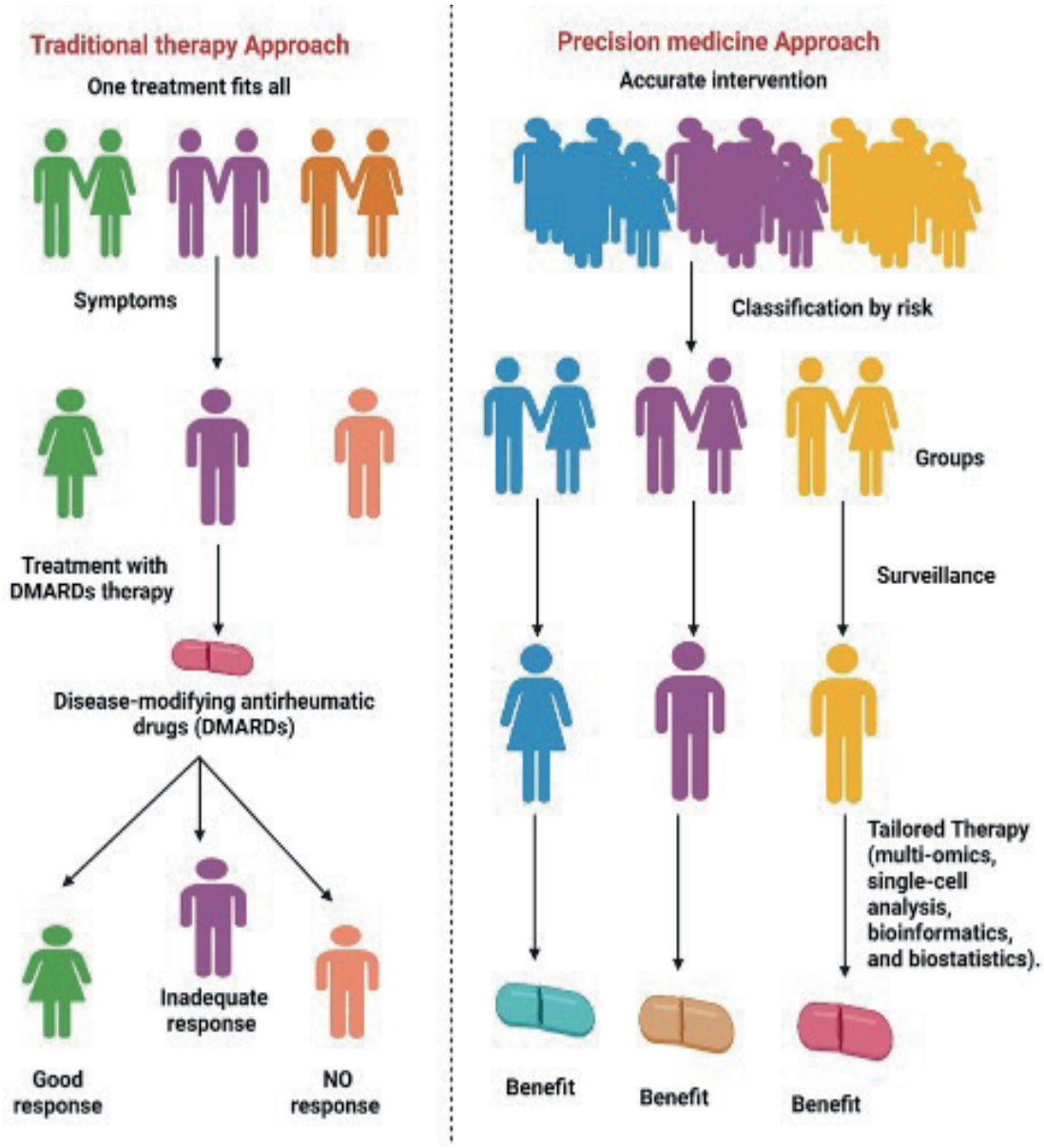


Figure 1: Traditional vs. Precision Medicine in Chronic Disease Management

It can be adapted according to the expectations of the patient, enhance the number of successful cases, and ultimately reduce expenditures within a certain time. The chapter will discuss care navigation to determine how it would enhance the right application of precision medicine or the patient-centered care that patients would have to embrace together with chronic illnesses that each patient would have to live with during the duration of this study. Both precise medicine and care coordination of chronic disease are the real visions of the future for the healthcare industry of progressive patient-centered care that is efficient and, most importantly, financially sustainable.

2. Understanding Chronic Diseases

Chronic diseases, such as those that last for one year or more, are a recurrent public health occurrence. This broad category includes many syndromes of different etiologies, but they all have many things in common. They are chronic, have slow progression, and have multiple factors behind them (Table 1).

Table 1: Chronic Diseases: A Global Burden

Disease	Prevalence (Global)	Main Risk Factors	Economic Burden (USD Billions)	References
Cardio-vascular Disease	32%	Unhealthy lifestyle (smoking, diet, inactivity), high blood pressure, cholesterol	$1,044	(Bovet & Paccaud, 2011)
Cancer	10%	Tobacco, unhealthy lifestyle, carcinogens	$439	(Bode et al., 2016)
Chronic Respiratory	6%	Smoking, pollution, occupational hazards	$383	(Viegi et al., 2001)
Diabetes	9.3%	Unhealthy lifestyle, genetics	$327	(Arokiasamy et al., 2021)
Mental Disorders	Varies	Genetics, stress, trauma, social factors	$2,500	(Muir & Zegarac, 2001)

2.1 Common Chronic Diseases

Among the most prevalent chronic diseases globally are: These are the principal chronic conditions:

Diabetes: Initially, this is a metabolic disease that leads to high blood sugar levels, and to the present day, has affected over 420 million population (Ning et al., 2022). It is associated with presenting with cardiovascular diseases, peripheral neuropathy, nephropathy, and retinopathy among others.

Cardiovascular diseases: Coronary artery diseases, stroke, and heart failure are some of the diseases that constitute NCDS and they are among the main causes of death worldwide. Thus, hypertension, dyslipidemia, smoking, and physical inactivity are considered to be the factors that are potential determinants of the condition; however, other factors are considered to be detrimental to the situation (Matei et al., 2018).

Cancer: An account of diseases that involve the uncontrolled growth of cells and the spread of tissue; there are numerous types of cancers differing in results and management (Souhami & Tobias, 2008).

Chronic respiratory diseases: Other diseases, including COPD and Asthma, caused by cigarette smoking and other pollutants, cause extreme ill health and deaths all over the world (Gan et al., 2022).

Mental health disorders: This explains that typical mental disorders, including depression, anxiety, bipolar condition, or any other related disorders that drastically affect the quality of living of a patient, also have a lasting impact on the physical and overall health of a patient (Young & Grunze, 2013).

2.2 Chronic Diseases and Its Impacts on the Health and the Wealth of the Nation

Resolution with chronic diseases and illnesses involves pain in the social, psychological, and economic, as well as in the physical domain since chronic diseases transcend healthcare facilities, cultures, and borders. One of the most significant health risks in most countries, contributing to the cost aspect of health care systems, is complications due to chronic diseases since they form the largest component of health care costs. This condition also leads to low-quality work, work absenteeism, and premature death, making this a fiscal burden to most families and societies (Antczak & Miszczyńska, 2021). Also, with more patients getting affected by chronic diseases, the problem that arises is how one manages the same for a long time, which is demanding, sophisticated, and

resource-intensive.

2.3 Defects of the Traditional Model of Chronic Condition Management

In their view, while the conventional disease management models offer the required primary care for chronic diseases, they fall short of offering sufficient and comprehensive care for modern-day health needs. These approaches frequently rely on:

One-size-fits-all models: This indicates that treatment plans utilize some label and do not factor in each patient's genetic makeup and the environment they live (Squassina et al., 2010), as well as their lifestyle likely to enhance their susceptibility to the disease and the rate of the disease's progress.

Limited patient engagement: Another important implication is that patients' decision-making regarding affairs that influence their care may not be well exercised (Blustein, 1993).

Fragmented care: Numerous specialists can treat chronic disease, and there is little communication between providers, which results in fragmented care (Cortis et al., 2016). These challenges, therefore, justify why chronic disease management has to move away from this previously described traditional model of care and opt for a modern, patient-centered, proactive model of care. As for the shortcomings mentioned above, precision medicine and care navigation can be regarded as solutions that can help eliminate those negative tendencies and significantly improve the quality of life in patients with chronic diseases.

3. The Concept of Precision Medicine

Precision medicine as a concept and a form of delivering care in the healthcare sector can be classified as new, and it is described as the method used in the prevention, diagnosis, and treatment of disease based on characteristic features (Dugger et al., 2018). This is because to treat patients affected by diseases, one has to recognize the importance and uniqueness of every individual in genetic make-up, social backgrounds, behaviors, and manifestations of the illness. Thus, concerning these factors that may differ for any particular patient, precision medicine is constructed as the attempt to supply treatments that have better results and fewer side effects than standard treatments for any patient that may receive it.

3.1 Definition and Principles

Precision medicine could be described as the approach toward patients with diseases by which the medical approach is methodologically different, relying on the patient's genes, environment, and lifestyle (Gray et al., 2020). Since the 'blanket' form of treatment is conventional, or for a considerable period has been conventional, let us, precision medicine recognizes the differences in human biology and, thus, also in diseases and does not treat each patient as if his or her condition is similar to the other patient. The fundamental principles underpinning precision medicine include: The key ideas or the foundations of precision medicine comprise:

Individual variability: They know that advanced precision medicine patients are not the same; hence, failure to respond the same to certain treatments may be due to differences in genotypes, environment, or even lifestyle (Kaur et al., 2017).

Molecular profiling: This is the process through which the biomolecules of a person are sequenced; this person profiles the proteomes and metabolomes. This information can contain genetic drift, molecular change, and even other aspects concerning patients' ability to contract the disease, its progression, and subsequent treatment (Aranda-Anzaldo, 2001).

Targeted therapies: Precision medicine pulled the treatments that were being offered and administered from the molecular data of the person's illness and the molecular profile of the person in particular. This will be particularly helpful instead of the usual conventional treatments that are

normally toxic to the body (Stephenson, 2011).

Data-driven decision-making: Precision medicine is dependent on the theories holding that large quantities of data are sourced from patients, their records, and other sources such as EHRs and genomics. That information allows healthcare providers to develop association relations that are useful in the creation of individualized therapy (Bush et al., 2020).

Patient-centered care: However, what must be taken into account is that precision medicine is empowered by patients' engagement in decision-making processes. This way, a patient can receive data on their recovery state and possible therapies and then select the treatment that is consistent with their values and preferences (Knoepke et al., 2022).

3.2 History and Development

The essence of PM began much earlier than the term's coinage, less than two decades ago (Table 2). Physicians observed patients' behavior centuries before the present time, saying that patients' reactions are variable even though they are physically ill in the same manner, and thus, it is unethical to treat all patients in the same manner based on their judgment of the matter. However, with the introduction of the scientific technology of molecular biology and genomics in the late twentieth century, the concept of precision medicine got a new look (Cardon & Harris, 2016).

Table 2: Milestones in Precision Medicine

Era	Milestone	Significance	References
Ancient Medicine	Personalized medicine based on observation	Laid groundwork for individualized treatment.	(Issa, 2007)
19th Century	Discovery of blood types	Enabled safe blood transfusions.	(Biro, 2022)
Mid-20th Century	Pharmacogenetics (genetic variation in drug response)	Tailored drug therapies to individual patients.	(RAMEEZ et al., 2023)
1990s	Human Genome Project initiated	Paved the way for genomics-based medicine.	(Olson & Berger, 2012)
2000s	The Human Genome Project completed	Identification of disease-related genetic markers.	(Mundy, 2001)
2010s	Rise of precision medicine targeted therapies for genetic mutations	Personalized treatment for cancer and other diseases.	(Jäger et al., 2021)
2020s & beyond	Advancements in genomics, proteomics, metabolomics	More comprehensive personalized treatment approaches.	(Su et al., 2021)
Future	Integration of AI and big data analytics	Refined precision medicine and improved disease prediction and treatment response.	(Sahu et al., 2022)

The Human Genome Project sequenced all the genes of the human body, an effort acclaimed for putting at the disposal of mankind all the codes that one would require to construct, sustain as well as repair the human body (Gannett, 2008). One of the major findings was biomarkers, to which further invention of diagnostic machinery, proper treatment, and tailored treatment plans were added in later years. Since then, great advances have been made in precision medicine because of available technologies such as genomic sequencing, bioinformatics, and data analysis. Earlier, the funding for genomic sequencing was high; it was not feasible for clinical uses, but it has revolved (Kwong et al., 2015). Thus, the number of genetic alterations that cause diseases has been determined.

3.3 Key Components: Genomics, Proteomics, and Metabolomics

Precision medicine applies a top-down approach of multiple levels of molecular characterization of a patient, which allows for a better overall reflection of the patient's condition. The key components of this approach include: While adopting this approach, some of the aspects include:

Genomics: On the other hand, is a branch of science that deals with an individual's complete genetic makeup or the analysis of all the genes. Genetic information may point to the exact gene that is involved or affected in some disease or specific changes that cause the said individual to point to specific diseases or reactions to certain other therapies (King et al., 2002). Therefore, the second generation of sequencing techniques during the last few years has helped to realize the idea of individual DNA rapidly and cheaply, which enhanced the actual implementation of the concept of personalized medicine.

Proteomics: Regarding proteomics, it is possible to give a relatively straightforward definition of this term that can be stated as such. This discipline is large-scale research of proteins of an organism or a certain cell. Since proteins are the functional molecules within a cell, with people's body's workforce being employed by the cell most, it can only be that the concentration and activities of these proteins can become an area of concern in disease processes. Proteomic analysis can, therefore, offer biomarkers relating to the disease diagnosis and, additionally, the potential severity and reaction of the disease to the treatment plan (Bowser & Lacomis, 2009). Therefore, if one comprehends how proteins are employed in diseases, that person can develop cures focusing on such irregularities.

Metabolomics: Therefore, it may be defined as the sub-discipline of the biology involved with identifying small molecules referred to as 'metabolites.' It is specified that metabolites are the final career products of metabolism, and their concentration denotes an individual's physiological condition and disease condition. Metabolomic analysis can determine disease risk factors, prognosis indexes, and treatment effect evaluation and unveil the pathogenesis of the diseases (Gonzalez-Covarrubias et al., 2022).

4. Interventions tailored for patients in Chronic Diseases Management

Precision medicine is revolutionizing the management of chronic diseases right from its premise of generalizability in one population to that of individual special nongranular treatment as applicable to every patient (Wouters et al., 2021). Thus, by using genetic profiling, individualized treatment and therapy, and biomarker-based outcome control, there are great advancements in the diagnosis as well as treatment of illness and diseases, resulting in greater effectiveness and efficacy of prognosis for patients and the healthcare system as a whole (Figure 2).

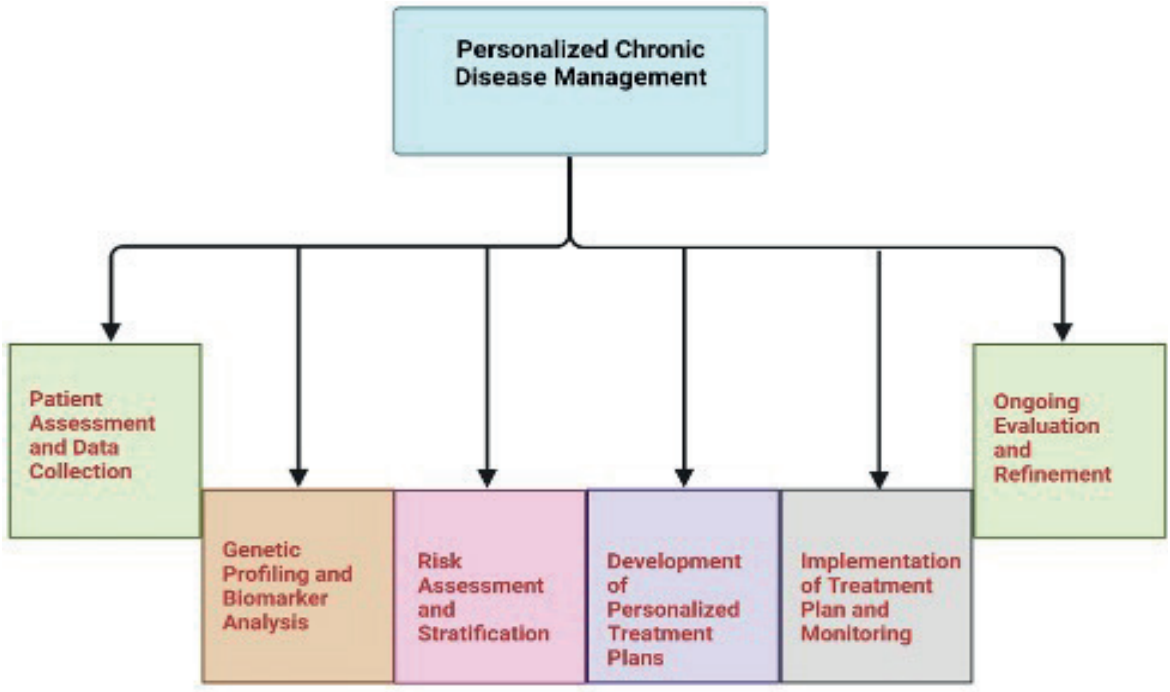


Figure 2: Personalized Chronic Disease Management

4. 1 Genetic profile and risk prediction

In personalized medicine, genetic profiling is a procedure that aims to analyze all the genome characteristics that point to risk factors, disease development, and treatment outcomes (Goulielmos et al., 2016). Through the demystification of the human genome, which includes diseases that may run in one's family as well as their odds of developing a myriad of chronic illnesses, healthcare practitioners can improve the odds of predicting diseases prone to affect a particular patient and the preventive measures to be taken.

Cardiovascular Disease: Polygenic risk scores, calculated based on multiple genetic variants, recently came into light as one of the most effective tools for estimating the particular patient's risk of the development of coronary artery disease (Gladding et al., 2020). Thus, clinicians can advise clients to change their dietary habits or to engage in physical activity; in high-risk clients, counsel them to start on statins to decrease the risk.

Cancer: DNA bio-markers such as the BRCA1 and BRCA2 genes can be tested, and it identifies customers or group members that are at a very high predisposition for contracting breast and ovarian cancer (Holman, 2014). Such knowledge can be used for individual risk management to reduce risk or the subsequent measures that may save lives if early detection, preventive surgeries, or medication with chemopreventive effects are indicated.

Neurodegenerative Diseases: Specific loci of the APOE gene coded for ApoE have been shown to have a significant linkage to the development of ADR (Cacabelos et al., 2010). Currently, no definitive cure exists for Alzheimer's, but high-risk people's early identification can aid in enrolling them in cognitive maintenance programs or experimental treatment hypotheses to perhaps postpone disease development or contraction.

Pharmacogenomics: The researchers that differences between people may be mitigated because genetic differences affect drug use. Pharmacogenomic testing involves stratifying genetic markers that would point out the effectiveness of drugs and the risk of adverse reactions (Tzvetkov

& von Ahsen, 2012). Thus, clinicians would be able to select the right drugs or dosages for patients, improving healthcare outcomes with fewer cases of drug intolerance.

4. 2 Individualized Treatment Programs and Exercising

Precision medicine helps create individual treatment programs that are targeted to the molecular and genetic profile of a particular disease in the patient. This approach ensures optimal treatment response is achieved without undesirable side effects, hence enhancing the clients' progress and utilization of Health resources.

Oncology: Targeted treatment involves directing the treatment to the particular molecular alterations that make tumor cells grow rapidly. It has improved the management of several cancers. For example, patients with HER2-positive breast cancer are administered trastuzumab, which is a monoclonal antibody that corresponds to the HER2 receptor, meaning that it helps boost the rates of survival among those patients (Patel et al., 2020).

Inflammatory Diseases: Inflammatory Diseases: Biologic agents such as TNF-alpha inhibitors and IL-12/23 inhibitors have greatly transformed the approach to chronic inflammatory diseases from RA to IBD (Argollo et al., 2019). These therapies act specifically on the disease's cytokine production, and therefore, they are more effective in controlling the disease than broad traditional medicines.

Rare Diseases: The approaches of precision medicine have created new horizons for diagnostics and therapies for rare diseases with genetic backgrounds. That is why molecular diagnostics, identifying exact loci with certain mutations, allow the creation of specific therapies and gene therapies when the previous potential of medical treatment for patients with rare diseases was limited (Marwaha et al., 2022).

4.3 Role of Biomarkers in Monitoring and Prognosis

Biochemical markers indicative of a disease state are important to the intervention of precision medicine. They can be used to:

Monitor Disease Progression: Because biomarkers are measurable, they can be used by clinicians over a given time as markers for determining the impacts of the treatment plan given, detecting any signs of disease progression or relapse, and with this, making necessary changes as needed. For instance, glycated hemoglobin (HbA1c) is used in diabetes to evaluate the patient's overall glycemic control and to compare with the risk indices for complications (Kohnert et al., 2015).

Predict Treatment Response: Some of the biomarkers can help one understand his/her chances of having and responding to a particular type of therapy. Thus, the obtained data can be suitable for choosing therapy in which the patient would receive therapy potentially positively affecting their condition. For example, in breast cancer, the status of estrogen and progesterone receptors helps to determine the reaction to hormone treatment (McGuire et al., 1977).

Assess Prognosis: Biomarkers can provide a lot of information regarding the severity of the disease and its likely prognosis, which can be helpful in prognosis and decision-making concerning the aggressiveness of the therapy to be applied, if any. For instance, in heart failure, a higher concentration of brain natriuretic peptide (BNP) indicates poor prognosis, and hence, other drastic measures may be warranted (Sarhene et al., 2019). By incorporating a person's genes, specific treatments, and biomarker-based follow-up, it has substantially transformed the management of chronic diseases. This approach hands the control of patient care back into the hands of healthcare givers, where it rightfully belongs. Such an environment has exacted, timely, and anticipatory care delivery that results in better patient well-being and increased efficiency of the healthcare delivery system.

5. Technologies Enabling Precision Medicine

This discipline is in its embryonic stages, and more importantly, it heavily depends on technologies that enable the generation, extraction, and processing of big data, particularly from patients. In addition to offering increased insight into disease etiology, these technologies are also reshaping the way with which several chronic conditions are diagnosed, managed, and treated, thus creating the foundation for the development of novel and progressive, individualized approaches to medicine.

5. 1 Next-Generation Sequencing (NGS)

Next-generation sequencing (NGS) is a current revolution in bioinformatics in the progressing healthcare system, which can hand over whole-genome sequencing or particular selection sequences within a reduced time and cost (Satam et al., 2023). This has helped to expand the opportunities and ability to determine the genetic variations linked with the presentation, prognosis, and management of disease, allowing for the basic of targeted treatments (Figure 3).

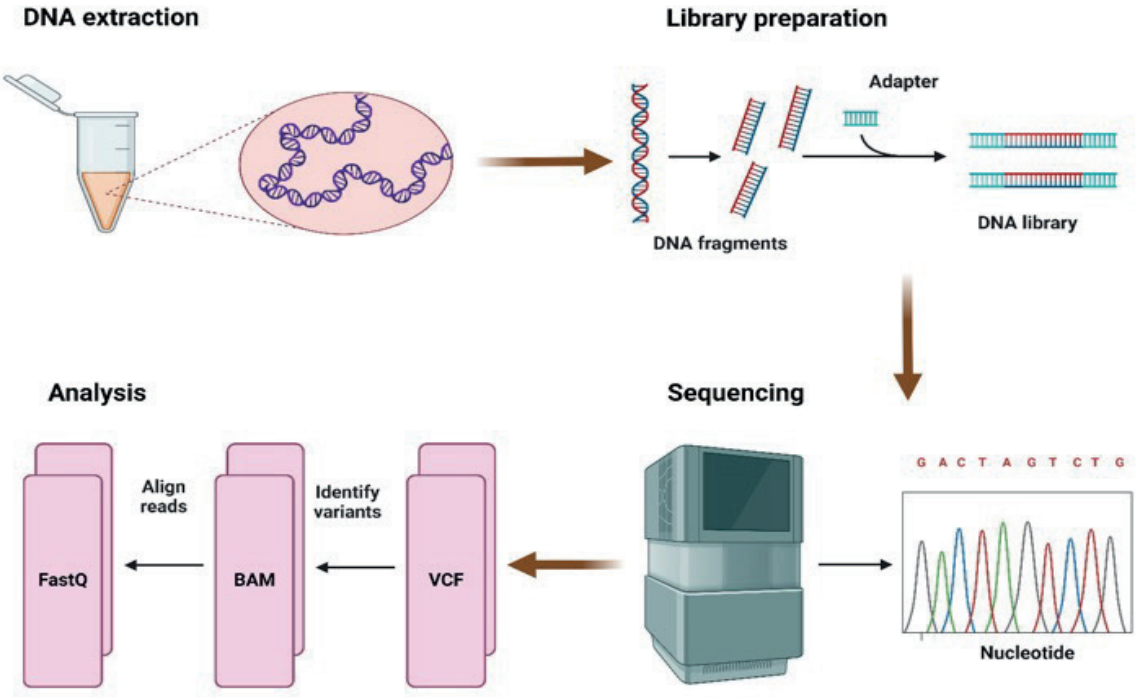


Figure 3. Unveiling the NGS tool of Precision Medicine

Disease Risk Assessment: The polygenic risk scores, made possible by NGS, integrate the effects of many genetic features and allow estimation of an individual's probability of developing complex disorders (Slunecka et al., 2021) including coronary artery disease, type 2 diabetes, and some forms of cancer. That is why this information can be used to sort people according to their risk and further provide them with preventive measures and early treatment.

Diagnosis: NGS can be used to identify most diseases, but it has found significant application in cancers and certain rare genetic disorders. Because NGS can detail certain genetic changes or fusion genes, it can be used to properly choose the right EPs and assess the patient's prognosis (Lanza et al., 2020). In most advanced cancers, there is a growing application of NGS-based tumor profiling to identify druggable mutations that can be readily treated to enhance patients' survival (Shibata, 2015).

Treatment Selection: Pharmacogenomics, one genre of application of NGS that studies the genes associated with how a patient metabolizes medications and how he or she responds to them,

is changing how we choose drugs for patients (Schwarz et al., 2019).

5. 2 Bioinformatics and BIG Data Analysis

The amounts of data produced by NGS and other omics technologies can only be analyzed and transformed into useful information with the help of robust bioinformatics algorithms and big data analytical approaches. It is well understood that exact and accurate algorithms and software are involved in analyzing genomic data, differentiating disease-related variants, and assessing them for their functional implications (Liu et al., 2022). Such tools can highlight genetic variants and estimate their effects on the proteins and even on their pathogenicity. In contrast, big data analysis uses machine computation and mathematical formulas to seek relationships in the big data set (Adadi, 2021). Approaches of this type can be employed to discover new biomarkers for diseases, new therapeutic targets for treatment, and assign disease risk and treatment outcome prediction models. The sub-field of big data analytics, namely machine learning, is expected to be employed to provide a more detailed understanding of the disease processes and patient paths. With the help of analyzing electronic health records, genomics, and other sources of patient information (Ohno-Machado et al., 2018).

5. 3 Wrist-worn Technologies and Mobile Healthcare (mHealth)

Mobile healthcare technologies and wearable devices are considered to transform chronic disease management by enabling patients' self-management (Stampe et al., 2021). It also supports the clinician's timely decision-making process. Some of the indicated devices include but are not limited to A fitness tracker, a Smartwatch, and a continuous blood sugar monitor Among other physiological and behavioral information that the devices may capture and aggregate are; heart rate, blood pressure, physical activity, quality of sleep and among others regarding the medicine (Figure 4).

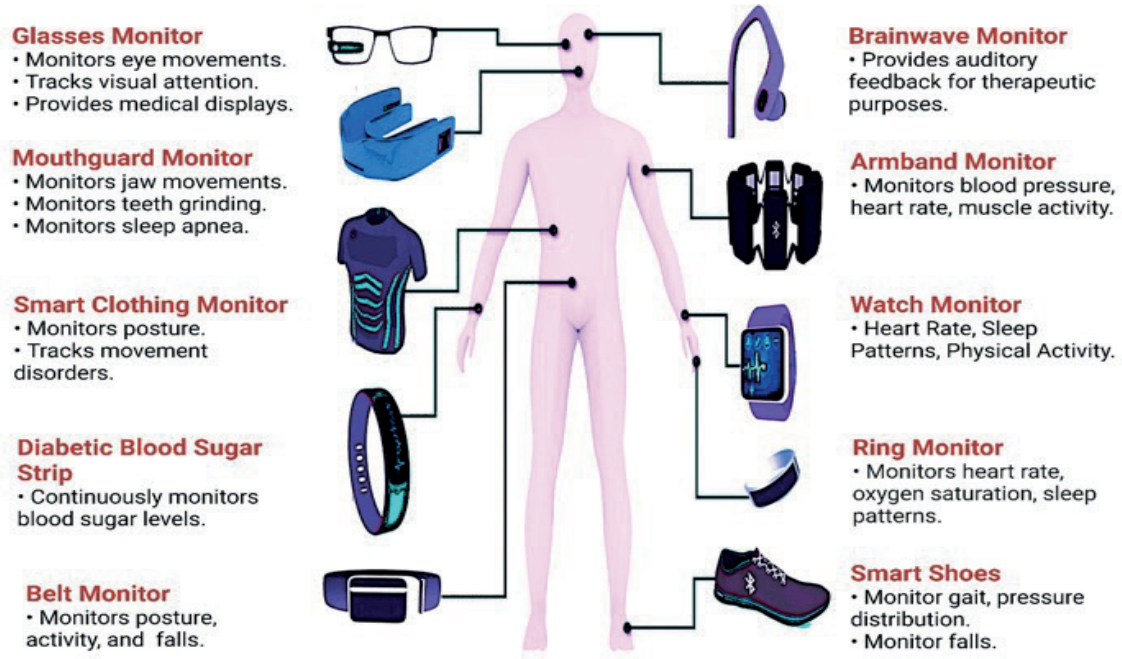


Figure 4. Unveiling the wearable tool of Precision Medicine

This continuous data is very useful in assessing the health state of a given individual, the prognosis of a disease, and the impact of management interventions. For instance, patients with diabetes can employ advanced devices such as continuous glucose monitors available to show their glucose levels in real-time, making it possible for a patient to adjust their insulin dose or change their diet. Likewise, hypertensive patients can use home blood pressure monitoring using wearable

equipment that helps them detect changes in blood pressure and help alter the medication schedule accordingly (Rastegar et al., 2020). Mobile health apps can increase the knowledge of patients about their conditions and possible ways for their treatment and, thus, improve the management of chronic illnesses (Piette et al., 2015). The mentioned apps can include features such as taking medicine on time, giving out information, helping track symptoms, and arranging an online appointment with a doctor. Offering patients mHealth technologies can help to improve the schedule of treatments and to increase the compliance of patients, which in turn can increase the levels of disease control and, ultimately, the quality of health outcomes.

6. Case Studies: Applying Precision Medicine

The potential of precision medicine is perhaps better illustrated in use-case scenarios that tell the success story of how patients' lives changed for the better with this new approach to disease care. Further, considering real-life cases will be informative. It will be informative to discover how this individualized approach is transforming the sphere of healthcare and enhancing patients' results.

6. 1 Diabetes Management: Personalised Insulin therapy

Diabetes mellitus, particularly its type 1 and 2 with high blood glucose levels must be closely supervised to avoid effects (Perkins et al., 2021). Classically, insulin treatment has been formulated by trial and error with the help of blood glucose data and patients' testimonials. Nevertheless, this concept is changing with the help of precision medicine that utilizes genetic data for Insulin therapy. For instance, macro genetics analyses of RCTs have found genes that determine insulin sensitivity and secretion, which can be used in the assessment of the given individual's response to various types of insulins (Jaacks et al., 2012). Clinicians genotype patients for these variants that help in personalizing insulin therapy based on the type of insulin, dosage, and frequency of administration. It can enhance glycemic control, decrease the incidence of hypoglycemia, and extend patients' life expectancies in diabetes mellitus. Furthermore, there is also the modern CGM, integrated with machine learning systems; currently, these are used to create closed-looped insulin delivery systems during which the bolus and the basal insulin doses are prescribed based on the current glucose levels (Mohebbi, 2021). For this reason, the 'artificial pancreas', therefore, holds the prognosis of modifying and managing the diabetic patient since through it, the body requisites of insulin are determined, and the amount of the hormone that is administered is regulated without much participation from the patient.

6. 2 Cardiovascular Diseases

In the greater majority of types of cardiovascular pathologies, the leading causes of death are chronic, and ought to be treated as such, minimum, for the remainder of one's days. Treatment is becoming enriched in such a way through precision medicine concerning the prescription and consumption of drugs through the patient's genotype (Singh, 2020). Regarding the application of pharmacogenomics in the use of drugs filed under the individual patient category, the best example is the use of warfarin. The anticoagulant warfarin is a drug well included in the list of drugs with many gene interactions varying by patients' genetic polymorphisms in the CYP2C9, and VKORC1 genes (de Freitas Campos et al., 2023). By genotyping the patients for such variants, the clinicians who will administer the drug will be able to determine the patient's response to warfarin and give the first dose in the right measure that will not cause bleeding-related side effects, thus enhancing the effectiveness of the media even on patients with comorbidity disorders. For instance, the test for genetic screening of the population to detect persons with FH, which is a hereditary disease that leads to high levels of LDL cholesterol (Berberich & Hegele, 2019). FH can also be tested genotypically; therefore, patients can begin taking lipid-lowering drugs, including statins and PCSK9 inhibitors, to attempt to minimize cardiovascular diseases.

7. Case Studies

The use of insight in the engineering of precision medicine applies to every domain of chronic diseases. Let's delve deeper into two specific areas where precision medicine has made significant strides: cancer patients who are going through chemotherapy as well as other individuals who have chronic diseases of the respiratory system.

7.1 Cancer Treatment: Targeted Therapy and Immuno-therapy

Cancer is a systems genetic and intra-tumor retreating molecular heterogeneous disease that previously was treated with broad interventions such as chemotherapy and radiotherapy, which has severe side effects (Kwapisz, 2022). Precision medicine has now brought about the concept of targeted therapy and immunotherapy, which envelopes the identity of molecular characteristics of each tumor of each patient.

Targeted Therapies: Such therapies are meant to deprive certain critical molecules or pathways for cancer cells' survival and growth. For example, patients with chronic myeloid leukemia (CML) with the BCR-ABL1 fusion gene can receive tyrosine kinase inhibitors (TKIs) such as imatinib due to the specificity of the latter for the identified oncoprotein (De Novellis et al., 2021). Likewise, lung cancer patients who were positive for EGFR mutation can be treated with EGFR inhibitors that have shown an increased survival rate compared to conventional chemotherapy (Tang et al., 2019).

Immunotherapy: This approach works based on the principles of immunology to eliminate the existence of cancer cells. Generally, immune checkpoint inhibitors, including PD-1, and CTLA-4 inhibitors, have been described as having high success rates in the eradication of different cancer types, including melanoma, lung, and kidney cancer (Wojtukiewicz et al., 2021). Cytotoxic therapies are effective in removing the suppressive messages circling in the body, which would otherwise prevent the immune system from attacking the cancer cells.

7.2 Chronic Respiratory Diseases

Two of the long-term respiratory illnesses are diseases resulting from various causes that have characteristic manifestations such as asthmatic and chronic obstructive pulmonary diseases. Precision medicine is raising awareness of such diseases and helping to create improved diagnostic and treatment solutions.

Precision Diagnosis: Molecular phenotyping with gene expression patterns and protein biomarkers, as well as inflammatory mediators, is growing to be implemented with patients with asthma and COPD to differentiate subgroups (De Ferrari et al., 2016). This enables better diagnosis and identification of the set of patients who gain more benefits from these treatments. For instance, patients with eosinophilic asthma comprising increased eosinophils in the bronchi have benefited from IL-5 antagonists (Roufosse, 2018).

Precision Treatment: Global control strategies for asthma and COPD involve the use of ICS as the 'gold standard,' but there is a large variability in response to these treatments. The pharmacogenomic research reveals the genetic factors that affect the ICS's efficacy and, therefore, explains why certain patients benefit more from ICS than others (Matera et al., 2017). This knowledge can then be applied by clinicians in choosing the right ICS dosage and form for the patient's case.

Personalized Management: Thus, precision medicine is also opening the prospects for individualized control of chronic respiratory diseases with digital health and wearable technology. It is possible to have tools that can gather data in real-time regarding the patient's lung functioning, medication intake, and severity of symptoms allowing the clinician to assess disease progression and adjust the course of action as necessary (Mackay et al., 2018). Precision medicine is slowly revolutionizing the way that chronic diseases are being handled, especially in the treatments being offered. Several examples include diabetes (personalized insulin therapy), cardiovascular diseases

(genotype-based drug diets), cancer (genotype-based therapy and immunotherapy), and chronic respiratory diseases (precision diagnosis and treatment) (Villagómez-Guzmán & Quiroz, 2024). With these examples, the application of precision medicine has the potential to change how patients are managed, resulting in better outcomes.

8. Implementing Precision Medicine into Practice

Precision medicine adopts a broad and complex concept, which can be implemented in various approaches and tackle different issues according to the adaptation and utilization of precision medicine in routine clinical practice. It entails policy and practice advancements that enhance safety and exert multi-professional collaboration and education with patients to enhance the benefits relevant to this new conceptual model of healthcare.

8.1 Implementation Strategies and Best Practices

Implementing precision medicine in clinical practice requires a well-structured approach that addresses key considerations: subfactors referred to in this article in clinical practice of PM which consist of the following:

Infrastructure and Resources: It has been briefly pointed out that constructing the capacity that forms the basis for genomics involves using appropriate generic sequencing technologies, assembling bioinformatics teams, and setting up storage and analysis datasets. These resources are critical in creating and analyzing big data from genomics and clinics, which is the basis of precision medicine (Xue et al., 2016).

Clinical Decision Support Tools: Precision medicine data must be incorporated into EHR, and CDS tools must be created to be easily implemented in regular clinical practice (Sitapati et al., 2017). Computerized decision-support systems enable clinicians to receive alerts and recommendations on a patient's risk level and the appropriate treatment plan depending on the genomic makeup.

Education and Training: Education and training are crucial components of enhancing PM, and healthcare professionals need extensive programs. Such training involves precision medicine, genetic counseling, genomics interpretation, and other forensic-related challenges and ethical issues from genomic information in clinical practice (Alshehhi et al., 2023). Relevant continuous professional development programs can demonstrate that healthcare providers are in touch with the advancements in the sphere.

Reimbursement and Policy: Existential issues such as policy formulation and reimbursement models that compel the use and procurement of PM also affect technology adoption (Muthelo, 2022). This might include the inclusion of genetic testing, targeted therapies, precision medicine, and other relevant treatment services by health insurance companies. Also, the policies and infrastructures for sharing and cooperation between different healthcare organizations can help to create more extensive datasets needed for the development of precision medicine and its applications.

8.2 Features of Research and Setting of Programs

In managing chronic conditions, patient-centered interprofessional care teams are usually formed by the PCP, specialists, nurses, pharmacists, social workers, and other stakeholders (Mohiuddin, 2020). Such an integrated care model may be especially valuable for patients with chronic disease co-morbidity, facilitating the communication between different healthcare providers, consistent assessment of patients' medication lists, and overall coordinated co-management of coexisting diseases.

8.3 Role of Healthcare Providers and Patient Education

Physicians remain the linchpin in translating precision medicine into a reality in the wards, clinics, and operating theaters. They also should be up to date regarding the progression of precision

medicine, existing genetic tests, intentionally targeted therapies, and other clinical support systems. Also, they should be able to explain the complicated genetic information to the patient concisely and easily understandable, thus equipping the patient with sufficient information to make the necessary decisions regarding her treatment. Lack of adequate knowledge about the diseases is one of the major shortcomings that can be overcome by educating the patients through pamphlets that they can take home, videos, and genetic counseling.

9. Ethical, Legal and Social Issues

9.1 Ethics of genetic testing and data privacy

Some of the key issues of ethical concern being highlighted by the use of genetic testing include the patient's control and self-determination, the autonomy of the patient, and the notion of the patient's consent.

Autonomy and Informed Consent: Patients must be free to make certain decisions as professionals or not to take certain tests such as genetic testing. Thus, any genetic test must be preceded by the patient's informed consent, where they are to be informed of the test's purpose, its possible risks and benefits, and any possible outcome that may arise (Green et al., 2004). It involves dimensions such as medical geneticists' approaches to alert patients and their families of incidental findings and how they would address findings in genetics not relevant to the reason for testing.

Genetic Discrimination: The concern over job, insurance, or other social preconceptions arising from a person's genetic profile continues to be a concern among many people (Lovejoy, 2000). Measures such as GINA, Genetic Information Nondiscrimination Act in the United States offer some antidote, but questions arise on the possibility of these laws containing holes that may be exploited by one form of discriminative technique or the other, and the general need for stronger legal frameworks to curb discrimination based on genetic results.

Data Privacy and Security: Precision medicine requires the collection and analysis of large quantities of a patient's genetic and personal health information that is considered private and confidential, thus increasing the risk of privacy and security breaches (Li, 2016).

9.2 Legal Environment and Related Issues

The rapid pace of technological advancements in precision medicine has outpaced the development of legal and regulatory frameworks, posing several challenges: Consequently, the integration has led to several challenges highlighted here below due to the alarming rate of technological advancements in precision medicine as opposed to the formulation of legal and regulatory measures.

Intellectual Property Rights: Concerns connected with the patenting of genes and approaches to diagnostic techniques and therapies can cause some limitations in access to medicine and slow down advancement (Arjmand et al., 2020). It is still challenging to achieve an appropriate level of encouraging further research and development and accessible precision medicine in terms of law and policy.

Regulatory Oversight: Writing that addresses the presently prevailing actual-law frameworks for precision medicine needs to be mindful of three important facts: The use of new genomic tests and targeted therapies must be protected to avoid any safety or efficacy issues, yet the rapidly growing technologies surpass the approval processes (Phillips et al., 2018). Issues of interest include the ever-raging debate on how to foster innovation while at the same time protecting the lives of the patients.

Liability and Malpractice: Such employment of genomic information in clinical practice leads to many concerns concerning liability and medical malpractice (Pike et al., 2014). If the

patient gets an adverse outcome from incorrect genetic analysis or the absence of appropriate genetic markers, then defining fault for it is challenging. This means that there is a need to have clear-cut guidelines and standards that have to be followed regarding the use of genomic information in clinical practice to minimize the risks.

9.3 Accessibility and Social Equity Problems

It is, therefore, extremely relevant to consider the ethical and social implications of the achievement of precision medicine, particularly concerning the ideal of fairness in the distribution of the interventions in question.

Cost and Affordability: Targeted therapies and genetic testing can be costly and, therefore, out of reach for many people, especially those with low incomes or insufficient insurance coverage (Adachi et al., 2023). If precision medicine widens the gap between the 'haves' and the 'have-nots,' as indicated in the case of cost barriers and affordability, then it will further users' woes.

Health Disparities: This is because precision medicine is pointed out to pose a threat of increasing existing inequalities in health outcomes (Vodovotz et al., 2020). Clinical studies in specific diseases and their treatment require ethnically and racially diverse sample participants to guarantee that precision medicine outcomes will not be sensitive to race, ethnicity, or socioeconomic status.

Public Understanding and Trust: Precision medicine is now embodied in the broader context of personalized medicine that designs individual treatments based on characteristics that encompass not only genes but also other facets of an individual's life; therefore, for people to have confidence in this paradigm, veterinarians must make it transparent, educate and engage. The general population also requires knowledge about the opportunities and challenges of precision medicine and the moral and social impacts of the approach to make a rational choice regarding their overall health (Maeckelberghe et al., 2023). Therefore, dissecting the components of the final ethical, legal, and social implications question is critical to properly and fairly implementing precision medicine. When these challenges are preemptively solved, precision medicine promises to revolutionize healthcare to the advantage of all people.

10. Precisely, Managing the Future of Precision: Medicine

With the advancement of precision medicine, the latest trends and new advancements or inventions are said to bring greater change to the management of chronic ailments. This future trajectory includes such specifics as the application of the newest technologies, such as liquid biopsies and single-cell sequencing, the establishment of artificial intelligence and machine learning, and increased focus on preventive and, at best, early-diagnosis approaches.

10.1 New Directions and Advances

Several promising trends are shaping the future of precision medicine and hold the potential to impact chronic disease management significantly: Several promising trends are shaping the future of precision medicine and hold the potential to impact chronic disease management significantly:

Liquid Biopsies: Blood or other body fluids-based liquid biopsies which comprise circulating tumor DNA (ctDNA), RNA, or other biomarkers are recognized as a tissue biopsy surrogate for cancer diagnosis, monitoring, and treatment choice (Shegekar et al., 2023). Lung cancer has been proven to be diagnosed at an early stage, identify the molecular residual disease, and evaluate the response to treatment in real-time with the help of this technology. In chronic ailments also, liquid biopsies could help in observing the status of the disease and the appearance of complications without always having to perform invasive procedures (Perales et al., 2021).

Single-Cell Sequencing: Thus, single-cell sequencing technologies that enable the assessment of the genome, transcriptome, or epigenome of individual cells reveal essential information about

cell heterogeneity and the pathogenesis of various diseases (Kamies & Martinez-Jimenez, 2020). The sort of analysis possible at this level can help to distinguish between healthy and diseased cells, discover rare populations of cells promoting disease, and discover new targets for therapies. In chronic illnesses, single-cell sequencing might allow additional insight into the interactions between different cell types and molecular apparatuses and, consequently, improve treatment strategies and practices.

Gene Editing Technologies: Gene editing tools such as CRISPR-Cas9 hold the promise of replacing a bad gene with a good one, meaning that genetic diseases have possible cures in the form of editing tools (Bhattacharjee et al., 2022). Despite being largely present only in research, gene editing could revolutionize the future of precision medicine, with rare inherited conditions possibly being treated in this way in the future.

10.2 AI and Machine Learning

AI and Machine learning are now significant tools that are becoming almost mandatory to work in precision medicine as these technologies help researchers and clinicians analyze the data and mine the patterns from these sets, which are difficult for humans to handle.

Image Analysis: X-rays, CT scans, and MRI can be analyzed with the help of algorithms enabled by Artificial Intelligence to diagnose complex and simple patterns within the images that may be out of reach of human eyes (Najjar, 2023). This can help in the early detection of different chronic illnesses such as cancer, cardiovascular, and neurological disorders, hence integrating early interventions to enhance performance.

Risk Prediction: Universal computing and AI used in the ML frameworks can combine multiple forms of data, from genomic data and electronic health records to environmental exposures, to create accurate risk estimate models for different chronic diseases (Zahid et al., 2021). Such models could pinpoint people who are most likely to get afflicted by certain diseases, allowing the application of measures to prevent the diseases early.

Treatment Optimization: Clinical and molecular data can be processed to create individual patient response profiles for various treatments that AI algorithms could use (Elemento et al., 2021). This information can assist in the choice of multiple treatment options that would increase therapeutic outcomes and reduce toxicity. AI technologies can also assist with tracking patients' responses to treatment in real time to make changes to the process and focus on patient-centered care.

10.3 Possible Preventive Medicine and Early Detection

It's one of the key strengths of the approach, where precision medicine has the potential of moving the healthcare system away from one that is fundamentally reactive to one that seeks to prevent diseases and intervene early when necessary. Special attention should be paid to genetic testing, risk prediction, and advanced diagnostics in achieving early identification of people who may develop chronic diseases in the future, which allows practicing the prevention needed for lifestyle changes and chemoprevention or early intervention. The advantages of this approach may consist in preventing or postponing some chronic diseases, thus providing better health and institutional results, not to mention decreased costs (Organization, 2013).

11. Challenges and Barriers

It is evident that precision medicine creates great promise; however, applying and offering precision medicine to the public equitably has some hurdles and obstacles. These are various challenges, which are technical, scientific, economic, and social, and that require involve of all the stakeholders in the healthcare organization (Table 4).

Table 4: Challenges and Barriers to Widespread Adoption of Precision Medicine

Barrier Category	Specific Barrier	Potential Solutions	References
Technical	Data privacy, standardization, interpretation, access	Encryption, universal formats, cloud storage, user-friendly tools, telemedicine.	(Akotaobi, 2023)
Economic	High costs, reimbursement, lack of incentives	Subsidies, insurance coverage, new payment models, partnerships.	(Ndayishimiye et al., 2023)
Social	Ethics, awareness, disparities, discrimination	Guidelines, education, equitable access, anti-discrimination laws.	(Scott, 2023)

11.1 Drag and Drop Environment

Despite the remarkable progress made in precision medicine, several technical and scientific hurdles remain: Despite the remarkable progress made in precision medicine, several technical and scientific hurdles remain:

Data Integration and Interpretation: The flow, heterogeneity, and complexity of data produced by genomic sequencing, proteomics, metabolomics, and similar techniques generate several issues related to data integration, analysis, and interpretation (Santiago-Rodriguez & Hollister, 2021). To transform this paradigm into a biologist's everyday reality, standardization of data formats, consistent bioinformatics resources, and intelligent ML models are the keys. Moreover, superimposing multi-omics data with clinical and environmental data needs considerable and compatible utility to organize the databanks, given the intricacy and heterogeneity of incoming data.

Unraveling Disease Complexity: Most chronic diseases are polygenic and multifactorial, meaning there are numerous interactions between the many genes, both in the inhabitants and their microenvironments and lifestyles (Butnariu et al., 2022). Acknowledging and comprehending such complex relationships is still one of the major scientific tasks. It has to be based on massive multi-center investigations, long-term data collection, and problem-solving methods that are novel in data analysis and modeling to uncover disease mechanisms and design individual-based risk prediction models.

Limited Clinical Utility: Although genomic information can offer many tangible data like the risk factors for disease or a candidate's reaction to treatment, it is not always easy to use in clinical practice (Suter, 2015). Most common genetic variants are associated with modest changes in risk, and the effects of those variants may be nuanced by the environment and lifestyle. Moreover, there is not adequate clinical evidence for many genomic tests and targeted therapies, which cannot be adopted at the clinical level. Additional studies are required to support the outcome of genomic results and develop standard protocols to implement them in medical practice (Alarcón Garavito et al., 2023).

Ethical and Regulatory Considerations: Warning issues of precision medicine include, but are not limited to, issues to do with informed consent, data privacy, genetic discrimination, and issues of incidental findings, again call for improved ethical scrutiny and guidance (Beskow et al., 2018). Maintaining a balance between embracing innovation and protecting the patient's rights and their privacy is quite a task in ethics. Further, the complex and shifting global regulatory environment should be aligned with the fast-growing options in Precision Medicine technologies for protecting the consumer as well as building trust and developing components of IP and Accessing healthcare.

11.2 Indicators; Barriers to Access and Quality Education: Economic and Financial Aspects

The challenges concerning precision medicine's cost and feasibility are diverse and significant; they affect the delivery of precision medicine to the population.

Cost of Genomic Testing: While the costs have reduced gradually over the years, it remains a very costly procedure that is unaffordable to the majority of people as well as healthcare facilities (Organization, 2007). This can lower the chances of the patients being given the genomic tests especially if they have no adequate insurance or belong to the minority groups. The fact that the accessibility of genomic tests is becoming a pressing issue implies that cost reduction, insurance coverage, and the creation of new types of financing are critical in terms of the organizational perspective.

Cost of Targeted Therapies: Although it was established that targeted therapies are normally more effective as compared to traditional approaches to treatment, these drugs are normally quite expensive (Waterhouse et al., 2006). These therapies have been known to be costly whereby they are inconveniencing to the patients, in addition to being costly to equip healthcare facilities hence leading to a lot of debates regarding its cost-effectiveness. Additionally, the long-term benefit of some of the incorporated targeted therapies is still not quite established and, therefore, efficient control.

Reimbursement Challenges: The payment of precision medicine is still uncontrolled, and the payment methods are not very similar. Most genomic tests and targeted treatments are not covered by insurance or not reimbursed. The standardization of insurance coverage for genomic tests is different depending on the insurance provider or available test/treatment options (Schoonmaker, 1998). Nevertheless, when insurance reimbursements are low and sporadic, they may become a problem concerning money on the patient's side and the future advancement of precision medicine in actual healthcare facilities.

11.3 The Health Care Disparities

Therefore, the most fitting illustration of the kind of distribution of healthcare that has been accused of being prejudicial to accessing quality care is when precision medicine reinforces socio-economic healthcare disparities (Singh, 2023). Medical racism is illustrated through guidelines related to who receives a genetic test, targeted treatments, and other aspects of precision medicine. To address these disparities, a concerted effort is needed. To overcome all these disparities, the following strategies have to be undertaken:

Increase Diversity in Research and Clinical Trials: This implies that people of diverse races, ethnicities, and SES should participate in research and clinical trials to ensure that safe and effective mechanisms of precision medicine are developed for each population group (Washington et al., 2023).

Improve Access to Genetic Counseling: Genetic counseling is very important because it entails patient education to underscore genetic test results for a mutually appropriate management plan (Burke et al., 2007). To address this challenge, patients must receive the care and attention they need to survive in precision medicine; therefore, more genetic counseling services must be made available to people in regions with limited services.

Educate Healthcare Providers and the Public: Hence, it is only clear to educate consultants and the public about the existence of precision medicine so that optimal outcomes are obtained from the technology and patients are informed about their right to choose. This entails that patients and the public receive information such as the benefits and risks of genetic testing, targeted therapies, and any other precision medicine intervention (Rose, 2013). These are the challenges or will be, together with the barriers that hinder precision medicine's offering exact use and contributing great

value to the healthcare system for patients with chronic diseases.

12. Conclusion

By the method of precision medicine, it has been further predicted that the control of chronic diseases is set to start being done in a different technique than the conventional technique of controlling diseases, and this is the traditional one-size-fits-all technique of controlling chronic diseases. Precision medicine makes use of genomic sequencing, multi-omics, intelligence with AI, and other uses, including mobile health technologies for the improvement of identification of the risk factors affecting an individual's disease, determination of the various personalized treatment options available for the addressed disease, and the utilization of applications of technology, as well as other available approaches for the prevention of the concerned disease that can be optimally utilized in a personalized manner. The case examples of precision medicine implementation that could potentially be seen throughout the given chapter and the case subject matter depict and exemplify the benefits of such an approach regarding the management of different chronic diseases diabetes mellitus, cardiovascular diseases, cancer, chronic respiratory diseases, and many others. Thus, implementing PM as one of the significant components of daily clinical practice is not entirely problem-free. Data integration and analysis still remain a problem, as well as comprehensiveness and heterogeneity of the diseases, problems in funding, and last but not least, regulatory, legal, and ethical issues are important problems that have to be solved by all the stakeholders. However, there is a positive prognosis for the application of precision medicine in the future. Technologies like liquid biopsies that are not currently part of the equation, single-cell sequencing, and more attractive gene editing technologies are new possibilities for enhancing the performance of individualized therapy. In addition, its usage will have a definite role to play when it comes to raising the rate of novelties in disease identification and treatment. To conclude, it is vital to note that more progress and rational utilization of precision should assist in equalizing access to it, and its ethical and social impacts are to be described and mitigated; interdisciplinary cooperation remains the most important goal for scientists, clinicians, patients, and policymakers. With this new focused change approach and facing the future challenges that this endeavor implies; it is possible to launch a new epoch of patient-centered efficaciousness and long-term management of chronic diseases for millions of people worldwide.

References

Adachi, T., El-Hattab, A. W., Jain, R., Nogales Crespo, K. A., Quirland Lazo, C. I., Scarpa, M., Summar, M., & Wattanasirichaigoon, D. (2023). Enhancing equitable access to rare disease diagnosis and treatment around the world: a review of evidence, policies, and challenges. International Journal of Environmental Research and Public Health, 20(6), 4732.

Adadi, A. (2021). A survey on data-efficient algorithms in big data era. Journal of Big Data, 8(1), 24.

Akotaobi, G. C. (2023). Barriers to Storing and Accessing Personal Sensitive Healthcare Data in the Internet Cloud: A Qualitative Study Colorado Technical University].

Alarcón Garavito, G. A., Moniz, T., Deom, N., Redin, F., Pichini, A., & Vindrola-Padros, C. (2023). The implementation of large-scale genomic screening or diagnostic programmes: A rapid evidence review. European Journal of Human Genetics, 31(3), 282-295.

Alshehhi, A., Almarzooqi, A., Alhammadi, K., Werghi, N., Tay, G. K., & Alsafar, H. (2023). Advancement in human face prediction using DNA. Genes, 14(1), 136.

Antczak, E., & Miszczyńska, K. M. (2021). Causes of sickness absenteeism in Europe—analysis from an intercountry and gender perspective. International Journal of Environmental Research and Public Health, 18(22), 11823.

Aranda-Anzaldo, A. (2001). Cancer development and progression: a non-adaptive process driven by genetic drift. Acta Biotheoretica, 49, 89-108.

Argollo, M. C., Allocca, M., Furfaro, F., Peyrin-Biroulet, L., & Danese, S. (2019). Interleukin-23 blockers: born to be first-line biologic agents in inflammatory bowel disease? Current Pharmaceutical Design, 25(1), 25-31.

Arjmand, B., Larijani, B., Sheikh Hosseini, M., Payab, M., Gilany, K., Goodarzi, P., Parhizkar Roudsari, P., Amanollahi Baharvand, M., & Hoseini Mohammadi, N. s. (2020). The horizon of gene therapy in modern medicine: advances and challenges. Cell Biology and Translational Medicine, Volume 8: Stem Cells in Regenerative Medicine, 33-64.

Arokiasamy, P., Salvi, S., & Selvamani, Y. (2021). Global burden of diabetes mellitus. In Handbook of global health (pp. 1-44). Springer.

Berberich, A. J., & Hegele, R. A. (2019). The complex molecular genetics of familial hypercholesterolaemia. Nature Reviews Cardiology, 16(1), 9-20.

Beskow, L. M., Hammack, C. M., & Brelsford, K. M. (2018). Thought leader perspectives on benefits and harms in precision medicine research. PloS one, 13(11), e0207842.

Bhattacharjee, G., Gohil, N., Khambhati, K., Mani, I., Maurya, R., Karapurkar, J. K., Gohil, J., Chu, D.-T., Vu-Thi, H., & Alzahrani, K. J. (2022). Current approaches in CRISPR-Cas9 mediated gene editing for biomedical and therapeutic applications. Journal of Controlled Release, 343, 703-723.

Biro, G. P. (2022). Erythrocyte transfusion: brief history and current practice. In Blood substitutes and oxygen biotherapeutics (pp. 3-19). Springer.

Blustein, J. (1993). The family in medical decisionmaking. The Hastings Center Report, 23(3), 6-13.

Bode, A. M., Dong, Z., & Wang, H. (2016). Cancer prevention and control: alarming challenges in China. National science review, 3(1), 117-127.

Bovet, P., & Paccaud, F. (2011). Cardiovascular disease and the changing face of global public health: a focus on low and middle income countries. Public Health Reviews, 33, 397-415.

Bowser, R., & Lacomis, D. (2009). Applying proteomics to the diagnosis and treatment of ALS and related diseases. Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine, 40(5), 753-762.

Burke, W., Zimmern, R. L., & Kroese, M. (2007). Defining purpose: a key step in genetic test evaluation. Genetics in Medicine, 9(10), 675-681.

Bush, C. L., Blumberg, J. B., El-Sohemy, A., Minich, D. M., Ordovás, J. M., Reed, D. G., & Behm, V. A. Y. (2020). Toward the definition of personalized nutrition: a proposal by the American Nutrition Association. Journal of the American College of Nutrition, 39(1), 5-15.

Butnariu, L. I., Gorduza, E. V., Florea, L., Țarcă, E., Moisă, Ș. M., Tradafir, L. M., Cojocaru, E., Luca, A.-C., Stătescu, L., & Bădescu, M. C. (2022). The Genetic Architecture of the Etiology of Lower Extremity Peripheral Artery Disease: Current Knowledge and Future Challenges in the Era of Genomic Medicine. International journal of molecular sciences, 23(18), 10481.

Cacabelos, R., Fernández-Novoa, L., Martínez-Bouza, R., McKay, A., Carril, J. C., Lombardi, V., Corzo, L., Carrera, I., Tellado, I., & Nebril, L. (2010). Future trends in the pharmacogenomics of brain disorders and dementia: Influence of APOE and CYP2D6 variants. Pharmaceuticals, 3(10), 3040-3100.

Cardon, L. R., & Harris, T. (2016). Precision medicine, genomics and drug discovery. Human molecular genetics, 25(R2), R166-R172.

Clim, A., Zota, R. D., & Tinica, G. (2019). Big Data in home healthcare: A new frontier in personalized medicine. Medical emergency services and prediction of hypertension risks. International Journal of Healthcare Management, 12(3), 241-249.

Cortis, L. J., Ward, P. R., McKinnon, R. A., & Koczwara, B. (2016). Breaking the silos: Integrated care for cancer and chronic conditions. Cancer and Chronic Conditions: Addressing the Problem of Multimorbidity in Cancer Patients and Survivors, 287-313.

De Ferrari, L., Chiappori, A., Bagnasco, D., Riccio, A. M., Passalacqua, G., & Canonica, G. W. (2016). Molecular phenotyping and biomarker development: are we on our way towards targeted therapy for severe asthma? Expert review of respiratory medicine, 10(1), 29-38.

de Freitas Campos, E. I., Gomes, K. B., Ribeiro, D. D., Puurunen, M. K., Oliveira Magalhães Mourão, A. d., Ferreira, I. G., da Costa Rocha, M. O., de Souza, R. P., & Parreiras Martins, M. A. (2023). Influence of polymorphisms in CYP2C9, VKORC1, MDR1 and APOE genes on the warfarin maintenance dose in Brazilian patients. Pharmacogenomics, 24(13), 701-712.

De Novellis, D., Cacace, F., Caprioli, V., Wierda, W. G., Mahadeo, K. M., & Tambaro, F. P. (2021). The TKI era in chronic leukemias. Pharmaceutics, 13(12), 2201.

Dugger, S. A., Platt, A., & Goldstein, D. B. (2018). Drug development in the era of precision medicine. Nature Reviews Drug Discovery, 17(3), 183-196.

Duncan, E., Glaros, A., Ross, D. Z., & Nost, E. (2021). New but for whom? Discourses of innovation in precision agriculture. Agriculture and Human Values, 38, 1181-1199.

Elemento, O., Leslie, C., Lundin, J., & Tourassi, G. (2021). Artificial intelligence in cancer research, diagnosis and therapy. Nature Reviews Cancer, 21(12), 747-752.

Fitzgerald, D., Ashcroft, R., Hollin, G., Karkazis, K., King, N. B., Landecker, H., Langlitz, N., Lentzos, F., Meyers, T., & Niewöhner, J. (2020). Lockdown texts. In: Springer.

Gan, H., Hou, X., Zhu, Z., Xue, M., Zhang, T., Huang, Z., Cheng, Z. J., & Sun, B. (2022). Smoking: a leading factor for the death of chronic respiratory diseases derived from Global Burden of Disease Study 2019. BMC pulmonary medicine, 22(1), 149.

Gannett, L. (2008). The human genome project.

Gladding, P. A., Legget, M., Fatkin, D., Larsen, P., & Doughty, R. (2020). Polygenic risk scores in coronary artery disease and atrial fibrillation. Heart, Lung and Circulation, 29(4), 634-640.

Gonzalez-Covarrubias, V., Martínez-Martínez, E., & del Bosque-Plata, L. (2022). The potential of metabolomics in biomedical applications. Metabolites, 12(2), 194.

Goulielmos, G. N., Zervou, M. I., Myrthianou, E., Burska, A., Niewold, T. B., & Ponchel, F. (2016). Genetic data: The new challenge of personalized medicine, insights for rheumatoid arthritis patients. Gene, 583(2), 90-101.

Gray, I. D., Kross, A. R., Renfrew, M. E., & Wood, P. (2020). Precision medicine in lifestyle medicine: the way of the future? American Journal of Lifestyle Medicine, 14(2), 169-186.

Green, M. J., Peterson, S. K., Baker, M. W., Harper, G. R., Friedman, L. C., Rubinstein, W. S., & Mauger, D. T. (2004). Effect of a computer-based decision aid on knowledge, perceptions, and intentions about genetic testing for breast cancer susceptibility: a randomized controlled trial. Jama, 292(4), 442-452.

Holman, C. M. (2014). The Critical Role of Patents in the Development, Commercialization, and Utilization of Innovative Genetic Diagnostic Tests.

Issa, A. M. (2007). Personalized medicine and the practice of medicine in the 21st century. McGill Journal of Medicine: MJM, 10(1), 53.

Jaacks, L. M., Wylie-Rosett, J., & Mayer-Davis, E. J. (2012). Diabetes. Present Knowledge in Nutrition, 806-832.

Jäger, P., Twarock, S., & Haas, R. (2021). Prognostic Parameters in Myeloid Malignancies in a Historical Context–From Microscopy to Individualized Medicine. Current Drug Targets, 22(2), 202-213.

Kamies, R., & Martinez-Jimenez, C. P. (2020). Advances of single-cell genomics and epigenomics in human disease: where are we now? Mammalian Genome, 31(5), 170-180.

Kaur, J., Rahat, B., Thakur, S., & Kaur, J. (2017). Trends in precision medicine. In Progress and challenges in precision medicine (pp. 269-299). Elsevier.

King, R. A., Rotter, J. I., & Motulsky, A. G. (2002). The genetic basis of common diseases. Oxford university press.

Knoepke, C. E., Chaussee, E. L., Matlock, D. D., Thompson, J. S., McIlvennan, C. K., Ambardekar, A. V., Schaffer, E. M., Khazanie, P., Scherer, L., & Arnold, R. M. (2022). Changes over time in patient stated values and treatment preferences regarding aggressive therapies: insights from the DECIDE-LVAD trial. Medical Decision Making, 42(3), 404-414.

Kohnert, K.-D., Heinke, P., Vogt, L., & Salzsieder, E. (2015). Utility of different glycemic control metrics for optimizing management of diabetes. World journal of diabetes, 6(1), 17.

Kwapisz, D. (2022). Cancer Immunotherapy Clinical Trials. In Handbook of Cancer and Immunology (pp. 1-24). Springer.

Kwong, J. C., McCallum, N., Sintchenko, V., & Howden, B. P. (2015). Whole genome sequencing in clinical and public health microbiology. Pathology, 47(3), 199-210.

Lanza, G., Calì, F., Vinci, M., Cosentino, F. I. I., Tripodi, M., Spada, R. S., Cantone, M., Bella, R., Mattina, T., & Ferri, R. (2020). A Customized Next-Generation Sequencing-Based Panel to Identify Novel Genetic Variants in Dementing Disorders: A Pilot Study. Neural Plasticity, 2020(1), 8078103.

Li, J. (2016). Genetic information privacy in the age of data-driven medicine. 2016 IEEE International Congress on Big Data (BigData Congress),

Liu, Y., Yeung, W. S., Chiu, P. C., & Cao, D. (2022). Computational approaches for predicting variant impact: An overview from resources, principles to applications. Frontiers in genetics, 13, 981005.

Lovejoy, W. (2000). Ending the genetic discrimination barrier: Regaining confidence in preconception, prenatal, and neonatal genetic testing. S. Cal. L. Rev., 74, 873.

Mackay, A. J., Kostikas, K., Murray, L., Martinez, F. J., Miravitlles, M., Donaldson, G., Banerji, D., Patalano, F., & Wedzicha, J. A. (2018). Patient-reported outcomes for the detection, quantification, and evaluation of chronic obstructive pulmonary disease exacerbations. American journal of respiratory and critical care medicine, 198(6), 730-738.

Maeckelberghe, E., Zdunek, K., Marceglia, S., Farsides, B., & Rigby, M. (2023). The ethical challenges of personalized digital health. Frontiers in medicine, 10, 1123863.

Marwaha, S., Knowles, J. W., & Ashley, E. A. (2022). A guide for the diagnosis of rare and undiagnosed disease: beyond the exome. Genome medicine, 14(1), 23.

Matei, Ș., Cutler, S. J., Preda, M., Dorobanțu, M., Ilinca, C., Gheorghe-Fronea, O., Rădulescu, L., Oprescu, N., Deaconu, A., & Zorilă, C. (2018). The relationship between psychosocial status and hypertensive condition. Current Hypertension Reports, 20, 1-13.

Matera, M. G., Rinaldi, B., Calzetta, L., & Cazzola, M. (2017). Pharmacogenetic and pharmacogenomic considerations of asthma treatment. Expert opinion on drug metabolism & toxicology, 13(11), 1159-1167.

McGuire, W., Horwitz, K., Pearson, O., & Segaloff, A. (1977). Current status of estrogen and progesterone receptors in breast cancer. Cancer, 39(6), 2934-2947.

Mohebbi, A. (2021). A Machine Learning Approach to Treatment Improvement in Type 2 Diabetes using Glucose Data.

Mohiuddin, A. K. (2020). The role of the pharmacist in patient care: achieving high quality, cost-effective and accessible healthcare through a team-based, patient-centered approach. Universal-Publishers.

Moon, S., Jambert, E., Childs, M., & von Schoen-Angerer, T. (2011). A win-win solution?: A critical analysis of tiered pricing to improve access to medicines in developing countries. Globalization and health, 7, 1-11.

Muir, T., & Zegarac, M. (2001). Societal costs of exposure to toxic substances: economic and health costs of four case studies that are candidates for environmental causation. Environmental health perspectives, 109(suppl 6), 885-903.

Mundy, C. (2001). The human genome project: a historical perspective. Pharmacogenomics, 2(1), 37-49.

Muthelo, R. G. (2022). An Integrated Decision-making Model for Evaluating Public Sector Construction Bids University of Johannesburg].

Najjar, R. (2023). Redefining radiology: a review of artificial intelligence integration in medical imaging. Diagnostics, 13(17), 2760.

Ndayishimiye, C., Tambor, M., & Dubas-Jakóbczyk, K. (2023). Barriers and Facilitators to Health-Care Provider Payment Reform–A Scoping Literature Review. Risk Management and Healthcare Policy, 1755-1779.

Ning, C., Jiao, Y., Wang, J., Li, W., Zhou, J., Lee, Y.-C., Ma, D.-L., Leung, C.-H., Zhu, R., & Wang, H.-M. D. (2022). Recent advances in the managements of type 2 diabetes mellitus and natural hypoglycemic substances. Food Science and Human Wellness, 11(5), 1121-1133.

Ohno-Machado, L., Kim, J., Gabriel, R. A., Kuo, G. M., & Hogarth, M. A. (2018). Genomics and electronic health record systems. Human molecular genetics, 27(R1), R48-R55.

Olson, S., & Berger, A. C. (2012). Genome-Based Therapeutics: Targeted Drug Discovery and Development: Workshop Summary. National Academies Press.

Organization, W. H. (2007). Financing long-term care programmes in health systems, with a situation assessment in selected high-, middle-and low-income countries.

Organization, W. H. (2013). Health 2020: A European policy framework and strategy for the 21st century. World Health Organization. Regional Office for Europe.

Patel, A., Unni, N., & Peng, Y. (2020). The changing paradigm for the treatment of HER2-

positive breast cancer. Cancers, 12(8), 2081.

Perales, S., Torres, C., Jimenez-Luna, C., Prados, J., Martinez-Galan, J., Sanchez-Manas, J. M., & Caba, O. (2021). Liquid biopsy approach to pancreatic cancer. World journal of gastrointestinal oncology, 13(10), 1263.

Perkins, B. A., Sherr, J. L., & Mathieu, C. (2021). Type 1 diabetes glycemic management: Insulin therapy, glucose monitoring, and automation. Science, 373(6554), 522-527.

Piette, J. D., List, J., Rana, G. K., Townsend, W., Striplin, D., & Heisler, M. (2015). Mobile health devices as tools for worldwide cardiovascular risk reduction and disease management. Circulation, 132(21), 2012-2027.

Pike, E. R., Rothenberg, K. H., & Berkman, B. E. (2014). Finding fault? Exploring legal duties to return incidental findings in genomic research. The Georgetown law journal, 102, 795.

RAMEEZ, M., KHAN, A. U., & Ali, R. (2023). BREAKTHROUGHS IN DISEASE PREVENTION AND TREATMENT. CURRENT STUDIES IN HEALTH AND LIFE SCIENCES, 431.

Rastegar, S., GholamHosseini, H., & Lowe, A. (2020). Non-invasive continuous blood pressure monitoring systems: current and proposed technology issues and challenges. Physical and Engineering Sciences in Medicine, 43, 11-28.

Reichenberg, L. W., & Seligman, L. (2016). Selecting effective treatments: A comprehensive, systematic guide to treating mental disorders. John Wiley & Sons.

Rose, N. (2013). Personalized medicine: promises, problems and perils of a new paradigm for healthcare. Procedia-Social and Behavioral Sciences, 77, 341-352.

Roufosse, F. (2018). Targeting the interleukin-5 pathway for treatment of eosinophilic conditions other than asthma. Frontiers in medicine, 5, 49.

Sahu, M., Gupta, R., Ambasta, R. K., & Kumar, P. (2022). Artificial intelligence and machine learning in precision medicine: A paradigm shift in big data analysis. Progress in molecular biology and translational science, 190(1), 57-100.

Santiago-Rodriguez, T. M., & Hollister, E. B. (2021). Multi 'omic data integration: A review of concepts, considerations, and approaches. Seminars in Perinatology,

Sarhene, M., Wang, Y., Wei, J., Huang, Y., Li, M., Li, L., Acheampong, E., Zhengcan, Z., Xiaoyan, Q., & Yunsheng, X. (2019). Biomarkers in heart failure: the past, current and future. Heart failure reviews, 24, 867-903.

Satam, H., Joshi, K., Mangrolia, U., Waghoo, S., Zaidi, G., Rawool, S., Thakare, R. P., Banday, S., Mishra, A. K., & Das, G. (2023). Next-generation sequencing technology: current trends and advancements. Biology, 12(7), 997.

Schoonmaker, M. M. (1998). Reimbursement issues in genetic testing: The role of the payer in the diffusion of new medical technologies. The Johns Hopkins University.

Schwarz, U. I., Gulilat, M., & Kim, R. B. (2019). The role of next-generation sequencing in pharmacogenetics and pharmacogenomics. Cold Spring Harbor Perspectives in Medicine, 9(2), a033027.

Scott, S. L. (2023). A Qualitative Study: Exploring Federal Employees' Perceptions of Barriers to Effective Diversity, Equity, Inclusion, and Accessibility Education in Federal Government Trident University International].

Shegekar, T., Vodithala, S., & Juganavar, A. (2023). The emerging role of liquid biopsies in revolutionising cancer diagnosis and therapy. Cureus, 15(8).

Shibata, T. (2015). Current and future molecular profiling of cancer by next-generation sequencing. Japanese Journal of Clinical Oncology, 45(10), 895-899.

Singh, D. B. (2020). The impact of pharmacogenomics in personalized medicine. Current Applications of Pharmaceutical Biotechnology, 369-394.

Singh, S. (2023). Racial biases in healthcare: Examining the contributions of Point of Care tools and unintended practitioner bias to patient treatment and diagnosis. Health, 27(5), 829-846.

Singh, S., Sarma, D. K., Verma, V., Nagpal, R., & Kumar, M. (2023). Unveiling the future of metabolic medicine: omics technologies driving personalized solutions for precision treatment of metabolic disorders. Biochemical and biophysical research communications.

Sitapati, A., Kim, H., Berkovich, B., Marmor, R., Singh, S., El-Kareh, R., Clay, B., & Ohno-Machado, L. (2017). Integrated precision medicine: the role of electronic health records in delivering personalized treatment. Wiley Interdisciplinary Reviews: Systems Biology and Medicine, 9(3), e1378.

Slunecka, J. L., van der Zee, M. D., Beck, J. J., Johnson, B. N., Finnicum, C. T., Pool, R., Hottenga, J.-J., de Geus, E. J., & Ehli, E. A. (2021). Implementation and implications for polygenic risk scores in healthcare. Human genomics, 15(1), 46.

Souhami, R., & Tobias, J. S. (2008). Cancer and its management. John Wiley & Sons.

Squassina, A., Manchia, M., Manolopoulos, V. G., Artac, M., Lappa-Manakou, C., Karkabouna, S., Mitropoulos, K., Zompo, M. D., & Patrinos, G. P. (2010). Realities and expectations of pharmacogenomics and personalized medicine: impact of translating genetic knowledge into clinical practice. Pharmacogenomics, 11(8), 1149-1167.

Stampe, K., Kishik, S., & Müller, S. D. (2021). Mobile health in chronic disease management and patient empowerment: exploratory qualitative investigation into patient-physician consultations. Journal of Medical Internet Research, 23(6), e26991.

Stephenson, C. (2011). The Complementary Therapist's Guide to Conventional Medicine E-Book: The Complementary Therapist's Guide to Conventional Medicine E-Book. Elsevier Health Sciences.

Su, M., Zhang, Z., Zhou, L., Han, C., Huang, C., & Nice, E. C. (2021). Proteomics, personalized medicine and cancer. Cancers, 13(11), 2512.

Suter, S. M. (2015). Genomic Medicine-New Norms regarding Genetic Information. Hous. J. Health L. & Pol'y, 15, 83.

Tang, W., Li, X., Xie, X., Sun, X., Liu, J., Zhang, J., Wang, C., Yu, J., & Xie, P. (2019). EGFR inhibitors as adjuvant therapy for resected non-small cell lung cancer harboring EGFR mutations. Lung Cancer, 136, 6-14.

Tzvetkov, M., & von Ahsen, N. (2012). Pharmacogenetic screening for drug therapy: from single gene markers to decision making in the next generation sequencing era. Pathology-Journal of the RCPA, 44(2), 166-180.

Viegi, G., Scognamiglio, A., Baldacci, S., Pistelli, F., & Carrozzi, L. (2001). Epidemiology of chronic obstructive pulmonary disease (COPD). Respiration, 68(1), 4-19.

Villagómez-Guzmán, A. K., & Quiroz, I. V. (2024). Human Diseases and Recent Biotechnology Breakthroughs in Curbing Diseases. Biotechnology and Drug Development for Targeting Human

Diseases, 9, 165-187.

Vodovotz, Y., Barnard, N., Hu, F. B., Jakicic, J., Lianov, L., Loveland, D., Buysse, D., Szigethy, E., Finkel, T., & Sowa, G. (2020). Prioritized research for the prevention, treatment, and reversal of chronic disease: recommendations from the lifestyle medicine research summit. Frontiers in medicine, 7, 585744.

Washington, V., Franklin, J. B., Huang, E. S., Mega, J. L., & Abernethy, A. P. (2023). Diversity, equity, and inclusion in clinical research: a path toward precision health for everyone. Clinical Pharmacology & Therapeutics, 113(3), 575-584.

Waterhouse, D., Gelmon, K., Klasa, R., Chi, K., Huntsman, D., Ramsay, E., Wasan, E., Edwards, L., Tucker, C., & Zastre, J. (2006). Development and assessment of conventional and targeted drug combinations for use in the treatment of aggressive breast cancers. Current cancer drug targets, 6(6), 455-489.

Who, J., & Consultation, F. E. (2003). Diet, nutrition and the prevention of chronic diseases. World Health Organ Tech Rep Ser, 916(i-viii), 1-149.

Wojtukiewicz, M. Z., Rek, M. M., Karpowicz, K., Górska, M., Polityńska, B., Wojtukiewicz, A. M., Moniuszko, M., Radziwon, P., Tucker, S. C., & Honn, K. V. (2021). Inhibitors of immune checkpoints—PD-1, PD-L1, CTLA-4—new opportunities for cancer patients and a new challenge for internists and general practitioners. Cancer and Metastasis Reviews, 40, 949-982.

Wouters, R. H., van der Graaf, R., Rigter, T., Bunnik, E. M., Ploem, M. C., de Wert, G. M., Dondorp, W. J., Cornel, M. C., & Bredenoord, A. L. (2021). Towards a responsible transition to learning healthcare systems in precision medicine: ethical points to consider. Journal of Personalized Medicine, 11(6), 539.

Xue, Y., Lameijer, E.-W., Ye, K., Zhang, K., Chang, S., Wang, X., Wu, J., Gao, G., Zhao, F., & Li, J. (2016). Precision medicine: what challenges are we facing? Genomics, Proteomics and Bioinformatics, 14(5), 253-261.

Young, A. H., & Grunze, H. (2013). Physical health of patients with bipolar disorder. Acta Psychiatrica Scandinavica, 127, 3-10.

Zahid, A., Poulsen, J. K., Sharma, R., & Wingreen, S. C. (2021). A systematic review of emerging information technologies for sustainable data-centric health-care. International Journal of Medical Informatics, 149, 104420.

About The Authors

Maria Nazir is an MPhil Scholar of Microbiology at the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur, Pakistan. She is involved in a National Research Program for Universities (NRPU) Project, with research interests in Molecular Characterization. She has submitted abstracts to various conferences and authored and coauthored of several book chapters. Her research focuses on the isolation and Molecular characterization of Corynebacterium pseudotuberculosis and their applications in promoting animal health. Her interested research criteria are based on genetics, molecular biology, and bioinformatics.

Email: nazirmaria545@gmail.com ORCID 0009-0004-6714-6212

Mr. Hameer Khan Khaskheli received his Master's in 2023 from the University of Padova, Italy. He is currently a Research Assistant in the Department of Biomedical Sciences at the University of Padova, Italy. His research expertise spans Molecular Biology, Cancer Biology, Medical Immunology, Stem Cell Research, and Precision Medicine. His primary focus is the intricate regulation of protein phosphorylation by kinases and phosphatases - critical processes often dysregulated in cancer and other diseases. He has an extensive record of publications in prestigious national and international journals and has authored two book chapters with a reputable publisher.

Email: hameerkhan.khaskheli@studenti.unipd.it ORCID 0009-0002-9622-9282

Dr. Nighat Batool completed her PhD in Pharmaceutical Sciences from Sargodha University, Sargodha, Pakistan. She is an Assistant Professor of Pharmaceutics at the Pharmacy Department of Pak-Austria Fachhochschule Institute of Applied Science and Technology Mang Haripur. Her research interests include Hydrogels, Microspheres, Pelletisation, Floating tablets, and Controlled release drug delivery systems. She has written more than 17 research articles in well-reputed national and international journals. She has also written book chapters.

Email: nighatbatool2352@gmail.com. ORCID: 0000-0002-9449-4624

Dr. Rumaisa Nawal received her MBBS degree in 2024 from Multan Medical and dental college. She is a house officer in Bhawal Victoria Hospital, Pakistan. She has done internship program at District Headquarters Lodhran.

Email: rumaisanawal9@gmail.com ORCID:0009-0000-1903-8365

Minal Hussain graduated from Cholistan University of Veterinary and Animal Sciences in Bahawalpur Pakistan. He continues his postgraduate study in Microbiology from Cholistan University of Veterinary and Animal Sciences Bahawalpur. Her research interest is in Bacteriophages, Bacteriology, Molecular cell biology, and Microbial genetics etc. She has published few book chapters in international journals.

Email: 2019-cu-bios-023@cuvas.edu.pk ORCID: 0009-0004-0143-5644

Dr. Danish Riaz received his PhD (Zoology) in 2018 from Government College University Faisalabad, Pakistan. He is serving as Assistant Professor of Zoology at the Department of Zoology, Division Science and Technology, University of Education Lahore Pakistan. His research interests include Biological Science with a specialization of animal biotechnology and Fisheries. He has published over 34 research articles in well-reputed national and international journals. He also has written book chapters.

Email: danish.riaz@ue.edu.pk ORCID-0000-0002-6137-8993

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as "Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone". His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

Dr. Muhammad SAFDAR earned his PhD in Molecular Biology and Genetics from Gaziantep University, Turkey. He is Lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 70 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

E-mail: msafdar@cuvas.edu.pk ORCID: 0000 0002 3720 2090

To Cite This Chapter

NAZIR M et al., (2024). Revolutionizing chronic disease management with precision medicine and navigating. In Current Studies in Health and Life Sciences 2024 (pp.103-128). ISRES Publishing.

Microbiome and Autoimmune Diseases

Muhammad Masood AHMED

Fahad ULLAH

Muhammad Nazir UDDIN

Muhammad SAFDAR

1. Introduction to the Microbiome and Autoimmunity

The discovery of human microbiome has revolutionized our understanding of health and disease. These microbes, which live in various parts of the body; play different roles and as well as essential for the body's overall health. Recent innovations in genomics, especially the Human Microbiome Project (HMP), have shown that microbiota intertwines with the host in a complex process (Wang et al., 2017). The gut microbiota, which harbors the highest density of microbes that impact digestion, synthesis vitamins (Bengmark, 2013). Microbiomes present in other body sites such as skin, oral and respiratory microbiota are understood to have a considerable influence on site-specific and overall health.

The human body has a complex mechanism known as the immune system, which is primarily designed to safeguard the body (Parkin & Cohen, 2001). However, a snag may happen that may result in the immune system attacking a part of the body, leading to Autoimmune Diseases. These diseases are numerous and polygenic and many are known to be influenced by both genetic and environmental responses (Migliore & Coppedè, 2009). Recent literature supports that the microbiome-autoimmune connection has a significant role in the development of autoimmune diseases. Under this interaction, it is evident that the two, that is the microbiome and the immune system are interrelated as they respond to each other. Dysbiosis, characterized by abnormal microbiota, and is linked to various autoimmune diseases that encompass inflammatory bowel disease(IBD), according to research (de Oliveira et al., 2017).

Further explanations reveal how the microbiome affects autoimmune diseases: SCFAs are related to the microbial activities and have the ability to exert immunomodulatory effects, influence the regulatory T cell balance (Ratajczak et al., 2019). The autoimmune reactions can also be attributed to the molecular mimicry, where microbial antigens are similar to host antigens. Secondly, if the gut barrier is compromised, it allows luminal microbial components to directly enter the blood stream and potentially worsen systemic inflammation and autoimmune processes (Wells et al., 2017).

This shift in the concept of microbiome, particularly with reference to autoimmune diseases has, significant implication for both fields of study. It offers the chance for a clinical focus in Phillipsburg, to emerge and establish pharmacological strategies based on the disruption of microbiota to correct immunological disorders (Duarte-Chavez et al., 2018). Possible solutions may include use of probiotics as well as prebiotics, diet change and a process called fecal microbiota transplantation (FMT). Subsequently, targeting of biomarkers with links to specific autoimmune diseases would mean early identification and diagnosis of the disease, and elevating the management of autoimmune diseases to the next level: the potential of biomarkers in autoimmune diseases (Giacomelli et al., 2019).

2. The Human Microbiome: A Diverse Ecosystem

The human microbiome is an extensive and multifaceted system comprising trillions of microbes that reside within and on the human bodies, encompassing microbes, viruses, fungi, and archaea (Hoffmann et al., 2016). These microbes inhabit characteristic body locations, introducing

themselves as specific communities that functions to fulfill a range of critical roles for the human body. A more substantial and diverse compartment is the gut microbiome which is inhabited by approximately 100 trillion microbes of Firmicutes and Bacteroidetes phyla (Rinninella et al., 2019). These microbes are essential for digestion processes, the biosynthesis of vitamins and the body's defense mechanisms.

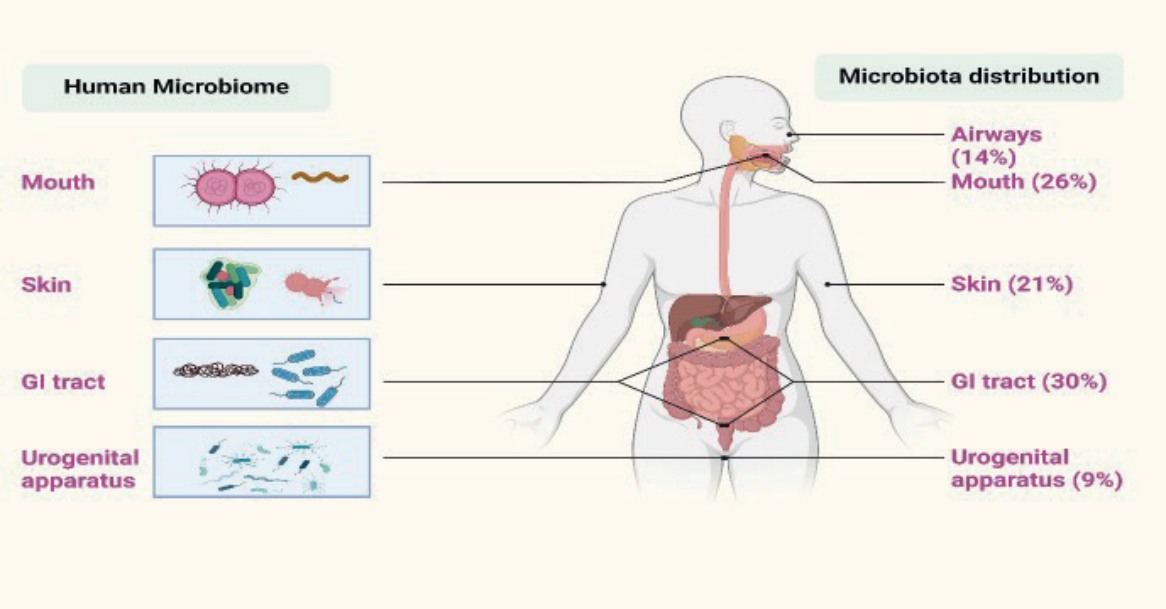


Figure 1. Microbiome and Autoimmunity

The skin microbial communities can differ among various different parts of the body; wet body regions have a different microbial population compared to the dry ones (Rosenthal et al., 2011). Cutaneous commensal flora include Staphylococcus, Corynebacterium and Propionibacterium species; These bacteria has a significance role in maintaining skin homeostasis to prevent colonization of skin by bad pathogens (Percival et al., 2012).The oral biofilm, a diverse ecosystem involving bacteria, fungi and viruses, also contains specific bacterial genera that are involved in the initial breakdown processes and the antagonism of pathogens: Streptococcus, Actinomyces and Fusobacterium. Subtypes of bacteria, including Streptococcus, Haemophiles, and Neisseria, contribute to the lung microbiome's function in patency and protecting against microbial invasion (García et al., 2016).

The microbiome has been credited with indispensable metabolic, protective, and immune-regulatory functions (Samuelson et al., 2015). The colonic microbiota metabolizes non- digestible carbohydrates into SCFAs, which are necessary for colon function and exert an array of general anti- inflammatory functions. They also manufacture important vitamins that are integral part of the body such as vitamin K and the B vitamin group (Shearer & Newman, 2008). By outcompeting for space and nutrients, the microbiome inhibits pathogens through their action of occupying the valuable niche, directly killing pathogens, and inducing host antimicrobial peptides. Additionally, the microbiome modulation of immune systems, including the ability to determine the difference between objects that can have a negative impact and those that are safe, immune tolerance, as well as efficient responses to pathogens (Tamburini et al., 2016).

As we know that human microbiome is a intricate system that is 'constructed' immediately after birth and modified by different factors throughout the lifespan. It explicitly exhibits how the mode of delivery affects the determining initial microbial colonization, directly from the mothers' microbiota for infants delivered through the vaginal route and skin and environmental microbes for those delivered through the cesarean section (Nuriel-Ohayon et al., 2016). Diet has a significant impact on microbiota, with microbial counts increasing in individuals taking the habitual Diet of breastfeeding supporting the growth of Bifidobacteria in the gut and high-fiber diet supporting the growth of diverse microbiota in adults (Francino, 2016). Lifestyle factors and the environment

also affect the population of microorganisms within the body, suggesting that there may be fewer microbial species in non-rural contexts due to hygienic practices of modernity.

The concept of microbiome is still comparatively new to the discussion of specific disease manifestation, but recent studies do suggest that the microbiome is connected to autoimmune diseases in some way (De Luca & Shoenfeld, 2019). The human body microbiota is unbalanced, which is popularly known as dysbiosis, in most autoimmune diseases. It has been reported that there are changes in the composition of gut microbiota of RA patients and diabetic, multiple sclerosis (MS) and healthy control indicating that altered microbiome may be related to the development and severity of autoimmune diseases (Chen et al., 2016).

3. Autoimmune Diseases: When the Immune System Goes Awry

Autoimmune diseases can be described as illnesses that occur when the immune system which is supposed to safeguard the body, starts threatening it instead (Condemi, 1992). This immune system disorganization makes the body experience constant inflammation, tissue necrosis, and impaired organ functions. Genetic factors, environmental contaminants, and microbial infections can be found to be associated with these diseases (Ashbolt, 2004).

There exist various pathways that are involved in the erosion of immune tolerance, a prominent feature observed in autoimmune diseases. Autoimmune disease has a highly genetic, with some genes making one vulnerable to the bacteria or other infections. The concept of molecular mimicry is whereby the foreign antigens share some similarities with host antigens and this is what leads to the cross immune attack on both pathogens and tissues (Segal & Shoenfeld, 2018). Autoimmune disease develops when a pathological process excites immune cells, which react with a high level of pathogenicity against self-antigens. This leads to epitope spreading, where the initial response increases in scale to attack other unrelated self-antigens, increasing the severity of the particular disease in question. Environmental factors such as infections, drugs and toxins also act as an environmental cause that can lead to the onset or exacerbation of autoimmune diseases (Molina & Shoenfeld, 2005).

There are more than eighty sorts of autoimmune diseases; all these diseases conduct an impact on different tissues and organs. Rheumatoid arthritis is a long-term disease characterized by inflammation affecting the joints resulting in pain, stiffness and swelling (Grassi et al., 1998). Systemic lupus erythematosus (SLE) is a chronic or relapsing systemic disease and disturbs several organs, in which autoantibodies can be produced against different cellular components. (Johnston Jr & Joy, 2001).

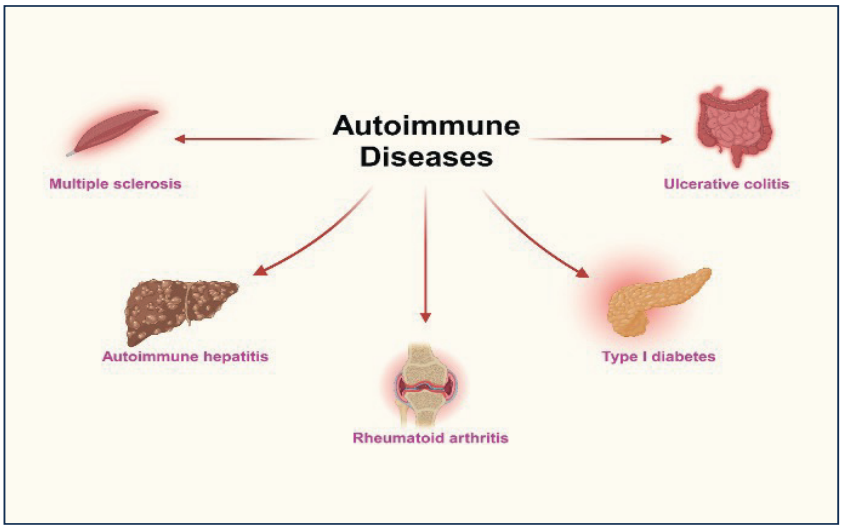


Figure 2. Autoimmune Diseases

It may prove a difficult proposition to diagnose autoimmune diseases especially bearing in mind that their manifestations are numerous and diverse (Touitou & Koné-Paut, 2008). It may involve a general physical examination and or assessments, serologic tests (autoantibodies), and imaging tests (like radiography, MIR, USG). Sometimes, histological samples obtained by biopsy may be required to affirm the diagnosis.

Autoimmune diseases' treatment is accomplished by moderating the immune system's activity, diminishing inflammation, and decreasing disease manifestations (Goodnow, 2001). The interventions include NSAIDs, corticosteroids, synthetic disease-modifying antirheumatic drugs DMARDs, and biologic agents (Smolen et al., 2017). Lifestyle changes which involve dietary changes, exercise regimes, and stress management can also be of immense assistance. Lifestyle changes in chronic illness patients, such as physical therapy and occupational therapy, can show remarkable enhancements in movement and function (Pedersen & Saltin, 2006).

Recent studies have brought the concept of microbiome involvement in autoimmune diseases to the spotlight. An inequity in the microbial makeup of the body, known as dysbiosis and has been positively associated with autoimmune diseases. With emerging evidences for the role of the gut microbiome in diseases such as RA, T1D, and MS, the variations in the gut microbiome composition have been an issue of interest (Vijay & Valdes, 2022). Such pathways of the microbial communication with the immune regulations are microbial metabolite and pattern recognition receptors. MIMS If the balance of the microbiota is shifted dysbiosis-interactions between the bacterial strains, the interaction of the bacteria with the epithelium, epithelium with the underlying tissue, the tight junctions and the permeability of the epithelial layer can be altered and promote further inflammation to the system and can stimulate autoimmune reactions (Yu et al., 2012).

Since microbiome is the mainly involved in the development of autoimmune diseases, it is quite logical to consider the manipulation of the microbiome as a viable strategy for the treatment of autoimmune diseases. Interpositions such as probiotics, prebiotics, nutrition modification, and fecal microbiota transplantation (FMT) are under trials for the restoration of PAH symbiosis and the dampening down of autoimmune responses (Flandroy et al., 2018). Future studies can potentially give better understanding of the effects of microbiome and immune system, which gives hope that people with autoimmune diseases can be alive better through innovative therapeutic strategies.

4. Microbiome-Immune Crosstalk: A Delicate Balance

Both the immune system and microbiota are constantly actively interacting through bidirectional communication necessary for optimal health (Zheng et al., 2020). This interplay is termed microbiome-immune crosstalk, and understanding these interactions is critical to deciphering how dysbiosis, perturbations in microbial communities, can contribute to immune system disorders such as autoimmunity.

The immune system is a coordinated group of defenses in the body, comprising of various cells, tissues, and organs. It consists of two main components: non-specialized immunity also known as the natural immunity, which is the first line of defense, and specialized immunity also known as the acquired immunity which forms the second line of defense (Spoel & Dong, 2012). There is also the innate system which comprises of barriers such as skin, and immune cells like the macrophages and neutrophils while the second is the adaptive immunity consist of lymphocytes comprised of the B and T cells that are selective to the antigens in question.

The interactions between microbiome and immune system are not well understood but can happen in several ways (Maynard et al., 2012). Some of the metabolites include short-chain fatty acids (SCFAs) that have immunosuppressive characteristics and stimulate Treg cells which are involved in immune tolerance. Cells involved in innate immunity contain molecules called pattern recognition receptors (PRRs) that bind to microbial molecules and affect the immune response. We found that mucosal immunity especially in the GALT site has important function in taking samples

of microbial antigens and immune cell education (Kawai & Akira, 2010). The Intestinal epithelial barrier is involved in preventing the microbes from crossing into the systemic circulation while the microbiome supports the epithelium. Microbes also modulate cytokine production which are chemical mediators involved in immune system communication (Thomas & Versalovic, 2010).

Imbalance in the two complexes, microbiome, and immunity, can cause disruption in the system, dysbiosis and immune dysregulation, autoimmune diseases. These are infection, antibiotics, diet, and stress among them though there may be other causes, as well. The pathogenesis of Visceral leishmaniasis begins from increased permeability of the intestine ("leaky gut") and additionally increases the blood circulation of microbial products that cause inflammation (Slyepchenko et al., 2016). Dysbiosis can also change immunological biases for inflammation, IMDs reducing T regs, and activating PRRs. Also, molecular mimicry, through which microbial antigens resemble self-antigens and initiate the autoimmune response in the susceptible host.

Some examples of microbiome-immune communication in autoimmune disorders include Rheumatoid arthritis (RA), Type 1 diabetes (T1D) and Multiple sclerosis (MS) (Zheng et al., 2020). For example, in RA, a more significant number of Prevotella copri have been linked to the development of the disease. In T1D, research has shown a connection of dysbiosis with both less bacterial richness and variations in certain bacterial populations. Literature on MS reports changes in the gut microbiota in the following ways: reduced ratio of anti-inflammatory bacterial strains and increased ratio of pro-inflammatory bacteria (Cristofori et al., 2021).

Knowledge regarding this crosstalk unveils novel pharmacological possibilities. There are various ways of altering the microbiome balance including probiotics, prebiotics, diet modification, and fecal microbiota transplant (FMT) (Cammarota et al., 2014). Other antimicrobial strategies that are under development are targeted therapies for individual microbial Immune interactions. Thus, studying these mechanisms and their consequences would help generate new ideas and solutions to eliminate autoimmune diseases.

5.Gut Microbiome and Autoimmunity: The Gut-Immune Axis

The gut microbiome states to the microbial community that resides in the human gastrointestinal tract and it has been earlier established that the microbiome plays a critical role in determining overall health and disease, especially in relation to autoimmunity (Thursby & Juge, 2017). The interactions between the gut and the immune system form a bidirectional communication system with the microbiota and are effective in maintaining the immune system and preventing autoimmune diseases. This crosstalk is complex and includes the GALT (gut-associated lymphoid tissue), the mucosal barrier, microbial metabolites, or immunocytes (Laissue et al., 1993). Role of Gut Microbiota in autoimmune disease is shown in below figure.

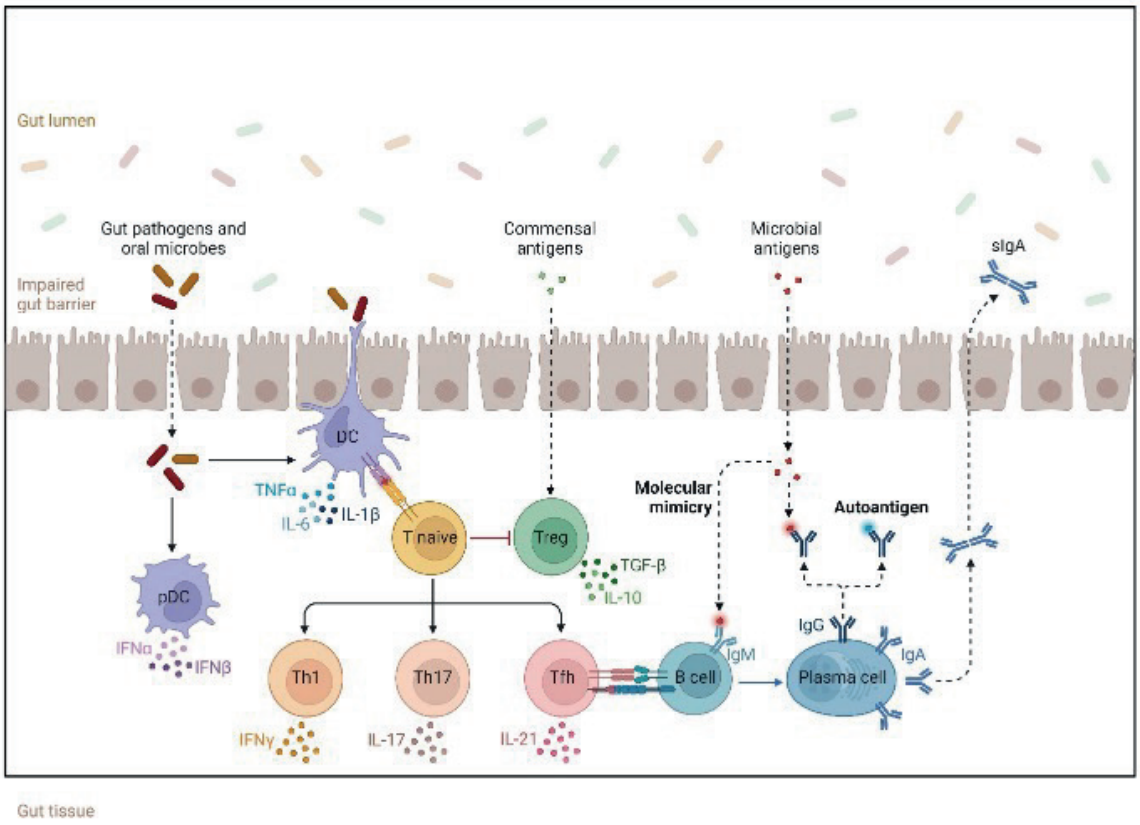


Figure 3. Role of the Gut Microbiota in Autoimmune Diseases

GALT makes up a major proportion of the immune cells, and it plays a crucial role in analyzing antigens from the gut and make the right responses. The intestinal epithelium also serves as a barrier whose primary function is to deny pathogenic organisms and their products entry into the systemic circulation (Powell, 1981). Saturated fatty acids can also influence immune function via preserving gut integrity and regulating inflammation and Tregs. The GI tract mucosa contains immune cells which, interacting with microbial antigens, get differentiated into Tregs or effector T cells that modulate immune response (Acheson & Luccioli, 2004).

An anomalous distribution of the microbiota, termed dysbiosis and it is the key contributor to the expansion of autoimmune diseases. This can alter the permeability of the gut, allowing toxins to penetrate the intestinal lining and enter the systemic circulation resulting in autoimmune type inflammation. Additionally, dysbiosis causes chronic inflammation, which enhances pro-inflammatory cytokines and shortages anti-inflammatory cytokines to aggravate autoimmune diseases. Furthermore, such shifts in microbiota composition affect the development and the functionality of immune cells and lead to immune intolerance and autoimmunity.

Autoimmune diseases like RA, T1D, MS, and IBD have been linked to dysbiosis. For example, in early RA the levels of Prevotella copri are increased, as well as in T1D there is reduced diversity of microbiota and some bacterial shifts in T1D (Miyauchi et al., 2023). In MS, it has been revealed that there are reduces the number of anti-inflammatory microbes and the number of pro-inflammatory microbes has been found to be high. IBD contributes to the dilution of effective bacteria, as well as the proliferation of pathogenic bacteria that cause chronic inflammation.

It showed that SCFAs which benefits gut and immune system and Toll like receptors which senses microbial signals to trigger immune response are the two interconnected components of microbiome and Immune system. Immunological tolerance is kept by Tregs which are regulated by the GM but dysbiosis reduces their number and functionality. It is established that some microbial

antigens are capable of inducing autoimmune reactions due to cross-reactivity with self-antigens in susceptible persons (Cooke et al., 1983).

Probiotics, prebiotics, diet modifications, and FMT are therapeutic interventions that may provide an option for tackling autoimmune diseases (Mangalam et al., 2021). Some of the aids include prebiotics which help in the restoration of the friendly bacteria while the probiotics assist in restoring the balance of the immune system. There is evidence that dietary modification to the Mediterranean diet reduces inflammation and has a positive effect on the microbiome. FMT involves the deposition of stool from a healthy individual is termed as FMT and this can assist in reconstructing the impaired functions. Having an understanding of the interaction between the microbes and the immune system will help encourage the use of focused treatments to enhance the synthesis of SCFAs or to nurture the growth of healthy bacteria in the body (Parada Venegas et al., 2019).

6. Beyond the Gut: Other Microbiomes in Autoimmunity

While autoimmunity perturbation is assigned to gut microbiota, the skin, mouth, lung, and urogenital tract microbiota are also significant, and their dysbiosis exists (De Pessemier et al., 2021). All of these microbiomes have various touch points with the immune system and factors that can influence the development and progression of autoimmune diseases. Oral biofilm states to a complex and ever-changing community of microorganisms such as bacteria, fungi, and viruses that make close associations with the teeth, gums, and tongue and plays a critical role in oral diseases and immune system functioning. Disharmony of the microflora of the oral cavity can affect different organs and tissues adversely and is believed to be involved in the development of certain autoimmune diseases such as rheumatoid arthritis due to systemic inflammation and molecular mimicry. Eubacteria lung microbiome is present in less number but diverse and has an essential impact on the respiratory tract and the immune response (Shukla et al., 2017).

The urogenital microbiota is relatively host specific and can be qualitatively and quantitatively altered by many factors, making it crucial to urogenital health. Dysbiosis is supposed to be one of the factors contributing to the shift in the urogenital microbiota which may be the cause of autoimmune urogenital diseases such as interstitial cystitis and autoimmune thyroiditis.

Thus, the regulation of these SITE-OTHERS by use of the concepts of probiotics, prebiotics, and antimicrobial targeting can be considered as therapeutic management strategies for autoimmune diseases (Shihata, 2004). Higher awareness and knowledge of these microbial communities regarding immune modulation may create a path to new therapies if autoimmune diseases impact multiple organs.

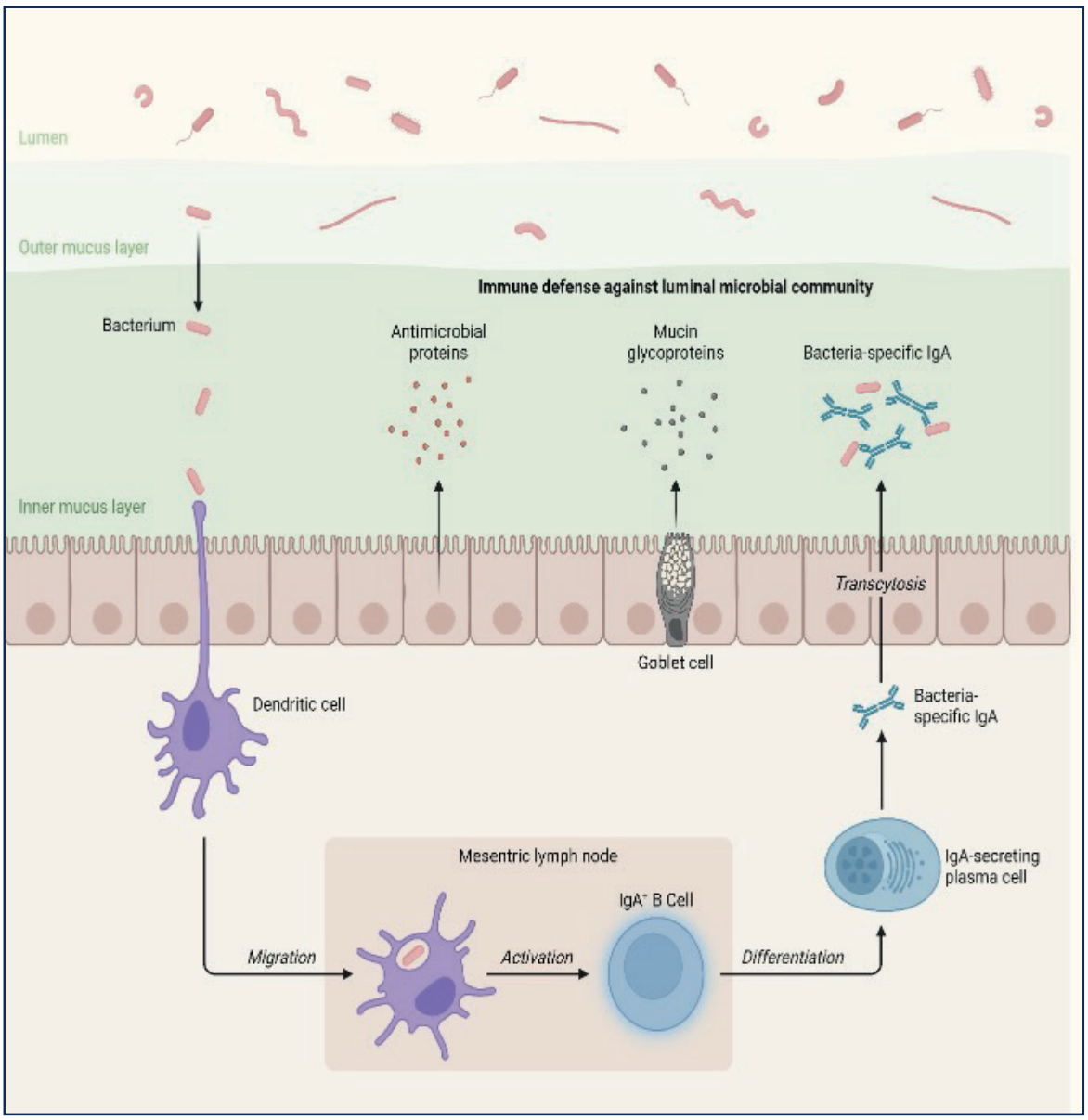


Figure 4. Intestinal Immune Défense Against Luminal Microbes

7. Therapeutic Potential: Harnessing the Microbiome for Treatment

Autoimmune diseases are expected to be influenced by gut microbiota and thus represent an extensive application target in medicine. This includes the introduction of naturally occurring or synthetically produced beneficial microorganisms or substrates, shift in diet, FMT and other novel microbiota modification therapies for disease (Quigley & Gajula, 2020).

The standard definition of probiotics is live bioactive microorganisms that are beneficial to the host, which can be achieved by intake of adequate quantities of such microorganisms. They operate through enhancing the mechanical and chemical barrier of the gut, modulating immune responses and producing antibiotics. However, it is evident from available research, that probiotics could prove beneficial in managing IBD, RA and MS.

Prebiotics are termed as non-hydrolysable agents or non-digestible oligosaccharides that act as factors enhancing the population of the beneficial bacteria in the GI tract. These extend the production of short-chain fatty acids (SCFAs) that contain anti-inflammatory properties and enable the development of favorable bacterial strains. A encouraging evidence regarding the use of Prebiotin was also witnessed in IBD, IBS and autoimmune diabetes (Sanders et al., 2019).

One aspect that deserves even more attention is that dietary interventions are the only possible approach to the change of the microbiome and immune response. According to research, there is information that shows that certain diets like the Mediterranean diet and low FODMAP diet aid in reducing inflammation and boost immune responses (García-Montero et al., 2021). These trials can be used to deduce some foods to eliminate from one's diet since their consumption is likely to aggravate autoimmune disease symptoms. These includes the farm to fork strategy for food and nutrition or the consumption map to specified microbiome characteristics and moderation for microbiota optimization.

This treatment process involves transferring stool sample from a normal person to a patient who has dysbiosis in order to improve microbial issues. FMT has also been very effective in treating recurrent C difficile infection and has been employed to reasonable extent for management of IBD and other autoimmune bowel disease related cases (Borody & Khoruts, 2012).

The future continuous lines of microbiome-based medication include symbiotic that is both probiotics and prebiotics, postbiotic which is the metabolites that the probiotics yield, phage therapy which uses the viral particles to counter specific bacterial types plus the microbiome modulation drugs. They are more beneficial in treating autoimmune diseases because they provide prospects at achieving new balance of the microbial community and immunologic functioning (Tlaskalová-Hogenová et al., 2004).

Table: Microbiome-Based Therapeutic Interventions for Autoimmune Diseases

Microbiome-Based Therapies	**Description**	**Potential Applications**
Probiotics	Live microorganisms that confer health benefits to the host.	Inflammatory Bowel Disease (IBD), Rheumatoid Arthritis (RA), Multiple Sclerosis (MS)
Prebiotics	Non-digestible food ingredients that promote the growth of beneficial bacteria in the gut.	IBD, Irritable Bowel Syndrome (IBS), Autoimmune Diabetes
Dietary interventions	Modification of food intake to alter gut microbiota and immune response.	Inflammatory Bowel Disease, Rheumatoid Arthritis
Fecal Microbiota Transplant (FMT)	Transfer of stool from a healthy donor to restore a healthy gut microbiome in a recipient.	Recurrent Chloridoids difficile infection, IBD
Emerging therapies	Symbiotic (probiotics + prebiotics), postbiotics (metabolites produced by probiotics), phage therapy (use of viruses to target specific bacteria), microbiome-modulating drugs.	Various autoimmune diseases

8. Future Directions and Challenges

The revelation of the functioning of microbiome in autoimmune diseases has helped to expand the paradigm in the field of study and treatment (Kaufmann, 2019). Areas that need further research include the geographical mapping of microbiota to determine the distribution of microbes within designated areas, functional analysis of microbial consortiums, and analysis of the symbiotic relationship between the host and microbiota. Interpreting research to therapeutics entails precision-driven microbiome therapies, new therapeutic approaches such as symbiotic and postbiotics, and conceptualizing the microbiome therapy guidelines and standards.

Major concerns in this field include microbiome heterogeneity, evaluating the risk and potential side effects of all therapies, and patient awareness of the microbiome and its function in the body. There are also more general questions related to the ethical and societal impact, including how to

provide equal and fair access to the pros of microbiome-based treatments, how to protect patients' data privacy, and how to address the public and make people trust those innovations.

Thus, the knowledge of the microbiome, translation of the research findings into useful treatment and management strategies, tackling barriers, and the ethical aspects could help maximize the potential of the microbiome to enhance the quality of life for the autoimmune disease sufferers.

9. Conclusion

It can be stated that the relations of the human microbiome with immunity as a topic that can be highly effective in the development of auto immune diseases. Specifically, the intricate inter– and interrelation between the aforementioned microbes/toxins and the immune system as a whole, not to mention the trillion-shaped microbial orchestra existing inside or on us, may shed light on the multiple faces of autoimmunity and prompt the creation of unprecedented immunotherapies. Furthermore, by comparing what the composition of the microbiome is, and how it can interrupt and speak to the immune system, or if therapeutic-solutions based on microbiome may actually contribute to understanding the extent to which the microbiome seems to manage and transform the immune system to counter autoimmune diseases we have recovered a sense of the ways in which it might work. Therefore, as more have been done to find out how the host microbiota signals the immune system there is no doubt that microbiome holds enormous opportunities in generating new and wider horizons in autoimmune diseases prevention, detection and control. Therefore, there is a hope that through the implementation of the ability to use potential microbiome, it will be possible to show the theoretical and proof-base for the individual and selective methods for treating such diseases that will give people with such ailments a desired and better quality of life. However, some limitations can be circumvented in the future, so it can be concluded that the prospects for the development of the microbiome in autoimmunity are impressive as part of the concept of personalized medicine micro biome in health and disease.

REFERENCES;

Acheson, D. W., & Luccioli, S. (2004). Mucosal immune responses. Best Practice & Research Clinical Gastroenterology, 18(2), 387-404.

Ashbolt, N. J. (2004). Microbial contamination of drinking water and disease outcomes in developing regions. Toxicology, 198(1-3), 229-238.

Bengmark, S. (2013). Gut microbiota, immune development and function. Pharmacological research, 69(1), 87-113.

Borody, T. J., & Khoruts, A. (2012). Fecal microbiota transplantation and emerging applications. Nature reviews Gastroenterology & hepatology, 9(2), 88-96.

Cammarota, G., Ianiro, G., Bibbò, S., & Gasbarrini, A. (2014). Gut microbiota modulation: probiotics, antibiotics or fecal microbiota transplantation? Internal and emergency medicine, 9, 365-373.

Chen, J., Chia, N., Kalari, K. R., Yao, J. Z., Novotna, M., Paz Soldan, M. M., Luckey, D. H., Marietta, E. V., Jeraldo, P. R., & Chen, X. (2016). Multiple sclerosis patients have a distinct gut microbiota compared to healthy controls. Scientific reports, 6(1), 1-10.

Condemi, J. J. (1992). The autoimmune diseases. Jama, 268(20), 2882-2892.

Cooke, A., Lydyard, P., & Roitt, I. (1983). Mechanisms of autoimmunity: a role for cross-reactive idiotypes. Immunology Today, 4(6), 170-175.

Cristofori, F., Dargenio, V. N., Dargenio, C., Miniello, V. L., Barone, M., & Francavilla, R. (2021). Anti-inflammatory and immunomodulatory effects of probiotics in gut inflammation: a

door to the body. Frontiers in immunology, 12, 578386.

De Luca, F., & Shoenfeld, Y. (2019). The microbiome in autoimmune diseases. Clinical & Experimental Immunology, 195(1), 74-85.

de Oliveira, G. L. V., Leite, A. Z., Higuchi, B. S., Gonzaga, M. I., & Mariano, V. S. (2017). Intestinal dysbiosis and probiotic applications in autoimmune diseases. Immunology, 152(1), 1-12.

De Pessemier, B., Grine, L., Debaere, M., Maes, A., Paetzold, B., & Callewaert, C. (2021). Gut–skin axis: current knowledge of the interrelationship between microbial dysbiosis and skin conditions. Microorganisms, 9(2), 353.

Duarte-Chavez, R., Wojda, T. R., Zanders, T. B., Geme, B., Fioravanti, G., & Stawicki, S. P. (2018). Early results of fecal microbial transplantation protocol implementation at a community-based university hospital. Journal of Global Infectious Diseases, 10(2), 47-57.

Flandroy, L., Poutahidis, T., Berg, G., Clarke, G., Dao, M.-C., Decaestecker, E., Furman, E., Haahtela, T., Massart, S., & Plovier, H. (2018). The impact of human activities and lifestyles on the interlinked microbiota and health of humans and of ecosystems. Science of the total environment, 627, 1018-1038.

Francino, M. (2016). Antibiotics and the human gut microbiome: dysbioses and accumulation of resistances. Frontiers in microbiology, 6, 164577.

García-Montero, C., Fraile-Martínez, O., Gómez-Lahoz, A. M., Pekarek, L., Castellanos, A. J., Noguerales-Fraguas, F., Coca, S., Guijarro, L. G., García-Honduvilla, N., & Asúnsolo, A. (2021). Nutritional components in Western diet versus Mediterranean diet at the gut microbiota–immune system interplay. Implications for health and disease. Nutrients, 13(2), 699.

García, B., Merayo-Lloves, J., Martin, C., Alcalde, I., Quirós, L. M., & Vazquez, F. (2016). Surface proteoglycans as mediators in bacterial pathogens infections. Frontiers in microbiology, 7, 220.

Giacomelli, R., Afeltra, A., Alunno, A., Bartoloni-Bocci, E., Berardicurti, O., Bombardieri, M., Bortoluzzi, A., Caporali, R., Caso, F., & Cervera, R. (2019). Guidelines for biomarkers in autoimmune rheumatic diseases-evidence based analysis. Autoimmunity reviews, 18(1), 93-106.

Goodnow, C. C. (2001). Pathways for self-tolerance and the treatment of autoimmune diseases. The Lancet, 357(9274), 2115-2121.

Grassi, W., De Angelis, R., Lamanna, G., & Cervini, C. (1998). The clinical features of rheumatoid arthritis. European journal of radiology, 27, S18-S24.

Hoffmann, A. R., Proctor, L., Surette, M., & Suchodolski, J. (2016). The microbiome: the trillions of microorganisms that maintain health and cause disease in humans and companion animals. Veterinary pathology, 53(1), 10-21.

Johnston Jr, R. B., & Joy, J. E. (2001). Multiple sclerosis: current status and strategies for the future.

Kaufmann, S. H. (2019). Immunology's coming of age. Frontiers in immunology, 10, 453189.

Kawai, T., & Akira, S. (2010). The role of pattern-recognition receptors in innate immunity: update on Toll-like receptors. Nature immunology, 11(5), 373-384.

Laissue, J. A., Chappuis, B., Müller, C., Reubi, J., & Gebbers, J.-O. (1993). The intestinal immune system and its relation to disease. Digestive Diseases, 11(4-5), 298-312.

Mangalam, A. K., Yadav, M., & Yadav, R. (2021). The emerging world of microbiome in

autoimmune disorders: Opportunities and challenges. Indian journal of rheumatology, 16(1), 57-72.

Maynard, C. L., Elson, C. O., Hatton, R. D., & Weaver, C. T. (2012). Reciprocal interactions of the intestinal microbiota and immune system. Nature, 489(7415), 231-241.

Migliore, L., & Coppedè, F. (2009). Genetics, environmental factors and the emerging role of epigenetics in neurodegenerative diseases. Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis, 667(1-2), 82-97.

Miyauchi, E., Shimokawa, C., Steimle, A., Desai, M. S., & Ohno, H. (2023). The impact of the gut microbiome on extra-intestinal autoimmune diseases. Nature Reviews Immunology, 23(1), 9-23.

Molina, V., & Shoenfeld, Y. (2005). Infection, vaccines and other environmental triggers of autoimmunity. Autoimmunity, 38(3), 235-245.

Nuriel-Ohayon, M., Neuman, H., & Koren, O. (2016). Microbial changes during pregnancy, birth, and infancy. Frontiers in microbiology, 7, 1031.

Parada Venegas, D., De la Fuente, M. K., Landskron, G., González, M. J., Quera, R., Dijkstra, G., Harmsen, H. J., Faber, K. N., & Hermoso, M. A. (2019). Short chain fatty acids (SCFAs)-mediated gut epithelial and immune regulation and its relevance for inflammatory bowel diseases. Frontiers in immunology, 10, 424615.

Parkin, J., & Cohen, B. (2001). An overview of the immune system. The Lancet, 357(9270), 1777-1789.

Pedersen, B. K., & Saltin, B. (2006). Evidence for prescribing exercise as therapy in chronic disease. Scandinavian journal of medicine & science in sports, 16(S1), 3-63.

Percival, S. L., Emanuel, C., Cutting, K. F., & Williams, D. W. (2012). Microbiology of the skin and the role of biofilms in infection. International wound journal, 9(1), 14-32.

Powell, D. (1981). Barrier function of epithelia. American Journal of Physiology-Gastrointestinal and Liver Physiology, 241(4), G275-G288.

Quigley, E. M., & Gajula, P. (2020). Recent advances in modulating the microbiome. F1000Research, 9.

Ratajczak, W., Rył, A., Mizerski, A., Walczakiewicz, K., Sipak, O., & Laszczyńska, M. (2019). Immunomodulatory potential of gut microbiome-derived short-chain fatty acids (SCFAs). Acta Biochimica Polonica, 66(1), 1-12.

Rinninella, E., Raoul, P., Cintoni, M., Franceschi, F., Miggiano, G. A. D., Gasbarrini, A., & Mele, M. C. (2019). What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. Microorganisms, 7(1), 14.

Rosenthal, M., Goldberg, D., Aiello, A., Larson, E., & Foxman, B. (2011). Skin microbiota: microbial community structure and its potential association with health and disease. Infection, Genetics and Evolution, 11(5), 839-848.

Samuelson, D. R., Welsh, D. A., & Shellito, J. E. (2015). Regulation of lung immunity and host defense by the intestinal microbiota. Frontiers in microbiology, 6, 158648.

Sanders, M. E., Merenstein, D. J., Reid, G., Gibson, G. R., & Rastall, R. A. (2019). Probiotics and prebiotics in intestinal health and disease: from biology to the clinic. Nature reviews Gastroenterology & hepatology, 16(10), 605-616.

Segal, Y., & Shoenfeld, Y. (2018). Vaccine-induced autoimmunity: the role of molecular mimicry and immune crossreaction. Cellular & molecular immunology, 15(6), 586-594.

Shearer, M. J., & Newman, P. (2008). Metabolism and cell biology of vitamin K. Thrombosis and haemostasis, 100(10), 530-547.

Shihata, A. (2004). The proteolytic activity of yoghurt and probiotic bacteria for the improved viability of probiotic bacteria in fermented milk products Victoria University of Technology].

Shukla, S. D., Budden, K. F., Neal, R., & Hansbro, P. M. (2017). Microbiome effects on immunity, health and disease in the lung. Clinical & translational immunology, 6(3), e133.

Slyepchenko, A., Maes, M., Machado-Vieira, R., Anderson, G., Solmi, M., Sanz, Y., Berk, M., A Kohler, C., & F Carvalho, A. (2016). Intestinal dysbiosis, gut hyperpermeability and bacterial translocation: missing links between depression, obesity and type 2 diabetes. Current pharmaceutical design, 22(40), 6087-6106.

Smolen, J. S., Landewé, R., Bijlsma, J., Burmester, G., Chatzidionysiou, K., Dougados, M., Nam, J., Ramiro, S., Voshaar, M., & Van Vollenhoven, R. (2017). EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Annals of the rheumatic diseases, 76(6), 960-977.

Spoel, S. H., & Dong, X. (2012). How do plants achieve immunity? Defence without specialized immune cells. Nature reviews immunology, 12(2), 89-100.

Tamburini, S., Shen, N., Wu, H. C., & Clemente, J. C. (2016). The microbiome in early life: implications for health outcomes. Nature medicine, 22(7), 713-722.

Thomas, C. M., & Versalovic, J. (2010). Probiotics-host communication: modulation of signaling pathways in the intestine. Gut microbes, 1(3), 148-163.

Thursby, E., & Juge, N. (2017). Introduction to the human gut microbiota. Biochemical journal, 474(11), 1823-1836.

Tlaskalová-Hogenová, H., Štěpánková, R., Hudcovic, T., Tučková, L., Cukrowska, B., Lodinová-Žádnıková, R., Kozáková, H., Rossmann, P., Bártová, J., & Sokol, D. (2004). Commensal bacteria (normal microflora), mucosal immunity and chronic inflammatory and autoimmune diseases. Immunology letters, 93(2-3), 97-108.

Touitou, I., & Koné-Paut, I. (2008). Autoinflammatory diseases. Best practice & research Clinical rheumatology, 22(5), 811-829.

Vijay, A., & Valdes, A. M. (2022). Role of the gut microbiome in chronic diseases: a narrative review. European journal of clinical nutrition, 76(4), 489-501.

Wang, B., Yao, M., Lv, L., Ling, Z., & Li, L. (2017). The human microbiota in health and disease. Engineering, 3(1), 71-82.

Wells, J. M., Brummer, R. J., Derrien, M., MacDonald, T. T., Troost, F., Cani, P. D., Theodorou, V., Dekker, J., Méheust, A., & De Vos, W. M. (2017). Homeostasis of the gut barrier and potential biomarkers. American Journal of Physiology-Gastrointestinal and Liver Physiology, 312(3), G171-G193.

Yu, L. C.-H., Wang, J.-T., Wei, S.-C., & Ni, Y.-H. (2012). Host-microbial interactions and regulation of intestinal epithelial barrier function: From physiology to pathology. World journal of gastrointestinal pathophysiology, 3(1), 27.

Zheng, D., Liwinski, T., & Elinav, E. (2020). Interaction between microbiota and immunity in health and disease. Cell research, 30(6), 492-506.

About The Authors

Muhammad Masood Ahmed is an Associate Professor of Pharmacology and the Head of the Pharmacy College at Nishtar Medical University in Multan, Pakistan. His research interests include immunology, medicine, pathology, angiogenesis, and oncology. Dr. Ahmed has made significant contributions to these fields through his extensive research, publications, and presentations at various conferences. His work has been instrumental in advancing knowledge and understanding in these critical areas of medical science.

Email:masoodkarni786@gmail.com ORCID: 0000-0002-4432-9583

Fahad Ullah holds a Master of Philosophy in Microbiology from the Institute of Basic Medical Sciences at Khyber Medical University in Peshawar, Pakistan. His research focused on the inhibition of efflux pumps in Pseudomonas aeruginosa. Fahad has a keen interest in Molecular Microbiology and Bioinformatics, areas in which he continues to expand his expertise.

Email: fahadullah620@gmail.com ORCID: 0009-0006-7685-7141

Muhammad Nazir Uddin is an Associate Professor at the Centre for Biotechnology and Microbiology (CB&M) at the University of Swat. With expertise in mycology and soil microbiology, he has supervised more than 100 M.Phil. and Ph.D. students in various microbiology fields. Dr. Nazir Uddin is currently focused on the potential of medicinal plant-based phytochemicals as alternative therapeutic approaches. His research involves using computational drug design and in silico tools to develop new treatments. His dedication to advancing microbiological research and exploring innovative therapeutic solutions is evident in his extensive supervision and current projects.

Email: nazir@uswat.edu.pk ORCID: 0000-0002-2339-1062

Dr. Muhammad SAFDAR earned his PhD in Molecular Biology and Genetics from Gaziantep University, Turkey. He is Lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 70 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

E-mail: msafdar@cuvas.edu.pk ORCID: 0000 0002 3720 2090

To Cite This Chapter

Ahmed M.M. et al., (2024). PMicrobiome and Autoimmune Diseases. In Current Studies in Health and Life Sciences 2024 (pp.134-146). ISRES Publishing.

Rebooting The Body's Defense: Innovations in Immunotherapy Treatment

Maria NAZIR

Aansa TAHREEM

Fatima SAGHEER

Rumaisa NAWAL

Shafeeq ur REHMAN

Muhammad SAFDAR

Mehmet OZASLAN

1. Introduction

The immune system can be described as the combination of our internal, molecular, cellular, and other processes to suit an entire defense mechanism we need during the fight with countless external agents (Paul, 2012). This is also the best way of keeping us healthy It is very effective in that it has no way for the pathogens i.e. viruses and bacteria to use by is impossible for them to adapt to the environment allowing our body to fight the infection. Two different kinds of activities involve the use of a foreigner's forces to drive foreigners away from our territory, while the other type is the locating and damaging of erratic cells such as those that can lead to cancer. Nevertheless, the immune system may have problems with this war on the enemy when they cross over the borders of the defensive system when autoimmunity causes malfunction of the immune system against its healthy part, and when cancer becomes a sales squad of cells that fights against the rest of the body parts. Therapy is obtained from Immunology, and medical researchers are in extremely busy work. Immunotherapy will make a great revolution in medicine, pushing the body's immune system (as shown in Table 1) against those invaders (Khan & Lopez, 2023).

Immunotherapy which was a concept now become a fact of life and is being practiced, it is giving way to a new face of cancer, and autoimmune diseases, and, may even prove useful in infectious disease treatment. This chapter will take us back in time, to where the foundations of immunotherapies were built, what information this knowledge is based on, and into the front-line technology that changes the lives of thousands of patients around the globe. That a thought that was only an idea back then has become today's clinical reality is great evidence for scientific development and life expectancy prolonging. The earliest immunotherapies generally employed the potency of antibodies, which are the proteins that are highly specific and only distinguish the foreign substances or dangerous cells, and after identifying them, label them for destruction by the immune system (Sompayrac, 2022). In addition to viral diseases like measles, smallpox, and polio that the vaccines held responsible for the decline in level of morbidity and mortality, the human immune system also serves as a teacher that nourishes it. However, the original versions had the great power of symbol and emotion lived differently by different people.

Table 1: Milestones in Immunotherapy Development

Decade	Milestone	Significance	Reference
1800s	Coley's Toxins	Concept of immunotherapy in the early stages	(Ventola, 2017)
1950s	Tumor antigens & interferons	The ability of the immune system to fight cancer	(Williams & Williams, 2019)
1970s	BCG vaccine for bladder cancer	First approved immunotherapy	(Cole et al., 2023)
1980s	Monoclonal antibodies	Targeted therapy revolution	(Falzone et al., 2018)
1990s	IL-2 for metastatic kidney cancer	First cytokine therapy	(FIGLIN, 1999)
2000s	Dendritic cell vaccines & sipuleucel-T	Personalized immunotherapy	(Srivastava et al., 2019)
2010s	Checkpoint inhibitors & CAR-T therapy	Transformative cancer treatment	(Nash et al., 2021)
2020s	Continued advancements	Refining and exploring new therapies	(Neukart, 2024)

The real-world understanding of molecular biology's latest achievements and a deeper look at the main principles of the immune system work were kind of groundwork for the presently progressing immunotherapy. Through the studies, scientists are now more educated about the immune system at the deep level and its ability to serve its purpose well. The shroud of immunological suppression is another line of defense mechanism with the immune checkpoint which ensures that the immune system never gets overstimulated and seriously harms the tissue regardless of a healthy body's development. However, these cancerous cells can do such a thing that evades the immune detection mechanism. Therefore, they are not getting killed (Bhatia & Kumar, 2014). The same strategy – the immune checkpoint inhibitors, which are already in use, were specifically designed to counterbalance these signaling molecules that restrain the immune responses. That is how the immune system can foster its ability to cope with and defeat cancer cells. The recent innovation of monoclonal antibody therapy can be seen as a result of such practice of building molecules, which are designed and specified with a high safety of only binding of the cancerous cell molecules or components of the immune oscillatory system. These actions might favor the aggregation of immune cells at the malignant sites, although the oscillation of the immune system might be altered as well (Silva et al., 2023).

One cell therapy that has facilitated these researchers to dream this way is CAR-T cell therapy. It entails a form of therapy by which the T cells (a type of white blood cells) of a patient are genetically engineered and multiplied in a laboratory thereby resulting in an army of cells that can destroy cancer; this regime of therapy has them empowered with antibody-like receptors (Suryaprakash et al., 2023). CAR-T cells have the unique property of being able to eliminate the cancer cells and then keep monitoring them permanently. This eliminates the problem of recurrence of cancer as the cells can heal themselves in the case of relapse. Throughout cancer therapy, it is widely known that the biggest endeavors and achievements were in immunotherapy, however, the borders of this field are not set and they span beyond oncology. In contrast with the early days when there were no vaccines against cancer, the Smart vaccines of today are being designed in individualized ways - using fragments of a patient's tumor or targeting multiple cancer antigens. On the other hand, the exploitation of oncolytic viruses the case of which can selectively wipe out cancer cells utilizing stimulating anticancer immune responses is a promising pathway for cancer treatment (Rahman & McFadden, 2021).

2. Understanding the Immune System

During the body's struggle with the destructive agents, the human complex system of death, as well as reconstruction recreating processes, become especially the human immune system. This intricate network, which is both the outer buster and the inner doctor, guards us against a broad range of things from the outside and the inside that can potentially harm us. These include viruses, bacteria, and intestinal parasites as well as illnesses like tumors within us. For beginners, fasten your seatbelts and prepare to discover the fundamentals of this powerful force. The immune system broadly consists of two interconnected branches: the physiologic state of rest and the state of transition (Roy & Bagchi, 2020). The immune system has two pillars innate and adaptive immunity. the original immunity as well, which is responsible for the instant and non-specific reaction. This is a rapid-response group of cells that when deployed activate a huge passage of macrophages and neutrophils over the invader to surround them and then engulf them, additionally, they release signals that induce inflammation which is a highly effective anti-microbial response (Pallister & Watson, 2010). It is the natural course; the specialized adaptive immune system earns more time as a sensor (of the attack) but at the same time, the same system becomes supremely specialized and highly effective as consumers of the disease-causing factors that impose the attack on the organism. It is necessary to consider lymphocytes which are two different types of cells, such as T cells and B cells, that are part of an adaptive system. The T-cells are known as the cellular base for the immune reaction, they carry the role of killing the infected and cancerous cells that must be eliminated from the body to let the immune response function efficiently (Kartikasari et al., 2019). Nevertheless, by comparison, the B cells are the predominant cell type in the humoral immunity and specific antibody formation (as shown in Figure 1). This procedure is centrally based on the production of highly selective proteins whose mechanisms are of paramount importance. It is also worth noting that these proteins not only have a high affinity to toxic pathogens but are also able to detoxify them, alongside the subsequent processing and further utilization of the debris by the macrophages (Brüne et al., 2013). On the one hand, the immunological system needs foolproof strategies for perceiving threats but on the now, such systems also have to be well-regulated to avoid the self-wrecking of healthy tissues. Another aspect is that the class of immune checkpoints never allows the immune system to be in an excessive state. The immunity process for the body is being lost therefore the body's self can be attacked by the immunity. Contrary to this, some cancer cells can dodge the interception and therefore do not come under the immune checkpoint regulation.

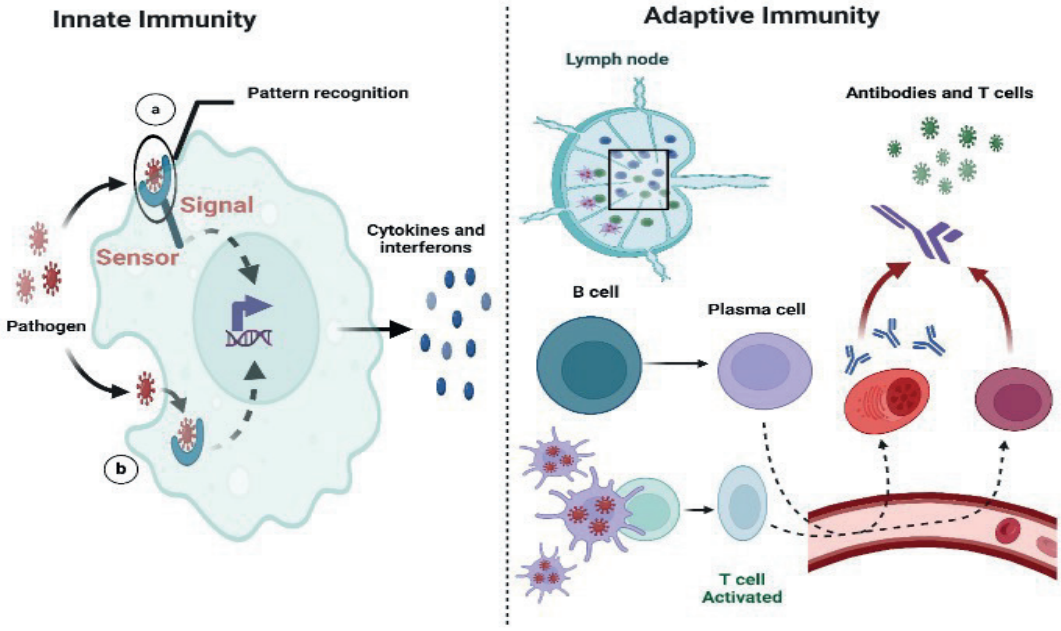


Figure 1. Understanding the Immunity

The labors aimed at the increase of knowledge from the cellular and molecular natural environment of the immune system are proof of the progression of immunotherapy. Scientists have lastly revealed a new immune cell type that mainly functions in differentiating development and suppression of the activation phase, as very important tasks. The most appropriate scheme is regulatory T cells (Treg) which operate as suppressors of immune responses and hence are good candidates in mitigating autoimmune illnesses and recipient organ transplants (Romano, 2015). The possibility that the trillions of microbes constituting the microbiome which are the hosts of the human body, may be the essence of innately immune system function, and eventually be a primary force in the child development stage has been revealed. The gut microbes play these noteworthy signals that bring the balanced responses from the immunological side to industriously produce the best immune responses. The slight shift in the differing proportions of the microbiome of an individual may cause a rise in psychiatric disorders and autoimmune diseases (Muszer et al., 2015).

The immune system is not a static object, rather this is a dynamic base on which many reactions take place during our life. The immune system responds effectively against pathogens when the balance is maintained. Genetics aspects are the factors that influence the emergence of some illnesses and reviving the immunity system (Lazar et al., 2018). Our body and microbes live alongside us in intimate symbiotic relationships, when we encounter stress, we modify our diet, along with our exposure to the organisms belonging to this environment; these factors all affect the immune system.

3. Evolution of Immunotherapy

The fact that manipulating the way the immune system works to combat disease has been around as far back as several hundred years ago. The earliest immunotherapies that were uncovered were with these pathogenic agents directly infused to generate immunity on an automatic base. This period saw the beginning of several very important inventions, particularly the vaccine against smallpox, found by Edward Jenner in the 18th century. This is a widely recognized milestone, which brought a new era in medicine, as well as a significant step in that direction (Wu et al., 2019). Furthermore, genetics got new advancements by recognizing antibodies as a new phenomenon (as shown in Table 2). As the exact method of this compound to treat different diseases especially, of course, was known since the late 1800s and is mentioned in the literature as well, it can be said that the moment of a tremendous jump in production was organized in the 1970s when the culture of monoclonal antibodies (specific antibodies developed from single cells) was finally synthesized which was achieved. As of today, the first monoclonal antibody licensing for oncology therapies happened in 1997 year (Lu et al., 2020). The second therapy majorly was monoclonal antibody treatments that were a cornerstone of cancer treatment for many types including autoimmune conditions like rheumatoid arthritis and Crohn’s disease (Flevaris & Kontoravdi, 2022).

Table 2: Evolution of Immunotherapy

Period	Key Advancements	Reference
The late 1800s	Coley's Toxins are bacterial toxins used to stimulate tumors.	(Löwy, 2003)
The early 1900s	BCG vaccine was initially developed for tuberculosis treatment and later found to be effective for treating bladder cancer as well.	(Ikryannikova et al., 2023)
Mid 1900s	Recognition of tumor antigens by the immune system is facilitated by interferons.	(Tian et al., 2022)
Late 1900s	Therapy that is targeted and enhanced using monoclonal antibodies and IL-2.	(Helmy et al., 2013)
The early 2000s	Personalized therapy with dendritic cell vaccines and sipuleucel-T.	(Mukherjee et al., 2022)
2010s	Checkpoint inhibitors & CAR-T therapy have completely transformed the way we treat patients.	(Zhang et al., 2023)
Future	Ongoing developments in the field of combination and personalized therapies.	(Dey et al., 2023)

Cancer vaccination is not a modern invention but is a central theme without tangible results from millennia ago. Elimination treatment procedures have been the major choice in cancer treatment for a long time by targeting some tumor cells or tumor antigens to cue the immune system for cancer marker recognition. Nevertheless, they raised the theoretical vision, but the vaccine in practical applications did not provide us with highly durable and predictable clinical outcomes. The achievements in the field of cancer vaccination design are much more limited compared to expected because of the immunoreactive ability problem. However, the targets for immunogenicity are identified more accurately, and the immune evasion mechanisms and delivery systems for the tumors are fully understood. New stages for cancer vaccines are opened up (Fan et al., 2023). Such an important move was the discovery of immune checkpoints in the 1990s as well as the advent of immuno-oncology (Wilky, 2019). Yet the world of scientific research cannot stand eternally at a halt – James Allison and Tasuku Honjo found CTLA-4 and PD-1 to be the major two "brake pads" that may lead to uncontrolled immune responses. The process of this research led to another discovery that is commonly called immune checkpoint inhibitors a kind of medicine that seemed to be a real solution to the cancer disease problem (Dobosz & Dzieciątkowski, 2019). The immune checkpoint inhibitors, for example, ipilimumab (anti-CTLA-4) and nivolumab (anti-PD-1) have been accounted for being widely used in the treatment of cancer patients over the last few years. They exert their immune suppression activity by blocking the signaling pathways employed by malignant cells for their benefit; thus, enabling the immune system to completely unleash its potential for a total annihilation of tumor cells.

The past several years have witnessed new cell therapies establishing themselves as an immunotherapy field sub-specialty, Secondly, destitution in this cancer treatment was a telling signification of how the transplanting of immunity cells can be a great weapon in combatting this disease. CRISPR-Cas9 is a modern CRISPR technology capable of removing genetic material or inserting it in a target cell (Gupta et al., 2019), such as a T cell or any kind of cancer cell, allowing it to fight cancer cells and perform anti-cancer activities more effectively. Advancement attained in the field of CAR-T cell therapy based on breakthroughs seen in leukemia and lymphoma has resulted in FDA approval of CAR-T cells as a treatment in many blood cancer recipes, thereby opening a new path for adding the cure to the immunotherapy armory (Shouval et al., 2022). Another great area wherein advanced research should be undertaken is the oncolytic viruses applied as a treatment. These arrays of infections can specifically target and destroy malignant cells that block cancer spread. Likewise, the anti-tumor activity of a virus does not only include its direct toxicity to tumor cells but also facilitates the patient's immune response, implying that the oncolytic virus

is advantageous in terms of both mechanisms (Raja et al., 2018).

Although there are currently problems with immunotherapy delivery, which are mainly connected with personalized treatment, scientists continue working on overcoming them (Raja et al., 2018). Scientists are enlightening the community after depicting the relationship between cancer characteristics, the implantation of the composition of immune systems, and varieties of the microbiome of a particular patient, and these data will be useful in making an effective selection of a particular patient for a specific treatment. This special kind of treatment program can bring the best result out of it and will make sure that unnecessary side effects are avoided. This makes individualized immunotherapy more targeted to the disease-specific patient and proteins (Krzyszczyk et al., 2018).

4. Immune Checkpoint Inhibitors

Immune checkpoints are an intrinsic immunity system regulatory system that prevents the immune system from generating a rampage in which harmful effects to the body's organs are their results. They function as protective units and stop the needless launch of pro-inflammatory cytokines, which over time could produce autoimmune diseases (Manik & Singh, 2022). On the other hand, the cabu immunosystem has also developed some natural barriers to protect the body against cancer including cells like immune cells and antibodies. While this is the case, pathologists tell us that cancer cells are in some ways super smart and can take advantage of the system that our immune cells try to fight with them. It is as if the cancer cells disguise themselves so cleverly that the immune system cannot identify and destroy them, resulting in cancer cells multiplying and spreading to other organs (Šmardová, 2024). Immunoadjuntants have brought a revolution in the treatment of cancer by, on the one side, inducing cell death and on the other side exposing the cancer cells to the immune system. The two essential checkpoint pathways histrionic proteins CTLA-4 and PD-1/PD-L1, are located in several immune cells. At present, checkpoint blockade drugs have become monoclonal antibodies that can be considered as immunotherapies. These checkpoint inhibitors will oppose the checkpoint brake and enable constant signaling. Hence, those therapies will hold heat, and at that time, the T cell, which is one of the major cell-mediated arms of the immune system, (as shown in Figure 2) can detect and kill particular cancer cells that were marked (Kumar et al., 2021).

Some clinical trials showed some cancers as very responsive to immunotherapy. When these cancers lose control over immunity, they are highly sensitive to checkpoint inhibitors. Characterized by the highest rate of response are melanomas, lung cancers of certain types, head and neck cancers, renal cancer as well liver carcinomas among others that have withstood several years of immunotherapy reliant on checkpoint inhibitors (Bridge et al., 2018). Analyzing checkpoint immunotherapy drugs that specifically work against cancers has already gained its mark as a weapon against cancer treatments. The FDA authorizes an expanding number of cancers including melanoma, NSCLC, and kidney cancer so that immune checkpoint inhibitors can be activated against the aforementioned cancers. Later, the PD-1 / PD-L1 pathway was found to be the other next target, allowing ipilimumab (anti-CTLA-4) to be approved in 2011(Chae et al., 2018). Thereafter the development of other drugs also took place including nivolumab, pembrolizumab, atezolizumab, and others.

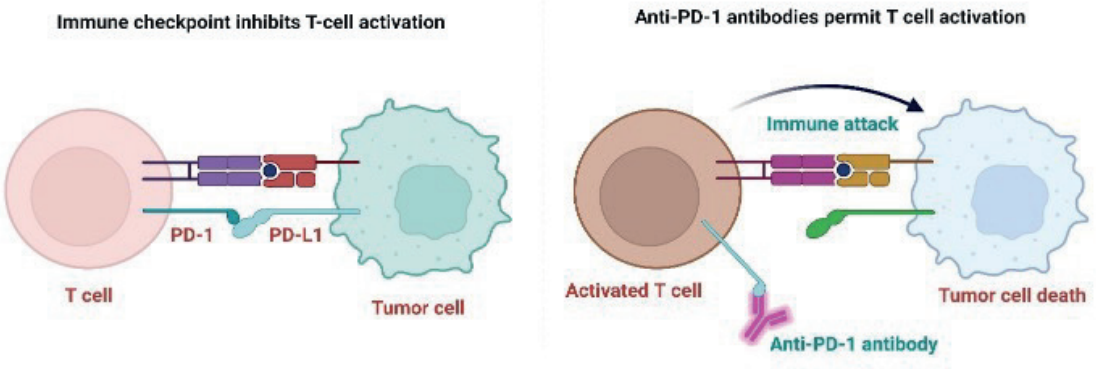


Figure 2. Immune Checkpoint Inhibitors in T-Cell

Though this medicine may not one hundred percent duplicate all vitalities provided by nature, it will still provide so many advantages that can never be overlooked. It is vital to stress that not all cancer cases can be cured utilizing immune checkpoint inhibitors and that some are the ones with high response levels, some the others with low response levels. Identifying specific patients who are most susceptible to certain checkpoint inhibitors and the exact role of immunotherapy is no doubt the aim of the research (Wojtukiewicz et al., 2021). The key lesson from this experience has been to start to use a thinking process that is critical and more independent. On top of that, I have learned to manage myself outside the dependence on others as well as how to take ownership of my health care. Also, biomarkers such as PD-L1 expression level and tumor cell mutation status give a clue as to when a patient is most likely to benefit from checkpoint blockade treatment (Fujii et al., 2018). Anti-immune checkpoints crazy the brakes of the immune system, which is supposed to preserve and promote good health in the body. As a side effect of this drug mode of operation, there are some cases of immune-induced illnesses. Meanwhile, organ inflammations such as skin and gut, that require close monitoring, introducing other immune-suppressive therapy are also brought in for unforeseen events (Rapoport et al., 2017). At the moment, scientists are working on a scale-up process of checkpoint inhibitor production which is based on the entire cells and cell lines that are specially engineered for this. Checkpoint inhibitors are the other approach where an array of these inhibitors is employed in certain combinations or just a single one of them could be administered. A patient with one cancer and another will especially benefit a therapy with a CTLA-4 substance and a PD-1 substance while other people can show lower effectiveness from such treatment to a CTLA-4 treatment separately. Finally, a demand for more clinical studies into combining immunotherapy with conventional treatment modes like chemotherapy, radiology, and targeted therapies is another key area with some thrilling studies about new and effective methods of treatment (Kamrani et al., 2023).

5. CAR-T Cell Therapy

Chimeric antigen receptor gene transfer therapy which is also known as CAR T cell therapy is a game changer in the field of cancer immunotherapy and this case, the cells are redesigned to ensure that patients are no longer bedridden by this deadly disease but that they are each other and all the resources they need to fight cancer. The output confirms the point that CAR-T cell therapy is a variable that can be used and redesigned (as shown in Figure 3) for the fight against the disease (Ahmed, 2021).

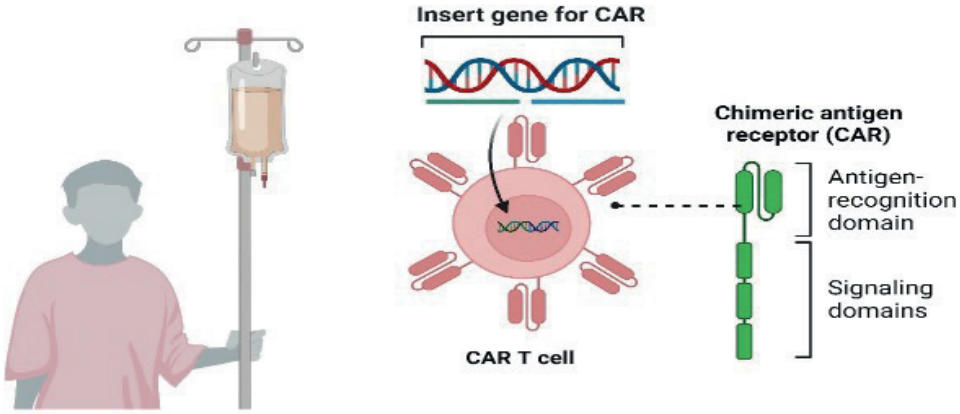


Figure 3. Overview of CAR-T Cell Therapy

The T cells, which are a type of white blood cells, are the immunity combatants in our body and are very impart in our immunity system. They will mark out and obliterate both them and the transformed health cells. T cells can target these cells, which have unfastened those cells that betray, but cancer cells still suppress these T cells, which enhances these cells' ability to proliferate. CAR-T cell therapy blade pens novel pathways for the editing of T cells to enhance their ability to not only recognize but also eradicate even the most wicked cancer cells as targeted and persistent as these cells (Han, 2016). This approach entails "arming" patients' T cells which are the body's defenders by introducing CARs into them such that the T cells can function as though they are customized fighters eliminating cancer cells this way (Ayala, 2016). On the very, first step, collecting the patient's T cells by taking out his blood with the standard method of blood donation. Cells from the blood are drawn in the lab and through genetic engineering, the DNA molecules within them are redone to provide this specific receptor molecule of chimeric antigen receptor (CAR). The CAR is comprised of the antibody and T-cell receptors since they are the trigger mediators. The role of the antigen binding potential of CAR is to properly couple the CAR to an antigen (complementary protein) on the surface of the cancer cell, thereby giving precision to a harpoon on the carrier which in turn binds the cancer cell to the CAR-T cell. Finally, when the tumor cell sticks to the CAR receptor, a certain cell subset of the innate and adaptive immunity will recognize them as targets (Willcox et al., 2020). These C-AR T-cells are then graded and placed in the laboratory to enhance their replication, since they multiply exponentially in can be taken in millions. Therefore, when the CAR-T cells are decided as ready, they enter through the bloodstream to join the patients. Indeed, this cell transfer can be in a way regarded as an internal and living drug. Following on, the CAR-T cells would be the ones now seeking and destructing the cancer cells having installed their antigen distinctly. Rather chemotherapy drugs are more approaches to treat cancer that are only in use single time, the CAR-T cells can multiply inside the patient, which provides the opportunity to achieve a long period at which active cancer can be fought (Safarzadeh Kozani et al., 2022).

Although the CAR-T cell technology mainly focuses on blood-conditioned cancers (leukemia or lymphoma), (as shown in Figure 4) it is the early clinical trials that indicate positive responses. This therapy is really useful in case of recurrence or when the patients attend other treatment modes and response is poor, especially for those whose aggressiveness doesn't respond to other measures. Here CAR-T gives only hope for remission and chances for cure. Over FDA-approved cell therapy drugs for the indication of treating cancers as well (Mitra et al., 2023). Despite the benefits CAR-T therapy provides by being a very strong technique it also comes with its risks and dangers. Cytokine Release Syndrome (CRS), A broad-spectrum systemic inflammation effect that arises from a rapid expansion of CAR-T cells, is a very severe and, sometimes, even fatal

complication (Cobb & Lee, 2021). Realizing CRS may lead to flu-like illness where the body can attain a fever at times. At times, stressors may become more severe, potentially leading to a triad of disorders. Organ harm can be a consequence. Neuronal toxicity is said to be one possible complication that can be experienced by patients after the CAR-T cell treatment, the severity of the side effects ranges from minor symptoms like seizures and confusion to serious conditions. On a more optimistic note, is the fact that researchers have devised some practical ways in which the side effects of the rigid protocol can be managed. This has led to gradual progress in the safety of CAR-T therapy (Cauchon et al., 2019).

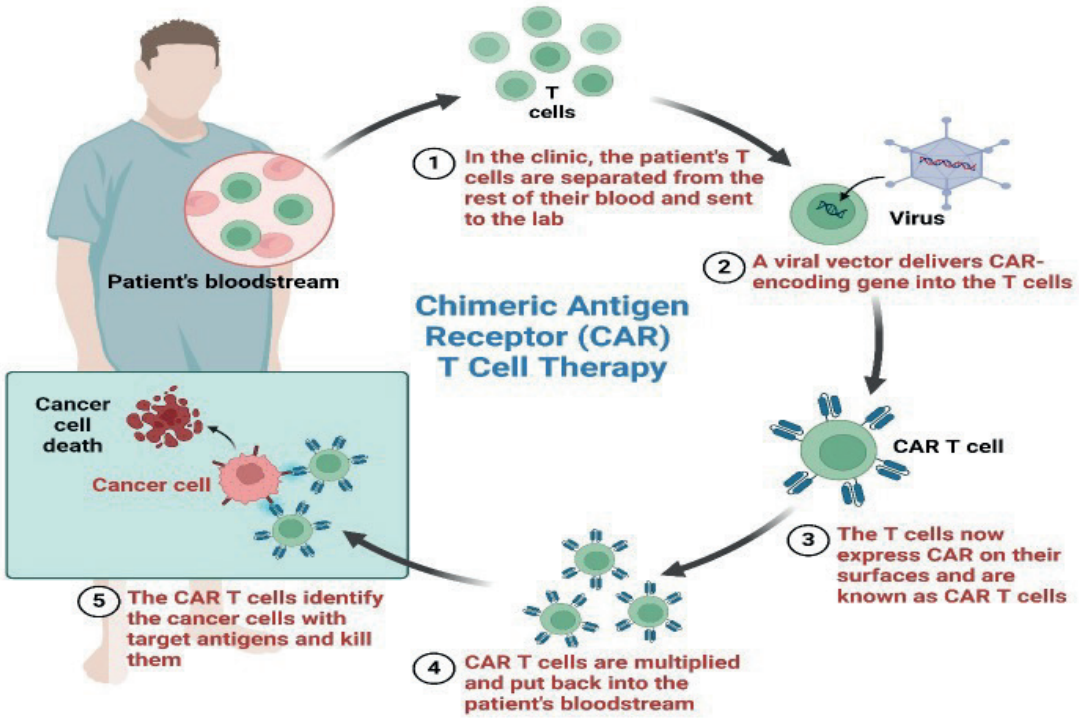


Figure 4. Process of CAR-T Cell Therapy

The therapy CAR-T is a promising innovation with a growing branch that implies the better carrier of this treatment is getting closer and closer. Given the already successful track record as far as blood cancer treatment, the scientists continue to work on tackling this by offering alternative ways of treating solid tumors. By contrast, solid tumors comprise considerably more multifarious problems than liquids due to the cells of the CAR-Ts being near solid masses and the deformation of the latter (Clark et al., 2019). Investigators search for ways how to create an advanced generation of CAR-T cells with higher potency and avoid related problems by using this approach for those types of cancer that are not very responsive now. Additionally, to the investigative domains for future research include that of genetically engineered, normal donor-derived CAR-T cells in substitution of the patient's cells. On the other hand, this means the patients don't have to incur the high cost associated with an expensive customization process, so the availability of mass-produced products can have a positive effect due to easier treatment access. Moreover, CRISPR techniques among other molecular biology tools could be used for the acceleration of the process allowing the level of changes to another level (Nidhi et al., 2021).

6. Monoclonal Antibody Therapy

On the whole, CD19-specific chimeric antigen receptor (CAR) T cell therapy stands at the boundary of immunotherapy, being both a scissor and a stitcher to disarm and rearm the patient's cells into anticancer machine guns. It means a novel epoch devoted to custom-tailored medicine

that employs patients' reservoirs those powers that stabilize their bodies (as shown in Figure 5). T cells provide cellular bases for immune response by attacking and disabling the cells affected by the harmful intruder. But on the other hand, cancer cells retain such intrinsic powers for evading immune detection. In comparison to CAR-T cell therapy, this kind of treatment is not powerful enough to do over the immunosuppressive state that is often associated with cancer cells (Safarzadeh Kozani et al., 2022). Generally, the process starts with a T cell provided from one of the patient's blood donation kinds which is conducted as irregularly as possible. In the laboratory, the CAR T cells take a new gene which includes it within a chimeric receptor as long as CAR. In addition to it, this certain molecule has one part that appears as an antibody and attaches itself to the antigen on the surface of the cancer cells. This specific targeting portion has been imprinted with engineered components that come from T cell receptors, which, when these T cell receptors are attached to cancerous cells, may increase the destruction power of the cell towards the cancer cell (Liu et al., 2020).

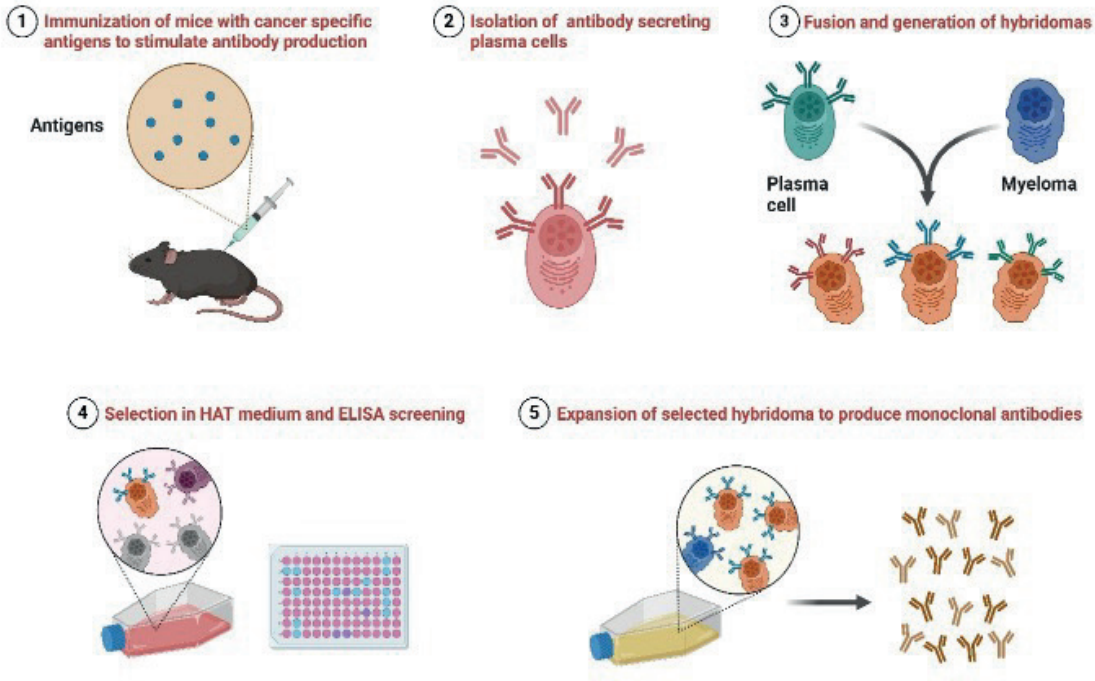


Figure 5. Monoclonal Antibody Productions

These CAR-T Cells are then expanded to millions in the lab in weeks instead of taking months to reach the clinical stage of treatment. This is how the conjugated antibodies, if present in a person's blood, resemble a "living drug" that selectively searches and eliminates cancer cells that bear the target antigen (Afsahi, 2023). Unlike traditional chemotherapy which has intermittent on-and-off effects, the CAR-T cells are free of such constraints, thus having the ability to live the recipients and keep tabs on possible cancer recurrence. While at present CAR-T therapy has proved to be very promising in the treatment of blood cancers, especially leukemias, and lymphoma, it has not yet been able to bring encouraging results in the treatment of solid tumors (as shown in Figure 6). Here it has acted as a means to make patients who undergo successful therapies take it easy as well and issues with efficacy in other cancer treatment procedures disappear. These FDA-certified, multi-disciplinary treatment trials can be accounted for as Phase I and Phase II clinical trials approved by the FDA, and the statistics show a significant effect of the treatment on blood cancers (Armstrong, 2015).

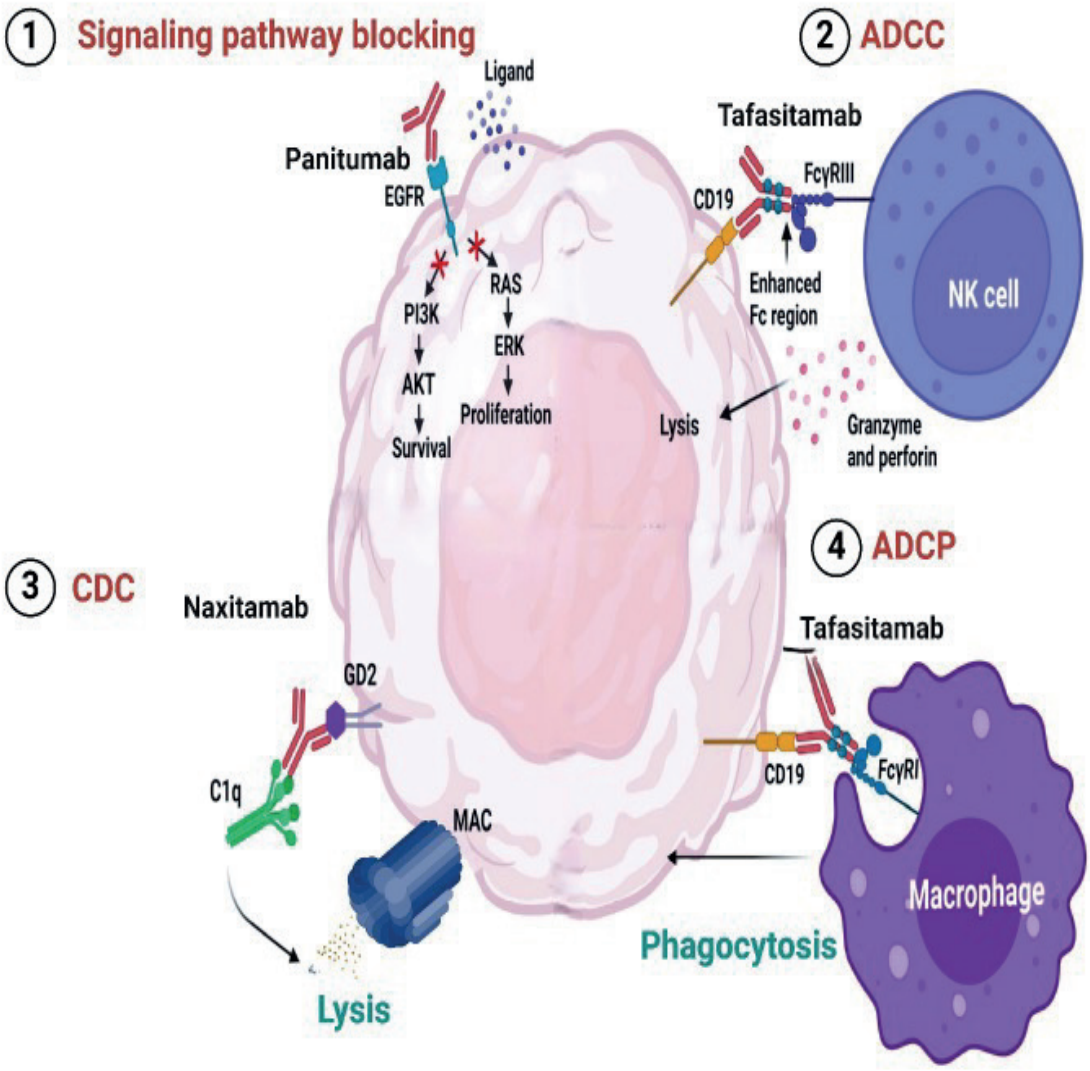


Figure 6. Monoclonal Antibody Binding to a Target Protein on a Cancer Cell

While the CAR-T breakthrough treatment seems to be a gaming-changing therapy, the approach comes with its weaknesses which should be addressed. Cytokine release syndrome (CRS) or a "systemic inflammatory reaction produced by very rapid CAR-T cell activity may be moderate as influenza-like disease or worse as multi-organ damage. The issues related to toxic signage like salt anions that may lead to confusion or epilepsy are highlighted in the sentence that follows. However, this can be summed up by the use of management strategies, made possible to restore patient safety to the highest possible level. This can be made through the gathering of information from patients, doctors, and the manufacturer of the drug. This can be followed by extensive research on the adverse effects of such therapy (Garrison Jr et al., 2007). While CAR-T cell therapy shows promising results, we are enjoying remarkable achievements. Overall, without these complex diverse microenvironments of solid tumors, there is always one of the major issues with infiltrating CAR-T cells. The researchers aim to deliver the novel CAR-T cells to the next generation with the ability to tackle the obstacles and thus reach the intended mutated cells (Kapoor-Narula & Lenka, 2022).

7. Cancer Vaccines and Oncolytic Viruses

The vaccine for cancer and oncolytic virus is a new and emerging technology scrum that builds the immune system for the anti-tumor effects or treatment. Even though these limits might

appear unapparent a great approach for overcoming them has been presented as progress in tumor immunology and bioengineering that reawakened a very tenuous research area. Vaccines designed for the prevention or treatment of cancer differ greatly from the common vaccines which aim to protect new people from viruses or germs (as shown in Figure 7). They do not use the prophylactic method by protecting healthy cells and identifying sick ones but 'train' the immunities system to accustom itself to tumor cell identification and subsequent eradication. Cancer vaccination could be launched in several forms, such as vaccines. Some CAR-T cells express humanized antigens (proteins) while others prefer the expression of tumor tissue fragments. Simultaneously, methods can take the shape of personalized vaccines that are put to combat those patients who have mutations in tumors, which result in highly specific target vaccines(Fennemann et al., 2019). Cancer vaccine fundamentally aims to prime the body against cancer-associated targets and take the immune response as its goal. For those vaccines, adjuvants are part of the package that increases the immune response and directs it in a desired way, thus leading to efficiency. Geneticists are putting efforts into developing different types of vaccine delivery systems such as nanoparticles and specific virus-like structures to increase efficacy levels and the target immune cells are collected(Iyer et al., 2022).

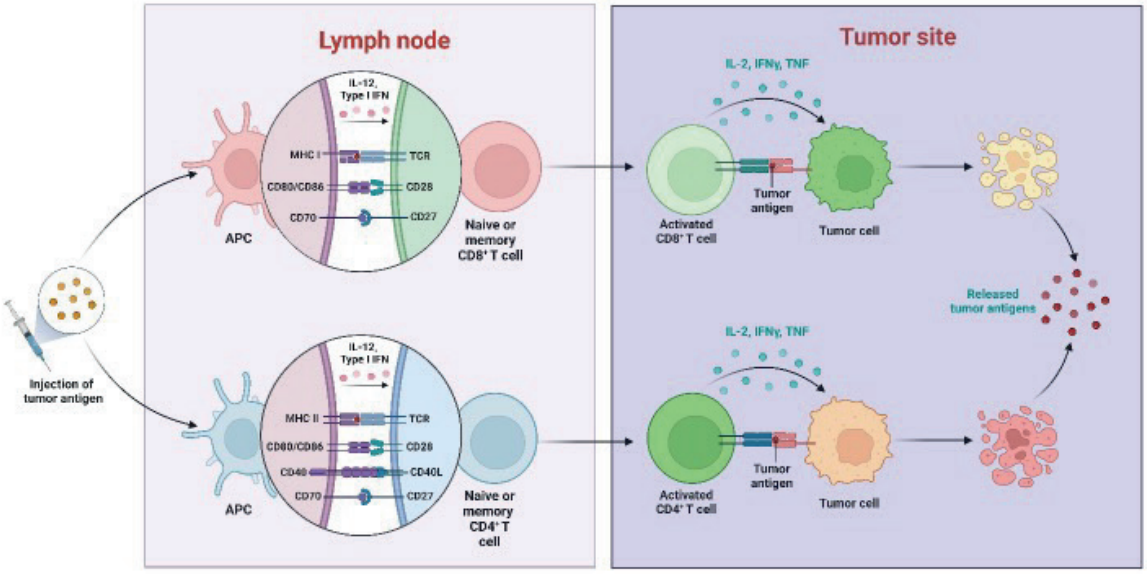


Figure 7. Cancer Vaccine Stimulating the Immune System

Vaccine-associated mortality with cancer vaccines remains a longstanding myth in which the clinical trials of vaccination work sporadically. On one hand, cancer cells gaining the ability to escape immune system detection by an entirely new mechanism inspires the field with more and more questions and the models come out to explain the process of immune evasion. These cases include a co-treatment where cancer vaccines completely stop cancer which is superseded by the checkpoint inhibitors that just combine, they work together. It is additionally found that scientists are making vaccines that seek different cancer antigens simultaneously. This is, in a way, posing a challenge for the immune system to target these different antigens (Han et al., 2021). Oncolytic Viruses have been developed as a special type of virus or selected and modified whose job is to home and destroy cancer cells only (Lawler et al., 2017). They are a little two-faced in the sense that they can be pretty convincing at the moments when they are most talked about. The second one is that immunotherapy can induce one's immune system by blocking the effects of the body on the tumor cells. To start with, the tumor cells release cancer-pheromones as well as viral compounds due to their death. This together sends a signal to a large enough immune system to attack the dangerous processes within the cancer cells. Thus the oncolytic virus is fighting not only through the direct tumor-killing effect but is also able to overrule the tumor which is poor in immune cells till it turns it "hot" and activates immune cells (Lin et al., 2023).

The researches on oncolytic virotherapy are not limited only to one virus kind. Another famous example is the T-VEC virus which got its trial permission for use by the FDA in patients with advanced melanoma which was caused by the herpes simplex virus (Shalhout et al., 2023). The first era of oncolytic virus research was characterized by restricting factors with the actual targeting, modification, and adjusting of safety-enhancing features, and by now, these genetically modified viruses are optimized for the treatment of cancer. Another direction of research to be kept in mind is combinational therapy with concurrent use of oncolytic viruses along with other anticancer agents. The association of oncolytic viruses and checkpoint inhibitors may be a truly fruitful one, which would induce a more comprehensive immune response that the virus can only cause only (Martikainen & Essand, 2019). Another thing is that researchers are using these viruses as a source of oncolysis through which other therapeutic agents are directed toward the tumor. This is a multimodal way to exhibit anti-cancer effects by a single therapy. Two remarkable areas of cancer vaccine and oncolytic virus technologies are all now being spread out most exuberantly.

8. Future Directions and Challenges

What was the latest immunotherapy, for instance, is now not old yet compared to how quickly it has advanced in years. However, immunotherapy is an ever-changing profession. Overcoming resistance is paramount. This practice of medicine has shown the ability to stimulate very strong responses in selected cases, but not every immunotherapy is as effective and some individuals might not even respond to the treatment. Identifying patients in whom resistance will be more likely will, therefore, build the basis for coming up with corresponding schedules that could ensure a larger number of them derive the best from this treatment. One is how complex the cancer cell structures within the tumor are, the other is how complicated the tumor microenvironment is, and the other is the gut microbiome makeup (Nejman et al., 2020). To optimize effectiveness in the future, multi-directional tactics, rather than a one-way approach, are likely to be the standard. Combining several sorts of immunotherapies, for instance, administering checkpoint inhibitors in tandem with CAR-T cell therapy, or cancer vaccines is likely to stimulate more forceful treatment approaches (Marshall & Djamgoz, 2018). Alongside this, NLA-121 is still carried out for use with other traditional treatment modalities like chemotherapy and radiotherapy, which might improve their therapeutic efficiency. While this last option may have a few conditions with its usage which may cause side effects in the patients, saving their lives is still very important.

Identifying biomarkers that are not immunology-specific relies on a critical process. Right now, the options to determine the efficiency possibilities are rather limited that is, knowing which outcome is most likely in different treatments is very difficult. Similarly, the selection of suitable therapy types, relating to genetic testing of the cancer, immune system cell, or stomach microbiome markers, will be an approach for the doctors to make their decision in a personalized manner. As to the benefits of cancer treatment, it stands out in being so specific that it can be sharpened out to meet the best-matched dose including the stooping of the causes of wastage and expenses (Suri, 2022). One of the big issues to solve is how to expand the accessibility of immune therapy to the wider population. Nevertheless, cancers in the blood can be so remarkable that it still needs a lot to solve lymphoid ones on the other hand where the conversion of advantages to solid tumors is a research field that is pressing for now. Once next-generation CAR-T science emerges that focuses on striking strategic locations on oncolytic viruses, and also the latest vaccine designs are revealed it will possibly result in the invention of many modes of cancer treatment (Safarzadeh Kozani et al., 2022).

Another immunotherapeutic approach, instead of destroying and killing the body's invaders, can serve as a means of treating diseases such as cancer, besides autoimmune diseases because of its mode of action. The first successful and useful targeting therapy called “rheumatoid arthritis” that are helpful for various targeted antibody-based therapies has been the one to walk this way (Ferrari et al., 2015). The researchers now start the task of proportionally looking upon mechanisms of immune regulatory cells or switching the wayward immune response in autoimmune diseases and also they

have opened up the new potential to be tackled by tomorrow's therapy. Immunosuppressive therapy approach very soon might be substituted by advanced treatment methods and, therefore, they will be much less ore detrimental in aspects of the sick side effects than their precedents (Abedon, 2019). The development of 'ready-made' solutions on the one hand in combination with a simplification in the production process along with a detailed investigation of whether the application of synthetic biology purposes may be used to reduce the level of the price and to increase the supply levels of these treatments that save people's lives should be done.

9. Conclusion

One is clear: immunotherapy is the newest approach to cancer, which is already being implemented now. Sometimes the things that fascinated scientists for years and were considered the most complicated phenomena of the immune system are the things that take the credit for the currently observed effects. Immune therapy changed the face of how cancer is treated radically and not just by paving the way for yet untapped promise for other diseases. Though problems persist around plagiarism, these technologies are very quickly improving. The fact is that immunotherapy is just in its infancy, and now we see the concept of the immune system of the highest level of complexity. As the tool, the direction of the future immunotherapy is being developed which is aimed to generate strong and specific therapies. Immunotherapy is, in consequence, the summation of progress in medical biology and of course, it gives the hope of writing the medicine's future.

References

Abedon, S. T. (2019). Use of phage therapy to treat long-standing, persistent, or chronic bacterial infections. Advanced Drug Delivery Reviews, 145, 18-39.

Afsahi, A. (2023). Augmentation of anti-myeloma engineered T cells by pharmacological or genetic interventions

Ahmed, M. M. E. (2021). CAR-T cell therapy: current advances and future research possibilities. Journal of Scientific Research in Medical and Biological Sciences, 2(2), 86-116.

Armstrong, V. (2015). Indonesian Day. Vox Sanguinis, 109(2), 1-96.

Ayala, L. (2016). Cybersecurity for hospitals and healthcare facilities. Berkeley, CA.

Bhatia, A., & Kumar, Y. (2014). Cellular and molecular mechanisms in cancer immune escape: a comprehensive review. Expert review of clinical immunology, 10(1), 41-62.

Bridge, J. A., Lee, J. C., Daud, A., Wells, J. W., & Bluestone, J. A. (2018). Cytokines, chemokines, and other biomarkers of response for checkpoint inhibitor therapy in skin cancer. Frontiers in medicine, 5, 351.

Brüne, B., Dehne, N., Grossmann, N., Jung, M., Namgaladze, D., Schmid, T., von Knethen, A., & Weigert, A. (2013). Redox control of inflammation in macrophages. Antioxidants & redox signaling, 19(6), 595-637.

Cauchon, N. S., Oghamian, S., Hassanpour, S., & Abernathy, M. (2019). Innovation in chemistry, manufacturing, and controls—a regulatory perspective from industry. Journal of Pharmaceutical Sciences, 108(7), 2207-2237.

Chae, Y. K., Arya, A., Iams, W., Cruz, M. R., Chandra, S., Choi, J., & Giles, F. (2018). Current landscape and future of dual anti-CTLA4 and PD-1/PD-L1 blockade immunotherapy in cancer; lessons learned from clinical trials with melanoma and non-small cell lung cancer (NSCLC). Journal for immunotherapy of cancer, 6, 1-27.

Clark, D. J., Dhanasekaran, S. M., Petralia, F., Pan, J., Song, X., Hu, Y., da Veiga Leprevost,

F., Reva, B., Lih, T.-S. M., & Chang, H.-Y. (2019). Integrated proteogenomic characterization of clear cell renal cell carcinoma. Cell, 179(4), 964-983. e931.

Cobb, D. A., & Lee, D. W. (2021). Cytokine release syndrome biology and management. The Cancer Journal, 27(2), 119-125.

Cole, K., Al-Kadhimi, Z., & Talmadge, J. E. (2023). Highlights into historical and current immune interventions for cancer. International Immunopharmacology, 117, 109882.

Dey, A., Mitra, A., Pathak, S., Prasad, S., Zhang, A. S., Zhang, H., Sun, X.-F., & Banerjee, A. (2023). Recent advancements, limitations, and future perspectives of the use of personalized medicine in treatment of colon cancer. Technology in Cancer Research & Treatment, 22, 15330338231178403.

Dobosz, P., & Dzieciątkowski, T. (2019). The intriguing history of cancer immunotherapy. Frontiers in immunology, 10, 496087.

Falzone, L., Salomone, S., & Libra, M. (2018). Evolution of cancer pharmacological treatments at the turn of the third millennium. Frontiers in Pharmacology, 9, 421926.

Fan, T., Zhang, M., Yang, J., Zhu, Z., Cao, W., & Dong, C. (2023). Therapeutic cancer vaccines: advancements, challenges, and prospects. Signal Transduction and Targeted Therapy, 8(1), 450.

Fennemann, F. L., de Vries, I. J. M., Figdor, C. G., & Verdoes, M. (2019). Attacking tumors from all sides: personalized multiplex vaccines to tackle intratumor heterogeneity. Frontiers in immunology, 10, 454555.

Ferrari, M., Onuoha, S. C., & Pitzalis, C. (2015). Trojan horses and guided missiles: targeted therapies in the war on arthritis. Nature Reviews Rheumatology, 11(6), 328-337.

FIGLIN, R. A. (1999). Renal cell carcinoma: management of advanced disease. The Journal of urology, 161(2), 381-387.

Flevaris, K., & Kontoravdi, C. (2022). Immunoglobulin G n-glycan biomarkers for autoimmune diseases: Current state and a glycoinformatics perspective. International journal of molecular sciences, 23(9), 5180.

Fujii, T., Naing, A., Rolfo, C., & Hajjar, J. (2018). Biomarkers of response to immune checkpoint blockade in cancer treatment. Critical reviews in oncology/hematology, 130, 108-120.

Garrison Jr, L. P., Neumann, P. J., Erickson, P., Marshall, D., & Mullins, C. D. (2007). Using real-world data for coverage and payment decisions: the ISPOR real-world data task force report. Value in health, 10(5), 326-335.

Gupta, D., Bhattacharjee, O., Mandal, D., Sen, M. K., Dey, D., Dasgupta, A., Kazi, T. A., Gupta, R., Sinharoy, S., & Acharya, K. (2019). CRISPR-Cas9 system: A new-fangled dawn in gene editing. Life sciences, 232, 116636.

Han, L., Peng, K., Qiu, L.-Y., Li, M., Ruan, J.-H., He, L.-L., & Yuan, Z.-X. (2021). Hitchhiking on controlled-release drug delivery systems: opportunities and challenges for cancer vaccines. Frontiers in Pharmacology, 12, 679602.

Han, X. (2016). Engineering Chimeric Antigen Receptor T Cells towards Enhanced Safety and Efficacy in Cancer Immunotherapy University of Southern California].

Helmy, K. Y., Patel, S. A., Nahas, G. R., & Rameshwar, P. (2013). Cancer immunotherapy: accomplishments to date and future promise. Therapeutic delivery, 4(10), 1307-1320.

Ikryannikova, L. N., Gorokhovets, N. V., Belykh, D. A., Kurbatov, L. K., & Zamyatnin Jr, A. A. (2023). Bacterial Therapy of Cancer: A Way to the Dustbin of History or to the Medicine of

the Future? International journal of molecular sciences, 24(11), 9726.

Iyer, S., Yadav, R., Agarwal, S., Tripathi, S., & Agarwal, R. (2022). Bioengineering strategies for developing vaccines against respiratory viral diseases. Clinical microbiology reviews, 35(1), e00123-00121.

Kamrani, A., Hosseinzadeh, R., Shomali, N., Heris, J. A., Shahabi, P., Mohammadinasab, R., Sadeghvand, S., Ghahremanzadeh, K., Sadeghi, M., & Akbari, M. (2023). New immunotherapeutic approaches for cancer treatment. Pathology-Research and Practice, 154632.

Kapoor-Narula, U., & Lenka, N. (2022). Cancer stem cells and tumor heterogeneity: Deciphering the role in tumor progression and metastasis. Cytokine, 157, 155968.

Kartikasari, A. E., Prakash, M. D., Cox, M., Wilson, K., Boer, J. C., Cauchi, J. A., & Plebanski, M. (2019). Therapeutic cancer vaccines—T cell responses and epigenetic modulation. Frontiers in immunology, 9, 429150.

Khan, A., & Lopez, M. (2023). Advances In Immunotherapy: A Comprehensive Review Of Medical Science. The Research of Medical Science Review, 1(01), 1-9.

Krzyszczyk, P., Acevedo, A., Davidoff, E. J., Timmins, L. M., Marrero-Berrios, I., Patel, M., White, C., Lowe, C., Sherba, J. J., & Hartmanshenn, C. (2018). The growing role of precision and personalized medicine for cancer treatment. Technology, 6(03n04), 79-100.

Kumar, A. R., Devan, A. R., Nair, B., Vinod, B. S., & Nath, L. R. (2021). Harnessing the immune system against cancer: current immunotherapy approaches and therapeutic targets. Molecular biology reports, 1-21.

Lawler, S. E., Speranza, M.-C., Cho, C.-F., & Chiocca, E. A. (2017). Oncolytic viruses in cancer treatment: a review. JAMA oncology, 3(6), 841-849.

Lazar, V., Ditu, L.-M., Pircalabioru, G. G., Gheorghe, I., Curutiu, C., Holban, A. M., Picu, A., Petcu, L., & Chifiriuc, M. C. (2018). Aspects of gut microbiota and immune system interactions in infectious diseases, immunopathology, and cancer. Frontiers in immunology, 9, 1830.

Lin, D., Shen, Y., & Liang, T. (2023). Oncolytic virotherapy: basic principles, recent advances and future directions. Signal Transduction and Targeted Therapy, 8(1), 156.

Liu, W. L., Zou, M. Z., Qin, S. Y., Cheng, Y. J., Ma, Y. H., Sun, Y. X., & Zhang, X. Z. (2020). Recent advances of cell membrane-coated nanomaterials for biomedical applications. Advanced Functional Materials, 30(39), 2003559.

Löwy, I. (2003). Immunotherapy of cancer from Coley's toxins to interferons: Molecularization of a therapeutic practice. Molecularizing Biology and Medicine: New Practices and Alliances, 1920s to 1970s, 233.

Lu, R.-M., Hwang, Y.-C., Liu, I.-J., Lee, C.-C., Tsai, H.-Z., Li, H.-J., & Wu, H.-C. (2020). Development of therapeutic antibodies for the treatment of diseases. Journal of biomedical science, 27, 1-30.

Manik, M., & Singh, R. K. (2022). Role of toll-like receptors in modulation of cytokine storm signaling in SARS-CoV-2-induced COVID-19. Journal of medical virology, 94(3), 869-877.

Marshall, H. T., & Djamgoz, M. B. (2018). Immuno-oncology: emerging targets and combination therapies. Frontiers in oncology, 8, 315.

Martikainen, M., & Essand, M. (2019). Virus-based immunotherapy of glioblastoma. Cancers, 11(2), 186.

Mitra, A., Barua, A., Huang, L., Ganguly, S., Feng, Q., & He, B. (2023). From bench to bedside: the history and progress of CAR T cell therapy. Frontiers in immunology, 14, 1188049.

Mukherjee, B., Al Hoque, A., Chakraborty, A., Chakraborty, S., Dutta, L., Dutta, D., Banerjee, S., Dhara, M., & Deepa, R. M. (2022). Recent developments in cancer vaccines: where are we? Nanotherapeutics in Cancer Vaccination and Challenges, 29-75.

Muszer, M., Noszczyńska, M., Kasperkiewicz, K., & Skurnik, M. (2015). Human microbiome: when a friend becomes an enemy. Archivum immunologiae et therapiae experimentalis, 63, 287-298.

Nash, A., Aghlara-Fotovat, S., Hernandez, A., Scull, C., & Veiseh, O. (2021). Clinical translation of immunomodulatory therapeutics. Advanced Drug Delivery Reviews, 176, 113896.

Nejman, D., Livyatan, I., Fuks, G., Gavert, N., Zwang, Y., Geller, L. T., Rotter-Maskowitz, A., Weiser, R., Mallel, G., & Gigi, E. (2020). The human tumor microbiome is composed of tumor type–specific intracellular bacteria. Science, 368(6494), 973-980.

Neukart, F. (2024). Towards sustainable horizons: A comprehensive blueprint for Mars colonization. Heliyon.

Nidhi, S., Anand, U., Oleksak, P., Tripathi, P., Lal, J. A., Thomas, G., Kuca, K., & Tripathi, V. (2021). Novel CRISPR–Cas systems: an updated review of the current achievements, applications, and future research perspectives. International journal of molecular sciences, 22(7), 3327.

Pallister, C., & Watson, M. (2010). Haematology. Scion Publishing Ltd.

Paul, W. E. (2012). Fundamental immunology. Lippincott Williams & Wilkins.

Rahman, M. M., & McFadden, G. (2021). Oncolytic viruses: newest frontier for cancer immunotherapy. Cancers, 13(21), 5452.

Raja, J., Ludwig, J. M., Gettinger, S. N., Schalper, K. A., & Kim, H. S. (2018). Oncolytic virus immunotherapy: future prospects for oncology. Journal for immunotherapy of cancer, 6, 1-13.

Rapoport, B. L., van Eeden, R., Sibaud, V., Epstein, J. B., Klastersky, J., Aapro, M., & Moodley, D. (2017). Supportive care for patients undergoing immunotherapy. In: Springer.

Romano, M. (2015). In vitro characterisation and expansion of human regulatory T cells for their in vivo application in the induction of tolerance in haematopoietic stem cell and solid organ transplantation.

Roy, S., & Bagchi, B. (2020). Fluctuation theory of immune response: A statistical mechanical approach to understand pathogen induced T-cell population dynamics. The Journal of Chemical Physics, 153(4).

Safarzadeh Kozani, P., Safarzadeh Kozani, P., Ahmadi Najafabadi, M., Yousefi, F., Mirarefin, S. M. J., & Rahbarizadeh, F. (2022). Recent advances in solid tumor CAR-T cell therapy: driving tumor cells from hero to zero? Frontiers in immunology, 13, 795164.

Shalhout, S. Z., Miller, D. M., Emerick, K. S., & Kaufman, H. L. (2023). Therapy with oncolytic viruses: progress and challenges. Nature Reviews Clinical Oncology, 20(3), 160-177.

Shouval, R., Alarcon Tomas, A., Fein, J. A., Flynn, J. R., Markovits, E., Mayer, S., Olaide Afuye, A., Alperovich, A., Anagnostou, T., & Besser, M. J. (2022). Impact of TP53 genomic alterations in large B-cell lymphoma treated with CD19-chimeric antigen receptor T-cell therapy. Journal of clinical oncology, 40(4), 369-381.

Silva, J. L., Foguel, D., Ferreira, V. F., Vieira, T. C., Marques, M. A., Ferretti, G. D., Outeiro, T. F., Cordeiro, Y., & de Oliveira, G. A. (2023). Targeting biomolecular condensation and protein

aggregation against cancer. Chemical Reviews, 123(14), 9094-9138.

Šmardová, J. (2024). What tumors teach us: Parallels in cell and human behavior (Vol. 2). Masarykova univerzita.

Sompayrac, L. M. (2022). How the immune system works. John Wiley & Sons.

Srivastava, S. R., Ramana, J., & Lahmo, P. (2019). T-Cell Immunotherapies Market 4th Edition 2019-2030.

Suri, V. K. (2022). Functional Automation and Digital Transformation. Dorrance Publishing.

Suryaprakash, R. T. C., Safi, M. A. A., Alonazi, N., Alsieedi, A. A., & Kujan, O. (2023). Immunotherapy and Cancer Stem Cells. Molecular Targets and Cancer Therapeutics (Part 2), 165.

Tian, Y., Xie, D., & Yang, L. (2022). Engineering strategies to enhance oncolytic viruses in cancer immunotherapy. Signal Transduction and Targeted Therapy, 7(1), 117.

Ventola, C. L. (2017). Cancer immunotherapy, part 1: current strategies and agents. Pharmacy and therapeutics, 42(6), 375.

Wilky, B. A. (2019). Immune checkpoint inhibitors: The linchpins of modern immunotherapy. Immunological reviews, 290(1), 6-23.

Willcox, C. R., Mohammed, F., & Willcox, B. E. (2020). The distinct MHC-unrestricted immunobiology of innate-like and adaptive-like human γδ T cell subsets—Nature's CAR-T cells. Immunological reviews, 298(1), 25-46.

Williams, C. K. O., & Williams, C. K. O. (2019). Historical Perspectives. Cancer and AIDS: Part I: An Historical Perspective, 15-59.

Wojtukiewicz, M. Z., Rek, M. M., Karpowicz, K., Górska, M., Polityńska, B., Wojtukiewicz, A. M., Moniuszko, M., Radziwon, P., Tucker, S. C., & Honn, K. V. (2021). Inhibitors of immune checkpoints—PD-1, PD-L1, CTLA-4—new opportunities for cancer patients and a new challenge for internists and general practitioners. Cancer and Metastasis Reviews, 40, 949-982.

Wu, C., Wang, A. C., Ding, W., Guo, H., & Wang, Z. L. (2019). Triboelectric nanogenerator: a foundation of the energy for the new era. Advanced Energy Materials, 9(1), 1802906.

Zhang, T., Kurban, E., & Wang, Z. (2023). Neoantigens: The Novel Precision Cancer Immunotherapy. Biologics, 3(4), 321-334.

About The Authors

Maria Nazir is an MPhil Scholar of Microbiology at the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur, Pakistan. She is involved in a National Research Program for Universities (NRPU) Project, with research interests in Molecular Characterization. She has submitted abstracts to various conferences and authored and coauthored of several book chapters. Her research focuses on the isolation and Molecular characterization of Corynebacterium pseudotuberculosis and their applications in promoting animal health. Her interested research criteria are based on genetics, molecular biology, and bioinformatics.

Email: nazirmaria545@gmail.com ORCID 0009-0004-6714-6212

Aansa Tahreem earned a Bachelor's in applied microbiology from the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur Pakistan. Currently, she is doing an M. Phil in Microbiology from the University of Veterinary and Animal Sciences (UVAS) in Lahore Pakistan. Her research interests are in Microbial genetics, Molecular biology, soil microbiology, plant Microbiology, and food quality and its application. She has a single publication in international journals.

E-mail: aansa45tehreem@gmail.com ORCID: 0009-0001-6208-8090

Dr. Rumaisa Nawal received her MBBS degree in 2024 from Multan Medical and dental college. She is a house officer in Bhawal Victoria Hospital, Pakistan. She has done internship program at District Headquarters Lodhran.

Email: rumaisanawal9@gmail.com ORCID:0009-0000-1903-8365

Ms. Fatima Sagheer doing MPhil in Biotechnology at The Islamia University of Bahawalpur. Her research interests include Bioremediation & Biotransformation of environmental Contaminants using microbes.

Email: fatimasagheer336@gmail.com ORCID: 0009-0002-8381-1089

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as “Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone”. His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

Dr. Muhammad SAFDAR earned his PhD in Molecular Biology and Genetics from Gaziantep University, Turkey. He is Lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 70 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

E-mail: msafdar@cuvas.edu.pk ORCID: 0000 0002 3720 2090

Prof. Dr. Mehmet ÖZASLAN received his PhD in 1995 Institute of Natural Sciences at Cukurova University, Turkiye. He is a Professor in Molecular Biology and Genetics. His research interests are included Cancer Genetics, Molecular Virology, Molecular Genetics, Microbiology, and Genetic mutations etc. He has published more than 200 research articles in national and international well reputed journals. He also has written many book chapters as well as edited books. He is an editor and editor-in-chief of many well-reputed national and international journals.

E-mail: ozaslanmd@gantep.edu.tr, ORCID: 0000 0001 9380 4902

To Cite This Chapter

NAZIR M et al., (2024). Rebooting the body's defense: innovations in immunotherapy treatment. In Current Studies in Health and Life Sciences 2024 (pp.145-162). ISRES Publishing.

A Healthy Planet, Healthy People: Exploring The Links Between Environment and Health

Maria NAZIR

Tehreem ZAHRA

Arifa MEHREEN

Tasneem MURTAZA

Jamal Muhammad KHAN

Shafeeq Ur REHMAN

1. Introduction

While the perception of human health being synonymous with the environment is not commonly practiced, its correlation is as absolute as the sunlight to life on Earth. Air, a heterogeneous entity that constitutes oxygen, the major component that is a necessity for life and water for consumption the food we eat, and the environment where we live are the essential elements of health. The intertwining nature of the environmental crises and the human health implications commands that this channel be considered as one of the factors in the policy development and the remedial action taken to sustain the ecological system and humankind. This chapter specifies the environmental health sector, a discipline that is considered to be very wide, as it shows how the environment inhabited by human beings has either a positive or negative impact on health (as shown in Figure 1). First of all, the main ecological health principles involve the understanding that people are perhaps the most connected to nature (Sandifer et al., 2015) which shows that environmental change can lead to changes in health outcomes in all aspects of life (from mental to physical) and consequently it can take years to restore the state, and the appearance of some diseases might be experienced as a result by some part of the population. An intricate web of factors such as air, water, and soil quality, biodiversity, and climate patterns influence how well people are and how sick they get. They typically launch either chemical effects e.g. air and water pollution or biological threats such as pathogens and allergens. Environmental health, which promotes perfect accommodation and sanitation faces, also has social and economic aspects. Analyzing these natural components of the environment aids in the adoption of fitting approaches in treatment, low risk of diseases, and thereby improving wellbeing.

The environment threatens life and can harm it in myriad ways via direct as well as indirect ways. The scary list of the ways polluted air and water can contaminate organisms includes all that bad air to breathe and eating and drinking unsafe food. When one touches the skin of s/he chemicals and toxins, it is equivalent. People and communities are prone to health hazards that become worse over time as they face various kinds of living, jobs, locations, and health associated with socioeconomic position, behaviors, and inequalities (DeFur et al., 2007). Environmental health research refers to studies that focus on quantification and in-depth portrayal of the prevalence of health outcomes that correlate with the indicated level of exposure. This could be, for example, some acute (bacterial) diseases like food poisoning and respiratory infections and injuries due to weather-related extreme weather events. Also, some chronic diseases like cancer, cardiovascular disease, dementia, and autoimmunity may have been experienced from the long-term pollution of the environment over time as claimed by (Kim et al., 2020).

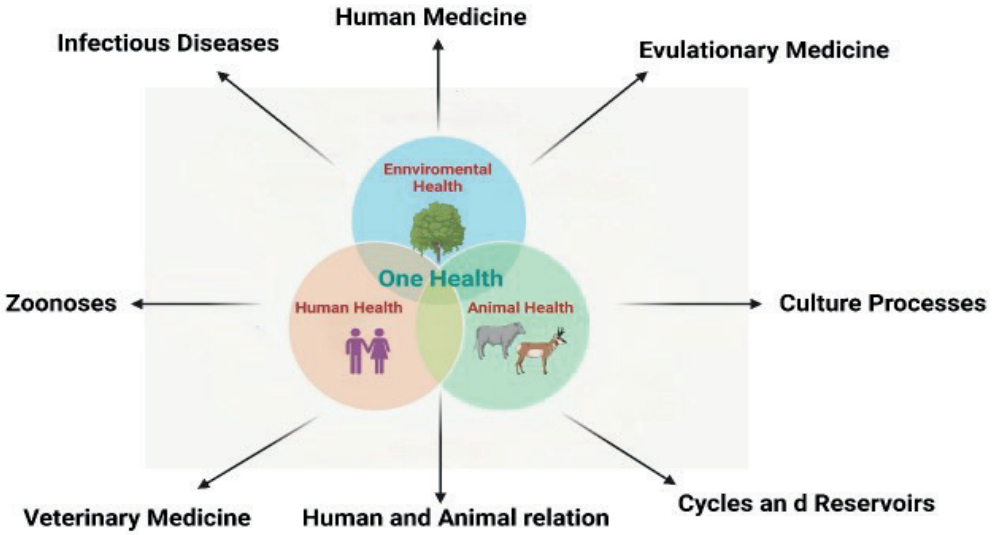


Figure 1. One Health Concept

The ambient environment of the healthcare spot is also complex, and the parameters might be altered more often. For example, the correlation may be unidirectional, similar to that between a child's lead contact and delays in development. Yet at times, these bonds echo in the chords. For this point, let us look at a visual example of how climate change results in different disease types such as malnutrition from changes in farming which brings the number of dengue and malaria cases up in different areas (Kim et al., 2020). The chapter's main agenda is to enlighten the new and old debates that show the link between environmental health and the health of humans. Set down the standard pollution questions concerning air and water, but also share the wider concerns connected with nutrition, global warming, and conserving biological diversity to a healthy society. Last but not least, attaining a sharp eye on how our locality and the external environment are related to our health is necessary before browsing further steps that will lead to a healthier life as well as a safer environment.

2. Environmental Determinants of Health

The ecology of this century is a critical factor in human health competition. The major problems of carbon emissions, the acid rain phenomena, the decreasing of artwork, and the exhaustion of resources, have the lesser concern compared to climate change (Karpudewan et al., 2015). Origins of the warming planet are manifold and multifarious meaning they permeate the macro environment responding differently to different weather patterns and processes. Climate change is generally referred to as a clampdown multiplier on a wide array of health concerns that already exist in different parts of the world while also exacerbating the health inequality experienced in all countries. It is now the moment to focus on and speak of several important factors of climate change that will knock your health. The expansion of heat waves, floods, droughts, forest fires, and storm occurrences in certain areas leads to direct consequences that threaten life and infrastructure. This becomes the failure key element, as people can suffer physical harm, eviction, and even not have the opportunity to go to clinics during such times(Comfort et al., 2015). The top contributor to the worsening of the heatwave is also the heat rise which is a very dangerous factor, as heat-related illnesses increase predominantly in elderly and sick individuals as well. In some areas,

the forces of F injected air pollution in different ways. This increased level of ozone induces the production of ground-level ozone which from now on is only becoming worse in the condition of respiratory diseases (as shown in Table 1). Similarly, during wildfires of this kind, huge numbers of particulates and polluting gases are sent into the air causing it to get polluted, and yet, various consequences other than impacts from climate change have been noted as well. The second example is that seasons become longer so there are many pollens which makes asthma and allergies even worse (Barnes, 2018).

Table 1: Environmental Determinants of Health and Their Impact (Prüss-Ustün et al., 2017)

Determinant Type	**Examples**	**Health Impacts**
Physical	Air pollution, radiation, noise, extreme weather	lead to respiratory diseases, cancer, hearing loss, heatstroke, injuries, and mental health impacts.
Chemical	Toxic substances like lead, mercury, pesticides, and endocrine disruptors	neurological damage, cancer, reproductive problems, and hormonal imbalance.
Biological	Bacteria, viruses, parasites, and allergens	It causes infectious diseases like cholera and malaria, as well as allergies and asthma.
Social	Quality of housing, availability of healthcare, economic status	chronic illnesses, mental health issues, physical injuries, and heightened susceptibility to other factors.

Unpredictable weather patterns as a result of climate change have caused the interruption of agro-ecosystems which have affected crop yield as well as lowered the nutritional content of various food products. Extreme cases like flooding and droughts are often the very reason for the instability and insecurity of the food supply, which can lead to a food deficit situation in some areas that are already very fragile (Mohamed, 2017). Community hazards have been identified in both the cases of under nutrition and malnutrition among children which may be the situation that sets the path for such a community to be a health burden forever. Changing the direction of rainfall, flooding occurrences and droughts result adversely in the adverse effects on water quality and drainage and sanitation system. There could be a transmission of person-derived bacteria from water bodies into the community raising cases of diseases like cholera and typhoid which are more common in low-hygiene areas. The hottest temperatures and the unusual imbalances in the precipitation make many vector species that are spreaders of diseases overgrow, which live long and expand their regions. It is even possible for these usually local diseases, such as malaria, dengue, and zika, to spread to the areas where there were previously none, thus threatening human lives even more in the regions in which these diseases already prevail (Chala & Hamde, 2021).

This is very difficult to feel certain of an accurate definition of the mental well-being consequences affected by climate change as these effects are very diverse. Oncoemokrediton severe weather and way of life complexities may lead to psychological problems, like PTSD. Different changes; whether short-term changes like the alterations of agriculture or long-term changes that cause the reduction of livelihoods microbiologists' feelings of anxiety and depression in association with suicide (Kim et al., 2014). The effects of climate change on health are two-fold, they do not only not affect all populations similarly, but they also, do not only affect them at the same o or on the same level. Among the many socioeconomic groups people that are the youth, the elderly, and people with pre-existing medical problems as well as individuals living in slums, those who are marginalized are the ones who are hit the hardest by the devastating effects of climate change. Climate change is currently seen as a threat multiplier, a process by which climate change is escalated as well as worsened, and thus leads to health inequities that already exist (Friel, 2019).

Climate disasters have taken on multiple dimensions of the threat to public health. Nevertheless, the mentioned issue should be dealt with, as it has always required collective action for climate change reduction by inhibiting carbon emissions levels and enhancing the energy sources to renewable ones. So along with the development of adaption systems to cope with it will also require that healthcare systems and communities become more resilient to such unprecedented environmental events. This approach includes the establishment of diverse early warning mechanisms for extreme weather, monitoring of world diseases, erection of structures constructed to climate change demands, and mental health support facilities (Pinheiro & Luís, 2020). One of the most serious effects of climate change on both the ecosystem and human beings is an inseparable relationship between our planet's health and humans' health. Presenting this challenge may be a structured and fair-based international action, which could protect not only the present population of the local community but also their prosperity.

3. Air Quality and Respiratory Health

Around 6% of deaths are caused by the worsening in air condition leading to respiratory allergies and infection air pollution, as multi-component wood-blacken peril, for years has been extensively talked about, especially by inhabitants of urban areas and industrial places. Air pollution can act as a catalyst for various complications thereby resulting in the interplay of existing respiratory diseases, and chances of riding chronic respiratory diseases, subsequently radiating negatively on our lives and shorter lifespans. Now sit back a second and we move to a specific level of the issue dealing with the primary pollutants and their recognition in the respiratory system. PM, in other words, those minute particulate elements of which air is made and which inhalation passes right through to the lungs, is a major cause of pollution (Akther et al., 2019). It is burnt up all vehicle emissions and energy-producing facilities as well as the events made due to forest fires, generally speaking, are the major sources of air pollution. Smaller particles, like PM2. (as shown in Figure 2) aside an inevitable aspect is that 90% of these particles are categorized as ultrafine (i.e. having a diameter less than 2. 5 μm) forms that are much riskier to attain the terminal bronchioles(Isaxon, 2014). Inflammation of the airways and a decrease in lung function are two other adverse effects that could lead to an increase in asthma severity for the patient. Ozone that is produced from the nitrogen oxides from vehicles and industries and the organic air pollutants can scatter UV radiation directly under the sun and return it to the earth, thus becoming harmful to all living beings. In the polluted air, there is the hazardous gas ozone which is an irritant and a swelling agent in the airways that can cause respiratory problems when it is mixed with other pollutants and airborne particles (Patocka & Kuca, 2014).

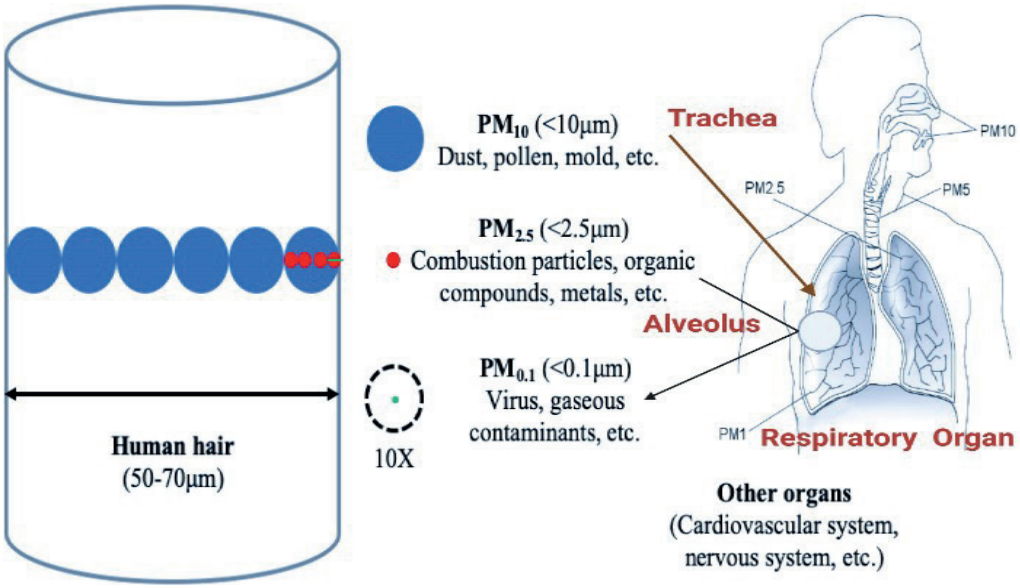


Figure 2. Impact of PM2.5 on respiratory disease.

After the air contamination is done, fewer areas are still left for breathing and as a consequence, the lung capacity is reduced in general. Nitrogen dioxide (NO2) is most frequently emitted by vehicular transportation and power stations. It is one of the major causes of respiratory irritation which ultimately results in lung development problems in kids and heightens susceptibility to lung infections (Goldizen et al., 2016). The influence remains a known risk trigger for both asthma and COPD development. Sulfur Dioxide (SO2), coming from the sulfurous chemicals discharged into the environment that burn fossil fuel, is a very good contact irritant, especially the persons who have abnormal conditions in the respiratory system (Verma et al., 2021). In other words, through air pollution, asthmatic patients experience complications of their illness and the pulmonary ward of the hospital experiences the heaviest workload (as shown in Figure 3). It is not just individual pollutant effects that contribute to the elevated risks of impaired respiratory function; overall air pollution is the underlying factor. These chemicals cause many diseases in the body's organs thereby down-regulating the body's immune systems and this results in the general architecture and the body cells being toxic. Those who stay in pollution levels of high (egg. smog) are more susceptible to respiratory diseases, like asthma, Chronic Obstructive Pulmonary Disease, lung cancer, or pneumonia, than the ones whose air is not polluted and of better quality (Saxena & Sonwani, 2019).

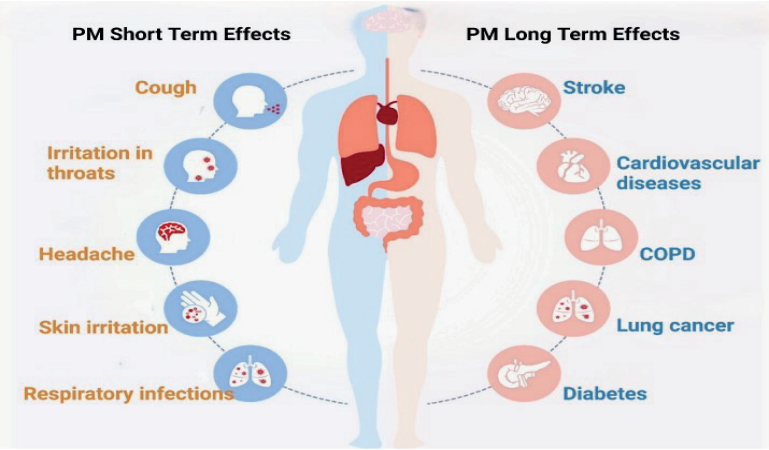


Figure 3. Effects of PM2.5

Combating the health issue from air quality deterioration, therefore, contemplates working out all the problems whatsoever. It is required to undertake changes to the already existing energy sources either by solar, wind, or other renewables or with stricter emissions limits from cars and power stations. Instruction can be considered as one of the chief factors for improving urban air quality (Fripp, 2012). Most of the measures like public transit, bicycling, and walking may help make significant amendments to urban air quality. While emitting information should be tracked and limited, such expenses need to be aimed at being raised for further investment in clean technologies. For individuals, the first step is to be mindful of the issue and check the air quality on websites regularly, regarding special populations, they are of utmost importance, and on poor air quality days anyone with health issues should avoid exhausting even physical activities are the procedures. The effect of air pollution on respiratory health becomes more alarming given the seriousness of the cause. It has grown to a stage that now counts as a health menace. Pollution control is a multi-faceted program and it should focus not only on environmental objectives but also be people-centered (Singh & Kumar, 2018). Breathing clean fresh air ensures the physical and mental health of every individual.

4. Water Quality, Waterborne Diseases, and Disease-Free Water Source.

The availability of drinking water being a fundamental necessity is not only a health and welfare enhancer but also an economic activity stimulant (as shown in Figure 4). Aggravating the health issue is that the contaminations in water are, actually one of the most powerful threats to the well-being wherever in the world. Contrarily, the withdrawal of water may bring advantages

in many cases but also may create some problems like waterborne diseases caused by bacteria which can easily grow when water is polluted. According to this, diarrheal diseases have led to unhealthier illnesses and deaths, but this is more inevitable in areas where sanitation infrastructures are inaccessible (Nagtegaal et al., 2020).

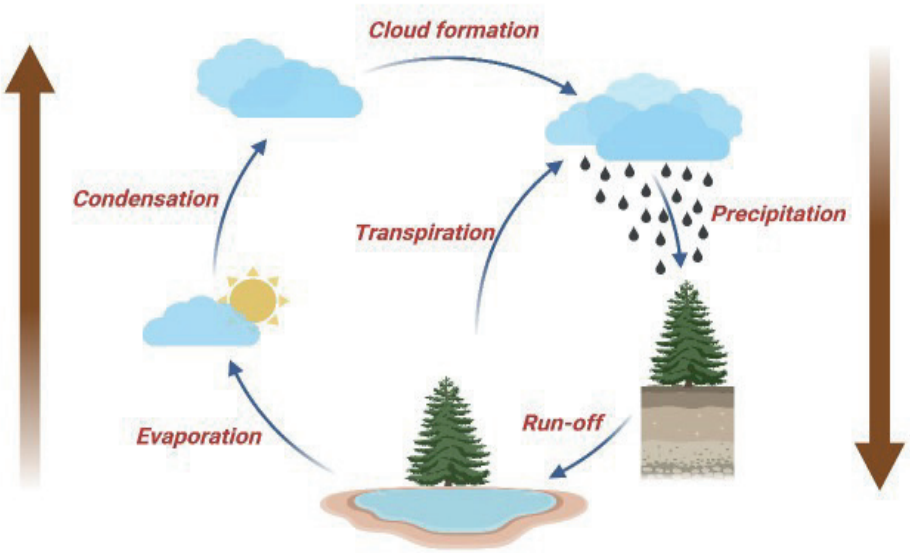


Figure 4. Water Cycle

Unsanitary sources of drinking water have pronounced implications, both in terms of public health, and they are associated with economic and global development, literacy, and other social development. Water is our body's holy grail in every physiological operation from eliminating wastes, maintaining the body temperature, and transporting or dissolving nutrients. Piled water is likely to impair the coordination of healthy functioning of these vital systems (Gillen, 2013). The type of illnesses that mostly kill the children in poor countries such as dysentery and cholera, are a result of unclean water that has contamination of bacteria, viruses, and parasites. The situation is made worse by the fact that the poor countries, which host the most children, are the places where these diseases are present. Child mortality was high before the advent of clean water because many water-borne diseases found their way to people through drinking contaminated water (Organization, 2019). Cholera disease is the name which organism named as Vibrio cholerae has caused. The occurrence of dehydration could be the outcome if proper medical treatment is not provided, which in turn, might lead to death. Typhoid fever is commonly known to be deadlier. The initial symptoms present high fever, fatigue, and vomiting, whereas, in severe conditions, it develops into a critical life-threatening situation. Examples of virus types capable of causing gut-type diseases like rotavirus, norovirus or infectious hepatitis are those transmitted via importing polluted water. Giardiasis and Schistosomiasis, both of which are caused by germs that are similar to parasites, are among the most widespread ailments that affect the lives of people (Cox, 2002). However, this is not to disregard the violation of the right to health which is caused by diarrhea which is the illness we often and more frequently pay attention to. The consequences of water quality issues on a community's status are more than that. The emerging danger of chemical contamination, in fact, in numerous instances being stealthy and underhandedly is a rather experienced issue. When a production land is used, pollutants sources change into it by introducing pesticides and fertilizers to water body systems. The case is entirely different with trace elements (such as lead, arsenic, and mercury) that industrial effluents and poor management of waste bring. Hexavalent heavy metals exhibit a vast range of effects depending on the substance (Azeez et al., 2021). These chemical

substances, equally demanding, release these relatively harmful effects to humans. Lead, even though is a primary reason the younger children's IQ decreases, the long-term effect on the entire brain of these children shows permanent brain consequences. Just because arsenic is present does not mean that causing cancer, cardiovascular disease, and diabetes is a simple act. These chemicals disrupt bee cycle activity in such a way that they turn their natural actions harmful and in the long run, they may affect their procreation development (Leska et al., 2021).

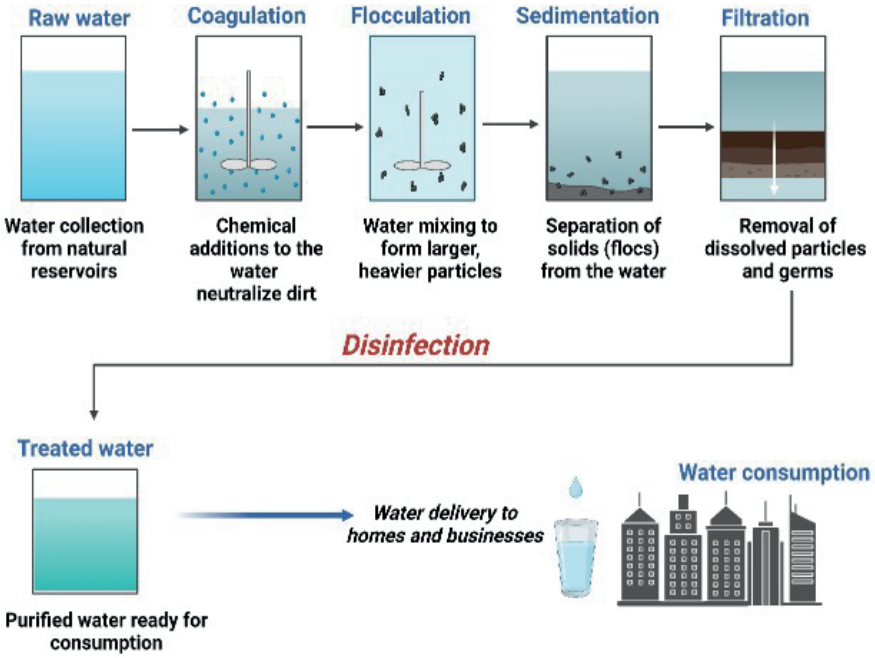


Figure 5. Water Cycle and Potential Contamination Points.

The quality of water that goes beyond only serving as a medium for drinking is also another matter. A quality of low sanitation, which one can come to have when the water is used for bathing, washing clothes, and irrigating, can negatively influence one's health. Yes, direct contact having physical contact with the person who is infected one might be not exposed, but still, it can be a low-level health threat. Water stewardship consists not only of water sources such as rivers, lakes, and aquifers. It reaches transmission systems to reach homes and communities through the treatment of water (Pokhrel et al., 2022).

The combination of quality of water and diarrhea illnesses requires understanding strategy to the core. Along with this scheduled investing in environmental sanitization interventions is the primary concern of these most underserved communities where the data has shown to have many disease transmission routes (Howard et al., 2020). The point to be considered is that the supply of improved toilet facilities which keep feces within themselves and keep them from the areas of a freshwater source should be the central issue. Besides that, preparing reliable plans covering the issue of clean water for drinking, hygiene, and domestic use is the other vital cover. This can be manifested in varied ways such as; the use of different water purification processes, protecting watersheds, and creating reliable water distribution networks. Apart from water quality issues, wastewater treatment is also an issue. The micro bio contamination test and the chemical pollutants test are tested sporadically to be in a better position to deal with issues at an early stage. Setting very rigorous rules and checking for industrial water pollution by neighborhood activities such as factories, agriculture, and waste, as well as collecting waste, are very important for preventing pollution. Including in public awareness campaigns lessons of water safety and hygiene does even

more as community members learn and begin to take steps towards being safe for themselves and their families (Allender et al., 2013).

Harmonizing a shared convention or a unanimous set of guidelines at the international level, researching water resources, and engaging in joint water management among countries creates a platform that should define the water management agenda (McIntyre, 2016). An increase in water scarcity as a result of extreme events, like population growth and the changing climate, impacts the lives of the most vulnerable, especially the country's poor people. Safe water is not an issue of just helping protect people from a particular illness, but something even more fundamental that is, monitoring the health of the children and communities, and emerging parity in life (as shown in Figure 5). Clean water leads to stronger human characteristics and enables people to produce good results, get rich, and help other people too in the growth of their community.

5. Food Safety and Nutrition

All nutrients will be derived from the food although they can bring us diseases if they are not carefully treated and prepared. Intestinal diseases are another public health issue contributed by food. Examples are Salmonella, E. coli, Norovirus, and parasites as they can be spread through foods, causing sometimes life-threatening illness (Flint et al., 2012). They may be short-term lead to minimal side effects such as nausea and can be even life-threatening in extreme cases. Contamination can arise at each step of the food chain, from farming and processing at initial levels and cooking at a later point. Concerning it, the molds or certain bacteria species are at most capable of producing toxins on the surface of the food that they eat, which then may become diseases that make us sick. Microbial contaminants are just one of the many unsafe components of food, and chemical residues like pesticides or metal contaminations which accidentally find their way into the food and enter the mainstream are yet another example that can be cited (Landrigan et al., 2018). The connection between food and health is not confined to only the food intake, but beyond that, it encompasses the quality of diets. The foundation of normal activities in people begins with regular balanced nutrition in the sense that this nutrition regulates growth and development processes, strengthens the human immune system, and serves as protection from various chronic diseases (Sardesai, 2011). Poor dietary habits are; being deficient in foods, consuming too many unhealthy foods, and consuming those foods in large quantities; which causes a lot of diseases to be common in large parts of the world.

6. Climate Change and Health Impacts

Climate-Exacerbated Health Crises Pose Not Only a Public Health Menace but also Significant Amounts of the Soft of Sickness and Diseases. While "normal" devastating weather events such as hurricanes, floods, wildfires, and droughts which used to occur from time to time are daily an occurrence today and cause casualties, injuries, displacement of the population, health facilities disruption, and livelihoods loss (Bell et al., 2018). There is the potential for problems even though heat waves carry danger to certain population groups. For example, the probability of heat stroke heat stress, and aggravation of cardiovascular and respiratory diseases increases. Climate change continues to become a factor setting the stage for an epidemic arising with diseases like Zika that are affected by temperature changes. Less likely would the collective range of such disease vectors, like mosquitoes and ticks, be affected by the temperature rise and a shift in the rainfall patterns, eventually extending their geographic positions (as shown in Figure 6). Thus, malaria, dengue, and vector-borne diseases like Lyme will spread further. At the top of the list, we should remember the negative consequences of climate change and farming the so-called "agricultural problems. " Moreover, food security and scarcity of food due to malnutrition (Herforth, 2010).

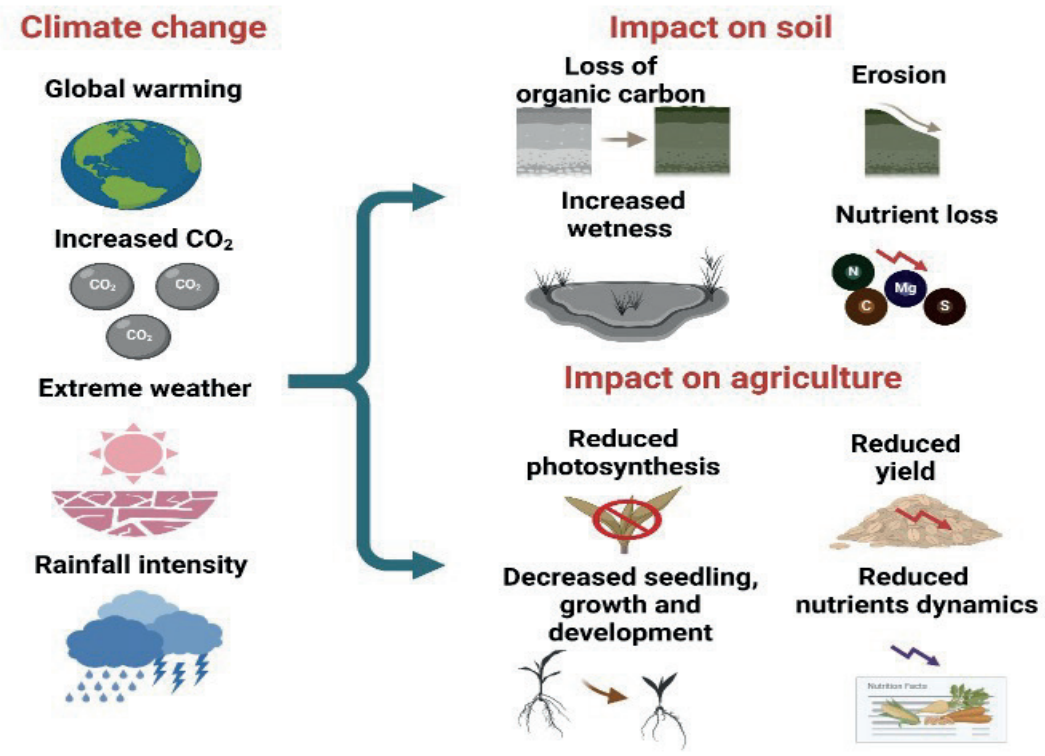


Figure 6. Global Vulnerability to Climate-Related Health Threats

7. Biodiversity and Ecosystem Health

Diversity of life, the distinctive components of life and nature, has the biggest role even if it may not be visible when examining the link between your health to the health of human beings. Human crop ecosystems provide valuable services to us, often detailing in a considerable amount. They uphold this by holding the atmosphere in which we breathe without toxic particles, heath of water, nutrients from and into the earth, and ecosystems that sustain food production. Ecosystems in the border zone might be compared with the strong columns supporting any building and the building can hardly micro vibrate or collapse when being shaken by the shocks (Hsu, 2024). Simply, habitat loss is the consequence of deforestation, increasing the available land for agriculture, and urbanization which is the main threat to biodiversity. However, the destruction of ecosystems is the reason that we are losing plants and animals in the process. Moreover, disturbing natural balance, which supports our existence as well as our health, is our stake. The studies have also found that the reduction of local biodiversity leads to an altered way of transmission of contagious diseases. More specifically, habitat loss leads to the increase of the animal's close standstill and brushing of humans, cattle, or wildlife species. This is a feature that makes an epidemic occur and spread, as the number of COVID-19 cases shows as an example to be seen (Liu et al., 2021). The combination of these things makes biodiversity to be an issue of large importance to food security. A colorful mixture of crop types, besides the role of pollinators, is the factor of the long-term origin of food production. This is mainly the duo of attacks from pests, diseases, and climate change. However, the role of healthy marine life in nutrition and providing healthy food to more than billions of people who also reside on the coast is a very crucial basic component (Tacon & Metian, 2013). Moreover, if exploitation of marine resources and other types of species' destruction are out of control, there will be a loss of biodiversity, thus raising questions about human survival and food supply.

As research progresses and further connection between our well-being and biodiversity becomes more evident, it appears to be natural that our minds accept this information and learn, act, and behave in a way that helps us on several levels. Researchers found out that humans who live in close connection to nature and are rich in all kinds of diversity, decrease their depression, stress,

and general good mood, and allow them to think well (Sandifer et al., 2015). A growing number of scientists see nature connectedness (which is the kind of feeling when somebody understands their connection with the natural world) as the most important factor that helps to create a full and healthy life. Also, the diversity of habitats is considered an endless source of remedies for health care formulas. New treatments based on natural products are being discovered today by scientists, and similar molecular components used in them are being identified for the first time as the effects of existing drugs in completely different organisms (Harvey et al., 2015). Currently, this is about withholding the disappearance of the species without which we can never hope to find the ones capable of synthesizing the drugs used to treat various kinds of diseases. More than that functions of healthy and well-maintained ecosystems as well as their diversity of species play the role of the regulator of climate and the additional buffer in case of natural disasters which also along with giving benefits for health do their part in providing a better quality of air and water. Conserving biodiversity and healing once degraded ecosystems is an investment into health and prosperity and not only is it about environmental defense. The programs that address such sustainable land and watershed management harvest forest conservation, sea life protection, as well as ecosystem restoration, cannot be left out since different humans must share a planet that is their home (Chapin III et al., 2011).

8. Mitigation and Adaptation Strategies

Addressing the multifaceted health risks posed by environmental changes requires a two-pronged approach: mitigation and adaptation are the main activities directed by the ultimate goal which is the preservation of a healthy ecosystem. The measures intended to diminish several agents of pollution/environmental degradation are called mitigation strategies. The cause of these root problems is, for example, climate change, and they should be required to be dramatically reduced or eliminated as fast as it is possible. On the contrary, we are looking for ways to enhance the resiliency of the communities through a gradual activity even in the presence of climate change-determined health hazards (as shown in Table 2). The next sentence is dedicated to discussing finding a solution to the problem. The decline of coal and subsequent emissions led to the emphasis on renewable sources. In this case, such sources of alternative energies as the sun, wind, and geothermal wells are going to replace coal and other types of fossil fuels, which means that the emission of harmful air pollutants and greenhouse gases will be reduced (Shahsavari & Akbari, 2018). These sectors are considered the channels of energy where energy efficiency i.e. buildings, industries, and transportation can be used to reduce pollution and thus, conserve resources. One of the top priorities that are required from decision-makers and actors in the agricultural sector is to intimate actors with the environmentally friendly agricultural system, which will decrease the negative environmental impact or damage of soil, and they need to improve the use of pesticides with less toxic chemo ga mics. As well as this, green development, such as fair and sustainable distribution of goods as well as walks to parks, public transport, and green spaces all not only improve the bio-diversity health of the ecosystem but also provide an extra benefit of physical activity by encouraging people to move around more and deter air pollution (Carlin et al., 2016).

Table 2: Mitigation vs. Adaptation Strategies for Environmental Health (Delpla et al., 2021)

Strategy	Goal	Examples	Potential Benefits	Potential Drawbacks
Mitigation	Decrease the factors contributing to climate change and environmental damage	shifting towards renewable energy, sustainable farming, and lowering emissions.	include fresher air and water, enhanced health, and minimizing the likelihood of disasters	International collaboration is necessary for significant upfront expenses and a chance of economic disturbances.
Adaptation	Develop resilience and safeguard communities from environmental change	implementing early warning systems, disaster preparedness measures, infrastructure enhancements, and disease surveillance programs.	lead to decreased vulnerability to disasters, better health results, and saved lives.	limited long-term effectiveness and a risk of maladaptation.

Adaptation strategies are of the first class because they are mostly demanded in the health area, climate change and their outcomes, as well as the events. This, therefore, includes building the resilience of healthcare systems to have them adequately equipped to deal with climate-related diseases and any other epidemics following these extreme events. Social awareness and disaster management protocols often decrease mortality by ensuring the safe evacuation of the population to shelters that are high enough or by taking the necessary precautions to protect themselves. House owners, essential services, and other entities living in the community place their trust in the construction of stronger infrastructure that's highly resistant to the impacts of flooding, extreme temperatures, and other kinds of disasters (Council et al., 2011).

Such resistant infrastructure reduces the extension of long-term damages resulting from natural disasters. Planting and aquaculture will be conducted to grow code drought-resistant crops, while the approaches to minimize food loss help farmers adapt for the future where climate change is the rule. The proper management and preservation of naturally developing biospheres, such as wetlands and forests aid nature itself in building up a buffer against natural calamities or disasters like storms, floods, and extreme temperature modification (Upadhyay, 2020). Aside from the provision of mental health counseling, recyclable and reusable services will give the individuals and community opportunities to live past climate change-related stress, anxiety, and trauma. Nevertheless, these mitigation and adaptation have their dual role in time to help our species withstand the war against climate change. While the mitigation strategies become too narrow for the current situation, the adaptation processes through fast tools ensure the present livelihood of the affected communities. It is on that note that the entire sustainability agenda integrates. The two-pronged tactic works to eliminate of poverty and installation of access to safe water and sanitation facilities that would facilitate equity and adapt vulnerable populations to environmental catastrophes (Dulal et al., 2009). To triumph over the medical impacts of ecological variability, the move should be embraced by society in general and the battle must be led on a global level. The policy could be the first in the implementation of sustainable technology/practices. Furthermore, international cooperation should take place as it would ensure that communities subjected to environmental pollution do not suffer many health burdens (Manisalidis et al., 2020). Efficient, disengaging environmental and human health actions due to their integrated nature automatically become ways to effectively reduce the risks from and adapt to various threats not only to our planet but also to ourselves to realize a unified and healthier world with everyone.

9. Conclusion

The health we enjoy is as closely related to the environment we live in, as our lungs and heart. At the end of the chapter, we learned that climate change is not per se bad or good, but if it overcomes the stable rainy cycles with less rain, the amount of food produced will be reduced, on the other hand, if it reduces oxygen levels, the levels of respiratory diseases will get higher. The environmental personification risk is an umbrella term for the challenges that already seem typical like air pollution and waterborne diseases among others as well as the emerging ones currently taking over the world like climate change, biodiversity loss, and chemical spectrum. The sector of environmental health human promotion is the core point. The undeniable evidence calls in the disproportionately urgency for the actionable laws that follow the goal of prevention of environmental risks and thus preserving the good health of people. The substitution of cleaner energy sources, the use of sustainable methods, and building a community to be able to withstand any challenge are not only the marks of green goals but of an individual's welfare and betterment as well. Learning how ecological disturbances and ill health are connected leads to the conclusion that joint action (of those disciplines) is an essential element when dealing with environmental problems and health. People from various fields such as health workers, environment science, policymakers, and residents are the key sources required for creating effective solutions. The issue of ecosystem protection is deeply rooted not only in the state agenda but in a global one as well, therefore, it opens up the way for transnational cooperation. By giving an ecology that it can live in a residents will get better lives. Environmental sustainability of the future, the one that is inhabited by both humans and nature side by side, needs to start with rethinking our consumption patterns and the patterns of production and relations for both humans and nature just as well. This metamorphosis presents an advantage on two fronts: on one hand, it changes the current lives of people in an upward way that benefits many individuals, and on the other hand, it helps discharge health issues and build reserves that will ensure that future generations will not only show stability but will be prosperous as well. The wellness of the planet as well as ours is connectedly irremissible. We should take action now to do something that is needed to overcome the stalemate and change the current situation to attain a desirable end.

References

Akther, T., Ahmed, M., Shohel, M., Ferdousi, F. K., & Salam, A. (2019). Particulate matters and gaseous pollutants in indoor environment and Association of ultra-fine particulate matters (PM 1) with lung function. Environmental Science and Pollution Research, 26, 5475-5484.

Allender, J., Rector, C., Rector, C., & Warner, K. (2013). Community & public health nursing: Promoting the public's health. lippincott williams & wilkins.

Azeez, N. A., Dash, S. S., Gummadi, S. N., & Deepa, V. S. (2021). Nano-remediation of toxic heavy metal contamination: Hexavalent chromium [Cr (VI)]. Chemosphere, 266, 129204.

Barnes, C. S. (2018). Impact of climate change on pollen and respiratory disease. Current allergy and asthma reports, 18, 1-11.

Bell, J. E., Brown, C. L., Conlon, K., Herring, S., Kunkel, K. E., Lawrimore, J., Luber, G., Schreck, C., Smith, A., & Uejio, C. (2018). Changes in extreme events and the potential impacts on human health. Journal of the Air & Waste Management Association, 68(4), 265-287.

Carlin, C., Cormican, M., & Gormally, M. (2016). Health benefits from biodiversity and green infastructure. Environmental Protection Agency, Johnstown Castle, Ireland.

Chala, B., & Hamde, F. (2021). Emerging and re-emerging vector-borne infectious diseases and the challenges for control: a review. Frontiers in public health, 9, 715759.

Chapin III, F. S., Power, M. E., Pickett, S. T., Freitag, A., Reynolds, J. A., Jackson, R. B.,

Lodge, D. M., Duke, C., Collins, S. L., & Power, A. G. (2011). Earth Stewardship: science for action to sustain the human-earth system. Ecosphere, 2(8), 1-20.

Comfort, M., Lopez, A. M., Powers, C., Kral, A. H., & Lorvick, J. (2015). How institutions deprive: Ethnography, social work, and interventionist ethics among the hypermarginalized. RSF: The Russell Sage Foundation Journal of the Social Sciences, 1(1), 100-119.

Council, N. R., Earth, D. o., Studies, L., Sciences, B. o. E., Committee, G. S., & Resilience, C. o. P.-P. S. C. t. E. C. D. (2011). Building community disaster resilience through private-public collaboration. National Academies Press.

Cox, F. E. (2002). History of human parasitology. Clinical microbiology reviews, 15(4), 595-612.

DeFur, P. L., Evans, G. W., Hubal, E. A. C., Kyle, A. D., Morello-Frosch, R. A., & Williams, D. R. (2007). Vulnerability as a function of individual and group resources in cumulative risk assessment. Environmental health perspectives, 115(5), 817-824.

Delpla, I., Diallo, T. A., Keeling, M., & Bellefleur, O. (2021). Tools and methods to include health in climate change adaptation and mitigation strategies and policies: a scoping review. International Journal of Environmental Research and Public Health, 18(5), 2547.

Dulal, H. B., Shah, K. U., & Ahmad, N. (2009). Social equity considerations in the implementation of Caribbean climate change adaptation policies. Sustainability, 1(3), 363-383.

Flint, H. J., Scott, K. P., Louis, P., & Duncan, S. H. (2012). The role of the gut microbiota in nutrition and health. Nature reviews Gastroenterology & hepatology, 9(10), 577-589.

Friel, S. (2019). Climate change and the people's health (Vol. 2). Small Books Big Ideas in Popul.

Fripp, M. (2012). Switch: a planning tool for power systems with large shares of intermittent renewable energy. Environmental science & technology, 46(11), 6371-6378.

Gillen, C. M. (2013). The Hidden Mechanics of Exercise: Molecules That Move Us. Harvard University Press.

Goldizen, F. C., Sly, P. D., & Knibbs, L. D. (2016). Respiratory effects of air pollution on children. Pediatric pulmonology, 51(1), 94-108.

Harvey, A. L., Edrada-Ebel, R., & Quinn, R. J. (2015). The re-emergence of natural products for drug discovery in the genomics era. Nature Reviews Drug Discovery, 14(2), 111-129.

Herforth, A. (2010). Promotion of traditional African vegetables in Kenya and Tanzania: a case study of an intervention representing emerging imperatives in global nutrition.

Howard, G., Bartram, J., Brocklehurst, C., Colford Jr, J. M., Costa, F., Cunliffe, D., Dreibelbis, R., Eisenberg, J. N. S., Evans, B., & Girones, R. (2020). COVID-19: urgent actions, critical reflections and future relevance of 'WaSH': lessons for the current and future pandemics. Journal of water and health, 18(5), 613-630.

Hsu, L.-h. (2024). "Because the bees buzz underground,/we have earthquakes": Chen Li's The Edge of the Island at the Brink of the Anthropocene Ruin. Concentric: Literacy & Cultural Studies, 50(1).

Isaxon, C. (2014). Aerosol characterization in real life and a methodology for human exposure studies in controlled chamber settings.

Karpudewan, M., Roth, W.-M., & Chandrakesan, K. (2015). Remediating misconception on

climate change among secondary school students in Malaysia. Environmental Education Research, 21(4), 631-648.

Kim, H., Kim, W.-H., Kim, Y.-Y., & Park, H.-Y. (2020). Air pollution and central nervous system disease: a review of the impact of fine particulate matter on neurological disorders. Frontiers in public health, 8, 575330.

Kim, K.-H., Kabir, E., & Ara Jahan, S. (2014). A review of the consequences of global climate change on human health. Journal of Environmental Science and Health, Part C, 32(3), 299-318.

Landrigan, P. J., Fuller, R., Acosta, N. J., Adeyi, O., Arnold, R., Baldé, A. B., Bertollini, R., Bose-O'Reilly, S., Boufford, J. I., & Breysse, P. N. (2018). The Lancet Commission on pollution and health. The lancet, 391(10119), 462-512.

Leska, A., Nowak, A., Nowak, I., & Górczyńska, A. (2021). Effects of insecticides and microbiological contaminants on Apis mellifera health. Molecules, 26(16), 5080.

Liu, X., Huang, J., Li, C., Zhao, Y., Wang, D., Huang, Z., & Yang, K. (2021). The role of seasonality in the spread of COVID-19 pandemic. Environmental research, 195, 110874.

Manisalidis, I., Stavropoulou, E., Stavropoulos, A., & Bezirtzoglou, E. (2020). Environmental and health impacts of air pollution: a review. Frontiers in public health, 8, 505570.

McIntyre, O. (2016). The emergence of the'common management'approach to international watercourse governance and its significance for environmental protection.

Mohamed, A. A. (2017). Food security situation in Ethiopia: a review study. International journal of health economics and policy, 2(3), 86-96.

Nagtegaal, I. D., Odze, R. D., Klimstra, D., Paradis, V., Rugge, M., Schirmacher, P., Washington, K. M., Carneiro, F., & Cree, I. A. (2020). The 2019 WHO classification of tumours of the digestive system. Histopathology, 76(2), 182.

Organization, W. H. (2019). WHO global report on traditional and complementary medicine 2019. World Health Organization.

Patocka, J., & Kuca, K. (2014). Irritant compounds: respiratory irritant gases. Milit Med Sci Lett, 83(2), 73-82.

Pinheiro, M. D., & Luís, N. C. (2020). COVID-19 could leverage a sustainable built environment. Sustainability, 12(14), 5863.

Pokhrel, S. R., Chhipi-Shrestha, G., Hewage, K., & Sadiq, R. (2022). Sustainable, resilient, and reliable urban water systems: making the case for a “one water” approach. Environmental Reviews, 30(1), 10-29.

Prüss-Ustün, A., Wolf, J., Corvalán, C., Neville, T., Bos, R., & Neira, M. (2017). Diseases due to unhealthy environments: an updated estimate of the global burden of disease attributable to environmental determinants of health. Journal of public health, 39(3), 464-475.

Sandifer, P. A., Sutton-Grier, A. E., & Ward, B. P. (2015). Exploring connections among nature, biodiversity, ecosystem services, and human health and well-being: Opportunities to enhance health and biodiversity conservation. Ecosystem services, 12, 1-15.

Sardesai, V. (2011). Introduction to clinical nutrition. CRC press.

Saxena, P., & Sonwani, S. (2019). Criteria air pollutants and their impact on environmental health (Vol. 1). Springer.

Shahsavari, A., & Akbari, M. (2018). Potential of solar energy in developing countries for reducing energy-related emissions. Renewable and Sustainable Energy Reviews, 90, 275-291.

Singh, J., & Kumar, S. (2018). Sustainable human security: A paradigm shift. International Journal of Research in Social Sciences, 8(7), 311-319.

Tacon, A. G., & Metian, M. (2013). Fish matters: importance of aquatic foods in human nutrition and global food supply. Reviews in fisheries Science, 21(1), 22-38.

Upadhyay, R. K. (2020). Markers for global climate change and its impact on social, biological and ecological systems: A review. American Journal of Climate Change, 9(03), 159.

Verma, R. K., Sankhla, M. S., Parihar, K., Kumar, R., & Verma, M. K. (2021). The study of assessing the impact on environment by the noxious airborne chemicals: a review. Biointerface Res Appl Chem, 11, 10844-10863.

About The Authors

Maria Nazir is an MPhil Scholar of Microbiology at the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur, Pakistan. She is involved in a National Research Program for Universities (NRPU) Project, with research interests in Molecular Characterization. She has submitted abstracts to various conferences and authored and coauthored of several book chapters. Her research focuses on the isolation and Molecular characterization of Corynebacterium pseudotuberculosis and their applications in promoting animal health. Her interested research criteria are based on genetics, molecular biology, and bioinformatics.

Email: nazirmaria545@gmail.com ORCID 0009-0004-6714-6212

Tehreem Zahra is M.Phil. Scholar of Food Science and Technology at the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur, Pakistan. Her research focuses on food nutrition and its impact on the human body, with a particular interest in the role of postbiotics in cancer treatment. She is actively investigating how postbiotics can contribute to healthy outcomes in cancer therapy. Tehreem is dedicated to advancing knowledge in this crucial area of food science.

Email: 2019-cu-food-051@student.cuvas.edu.pk ORCID: 0009-0001-2861-5571

Arifa Mehreen is an Assistant Professor of Zoology at the University of Agriculture Faisalabad (UAF). Her research focuses on the antimicrobial properties of natural products, drug formulation and pharmacokinetics, and characterization of bacterial pathogens. She has studied the antimicrobial and toxicological effects of Origanum vulgare, developed a fixed-dose combination drug for

cardiovascular disease, and investigated the characteristics of Staphylococcus aureus strains.

E-mail: arifa.mehreen@uaf.edu.pk ORCID: 0000-0001-5899-8027

Tasneem Murtaza working as zoologist in Zoological survey of Pakistan under ministry of climate change, Islamabad. She is a biological scientist who studies animals and their interactions with their environments. Study animals in controlled or natural environments to understand their behavior, physiology, development, and evolution. Conduct research, collect and analyze data, and publish findings in scientific journals. Collaborate with other scientists, conservationists, and policymakers to develop and implement conservation strategies. Teach and mentor students, interns, or junior scientists. Working experience with universities, colleges, or research institutes. Government agencies (e.g., wildlife services, conservation departments). Non-profit organizations (e.g., wildlife conservation societies). Private industry (e.g., environmental consulting, zoos, aquariums).

Email: tasneem.zsp@gmail.com ORCID:0009-0007-6542-8066

Dr. Jamal Muhammad Khan is an Assistant Professor in the Department of Parasitology at Cholistan University of Veterinary and Animal Sciences, Bahawalpur, Pakistan. His research focuses on infections caused by blood-sucking mosquitoes and their impact on host health. He has published papers on cancer-related genes and presented on topics like parasite-based organic farming, climate change-induced infections, and transgenic parasites as vaccine vectors. He is particularly interested in the interactions between parasites, their environment, and cancer in humans. Dr. Jamal Muhammad Khan also explores using transgenic parasites to combat coccidiosis in poultry and reviews for journals such as Aging-US and Frontiers in Genetics.

Email: jamalmkhan@cuvas.edu.pk ORCID: ORCID: 0000-0003-1208-761X

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as “Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone”. His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

To Cite This Chapter

NAZIR M et al., (2024). A healthy planet, healthy people: exploring the links between environment and health. In Current Studies in Health and Life Sciences 2024 (pp.164-178). ISRES Publishing.

Investigating The Role of The Microbiome in Health and Disease

Arifa MEHREEN

Quratulane GILLANI

Ayesha Bintay FAROOQ

Rumaisa NAWAL

Maria NAZIR

Minal HUSSAIN

Shafeeq ur REHMAN

Muhammad SAFDAR

Introduction

The human body harbors a vast and vital community of microorganisms known as the microbiome, comprising bacteria, viruses, fungi, and other organisms. Recent advances in sequencing technology have unequivocally demonstrated the crucial role of the microbiome in human health (Gebrayel et al., 2022). This chapter will deliver a comprehensive overview of the microbiome, encompassing its definition, composition, impact on health, and potential treatment applications. The microbiome encompasses all microorganisms (as shown in Table 1) residing in different body parts, with the highest concentration found in the gastrointestinal tract and other mucosal surfaces. The complex ecosystem of bacteria in the human body is predominantly composed of the phyla Bacteroidetes and Firmicutes (Rinninella, Raoul, et al., 2019). The microbiome is influenced by various factors, making it a multifaceted process. Genetics, birth methods, antibiotic use, and environmental influences are significant, but the role of a healthy diet is particularly emphasized (Fletcher, 2015).

Table 1: The Human Microbiome: A Quantitative Overview

Microbiome Marvel	**Astonishing Value**	**Explanation**	**References**
Total Microbial Cells	~38 trillion	The microbiome's vast influence is emphasized by outnumbering human cells.	(Bolan, 2019)
Diversity of Species	Thousands	This category comprises diverse microorganisms such as bacteria, viruses, fungi, and other organisms with distinct functions.	(Coleman & Whitman, 2005)
Weight of Microbes in Gut	2-5 pounds (0.9-2.3 kg)	Of equal weight to the human brain, highlighting its significance towards digestion, immunity, and general well-being.	(Mocanu, 2021)
Microbial to Human Cell Ratio	~1.3:1	Shows the important function that microorganisms have in human biology and physiology.	(Salvucci, 2019)

Numerous studies have highlighted the strong influence of diet on the gut microbiome. The composition and diversity of the gut microbiome have a mutually beneficial relationship with the host. Gut bacteria break down complex carbohydrates, produce essential vitamins, and contribute to the production of short-chain fatty acids (SCFAs), which significantly impact health (Portincasa

et al., 2022). Additionally, the gut microbiome goes beyond nutrient production and digestion. It plays a crucial role in training and regulating the immune system, safeguarding the body against excessive activation (which can lead to inflammation) and insufficient activation (due to reduced pathogen defense) (Shao et al., 2021). An effective microbiome function acts as a defense against potential invasion by harmful pathogens (McLaren & Callahan, 2020). Increasing evidence suggests that an imbalance in gut bacteria, known as dysbiosis, is connected to chronic conditions such as inflammatory bowel disease (IBD), as well as non-digestive conditions like type II diabetes, obesity, and contact allergies.

2. Understanding the Human Microbiome

The human microbiome is an intricate and dynamic ecosystem that hosts a myriad of microorganisms, including bacteria, viruses, fungi, archaea, and other unicellular life forms that are too small to be seen with the naked eye. These microorganisms, collectively known as microbiota, are distributed throughout various body regions, such as the skin, oral cavity, and urogenital track (as shown in Figure 1). However, the largest microbial population that can be found in the human body is represented by the gastrointestinal microbiota, with the largest part of it residing in the large intestine (Hillman et al., 2017). Microorganisms present and living inside of the stomach are known as the 'gut microbiome'. These microbes are therefore among this diverse community that plays various roles in the physiological functions of the body including digestion, absorption of nutrients, and Immune regulation (as shown in Table 2). The complex interplay between the human body and the gut microbiota has become the focus of attention in scientific research due to the growing understanding of their significance in human health and pathology (Afzaal et al., 2022).

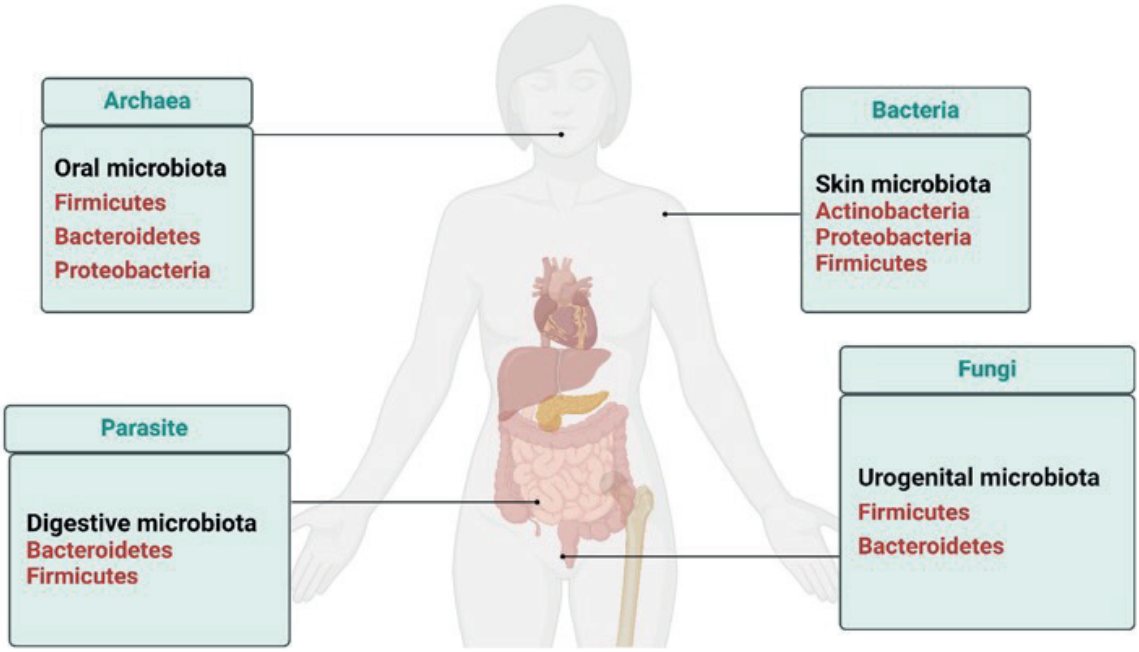


Figure 1. Composition of the Human Microbiome

The gut microbiome is defined as a complex community of microbial specimens that can inhabit the human intestine. Over 1,000 bacterial species have been discovered with two of the most abundant being phyla Bacteroidetes and Firmicutes (Zafar & Saier Jr, 2021). Furthermore, smaller species of Prokaryotes, Actinobacteria, Proteobacteria, and Verrucomicrobiaia have also been present in the environment (Fujimoto, 2012). It is critical to comprehend the complex interactions between these biotic structures and the numerous factors affecting the populations, to enhance and improve the knowledge of microbiome functionality. Every anatomical site of the human body has

its niche with specific conditions to which the microbial community occupying it has to adapt to perform specific physiological functions. That's because it is the gut microbiome that is involved in the digestive process and therefore, it is capable of deriving those nutrients from foods, even from those intricate dietary compounds without which we would be lacking. Not only does it produce vitamins and SCFAs, but these products are also vital for energy metabolism and the gut environment, respectively (Blaak et al., 2020). Another function of the gut microflora is related to the immune system, with both playing significant roles in protecting the body against diseases.

Table 2: Relative Abundance of Major Bacterial Phyla in Different Body Sites.

Body Site	Dominant Bacterial Phyla	Functions	References
Gut	Bacteroidetes, Firmicutes	Breaking down food, absorbing nutrients, producing vitamins, regulating the immune system, and shielding against pathogens.	(Zhang et al., 2015)
Skin	Actinobacteria, Proteobacteria, Firmicutes	Defense against harmful microorganisms, upkeep of skin's protective barrier, control of inflammatory responses	(Dou et al., 2019)
Oral Cavity	Firmicutes, Bacteroidetes, Proteobacteria	Maintaining oral health and preventing dental illnesses.	(Wade, 2013)
Respiratory Tract	Firmicutes, Bacteroidetes, Proteobacteria	Respiratory infections, possible involvement in lung health	(Shima et al., 2016)

It is also important to state that the human microbiome is not a stable community of microorganisms but rather a dynamic community shaped by genetic and environmental factors (as shown in Table 2). An intake of a healthy diet can go down and even change the human metabolism, the working of the vital organs, and even the behavior patterns. Immunomodulation Prescribing extended periods of dietary pattern changes affects the microbial community residing in the intestines (Leeming et al., 2019). Some factors include mode of birth, where the child was born by either vaginal, CS, antimicrobial use, age, and exposure to animals, particularly pets or farms among others (Renz & Skevaki, 2021).

3. The Gut Microbiome and Health

The human body thus has a populace of diverse microorganisms that make up a huge network that is referred to as the human microbiota. This system includes bacteria, viruses, fungi, archaea, and many other microorganisms that are minute to the naked eye. Although bacteria of different types are divided based on their specialization in the skin, mouth, and urogenital tract, the largest colony and variety are found in the large intestine known as the 'gut microbiota (Matter, 2019).

Table 3: Factors Influencing Gut Microbiome Composition (Kumbhare et al., 2019)

Factor	Impact on the Gut Microbiota	Examples
Diet	Diet plays a significant role in determining the composition of microbial communities that are influenced by extended dietary habits.	Diets rich in fiber enhance diversity, while Western diets (high in fat and low in fiber) reduce diversity.
Lifestyle	Physical activity, amount of rest, and stress levels affect the types of microorganisms living in the body.	Engaging in more physical activity can result in positive changes dysbiosis can be caused by chronic stress.
Medications	Antibiotics can disturb the balance of bacteria in the gut, which may result in dysbiosis.	Prolonged antibiotic usage leads to lower variety and higher likelihood of Clostridium difficile infection.

Factor	Impact on the Gut Microbiota	Examples
Genetics	Genes of the host have an impact on the environment and mold the microbiome.	Inherited genes can impact the makeup of the gut microbiome for specific illnesses.
Environment	Early-life experiences and continuing environmental elements can impact the development of the microbiome.	The way a baby is born (vaginal or C-section), contact with pets or farm animals, and where someone lives can impact the makeup of their microbiome.

The gut microbiome exhibits a remarkably high level of diversity, encompassing an estimated 10,000 to 50,000 strains within the average human. Recent research by (DE GIANI, 2022) has revealed that the preponderance of bacterial species in this milieu exceeds 1000, predominantly comprising the Phyla of Bacteroidetes and Firmicutes. Additionally, Actinobacteria, Proteobacteria, and Verrucomicrobia, while present in lower quantities, play ancillary roles. A comprehensive understanding of the intricate interplay between fiber diet interactions and microflora, along with their abundance elements, is imperative for gaining insights into the dynamic nature of the microbiome (as shown in Table 3).

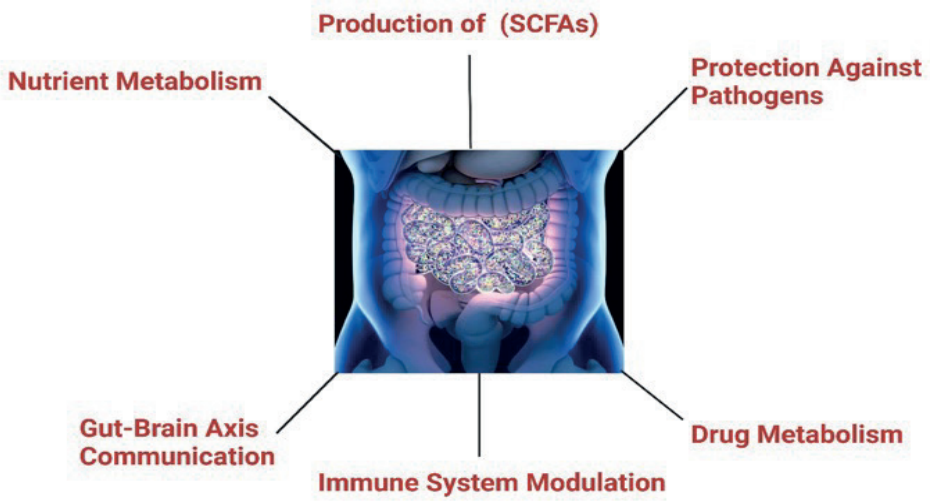


Figure 2. Gut Microbiomes and their functions

The human body encompasses a diverse resident microbial community within each specific niche, demonstrating distinct diversity by specific ecological and physiological functions (as shown in Figure 2). Notably, the gut microbiome, comprising the microbial population in the gastrointestinal tract, holds profound significance in facilitating the digestion process by enabling the extraction of nutrients from complex dietary components that would otherwise remain indigestible. In addition, the microbiome is involved in the production of various vital vitamins comprising certain B-group vitamins and SCFAs for energy requirements and intestinal barrier integrity (LeBlanc et al., 2017). Furthermore, through the integration of signaling pathways, the gut microbiome helps in the regulation of known immune cells to determine between pathogenic and helpful organisms. The human microbiome is not static but rather dynamic, influenced by a complex interplay of genetics and environment. Diet and daily habits play a significant role in determining an individual's health. Long-term dietary patterns, particularly the intake of protein and carbohydrates, are major contributors to the composition of the gut microbiota (Rinninella, Cintoni, et al., 2019). Lifestyle factors such as exercise, sleep, and stress also leave an imprint on the microbiome (Gültekin et al., 2021). Early

environmental exposures, such as the mode of delivery at birth (vaginal birth or Cesarean section), as well as maternal factors like pet ownership and farm exposure, have substantial effects on the developing immune system and the diversity of microbes (García-Serna et al., 2021).

4. Microbiome Dysbiosis and Disease

The complicated and one-sided equilibrium in our microbial community determines whether our health status is intact. Taxa disorders or dysbiosis is a condition of the disproportion in the levels of the bacteria within the microbiome as a transient state of insufficient number of beneficial bacteria and sometimes the appearance of potentially harmful microbes (Ceballos et al., 2021). Gut dysbiosis, these types of fluctuations in the gut microbiota, may indeed bring major health risks to the human system (as shown in Figure 3). Dysbiosis interferes with the mission-critical microbial processes that a healthy commensal community can carry out. It results in the ability of body functions to integrate foods, generate vitamins and SCFAs, regulate immunity, and resist pathogenic bacteria. In addition to that, dysbiosis brings about a situation where there is a smaller degree of inflammation, which is the origin of various chronic diseases (Potrykus et al., 2021).

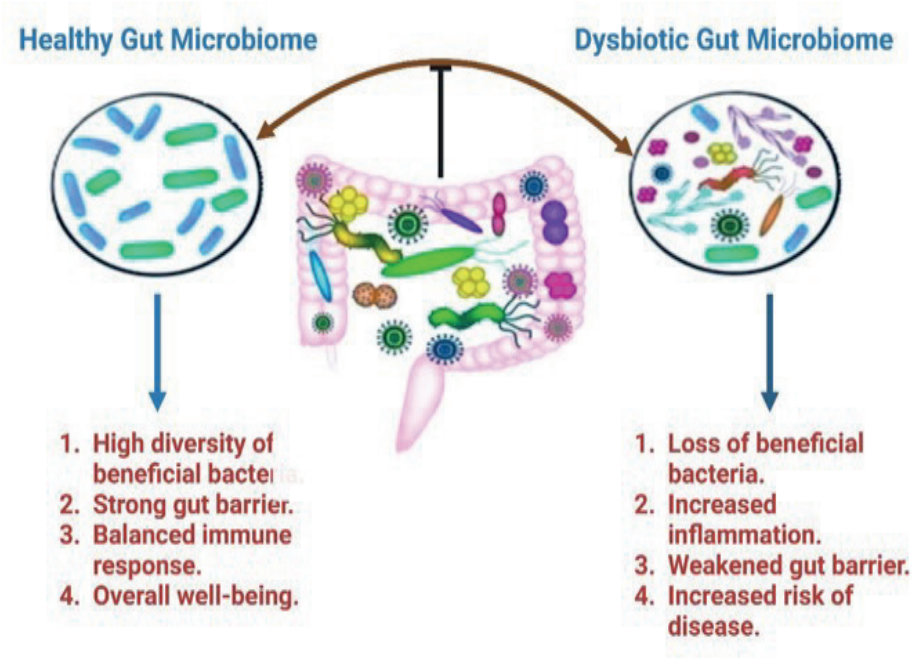


Figure 3. Microbiome Dysbiosis and Disease

Inflammation, genetics, and environment could play a role in the development of several, local, and systemic diseases that, research suggests, have a firm link to dysbiosis. Here's a look at how microbiome disruptions may factor into disease development and progression (as shown in Table 4).

4.1. Inflammatory bowel diseases (IBD): The fermentation imbalance is the nascent phenomenon of IBD, containing diseases such as Crohn's or ulcerative colitis. A consequence of interruption in the microbiome balance of the gut is the appearance of abnormal immune responses, which lead to the appearance of chronic intestinal inflammations (Pullaiah, 2016). The Imbalance in the gut microorganisms, if severe, may be among the causes of IBD and is believed to promote it.

4.2. Metabolic syndrome and Type 2 diabetes: Dysbiosis can handle energy control, insulin sensitivity, and fat handling through this mechanism, giving a reason for insulin resistance and metabolic disorders. Hosting gut microbes, in turn, affects host metabolism, reducing processed

food intake and lowering the host's body fat. The elevated probability of developing obesity and type 2 diabetes due to the emergence of these factors is one of the risks (Wu et al., 2014).

4.3. Irritable bowel syndrome (IBS): However, it is not as straightforward as in an IBD case, because dysbiosis is present but not strongly diagnosed in IBS patients. The specific gut microbial pattern that is connected to IBS has influences on abdominal pain, bloating, and changes in bowel habits symptoms (Duan et al., 2019).

4.4. Atopic diseases (Eczema, Asthma, Allergies): There are now studies that link a dysbiosis of children`s baby`s stomach flora in infancy with an increased risk of allergy, a pruritus called atopic dermatitis, and asthma. Disruption of the microbiome during the fetal period and infancy interferes with the formation of the immune system's regulatory system and leads to hyperactivity and allergies (Donald & Finlay, 2023).

4.5. Neurological and Neuropsychiatric conditions: The gut-brain axis is an active research area analyzing the complex dialogue between our gut microbiota and the brain. Disruption or imbalance in the microbiome has been demonstrated to be associated with illnesses such as Parkinson's disease and multiple sclerosis. Researchers are researching the possible influence of social networking on mental health conditions including anxiety, depression, and autism spectrum disorders(Donald & Finlay, 2023).

5. The Microbiome as a Therapeutic Target

Microbiome is more and more being respected as those microorganisms do not participate in your wellbeing only but also have a considerable influence on the development of diseases along with a wide array of other phenomena. During the last decade, microbiome research has become one of the dominating issues among scientists, which has led to its increasing popularity (Cullen et al., 2020).

Table 4: Microbiome-Associated Diseases and Potential Therapeutic Interventions

Disease	**Potential Microbiome Changes**	**Therapeutic Interventions**	**References**
Obesity	Reduced variety, higher ratio of Firmicutes to Bacteroidetes.	Diet changes, prebiotics, probiotics, FMT	(Sankararaman et al., 2023)
Inflammatory Bowel Disease (IBD)	Reduced variety, decline in helpful bacteria, rise in inflammatory microbes	Diet adjustments, prebiotics, probiotics, fecal microbiota transplantation (as studied), particular medications	(Durchschein et al., 2016)
Type 2 Diabetes	Changed biochemical routes, and decreased levels of bacteria that generate butyrate.	Dietary measures, prebiotics, probiotics (limited evidence)	(Bordalo Tonucci et al., 2017)
Irritable Bowel Syndrome (IBS)	Altered microbial composition and function	Dietary changes, probiotics	(Staudacher & Whelan, 2016)

Some of the core strategies under development and clinical investigation include: When it comes to cancer, arising from different biological origins is one of the reasons why it's incurred. Besides environmental and behavioral factors, each type of cancer is particularly caused by different gene mutations (Sankpal et al., 2012). Hence, the core strategies in development and clinical investigation in which:

5.1. Dietary interventions: It is well known that diet is more salient to the microbiome, impacting both composition and function. Although dietary modulation is thought to be a controversial

technique (as shown in Table 3) for structuring the microbiota, it is widely recommended by health professionals and nutritionists (y Abreu et al., 2021). The same diets will need to emphasize the role of fiber in plants which is meant for improving the quality of microorganisms needed for good digestion. Notwithstanding, the brew drinkers, the grains community as well and the vegetable community may find themselves fortunate to be alive as it will be possible to preserve their population, which is a healthy habit. The bad fats and excessive sugar in the blatantly processed and purified food varieties are the major contributors to weight gain and obesity (Kwan & Graves, 2013). Switching to traditional Mediterranean eating is to be seen among the most important principles of food combination with high nutritional content. Besides, this might be just a starting phase which may result in significantly improved chronic disease management longer-term.

5.2. Probiotics: Correctly processed probiotics involve the living microorganisms that are supposed to be a part of obligatory nutrition for the human body (Awaisheh, 2012). Also, if a necessary amount is not received by the human body due to improper diet, then, it affects the health in a very negative way. The following foods contain these species of Lactobacillus and Bifidobacterium of the deltaccaecithe genera of bacteria. The aim is to eliminate the microbes that cause seals and enhance the ones that support health at the same time (seen in Figure 5). In addition, a significant milestone is the use of probiotics in managing intestinal bowel syndrome (IBS) and antibiotic-associated diarrhea, (as shown in Table 4) a factor that has made such products so popular nowadays (Reque & Brandelli, 2022). Nevertheless, researchers at the same time are more and more thinking that if allergens strictly mean a particular kind of group, then people of this kind group are probably born with no ventilated disease or at all sinuses.

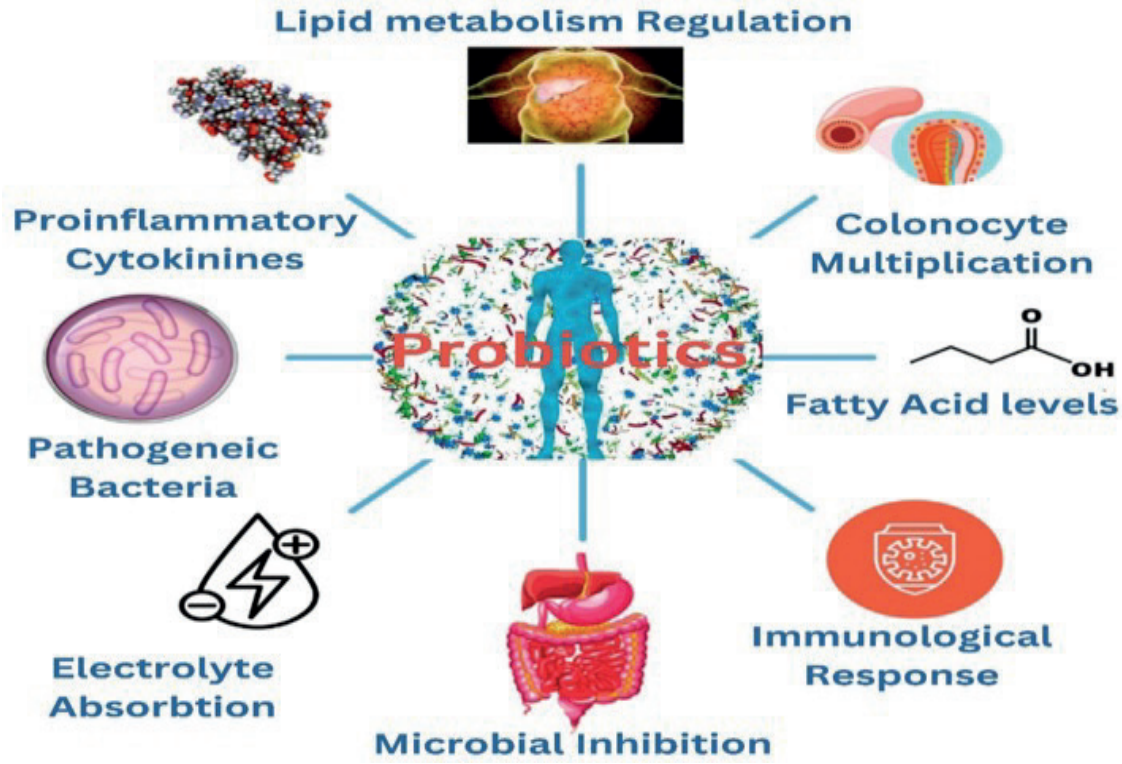


Figure 5. Probiotics

5.3. Prebiotics: These are examples of unfermentable dietary fibers (mostly resistant starches, fructans, and galactooligosaccharides) and they nourish the gut where there are good micro-organisms for the beneficial bacteria to thrive. The increase in the count of health-promoting bacteria in the intestines due to prebiotics (Lordan et al., 2020) is the main thing and with it there is an increase in their capability to carry out their objective. The dietary supplement is usually filled with inulin and Fos due to the presence of GOS (galactooligosaccharides) in daily routine (Mutanda et al., 2014). Attention will be paid precisely to the prebiotic efficacy of the co-treatment, along with

other factors. The investigators may well establish there will be a decreased incidence of diseases such as, for instance, inflammatory bowel disease or metabolic diseases.

5.4. Fecal microbiota transplantation (FMT): This technique is done by seeding the recipient with a healthy microbiome of the donor's dysbiotic gut and there are some methods through which this is done by the researcher. The objective is to gradually add some of the bacteria back and the microbial environment to get their balance back and digestion intact is what Goal is aiming for. This once-a-year Follow the Money (FMT) trial was the core evidence that the appearance of this issue cannot be underestimated and it is one of such ways to cure recurrent C. difficile. (1) The first weakness in antibiotics is (2) rising concern because of antibiotic resistance, MDR bacteria then (3) are a threat because of the emergence of multi-drug resistant bacteria. To illustrate, the antibiotic-resistant probability (MDR) is higher than the point made by the traditional drug (Tarín-Pelló et al., 2022). The other approach, as well as the Humanized Microbiota Transplantation (seen in Figure 7), is also considered to be applied to deal with diseases that are complex just as IBD, metabolic disorders, and psychological conditions subject to a lot of risk assessment and long-term safety studies.

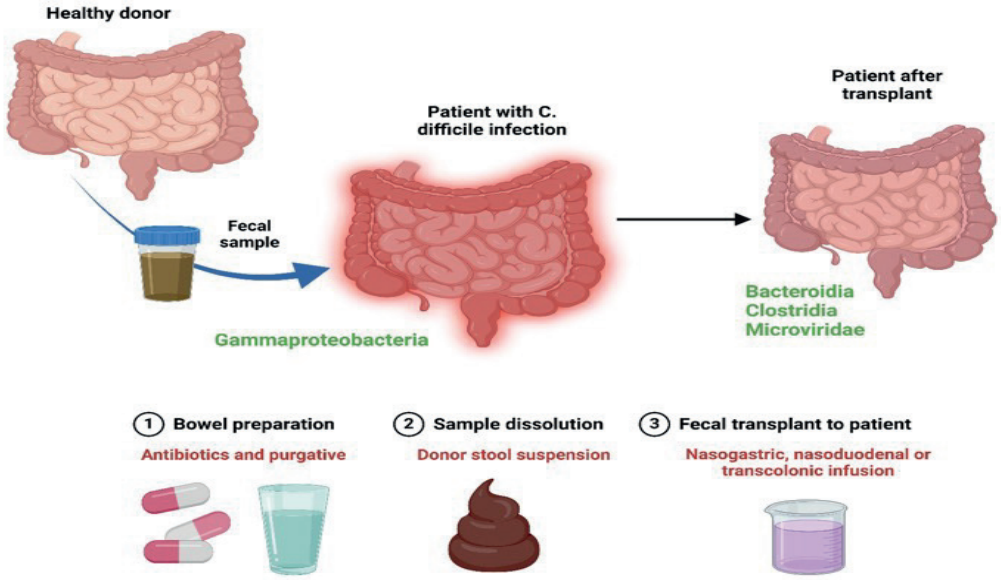


Figure 6. Fecal Microbiota Transplantation (FMT)

To boost the efficacy of our therapy, we intend to integrate dietary interventions based on prebiotics, probiotics, and fecal microbiota transplantation (FMT), as tools that are capable of dealing with this deficiency (Perillo et al., 2020). The level of the microbiome-targeted therapy is however at the initial stage of development and more research is required. A department with clinical evidence as a base should be observed as a possible route for the cure of many diseases. Still, there are some key considerations in which a certain selection of people can be quite special in some situations:

5.4.1 Specificity: Investigators cannot depend on low-grade kind of probiotics and prebiotics. They are of no effective good outcome! The microbes in some cases may carry out some tasks other than acting as antagonists. This is particularly notable when a patient already has other problematic conditions. Specifically, that is, the treatment and everyday supplementations most probably will not have an effect as required (Nieuwenhuizen et al., 2010).

5.4.2 Regulation: The governance leans toward the sovereign or national institutions, yet each country decides whether there will be governing for folic acids, prebiotics, and fecal microbial transplantation. The boundary between drugs and medication now is becoming a grey area as both

a type of medication fall into the group of supplements while the other may be used as a drug (Herzberg, 2010). In the course of this theme, it is important to ensure the tighter implementation of laws going with the advancement of these inventions from funding some market gaps to uniform medical use.

5.4.3 Individual variability: The specificity of the microbial population in the human microbial context varies thereby; the effect of the therapy on the microbial communities may vary widely from one patient to another (Mira et al., 2017). Apart from the genetic factors, eating habits and a way of life also matter much as regards determining which treatment method should be applied to the patients, who in the long run can have the outcome of becoming either well or worse. Detecting these parameters is fundamental, so it may be possible, to be accurately specialized in personalized treatments for these people.

5.4.4. Potential risks: Probiotics comprise live microorganisms, so as a general rule, they are free from side effects. However, some populations like those with reduced immunity natural or immune-suppressed due to an underlying condition can be adversely affected by probiotics. FMT has a chance of contamination and spreading unknown pathogens or microbes, which may not be beneficial and acceptable. The members of such a microbe might be harmful to the ill person (Manges et al., 2016). It can indicate the screening of donors to further prevent this situation. The unanswered questions regarding the FMT after prolonged use trials are the most dreading issue for clinicians.

6. Advancements in Microbiome Research

The microbiome research has dramatically undergone a revolution that is the outcome of improved new technologies and instruments used for diagnosis. Some key developments expanding our understanding of the microbiome include Some noteworthy findings, shedding light on the complexity of the microbiome in particular, as follows:

6.1. Large-scale cohort studies and biobanks: As of right now, a massive number of projects as the Human Microbiome Project exist that are responsible for amassing huge amounts of information about microbial diversity. This targeting of the relationship between microbiome's modifications and diseases gives mushrooms for study (Jayachandran et al., 2017). The biobanks, as tissues linked to health records, are used for the longitudinal studies which are focused on establishing exact long-term communication between microbiome and health. Big data, it is now, tells a story that is shaping the factors or identifying any possible biomarkers with a much higher outcome.

6.2. Refinement of culturomics: A thing that was a common view in this field was that not many small gut microbes were able to turn into laboratory research, and hence the prior learnings were greatly based on ‘easily grown species. The emergent technologies of complex growth media and conditions as well as isolation and studying proposals of more diverse microorganisms deliver quite profound scientific knowledge reinforcement beyond one 'culturable' microbiome (Iqbal et al., 2024). This handover lets us fill in the distance separating the level of detail that can be now well provided in the sequence proceeding and the extent of experimental exploration.

6.3. Animal models: For mice studies, researchers are the ones who set the ideal conditions that will set the condition where they get to notice the effect of the changes in the microbiome, their mechanisms, and also the effects of new medications targeting the microbiome. The sterile mice (without natural microbiota) and also have low or absent microbiome are used to uncover the effect of introducing selected bacterial species only or communities as well as to observe the effect on health and disease in a very well-controlled situation (Kostic et al., 2013). The groups noted the metagenome, metatranscriptome, and metabolomes were the new-generation techniques and technologies for microbiome research (Anandaraj et al., 2021). The field of microbiome has become more polished and with the steady evolution of an accurate and precise set of research

tools a great tool for future research is created. Here's a look at some key techniques in which:

6.3.1. Metagenomics: The process of obtaining DNA from microbial populations is based on addressing the microbiome and then using direct sequencing. This viable strategy is not similar to just all the bacteria, viruses, and microbes, but forms a complete picture of the microbes forming into communities and containing their diversity. The researchers investigate whether there is a certain species or simply provide the data to know the number and their genes as they may be antibiotic resistant or the generation of vital metabolic functions (Crofts et al., 2017). The snapshot of genetic talents is preserved among different organisms that make up the metagenome.

6.4.2. Metatranscriptomics: In contrast, synchronous instruction, especially for massively open online courses (MOOCs), has increasingly become necessary to keep student engagement. The collection of the gene expression profiles and then the presence of certain microbes is ensured in addition to their genes that are active at a given period as well as what their function and activity are concerned (Franzosa et al., 2014).

6.4.3. Metabolomics: Gut microbial activity analyzing the small molecules that are produced by the microbes will be the direct evidence of the microbial species' capability functional activities as well the indication of how the microbes interact with each other. Metabolome can be used to determine the effective molecules and these are either supportive of breeding farm animal health or they have elevated susceptibility to the animals getting the disease (Sun et al., 2019). One as a caveat, the translation the metabolites can reach and the creation of the chemical language and to assess how it affects physiology is possible.

7. Future Directions

The narrow Transition that the microbiome research field is facing is however very purposeful because it holds a huge promise. Here are some key areas likely to see significant advancements in the coming years. The following are the prominent fields in which:

7.1. Precision Medicine: Integrating microbiome analysis into the person’s health tracker, genetic weaknesses, and lifestyle factors is a main element that may be employed to implement microbiome-concentrated adjustments. It can be the case that not only do the dietary recommendations need tailoring but also the choice of such probiotics or even the FMT is the treatment key to enhancing results while reducing side effects (Scott et al., 2015).

7.2. Expanding beyond the gut: The attention is on the gut microbiome which has been widely explored. Nonetheless, the field is increasingly diversifying to the other domains of the body such as the skin, the airways, and the mouth. These microbial options may well be identified through tamponade therapy, skin disorders including eczema and prostatitis, and even lung diseases, which could help in the future developments of newer medical standards (EDITION, 2013).

7.3. Novel therapeutic targets: Highlighting the mysterious ways microbiota converses with our human body in an interconnected system, hope may arise to improve the therapeutic prospects of future medicine. This approach could involve the substantially complex production of probiotics or prebiotics which are intelligently designed to work with metabolic pathways, reducing inflammation or strengthening the immune system, which is necessary for multiple health issues (Kouhounde et al., 2022).

7.4. Bioengineered microbes: Synthetic biology as an entirely new space allows one to create these microorganisms which may be purely designed following the specific needs of the environment. Such genetically modified microbes could be administered to a patient's body directly to allow them to produce an intragastrical medication that could carry the medication, neutralize any potential metabolic products, or even improve the potency of the current medication.

7.5. Addressing regulatory challenges: The hyper-accumulative dynamics of immunotherapies development require the governmental and scientific communities to hold a conversation on the governing rules and regulations to ensure the patient safety and effectiveness of these novel treatments (Garg et al., 2022). Consequently, the standards, which protect patients from being victimized and, in addition, guarantee the proper and ethically sound application of microbiology in practice will be developed.

8. Conclusion

The human Microbiome, the microorganisms that inhabit our bodies are sometimes less known, is a very huge, quite still unknown ecosystem, with a large number of them firmly connected to our health and well-being. Microbiome research is a place of the child of a new exploration on the creating agency are recruiting significance of microbes in the general physiological procedures and their susceptibility to various diseases. Making future drugs of the top-notch kind by reprogramming the bacterial gut for health-benefiting purposes is an excellent prospect for medicine development. Rather than facing up to the problem with such a narrow array of weapons, the opening of microbiome-based interventions to the public is a continuous process at the early stage. Such therapy is a type of very promising treatment with an extensive patient population who otherwise will have to take the old-style therapies which are very conservative.

References

Afzaal, M., Saeed, F., Shah, Y. A., Hussain, M., Rabail, R., Socol, C. T., Hassoun, A., Pateiro, M., Lorenzo, J. M., & Rusu, A. V. (2022). Human gut microbiota in health and disease: Unveiling the relationship. Frontiers in microbiology, 13, 999001.

Anandaraj, M., Manivannan, S., & Umadevi, P. (2021). Rhizosphere Microbiome: The Next-Generation Crop Improvement Strategy. Environmental and Agricultural Microbiology: Applications for Sustainability, 243-256.

Awaisheh, S. S. (2012). Probiotic food products classes, types, and processing. In Probiotics. Intechopen.

Blaak, E., Canfora, E., Theis, S., Frost, G., Groen, A., Mithieux, G., Nauta, A., Scott, K., Stahl, B., & Van Harsselaar, J. (2020). Short chain fatty acids in human gut and metabolic health. Beneficial microbes, 11(5), 411-455.

Bolan, S. S. (2019). GUT MICROBES–HEAVY METAL (LOID) INTERACTIONS.

Bordalo Tonucci, L., Dos Santos, K. M. O., De Luces Fortes Ferreira, C. L., Ribeiro, S. M. R., De Oliveira, L. L., & Martino, H. S. D. (2017). Gut microbiota and probiotics: Focus on diabetes mellitus. Critical reviews in food science and nutrition, 57(11), 2296-2309.

Ceballos, D., Hernández-Camba, A., & Ramos, L. (2021). Diet and microbiome in the beginning of the sequence of gut inflammation. World Journal of Clinical Cases, 9(36), 11122.

Coleman, D. C., & Whitman, W. B. (2005). Linking species richness, biodiversity and ecosystem function in soil systems. Pedobiologia, 49(6), 479-497.

Crofts, T. S., Gasparrini, A. J., & Dantas, G. (2017). Next-generation approaches to understand and combat the antibiotic resistome. Nature Reviews Microbiology, 15(7), 422-434.

Cullen, C. M., Aneja, K. K., Beyhan, S., Cho, C. E., Woloszynek, S., Convertino, M., McCoy, S. J., Zhang, Y., Anderson, M. Z., & Alvarez-Ponce, D. (2020). Emerging priorities for microbiome research. Frontiers in microbiology, 11, 491374.

DE GIANI, A. (2022). Impact of prebiotics and probiotics on gut microbiota and human health.

Donald, K., & Finlay, B. B. (2023). Early-life interactions between the microbiota and immune system: impact on immune system development and atopic disease. Nature Reviews Immunology, 23(11), 735-748.

Dou, J., Zeng, J., Wu, K., Tan, W., Gao, L., & Lu, J. (2019). Microbiosis in pathogenesis and intervention of atopic dermatitis. International Immunopharmacology, 69, 263-269.

Durchschein, F., Petritsch, W., & Hammer, H. F. (2016). Diet therapy for inflammatory bowel diseases: The established and the new. World Journal of Gastroenterology, 22(7), 2179.

EDITION, F. (2013). Standard Treatment Guidelines and Essential Medicines List.

Fletcher, S. (2015). Understanding the contribution of environmental factors in the spread of antimicrobial resistance. Environmental health and preventive medicine, 20, 243-252.

Franzosa, E. A., Morgan, X. C., Segata, N., Waldron, L., Reyes, J., Earl, A. M., Giannoukos, G., Boylan, M. R., Ciulla, D., & Gevers, D. (2014). Relating the metatranscriptome and metagenome of the human gut. Proceedings of the National Academy of Sciences, 111(22), E2329-E2338.

Fujimoto, M. (2012). Microbial succession on the lake sturgeon egg surface: Mechanisms shaping the microbial community assembly during succession and the effect of microbial successional processes on host life history traits. Michigan State University. Microbiology and Molecular Genetics Ecology ….

García-Serna, A. M., Martín-Orozco, E., Hernández-Caselles, T., & Morales, E. (2021). Prenatal and perinatal environmental influences shaping the neonatal immune system: a focus on asthma and allergy origins. International Journal of Environmental Research and Public Health, 18(8), 3962.

Garg, R., Garg, R., & Eddy, N. O. (2022). Handbook of research on green synthesis and applications of nanomaterials. IGI Global.

Gebrayel, P., Nicco, C., Al Khodor, S., Bilinski, J., Caselli, E., Comelli, E. M., Egert, M., Giaroni, C., Karpinski, T. M., & Loniewski, I. (2022). Microbiota medicine: towards clinical revolution. Journal of translational medicine, 20(1), 111.

Gültekin, F., Akın, S., İzler, K., & Kalkanlı, S. (2021). The Key to Strong Immunity: Lifestyle. Academic Platform Journal of Halal Lifestyle, 3(2), 90-107.

Herzberg, D. (2010). Happy pills in America: from Miltown to Prozac. JHU Press.

Hillman, E. T., Lu, H., Yao, T., & Nakatsu, C. H. (2017). Microbial ecology along the gastrointestinal tract. Microbes and environments, 32(4), 300-313.

Iqbal, S., Begum, F., Ullah, I., Jalal, N., & Shaw, P. (2024). Peeling off the layers from microbial dark matter (MDM): recent advances, future challenges, and opportunities. Critical Reviews in Microbiology, 1-21.

Jayachandran, M., Xiao, J., & Xu, B. (2017). A critical review on health promoting benefits of edible mushrooms through gut microbiota. International journal of molecular sciences, 18(9), 1934.

Kostic, A. D., Howitt, M. R., & Garrett, W. S. (2013). Exploring host–microbiota interactions in animal models and humans. Genes & development, 27(7), 701-718.

Kouhounde, S., Adéoti, K., Mounir, M., Giusti, A., Refinetti, P., Otu, A., Effa, E., Ebenso, B., Adetimirin, V. O., & Barceló, J. M. (2022). Applications of probiotic-based multi-components to human, animal and ecosystem health: concepts, methodologies, and action mechanisms. Microorganisms, 10(9), 1700.

Kumbhare, S. V., Patangia, D. V., Patil, R. H., Shouche, Y. S., & Patil, N. P. (2019). Factors influencing the gut microbiome in children: from infancy to childhood. Journal of biosciences, 44, 1-19.

Kwan, S., & Graves, J. (2013). Framing fat: Competing constructions in contemporary culture. Rutgers University Press.

LeBlanc, J. G., Chain, F., Martín, R., Bermúdez-Humarán, L. G., Courau, S., & Langella, P. (2017). Beneficial effects on host energy metabolism of short-chain fatty acids and vitamins produced by commensal and probiotic bacteria. Microbial cell factories, 16, 1-10.

Leeming, E. R., Johnson, A. J., Spector, T. D., & Le Roy, C. I. (2019). Effect of diet on the gut microbiota: rethinking intervention duration. Nutrients, 11(12), 2862.

Lordan, C., Thapa, D., Ross, R. P., & Cotter, P. D. (2020). Potential for enriching next-generation health-promoting gut bacteria through prebiotics and other dietary components. Gut microbes, 11(1), 1-20.

Manges, A. R., Steiner, T. S., & Wright, A. J. (2016). Fecal microbiota transplantation for the intestinal decolonization of extensively antimicrobial-resistant opportunistic pathogens: a review. Infectious Diseases, 48(8), 587-592.

Matter, W. M. (2019). The Development of the Human Microbiome. The microbiome: Interactions with organ systems, diet, and genetics, An Issue of Gastroenterology Clinics of North America, Ebook, 357.

McLaren, M. R., & Callahan, B. J. (2020). Pathogen resistance may be the principal evolutionary advantage provided by the microbiome. Philosophical Transactions of the Royal Society B, 375(1808), 20190592.

Mira, A., Simon-Soro, A., & Curtis, M. (2017). Role of microbial communities in the pathogenesis of periodontal diseases and caries. Journal of clinical periodontology, 44, S23-S38.

Mocanu, V. (2021). Harnessing Gut Microbial Modulation in Chronic Inflammatory Gastrointestinal Disease.

Mutanda, T., Mokoena, M., Olaniran, A., Wilhelmi, B., & Whiteley, C. (2014). Microbial enzymatic production and applications of short-chain fructooligosaccharides and inulooligosaccharides: recent advances and current perspectives. Journal of Industrial Microbiology and Biotechnology, 41(6), 893-906.

Nieuwenhuizen, W. F., Weenen, H., Rigby, P., & Hetherington, M. M. (2010). Older adults and patients in need of nutritional support: review of current treatment options and factors influencing nutritional intake. Clinical nutrition, 29(2), 160-169.

Perillo, F., Amoroso, C., Strati, F., Giuffrè, M. R., Díaz-Basabe, A., Lattanzi, G., & Facciotti, F. (2020). Gut microbiota manipulation as a tool for colorectal cancer management: recent advances in its use for therapeutic purposes. International journal of molecular sciences, 21(15), 5389.

Portincasa, P., Bonfrate, L., Vacca, M., De Angelis, M., Farella, I., Lanza, E., Khalil, M., Wang, D. Q.-H., Sperandio, M., & Di Ciaula, A. (2022). Gut microbiota and short chain fatty acids: implications in glucose homeostasis. International journal of molecular sciences, 23(3), 1105.

Potrykus, M., Czaja-Stolc, S., Stankiewicz, M., Kaska, Ł., & Małgorzewicz, S. (2021). Intestinal microbiota as a contributor to chronic inflammation and its potential modifications. Nutrients, 13(11), 3839.

Pullaiah, T. (2016). Biotechnological approaches for sustainable development. Regency

Publications, New Delhi.

Renz, H., & Skevaki, C. (2021). Early life microbial exposures and allergy risks: opportunities for prevention. Nature Reviews Immunology, 21(3), 177-191.

Reque, P. M., & Brandelli, A. (2022). An introduction to probiotics. In Probiotics (pp. 1-17). Elsevier.

Rinninella, E., Cintoni, M., Raoul, P., Lopetuso, L. R., Scaldaferri, F., Pulcini, G., Miggiano, G. A. D., Gasbarrini, A., & Mele, M. C. (2019). Food components and dietary habits: keys for a healthy gut microbiota composition. Nutrients, 11(10), 2393.

Rinninella, E., Raoul, P., Cintoni, M., Franceschi, F., Miggiano, G. A. D., Gasbarrini, A., & Mele, M. C. (2019). What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. Microorganisms, 7(1), 14.

Salvucci, E. (2019). The human-microbiome superorganism and its modulation to restore health. International journal of food sciences and nutrition, 70(7), 781-795.

Sankararaman, S., Noriega, K., Velayuthan, S., Sferra, T., & Martindale, R. (2023). Gut microbiome and its impact on obesity and obesity-related disorders. Current gastroenterology reports, 25(2), 31-44.

Sankpal, U. T., Pius, H., Khan, M., Shukoor, M. I., Maliakal, P., Lee, C. M., Abdelrahim, M., Connelly, S. F., & Basha, R. (2012). Environmental factors in causing human cancers: emphasis on tumorigenesis. Tumor Biology, 33, 1265-1274.

Scott, K. P., Jean-Michel, A., Midtvedt, T., & van Hemert, S. (2015). Manipulating the gut microbiota to maintain health and treat disease. Microbial ecology in health and disease, 26(1), 25877.

Shao, T., Verma, H. K., Pande, B., Costanzo, V., Ye, W., Cai, Y., & Bhaskar, L. (2021). Physical activity and nutritional influence on immune function: an important strategy to improve immunity and health status. Frontiers in physiology, 12, 751374.

Shima, K., Coopmeiners, J., Graspeuntner, S., Dalhoff, K., & Rupp, J. (2016). Impact of micro-environmental changes on respiratory tract infections with intracellular bacteria. FEBS letters, 590(21), 3887-3904.

Staudacher, H. M., & Whelan, K. (2016). Altered gastrointestinal microbiota in irritable bowel syndrome and its modification by diet: probiotics, prebiotics and the low FODMAP diet. Proceedings of the Nutrition Society, 75(3), 306-318.

Sun, H., Plastow, G., & Guan, L. (2019). Invited review: Advances and challenges in application of feedomics to improve dairy cow production and health. Journal of Dairy Science, 102(7), 5853-5870.

Tarín-Pelló, A., Suay-García, B., & Pérez-Gracia, M.-T. (2022). Antibiotic resistant bacteria: current situation and treatment options to accelerate the development of a new antimicrobial arsenal. Expert Review of Anti-infective Therapy, 20(8), 1095-1108.

Wade, W. G. (2013). The oral microbiome in health and disease. Pharmacological research, 69(1), 137-143.

Wu, Y., Ding, Y., Tanaka, Y., & Zhang, W. (2014). Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. International journal of medical sciences, 11(11), 1185.

y Abreu, A. A., Milke-García, M., Argüello-Arévalo, G., Calderón-de la Barca, A., Carmona-Sánchez, R., Consuelo-Sánchez, A., Coss-Adame, E., García-Cedillo, M., Hernández-Rosiles, V., & Icaza-Chávez, M. (2021). Dietary fiber and the microbiota: A narrative review by a group of experts from the Asociación Mexicana de Gastroenterología. Revista de Gastroenterología de México (English Edition), 86(3), 287-304.

Zafar, H., & Saier Jr, M. H. (2021). Gut Bacteroides species in health and disease. Gut microbes, 13(1), 1848158.

Zhang, Y.-J., Li, S., Gan, R.-Y., Zhou, T., Xu, D.-P., & Li, H.-B. (2015). Impacts of gut bacteria on human health and diseases. International journal of molecular sciences, 16(4), 7493-7519.

About The Authors

Arifa Mehreen is an Assistant Professor of Zoology at the University of Agriculture Faisalabad (UAF). Her research focuses on the antimicrobial properties of natural products, drug formulation and pharmacokinetics, and characterization of bacterial pathogens. She has studied the antimicrobial and toxicological effects of Origanum vulgare, developed a fixed-dose combination drug for cardiovascular disease, and investigated the characteristics of Staphylococcus aureus strains.

E-mail: arifa.mehreen@uaf.edu.pk ORCID: 0000-0001-5899-8027

Dr Qurat-ul-Ane Gillani is an Assistant Professor of Zoology at Women's University Multan. Her research primarily focuses on the effects of various substances on animal physiology and behavior, particularly in mice. She has investigated the impact of nickel chloride on fish, plant extracts on mice, and the neurological mechanisms of COVID-19. Additionally, her work has explored the role of GABAB receptor antagonists on behavior, hematology, and biochemistry in mice models, sometimes with a focus on neonatal brain damage. She has also researched detecting blood parasites in cattle.

E-mail: anneegillani@wum.edu.pk ORCID: 0000-0002-1068-4472

Ayesha Bintay Farooq is a researcher in the Department of Physiology, Life Sciences, at Government College University Faisalabad, Pakistan. Her primary research interests lie in the field of neuroscience, with a particular focus on neuroimaging. Ayesha is dedicated to exploring the intricacies of brain function and structure through advanced imaging techniques. Her work aims to enhance the understanding of neural processes and contribute valuable insights to the field of neuroscience.

Email: ayeshabintyfarooq@gcuf.edu.pk ORCID: 0009-0003-7009-222X

Maria Nazir is an MPhil Scholar of Microbiology at the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur, Pakistan. She is involved in a National Research Program for Universities (NRPU) Project, with research interests in Molecular Characterization. She has submitted abstracts to various conferences and authored and coauthored of several book chapters. Her research focuses on the isolation and Molecular characterization of Corynebacterium pseudotuberculosis and their applications in promoting animal health. Her interested research criteria are based on genetics, molecular biology, and bioinformatics.

Email: nazirmaria545@gmail.com ORCID 0009-0004-6714-6212

Dr. Rumaisa Nawal received her MBBS degree in 2024 from Multan Medical and dental college. She is a house officer in Bhawal Victoria Hospital, Pakistan. She has done internship program at District Headquarters Lodhran.

Email: rumaisanawal9@gmail.com ORCID:0009-0000-1903-8365

Minal Hussain graduated from Cholistan University of Veterinary and Animal Sciences in Bahawalpur Pakistan. He continues his postgraduate study in Microbiology from Cholistan University of Veterinary and Animal Sciences Bahawalpur. Her research interest is in Bacteriophages, Bacteriology, Molecular cell biology, and Microbial genetics etc. She has published few book chapters in international journals.

Email: 2019-cu-bios-023@cuvas.edu.pk ORCID: 0009-0004-0143-5644

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as “Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone”. His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

Dr. Muhammad SAFDAR earned his PhD in Molecular Biology and Genetics from Gaziantep University, Turkey. He is Lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 70 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

E-mail: msafdar@cuvas.edu.pk ORCID: 0000 0002 3720 2090

To Cite This Chapter

MEHREEN A et al., (2024). Investigating the role of the microbiome in health and disease. In Current Studies in Health and Life Sciences 2024 (pp.180-194). ISRES Publishing.

Breaking Barriers: Advancements in Genomic Research and CRISPR Technology

Maria NAZIR

Tasawar ABBAS

Maham SHAHZADI

Shafeeq ur REHMAN

Muhammad EJAZ

Muhammad SAFDAR

1. Introduction

Genetics is the key to Uncovering the mysteries and putting life through the constant search for hiding points there is the deciphering the mystery of human health and illness and a transition to the envoy of the agricultural and genome technology, the world has stepped into the age of discoveries unparalleled. CRISPR, gene-editing application, as its technology has been created, revolutionized the modern science sphere to give us the necessary tools that allow us to accurately and competently make adjustments and changes in the gene regions. This chapter explores the origin of genetics research and the offshoots of CRISPR technology (as shown in Figure 1) stemming from historical background, which made it possible to reach the modern state of acceptable knowledge currently introduced as a breakthrough in one of the diverse research areas like genetics, medicine, and even human nature transformation. It can be deduced that the presence of modern genomics would not have been possible without the results of the 19th century conducts of Gregor Mendel, who discovered the patterns of inheritance of peas plants and captured the concept of genes for the first time (Mendel, 1866). The 20th century witnessed significant breakthroughs: its spiral shape, the genetic code's functionality, and genes' transportation as a means (Aldridge, 1996). Genomics reached a high level of achievement when a worldwide research project known as The Human Genome Project was launched in 2003. This project determined the full sequence of the genome, (as shown in Table 1) which is referred to as the beginning of the genomic era (Hood & Rowen, 2013). Nevertheless, those developments are moving in countries that are far distant, but earlier, a low-profile mechanism of gene editing that is peculiar to gram-positive bacteria will later have an incredible impact on gene control in organisms. The CRISPR-Cas feature is a genomic structure found in the bacteria and archaeal domain, that works in the same way that immunity does against viruses. The science community and those working in scientific research, including people like Jennifer Doudna and Emmanuelle Charpentier, have recently unveiled a potential tool known as CRISPR-Cas9 that has the programming ability (Doudna & Charpentier, 2014).

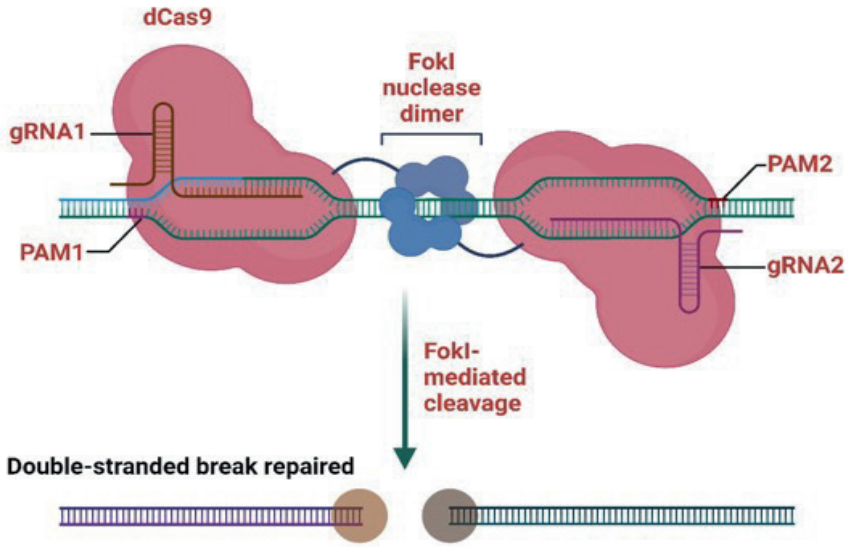


Figure 1. Overview of CRISPR Technology

Indisputably, the urgency of grasping the role of CRISPR at the base or 'genomic level, is not an exaggeration. The evolution, in DNA sequencing methods, now allows scientists to read the biological code of organisms and discover those letters' corresponding sequences, which are the A, C, T, G (Kchouk et al., 2017). Through the application of genome mapping and annotation processes that identify essential genes, regulatory elements, and those that might be related to certain health problems, the raw genetic data is interfaced with a functional interpretation. The CRISPR works like a pair of DNA scissors, with a sharp-bladed tool that is capable to slit the desired place in the DNA chain. An introduced Cas9 protein along with a guide, that is modifiable, creates a cut at the exact place of the targeted mutation (Ceasar et al., 2016). This editing has far-reaching potential: the particular gene, a mutation, or a disease-causing insertion of some kind. The gene editing efficiency has been improved, and the capacity for customization has opened the floodgates for novel research projects due to its easy handling and adaptability.

The level of the perfunctory development of the subjects of genetics science raises difficulties which can be the people set for experimentation. The emergence of next-generation sequencing provides the perspective of whole population-scale studies, which uncovers genetic risk in complex disease or evolutionary mechanisms that were overshadowed through only species' relationships. The production of agricultural inputs by CRISPR is anything but minor, which results in higher yield, more resilience, and a better quality crop (Buzdin et al., 2021). It is the advanced gene editing technologies that can be exemplified as a possible solution to how the approach to treating genetic disorders can be modified. Using cancer, leukemia, or blindness of a gene origin, these gene changes can be able to be taken care of easily. One of the illustrations provided by the world movement effort led by Yin and his team is environmental degradation, which they argue is caused by anthropogenic activities (Cantelon & Letters, 2000). On the contrary, genome studies and CRISPR-Cas9 technology, as with any other of the developments, hold its own, as well as several, mentionable drawbacks and limitations too. In addition to off-target effects, there remains a high risk of introducing new mutations when modifications are made outside of the precise locus, and only a few genome sites are expected to be immune to these adverse changes. Another issue that

remains practically unresolved is the development of safe and effective routes of specific cell and tissue targeting, which is an important area to concentrate on presently (Das et al., 2009). The ethics of germline editing (editing carried in inheritance) shows that the opinions of the society have to be well-monitored with the consenting process (Jorqui-Azofra, 2020).

For various people, many opportunities for the future are seen in the fact that genomics and CRISPR technology are of important areas of progress. The goal is in the area of capturing changes in the technology which will get the precision in higher and efficiency in productivity to work with gene editing (Rees & Liu, 2018). Genome data analysis can potentially be minimized because the intersection of AI and machine learning can crack the way of research. This chapter, which will start with a deep investigation of genome research progress, covers the case of how CRISPR techniques revolutionized the scientific discipline through the multidisciplinary approach and concludes with the history of controversies and ethical dilemmas provoked by the development will be an instructing trip. Get yourself ready and click on the button to start the revolution in your mind to search for the truth and the best method to uncover the mystery of its course.

2. Historical Context

In the present case, it is a story that goes through thousands of years and that has extremely deep and elaborate roots talking about an understanding of how inheritance and fundamental laws of passed-on traits operate throughout generations (as shown in Table 1). The key contribution of Gregor Mendel, who thoroughly explored the physiological problem of pea plants during the time, was the birth of modern genetics (Smýkal et al., 2016). Here he comes to recall how the heredity pattern for plants was described which eventually established the concept of gene as the discrete entity or agent (Mendel, 1866). Nonetheless, the true genre that family mysteries would belong to was hidden, only to be uncovered after the generations. The 20th century was a progressive scientific discovery realization engine chain that gave the genetic base that is determinant to success. The year 1953 was the framework for the science which was laid down by Watson and Crick when they disclosed the structure of DNA, and how the fundamentals of genetics were double- (Watson & Crick, 1953) (Borus, 2020). These years ahead are seeing how DNA code is broken into single amino acids so that it can be understood how they are ordered by signaling codes to manufacture cells. The beginning of the 1970s has brought scientists the most dramatic change ever with the help of recombinant DNA technology, which allows them to split and edit genes (Khalil, 2020). At this point, the application of genetic engineering to the human has become feasible.

Table 1: Milestones in Genomics and CRISPR Research

Year	Milestone	Significance	Reference
1866	Gregor Mendel's laws of inheritance	Foundation for genetics	(El-Hani, 2015)
1953	Discovery of DNA's double helix structure	Understanding the molecular basis of heredity	(Franklin & Franklin)
1977	Sanger sequencing developed	initial technique used to identify the sequence of nucleotides in DNA.	(Early, 1987)
1983	Invention of polymerase chain reaction (PCR)	amplifying DNA to analyze and manipulate it.	(Ahmed & Khosa, 2010)
1990	Launch of the Human Genome Project	International effort to sequence the entire human genome	(Naidoo et al., 2011)
2003	Completion of the Human Genome Project	Reference sequence aids in comprehending human genetics and disease.	(Moraes & Góes, 2016)

Year	Milestone	Significance	Reference
2005	Emergence of next-generation sequencing (NGS)	quicker, more affordable DNA sequencing, transforming genomic research.	(Sage, 2005)
2012	Discovery of the CRISPR-Cas9 system	ground-breaking genome editing tool with the ability to revolutionize medicine, agriculture, and biotechnology.	(Kaur et al., 2021)
2015	First clinical trial of CRISPR-Cas9 for cancer treatment	CRISPR-Cas9 shows promise in treating genetic illnesses and cancer.	(Ratan et al., 2018)
2018	Birth of first CRISPR-edited babies	Ethical concerns arise about the use of gene editing in humans.	(Doxzen & Halpern, 2020)

When the initial steps of the Human Genome Project were taken everything was in the process of registering with the general public. The international Consortium that was launched to directly target the sequence of the Human Genome and achieved the first Human Genome Sequencing from 1990 to 2003 is now representative of the Human Genome sequencing milestone (Naidoo et al., 2011). This revered feat had a two-faceted outcome: it not only enabled us to have a broad overview of our genes but it also unlocked a new and unstudied road to realizing the way our genes, environment, and genetic makeup converge. The Human Genome Project was notable for being the catalyst for a wide range of the most significant genetic engineering innovations which meant, among other things, that the cost of DNA sequencing equipment had gone down to be a hundred more times cheaper than it used to be while the speed rate had gone up accordingly. The gradual discovery of the CRISPR-Cas systems started in the 1980s when more microbiologists attempted to find an undisturbed territory (which was not in their maps at that time) (Wess, 2023). It is the fact that only the bacterial genomes were highlighted as the supposed carriers of these mysterious, repetitive sequences while the bilateral eukaryotes were not that instigated the scientists to have a paradigm shift, thus attributing the elusive sequence to the host cell's mode of protection against viral attack (Loverdos et al., 2019). While CAS system exploration still was ongoing and it was assumed that the viral DNA fragments were crucial to the functioning of the CAS system, in later research conducted in 2015, it was shown that bacteria were able to take in pieces of the virus' genomic information and as a result, to integrate the information into their own CAS gene segments. Then the parts serve as role models for RNA molecules, on which the Cas proteins operate and recall the same program to cut off a similar virus if it returns. This laid the foundation for the consequential discovery of the CRISPR-Cas9 systems that was disheveled by the work of Jennifer Doudna, Emmanuelle Charpentier, and others who exposed the true pathway of the CRISPR-Cas9. They showed that the system was able to be re-strategized to target and snip down not only viral DNA sequences but also the surrounding DNA passing onto the cells which in turn is being used to detect the genetic markers of the disease (Mugo, 2013). The wonder and hype about CRISPR were a consequence of its utility, flexibility, and inspiring breadth, the fact that it was the DNA-cutting technology that gave rise to the new “genetic engineering” era (Rademan, 2020).

3. Fundamentals of Genomics

Whole genomics is a combination of reading the code sequence of any living organisms, either mammal or plant, and the revealed sequences are a combination of A, C, G, and T basis. Despite the Human Genome Project's first phase producing tremendous technological advancements in the form of whole-genome sequencing, the latter years saw an even greater development of this sphere of research (as shown in Table 2). Initially, those early techniques were painstaking and less cost-effective for both of us. Novel techs of genomics have radically changed the face of the discipline. It is NGS (novel-gene sequencing) that makes a great contribution to this change. The history of their invention witnessed several genomic changes that led to thorough sequencing and

identification of genomic variation. NGS platforms precisely achieve high speed and high-throughput technology as those machines can read thousands or even millions of small DNA elements in every single research work (Satam et al., 2023). This, prospectively, drastically spiked the throughput thus cutting dollar investment and speeding up genomic research (as shown in Figure 2).

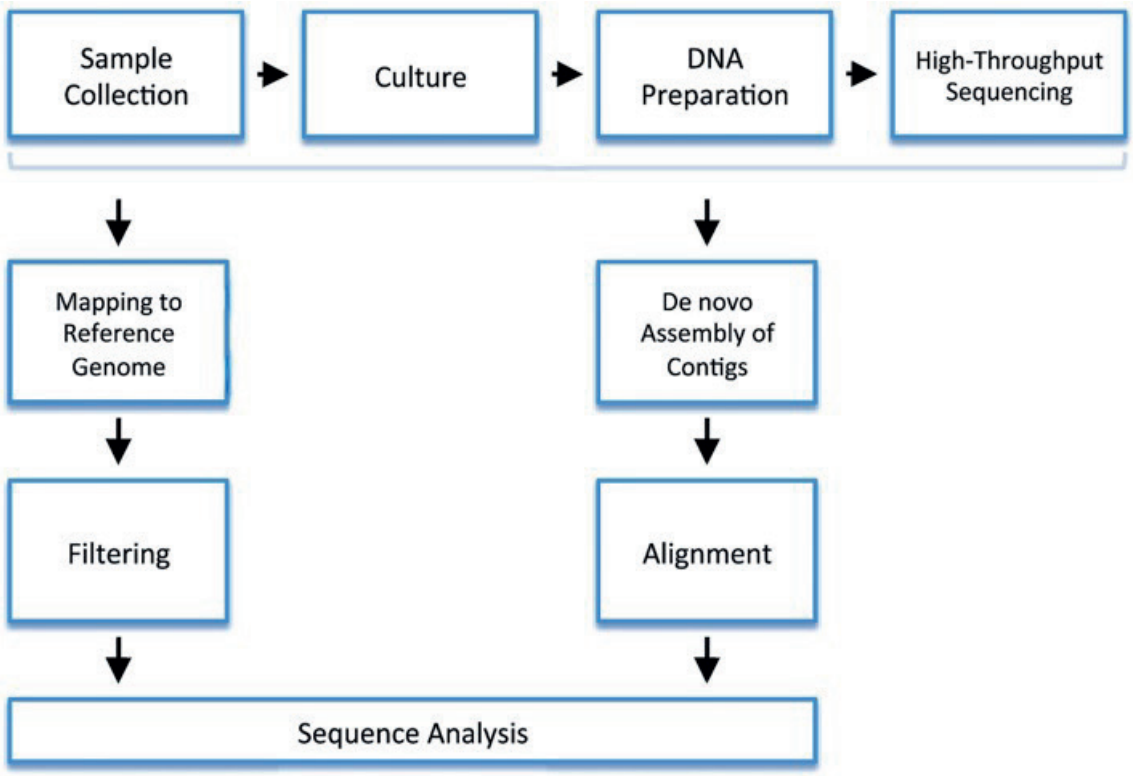


Figure 2. Genomic Sequencing Workflow

It is the case that what we have at hand today is not only based on the fact that new sequencing technologies are more advanced than those that preceded them, but they also can evolve higher than them. Since advanced next-gene sequencing technologies which directly observe the DNA and not only a few nucleotides at a time allow the detection of severe structural variations in the genome and resolving repetitive regions at a higher resolution, the authors (Rius et al., 2015) propose a relatively new approach to this problem. These developments expand the vistas of genomics and thus are adopted in science to make it more applicable. The following is to consider which of the sequencing methods we will use to read it. Genomics will learn aligning and snapshotting the genome. Short reads of the DNA are analyzed by computational analysis of the nucleotide sequence, to help reveal and uncover the order of the sequence in de novo assembly. Analysis of high-quality bioinformatics software is the key factor in the whole process, however, as it deals with massive quantities of data and finds the interested regions faster than people can (Luo et al., 2016).

Table 2: Comparison of Sequencing Technologies.

Disease	**Potential Microbiome Changes**	**Therapeutic Interventions**	**References**
Obesity	Reduced variety, higher ratio of Firmicutes to Bacteroidetes.	Diet changes, prebiotics, probiotics, FMT	(Sankararaman et al., 2023)
Inflammatory Bowel Disease (IBD)	Reduced variety, decline in helpful bacteria, rise in inflammatory microbes	Diet adjustments, prebiotics, probiotics, fecal microbiota transplantation (as studied), particular medications	(Durchschein et al., 2016)

Disease	Potential Microbiome Changes	Therapeutic Interventions	References
Type 2 Diabetes	Changed biochemical routes, and decreased levels of bacteria that generate butyrate.	Dietary measures, prebiotics, probiotics (limited evidence)	(Bordalo Tonucci et al., 2017)
Irritable Bowel Syndrome (IBS)	Altered microbial composition and function	Dietary changes, probiotics	(Staudacher & Whelan, 2016)

In this stage, the functional activities observed are at the low level but it is just the starting point. Annotation of genes is a procedure of identifying, or in other words, deciphering the message in the base sequence of the genome. It implies the process of determining the DNA segments that are the building materials of heredity, including the regulatory elements that control if a gene can be turned on or off. Correspondingly, the arrangement of the genome vs. well-known sequences in databases and the algorithmic models used are also of great importance here, since such models help to predict the character of a genome as well (Stanke et al., 2006). The additional benefit of sequencing is that we can spot different patterns where the number of nucleotides is not equal to the standard number, such as single nucleotide polymorphisms (SNPs) that contribute to some traits and disease-resistance or response to drugs. Genomics studies are those where the DNA coding sequence is examined and this information is historically composed. Human genome development rendered possible by sequence accuracy and interpretation of DNA sequences effectively creates a new perspective molecule that is a tool of research in most biological disciplines. The technologies offer a superficial analysis of gene expression and regulation, pattern of inheritance, and influence of environment, and also reveal the markers that are the fingerprint of the disease and which would be utilized in the development of small-scale therapies (Sharma et al., 2020).

4. CRISPR Technology: Principles and Applications

CRISPR-Cas systems, tools that are widely used in cutting-edge gene editing technology, derive their origin not just from viruses but also as a very smart anti-viral property of bacteria or archaea which somehow seems a prehistoric weapon. This one, para as microbial immune systems, bacilli and bacteriophages are the roles since organism. Microorganisms network with one another and fight back against the continuous invasion of strangers. This is like their own microbiota immunity. CRISPR designates a set of particular features on the chromosomes of bacteria which are the result of long, repetitive DNA sequences alternating with segments retrieved from viruses of earlier infections (Tajkarimi & Wexler, 2017). The bacteria permanently keep the genetic sequences from the portion of the invading viruses. The bacteria can later access these pieces of DNA in the CRISPR array when viruses attack the body again.

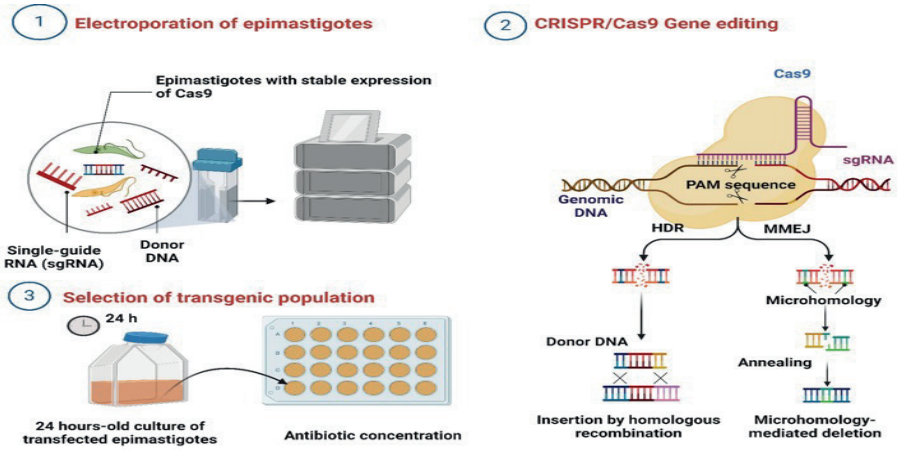


Figure 3. CRISPR-Cas9 Gene Editing

It is the very case of CRISPR-Associated Proteins (CAS) that are the real strong pillars upholding the technique. In the case of the CRISPR method, when the virus that the system has seen and defeated before tries to attack the system once again, the CRISPR molecule operates prophylactically, and, after converting into RNA molecules, the latter embodies the viral DNA. Along these guide RNAs, Cas proteins (same as Cas9 nuclease) are feeling bound and the molecular scissors are being cut for cutting the DNA (CHAKRABORTY & ACHARYA, 2017). In a similar way to the CASP 13 system, it defends the cells against viral intrusion and invading the processes by hunting for viral pieces that comply with the specific details given by the guide RNA. In contrast is seen when Cas9 of the host proteins present in the genomes, the double-stranded DNA scissors precisely inserted into the viral DNA that inhibits the virus from the opportunity to the host.

The most wonderful characteristic of CRISPR technology is that it generally has programmable attributes for DNA editing in organisms. This precision is achieved on purpose by scientists designing the gRNA (guide RNA) directed to the specific place of interest in the genome. The gRNA then interacts with the Cas9 protein resulting in its activation and further creating a double-stranded break portion at this targeted locus. This brings a double-strand break which, in turn, induces the mechanisms of the DNA natural repair. Consequently, the resulting recombination makes the correct replacement mutations to those that would have altered too much of the targeted gene. Furthermore, the CRISPR-Cas9 repair template is mutated and distorted into the cultivated site among other therapeutic approaches (Allen et al., 2019). On the other hand, CRISPR-Cas9 is characterized by a high degree of efficiency because it is capable of specifically targeting only one point in the genome, several alterations in the editing, and avoiding inaccurate changes. The base editing technique is considered tissue agnostic and non-inferring, as it has the attribute of being a programmable method through easily modifiable guide RNA, which makes it very diverse. Amongst that, CRISPR-Cas9 outshines, its predecessors in no other words than the perfection in the precision and efficiency while editing, making especially scissors, the zinc-finger nucleases, and TALENs look inferior (as shown in Figure 3). The single most important thing that gave it the needed edge over its competitors is its relative simplicity; which in turn has made it liked by researchers and professors in different fields and has found many engineering applications (Nilson, 2016).

5. Recent Genomic discoveries.

Genomics as everyone knows is a very mobile field with constant updates in the realm of science and medicine. These achievements open up the world of numerous alternatives. The positive feedback system has made the fast enrichment price and the fluency of sequencing of these recent developments, one of the key drivers of this high throughput. Genome sequencing with today's NGS (next generation sequencing) platforms can now produce plenty of data as opposed to in the past when the old platforms were used to generate this amount and lower of data in just a fraction of time and the cost (Metzker, 2010). One of the fields that are affected the most by the high-throughput sequencing revolution is the genomics research of many health conditions, and that has numerous causes. Analyzing the genomic ranges of hundreds or even millions of people has evolved as a critical part of a large-scale screening process using genome-wide association studies (GWAS), which scan for genetic variants including single nucleotide polymorphisms strongly associated with health problems including cancer, type 2 diabetes, or Alzheimer's disease (Uffelmann et al., 2021). Indeed, being involved in such investigations allowed gaining more knowledge of the sophisticated correlation between genetics and environmental factors as determinants for an individual's disease risk.

Table 3: Examples of CRISPR-based Crop and Livestock Improvement

Crop	**Modification**	**Benefit**	
Rice	Enhanced crop production and better grain quality	increased nutritional value and improved food safety.	(Mohidem et al., 2022)
Wheat	increased resistance against fungal diseases.	Decrease in crop losses and less use of pesticides	(Singh et al., 2016)
Tomato	Delayed fruit ripening leads to longer shelf life	reduced food waste and enhanced transportability.	(Adaskaveg & Blanco-Ulate, 2023)
Banana	Resistance to Panama disease, a fungal wilt disease	safeguards important staple crops in several areas.	(Dita et al., 2018)
Cattle	Polled (without horns)	enhanced animal welfare and decreased the necessity for painful dehorning.	(Knierim et al., 2015)

At one more level, that is the description of cancer on the molecular level, another area where the high-throughput sequencing technology is transforming our knowledge of cancer. The fact that analyzing a whole tumor in its typical cellular structure and without any unnecessary invasion was fundamental to cancer research and clinical medicine. Oncogenomic in this case consists of the identification of those mutations that are known to contribute to the development of the tumor in the patient. In addition, this may help in finding new therapeutic tactics and strategies (van Doorn et al., 2009). Those approaches based on analyzing the sequence of Chinese characters are more about guided medicine, being more specific in recognizing individual genomic patterns of a patient and treating each person individually. There are also genome studies of the interspecies variation or difference, which are powered by the high throughput sequencing technology; thus, researchers analyze how the gene sequences of the species spread around the world, how natural selection is involved in this species divergence and how the migration, gene recombination, and gene flow happen within the species. The advent of metagenomics technology in the study of microbiology has enabled such a radical change that it is currently possible to sequence entire microbial communities directly, without the need to culture the individuals apart (Garza & Dutilh, 2015). It is fun to observe these tiny but complex communities that grow on their own without the hassle of growing and handling each microbial crowd. Today, DNA sequencing is being changed through advances in techniques resulting in DNA analyses using those latest investigative approaches. The longer-read sequencing methods (capable of sequencing thousands of bases in one read) are thus an equally important technology to emerge. They came to cover most of the imperfections that could be seen in the former techniques and also assist in identifying repeated regions of genomes besides generating structural variations and a complex mixed sample in contrast to the DNA sequencing methods. However, this was not always the case for us as things went further and now the solution is available because of the newest development in single-cell sequencing. This technology made it possible to not only investigate the intercellular variations in tissue but also to understand what is happening on the level of a cell during the process of disease development (Kular et al., 2014).

The reality is that the rate at which genetic material research approaches its ways are gone through is impressive. The main motivation for the discovery of the more elementary parts of the genetic sequences will be the widespread ability for the users to decode and the authoritative level cost reduction (as shown in Table 3). In a sense, this means further exploration and identification of living creatures' genes, refining the diagnosis of diseases, and paving the way to medical, agricultural, and biotechnological transformation will require addressing this impending future (Fatima et al., 2024).

6. CRISPR Revolution: Transforming Biotechnology

Although the transformation of CRISPR-Cas9 into a widespread gene editing method gave a new impetus to the current biotechnology, providing the potential to be used in various immunological and medical fields. that plant breeding becomes more effective owing to CRISPR strategies since they are highly precise and, relative to the previous technologies, rather easy to use; as new paths in the genetic engineering of plants, animals, and microorganisms (as shown in Figure 4), this gives new opportunities to this field. The most important response from CRISPR that doesn't pull through is likely in agriculture. As for crop modification, scientists may use the CRISPR technology to build in useful characteristics such as better yield, tolerance to drought, disease resistance, or enriching food in good nutrients through the application of the technique developed by cross-breeding programs (Siddique et al., 2024) and this may be with no drawbacks of the earlier genetic method. As an exhibit, the resistance that biotechnology shows is that rice is the best in yield, wheat is disease resistant, and genetically engineered tomatoes last longer on shelves. All of these accomplishments are possible due to the significant benefit of the CRISPR approach that allows us to cross boundaries in plant species breeding because of the extremely fast speed, which at the same time makes it very good for crop development.

Besides the best CRISPR techniques application being implemented in livestock breeding, the CRISPR-Cas system can also be used to fight viral disease. Animal welfare is another main CRISPR application, along with it, improved productivity is also very likely to be obtained. Animals found on the planet Earth are characterized by an impressive diversity of them. Let us talk about the main function of the horns and tusk, they play a major role in the beauty of the animals and also make the sense of dignity, power, and toughness. Besides the effect on livestock, other application of CRISPR technology includes aquaculture in this regard the designers will be able to select some preside genes that will help in fast growth or being more resilient (Rexroad et al., 2019). In addition to its impact on agriculture, the technology can also be transformed which will lead to progress in other areas. CRISPR-based cell and animal models are not only accelerating the process of detecting cause-effect relationships between diseases and drugs but also, but they are also helping us to uncover gene functions that are involved in illnesses. CRISPR has the potential to transform gene therapy to allow for the delivery and correction of genetic mutations at a molecular level. It could be through editing mutations and phytonutrients that cause diseases. Clinical trials lie at the stage of Retinitis pigmentosa and sickle cell disease which are hereditary and it happens during the failure of the retina to function normally (Prateeksha et al., 2019).

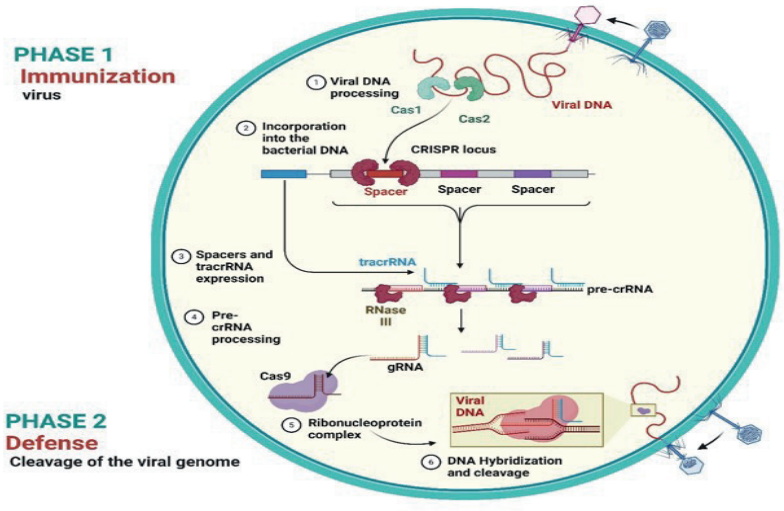


Figure 4. CRISPR-Cas9 Adaptive Immune System of Streptococcus pyogenes against Bacteriophages

CRISPR's ability to go over and beyond food security and industrial biotech as well as providing solutions that will secure a stable economic state will be the great beneficial aspect of gene editing. Human enablement through CRISPR for biodiesel production by way of developing new bio-based products such as biodegradable diapers (32 % natural fibers) and air pollutant decomposers is an example of an ongoing transformation through CRISPR. CRISPR in metabolic engineering, for instance, through introducing different traits, has been boosting ecology as the existence of petroleum-free alternatives is inspired through various spheres (Vigil et al., 2024).

It is difficult to say, how far biotechnology can be under the jurisdiction of CRISPR technology in the future, but the fact is that tomorrow is already represented by shining rays from our future. The gloomy picture of CRISPR-based tools will continue to be replaced gradually by its better versions, and it will finally be outshone by the dawning sun of uncomplicated platforms for gene editing and modification (de condoléances du Président Abdelaziz). High efficiency in delivery, as well as well-adapted ones, will make up for the lack of tasks that need to be addressed. CRISPR utilization in healthcare is just a big problem for the researchers who deal with such issues as off-target effects and the lack of efficient delivery systems. This will also call for innovation to be tackled by its developers. After all, we are actually at such an interesting period in a time frame when genetic engineering on a microscopic level with even a letter of the gene will open a way to yield crops, prevent and cure numerous diseases, and invent the tools for multiple problems.

7. Challenges and Future Directions

The Research of Genomics and CRISPR devices are incredibly optimistic yet criticized just as hard. They are known to come along with minimalities. Scientists are trying their best to reduce these risks by the methods available to them. Inventors have more challenges that need to address a higher level of innovativeness and will support the process of development in these industries. Being data a key issue in the genomic area, we should be aware of how to interpret this large amount of data provided by sequencers. It is noteworthy that although the velocity and cost of sequencing have decreased drastically compared to the early days, interpreting those sequences still requires too much bioinformatics. What the researchers are interested in investigating now is the genetic-modifying role of gene variations, particularly, those that are not located in the first known genes will be the object of subsequent research efforts. In addition, there is further insight regarding the fact that the entwining of genetic and environmental factors may be the critical determinant for disease or health after these, which remains a puzzling group (Dashti & Ordovás, 2021).

If Crispr technology is concerned the most difficult thing been take into account might be the fact off-target impacts sometimes occur. Different from mCRISPR-Cas9, at off-target locations, there is a chance of random but similar sequences to the target sequence. This can lead to accidental cutting at other locations along the genome instead of the target location. Further, it is potentially devastating gene-editing mistakes that would create hidden effects the mutations that could take place as a consequence of these undesirable effects. Although the researchers have designed the following strategies such as the advancement of the high-precision Cas9 variants for high specificity and an algorithm buildup for RNA design to decrease off-target effects, these strategies are no longer coping with a lot of challenges (Razzaq et al., 2021). Another matter that is difficult with is the introduction of components of CRISPR-Cas9 and their movement, especially in case there is the implantation of particular cells and tissues within the host organism. This is precisely why this thing is such an important characteristic when it comes to applying drugs to the human body. Research means the investigational studies that are based on the different forms of delivery methods such as viral vectors, and nanoparticles, and building the pre-assembled CRISPR-Cas complex (Lin et al., 2022). Making way for ethical perspectives is equally important when it comes to challenging technical issues. The possibility of CRISPR even in the human germline (sperm, eggs, and embryos) makes people turn to deep, unique morality which shows themselves in society(Greely, 2022). Filing up organic food will never be imagined by genetic engineering. However, these technologies can be misused in the future and may cause some unexpected long-term effects, posing questions like whether is it

ethically appropriate to 'design babies' or to practice some kind of eugenics in the future. However more important of these two elements than being merely a victim of these challenges is their ability to provide a driving force and set a pace for the designated adapting solution. Genomic data will be processed more sophisticatedly by single-cell sequencing and computational analysis which is possible via classical methods as a result of biological progress (Hwang et al., 2018). When you post something online, this isn't an issue that's occurring in absolute isolation somewhere; what you post becomes part of the overall Internet world. It means possible violations of privacy, security, and the overall process of the service. The area of genetic data processing and interpretation can be expedited and simplified by the usage of a combination of artificial intelligence and machine learning, which are part of the process of discovery (Gupta et al., 2021). Exploring the diversity of natural CRISPR-cas gene function has not yet opened ways to develop an expanded toolkit of new CRISPR enzymes with carefully engineered specific traits and others unnecessary for the chosen task. This rapidly evolving science and CRISPR use exposes us to an interesting junction where scientific discoveries and ethical/social issues are being debated together. It will be like a triangle where on one side there will be the long-term investigations, and on the other - the open and evident discussions of the possible amendments of these devices as the last would be the basis of the future enhancements of their performance and use in the medicine, agriculture and other industries of people's life.

8. Conclusion

This wave of genomic discoveries ushered by the appearance of CRISPR technology presents an awesome scientific revolution the result of which will be a victory over the unthinkable ability to control genetic information and to make use of it. The two historical events in the past that helped science to come up with an appropriate model, which was Mendel's peas and the Human Genome Project, have paved the way for a fruitful area of work. When the detection of CRISPR-Cas-based genome-engineering systems was done and then such a system was converted to an unparallel and very precise gene editing tool, there was created a new scientific setting in amending that DNA by having extreme control and return for performing the modification. The fastest-moving breed of science is called genome and it will help in the discovery of new treatments for a range of diseases. Such innovations empower us with wide-ranging sequencing and analysis technologies that make us aware of genes that lay the foundation for complex diseases, enigmas of the evolution unveiled, and healthcare diversified by adopting personalized medicine. CRISPR technology represents the focal point of biotechnology and provides diverse areas in such a way that innovation can be seen as the main element. From high-capacity plants and gene therapies to technological products, CRISPR plays an important part in fighting at least one of the problems of the first century. To make the fields that are trying to spend billions of dollars pass through the stages of ultimate professionalism and many dreams, they are recognizing the goal of correcting the errors or ethical issues through the efforts of research. Appropriate design of CRISPR tool, selection of valid genes, creation of gene delivery alternatives, and total appreciation of gene-environment interactions are about infrastructure for safe and effective implementation. An open discussion on genetic engineering from the ethical perspective as well as an inspection of germ-line gene editing will clarify whether the scientific discoveries are made ethically. Genome history will not be the same as in the past for the HERA human genome time and the technological breakthrough of CRISPR (Clustered, Regularly Interspaced Short Palindromic Repeats with similar structures with bacterial prokaryotic DNA). Scientists are just at the beginning of being able to uncover more mysteries as the methods are refined and the tools are developed. The more the techniques are being modified and the tools are adding up the more the expectation that the breakthrough that can change the world in the fields of medicine, agriculture, and biotechnology is increasing. Through these discoveries, we don't only see the development made on planet Earth in these regards but also get to see how our activities on our planet improve sustainability and reveal better understandings of the world around us. Such advancements in life sciences have brought both of them to this one point when humans are not only able to spot the unique pattern of the code of life but also able to change it.

References

Adaskaveg, J. A., & Blanco-Ulate, B. (2023). Targeting ripening regulators to develop fruit with high quality and extended shelf life. Current Opinion in Biotechnology, 79, 102872.

Ahmed, S., & Khosa, A. (2010). An introduction to DNA technologies and their role in livestock production: a review.

Aldridge, S. (1996). The thread of life: the story of genes and genetic engineering. Cambridge University Press.

Allen, F., Crepaldi, L., Alsinet, C., Strong, A. J., Kleshchevnikov, V., De Angeli, P., Páleníková, P., Khodak, A., Kiselev, V., & Kosicki, M. (2019). Predicting the mutations generated by repair of Cas9-induced double-strand breaks. Nature biotechnology, 37(1), 64-72.

Borus, A. (2020). James Watson, Francis Crick, Rosalind Franklin, and Maurice Wilkins: The Scientists who Revealed the Structure of DNA. The Rosen Publishing Group, Inc.

Buzdin, A. V., Patrushev, M. V., & Sverdlov, E. D. (2021). Will plant genome editing play a decisive role in "quantum-leap" improvements in crop yield to feed an increasing global human population? Plants, 10(8), 1667.

Cantelon, H., & Letters, M. (2000). The making of the IOC environmental policy as the third dimension of the Olympic movement. International review for the sociology of sport, 35(3), 294-308.

Ceasar, S. A., Rajan, V., Prykhozhij, S. V., Berman, J. N., & Ignacimuthu, S. (2016). Insert, remove or replace: A highly advanced genome editing system using CRISPR/Cas9. Biochimica et Biophysica Acta (BBA)-Molecular Cell Research, 1863(9), 2333-2344.

CHAKRABORTY, S., & ACHARYA, M. (2017). A "CRISPR" OVERVIEW OF GENOME EDITING: POTENTIALS AND CHALLENGES. SCIENCE AND CULTURE.

Das, M., Mohanty, C., & Sahoo, S. K. (2009). Ligand-based targeted therapy for cancer tissue. Expert opinion on drug delivery, 6(3), 285-304.

Dashti, H. S., & Ordovás, J. M. (2021). Genetics of sleep and insights into its relationship with obesity. Annual Review of Nutrition, 41, 223-252.

de condoléances du Président Abdelaziz, L. L'ex-premier ministre Michel Rocard nous a quittés: Parler vrai, honneur et dignité en politique.

Dita, M., Barquero, M., Heck, D., Mizubuti, E. S., & Staver, C. P. (2018). Fusarium wilt of banana: current knowledge on epidemiology and research needs toward sustainable disease management. Frontiers in Plant Science, 9, 398832.

Doudna, J. A., & Charpentier, E. (2014). The new frontier of genome engineering with CRISPR-Cas9. Science, 346(6213), 1258096.

Doxzen, K., & Halpern, J. (2020). Focusing on Human Rights: a framework for CRISPR germline genome editing ethics and regulation. Perspectives in Biology and Medicine, 63(1), 44-53.

Early, D. (1987). DNA sequencing.

El-Hani, C. N. (2015). Mendel in genetics teaching: some contributions from history of science and articles for teachers. Science & Education, 24, 173-204.

Ermini, L., & Driguez, P. (2024). The Application of Long-Read Sequencing to Cancer. Cancers, 16(7), 1275.

Fatima, G., Magomedova, A., & Parvez, S. (2024). Biotechnology and Sustainable Development. Shineeks Publishers.

Franklin, R., & Franklin, R. E. Who Discovered DNA? The Journey of Discovery.

Garza, D. R., & Dutilh, B. E. (2015). From cultured to uncultured genome sequences: metagenomics and modeling microbial ecosystems. Cellular and Molecular Life Sciences, 72, 4287-4308.

Greely, H. T. (2022). CRISPR people: The science and ethics of editing humans. MIT Press.

Gupta, R., Srivastava, D., Sahu, M., Tiwari, S., Ambasta, R. K., & Kumar, P. (2021). Artificial intelligence to deep learning: machine intelligence approach for drug discovery. Molecular diversity, 25, 1315-1360.

Hood, L., & Rowen, L. (2013). The human genome project: big science transforms biology and medicine. Genome medicine, 5, 1-8.

Hwang, B., Lee, J. H., & Bang, D. (2018). Single-cell RNA sequencing technologies and bioinformatics pipelines. Experimental & molecular medicine, 50(8), 1-14.

Jorqui-Azofra, M. (2020). Regulation of clinical xenotransplantation: A reappraisal of the legal, ethical, and social aspects involved. Xenotransplantation: Methods and Protocols, 315-358.

Kaur, H., Pandey, D. K., Goutam, U., & Kumar, V. (2021). CRISPR/Cas9-mediated genome editing is revolutionizing the improvement of horticultural crops: Recent advances and future prospects. Scientia Horticulturae, 289, 110476.

Kchouk, M., Gibrat, J.-F., & Elloumi, M. (2017). Generations of sequencing technologies: from first to next generation. Biology and Medicine, 9(3).

Khalil, A. M. (2020). The genome editing revolution. Journal of genetic engineering and biotechnology, 18(1), 68.

Knierim, U., Irrgang, N., & Roth, B. A. (2015). To be or not to be horned—Consequences in cattle. Livestock Science, 179, 29-37.

Kular, J. K., Basu, S., & Sharma, R. I. (2014). The extracellular matrix: Structure, composition, age-related differences, tools for analysis and applications for tissue engineering. Journal of tissue engineering, 5, 2041731414557112.

Kulski, J. K. (2016). Next-generation sequencing—an overview of the history, tools, and "Omic" applications. Next generation sequencing-advances, applications and challenges, 10, 61964.

Lin, Y., Wagner, E., & Lächelt, U. (2022). Non-viral delivery of the CRISPR/Cas system: DNA versus RNA versus RNP. Biomaterials Science, 10(5), 1166-1192.

Loverdos, K., Bellos, G., Kokolatou, L., Vasileiadis, I., Giamarellos, E., Pecchiari, M., Koulouris, N., Koutsoukou, A., & Rovina, N. (2019). Lung microbiome in asthma: current perspectives. Journal of Clinical Medicine, 8(11), 1967.

Luo, J., Wu, M., Gopukumar, D., & Zhao, Y. (2016). Big data application in biomedical research and health care: a literature review. Biomedical informatics insights, 8, BII. S31559.

Metzker, M. L. (2010). Sequencing technologies—the next generation. Nature reviews genetics, 11(1), 31-46.

Mohidem, N. A., Hashim, N., Shamsudin, R., & Che Man, H. (2022). Rice for food security: Revisiting its production, diversity, rice milling process and nutrient content. Agriculture, 12(6), 741.

Moraes, F., & Góes, A. (2016). A decade of human genome project conclusion: Scientific diffusion about our genome knowledge. Biochemistry and Molecular Biology Education, 44(3), 215-223.

Mugo, K. (2013). Down but Not Out: Becoming a Significant Leader at Home. Westbow Press.

Naidoo, N., Pawitan, Y., Soong, R., Cooper, D. N., & Ku, C.-S. (2011). Human genetics and genomics a decade after the release of the draft sequence of the human genome. Human genomics, 5, 1-46.

Nilson, L. B. (2016). Teaching at its best: A research-based resource for college instructors. John Wiley & Sons.

Prateeksha, Yusuf, M. A., Singh, B. N., Sudheer, S., Kharwar, R. N., Siddiqui, S., Abdel-Azeem, A. M., Fernandes Fraceto, L., Dashora, K., & Gupta, V. K. (2019). Chrysophanol: a natural anthraquinone with multifaceted biotherapeutic potential. Biomolecules, 9(2), 68.

Rademan, A. E. (2020). Creating expectations: the bioethics of genetics as reflected in selected South African media with specific reference to CRISPR-Cas9 Stellenbosch: Stellenbosch University].

Ratan, Z. A., Son, Y.-J., Haidere, M. F., Uddin, B. M. M., Yusuf, M. A., Zaman, S. B., Kim, J.-H., Banu, L. A., & Cho, J. Y. (2018). CRISPR-Cas9: a promising genetic engineering approach in cancer research. Therapeutic advances in medical oncology, 10, 1758834018755089.

Razzaq, A., Kaur, P., Akhter, N., Wani, S. H., & Saleem, F. (2021). Next-generation breeding strategies for climate-ready crops. Frontiers in Plant Science, 12, 620420.

Rees, H. A., & Liu, D. R. (2018). Base editing: precision chemistry on the genome and transcriptome of living cells. Nature reviews genetics, 19(12), 770-788.

Rexroad, C., Vallet, J., Matukumalli, L. K., Reecy, J., Bickhart, D., Blackburn, H., Boggess, M., Cheng, H., Clutter, A., & Cockett, N. (2019). Genome to phenome: improving animal health, production, and well-being–a new USDA blueprint for animal genome research 2018–2027. Frontiers in genetics, 10, 327.

Rius, M., Bourne, S., Hornsby, H. G., & Chapman, M. A. (2015). Applications of next-generation sequencing to the study of biological invasions. Current Zoology, 61(3), 488-504.

Sage, L. (2005). Faster, cheaper DNA sequencing. In: ACS Publications.

Satam, H., Joshi, K., Mangrolia, U., Waghoo, S., Zaidi, G., Rawool, S., Thakare, R. P., Banday, S., Mishra, A. K., & Das, G. (2023). Next-generation sequencing technology: current trends and advancements. Biology, 12(7), 997.

Sharma, P., Singh, I., Bohra, A., Singh, I. P., Tiwari, A., Sethi, M., Kushwah, A., & Singh, S. (2020). Updates of pigeonpea breeding and genomics for yield improvement in India. Accelerated Plant Breeding, Volume 3: Food Legumes, 109-141.

Siddique, A., Kalangutkar, A., & Kumari, P. (2024). Biotechnological approaches for crop improvement and production. Sustainable Agriculture: Nanotechnology and Biotechnology for Crop Production and Protection, 271.

Singh, R. P., Singh, P. K., Rutkoski, J., Hodson, D. P., He, X., Jørgensen, L. N., Hovmøller, M. S., & Huerta-Espino, J. (2016). Disease impact on wheat yield potential and prospects of genetic control. Annual review of phytopathology, 54, 303-322.

Smýkal, P., K Varshney, R., K Singh, V., Coyne, C. J., Domoney, C., Kejnovský, E., & Warkentin, T. (2016). From Mendel's discovery on pea to today's plant genetics and breeding:

Commemorating the 150th anniversary of the reading of Mendel's discovery. Theoretical and Applied Genetics, 129, 2267-2280.

Stanke, M., Schöffmann, O., Morgenstern, B., & Waack, S. (2006). Gene prediction in eukaryotes with a generalized hidden Markov model that uses hints from external sources. BMC bioinformatics, 7, 1-11.

Tajkarimi, M., & Wexler, H. M. (2017). CRISPR-Cas systems in Bacteroides fragilis, an important pathobiont in the human gut microbiome. Frontiers in microbiology, 8, 296628.

Uffelmann, E., Huang, Q. Q., Munung, N. S., De Vries, J., Okada, Y., Martin, A. R., Martin, H. C., Lappalainen, T., & Posthuma, D. (2021). Genome-wide association studies. Nature Reviews Methods Primers, 1(1), 59.

van Doorn, R., van Kester, M. S., Dijkman, R., Vermeer, M. H., Mulder, A. A., Szuhai, K., Knijnenburg, J., Boer, J. M., Willemze, R., & Tensen, C. P. (2009). Oncogenomic analysis of mycosis fungoides reveals major differences with Sezary syndrome. Blood, The Journal of the American Society of Hematology, 113(1), 127-136.

Vigil, T. N., Felton, S. M., Fahy, W. E., Kinkeade, M. A., Visek, A. M., Janiga, A. R., Jacob, S. G., & Berger, B. W. (2024). Biosurfactants as templates to inspire new environmental and health applications. Frontiers in Synthetic Biology, 2, 1303423.

Wess, L. (2023). The Curious World of Bacteria. Greystone Books Ltd.

About The Authors

Maria Nazir is an MPhil Scholar of Microbiology at the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur, Pakistan. She is involved in a National Research Program for Universities (NRPU) Project, with research interests in Molecular Characterization. She has submitted abstracts to various conferences and authored and coauthored of several book chapters. Her research focuses on the isolation and Molecular characterization of Corynebacterium pseudotuberculosis and their applications in promoting animal health. Her interested research criteria are based on genetics, molecular biology, and bioinformatics.

Email: nazirmaria545@gmail.com ORCID 0009-0004-6714-6212

Mr. Tasawar Abbas received his M. Phil in Molecular Biology from the National Center for Excellence in Molecular Biology University of Punjab Lahore Pakistan. He has one review article. He has worked in Forensic Serology, He has excellent knowledge of Genetics, STRs, genetic polymorphism also Stem cells, and virology. His research interests include stem cell therapies, Immunology, Human genetics and criminology.

Email: tasawarabbas333@yahoo.com ORCID: 0009-0002-7718-2634

Maham Shahzadi is a final-year BS Biotechnology student at Cholistan University of Veterinary and Animal Sciences, Bahawalpur (CUVAS). She is passionate about exploring the diverse applications of biotechnology to improve human health, agriculture, and marine ecosystems. Her research interests include developing novel diagnostics and therapeutics, enhancing crop yields and sustainability, and utilizing marine resources for drug discovery and environmental protection. With a strong academic background and a keen interest in cutting-edge research, Maham is poised to make significant contributions to the field of biotechnology.

E-mail: mahamshehzadi005@gmail.com ORCID: 0009-0005-9868-2162

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as "Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone". His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

Muhammad Ejaz earned Bachelor's in applied microbiology from Cholistan university of veterinary and animal sciences (CUVAS) Bahawalpur Pakistan. His research interest in Microbial genetics, Molecular biology, and food quality and its application.

Email: ijazrasheed334@gmail.com ORCID: 0009-0006-1709-6653

Dr. Muhammad SAFDAR earned his PhD in Molecular Biology and Genetics from Gaziantep University, Turkey. He is Lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 70 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

E-mail: msafdar@cuvas.edu.pk ORCID: 0000 0002 3720 2090

To Cite This Chapter

NAZIR M et al., (2024). Breaking barriers: advancements in genomic research and crispr technology. In Current Studies in Health and Life Sciences 2024 (pp.196-210). ISRES Publishing.

Stem Cell Research: Unloking The Potential for Regenerative Therapies

Maria NAZIR

Hameer Khan KHASKHELI

Ammara HAMEED

Tasawar ABBAS

Danish RIAZ

Shafeeq Ur REHMAN

Muhammad SAFDAR

1. Introduction

Stem cells have emerged as one of the brightest stars on the map, directing the course of modern medicine, and have attracted the attention of scientists as well as the common people. Such strategies of using the natural self-healing efficiencies of body tissues for curing such ailments is a new chapter in the history of medical science; it can be inferred that various diseases and injuries can be cured using the remedial advantages of regenerative medicine (Sorensen et al., 2022). In addition to this field, stem cells are some of the most exciting cells in biology owing to their ability to continue dividing for a rather long time and differentiate into many specialized cells (Hall & Watt, 1989). This double-faced characteristic of stem cells makes them useful resources for the treatment and regeneration of tissues, hence offering hope to patients with diseases that previously could not be treated. For instance, for neurodegenerative diseases such as Parkinson's and Alzheimer's disease, cardiovascular diseases, heart failure, and myocardial infarction stem cell therapy can be used in almost all the diseases that humans are unconsciously susceptible (Dawson et al., 1995). Thus, once people understand how different elements of stem cells' environment influence these cells, the scientific community will be paving the way for producing therapeutic approaches that could help millions of people with chronic pains and heal diseases as well as prolong human lifespan.

Scientists discovered that cell lineages could differentiate into all blood cells via the bone marrow hematopoietic stem cells (HSCs). It formulated the guidelines for bone marrow transplantation the only treatment for some forms of blood cancer and other hematological disorders. Stem cells were regarded as a priceless biomaterial; however, these cells were analyzed and researched in only several variations up to the end of the period of the nineteen nineties when hESCs were derived and cultured (Ericson, 2007). ESCs arise from the blastocyst and are noted for their Pluripotency or the ability of these cells to differentiate into any cell of the body, a process they derive from the blastocyst. This discovery gave way to subsequent surveys because people understood that stem cells are effective in solving different human diseases owing to their ability to repair tissues and organs. As a result of improving technological advancement and enhanced knowledge of stem cells, stem cell research has been boosted maximally over the last decade. However, with the later development of induced pluripotent stem cells (iPSCs), which is made by transforming an ordinary body cell into that which is almost embryonic, ethical considerations (Lewandowski & Kurpisz, 2016) that come with the use of ESCs are eliminated, although their totipotency is not opposed. It has allowed doctors to prescribe medication dependent on the personal traits of the patient, allow researchers to construct models of diseases, along with finding new medications. According to Shi et al., the consequent patient-specific nature of iPS cells enables the researcher to create a disease model in a dish, investigate the disease progression, and trial the drugs in a far more realistic setting. Besides, they serve purposes in regenerative medicine because the cells can be terminal to other types of cells for transplantations and tissue replacement (Ringe et al., 2002).

Moreover, findings have been made and reported that provide information on identifying numerous subpopulations of adult stem cells in different body parts. They contain tissue-specified stem cells that play vital roles in the homeostasis and repair of tissues, and the element potential of these tissues is discussed based on several diseases (Beerman & Rossi, 2015). For instance, MSCs derived from bone marrow have therapeutic use in autoimmune-related disorders, new blood vessel formation, and the replacement of damaged vital organ tissues. NSCs present the capability to replace flawed neurons and improve rehabilitation in global ischemia, neurological disorders, and spinal cord injury (Vishwakarma et al., 2014). Stem cell research has not been in vain as it extends direct medical application. At present, hematopoietic stem cell transplantation is known as a therapy for multiple blood diseases and kinds of cancer, and MSCs derived from bone marrow are used in autoimmune diseases and tissue regeneration. In ophthalmology, ESCs have been applied to produce layers of RPE in the treatment of one of the most prevalent causes of blindness, AMD (Schwartz et al., 2016). In this chapter, the reader will be first acquainted with the subject of stem cell research, especially emphasizing the differentiation of stem cells; they will also get a preview of the other types of stem cells, and, finally, the biological activities of stem cells will be explained in detail. Self-renewal and multipotent differentiation potential cells are known as stem cells; the different techniques used for isolation culture and manipulations of the stem cells and the development and advances made in the implementation of ideas into operation shall be understood. Thus, in the context of stem cells, let us clarify the position as to how we when it comes to confronting the current difficulties, are to shed light on the road that will incorporate regenerative medicine into a truly global picture beneficial for millions of people on earth.

2. Types of Stem Cells

Depending on their origin and differentiation potential, stem cells are categorically recognized in many categories. Since cells of different types have unique features and roles, it is crucial to understand them from the perspective of using stem cells in the literature of regenerative medicine.

2. 1 The first one develops from the Blastocyst

ESCs are isolated from the inner cell mass of early-stage embryos, preferably at the blastocyst stage, which is between five to seven days after fertilization (Desmarais et al., 2011). These cells are pluripotent, meaning they have the remarkable ability to differentiate into any cell type in the adult body, giving rise to all three germ layers. Some of the interesting features of stem cells include the ectoderm, mesoderm, and endoderm layer in humans. This makes ESCs versatile and this attribute is considered a plus in regenerative medicine since it can replace tissues that are destroyed or ravaged by diseases in the various body organs and systems (Figure 1). For instance, the scientific technique has been tested, and therefore, it is possible to differentiate ESCs into insulin-producing pancreatic beta cells to combat type 1 diabetes (Soria et al., 2001). However, the use of ESCs has been controversial because of its source, which is human embryos, a process most people consider to be eradicating human life. Even if an effort has been made to derive ESCs from other sources, such as somatic cell nuclear transfer (SCNT), the methods are still experimental and thus not clinically practicable (Šarić et al., 2010).

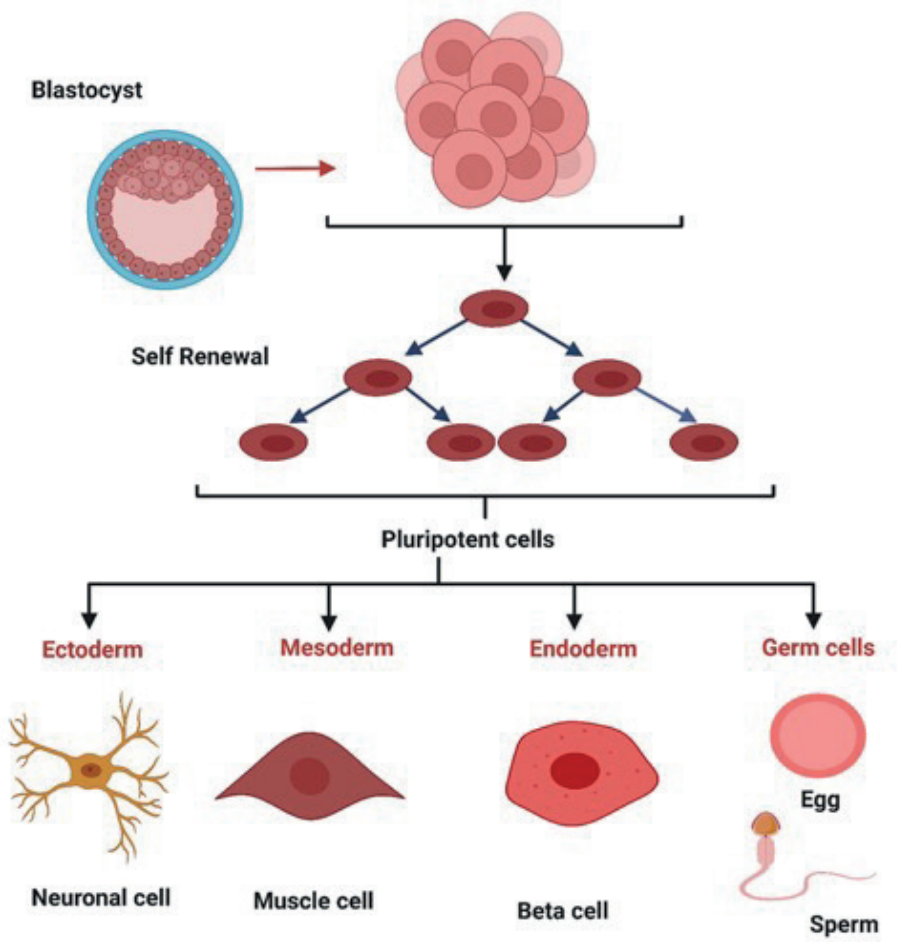


Figure 1. Human Embryonic Cell Differentiation

2. 2 Adult Stem Cells or Mesenchymal Stem Cells

Stem Cells These are stem cells that are taken from adults and are also known as postnatal stem cells are found in different parts of the body. This includes the bone marrow, adipose tissue of an adult, and umbilical cord blood of a newborn baby (Malgieri et al., 2010). Like any other stem cell, therefore, ESCs are pluripotent in their capabilities of differentiating into the various major cell types of an organism, while ASCs are multipotent, as many of the researchers would like to believe, by having the capability of differentiating into not more than three or four cell types of their lineage. For example, hematopoietic stem cells are found in the bone marrow, which can give rise to all the blood cells, or the mesenchymal stem which can transform into a bone cartilage or adipose tissue cell (Figure 2).

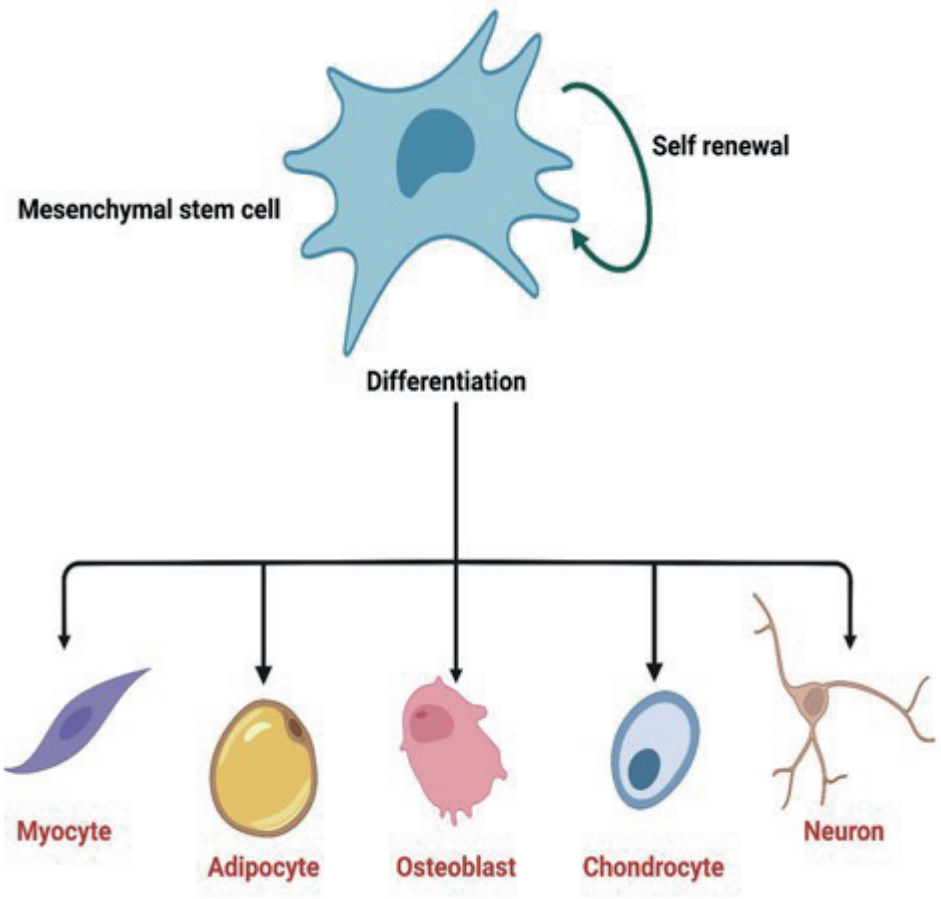


Figure 2. Adult Stem Cell differentiates to become Mesenchymal Stem Cell.

However, unlike ESCs, ASCs have certain advantages because of their low differentiation potential (Uzbas et al., 2015). They can be derived from adult people without ethical problems and can be reimplanted back into the body without facing rejection from the human body, unlike the ESCs. Moreover, some of the research has come across that some of these ASCs may have a specific property called the plasticity capacity through which it develops other cellular structures different from its source tissue(Sordi et al., 2017).

2. 3 Human embryonic stem cells (hESCs)

This involved using some chemicals to get a somatic cell to aspire to become an iPSC during the body's development processes. These cells are derived from normal somatic cells such as skin or blood cells and reprogrammed back to this state of embryonic stem cells through the agency of four genes, namely Oct4, Sox2, Klf4, and c-Myc (Zakrzewski et al., 2019). iPSCs are also known as pluripotent stem cells, just like ESCs, and this simply means that they can turn into any type of cell in the body as and when required. However, iPSCs do not come with some of the concerns of ESCs, for they can be differentiated from the easily obtainable adult cells. In addition, one can derive iPSCs from patients for disease studies, drug testing, and maybe possible regenerative medicine for each single patient. For example, researchers have used iPSCs of affected patients with genetic diseases; they observed the advancement of the disease on a plate and were able to establish possible therapeutic interventions (Bonaventura et al., 2021).

Nevertheless, the reprogramming process is related to altering genetic and epigenetic statuses, which affects the safety and function of iPSCs in clinical use. More research has to be done, and thereby, the quality control of the studies to establish how such matters can be handled to allow the

safe introduction of iPSC-based therapies into practice (Jha et al., 2021). Thus, all types of stem cells are different from one another by their peculiarities and treatments, which scientists have opened are almost infinite. Analyzing how the two human body parts have their individuality and how science is attempting to use stem cells and their capacity to self-renew, scientists are now able to come up with tonics that could go a long way in satisfying many medical needs.

3. Stem Cell Biology and Mechanisms

Stem cells are a particular kind of cell that possess different nature and characteristics from other cells. This paper describes the principal regulators of stem cell biology, which is fundamental information in stem cell-based therapeutic initiatives.

3. 1 Stem Cell Niches

Stem cells reside in shelters known as niches that are fundamental in the regulation of stem cells' properties. These niches provide mechanical substrate and also various bioactive molecules, cytokines, and factors of the extracellular matrix that control stem cell functions such as self-renewal, differentiation, and quiescence (Singh et al., 2019). Stem cell niche structure and organization can also be rather diverse concerning stem cells' overall tissue and differentiation. For example, the precise locality of HSCs is the bone marrow containing osteoblasts, endothelial cells, perivascular cells, and sympathetic neurons (Birbrair & Frenette, 2016). Known as niche cells, these cells employ various signals mostly through Notch/Wnt, SDF-1/CXCR4, and angiopoietin-1/Tie2 to regulate HSCs self-renewal, differentiation, and release (Portale, 2018). They are situated at the bottom of the crypts of Lieberkuhn and consist of Paneth cells and Lgr5 + stem cells (Schewe & Fodde, 2018). Despite wnt signaling for the renewing of the intestinal stem cells, notch signaling is not involved in the transmutation into various lineages of cells in the intestine (Foster et al., 2002). The stem cell niche is found to function as the master circuit, keeping a delicate balance between the stem cells' infinite division and differentiation. It improves the initiation of stem cell availability in the process of replacing tissues as individual life and also serves as a map for stem cells in case they are required to transform into certain cells for the formation of tissues, more so, for replacement and repair purposes (Saltzman, 2004). The changes of microenvironmental stimuli in the micro-territory fragment can lead to deviations in stem cell behavior and their participation in the diseases' progress, like cancers and degenerative diseases. For instance, the study highlighted how the modification of the bone marrow's place of dwelling leads to leukemia as well as other types of hematology-borne cancer.

3. 2 Microenvironments and Signaling Pathways

The stem cell niche is an active area summarized as the amalgamation of several signals that affect the stem cell functionality. These signaling pathways (Figure 3) include autocrine where the signals are synthesized and released by stem cells or paracrine factors coming from other stem cells or the surrounding matrix (Burchfield & Dimmeler, 2008). Some of the key signaling pathways involved in stem cell regulation include:

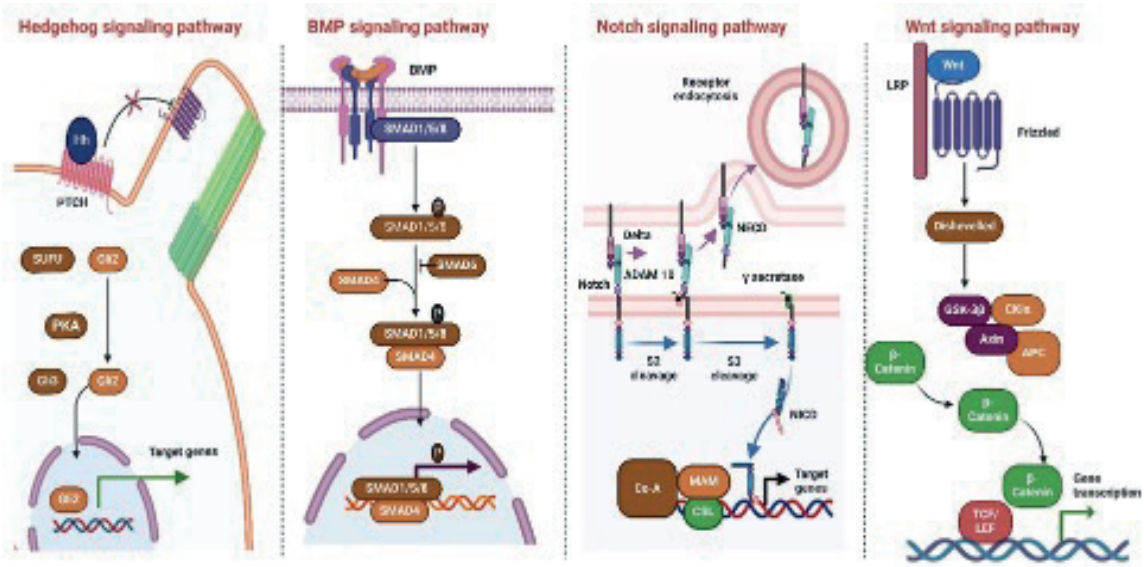


Figure 3. Different Signal Transduction Pathways

• **Notch signaling:** This pathway plays an especially critical role in the decisions that are made about cell lineage and is beneficial in maintaining the stem cells being 'pluripotent' while at the same time promoting differentiation into certain cells/tissues (Walia et al., 2012). For the hematopoietic system, Notch looked into the fate map of HSC concerning either maintaining cell proliferation or differentiating into the lymphoid or the myeloid lineage.

• **Wnt signaling:** The Wnt signaling pathway is involved in the regular development of an embryo and for the maintenance of tissue homeostasis and is essential for stem cell self-renewal, proliferation, and differentiation in different body tissues (Sokol, 2011). The Wnt signaling pathway helps in maintaining the ES and floor of the mouth iPS cells ' self-renewable states, while the inhibition of the Wnt signaling pathway plays a significant role in the differentiation process.

• **BMP signaling:** This has been relayed in diverse cell actions, including cell division, stem cell differentiation, and cell death, and is core to stem cell differentiation in various tissues. In the context of the bone marrow niche, BMP signaling assists in the same by restricting the HSCs into quiescence and hence assists in rewinding the long-term repopulating potential of these cells (Burel, 2022).

• **Hedgehog signaling:** In addition, this pathway participates in embryonic development and tissue stimulation and regulates the stem cell reaction in various tissues. In the skin, hedgehog signaling functions to retain Hair Follicle Stem cells in the G0 phase and regulate the emergence of hair structures (Zhang & Chen, 2024).

• **FGF signaling:** This pathway is used in processes like growth, development of cells, and movement and regulates stem cell activity in specific body regions. Anything that affects balanced FGF signaling directly affects ESCs and iPSCs' capacity to maintain their original embryonic stem cell state and their capacity to differentiate into lineages of the human body (Mong, 2013).

These signaling pathways can be interconnected, and this is how one obtains vast signal transduction networks that control stem cell functions in an idiosyncratic cell type and developmental phase. It is, therefore, important to understand these multiple interactions so that more precise treatments can be developed to modulate stem cell activity for therapeutic purposes.

3. 3 Differentiation and Plasticity

Differentiation is capable of specializing and supercilious the functions of the cells of the tissues and organelles. This process of differentiation is hereby described as a well-coordinated series of molecular changes in the cell, the pattern of genes, protein synthesis, and cell structure.

Stem cell's ability to respond to signals that cause their differentiation

This process of stem cell differentiation is a seemingly complex process that demarcates the genes to be turned on and the genes to be turned off through several factors, including both the intrinsic and the extrinsic factors. Modifications such as DNA methylation and histone acetylation alterations are used in the regulation of the gene in differentiation (Ikegami et al., 2009). Among the local key players, the most essential consists of those proteins capable of binding DNA sequences, which are, as a result, termed transcription factors because of their ability to switch target genes' activation or repression (Suter, 2020). Stem cells usually act according to the differentiation hierarchy; therefore, higher-order multipotent stem cells can differentiate in several cell types of a given lineage. In the process of differentiation, stem cell acquires partial characteristics of differentiation, which are prep producer cells for a particular lineage, but can go further to develop still other, more specialized IP cells before getting completely differentiated. For example, HSC in the hematopoietic system can differentiate to PCM or CLP, which in turn differentiate to virtually all blood cells such as red blood cells, the plates, as well as immune systems (Ranjitha, 2019). This implies that doing the differentiation process does not necessarily warrant this aspect of differentiation. Some stem cells are fully plastic because they either de-differentiate or trans-differentiate into other cell types under certain conditions. For instance, MSCs have been reported to trans-differentiate into ANLL-like cells, a discovery that should enable the application of such cells in the management of neurological diseases (Karpowicz, 2004). However, as regards the future of stem cells and their capability, this is still exceptional.

Factors Influencing Lineage Specification

The decision of which pathway to take is an action carried out by the stem cell through intrinsic and extrinsic processes. Other concurrent exogenous aspects include the epigenetic state of the stem cell at the onset and the switching on certain transcriptional factors as a prognosis of the stem cell's destination. The surrounding microenvironment, such as neighboring cells, signaling molecules, growth factors, and parts of the extracellular matrix, are the ones that provide the necessary signal to make destiny commitments (Lloyd-Lewis et al., 2019). The relative intrinsic and extrinsic force rates are pegged on certain environmental stimuli factors such as oxygen partial pressure, nutrient delivery, and biomechanical application. These can elicit so many responses in a cell that will spur the stem cell to either encourage or suppress the genes within and consequently determine its fate. For instance, hypoxia has been known to promote changes of MSCs to osteoblasts with the activation of nuclear factor HIF-1 (Ejtehadifar et al., 2015). Much effort has hence been directed at evaluating the complex signal transduction processes that guide stem cell differentiation as a way of rightly controlling the processes in a bid to provide the much-needed directions for innovative stem cell-based therapies.

3. 4 Self-Renewal and Proliferation

Stem cells can be released through self-renewal. This is the process of differentiating more stem cells that are phenotypically close to the original stem cell (Zipori, 2005). It is an important process of how the stock of stem cells in an individual is regenerated during a lifetime to enable tissue self-repair. However, at the same time, the uncontrolled capacity for self-renewal may lead to the formation of tumors and other diseases. This process of self-renewal and differentiation is controlled in a very similar way and helps to balance the tissue without the elimination of stem cells or an excessive amount of cell amplification. This balance is achieved via the presence of signaling pathways in the cell and additionally through transcription factors and epigenetic modifiers.

Molecular Pathways Regulating Self-Renewal

The records of the molecules, which include signals involved in the regulation of stem cell self-renewal, include the following. The Wnt signaling pathway is also used to control self-renewal capability, mainly in ESCs and ASCs (Jayaraman et al., 2021). Wnt signaling is useful in preserving the pluripotency of the cells due to the later activation of target genes such as c-Myc and cyclin D1, which are known genes that hinder the differentiation process (Sidrat et al., 2021). Furthermore, there are integrations of reprogramming pathways like Wnt with other signaling pathways such as Notch and TGF-β are involved in the regulation of the self-renewal process (Gordeeva, 2019). Another pathway that is also involved in stem cell self-renewal is the notched signaling pathway. While Hes1 belongs to the differentiation genes, it is, on the contrary, inhibited, while Bmi1, which is associated with stem cell self-renewal, is enhanced by NOTCH. This pathway is employed for the generation of renewal of HSCs, NSCs, and ISCs (Al-Jedai, 2008). Specifically well-described pathway that helps in stem cell survival, proliferation, and self-renewal is the PI3K/Akt signaling that is triggered by growth factors or cytokine. Downstream targets are launched, including the kinase mTOR (mechanistic target of rapamycin) mapped to photosynthesis and cell multiplication, besides FOXO transcription factors concerning genes associated with cell division and stress (Verma & Chatterjee, 2009). The same can be said about the ratio between the number of stem cells, in this case of the HaCaT cell line, and the differentiation of the cells at hand (Çetin et al., 2023). That is why regulating the stem cell cycle and determining the cell's developmental plan is critical for the tissue to remain stable. Therefore, cells of the body produce what might be referred to as an alarm in the form of inflammation whenever there is bodily tissue injury or damage, and the stem cells reproduce and begin to differentiate into a specific nutrient in a bid to replenish damaged lost cells. However, when these cells divide overly, they can then result in the formation of tumors or, if the division rate is inadequate, this could lead to tissue degeneration (Baba & Câtoi, 2007).

Several positive feedbacks avoid too numerous copies of the same cell type and negative feedbacks define the final fate of each given cell. Among these growth regulatory proteins, cyclins and cyclin-dependent kinases, and p 53 and Rb, the transcription factors that set the rate of cell division and the differentiation genes. HEPA growth factors such as EGF and FGF; cytokines such as IL-6, and cell adhesion molecules to get into the cell cycle and differentiate or to remain stem cells (Rhind & Russell, 2012). Hence, it bears a pertinent role as the stem cell niche in terms of right imposing stem cells' self-renewal and differentiation conditions. The niche signals may advise stem cell quiescence, which is a process of rather temporary withdrawal from the cell cycle with the intention of not depleting stem cells. Several processes attain this; creating inhibitory cytokines, including TGF-β, and obtaining quiescence-inducing niche cells (Moses, 2016). If tissue repair is needed, then the niche signals help the stem cells to proliferate and differentiate to replace the damaged or dead cells.

4. Methods Used in Stem Cell Research

This is because various procedures have been created for stem cell research. Through these procedures, stem cells can be isolated, grown, and manipulated. These techniques have assisted in enhancing knowledge of stem cell biology and given the basis for potential therapeutic applications.

Table 1: A list of methods that are employed in stem cells for isolation and culturing (Khan et al., 2018).

Technique	Stem Cell Type	Isolation Method	Culturing Method	Advantages	Limitations
Embryo Dissection	Embryonic Stem Cells (ESCs)	Manual dissection, laser dissection, immunosurgery	Feeder-dependent or feeder-free systems on specialized media	High pluripotency; Unlimited self-renewal potential	Ethical concerns; Risk of teratoma formation; Potential for immune rejection
Bone Marrow Aspiration/ Biopsy	Hematopoietic Stem Cells (HSCs)	Aspiration from iliac crest or sternum; Biopsy from iliac crest	Liquid cultures with growth factors; Co-culture with stromal cells	Relatively easy to obtain; Well-established protocols; No ethical concerns	Limited differentiation potential (blood cells only); Invasive procedure
Mobilized Peripheral Blood Collection	HSCs	G-CSF administration followed by apheresis (blood separation)	Similar to bone marrow culture	Less invasive than bone marrow aspiration; Higher yield of HSCs	Requires G-CSF administration; Possible side effects
Adipose Tissue Harvest	Mesenchymal Stem Cells (MSCs)	Liposuction or surgical excision	Adherent cultures on specialized media	Abundant source; Easy to obtain; Minimal ethical concerns	Lower differentiation potential compared to ESCs; Potential for contamination
Cell Reprogramming	Induced Pluripotent Stem Cells (iPSCs)	Transfection or transduction of reprogramming factors (Oct4, Sox2, Klf4, c-Myc) into somatic cells	Similar to ESC culture	Avoids ethical concerns of ESCs; Patient-specific cells possible; No immune rejection	Reprogramming efficiency can be low; Risk of genetic abnormalities; Concerns about long-term safety
Umbilical Cord Blood Banking	HSCs, MSCs	Collection of cord blood after birth	Cryopreservation for future use	Rich source of stem cells; Non-invasive; Easily accessible; No ethical concerns	Limited quantity available; Not suitable for all patients

4. 1. Biopsy and Enrichment of Stem Cell Samples

Another procedure that is usually traditional but fundamental in stem cell research is isolating stem cells from other sources. It is one of the early but very important processes inherent in stem cell research. Subsequently, many methods have been developed to derive various kinds of stem cells, which depend on the cell they belong to and the tissue they originate from.

Embryonic Stem Cells (ESCs): The stem cells that are commonly used are the Embryonic Stem Cells, which are collected from the inner mass of the blastocysts, which are termed the early stages of the embryos after fertilization. This isolation method could freeze some in vitro procedures, such as immunosurgery or laser disaggregation, to purify the ICM from the trophectoderm (Xu et al., 2014). This is a very sensitive process because the ESCs which is supposed to be isolated

must be healthy and, indeed, pluripotent. Subsequently, they can be grown on conditioned MEFs or serum-free using knockout (KO) basal media. These media formulations usually include KSR, bFGF, and LIF, maintaining pluripotency and minimizing differentiation of ESCs (Lee, 2013).

Adult Stem Cells (ASCs): ASCs are in various tissues and organs of the adult organism, for example, the bone marrow, adipose tissue, and umbilical cord blood. The isolation methods of ASCs are not the same, depending on the tissue origin as well as the stem cell type. For example, blood-making stem cells known as hematopoietic stem cells (HSCs) are usually isolated from the bone marrow or the peripheral blood by methods. Such as density-gradient centrifugation or fluorescence-activated cell sorting, where cells are sorted depending on the receptors on their surface. MSCs capable of in vitro self-renewal and differentiating into multiple lineages while also exerting immunosuppressive effects (Bassi et al., 2011). These are obtained by either adherence of the culture to plastic or by immuno-selecting the culture for MSC markers from either the bone marrow aspirate.

Induced Pluripotent Stem Cells (iPSCs): The generation of iPSCs also involves the reprogramming of adult somatic cells like the skin fibroblasts, blood cells, etc., back to the state of embryonic-like cells using factors. This reprogramming process is made possible by the transduced four transcription factors: The genes Oct-4, Sox-2, Klf-4, and c-Myc to be delivered into the somatic cells (Jatving & Schepers). For this reason, practices like viral transduction, non-integrating vectors, and direct gene delivery, including proteins, or even mRNA, have been used. Subsequently, the iPSCs are maintained in the same way as ESCs to retain their ability to remain stem cells and not differentiate.

4.2 Stem Cells in the Culture

Due to tissue and organ generation, it is vital to organize stem cell long-term preservation and stem cells' cultivation in a culture medium for experimental and clinical needs. This has to be offered in sterile ways and conditions like culture media, adequate growth amenities, and types of substrates. Common culture media for both ESCs and iPSCs are based media combined with FBS or recognized substitutes for FBS since they supply the needed nutrients and growth factors essential for the cells' sustainable growth. Besides, to manifest the ability of cells to differentiate into multiple lineages, bFGF and LIF are added to the culture medium since they help retain the undifferentiated state of such cells (Shoni et al., 2014).

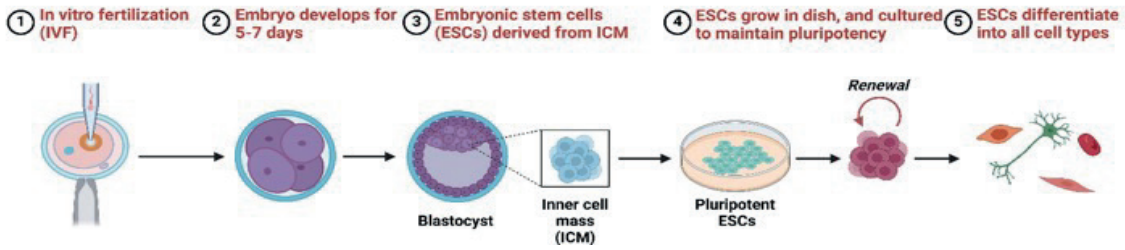


Figure 4. Stem Cell Isolation and Culture Method

Culture conditions of ASCs, including MSCs, are culture media containing FBS or hPL and specific growth factors and cytokine to support growth and maintain the ability of ASCs to differentiate into more than one cell lineage (Mangum et al., 2017). Therefore, specific cultural conditions may be necessary for various types of ASCs based on their characteristics and the conditions they specify. This is a feature that directly influences stem cells, this is in regards to the physical form of the culture system. Factors like oxygen tension, substrate stiffness, and cell density ways stem cell self-renewal, differentiation, and survival. For instance, low concentration of oxygen and high oxygen tension (hypoxia) enhances the self-renewal and survival of HSCs, and substrate stiffness controls the differentiation of MSCs into osteoblasts and adipocytes (X. Zhang

et al., 2022). Hence, it can be concluded that the stem cell isolation and culture methodology, or rather, their manipulation, has helped in the advancement of stem cell technology (Figure 4). The researchers are optimizing these techniques in every possible manner and the discovery of stem cell biology and realizing the potential in forming regenerating medicine and several other therapeutic methods.

4. 3 Genetic and Epigenetic Modification

In addition, there is germ-line engineering and/or epigenetic modification that has advanced the control of stem cells and enhanced any genetically defective genes. These techniques have greatly improved the likelihood and strength of studying stem cells, disease simulation, and possible treatments.

CRISPR/Cas9 and other Gene Editing Tools

Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR-associated protein 9 (CRISPR/Cas9) is an efficient and multimodal technique for stem cells' gene editing (Kato-Inui et al., 2018). A technique that allows for intentional genome modification by using double-strand breaks in the DNA that are then repaired either through NHEJ or HDR (Figure 5). NHEJ is relied on for gene disruption mostly in small insertions, while HDR is used in the generation either of single nucleotide variations (SNVs) or in s on inserting other sequences of interest in the genome. However, for the use of CRISPR/Cas9, has been used to genetically alter disorders in patient-specific iPSCs in stem cell research (Qin & Gao, 2016). For instance, some of the works revealed that the mutations associated with diseases such as cystic fibrosis, sickle cell anemia, and Duchenne muscular dystrophy can be repaired in iPSCs for autologous cell therapy. CRISPR/Cas9 has also been applied to introduce reporter genes and fluorescent tags into stem cells, tracking the behaviors and development as the stem cell differentiates (Bao et al., 2019). Hence, apart from the CRISPR/Cas9 system of gene editing, there are other modes of gene editing applied in stem cells, and they include the zinc finger nucleases (ZFNs) and the transcription activator-like effector nucleases (TALENs). These technologies utilize designed DNA binding proteins that affix to specific target sequences within the DNA to induce double-strand breaks that make gene editing quite easier, like that of CRISPR/Cas9 (Saber Sichani et al., 2023). Some of these technologies have been developed to some extent and implemented in practice, although less frequently than in the case of using recombinant proteins from the company's 'storehouse', because of the design and synthesis of the specific DNA-binding proteins required to control target genes.

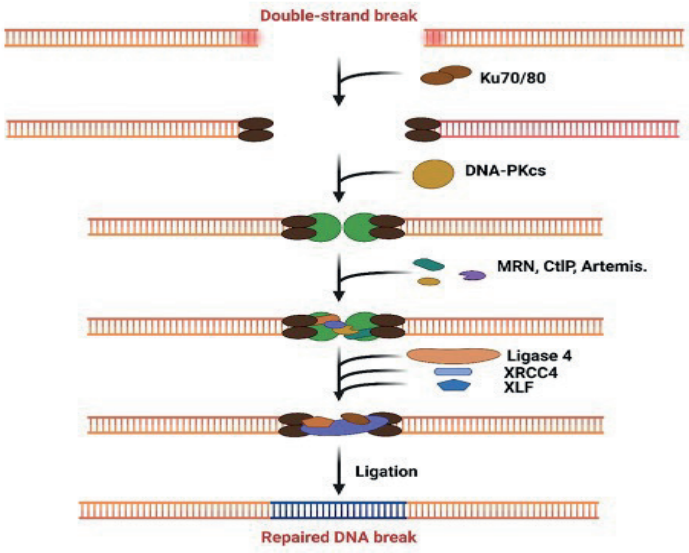


Figure 5. Mechanism of Non-Homologous End-Joining of Double-Strand Breaks

Epigenetic modifications and Their effects

Epigenetic changes are also executed through DNA and histones as a means of DNA methylation to regulate the extent of gene expression rather than the actual genetic code. These changes are particularly reversible and can be controlled by various signals from the environment or developmental needs; that is why they are the subject of the study of stem cells (Shenghui et al., 2009). DNA methylation is commonly defined as an addition of a methyl group to the cytosine base of the DNA molecule and is typically observed in CpG dimer (Ren et al., 2018). This alteration is mostly associated with gene silencing and has a crucial role in maintaining the specialized characteristics of cells. For instance, stem cells exhibit demonstrably finite DNA methylation, and these can be rewired during the embryo organism's development and cell specialization process. Concerning the histones, the covalent modifications involve acetylation, methylation, phosphorylation, and ubiquitination, and these occur on histone proteins. It also carries the ability to alter the conformation or chromatin to give more or less access to the transcription factors and other regulating proteins to transcribe genes (Todeschini et al., 2014). Histone modifications are crucial for maintaining stem cells in an undifferentiated or pluripotent state and for altering between these two states, that is, the self-renewing state or the differentiation state of stem cells. Thus, considering the specifics of the epigenetic process of manipulating stem cells, it is possible to conclude that another tool for controlling cell fate and function has been revealed. For instance, the small molecules and other epigenomic factors for the differentiation of iPSCs to several cell types required for regenerative medicine are under investigation. Also, it is mentioned that epigenetic changes are linked with many diseases including cancer. Research concerning epigenetic events in stem cells can thus offer fresh management solutions to numerous diseases (Dompe et al., 2020).

4. 4. Stem Cell Imaging and Tracking

Consequently, cell labeling methodologies and imaging techniques have become firmly established as essential tools in stem cell biology to help researchers follow stem cell development within culture plates and animal models (Eglen & Reisine, 2011). They contribute to acquiring information about alterations in the behavior of stem cells, their migration, development, interaction with the adjacent cells, and their use in clinical procedures, which aids in setting up stem cell therapies in clinics.

Approaches to the monitoring of mesenchymal stem cells

Many methods have been employed in staining stem cells; several factors influence the efficiency of staining the particular stem cells depending on the intended application and the type of stem cells as well as the localization and time limitation of the chosen technique.

1. Genetic Labeling: This approach has used stem cells which have been engineered to express reporter genes, which include fluorescent proteins such as green fluorescent protein (GFP) or bioluminescent enzymes such as luciferase; hence, they can be seen over time with their progeny (Jurgielewicz et al., 2017). This method is flexible and can be achieved by viral transduction or transfection or the use of transgenic animal explants expressing the reporter gene placed under the regulation of the stem cell, particularly the promoter. Genetic labeling is used in long-term stem cell tracking it provides data concerning stem cell differentiation potential and tissue integration (Stroh et al., 2011). However, it involves changing the cells' genes, which can prove risky as far as clinical application is concerned.

2. Cell Surface Markers: Stem cells have certain markers, which are proteins attached to the cell surface and help recognize the cell type. These markers can be targeted by antibiotics tagged by fluorescent dyes with the help of labels; these markers can be visualized with flow cytometry or immunofluorescence microscopy (B. Zhang et al., 2022). This method is rather noninvasive and barely affects the cell, though alterations in cell surface marker expression density prevent long-term identification of certain cells.

3. Magnetic Resonance Imaging (MRI): MRI has in no way been known to be injurious to the human body, and it can be utilized to track stem cells that have been labeled with magnetic nanoparticles (Cromer Berman et al., 2011). Body cells then consume these particles and make a signal that can be checked through MRI machines. This allows one to track the stem cells in live animals and, therefore, get substantial data on biodistribution, migration, and engraftment in the tissues. However, to some of the other imaging techniques MRI could be comparatively less sensitive and lower in spatial resolution.

4. Nuclear Imaging: Albeit the radioactivity of the radioisotope used to label the stem cells could be technetium 99m or indium III, gamma rays are produced that can be identified using SPECT and or PET scanners (Bal, 2007). This procedure makes positron emission tomography possible and can be used to study the distribution of stem cells and their migration in the entire body without biopsy, but the technique requires the usage of radioactive materials, which is a complication concerning safety. Throughout the course of this dissertation, two broad approaches that aim to provide a more in-depth insight into the tissue, cell, and subcellular level characteristics of diseases will be described:

5. In vitro imaging: Stem cell imaging can be done on culture dishes or any man-made structures, such as under the microscope. Histo-to-chemical analysis and live cell imaging procedures are immensely useful for researchers to analyze stem cells' morphological, growth, and developmental status and their mobilization in the same context. These techniques are important to investigate the consequences of different conditions: other interventions such as drugs, cytokines, or genetic manipulation on the stem cell's activity (Ceccarelli et al., 2020).

6. In vivo imaging: This includes attempting to visualize the stem cells in their most natural habitats, which are the living organisms. Positive results attained by this knowledge include bioluminescence imaging, MRI, SPECT, and PET, which assist the researcher in observing stem cell transplantation in life to determine the survival and engraftment potential of cells and their differentiation ability in host tissue, in addition to therapeutic efficiency. Therefore, imaging is of significant use in stem cell-based therapies' evaluation both preclinically and in clinical settings in vivo (Klontzas et al., 2021).

5. Applications in Regenerative Medicine

It becomes one of the most complex tissues in the body mainly due to the neurons and glial cells that make it up, though they are believed to have low inherent regenerative capabilities. However, stem cell research has opened new chances for neural recovery for SCIs and NDDs, and these are very good developments in neural treatment.

5.1 Repairing Spinal Cord Injuries

Medical consequences of spinal cord lesions are paralysis and loss of feeling in the regions of the body beneath the area of the injury because the connection between the brain and the rest of the body is interrupted. The current stem cell therapies are said to unlock ways of enhancing processes in neural repair that affect SCI patients' overall functionality (Zhang et al., 2019).

Neural Stem Cells (NSCs): Labeled NSCs, as they are long-lived cells found in the adult mammalian, which are capable of self-renewal and differentiation into any cell of the nervous system including neurons, astrocytes, and oligodendrocytes; they are the three major classes of cells of the nervous system (Daynac & Petritsch, 2017). The preceding studies have shown that the propriety of NSCs for transplantation in the ischemic spinal cord can promote axonal regeneration, oligodendrocyte reforming, and functional recovery in animals. NSCs release factors that have therapeutic attributes on damaged neurons in the following manners: generate new healthy neurons and launch opinions that support the survival and growth of neurons besides decreasing inflammation. The current literature's research studies show that several clinical trials regarding

NSC transplantation are still undergoing for treating SCI patients (Hu et al., 2021).

Mesenchymal Stem Cells (MSCs): However, because MSCs are not neural stem cells, they have been reported to hold some potential in SCI, the outcome of which appears from immunomodulatory and neuroprotective properties. Studies have shown that MSC transplantation restores the blood barrier, decreases inflammation, enhances endothelial cell growth, remodeling, and repair in the injured cord, and, therefore, the functional outcomes in animal models (Lv et al., 2021). Clinical trials are also useful in establishing the benefits of MSCs in addressing situations of SCI patients.

5.2 Repairing Neurodegenerative Diseases

Neurodegenerative diseases, such as Parkinson's, Alzheimer's, or ALS, are diseases in which neurons and any functions have started fading. Critics have contended that stem cell therapies can replace the neurons that are destroyed, safeguard other neurons from the disease's effects, and slow down or halt the disease's progression.

Neural Stem Cells (NSCs): Neurogenic stem cell transplants have also been studied in the context of various NDDs in animal models, and the reports have revealed positive outcomes (Guerreiro & Maciel, 2023). Thus, Demetri and colleagues show that with the help of NSCs and the creation of dopaminergic neurons in the brains of animal models of Parkinson's disease, it is possible to enhance motor function. Research in animal models has since shown that NSC transplantation leads to a decrease in amyloid plaques and an increase in neurogenesis apart from the enhancement of cognition for Alzheimer's disease (Fouad, 2019).

Induced Pluripotent Stem Cells (iPSCs): The generation of iPSCs with the characteristics of the patient has opened up new vectors for apprehending and designing drugs for NDDs (Vijay et al., 2023). This is important because if you have iPSC-derived neurons carrying the genes for a specific disease, you can ascertain or determine the cause of the disease besides experimenting with drugs on specific neurons in a plate, a technique that is referred to as pharmacogenomics or, more specifically, personalized medicine. Besides, iPSC is meant for medical application with cell replacement therapies; this concerns the fact that neurons generated from patients' iPSCs may be grafted into the brain to replace the damaged ones (Paolini Sguazzi et al., 2021).

5.3 Neural Stem Cells: A New Development in the Field

For the ONS, discoveries that have come up have been of immense importance in studying the expansion and application of the theory. Certain of the recent tactics that have been developed were to refine the process of isolation and multiplication of NSCs and viability in transplantation (Abati et al., 2019). Hence, there are ongoing efforts to try and use biomaterials and tissue engineering to form structures through which stem cells that are to be transplanted, will be given direction and support as far as their functionality is concerned. Furthermore, technological advancements, particularly in gene editing like CRISPR/Cas9, have eased the chances of controlling NSCs for enhanced treatment (Lee et al., 2020). For instance, CRISPR/Cas9 has been used to cure NDDs based on fixing a mutational mistake in a couple of iPSC-derived neurons, The World's First Gene Editing for NDD treatment (De Guidi, 2021). However, some limitations have been raised in the current studies, which constitute a preliminary barrier to translating such results into practice. Further studies have to be conducted to determine the standards concerning stem cell transplants, raise the rates of survival and integration of the stem cells, and ascertain the efficiency and security of stem cell therapy.

5.4 Applications in Regenerative Medicine: Musculoskeletal Regeneration

Joint and muscular disorders Such disorders involve the bones, cartilage, or muscles and are prevalent hence being painful to the patient. Stem cells as a source of regenerative medicine can be

viewed as a perspective for repairing and regenerating these tissues; thus, the further development of orthopedic therapy with better chances to improve patient's quality of life may be provided (Akpancar et al., 2016).

Bone Repair

Most of the time, the bone heals itself; therefore, this process involves calling for help only when the defect is of a certain size or the healing process is in danger for one reason or another. Thus, the inherent characteristic of stem cells, particularly MSCs, to transform into osteoblasts makes stem cells provide substantial solutions to bone regeneration (Hollý et al., 2021). MSCs can be harvested from BM, Adipose tissue, and UC, and the cells can be either directly transplanted into the bone defect or placed into bioengineered scaffolds. The research done on pre-clinic and clinical studies has shown that MSC enhances bone repair in diseases such as nonunion fractures, osteonecrosis, and spinal fusion.

Cartilage Repair

Chondrocytes, which are the cells with the ability to produce cartilage, are relatively poor at repair and regeneration mechanisms even though cartilage is a smooth, flexible connective tissue that lays the slippery floor on all bones that rub together in the joints (Nochehdehi et al., 2023). As a result, cartilage pathologies are associated with such clinical manifestations as pain and stiffness and osteoarthrosis as a form of degenerative-dystrophic changes in joints. The options for cartilage repair using stem cells include MSCs and chondrocytes or cartilage cells. MSCs can differentiate into chondrocytes and synthesize cartilage-specific ECM, therefore active in cartilage regeneration (Phull et al., 2016). Autologous chondrocyte implantation (ACI) involves the following procedures; first, the healthy cartilage cells are harvested from the patient. Next, those cells are cultured to make them look like healthy cells, and those cells are then implanted in the affected region. Some of the studies that have been conducted are as follows. ACI can be documented for reporting satisfactory results in the management of focal chondral and cartilaginous lesions in the knee (Jones & Peterson, 2007).

Muscle Repair

Such injuries tend to affect the basic structures and abilities of the affected body parts, with quality of life being seen more where muscles are involved. Among the cell-based therapies, some of the specific cells are muscle satellite cells and mesoangioblasts, which have the capability of muscle regeneration. These stem cells are present either between the muscle fibers or as a component of the nuclei of the muscle cells; their main functions are muscle hypertrophy and regeneration (Blaauw & Reggiani, 2014). The Mesoangioblasts are the kind of stem cells that are vessel-associated and dwelling in skeletal muscles; they can pen various kinds of cells with the help of fusion through which muscular fibers are also produced (Yedigaryan et al., 2022). Ex vivo, the future of these stem cells has demonstrated their ability to enhance muscle repair upon injury and boost strength and functioning (Qazi et al., 2019).

5.5 Applications in Orthopedic Treatments

Stem cell-based therapies are being investigated for a wide range of orthopedic applications, including research in stem cell applications for orthopedics has been active for numerous applications such as:

Osteoarthritis: MSCs and other stem cell types are discussed for the limitation or radical cure of OA by promoting cartilage regeneration and modulating the inflammation and immune responses (Liu et al., 2022).

Non-union fractures: MSCs, along with BMAC, consist of a mixture of stem and progenitor cells and are used to enhance bone formation in non-union fractures due to the body's inability to

heal (Haeusner et al., 2023).

Tendon and ligament injuries: At the time, many different stem cells, such as TDSCs and MSCs, have been investigated, and the tendon and ligament healing potentiality (Wei & Lu, 2021) of these cells has been studied for improving post-injurious healing and reducing the probability of re-injury. However, certain problems, such as the optimal way of delivering stem cells, the source of a constant stem cell supply for the patients, and the other effects of these anti-osteoporotic therapies in the perioperative period of the surgery, have not been optimized yet. Such modern approaches are focused on solving these problems and transferring the possible outcomes of preclinical investigations into clinical applications for managing musculoskeletal diseases.

5. 7 Applications in Regenerative Medicine: hematopoietic stem cell transplantation (HSCT)

Nevertheless, hematopoietic stem cell transplantation (HSCT) is the possible curative treatment method concerning the capabilities of hematopoietic stem cells (HSCs) to provide the repair of impaired or mutilated bone marrow (Alvin, 2021). HSCs are found in the BM, PB, and cord blood they are, by default, the only cells that make all the blood cells and are, therefore, ideal for re-populating BM of patients with diseased blood cell-making factories.

Treatments arise from the assessment of blood-related diseases and cancer genes

HSCT has, however, been useful in the management of a combination of hematological malignancies, for example, leukemia, lymphoma, and multiple myelomas (A Patel & Rameshwar, 2011). Railwayman is also applied in managing other nonneoplastic hematological diseases like aplastic anemia, sickle cell anemia, and thalassemia. HSCT can be either autologous, in which harvested Stem cells are used from the patient's/own marrow and Stem cells, which are harvested from the Stem cells of a related donor, or a matched unrelated donor and syngeneic Stem cells harvested from an identical twin. In the context of cancer treatment, HSCT serves two main purposes in which concerning cancer therapy, HSCT has two principal functions:

1. Myeloablative Therapy: To treat Hepatoid carcinoma, the patient is given a high intensity of chemotherapy or radiation to eliminate the cancerous cells in the bone marrow. While this treatment eliminates the body’s required, healthy HSCs tend to myelosuppression as well as make the patient immune deficient (DeFilipp et al., 2022).

2. Stem Cell Rescue: HSCs are transplanted by replacing the defective hematopoietic system of the body either from the patient’s bone marrow or from donor bone marrow, which is referred to as allogeneic transplant in cases where the patient's transplant, which is referred to as autologous transplant is not feasible. The HSCs are introduced in the bone marrow of the patients, where they differentiate into different kinds of blood cells, providing a direct replacement to the unhealthy cells or those that may be invaded by the disease (Kandarakov et al., 2022). In the case of nonmalignant hematologic diseases, the procedure for HSCT involves transplanting normal HSCs into the patients’ bodies to replenish normal blood and modify the character of hematological disorders.

Current State and Challenges in Organ Transplantation

HSCT has evolved over the years owing to the techniques of stem cell mobilization, collection, and processing, and changes in the condition for pre-transplant regimens, which has improved survival and less toxicity (Wade, 2023). Another difference is the increase in the use of peripheral blood stem cells (PBSCs) compared to bone marrow because it is easy to harvest and engraft faster. There have also been non-myeloablative or reduced-intensity preparations made for elderly patients and patients with previous illnesses; therefore, HSCT can be applied to more patients (Lekakis & De Lima, 2008). However, this field still poses some difficulties in the case of an increase in the complexity of HSCT and potential complications, including GVHD, infection, and organ toxicity

(Reis et al., 2016). The problem arises where the conditioning regimen of the donor stem cells recognizes the recipient's tissues as foreign entities and proceeds to produce immune cells to attack the target tissue, which may range from mild form to severe form. Morbidity concerns result from immunosuppression, which is witnessed after the conditioning regimen; acute organ toxicity tendings result from either the high dose chemotherapy or radiation therapy (Weichselbaum et al., 1980). Recovery research today entails efforts to minimize the mentioned complications; this involves donor-recipient compatibility, choice of regimen conditioning, and measures of combating GVHD (Timofeeva et al., 2022). New ways of promoting the culture of HSCs and engraftment are also being established to enhance the efficiency of the HSCT. Hematopoietic stem cell transplantation remains one of the key advancements in managing blood disorders and malignancy, as it offers definitive therapy to many of the affected clients. That is why new advancements in transplantation surgery, along with advancements in the management of such patients, have effectively improved the salvage modality of this intervention.

6. Roles in Disease Simulation and New Drugs Development

Due to the development of stem cells, especially iPSCs, disease modeling and drug discovery have been enhanced. Techniques of deriving the patient's iPSCs and their subsequent differentiation into multiple lineages have provided new roads toward understanding the pathogenesis of diseases, identifying biomarkers, and finding specific therapies for patients.

Disease Modeling

One serious deficiency of the present disease models is that they are either animal models or immortalized cell lines and do not represent human diseases regarding genetics and phenotype. Unlike this, iPSCs can be derived exclusively from patients with specific diseases with clearly identifiable genetic mutations and epigenetic tags identical to the patient's cells (Jang & Ye, 2016). This makes it possible to create disease models that replicate the human organism's status as it assists in understanding diseases' mechanisms and pathogenesis. For instance, iPSCs derived from patients with neurodegenerative diseases, Parkinson's and Alzheimer's disease, have been utilized in modeling such diseases and understanding the molecular activity and cellular signaling routes (Yefroyev & Jin, 2022). In this manner, it is possible to investigate the neuronal differentiation of iPSC, the appearance of a disease, or certain processes, such as the formation of aggregates and neuronal death in a plate. These models have assisted in identifying new therapies for all these diseases besides testing compounds that could assist in preventing or treating these diseases. Similarly, iPSCs of patients with Cardiomyopathy and Arrhythmia have been applied to fashion in vitro diseases of the Cardiovascular system and to compare the cellular phenotypes consequent to disease-relevant alleles. These models have assisted in elucidating the processes of cardiac dysfunctions and in the development of new drugs that operate at molecular levels (McGregor & Dunn, 2006).

Drug Screening and Toxicology

Thus, the stem cell-based disease models are beneficial in drug discovery and also in assessing the toxic effects. An existing technique in drug identification largely relies on animal testing, and success attained from such could be far from an actual estimate of successful drugs in man because of species differences (Liebsch et al., 2011). On the other hand, the cells derived from iPSCs represent a real human/system of speaking to evaluate the response to drugs and possible adverse effects. Thus, the iPSC-based HTS platforms for drug discovery have been developed so that a large number of compounds in the library can be tested for therapeutic potential. It can also identify small molecules that may preserve disease phenotypes, repair diseased cells, or modulate specific signaling pathways. There are also opportunities to compare the differences in drug sensitivity in the iPSC-derived cells originating from patients with different genetic profiles or disease types (Grskovic et al., 2011). Furthermore, the derived cells from the iPSCs can be used for the study of

the toxicity of the desired drug candidate on the stem cell's viability, proliferation, differentiation, and functional profile alteration (Genova et al., 2019). This makes it possible for the researchers to identify some of the safety problems before the drug is ready to be injected into patients, which goes a long way in preventing the impacts on the patients participating in clinical trials.

7. Future Directions and Recommendations

Stem cell research is a relatively new and rapidly developing branch of science in which discoveries can dramatically alter the functioning of medicine. However, some issues and ethical factors are also taken into consideration regarding the intended objectives for applying stem cell-based therapy.

Enhancing stem cell survival and engraftment: One of the major challenges of stem cell transplants is that cells do not fare very well because engraftment is fairly poor. The current strategy is to find a definitive mode of handling the problem of survival and integration of the transplanted cell into the host tissue; this uses ideas concerning biomaterials as well as tissue engineering (Mooranian et al., 2021).

Optimizing stem cell differentiation and maturation: Nevertheless, it is difficult to continue to possess the abilities of differentiation to various cell types, direct their differentiation, and substantiate that they become functional cells. Research should be done concerning the type of signals that promote the differentiation of stem cells into the desirable lineages and the culture conditions that promote the differentiation of stem cells into fully mature cells (Cai et al., 2007).

Addressing safety concerns: Even in cell therapy, the stem cells that are prospective for the treatment of diseases are still able to form tumors or are recognized as foreign bodies by the immune system of the body. The long-term safety of stem cell therapies also poses challenges for preclinical and clinical trials (Squillaro et al., 2016). It must be performed before the recipients' immune systems can be protected against harm resulting from the erroneous placement of these cells and their migration to locations that are problematic for the recipient's body.

Scaling up production and ensuring quality control: Because stem cell clinical application requires mass production of stem cells, this can only be achieved in a process that affords cell quality and consistency in the stem cell manufacturing process. Therefore, enhancing quality assurance and developing policies concerning stem cells is important to apply such findings to practice (Papassavas et al., 2015).

Personalizing stem cell therapies: Popular information technologies such as genomic and Precision medicine have provided options for personal stem cell therapies. They include disease/ Genetic Map responsive treatment. This strategy can also raise the efficiency of stem cell therapies because it identifies the prospect of a specific patient reacting positively to a treatment and minimizes the chances for an adverse outcome (Desgres & Menasche, 2019). Recommendations for future research and development include:

1. Investing in basic research: Stem cell therapies as safe, effective means of treatment, additional insight into stem cell biology, namely the mechanisms of stem cell self-renewal and determination as well as their interactions with the immediate environment, is needed (Li et al., 2022).

2. Developing standardized protocols: Another requirement is the severity of procedures applied to stem cells' isolation as well as their further cultivation and differentiation within cells, as this condition influences the possibility of achieving the same results in different labs or clinics (Sensebe et al., 2010).

3. Collaborating across disciplines: Stem cell research is an area of research that means that various professionals, engineers, biologists, clinicians, and regulatory scientists can implement

what has been learned in the laboratories (Wainwright et al., 2006).

4. Investing in education and outreach: Stem cell therapy is also an unclear area, so society and those offering care need to educate themselves on the positive changes that may result from the use of new technology and the dangers attributed to stem cell therapies (Einsiedel & Adamson, 2012). Due to stem cells' ability of future changes in the medical practice and millions of patients, it can be considered as one of the most significant discoveries. If one comprehends and manages to combat the difficulties and ethical issues arising in the course of completing the work of this chapter, advancing the efforts in researching, developing, and enlightening, one can contribute to the potential of stem cell therapies and open the possibility to enhance the future of the regenerative medicine.

8. Conclusion

Stem cell science has become one of the most promising fields in modern health care science, offering new directions in understanding diseases, treating them, and even regenerating tissues. Because of their properties, as well as their ability to replenish and convert themselves into any cell of choice, stem cells apply to creating new therapeutic models. In this chapter, researchers have differentiated stem cells in brief by classification, such as embryonic stem cells, adult stem cells, and induced pluripotent stem cells, and have tried to exhibit the picture regarding the differences and the features of each kind of stem cell broadly considering the possibilities of their use in the treatment of diseases. Two of them explained how stem cells operate and the factors, including stem cell microenvironments, signaling, and epigenetic mechanisms controlling self-renewal, differentiation, and plasticity. Furthermore, we have discussed the future application of stem cells in regeneration medicine, such as cardiovascular regeneration, neural regeneration, musculoskeletal tissue regeneration, and Hematopoietic stem cell transplantation. We have also mentioned using stem cells in disease modeling, which means disease and drug analysis and screening, as well as customized medicine. In total, the successes of stem cell research are quite sensational; nonetheless, the challenges remain critical. Stem cell-based therapies' safety and effectiveness, how the cells are delivered how the cells engraft and the ethics of the issues all are crucial in the attempt to translate discoveries in the lab to real-life scenarios. For this; as stem cell biology, engineering and the successful translation of such findings into medical applications progresses, stem cell-based therapies should have a promising future. Thus, stem cell research can be concluded to be a significant discovery in medical science that has transformed the very picture of the modern curing paradigm and, at the same time, opened up brand new vistas for the treatment of countless diseases. When proper respect is accorded to stem cells, human beings can advance the usefulness for reshaping tilted tissues and severe diseases and, in this way, boost health. The road might be full of challenges; however, the reward is priceless; thus, come up with the vision of a future where regenerative medicine will be the backbone of medicine.

References

A Patel, S., & Rameshwar, P. (2011). Stem cell transplantation for hematological malignancies: prospects for personalized medicine and co-therapy with mesenchymal stem cells. Current Pharmacogenomics and Personalized Medicine (Formerly Current Pharmacogenomics), 9(3), 229-239.

Abati, E., Bresolin, N., Comi, G. P., & Corti, S. (2019). Preconditioning and cellular engineering to increase the survival of transplanted neural stem cells for motor neuron disease therapy. Molecular Neurobiology, 56, 3356-3367.

Akpancar, S., Tatar, O., Turgut, H., Akyildiz, F., & Ekinci, S. (2016). The current perspectives of stem cell therapy in orthopedic surgery. Archives of trauma research, 5(4).

Al-Jedai, A. H. (2008). Notch signalling in CD34+ cells in chronic myeloid leukaemia. The

University of Manchester (United Kingdom).

Alvin, G. (2021). Cell therapy: the new approach to der-matology and dermatologic surgery. Clin Surg, 5(8), 1-14.

Baba, A. I., & Câtoi, C. (2007). Tumor cell morphology. In Comparative oncology. The Publishing House of the Romanian Academy.

Bal, C. (2007). Radio-isotopic techniques. In.

Bao, X., Adil, M. M., Muckom, R., Zimmermann, J. A., Tran, A., Suhy, N., Xu, Y., Sampayo, R. G., Clark, D. S., & Schaffer, D. V. (2019). Gene editing to generate versatile human pluripotent stem cell reporter lines for analysis of differentiation and lineage tracing. Stem Cells, 37(12), 1556-1566.

Bassi, Ê. J., Aita, C. A. M., & Câmara, N. O. S. (2011). Immune regulatory properties of multipotent mesenchymal stromal cells: where do we stand? World Journal of Stem Cells, 3(1), 1.

Beerman, I., & Rossi, D. J. (2015). Epigenetic control of stem cell potential during homeostasis, aging, and disease. Cell stem cell, 16(6), 613-625.

Birbrair, A., & Frenette, P. S. (2016). Niche heterogeneity in the bone marrow. Annals of the New York Academy of Sciences, 1370(1), 82-96.

Blaauw, B., & Reggiani, C. (2014). The role of satellite cells in muscle hypertrophy. Journal of muscle research and cell motility, 35, 3-10.

Bonaventura, G., Iemmolo, R., Attaguile, G. A., La Cognata, V., Pistone, B. S., Raudino, G., D'Agata, V., Cantarella, G., Barcellona, M. L., & Cavallaro, S. (2021). iPSCs: A preclinical drug research tool for neurological disorders. International journal of molecular sciences, 22(9), 4596.

Burchfield, J. S., & Dimmeler, S. (2008). Role of paracrine factors in stem and progenitor cell mediated cardiac repair and tissue fibrosis. Fibrogenesis & tissue repair, 1, 1-11.

Burel, M. (2022). Microenvironment Remodeling as a Novel Mechanism for Germline Stem Cell Competition New York University].

Cai, L., Ye, Z., Zhou, B. Y., Mali, P., Zhou, C., & Cheng, L. (2007). Promoting human embryonic stem cell renewal or differentiation by modulating Wnt signal and culture conditions. Cell research, 17(1), 62-72.

Ceccarelli, S., Pontecorvi, P., Anastasiadou, E., Napoli, C., & Marchese, C. (2020). Immunomodulatory effect of adipose-derived stem cells: the cutting edge of clinical application. Frontiers in Cell and Developmental Biology, 8, 236.

Çetin, E. A., Babayiğit, E. H., Özdemir, A. Y., Erfen, Ş., & Onur, M. A. (2023). Investigation of UV-treated mesenchymal stem cells in an in vitro wound model. In Vitro Cellular & Developmental Biology-Animal, 59(5), 331-345.

Cromer Berman, S. M., Walczak, P., & Bulte, J. W. (2011). Tracking stem cells using magnetic nanoparticles. Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, 3(4), 343-355.

Dawson, R., Beal, M. F., Bondy, S. C., DiMonte, D., & Isom, G. E. (1995). Excitotoxins, aging, and environmental neurotoxins: implications for understanding human neurodegenerative diseases. Toxicology and applied pharmacology, 134(1), 1-17.

Daynac, M., & Petritsch, C. K. (2017). Regulation of asymmetric cell division in mammalian neural stem and cancer precursor cells. Asymmetric Cell Division in Development, Differentiation and Cancer, 375-399.

De Guidi, C. (2021). Generation of induced pluripotent stem cells (iPSCs) lines deficient for genes associated with neurodevelopmental diseases using CRISPR/Cas9 technology. In.

DeFilipp, Z., Hefazi, M., Chen, Y.-B., & Blazar, B. R. (2022). Emerging approaches to improve allogeneic hematopoietic cell transplantation outcomes for nonmalignant diseases. Blood, The Journal of the American Society of Hematology, 139(25), 3583-3593.

Desgres, M., & Menasche, P. (2019). Clinical translation of pluripotent stem cell therapies: challenges and considerations. Cell stem cell, 25(5), 594-606.

Desmarais, J. A., Demers, S.-P., Suzuki, J., Laflamme, S., Vincent, P., Laverty, S., & Smith, L. C. (2011). Trophoblast stem cell marker gene expression in inner cell mass-derived cells from parthenogenetic equine embryos. Reproduction, 141(3), 321.

Dompe, C., Janowicz, K., Hutchings, G., Moncrieff, L., Jankowski, M., Nawrocki, M. J., Józkowiak, M., Mozdziak, P., Petitte, J., & Shibli, J. A. (2020). Epigenetic research in stem cell bioengineering—anti-cancer therapy, regenerative and reconstructive medicine in human clinical trials. Cancers, 12(4), 1016.

Eglen, R., & Reisine, T. (2011). Primary cells and stem cells in drug discovery: emerging tools for high-throughput screening. Assay and drug development technologies, 9(2), 108-124.

Einsiedel, E. F., & Adamson, H. (2012). Stem cell tourism and future stem cell tourists: policy and ethical implications. Developing world bioethics, 12(1), 35-44.

Ejtehadifar, M., Shamsasenjan, K., Movassaghpour, A., Akbarzadehlaleh, P., Dehdilani, N., Abbasi, P., Molaeipour, Z., & Saleh, M. (2015). The effect of hypoxia on mesenchymal stem cell biology. Advanced pharmaceutical bulletin, 5(2), 141.

Ericson, R. J. (2007). Bridging solutions to the religion and science conflict over human embryonic stem cell* research. George Mason University.

Foster, C. S., Dodson, A., Karavana, V., Smith, P., & Ke, Y. (2002). Prostatic stem cells. The Journal of Pathology: A Journal of the Pathological Society of Great Britain and Ireland, 197(4), 551-565.

Fouad, G. I. (2019). Stem cells as a promising therapeutic approach for Alzheimer's disease: a review. Bulletin of the National Research Centre, 43(1), 52.

Genova, E., Cavion, F., Lucafò, M., De Leo, L., Pelin, M., Stocco, G., & Decorti, G. (2019). Induced pluripotent stem cells for therapy personalization in pediatric patients: focus on drug-induced adverse events. World Journal of Stem Cells, 11(12), 1020.

Gordeeva, O. (2019). TGFβ family signaling pathways in pluripotent and teratocarcinoma stem cells' fate decisions: balancing between self-renewal, differentiation, and cancer. Cells, 8(12), 1500.

Grskovic, M., Javaherian, A., Strulovici, B., & Daley, G. Q. (2011). Induced pluripotent stem cells—opportunities for disease modelling and drug discovery. Nature Reviews Drug Discovery, 10(12), 915-929.

Guerreiro, S., & Maciel, P. (2023). Transition from animal-based to human induced pluripotent stem cells (iPSCs)-based models of neurodevelopmental disorders: Opportunities and challenges. Cells, 12(4), 538.

Haeusner, S., Jauković, A., Kupczyk, E., & Herrmann, M. (2023). cellularity in bone marrow autografts for bone and fracture healing. American Journal of Physiology-Cell Physiology, 324(2), C517-C531.

Hall, P. A., & Watt, F. M. (1989). Stem cells: the generation and maintenance of cellular diversity. Development, 106(4), 619-633.

Hollý, D., Klein, M., Mazreku, M., Zamborský, R., Polák, Š., Danišovič, Ľ., & Csöbönyeiová, M. (2021). Stem Cells and Their Derivatives—Implications for Alveolar Bone Regeneration: A Comprehensive Review. International journal of molecular sciences, 22(21), 11746.

Hu, X.-C., Lu, Y.-B., Yang, Y.-N., Kang, X.-W., Wang, Y.-G., Ma, B., & Xing, S. (2021). Progress in clinical trials of cell transplantation for the treatment of spinal cord injury: how many questions remain unanswered? Neural regeneration research, 16(3), 405-413.

Ikegami, K., Ohgane, J., Tanaka, S., Yagi, S., & Shiota, K. (2009). Interplay between DNA methylation, histone modification and chromatin remodeling in stem cells and during development. International Journal of Developmental Biology, 53.

Jang, Y.-Y., & Ye, Z. (2016). Gene correction in patient-specific iPSCs for therapy development and disease modeling. Human genetics, 135(9), 1041-1058.

Jatving, M., & Schepers, H. Induced pluripotent stem ce [] s: Wilt they be safe?

Jayaraman, S., Rajagopal, P., Periyasamy, V., Palaniyandi, K., Kumaran, R. I., Reddy, S. V., Balasubramanian, S., & Sambandam, Y. (2021). Signaling pathways influencing stem cell self-renewal and differentiation—special emphasis on cardiomyocytes. In Stem cells and aging (pp. 157-168). Elsevier.

Jha, B. S., Farnoodian, M., & Bharti, K. (2021). Regulatory considerations for developing a phase I investigational new drug application for autologous induced pluripotent stem cells-based therapy product. Stem Cells Translational Medicine, 10(2), 198-208.

Jones, D. G., & Peterson, L. (2007). Autologous chondrocyte implantation. Cartilage repair strategies, 137-165.

Jurgielewicz, P., Harmsen, S., Wei, E., Bachmann, M. H., Ting, R., & Aras, O. (2017). New imaging probes to track cell fate: reporter genes in stem cell research. Cellular and Molecular Life Sciences, 74, 4455-4469.

Kandarakov, O., Belyavsky, A., & Semenova, E. (2022). Bone marrow niches of hematopoietic stem and progenitor cells. International journal of molecular sciences, 23(8), 4462.

Karpowicz, P. A. (2004). A scientific and ethical investigation into the human retinal stem cell chimera: Manufacturing a monster? National Library of Canada= Bibliothèque nationale du Canada, Ottawa.

Kato-Inui, T., Takahashi, G., Hsu, S., & Miyaoka, Y. (2018). Clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein 9 with improved proof-reading enhances homology-directed repair. Nucleic acids research, 46(9), 4677-4688.

Khan, F. A., Almohazey, D., Alomari, M., & Almofty, S. A. (2018). Isolation, culture, and functional characterization of human embryonic stem cells: current trends and challenges. Stem cells international, 2018(1), 1429351.

Klontzas, M. E., Kakkos, G. A., Papadakis, G. Z., Marias, K., & Karantanas, A. H. (2021). Advanced clinical imaging for the evaluation of stem cell based therapies. Expert Opinion on Biological Therapy, 21(9), 1253-1264.

Lee, J., Bayarsaikhan, D., Bayarsaikhan, G., Kim, J.-S., Schwarzbach, E., & Lee, B. (2020). Recent advances in genome editing of stem cells for drug discovery and therapeutic application. Pharmacology & therapeutics, 209, 107501.

Lee, K.-H. (2013). Conditions and techniques for mouse embryonic stem cell derivation and culture. Pluripotent stem cells, 1, 85-116.

Lekakis, L., & De Lima, M. (2008). Reduced-intensity conditioning and allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia. Expert review of anticancer therapy, 8(5), 785-798.

Lewandowski, J., & Kurpisz, M. (2016). Techniques of human embryonic stem cell and induced pluripotent stem cell derivation. Archivum immunologiae et therapiae experimentalis, 64, 349-370.

Li, M., Jiang, Y., Hou, Q., Zhao, Y., Zhong, L., & Fu, X. (2022). Potential pre-activation strategies for improving therapeutic efficacy of mesenchymal stem cells: current status and future prospects. Stem cell research & therapy, 13(1), 146.

Liebsch, M., Grune, B., Seiler, A., Butzke, D., Oelgeschläger, M., Pirow, R., Adler, S., Riebeling, C., & Luch, A. (2011). Alternatives to animal testing: current status and future perspectives. Archives of toxicology, 85, 841-858.

Liu, S., Deng, Z., Chen, K., Jian, S., Zhou, F., Yang, Y., Fu, Z., Xie, H., Xiong, J., & Zhu, W. (2022). Cartilage tissue engineering: From proinflammatory and anti-inflammatory cytokines to osteoarthritis treatments. Molecular Medicine Reports, 25(3), 1-15.

Lloyd-Lewis, B., Mourikis, P., & Fre, S. (2019). Notch signalling: sensor and instructor of the microenvironment to coordinate cell fate and organ morphogenesis. Current opinion in cell biology, 61, 16-23.

Lv, B., Zhang, X., Yuan, J., Chen, Y., Ding, H., Cao, X., & Huang, A. (2021). Biomaterial-supported MSC transplantation enhances cell–cell communication for spinal cord injury. Stem cell research & therapy, 12, 1-16.

Malgieri, A., Kantzari, E., Patrizi, M. P., & Gambardella, S. (2010). Bone marrow and umbilical cord blood human mesenchymal stem cells: state of the art. International journal of clinical and experimental medicine, 3(4), 248.

Mangum, L. H., Natesan, S., Stone, R., Wrice, N. L., Larson, D. A., Florell, K. F., Christy, B. A., Herzig, M. C., Cap, A. P., & Christy, R. J. (2017). Tissue source and cell expansion condition influence phenotypic changes of adipose-derived stem cells. Stem cells international, 2017(1), 7108458.

McGregor, E., & Dunn, M. J. (2006). Proteomics of the heart: unraveling disease. Circulation research, 98(3), 309-321.

Mong, J. (2013). Integrating extrinsic and intrinsic cues to guide cell fate decisions: rational approaches in stem cell engineering. Karolinska Institutet (Sweden).

Mooranian, A., Jones, M., Ionescu, C. M., Walker, D., Wagle, S. R., Kovacevic, B., Chester, J., Foster, T., Johnston, E., & Kuthubutheen, J. (2021). Artificial cell encapsulation for biomaterials and tissue bio-nanoengineering: history, achievements, limitations, and future work for potential clinical applications and transplantation. Journal of Functional Biomaterials, 12(4), 68.

Moses, B. S. (2016). The role of miRNAs in niche regulation of ALL phenotype. West Virginia University.

Nochehdehi, A. R., Nemavhola, F., Thomas, S., & Maria, H. J. (2023). Cartilage Tissue and Knee Joint Biomechanics: Fundamentals, Characterization and Modelling. Elsevier.

Paolini Sguazzi, G., Muto, V., Tartaglia, M., Bertini, E., & Compagnucci, C. (2021). Induced

pluripotent stem cells (iPSCs) and gene therapy: a new era for the treatment of neurological diseases. International journal of molecular sciences, 22(24), 13674.

Papassavas, A., Chatzistamatiou, T. K., Michalopoulos, E., Serafetinidi, M., Gkioka, V., Markogianni, E., & Stavropoulos-Giokas, C. (2015). Quality management systems including accreditation standards. In Cord Blood Stem Cells and Regenerative Medicine (pp. 229-248). Elsevier.

Phull, A.-R., Eo, S.-H., Abbas, Q., Ahmed, M., & Kim, S. J. (2016). Applications of chondrocyte-based cartilage engineering: an overview. BioMed research international, 2016(1), 1879837.

Portale, F. (2018). Activin A as a new key factor in the leukemic bone marrow niche.

Qazi, T. H., Duda, G. N., Ort, M. J., Perka, C., Geissler, S., & Winkler, T. (2019). Cell therapy to improve regeneration of skeletal muscle injuries. Journal of cachexia, sarcopenia and muscle, 10(3), 501-516.

Qin, Y., & Gao, W.-Q. (2016). Concise review: patient-derived stem cell research for monogenic disorders. Stem Cells, 34(1), 44-54.

Ranjitha, B. (2019). A Study of Haematological Parameters and Bone Marrow Morphology of Pancytopenia in Adult Patients Rajiv Gandhi University of Health Sciences (India)].

Reis, M., Ogonek, J., Qesari, M., Borges, N. M., Nicholson, L., Preußner, L., Dickinson, A. M., Wang, X.-n., Weissinger, E. M., & Richter, A. (2016). Recent developments in cellular immunotherapy for HSCT-associated complications. Frontiers in immunology, 7, 500.

Ren, R., Horton, J. R., Zhang, X., Blumenthal, R. M., & Cheng, X. (2018). Detecting and interpreting DNA methylation marks. Current opinion in structural biology, 53, 88-99.

Rhind, N., & Russell, P. (2012). Signaling pathways that regulate cell division. Cold Spring Harbor perspectives in biology, 4(10), a005942.

Ringe, J., Kaps, C., Burmester, G.-R., & Sittinger, M. (2002). Stem cells for regenerative medicine: advances in the engineering of tissues and organs. Naturwissenschaften, 89(8), 338-351.

Saber Sichani, A., Ranjbar, M., Baneshi, M., Torabi Zadeh, F., & Fallahi, J. (2023). A review on advanced CRISPR-based genome-editing tools: base editing and prime editing. Molecular Biotechnology, 65(6), 849-860.

Saltzman, W. M. (2004). Tissue engineering: engineering principles for the design of replacement organs and tissues. Oxford university press.

Šarić, T., Mehrjardi, N. Z., & Hescheler, J. (2010). Alternative Embryonic Stem Cell Sources. Stem Cell Biology in Health and Disease, 101-143.

Schewe, M., & Fodde, R. (2018). Multitasking Paneth cells in the intestinal stem cell niche. In Advances in Stem Cells and their Niches (Vol. 2, pp. 41-75). Elsevier.

Schwartz, S. D., Tan, G., Hosseini, H., & Nagiel, A. (2016). Subretinal transplantation of embryonic stem cell–derived retinal pigment epithelium for the treatment of macular degeneration: an assessment at 4 years. Investigative ophthalmology & visual science, 57(5), ORSFc1-ORSFc9.

Sensebe, L., Krampera, M., Schrezenmeier, H., Bourin, P., & Giordano, R. (2010). Mesenchymal stem cells for clinical application. Vox Sanguinis, 98(2), 93-107.

Shenghui, H., Nakada, D., & Morrison, S. J. (2009). Mechanisms of stem cell self-renewal. Annual Review of Cell and Developmental, 25(1), 377-406.

Shoni, M., O Lui, K., G Vavvas, D., G Muto, M., S Berkowitz, R., Vlahos, N., & Ng, S.-W.

(2014). Protein kinases and associated pathways in pluripotent state and lineage differentiation. Current stem cell research & therapy, 9(5), 366-387.

Sidrat, T., Rehman, Z.-U., Joo, M.-D., Lee, K.-L., & Kong, I.-K. (2021). Wnt/β-catenin pathway-mediated PPARδ expression during embryonic development differentiation and disease. International journal of molecular sciences, 22(4), 1854.

Singh, A., Yadav, C., Tabassum, N., Bajpeyee, A., & Verma, V. (2019). Stem cell niche: Dynamic neighbor of stem cells. European journal of cell biology, 98(2-4), 65-73.

Sokol, S. Y. (2011). Maintaining embryonic stem cell pluripotency with Wnt signaling. Development, 138(20), 4341-4350.

Sordi, V., Pellegrini, S., Krampera, M., Marchetti, P., Pessina, A., Ciardelli, G., Fadini, G., Pintus, C., Pantè, G., & Piemonti, L. (2017). Stem cells to restore insulin production and cure diabetes. Nutrition, Metabolism and Cardiovascular Diseases, 27(7), 583-600.

Sorensen, J. R., Mcfaline-Figueroa, J., & Call, J. A. (2022). Pathophysiology of volumetric muscle loss and targets for regenerative rehabilitation. In Regenerative rehabilitation: From basic science to the clinic (pp. 177-225). Springer.

Soria, B., Skoudy, A., & Martin, F. (2001). From stem cells to beta cells: new strategies in cell therapy of diabetes mellitus. Diabetologia, 44, 407-415.

Squillaro, T., Peluso, G., & Galderisi, U. (2016). Clinical trials with mesenchymal stem cells: an update. Cell transplantation, 25(5), 829-848.

Stroh, A., Tsai, H.-C., Wang, L.-P., Zhang, F., Kressel, J., Aravanis, A., Santhanam, N., Deisseroth, K., Konnerth, A., & Schneider, M. B. (2011). Tracking stem cell differentiation in the setting of automated optogenetic stimulation. Stem Cells, 29(1), 78-88.

Suter, D. M. (2020). Transcription factors and DNA play hide and seek. Trends in cell biology, 30(6), 491-500.

Timofeeva, O. A., Philogene, M. C., & Zhang, Q. J. (2022). Current donor selection strategies for allogeneic hematopoietic cell transplantation. Human Immunology, 83(10), 674-686.

Todeschini, A.-L., Georges, A., & Veitia, R. A. (2014). Transcription factors: specific DNA binding and specific gene regulation. Trends in genetics, 30(6), 211-219.

Uzbas, F., May, I., Parisi, A., Thompson, S., Kaya, A., Perkins, A., & Memili, E. (2015). Molecular physiognomies and applications of adipose-derived stem cells. Stem cell reviews and reports, 11, 298-308.

Verma, D. P. S., & Chatterjee, J. (2009). TORing with cell cycle, nutrients, stress and growth. In (pp. 161-180): Wiley Online Library.

Vijay, A., Kaviya, M., Balakrishnan, A., & Sridhar, T. (2023). Polymers and nanomaterials as gene delivery systems. In Advances in Biomedical Polymers and Composites (pp. 513-539). Elsevier.

Vishwakarma, S. K., Bardia, A., Tiwari, S. K., Paspala, S. A., & Khan, A. A. (2014). Current concept in neural regeneration research: NSCs isolation, characterization and transplantation in various neurodegenerative diseases and stroke: A review. Journal of Advanced Research, 5(3), 277-294.

Wade, J. (2023). A Historical Review of Hematopoietic Stem Cell Transplantation: Developmental Advancements Then and Now. Senior Honors Theses.

Wainwright, S. P., Williams, C., Michael, M., Farsides, B., & Cribb, A. (2006). From bench to bedside? Biomedical scientists' expectations of stem cell science as a future therapy for diabetes. Social science & medicine, 63(8), 2052-2064.

Walia, B., Satija, N., Tripathi, R. P., & Gangenahalli, G. U. (2012). Induced pluripotent stem cells: fundamentals and applications of the reprogramming process and its ramifications on regenerative medicine. Stem cell reviews and reports, 8, 100-115.

Wei, B., & Lu, J. (2021). Characterization of tendon-derived stem cells and rescue tendon injury. Stem cell reviews and reports, 1-18.

Weichselbaum, R., Goebbels, R., & Lokich, J. (1980). Complications of Cancer Therapy. In Clinical Cancer Medicine: Treatment Tactics (pp. 325-354). Springer.

Xu, J., Li, Y., Xu, Y., Ding, C., Li, T., & Zhou, C. (2014). A simple and effective method for the isolation of inner cell mass samples from human blastocysts for gene expression analysis. In Vitro Cellular & Developmental Biology-Animal, 50, 232-236.

Yedigaryan, L., Martínez-Sarrà, E., Giacomazzi, G., Giarratana, N., van der Veer, B. K., Rotini, A., Querceto, S., Grosemans, H., Cortés-Calabuig, Á., & Salucci, S. (2022). Extracellular vesicle-derived miRNAs improve stem cell-based therapeutic approaches in muscle wasting conditions. Frontiers in immunology, 13, 977617.

Yefroyev, D. A., & Jin, S. (2022). Induced pluripotent stem cells for treatment of Alzheimer's and Parkinson's diseases. Biomedicines, 10(2), 208.

Zakrzewski, W., Dobrzyński, M., Szymonowicz, M., & Rybak, Z. (2019). Stem cells: past, present, and future. Stem cell research & therapy, 10(1), 1-22.

Zhang, B., & Chen, T. (2024). Local and systemic mechanisms that control the hair follicle stem cell niche. Nature reviews Molecular cell biology, 25(2), 87-100.

Zhang, B., Stone, M. R. L., Sanjaya, K., Łapińska, U., Pagliara, S., & Blaskovich, M. A. (2022). Application of antibiotic-derived fluorescent probes to bacterial studies. In Methods in Enzymology (Vol. 665, pp. 1-28). Elsevier.

Zhang, X., Zhang, S., & Wang, T. (2022). How the mechanical microenvironment of stem cell growth affects their differentiation: A review. Stem cell research & therapy, 13(1), 415.

Zhang, Z. G., Buller, B., & Chopp, M. (2019). Exosomes—beyond stem cells for restorative therapy in stroke and neurological injury. Nature Reviews Neurology, 15(4), 193-203.

Zipori, D. (2005). The stem state: Plasticity is essential, whereas self-renewal and hierarchy are optional. Stem Cells, 23(6), 719-726.

About The Authors

Maria Nazir is an MPhil Scholar of Microbiology at the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur, Pakistan. She is involved in a National Research Program for Universities (NRPU) Project, with research interests in Molecular Characterization. She has submitted abstracts to various conferences and authored and coauthored of several book chapters. Her research focuses on the isolation and Molecular characterization of Corynebacterium pseudotuberculosis and their applications in promoting animal health. Her interested research criteria are based on genetics, molecular biology, and bioinformatics.

Email: nazirmaria545@gmail.com ORCID 0009-0004-6714-6212

Mr. Hameer Khan Khaskheli received his Master's in 2023 from the University of Padova, Italy. He is currently a Research Assistant in the Department of Biomedical Sciences at the University of Padova, Italy. His research expertise spans Molecular Biology, Cancer Biology, Medical Immunology, Stem Cell Research, and Precision Medicine. His primary focus is the intricate regulation of protein phosphorylation by kinases and phosphatases - critical processes often dysregulated in cancer and other diseases. He has an extensive record of publications in prestigious national and international journals and has authored two book chapters with a reputable publisher.

Email: hameerkhan.khaskheli@studenti.unipd.it ORCID 0009-0002-9622-9282

Miss Ammara Hameed received her MS in Biochemistry from The Islamia University of Bahawalpur by securing a 3.87/4.00 CGPA, in Punjab. She is serving as a biology lecturer at Army Public School and College Bahawalpur. Her research interest criteria are based on genetics, molecular biology, and bioinformatics. The research title is " Detection of NBS1 Mutations in Leukemia and Lymphoma Patients". She has reported two NBS1 novel mutations in Leukemia and Lymphoma Patients in Pakistan. She has two book chapters and one research article related to breast cancer under process.

Gmail ID: ammarahameed09@gmail.com ORCID: 0009-0002-7337-2692

Mr. Tasawar Abbas received his M. Phil in Molecular Biology from the National Center for Excellence in Molecular Biology University of Punjab Lahore Pakistan. He has one review article. He has worked in Forensic Serology, He has excellent knowledge of Genetics, STRs, genetic polymorphism also Stem cells, and virology.His research interests include stem cell therapies, Immunology, Human genetics and criminology.

Email: tasawarabbas333@yahoo.com ORCID: 0009-0002-7718-2634

Dr. Danish Riaz received his PhD (Zoology) in 2018 from Government College University Faisalabad, Pakistan. He is serving as Assistant Professor of Zoology at the Department of Zoology, Division Science and Technology, University of Education Lahore Pakistan. His research interests include Biological Science with a specialization of animal biotechnology and Fisheries. He has published over 34 research articles in well-reputed national and international journals. He also has written book chapters.

Email: danish.riaz@ue.edu.pk ORCID-0000-0002-6137-8993

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as "Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone". His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell

biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

Dr. Muhammad SAFDAR earned his PhD in Molecular Biology and Genetics from Gaziantep University, Turkey. He is Lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 70 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

E-mail: msafdar@cuvas.edu.pk ORCID: 0000 0002 3720 2090:

To Cite This Chapter

NAZIR M et al., (2024). Stem cell research: unlocking the potential for regenerative therapies. In Current Studies in Health and Life Sciences 2024 (pp.212-237). ISRES Publishing.

The Never-Ending Battle: Strategies for Infectious Disease Control in The Face of Emerging Pathogens

Faizan ALI

Atif AHMED

Samra MAQSOOD

Minahal FATIMA

Minal HUSSAIN

Shafeeq Ur REHMAN

Muhammad SAFDAR

1. Introduction

Both natural processes, such as the development of pathogens over time, and human behavior and behaviors may cause newly emerging infectious illnesses. Natural processes include the evolution of pathogens over time. Population expansion, migration from rural regions to urban areas, international air travel, poverty, conflicts, and detrimental ecological changes as a result of economic development and land usage are some of the factors that have led to these changes. The transmission of infectious agents from animals to people is the cause of a significant number of newly discovered illnesses (Fong & Fong, 2017). The probability that humans may come into close contact with animal species that have the potential to be hosts of an infectious agent is certain to rise as the human population grows and extends into new geographical locations. It is simple to understand that this combination creates a significant danger to human health when that element is paired with increases in human density and mobility. This combination poses a hazard to human health. As a potential contributor to the growth of infectious illnesses, climate change is becoming an increasingly pressing reason for worry. Diseases can spread into new geographical regions when the temperature of the Earth increases, and various ecosystems are changed (Baker et al., 2022; Jones et al., 2008). Certain microorganisms, such as bacteria, viruses, and others, can evolve over time and acquire resistance to the medications used to treat illnesses caused by infections. Consequently, medicines that were beneficial in the past for the purpose of illness control are no longer suitable for this purpose. Vaccine coverage that is decreasing may lead to the resurgence of disease; hence, even when there is a vaccine that is both safe and effective, an increasing percentage of individuals opt not to be vaccinated against the illness (Baker et al., 2022; Trovato et al., 2020).

The plague in the fourteenth century, the Spanish flu of 1918, and, recently, the COVID-19 pandemic are examples of threats that have not disappeared but are constantly resembling one difference: they remain deadly. They underscore the need for constant alertness and creativity in how people address the spread of infectious diseases (Mack et al., 2007). Given the availability of new pathogens, conventional approaches to combating diseases do not suffice. One of the reasons why attempts to fight this disease proved so difficult is that various factors influenced its evolution, including changes in the environment, growing international travel, and mutations of the microbes that caused the disease (Levitt et al., 2010). Technological changes such as deforestation and climate change affect ecosystems in a way that the disease-causing pathogens seek new niches to thrive on. Globalization also helps in the speedy interconnectivity of people and the carriage of goods, helping to spread diseases. However, pathogens are not stateless entities; they change, and evolution may, on certain occasions, compromise their susceptibility to treatments (Flood et al., 2024).

Solving these problems is possible only through a complex set of measures. Healthcare, prevention, and early diagnosis programs are pivotal to preventing severe epidemics. It has been

found that prevention is highly effective, and such measures are usually manifested in vaccination and health promotion. Quarantine, isolation procedures, and antimicrobial agents are used to prevent cases from getting out of hand or spreading to the community (Choudhary, 2021). However, technology and innovation play a significant role in fighting economically threatening diseases. Some diagnostic tools, data analytics, and vaccine efficacy have contributed to improved knowledge of the current threats posed by emerging pathogens. International cooperation and policy frameworks support people's cooperation at the international level and the exchange of resources and information. This chapter provides an assessment of the various approaches used in managing infectious diseases and the ever-evolving nature of the task. Mainly, the emphasis is made on considering historical and modern techniques, the technologies that play a significant role in today's world, and global collaboration in the context of controlling infectious diseases (Tabish & Nabil, 2022).

1.1. Infectious Diseases

Infectious diseases originate from pathogenic organisms, including bacteria, viruses, fungi, or parasites. When the host is infected, these can enter the body, multiply, and cause symptoms and health complications. Infectious diseases can be passed on through direct contact with an affected individual, contact with objects or articles contaminated with the disease-causing agents, consumption of contaminated food or water, and through vectors such as insects or some animals (Kapasi, 2024). Infectious diseases are sicknesses caused by pathogens; these differ in degrees of severity, ranging from simple illnesses caused by microbes to fatal diseases caused by viruses that have the potential to spread through a population and cause cases of outbreaks, epidemics, or even pandemics (Adalja et al., 2019). Some of the well-known infectious diseases are influenza, tuberculosis, malaria, HIV/AIDS, COVID-19, and so on.

2. Emerging Pathogens

Newly identified microorganisms or old disease-causing organisms that are on the rise either have recently entered a population or exist but are spreading fast. These pathogens are relatively new and present substantial threats to human health since most people have not developed immunity against them, and most cures or vaccines are still being developed (Bloom & Cadarette, 2019). New pathogens can develop through several methods, such as genetic mutation, jump species, or change within the environment, which opens other paths to spread. Some newly identified pathogens include SARS-CoV-2, which led to COVID-19, Ebola, and Zika as discussed in Table 1(Mohapatra & Menon, 2022). Their sources could be fundamental activities like interactions between humans and animals, international and internal travel and trades, increased human encroachment into animal-inhabited areas, and environmental changes.

Table 1: Summary of pathogens with spillover, animal-to-human transmission, human-to-human transmission, or both with their interventions.

Pathogen	**Mode of transmission**	**Intervention**	**References**
Subcritical pathogens	Spillover	Reduction of human contact with camels Camel vaccination	(Dudas et al., 2018)
MERS			
Crimean-Congo hemorrhagic fever (CCHF)	Human-to-human (nosocomial)	Case isolation Contact precautions (PPE)	(Tsergouli et al., 2020)
Nipah	Spillover	Avoid consumption of palm sap Covers for palm sap collection vessels	(Nikolay et al., 2019)

Pathogen	Mode of transmission	Intervention	References
Avian influenza (H7N9)	"Spillover Human-to-human Both"	"Reductions in poultry exports Market disinfection Handwashing Social distancing Poultry trade regulations Health education campaigns"	(Stoto et al., 2019)
Post-elimination measles	"Spillover	Targeted vaccination of international travellers	(Hyle et al., 2019)
Monkeypox	"Spillover Both Human-to-human"	"Reduce contact with reservoir animals Smallpox vaccination Community-based interventions Improved diagnostics for early case detection Vaccinating healthcare workers"	(Reynolds & Damon, 2012)
Supercritical Pathogens			
Yellow fever	"oth Spillover Human-to-human"	"Vaccination of the general population Vector control Urban vector control"	(Ellwanger & Chies, 2018)
SARS-CoV	"Spillover Human-to-human"	"Culling civets Reducing contacts in live markets Culling civets Reducing contacts in live markets "	(Riley et al., 2003)
Ebola	" Spillover Human-to-human"	"Avoid contact with animals found dead Vaccination of nonhuman primates Safe burial Contact precautions (PPE) Drug treatments Ring vaccination"	(Jendrossek et al., 2019)
SARS-CoV-2	" Spillover Human-to-human "	"Market closure Social distancing Travel restrictions Contact precautions (PPE) Quarantine and isolation"	(Kraemer et al., 2020)

3. A Short History of Emerging Infectious Diseases

The establishment of human settlements and the subsequent development of agricultural practices created favorable circumstances for the creation and spread of infectious illnesses. The development of agriculture made it possible for people to remain in the exact location, and the rise in food production led to an increase in population density that was far higher than what could be maintained only by hunting and gathering. Because of this population density increase, a critical mass of individuals found it possible to maintain and transmit infectious and contagious illnesses. Additionally, some agricultural methods, notably the domestication of animals, led to a rise in the number of encounters between humans and animals and interactions between groups of animals of various species. Different species interacted with one another, creating the perfect environment for developing new infectious illnesses (Weiss & McMichael, 2004). The subsequent historical events that included migration, conflict, and commerce established a way by which disease epidemics

might be transmitted to new populations all across the globe (McNeill, 2010). Throughout human history, the distribution of infectious illnesses has occurred during societal upheaval and changes (McMichael, 2004). There is a possibility that infectious diseases were responsible for some events that occurred throughout history. An epidemic wiped out the population of ancient Greece, and the period known as the "Plague of Athens," which may have been caused by typhus, may have had a significant role in determining the result of the Peloponnesian war and the destiny of the state of Athens. Similarly, the 'Justinian Plague,' which is thought to have been caused by Yersinia pestis, had a significant impact on the Byzantine Empire and was responsible for the destruction of Constantinople when it occurred (Wagner et al., 2014). After fourteen centuries, the plague made its way to Europe via trade routes, which led to an exceptionally high fatality rate. The massive fall in population that occurred as a consequence throughout Europe contributed to a rise in social mobility and may have had a role in the development of changes in the political and economic structure (Alesina, 2013). Exploration and travel were other factors that contributed to the introduction of new infectious illnesses into populations that were vulnerable to them. For example, when the Spanish arrived in the Americas, they brought with them the diseases of measles and smallpox. These illnesses had a more significant effect on the native population than on the comparatively tiny troops that accompanied Cortez and Pizarro. The transmission of newly discovered illnesses was mostly one-sided, although it was not unidirectional. For instance, it is quite probable that Spanish explorers were the ones who brought syphilis to Europe (Weiss & McMichael, 2004).

Within the context of the Industrial Revolution, cities, with their quickly expanding populations, were highly influential in spreading infectious illnesses. This was especially true in Britain. As the people relocated from rural areas to urban areas to find employment in the newly constructed factories, migrants encountered overcrowding, longer working hours, and an inferior diet in comparison to their contemporaries who lived in rural communities over the same period diseases like TB, typhus, and smallpox were prevalent in urban areas. Measles, mumps, and scarlet fever were among the illnesses that contributed to the high rate of child death. Before the extensive implementation of contemporary sewage systems in the latter half of the 19th century, sewage was often responsible for directly contaminating water sources. Cholera has been abolished in the United States and the United Kingdom due to cleaner water sources; nonetheless, the spread of cholera continues to be caused by inadequate sanitation in many regions of the globe. Over the last several decades, advancements in technology and the general quality of life for certain people have resulted in new pathways for the spread of newly developing illnesses.

As a consequence of the growing number of people traveling, it is now possible for illnesses to spread from continent to continent in a matter of days rather than weeks or months. As a result, the proximity between people and infectious diseases can no longer be defined in terms of geographic distance. Furthermore, the elements responsible for the emergence of infectious diseases in one region of the globe may rapidly spread to other areas of the world. Additionally, the pursuit of natural resources and food sources has brought people into close contact with new species, increasing the likelihood of disease spillover (Daszak et al., 2000; Jones et al., 2013). This in conjunction with the ease with which both people and diseases can travel, has created an unprecedented opportunity for new diseases to emerge and spread (Polgreen & Polgreen, 2017).

3.1. Ancient and Medieval Times:

Early societies introduced measures of public health that included quarantining the infected individuals and isolation. Quarantine history could be traced back to the 14th century during what was then known as the black death; ships arriving in Venice were asked to stay in quarantine for forty days. It is stated that early attempts to control infectious diseases date back to Egypt, Greece, and China, where early cures and primary surgery by identification of herbs were mentioned (Conti, 2008).

3.2. 17th to 19th Century:

Substances that exist in large amounts but are not visible to the naked eye include microorganisms discovered by Antonie Van Leeuwenhoek in the 17th century. Thus, the development of the smallpox vaccine by Edward Jenner in 1796 provided insight into the functionality of vaccination in combating infectious ailments (Montero et al., 2024). The study carried out by John Snow identified contaminated water as the cause of cholera in London in 1854, and it stressed the significance of hygiene and cleanliness, signaling the start of epidemiology as a formal science (Tulchinsky, 2018).

3.3. Early 20th Century:

Louis Pasteur and Robert Koch helped establish germ theory that was major in managing infectious diseases by arriving at vaccines, antiseptics, and hygienic behavior. It would be best to mention that effective antibiotics appeared in the late 1940s, with penicillin being the first – and entirely revolutionized the approaches to bacterial infection treatment and the number of lives saved (Podolsky, 2015).

3.4. Mid to Late 20th Century:

One of the world's most significant successes in public health was the elimination of smallpox in 1980 with the help of a large-scale vaccination campaign conducted by WHO. Immunization, for instance, with the emergence of the poliomyelitis vaccine, lessens the impact of many contagious illnesses (Nathanson & Kew, 2010).

3.5. 21st Century:

New diseases such as SARS, H1N1 influenza, Ebola, Zika, and COVID-19 remain relevant assumptions for studying the possibilities of infectious disease control. Genomic sequencing, big data analytics, and artificial intelligence are new methods for managing and preventing infectious diseases (Dong et al., 2021).

4. Why is it Necessary to Focus on New and Reemerging Pathogens?

New strains of diseases present an actual and potential menace to the world's population. Several vital factors underscore the importance of addressing these threats:

4.1. Rapid Spread and Global Impact:

New pathogens possess the characteristics of epidemiology as international mobility has enhanced the ease of disease spread. An example is the COVID-19 global pandemic, which within months, affected almost all countries globally, leading to illnesses, numerous deaths, and economic disruptions. The integration of international supply networks and globalization contribute to the fact that the cases of the pandemic's outbreak in one region can negatively affect the entire world economy and health systems (Ibn-Mohammed et al., 2021).

4.2. Limited Preparedness and Response:

Emerging strains are a significant threat because the health systems may not prepare for such diseases because there is little information, few diagnostic methods, and no vaccinations or medicines available. The initial process is of utmost importance in managing new pathogens that threaten society, and this can only be done effectively if there are efficient surveillance mechanisms, quick diagnostic tools, and malleable health systems (Baqerkhani et al., 2022).

4.3. Public Health and Economic Consequences:

Disseminated things can rapidly infect a large number of people, overloading healthcare facilities and further worsening morbidity and mortality. Health centers, especially hospitals, are overburdened with patients, and normal outpatient services are likely to be affected. Pandemic

diseases are costly to the economy, resulting in health and related services expenditures, productivity loss, and economic development fluctuations. According to the World Bank the global cost of COVID-19 might be in trillions of dollars for global economies (Weiss et al., 2020).

5.Antimicrobial Resistance:

The use of antibiotics and other antimicrobial agents in the wrong or excessive quantities is a cause of resistant strains of bacteria, viruses, and other pathogens. This resistance hinders the management of infections, raising the rates of severe diseases and death. Crushing of antimicrobial resistance entails collaborative efforts worldwide and appropriate utilization and creation of further antimicrobial agents (Jani et al., 2021).

5.1 Need for Innovation and Collaboration:

Dealing with new pathogens requires constant studying, testing, and development of novel vaccines, drugs, and diagnostic techniques. This encompasses the use of the latest technology and encourages innovation in biomedical science. International cooperation must be achieved because diseases are not limited to a given country's/region's territory. It is crucial to stress that no single country can fight new threats alone; thus, international organizations, national governments, and the private sector must cooperate to share information, experience, and resources (Jones et al., 2009). Thus, the primary and secondary prevention of infectious diseases and the containment of new pathogens are vital to maintaining good health and well-being, guaranteeing economic growth, and preserving the world's stability. It is essential to look out and be ready to fight the next in a continuous struggle between man and pathogens. Emerging pathogens are new to a given population or are increasingly being identified in a population or regions of geographical distribution where they previously had negligible influence. Such pathogens are usually of new types or strains recently emerging or mutating from existing microbes. They tend to be more pathogenic, resistant to treatments, and can infect people of different species. Some of them include the coronavirus (COVID-19), the Ebola Virus, which is responsible for severe hemorrhagic fever ranging from moderate to severe in human beings, and the Zika Virus, which leads to congenital disabilities and neurological afflictions in human beings (McEntire et al., 2021). These include the H1N1 virus that caused the flu pandemic in 2009 and the MERS-CoV virus, which is widely known to cause the Middle East Respiratory Syndrome. The causes of infection re-emergence include ecological shift, climate change, movement of people and animals, goods and services, and microorganism characteristics, including drug and vaccine resistance. These changes in environmental inclinations, for instance, deforestation, urbanization, and fluctuation in climate make the interaction between humans and wildlife or between different species easier, thereby increasing the incidence of pathogens and zoonotic diseases. There are also the aspects of new pathogen creation through intensified livestock contact with people and administration of antibiotics to livestock to gain resistance strains (Harbarth et al., 2015).

Deliberate travel and transporting goods and services have created more chances for people to move across the globe, thus creating more authoritative chances for diseases to move across continents. Through today's means of transportation, viruses can quickly spread from one country to another; the globalization of the wildlife trade means that new strains of pathogens can be brought directly to human populations, as was the case with the SARS-CoV-1 virus outbreak concerning wild animal markets (Leite Junior et al., 2020). These factors are further compounded by microbial adaptation and resistance when it comes to the control of emerging pathogens. The genetic changes in the pathogen can also increase its virulence capacity to bypass the host's defence mechanisms or resist the effects of drugs. Horizontal gene transfer enables bacteria to use genes resistant to other bacteria, forming multi-drug-resistant organisms. The regular use of antibiotics and other antimicrobial substances puts pressure on the exertion of success of the existing strains of microorganisms (Emamalipour et al., 2020).

6. Surveillance and Early Detection

6.1. Significance of Surveillance Systems

Surveillance systems form the base of most public health interventions and are critical in controlling epidemics of infectious diseases. Interpretation and management of the surveillance enable the early detection of the events, the trends of diseases and the effects of the interventions. Surveillance is an organized and structured means of assembling, studying, and using operative health information to drive community decisions. They help in the early institution of control measures, thus preventing the spread of contagious illnesses and their effect on society. Surveillance systems also support cooperation and information sharing regarding international health threats, which are mandatory since the hazards are not confined to local or regional areas (Caballero-Anthony, 2006).

6.2. Modern Technologies in Diseases Diagnosis

Modern technology has boosted the vigour of disease detection, sharpening up the methodology of surveillance. Technologies of the present age offer effective ways of diagnosing and monitoring diseases and their spread long before they gain epidemic proportions.

6.2.1 Genomic Sequencing

Genomic sequencing is a modern innovation that involves the analysis of the total DNA or RNA of the pathogen and provides a clear view of the pathogen's genes. This information is invaluable for several reasons: This information is invaluable for several reasons:

6.2.2. Identification and Characterization: Molecular characterization aids in the proper type and description of the agents; they determine the pathogen's propensity to cause disease, how it spreads, and the drugs it can evade (Procop, 2007).

6.2.3. Tracking and Monitoring: By comparing sequences of the genes from various samples, the researchers can monitor the spread of pathogens or their evolution in the shortest time possible. This capability is beneficial in tracking the roots of the incidents and assessing the impact of new strains (Pybus & Rambaut, 2009).

6.2.4. Vaccine and Therapeutic Development: Knowing the relatedness of pathogens helps develop the best vaccine and ways of treating pathogen-related sicknesses. For example, quick sequencing of the virus SARS-CoV-2 paved the way for the fast development of COVID-19 vaccines (Riley & Blanton, 2018).

6.2.5. Outbreak Response: Sequencing offers essential information for public health interventions and includes elements of contact tracing, quarantining, and travel bans. In the years following COVID-19, human genomic data has depended on it to detect new strains and apply necessary preventive measures (Hill et al., 2021; Hoque et al., 2020). Therefore, the role of surveillance systems and capturing the opportunities with the latest technologies like genomic sequencing remain paramount in combating infectious diseases. These tools are essential because they help identify disease outbreaks early and the correct intervention to take and manage them, ensuring people's health worldwide.

Table 2: Challenges of current surveillance strategy

Type	Challenges	Suggestion
"Scarce international cooperation"	"(i) Current surveillance sources are not well-allocated around the world. (ii) Some countries are unwilling to share pathogen materials."	"Establishing a global effective surveillance system under the frame of WHO, through integrating current surveillance systems among various countries."
Technical shortage	"(i) Data analysis is lacking accuracy. (ii) Lacking sufficient capability of real-time and automatic surveillance. (iii) Lack of specificity and reliance on chief complaint data. (iv) Insufficiency in detecting unknown pathogen"	"(i) Using the big data technique based on multiple stream information for accurate surveillance. (ii) Using automatic biosensing detection techniques, combined with modern networking and communication technology. (iii) Interdisciplinary integration in high techniques including internet, big data and molecular detection. (iv) Developing multiplexed detection methods and novel gene sequencing techniques."
"Fragments in management"	Lacking enough coordinate and interoperability across agency borders to share data to meet the surveillance requirement	"Establishing well-integrated surveillance across different departments."
Others	(i) Privacy of protected health information	(i) Legislation to regulate surveillance activities.

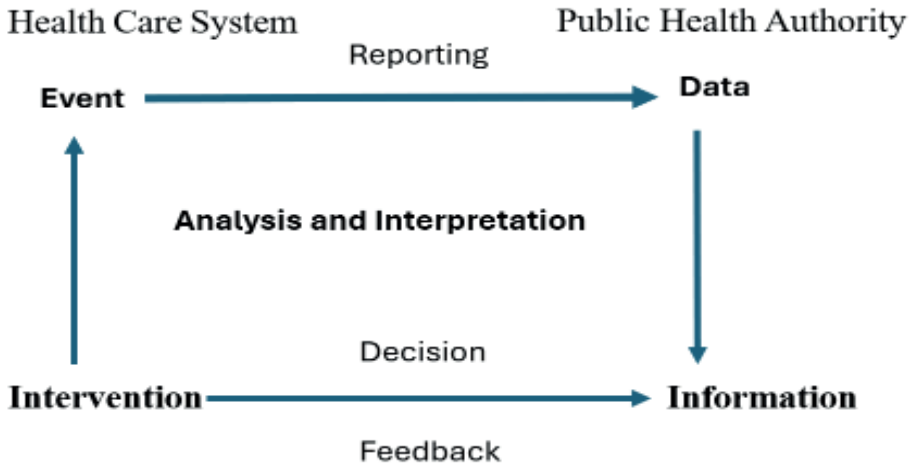


Figure 1. Framework for surveillance and response measures for emerging infectious disease.

6.3. Preventive Measures

6.3.1. Vaccination

Development and Deployment of Vaccination occupies one of the critical approaches to preventing infectious diseases. Vaccine development also goes through different phases: exploratory/research, pre-clinical/animal studies, clinical trials, and Regulatory approval. Once a vaccine is developed, especially once it goes through the process of being tested and trials to prove that it is safe for administration and effective in the war against a particular disease, it is produced and circulated in the community. These include using national immunization days, EPI sad calendar, and

unique target group campaigns. Vaccination campaigns have been proven to work, and smallpox has been completely eradicated. In contrast, polio has nearly been eradicated, and incidences of other diseases such as measles, mumps, and rubella have reduced significantly. Despite the accomplishments, vaccination programs present the following challenges. Lack of trust and false information can work against the nation's immunization programs. There are various challenges, like the cold chain problem and distribution of vaccines in hard-to-reach areas. These challenges were brought to light by the COVID-19 pandemic but, at the same time, proved economical and fast vaccine development and delivery. Measures like worldwide cooperation and progressive approaches like mRNA vaccines introduced new standards in vaccinology, which underlines that considering these problems is critical for attaining immunization coverage.

6.3.2. Public Health Campaigns

Hygiene and Sanitation Personal and environmental hygiene and sanitation are critical measures to prevent the spread of infectious diseases. Through education and improved sanitation, hand washing, food preparation, and other hygiene practices, the rates of diarrhea, cholera, and hepatitis A illness have significantly declined. The infrastructure includes a clean water supply and proper sewage systems. Indeed, health departments often initiate displays when epidemics occur to remind the audience of the potential consequences of insolent germs. Education and awareness programs and campaigns are crucial in the fight against diseases as they help change people's behavior and attitudes toward preventing the spread of diseases. Through these campaigns, awareness messages on the symptoms, mode of spread, and prevention methods of the diseases are transmitted through different media stations. Awareness is created through programs in schools and communities to have correct knowledge and practice to prevent disease spread. Efficient campaigns such as the HIV/AIDS campaign or the anti-smoking campaigns capture the essence of education in enhancing the population's health.

6.3.3. Measures Used in Quarantine and Isolation

Quarantine and isolation are essential to control contagious diseases, particularly during epidemics. To mean effective quarantine, people who may have been in contact with or are infected with the disease are isolated and cannot move around. Isolation, on the other hand, includes taking the already affected individuals from the larger population and putting them in isolation. These practices have been in existence for many years, from the times of epidemics such as that of the black death to the recent ones such as the COVID-19 virus. Implementing quarantine and isolation entails proper communication, facilities, and support structures for people in quarantine. Although these measures may inconvenience the public, they are very effective if implemented at the right time and properly to curb the spread of diseases. Thus, immunization, raising the population's awareness and education, and measures related to quarantine and isolation are among the crucial strategies to eliminate the threat of infectious diseases. These strategies limit the occurrence and transmission of diseases and the general ability of health frameworks.

6.4. Treatment Strategies

6.4.1. Antimicrobial Therapies: Broad categories in the treatments are antibiotics, which sub-treat bacterial infections; Antifungals, which treat fungal infections; and antiparasitic, which treat parasitic infections. It engages through either the extermination of the pathogens or the prevention of their growth.

6.4.2. Addressing Antibiotic Resistance

This is an emerging health problem of global proportions whereby bacteria change their structure and ability to be killed by antibiotics. Addressing antibiotic resistance involves multiple strategies: Educating patients and their caregivers to improve their understanding of the dangers of over-prescription of antibiotics using health facilities to install antibiotic stewardship programs

to enhance proper usage of the drugs, strengthening global surveillance to detect rising trends of AMR and characterize prevalent resistant strains (Harikumar & Krishanan, 2022) and increasing adherence to infection control measures in health facilities and communities to reduce the emergence and transmission of resistant organisms. Thus, the management strategies for infectious diseases include antiviral and antimicrobial medications, research for more therapeutic options, and combating drug-resistant bacteria. It is essential to control the present emergent diseases and anticipate and look forward to the challenge of new and re-emerging pathogens (Avershina et al., 2021).

6.4.3. Biotechnology Advancements

There are tremendous improvements that have been made by biotechnology in the diagnosis, treatment, and control of infectious diseases. Key areas of progress include:

6.4.3.1. Genomic Sequencing: Molecular biology techniques/western blotting techniques like next-generation sequencing (NGS) can be used to analyze many pathogen sequences simultaneously. This capability is extremely important for diagnosing and typing new pathogens, epidemiological surveillance, and studying and differentiating strains. Genomic sequencing played a crucial role in COVID-19 when new virus variants were discovered (Benito-Vicente et al., 2018).

6.4.3.2. Monoclonal Antibodies: Monoclonal antibodies are substances produced in the laboratory to resemble the human body's immune system when combating dangerous pathogens. These are employed in managing numerous infectious ailments such as COVID-19, Ebola, and respiratory syncytial virus (RSV). Antibody therapies have proven to be very effective in eliminating disease-causing agents and lowering the disease's severity (Mokhtary et al., 2022).

6.4.3.3. mRNA Technology: Lockdowns and mRNA technology, which has been hailed for having a role in developing a vaccine for COVID-19, is a breakthrough in developing vaccines. Currently, mRNA vaccines are introduced into the organism's mRNA, which are cells that produce the protein that causes an immune response and protects the organism against the virus. This technology presents a fast and efficient method to create vaccines against several diseases affecting humankind (Deering et al., 2014).

6.4.4. Big Data and AI in Disease Control

Big Data is the accumulation of an immense volume of data that is processed to uncover relationships, correlations, or tendencies, and this is mostly applied to studying the tendencies and patterns of diseases and people's behavior. In disease control, big data is used to: Epidemiological Surveillance: Track the disease occurrences by collecting and analyzing data from different sources, including health facilities, social media conversations, and mobile applications (Fung et al., 2015). Determine future incidences of the disease and areas that may experience high prevalence through movement information, climate, and other factors.

6.4.5. Artificial Intelligence (AI): The use of AI technologies such as machine learning and natural language processing improves the control of diseases by:

6.4.5.1. Early Detection: AI can also help diagnose diseases since one can feed the system with data and then group areas with symptoms characteristic of a particular disease, thus allowing officials to contain the disease quickly (Zeng et al., 2021).

6.4.5.2. Diagnostic Tools: A self-diagnosis auto system can be designed to analyze medical images, laboratory results, patient clinical details, and other related parameters so doctors and surgeons can diagnose infectious diseases aptly and speedily (Alqaissi et al., 2023; Asiri, 2024).

6.4.5.3. Public Health Interventions: AI can be used to design intervention strategies and assess the efficiency of intervention plans in containing the spread of diseases of particular interest in public health (Agrebi & Larbi, 2020). Therefore, in the contemporary world, technology and

innovation are significant determinants of healthcare as they increase disease prevention strategies' availability, effectiveness, and impact. Telemedicine, biotechnology, and applying big data and AI in diagnosing, treating, and preventing infectious diseases positively impact health and the healthcare system's capacity (Dogheim & Hussain, 2023).

6.5. Vector Control Strategies

Control measures are instrumental in eradicating vector-borne ailments, diseases that affect both man and animals and are passed on by agents like mosquitoes, ticks, fleas, and flies. The promotion of vector control aims to decrease or at least minimize these diseases' occurrence by addressing the vectors or their breeding grounds (Lobo et al., 2018). Here are some key strategies:

6.5.1. Vector Surveillance: Surveillance of the vectors is done by evaluating their population density, distribution, behavior, and ability to develop insecticide resistance. This proves helpful in planning and executing control measures in the fight against diseases (Fournet et al., 2018).

6.5.2. Habitat Modification: Modifying or eradicating the breeding place of vectors. These could mean emptying the water in which mosquitoes lay their eggs, cutting vegetation on which ticks like to feed, or better disposing of food waste that attracts flies (Takken & Knols, 2009).

6.5.3. Use of Insecticides: Insecticide spraying to eliminate adult vectors (adulticiding) and or their larvae (larviciding). This approach calls for a proper mode of insecticide selection, considering the efficiency, effects on the surrounding environment, and measures to counteract cases of resistance (Britch et al., 2019).

6.5.4. Biological Control: Release the natural enemies, parasites, or diseases of the vector species to control their populations and, for instance, use fish to eat mosquito larvae in water bodies to check their multiplication (Hajek & Eilenberg, 2018).

6.5.5. Community Engagement and Education: To create awareness of vectors and vector-borne diseases for the public and how to prevent them. Involving the communities in vector control efforts may improve the chances of observing control measures, making them sustainable (Rivera et al., 2023).

6.5.6. Integrated Vector Management (IVM): The proposed vector control method entails adopting multipronged strategies derived from the vector ecology of a given locality and disease epidemiology. IVM also underlines objective interventions and integration of interactions from different sectors (like health, environment, agriculture, etc.) (Dusfour et al., 2019). Vector control is, therefore, not one man's affair, and it should involve public health departments, environmental conservation departments, non-governmental organizations, and the general community. It is crucial in decreasing the rates of vectors and diseases affecting the populace's health and well-being (Wilson et al., 2020).

7. Emerging pathogens difficulties in their study and management

New diseases are dangerous for global health since they can evolve quickly, spread easily, and pressure countries' health services. It is equally important to note the following challenges as they are vital to formulating critical strategies in managing infectious diseases.

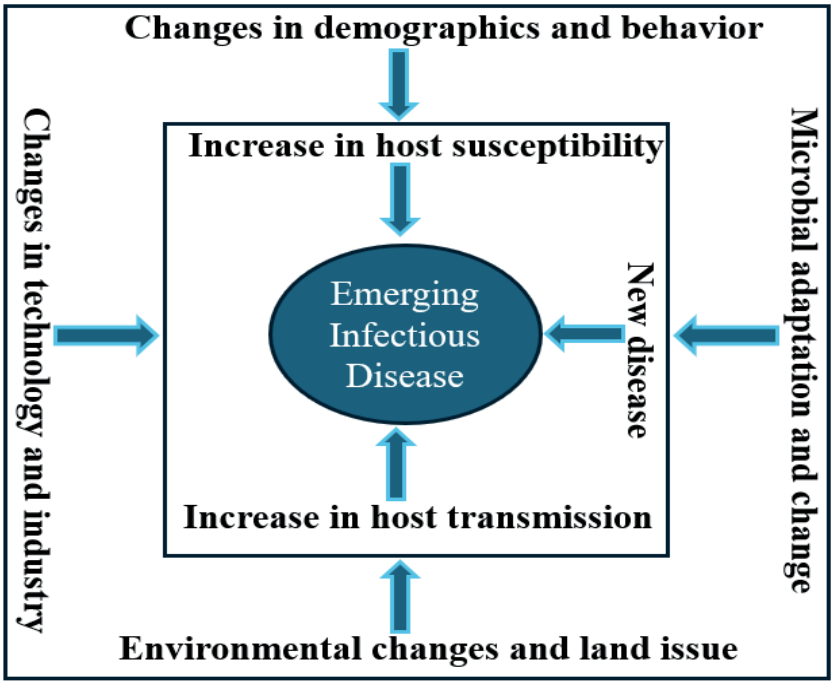


Figure 2: The major factors for the emergence of diseases

7.1. Rapid Gene Mutation and Adaptation

Influenza viruses and SARS-CoV-2, among other pathogens, can mutate rapidly by changing the genetic makeup of the virion. Such mutations may cause the appearance of new strains, much more virulent, transmissible, or immune to current medications and vaccines. This rapid mutation rate poses challenges in managing and eradicating the diseases since the new strains may not be inhibited by immunity offered by previous infections or vaccines (Manzanares-Meza & Medina-Contreras, 2020; Upadhyay, 2021).

7.2. Adaptation:

Viruses, for instance, can transform into other strains due to the availability of new hosts/ targets and vice versa (zoonotic diseases). For example, the Ebola virus and the coronaviruses or SARS, MERS, and the recent SARS-CoV-2 virus have crossed the species jump from animals to humans. This adaptability increases their likelihood of spreading infections in new and varied populations. The ability amplifies the extent of their capability to generate epidemics in other new communities (Olival et al., 2017).

7.3. Antimicrobial Resistance:

The mentioned processes, such as horizontal gene transfer, explain the adaptation of bacteria to antimicrobial agents leading to AMR. AMR contributes to the emergence of more potent bacteria and new diseases and prolongs patients' suffering and mortality. The emergence and growth of resistance are made worse by the improper and irrational use of antibiotics in human and veterinary practice and animal production (Thakur & Panda, 2017; Von Wintersdorff et al., 2016).

7.4. Globalization and Spread

7.4.1. Global Travel and Trade:

The circumstances and conditions the modern world provides contribute to the rapid spread of pathogenic agents. Epidemics can be transmitted through flight, and diseases move from one continent to another in hours, as evidenced by COVID-19. Also, through trade, items and animals are transported from one place to another, bringing pathogens to other parts of the world (Hulme, 2009; Kimball, 2016).

7.4.2. Urbanization:

High population and high rate of urbanization increase the population density, leading to the effective spread of infectious diseases. Populace centers are significant breeding grounds, where amenities such as sanitation and health care are hard to come by. The primary transmission mode is elevated human contact and low levels of hygiene, which are hallmarks of such facilities (Alirol et al., 2011; Neiderud, 2015).

7.4.3. Climate Change:

The climate also alters the breeding grounds and behaviors of vectors like mosquitoes and ticks, increasing incidences of vector-borne diseases like malaria, dengue, and Lyme disease. Alteration of climatic factors such as temperature, humidity, and rain affects the breeding of these vectors and their respective diseases (Biswas, 2022).

7.5. National and International Health Policies

One of the most crucial intervention targets is health policies at the national and international levels since they control and promote strategies for preventing infectious diseases. At the national level, health plans define the legal and organizational Epidemiological Surveillance and Disease Notification, Vaccination, Rational Use of Antimicrobials, and Health Promotion and Education (Anderson et al., 2019). They also help to promote the wise utilization of resources and readiness of health facilities in case of an outbreak. At the country level, health policies are guided by instruments such as the IHR, which enumerate countries' expectations in identifying, evaluating, reporting, and managing PHEs. They supplement international collaboration, which is essential for organized responses to health risks that have a global character (Ellwanger et al., 2021).

These health policies involve national and international guidelines and policies regarding the health of citizens. Healthcare policies at the country and global levels are central to planning and executing measures to prevent infection. The ministries of health at the national level draw out legal and institutional frameworks regarding disease surveillance and control, vaccination, antibiotics use, and health promotion. They help determine how funds are used and how healthcare institutions are ready for possible epidemics or other disease-endangering events. At the international level, health policies are embodied in the IHR, which outlines the commitment of countries to monitor, evaluate, notify, and address events of health importance. They enable people worldwide to collaborate and respond to threats whose impacts cross borders (Organization, 2021).

7.6. Organizations (e.g., WHO, CDC)

Infectious diseases are controlled by global and national organizations like WHO and CDC, which are some of the most critical organizations. WHO is a United Nations-related institution that offers international direction in health issues through leading global health initiatives, mobilizing and organizing international surveillance and response to diseases, and standard setting and providing technical cooperation for countries. CDC, being one of the most critical public health organizations in the United States, engages in scientific studies, offers recommendations for optimal delivery of disease prevention and control measures, and helps with the execution of those measures locally

and globally. Both organizations engage governments, non-governmental, and other actors to increase the resilience of health systems, disease monitoring, and health security globally (Cash & Narasimhan, 2000).

7.7. Legal and Ethical Issues of Disease Control

Legal and ethical issues are critical components of the management of infectious diseases. In legal terms, countries must regulate the protection of individual liberties and public health requirements to facilitate quarantine, isolation, and mandatory immunization for diseases while at the same time protecting the rights of the people (Organization, 2017). Ethical issues, therefore, relate to a) Fair and accountable implementation of public health interventions and b) the Dilemma of avoiding prejudice against vulnerable groups in the communities (Carter et al., 2011). Disease control is therefore anchored on several ethical principles such as informed consent, confidentiality, and the right to access one's records. Since Ebola is unusually lethal, matters of morality quickly show themselves during outbreaks regarding resource allocation and restrictions (Kass et al., 2019). Solving these issues implies compliance with the principles of ethics and legislation protecting human rights and justice. Hence, infectious disease policy and governance are essential for today's society. It starts with national and international health policies forming the backdrop for cooperative action since the phenomena affect many nations; while organizations such as the WHO and CDC function as leads as they facilitate the efforts in the society, legislation, and ethics serve as a balancing factor in ensuring that the action taken is fair and just to all as well as covers the entire population's need for health.

8. Future Directions and Innovations

8.1. New Trends in the Identification of Pathogens

Despite their traditionally inconspicuous role, emerging technologies are changing how societies identify pathogens and their presence. Current technologies that speed up genomics involve NGS, which again aids in identifying pathogens and allows for quick tracking of outbreaks. Diagnostics based on CRISPR are highly specific and transferrable to the field, allowing for early intervention even in a virus or bacteria (Bhattacharjee et al., 2021). The techniques in Biosensors and lab on the chip are advanced, which gives the result of the testing done at point care testing where the testing is done in minutes. Health technology enhances our capacity to identify and manage diseases that break out quickly, thus limiting their ability to spread (Umesha & Manukumar, 2018).

8.2. Data Analysis – Predictive Modeling and Forecasting

Forecasting and predictive modelling are indispensable paradigms in containing the spreading of infectious diseases, where historical and real-time data and AI are used to avoid infections. The machine learning algorithms use extensive data analysis, ranging from diseases, population, climate data, and other factors, to determine the likelihood of an epidemic and find possible outbreak areas. These models can also mimic a set of circumstances, assisting policymakers by planning and distributing all the resources. For example, possible scenario aids were used during the COVID-19 pandemic, predicting cases and actions related to the lockdown (Albalawi & Mustafa, 2022). Further development of AI and data assimilation will improve the steps that can be anticipated and taken to minimize the impacts of infection, thus making the measures taken by the public health organization much more anticipatory and effective (Zhao et al., 2024).

8.3. Ethics in the Control of Infectious Diseases

We are using new methods and technologies in the transmission of infectious diseases. Therefore, there are ethical issues that need to be discussed and realized. The application of one's biography into surveillance and utilization into predictive analysis significantly includes privacy and consent issues. Accomplishing purposeful and responsible collecting and analyzing of data

is essential while respecting people's rights. New technologies and treatments for diseases must be available to all since many patients can be discriminated against. Interventions that need to be introduced in organizational settings should be ethics-approved to not worsen existing disparities. Further, people's cooperation in implementing preventive and control measures, disease surveillance, and treatment are vital as the public requires confidence in the health systems. Therefore, there is a need to optimize multidisciplinary approaches to use new technologies for the prompt identification of infectious agents, the application of advanced modelling methods for anticipating disease emergence and investigating the ethical aspects toward proper respect of people's rights within the context of infectious disease prevention and control. Each of these innovations holds the potential to improve our capacity to prevent, diagnose, and manage the outbreak of contagious diseases and thereby create more robust health systems around the globe.

8.4. "One Health" Approach

The origin of around 70% of newly developing infectious illnesses in humans is zoonotic, and it is possible that there are almost 1.7 million viruses that have not yet been found in mammals and birds. Viral transmission of the Hendra and Nipah viruses, two henipaviruses that are associated with significant fatality rates, may occur when an individual comes into close contact with ill horses, pigs, or bats. Even before the coronavirus epidemic, scientists researching zoonotic illnesses have cautioned that actions such as uncontrolled wildlife trading, deforestation, and urbanization had moved humans closer to animals, raising the likelihood of viral spillovers (Cheng, 2022). These practices have brought people closer to animals. The Earth's human population is rapidly approaching 8 billion, yet nobody believes that the amount of contact between humans and animals will diminish. Instead of putting bats to death, experts believe that the most important thing is to lessen the likelihood of a catastrophic spillover. However, they admit that the forces of culture and the economy make reform challenging to achieve. According to several academics, the pandemic caused by the coronavirus highlights the need to adopt a more holistic approach known as "one health," which considers the health of humans, animals, and the environment to be interrelated. There is a need for a cultural transformation that begins at the community level and extends upwards about the manner in which we handle animals, as well as our comprehension of the hazards and biosecurity risks that we are putting ourselves in. maintaining the integrity of ecosystems rather than destroying them (Brulliard, 2020).

8.5. Emergency Preparedness

There has been a failure on a worldwide scale in terms of the coordination of operations, the integrity of public health systems and practices, and transparency. The strategy that governments have taken to address the difficulties posed by previous pandemics has been characterized by a lack of zeal. The majority of vulnerable groups were dismissed, which led to the loss of millions of lives that might have been avoided and had a negative impact on sustainable development. To protect populations, it is essential to have a sustainable vaccination strategy, to strengthen health systems and to broaden the coverage of health services, to address the global climate crisis, to have a better-prepared architecture that is driven by shared responsibility, and to integrate the international response to the risk of future pandemics with actions that are appropriate and definitive (Polgreen & Polgreen, 2017).

One of the most essential lines of protection against each newly discovered infection is the ability to recognize and identify it quickly. Considering the increasing rates of worldwide travel and commerce, which may make it possible for novel infectious illnesses to spread throughout the globe in time frames of days or weeks, surveillance must be conducted globally. The emergence of pathogens is an issue that affects the whole world. Initial outbreaks are the only way to accurately estimate the potential for a novel infection to spread across the human population. This can only be accomplished by carefully monitoring the outbreaks. In the not-too-distant future, it is quite probable that we will come across new species of agents that cause disease in humans. The ongoing

transmission of viruses from natural hosts to people and other animals is primarily attributable to human actions, such as implementing contemporary farming methods and expanding metropolitan areas. As a result, the most efficient method for preventing viral zoonosis is to keep the borders between natural reservoirs and human civilization intact, keeping in mind the notion of "one health." The following are three practical activities that may be taken to reduce the effect of future pandemics: improved monitoring of pathogen spillover and the construction of worldwide databases of viral genomes and serology; improved regulation of wildlife commerce; and a significant decrease in deforestation. These basic pandemic preventive efforts offer large co-benefits and cost less than one-twentieth of the lives typically lost each year due to newly developing viral zoonoses (Bernstein et al., 2022). It is known that there are 219 different types of viruses that are capable of infecting people. Although a significant number of human virus species have not yet been identified, there has been a noticeable slowdown in the pace at which species belonging to various families have been discovered. This may imply that there are limits to the possible range of variety. Phylogenetically conserved cell receptors are one of the few viable predictors of species leaps that may be found. Other putative predictors include species gaps. It seems that new human viruses will continue to originate, mostly from other mammals and birds, for the foreseeable future. This is something that appears to be practically unavoidable. It is necessary to have a worldwide monitoring system that is efficient at detecting new viruses (Woolhouse et al., 2012).

8.6. Primary Prevention of Pandemics

Every year, zoonoses are responsible for around one billion instances of disease and millions of deaths among people all over the world. Approximately sixty percent of newly discovered infectious illnesses that are reported on a worldwide scale are zoonoses. In the last three decades, more than thirty novel human infections have been identified, with seventy-five percent of these pathogens having their origins in animals. Viral infections are the root cause of illnesses that significantly risk the general population's health. Coronaviruses, Marburg syndrome: MERS and SARS-CoV-1, Human Immunodeficiency Virus (HIV), Hendra, Nipah virus (NiV), and the viruses responsible for Crimean-Congo hemorrhagic fever, Lassa fever, Ebola, Influenza A virus subtype H1N1, Asian highly pathogenic avian influenza (HPAI) A(H5N1) virus, or Rift Valley Fever (RVF) viruses have all been responsible for several epidemics in recent years. These epidemics were marked by high morbidity and death rates, and they mainly occurred in underdeveloped nations in South America, Africa, and Asia (Jones et al., 2008; Kulkarni et al., 2015). There is an increase in the frequency of epidemics, which are also growing and spreading further. They believe that we may anticipate around 3.3 million fatalities annually because of zoonotic outbreaks. This estimate is based on the Earth's present population, which is close to 8 billion people.

Among these preventative treatments, identifying viral infections is the most essential component. Inevitably, other epidemics will occur in the future. By enhancing healthcare for underprivileged populations that are located in close proximity to tropical forests, it would be possible to identify outbreaks of infectious diseases and limit their transmission before they can spread further. The investments in conservation and health systems that concentrate on spillover risk are investments in pandemic prevention. Pandemic prevention has the potential to save billions of dollars and millions of lives (Elias et al., 2021). When the first person falls unwell, new and improved mechanisms for identifying and monitoring possible health hazards will be implemented.

Additionally, the preservation of habitats for wild animals will be enforced, which will assist in the transition to a more preventive approach regarding maintaining people's health. Preventative measures are preferable to curative ones. Identifying newly emerging pathogens, which leads to the prompt implementation of preventative measures, has the potential to be very helpful in the fight against outbreaks of non-traditional illnesses. Nevertheless, there are a few specific difficulties that arise while doing surveillance for new diseases. It is necessary to address the deficiencies that currently exist in healthcare delivery systems as well as access to new developments in biological therapies. The importance of international collaboration in the fight against pandemics cannot be

overstated. As people continue to expand into wildlife areas, the danger of pandemics grows. This is because they are increasing the amount of interaction that animals and humans have with one another, which raises the risk of illnesses passed from one species to another. The following are three practical initiatives that have been recommended to lessen the effect of future pandemics: improved monitoring of pathogen spillover and the construction of worldwide databases of viral genomes and serology, improved regulation of wildlife commerce, and a significant decrease in deforestation. The cost of these core pandemic preventive efforts is less than one-twentieth of the value of the lives that are lost annually due to newly developing viral zoonoses, and they confer significant co-benefits. Scientific investigation, policy actions, and financial and organizational resources are required to prevent the next pandemic. It is estimated that primary pandemic prevention actions are remarkably inexpensive compared to the number of lives lost due to emerging viral zoonoses or the direct economic damage they cause (Elias et al., 2021; Tabish & Nabil, 2022).

9. Conclusion

Both natural processes and human behavior, including population expansion, migration, international air travel, poverty, conflicts, and ecological changes, cause infectious diseases. As the human population grows, the likelihood of humans coming into close contact with animal species that host infectious agents increases. Climate change and the evolution of microorganisms over time make traditional treatments no longer suitable for treating infections. The COVID-19 pandemic highlights the need for constant alertness and creativity in addressing the spread of infectious diseases. Conventional approaches are insufficient due to the availability of new pathogens, environmental changes, growing international travel, and mutations of pathogens. Solutions require healthcare, prevention, early diagnosis programs, vaccination, health promotion, and the use of diagnostic tools, data analytics, and vaccine efficacy. International cooperation and policy frameworks support people's cooperation and the exchange of resources and information. Emerging pathogens, such as SARS, H1N1, influenza, Ebola, Zika, and COVID-19, are crucial for studying infectious disease control due to their rapid spread, limited preparedness, public health and economic consequences, antimicrobial resistance, and need for innovation and collaboration. Genomic sequencing, big data analytics, and artificial intelligence are new methods for managing and preventing infectious diseases. Surveillance systems are essential for controlling contagious diseases and enabling early detection of events, trends, and interventions. Modern technologies like genomic sequencing have improved disease detection methods, allowing for identifying and characterizing pathogens, tracking and monitoring pathogen spread, and developing the best vaccines and treatments. Preventive measures include vaccination, which involves various phases, such as exploratory/research, pre-clinical/animal studies, clinical trials, and regulatory approval. Public health campaigns focus on hygiene, sanitation, education, and awareness programs to reduce disease spread. Quarantine and isolation measures are essential to control contagious diseases. Treatment strategies include vaccination, raising public awareness, and quarantine and isolation measures. Antimicrobial therapies, such as antibiotics, antifungals, and antiparasitics, treat bacterial, fungal, and parasitic infections. Biotechnology advancements, such as genomic sequencing, monoclonal antibodies, and mRNA technology, have significantly improved the diagnosis, treatment, and control of infectious diseases. Telemedicine, biotechnology, and applying big data and AI in disease control positively impact health and the healthcare system's capacity. Legal and ethical issues are critical components of disease control, involving regulation of individual liberties and public health requirements while protecting the rights of vulnerable groups. Future directions and innovations in pathogen identification include new technologies such as NGS, diagnostics based on CRISPR, biosensors, and chips.

References

Adalja, A. A., Watson, M., Toner, E. S., Cicero, A., & Inglesby, T. V. (2019). Characteristics of microbes most likely to cause pandemics and global catastrophes. Global catastrophic biological risks, 1-20.

Agrebi, S., & Larbi, A. (2020). Use of artificial intelligence in infectious diseases. In Artificial intelligence in precision health (pp. 415-438). Elsevier.

Albalawi, U., & Mustafa, M. (2022). Current artificial intelligence (AI) techniques, challenges, and approaches in controlling and fighting COVID-19: a review. International Journal of Environmental Research and Public Health, 19(10), 5901.

Alesina, A. (2013). Women, fertility, and the rise of modern capitalism. Science, 342(6157), 427-428.

Alirol, E., Getaz, L., Stoll, B., Chappuis, F., & Loutan, L. (2011). Urbanisation and infectious diseases in a globalised world. The Lancet infectious diseases, 11(2), 131-141.

Alqaissi, E., Alotaibi, F., Sher Ramzan, M., & Algarni, A. (2023). Novel graph-based machine-learning technique for viral infectious diseases: application to influenza and hepatitis diseases. Annals of Medicine, 55(2), 2304108.

Anderson, M., Schulze, K., Cassini, A., Plachouras, D., & Mossialos, E. (2019). A governance framework for development and assessment of national action plans on antimicrobial resistance. The Lancet infectious diseases, 19(11), e371-e384.

Asiri, M. A. A. (2024). An Agile Data Analytics Framework to Improve Healthcare Process Performance in Infectious Disease Propagation State University of New York at Binghamton].

Avershina, E., Shapovalova, V., & Shipulin, G. (2021). Fighting antibiotic resistance in hospital-acquired infections: current state and emerging technologies in disease prevention, diagnostics and therapy. Frontiers in Microbiology, 12, 707330.

Baker, R. E., Mahmud, A. S., Miller, I. F., Rajeev, M., Rasambainarivo, F., Rice, B. L., Takahashi, S., Tatem, A. J., Wagner, C. E., & Wang, L.-F. (2022). Infectious disease in an era of global change. Nature Reviews Microbiology, 20(4), 193-205.

Baqerkhani, M., Soleimanzadeh, A., Ghaleh, H. E., & Farzanehpour, M. (2022). Futurology and monitoring in the field of virology to deal with emerging diseases. Romanian Journal of, 125(2), 253.

Benito-Vicente, A., Uribe, K. B., Jebari, S., Galicia-Garcia, U., Ostolaza, H., & Martin, C. (2018). Validation of LDLr activity as a tool to improve genetic diagnosis of familial hypercholesterolemia: a retrospective on functional characterization of LDLr variants. International journal of molecular sciences, 19(6), 1676.

Bernstein, A. S., Ando, A. W., Loch-Temzelides, T., Vale, M. M., Li, B. V., Li, H., Busch, J., Chapman, C. A., Kinnaird, M., & Nowak, K. (2022). The costs and benefits of primary prevention of zoonotic pandemics. Science Advances, 8(5), eabl4183.

Bhattacharjee, G., Gohil, N., Lam, N. L., & Singh, V. (2021). CRISPR-based diagnostics for detection of pathogens. Progress in Molecular Biology and Translational Science, 181, 45-57.

Biswas, B. (2022). Effect of climate change on vector-borne disease. In Emerging issues in climate smart livestock production (pp. 263-316). Elsevier.

Bloom, D. E., & Cadarette, D. (2019). Infectious disease threats in the twenty-first century:

strengthening the global response. Frontiers in immunology, 10, 549.

Britch, S. C., Linthicum, K. J., Aldridge, R. L., Golden, F. V., & Walker, T. W. (2019). Visualizing efficacy of pesticides against disease vector mosquitoes in the field. JoVE (Journal of Visualized Experiments)(145), e58440.

Brulliard, K. (2020). The next pandemic is already coming, unless humans change how we interact with wildlife, scientists say. The Washington Post, 3.

Caballero-Anthony, M. (2006). Combating infectious diseases in East Asia: securitization and global public goods for health and human security. Journal of International Affairs, 105-127.

Carter, S. M., Rychetnik, L., Lloyd, B., Kerridge, I. H., Baur, L., Bauman, A., Hooker, C., & Zask, A. (2011). Evidence, ethics, and values: a framework for health promotion. American journal of public health, 101(3), 465-472.

Cash, R. A., & Narasimhan, V. (2000). Impediments to global surveillance of infectious diseases: consequences of open reporting in a global economy. Bulletin of the World Health Organization, 78, 1358-1367.

Cheng, A. (2022). New Langya virus that may have spilled over from animals infects dozens. The Washington Post, NA-NA.

Choudhary, S. (2021). A Review on Measures for Prevention of Community Transmission of COVID-19. Bioscience Biotechnology Research Communications, 14, 214-219.

Conti, A. A. (2008). Quarantine through history. International Encyclopedia of Public Health, 454.

Daszak, P., Cunningham, A. A., & Hyatt, A. D. (2000). Emerging infectious diseases of wildlife--threats to biodiversity and human health. Science, 287(5452), 443-449.

Deering, R. P., Kommareddy, S., Ulmer, J. B., Brito, L. A., & Geall, A. J. (2014). Nucleic acid vaccines: prospects for non-viral delivery of mRNA vaccines. Expert opinion on drug delivery, 11(6), 885-899.

Dogheim, G. M., & Hussain, A. (2023). Patient care through AI-driven remote monitoring: Analyzing the role of predictive models and intelligent alerts in preventive medicine. Journal of Contemporary Healthcare Analytics, 7(1), 94-110.

Dong, J., Wu, H., Zhou, D., Li, K., Zhang, Y., Ji, H., Tong, Z., Lou, S., & Liu, Z. (2021). Application of big data and artificial intelligence in COVID-19 prevention, diagnosis, treatment and management decisions in China. Journal of Medical Systems, 45(9), 84.

Dudas, G., Carvalho, L. M., Rambaut, A., & Bedford, T. (2018). MERS-CoV spillover at the camel-human interface. elife, 7, e31257.

Dusfour, I., Vontas, J., David, J.-P., Weetman, D., Fonseca, D. M., Corbel, V., Raghavendra, K., Coulibaly, M. B., Martins, A. J., & Kasai, S. (2019). Management of insecticide resistance in the major Aedes vectors of arboviruses: Advances and challenges. PLoS neglected tropical diseases, 13(10), e0007615.

Elias, C., Nkengasong, J. N., & Qadri, F. (2021). Emerging infectious diseases—learning from the past and looking to the future. New England Journal of Medicine, 384(13), 1181-1184.

Ellwanger, J. H., & Chies, J. A. B. (2018). Zoonotic spillover and emerging viral diseases–time to intensify zoonoses surveillance in Brazil. Brazilian Journal of Infectious Diseases, 22(1), 76-78.

Ellwanger, J. H., Veiga, A. B. G. d., Kaminski, V. d. L., Valverde-Villegas, J. M., Freitas, A.

W. Q. d., & Chies, J. A. B. (2021). Control and prevention of infectious diseases from a One Health perspective. Genetics and Molecular Biology, 44(1 Suppl 1), e20200256.

Emamalipour, M., Seidi, K., Zununi Vahed, S., Jahanban-Esfahlan, A., Jaymand, M., Majdi, H., Amoozgar, Z., Chitkushev, L., Javaheri, T., & Jahanban-Esfahlan, R. (2020). Horizontal gene transfer: from evolutionary flexibility to disease progression. Frontiers in cell and developmental biology, 8, 229.

Flood, C. M., Chen, Y., Deonandan, R., Halabi, S., & Thériault, S. (2024). Pandemics, Public Health, and the Regulation of Borders: Lessons from COVID-19. Taylor & Francis.

Fong, I., & Fong, I. (2017). Animals and mechanisms of disease transmission. Emerging Zoonoses: A Worldwide Perspective, 15-38.

Fournet, F., Jourdain, F., Bonnet, E., Degroote, S., & Ridde, V. (2018). Effective surveillance systems for vector-borne diseases in urban settings and translation of the data into action: a scoping review. Infectious diseases of poverty, 7, 1-14.

Fung, I. C.-H., Tse, Z. T. H., & Fu, K.-W. (2015). The use of social media in public health surveillance. Western Pacific surveillance and response journal: WPSAR, 6(2), 3.

Hajek, A. E., & Eilenberg, J. (2018). Natural enemies: an introduction to biological control. Cambridge University Press.

Harbarth, S., Balkhy, H. H., Goossens, H., Jarlier, V., Kluytmans, J., Laxminarayan, R., Saam, M., Van Belkum, A., Pittet, D., & participants, W. H.-A. I. R. F. (2015). Antimicrobial resistance: one world, one fight! In: Springer.

Harikumar, G., & Krishanan, K. (2022). The growing menace of drug resistant pathogens and recent strategies to overcome drug resistance: A review. Journal of King Saud University-Science, 34(4), 101979.

Hill, S., Perkins, M., von Eije, K. J., Benschop, K., Faria, N. R., Golubchik, T., Holmes, E., Kafetzopoulou, L., Lemey, P., & Minn Mak, T. (2021). Genomic sequencing of SARS-CoV-2: a guide to implementation for maximum impact on public health.

Hoque, M. N., Chaudhury, A., Akanda, M. A. M., Hossain, M. A., & Islam, M. T. (2020). Genomic diversity and evolution, diagnosis, prevention, and therapeutics of the pandemic COVID-19 disease. PeerJ, 8, e9689.

Hulme, P. E. (2009). Trade, transport and trouble: managing invasive species pathways in an era of globalization. Journal of applied ecology, 46(1), 10-18.

Hyle, E. P., Fields, N. F., Fiebelkorn, A. P., Walker, A. T., Gastañaduy, P., Rao, S. R., Ryan, E. T., LaRocque, R. C., & Walensky, R. P. (2019). The clinical impact and cost-effectiveness of measles-mumps-rubella vaccination to prevent measles importations among international travelers from the United States. Clinical Infectious Diseases, 69(2), 306-315.

Ibn-Mohammed, T., Mustapha, K., Godsell, J., Adamu, Z., Babatunde, K., Akintade, D., Acquaye, A., Fujii, H., Ndiaye, M., & Yamoah, F. (2021). A critical analysis of the impacts of COVID-19 on the global economy and ecosystems and opportunities for circular economy strategies. Resources, Conservation and Recycling, 164, 105169.

Jani, K., Srivastava, V., Sharma, P., Vir, A., & Sharma, A. (2021). Easy access to antibiotics; spread of antimicrobial resistance and implementation of one health approach in India. Journal of Epidemiology and Global Health, 11(4), 444-452.

Jendrossek, M., Edmunds, W. J., Rohan, H., Clifford, S., Mooney, T. A., & Eggo, R. M. (2019).

Health care worker vaccination against Ebola: Vaccine acceptance and employment duration in Sierra Leone. Vaccine, 37(8), 1101-1108.

Jones, B. A., Grace, D., Kock, R., Alonso, S., Rushton, J., Said, M. Y., McKeever, D., Mutua, F., Young, J., & McDermott, J. (2013). Zoonosis emergence linked to agricultural intensification and environmental change. Proceedings of the national academy of sciences, 110(21), 8399-8404.

Jones, B. D., Pascual, C., & Stedman, S. J. (2009). Power and responsibility: Building international order in an era of transnational threats. Rowman & Littlefield.

Jones, K. E., Patel, N. G., Levy, M. A., Storeygard, A., Balk, D., Gittleman, J. L., & Daszak, P. (2008). Global trends in emerging infectious diseases. Nature, 451(7181), 990-993.

Kapasi, Z. F. (2024). The immune system and infectious diseases and disorders. In Acute Care Physical Therapy (pp. 149-176). Routledge.

Kass, N., Kahn, J., Buckland, A., Paul, A., & Group, E. W. (2019). Ethics guidance for the public health containment of serious infectious disease outbreaks in low-income settings: lessons from Ebola. Baltimore: Johns Hopkins Berman Institute of Bioethics.

Kimball, A. M. (2016). Risky trade: Infectious disease in the era of global trade. Routledge.

Kraemer, M. U., Yang, C.-H., Gutierrez, B., Wu, C.-H., Klein, B., Pigott, D. M., Group†, O. C.-D. W., Du Plessis, L., Faria, N. R., & Li, R. (2020). The effect of human mobility and control measures on the COVID-19 epidemic in China. Science, 368(6490), 493-497.

Kulkarni, M. A., Berrang-Ford, L., Buck, P. A., Drebot, M. A., Lindsay, L. R., & Ogden, N. H. (2015). Major emerging vector-borne zoonotic diseases of public health importance in Canada. Emerging microbes & infections, 4(1), 1-7.

Leite Junior, D. P., Dantas, E. S. d. O., Costa, G. L. d., Pereira, R. S., Bonci, M. M., Ramos, R. T. B., Pires, R. A. A., Melhem, M. d. S. C., Felippe, P. A. N., & Paula, C. R. (2020). Global Trends of Emerging Infectious Diseases and the Impacts on Biodiversity: Spillover, Diversity and the Role of Bats in Evolutionary Relationships as Zoonotic Virus Reservoirs.

Levitt, A. M., Khan, A. S., & Hughes, J. M. (2010). Emerging and re-emerging pathogens and diseases. Infectious Diseases, 56.

Lobo, N. F., Achee, N. L., Greico, J., & Collins, F. H. (2018). Modern vector control. Cold spring harbor perspectives in medicine, 8(1), a025643.

Mack, A., Choffnes, E. R., Sparling, P. F., Hamburg, M. A., & Lemon, S. M. (2007). Global Infectious Disease Surveillance and Detection: Assessing the Challengesâ¬" Finding Solutions: Workshop Summary. National Academies Press.

Manzanares-Meza, L. D., & Medina-Contreras, O. (2020). SARS-CoV-2 and influenza: a comparative overview and treatment implications. Boletín médico del Hospital Infantil de México, 77(5), 262-273.

McEntire, C. R., Song, K.-W., McInnis, R. P., Rhee, J. Y., Young, M., Williams, E., Wibecan, L. L., Nolan, N., Nagy, A. M., & Gluckstein, J. (2021). Neurologic manifestations of the World Health Organization's list of pandemic and epidemic diseases. Frontiers in Neurology, 12, 634827.

McMichael, A. J. (2004). Environmental and social influences on emerging infectious diseases: past, present and future. Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 359(1447), 1049-1058.

McNeill, W. (2010). Plagues and peoples. Anchor.

Mohapatra, S., & Menon, N. G. (2022). Factors responsible for the emergence of novel viruses: An emphasis on SARS-CoV-2. Current Opinion in Environmental Science & Health, 27, 100358.

Mokhtary, P., Pourhashem, Z., Mehrizi, A. A., Sala, C., & Rappuoli, R. (2022). Recent progress in the discovery and development of monoclonal antibodies against viral infections. Biomedicines, 10(8), 1861.

Montero, D. A., Vidal, R. M., Velasco, J., Carreño, L. J., Torres, J. P., Benachi O, M. A., Tovar-Rosero, Y.-Y., Oñate, A. A., & O'Ryan, M. (2024). Two centuries of vaccination: historical and conceptual approach and future perspectives. Frontiers in public health, 11, 1326154.

Nathanson, N., & Kew, O. M. (2010). From emergence to eradication: the epidemiology of poliomyelitis deconstructed. American journal of epidemiology, 172(11), 1213-1229.

Neiderud, C.-J. (2015). How urbanization affects the epidemiology of emerging infectious diseases. Infection ecology & epidemiology, 5(1), 27060.

Nikolay, B., Salje, H., Hossain, M. J., Khan, A. D., Sazzad, H. M., Rahman, M., Daszak, P., Ströher, U., Pulliam, J. R., & Kilpatrick, A. M. (2019). Transmission of Nipah virus—14 years of investigations in Bangladesh. New England Journal of Medicine, 380(19), 1804-1814.

Olival, K. J., Hosseini, P. R., Zambrana-Torrelio, C., Ross, N., Bogich, T. L., & Daszak, P. (2017). Host and viral traits predict zoonotic spillover from mammals. Nature, 546(7660), 646-650.

Organization, W. H. (2017). WHO guidelines on ethical issues in public health surveillance.

Organization, W. H. (2021). WHO policy guidance on integrated antimicrobial stewardship activities.

Podolsky, S. H. (2015). The antibiotic era: reform, resistance, and the pursuit of a rational therapeutics. JHU Press.

Polgreen, P. M., & Polgreen, E. L. (2017). Emerging and re-emerging pathogens and diseases, and health consequences of a changing climate. Infectious Diseases, 40.

Procop, G. W. (2007). Molecular diagnostics for the detection and characterization of microbial pathogens. Clinical Infectious Diseases, 45(Supplement_2), S99-S111.

Pybus, O. G., & Rambaut, A. (2009). Evolutionary analysis of the dynamics of viral infectious disease. Nature Reviews Genetics, 10(8), 540-550.

Reynolds, M. G., & Damon, I. K. (2012). Outbreaks of human monkeypox after cessation of smallpox vaccination. Trends in microbiology, 20(2), 80-87.

Riley, L. W., & Blanton, R. E. (2018). Advances in molecular epidemiology of infectious diseases: definitions, approaches, and scope of the field. Microbiology spectrum, 6(6), 10.1128/microbiolspec. ame-0001-2018.

Riley, S., Fraser, C., Donnelly, C. A., Ghani, A. C., Abu-Raddad, L. J., Hedley, A. J., Leung, G. M., Ho, L.-M., Lam, T.-H., & Thach, T. Q. (2003). Transmission dynamics of the etiological agent of SARS in Hong Kong: impact of public health interventions. Science, 300(5627), 1961-1966.

Rivera, E. P., Arrivillaga, M. R., Juárez, J. G., De Urioste-Stone, S. M., Berganza, E., & Pennington, P. M. (2023). Adoption of community-based strategies for sustainable vector control and prevention. BMC Public Health, 23(1), 1834.

Stoto, M. A., Kang, M., Song, T., Bouey, J., Boyce, M. R., & Katz, R. (2019). At the frontier of the global battle against emerging infections: surveillance and management of avian influenza A (H7N9) in Guangdong Province, China. Journal of Global Health Reports, 3, e2019018.

Tabish, S. A., & Nabil, S. (2022). An age of emerging and reemerging pandemic threats. Health, 14(10), 1021-1037.

Takken, W., & Knols, B. G. (2009). Malaria vector control: current and future strategies. Trends in parasitology, 25(3), 101-104.

Thakur, S. D., & Panda, A. (2017). Rational use of antimicrobials in animal production: a prerequisite to stem the tide of antimicrobial resistance. Current science, 1846-1857.

Trovato, M., Sartorius, R., D'Apice, L., Manco, R., & De Berardinis, P. (2020). Viral emerging diseases: challenges in developing vaccination strategies. Frontiers in immunology, 11, 2130.

Tsergouli, K., Karampatakis, T., Haidich, A., Metallidis, S., & Papa, A. (2020). Nosocomial infections caused by Crimean–Congo haemorrhagic fever virus. Journal of Hospital Infection, 105(1), 43-52.

Tulchinsky, T. H. (2018). John Snow, cholera, the broad street pump; waterborne diseases then and now. Case studies in public health, 77.

Umesha, S., & Manukumar, H. (2018). Advanced molecular diagnostic techniques for detection of food-borne pathogens: Current applications and future challenges. Critical Reviews in Food Science and Nutrition, 58(1), 84-104.

Upadhyay, R. K. (2021). Climate induced virus generated communicable diseases: management issues and failures. Journal of Atmospheric Science Research, 4(2), 27-50.

Von Wintersdorff, C. J., Penders, J., Van Niekerk, J. M., Mills, N. D., Majumder, S., Van Alphen, L. B., Savelkoul, P. H., & Wolffs, P. F. (2016). Dissemination of antimicrobial resistance in microbial ecosystems through horizontal gene transfer. Frontiers in Microbiology, 7, 173.

Wagner, D. M., Klunk, J., Harbeck, M., Devault, A., Waglechner, N., Sahl, J. W., Enk, J., Birdsell, D. N., Kuch, M., & Lumibao, C. (2014). Yersinia pestis and the Plague of Justinian 541–543 AD: a genomic analysis. The Lancet infectious diseases, 14(4), 319-326.

Weiss, M. A., Schwarzenberg, A. B., Nelson, R. M., Sutter, K. M., & Sutherland, M. D. (2020). Global economic effects of COVID-19. Congressional Research Service Washington, DC.

Weiss, R. A., & McMichael, A. J. (2004). Social and environmental risk factors in the emergence of infectious diseases. Nature medicine, 10(Suppl 12), S70-S76.

Wilson, A. L., Courtenay, O., Kelly-Hope, L. A., Scott, T. W., Takken, W., Torr, S. J., & Lindsay, S. W. (2020). The importance of vector control for the control and elimination of vector-borne diseases. PLoS neglected tropical diseases, 14(1), e0007831.

Woolhouse, M., Scott, F., Hudson, Z., Howey, R., & Chase-Topping, M. (2012). Human viruses: discovery and emergence. Philosophical Transactions of the Royal Society B: Biological Sciences, 367(1604), 2864-2871.

Zeng, D., Cao, Z., & Neill, D. B. (2021). Artificial intelligence–enabled public health surveillance—from local detection to global epidemic monitoring and control. In Artificial intelligence in medicine (pp. 437-453). Elsevier.

Zhao, A. P., Li, S., Cao, Z., Hu, P. J.-H., Wang, J., Xiang, Y., Xie, D., & Lu, X. (2024). AI for science: predicting infectious diseases. Journal of Safety Science and Resilience.

About The Authors

Faizan Ali is doing BS Applied Microbiology from Cholistan university of veterinary and animal sciences (CUVAS) Bahawalpur Pakistan. His research interests are cell culture techniques, virology, genetics and molecular cell biology.

Email: faizansarwarali@gmail.com ORCID: 0009-0008-1066-7446

Mr. Atif Ahmed received his M. Phil. 2023 from CEMB, University of the Punjab l, Lahore. His research includes microbiology, molecular biology, and proteomics. He has published one research article in an international journal.

Email: atif.ahmed@cemb.edu.pk ORCID: 0000-0001-9571-1304

Samra Maqsood received her M.Phil. in Molecular Biology from the National Center of Excellence in Molecular Biology (CEMB), University of Punjab, Lahore, Pakistan. She is passionate about teaching and research in the fields of biomedical and forensic sciences. Her research interests include forensic serology, DNA typing, virology, stem cell therapies, and molecular biology techniques. She has worked on several research projects, including genetic polymorphism studies, DNA isolation, human genetics, and epidemiological studies on COVID-19.

Email: samramaqsoodmaqsood@gmail.com ORCID: 0009-0004-5674-1091

Minahal Fatima and She is doing M.Phil in Zoology, Wildlife and Fisheries from University of Agriculture, Fasilabad, Pakistan. Her research interest includes fish survival via changing the environmental factor. Not only the fish survive it also counts the progeny's survival. She has only one paper in International Journal and 12 Chapters in national and international Journals.

Email: fatimaabdulhameed08@gmail.com ORCID: 0009-0003-4387-6854

Minal Hussain graduated from Cholistan University of Veterinary and Animal Sciences in Bahawalpur Pakistan. He continues his postgraduate study in Microbiology from Cholistan University of Veterinary and Animal Sciences Bahawalpur. Her research interest is in Bacteriophages, Bacteriology, Molecular cell biology, and Microbial genetics etc. She has published few book chapters in international journals.

Email: 2019-cu-bios-023@cuvas.edu.pk ORCID: 0009-0004-0143-5644

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as “Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone”. His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

Dr. Muhammad SAFDAR earned his PhD in Molecular Biology and Genetics from Gaziantep University, Turkey. He is Lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 70 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

E-mail: msafdar@cuvas.edu.pk ORCID: 0000 0002 3720 2090

To Cite This Chapter

ALI F et al., (2024). The never-ending battle: strategies for infectious disease control in the face of emerging pathogens. In Current Studies in Health and Life Sciences 2024 (pp.240-262). ISRES Publishing.

The Role of Microbiome in Regenerative Medicine: A New Frontier

Maria NAZIR

Zubia RASHID

Amina Farrukh ALAVI

Muhammad Mudussair KHAN

Muhammad EJAZ

Shafeeq Ur REHMAN

Muhammad SAFDAR

I. Introduction

Tissue engineering or regenerative medicine is an upcoming therapeutic, scientific discipline that encompasses great potential in shaping the future of the healthcare industry. It is based on the concept that organs and organ function can be repaired or replaced by influencing cells, tissues, and organs to heal themselves (Sipe, 2002). This type of regenerative medicine, being an inter-disciplinary area, derives from stem cell therapy, tissue engineering, gene therapy, and immunomodulation, which, in other words, is a direct attempt to trigger the inherent self-healing in the body for tissue repair as well as regain functional losses. The application of regenerative medicine is diverse, with potential uses ranging from injuries and ulcers to osteoarthritis and other neurodegenerative diseases. In recent times, the field of regenerative medicine has increased the capacity to develop new therapies for organ failure that were simply unthinkable previously (Tandon et al., 2024). With few exceptions, regenerative medicine entails new therapies for increasingly common diseases and illnesses with the objective of enhancing the patient's lifestyle. Among the perspective directions of modern regenerative medicine, it is possible to distinguish a new branch of regenerative medicine, the microbiome that unites all microorganisms inhabiting the human organism. To date, the microbiome is defined as the aggregate of microorganisms, such as bacteria, viruses, fungi, and other microorganisms, that inhabit and interact within and on the exterior of the human body and is estimated to host at least 10^12 microorganisms (Wilson, 2018). The consistencies of microbiota, mainly the gut and skin-associated microbiota, have been shown to control several physiological functions, including metabolism, the immune system, and the brain and central nervous system (Malaviya et al., 2022). New data that became known in recent years showed that microbiota directly influences tissue repair, which means that these bacteria are involved in the regulation of the organism's inherent reparative capabilities (Xu & Hsia, 2018). This has led several researchers in the area of regenerative medicine to start emphasizing the use of microbiome and how it may be fitted into the area of regenerative medicine to enhance tissue repair, increase the healing rate, and reciprocally, the rate of success in regenerative medicine therapies. The microbiome influences tissue regeneration through various mechanisms, including in this context, the microbiome plays a part in tissue regeneration through the following processes:

Modulation of Immune Responses: The immune system has the task of balancing the ability of the cells to repair and regenerate the tissues, while the microbiome can manage the immunity network (Shavandi et al., 2020). The availability of useful microorganisms is the ability to activate constructive inflammation, which is to suppress pathological inflammation to create opportunities for tissue repair. On the other hand, dysbiosis- an unstable microbial community may result in inflammation and remodeling of the tissues' regenerative potential.

Promotion of Angiogenesis: Thus, the microbiome field exerts an influence on angiogenesis, which represents a significant form of tissue repair or the generation of new blood vessels. Based on the increase in VEGF, a product of the gene that regulates angiogenesis, some of the SCFAs'

effects on endothelial cells were shown to be positive (Gomes et al., 2023).

Influence on Stem Cell Function: The microbiome communicates/interacts with stem cells; these are undifferentiated cells that depend on signals to develop into various cells to form tissues for repair. To the realization that the bacteria of the gut are already capable of producing signaling factors that relate to stem cell activation, differentiation, and migration, therefore forming a basis for replacing dead or sick tissues (Oncel & Basson, 2022). The researchers build a new division of progressive scholarly works by applying microbiome elements to regenerative medicine. Hence, unraveling the complex interconnection of the microbiome with the regenerative processes is the key to the therapeutic strategies that unlock the full potential of the microbiome for healing and enhancing tissue repair, faster recovery, and better patient prognosis. This chapter is devoted to the description of the newest findings in this rapidly progressing field and the following topics will be discussed in detail.

2. Understanding the Microbiome

The understand the role of the microbiome in the approach of regenerative medicine, it is necessary to study its evolution, characteristics, and significance to the organism, with the additional consideration of factors that impact the intricate system of the microbiome.

2. 1 Composition and Diversity of the Human Microbiome

The human microbiome is a dynamic and complex individuals that care for trillions of microorganisms, of which sixty percent consist of bacteria, viruses, Fungi, and archaea (Nazir et al., 2024). This population interacts with various body surfaces, and these include skin, oral mucosa, respiratory system, and urogenital system. However, the highest microbial density and the research emphasis is on the gastro-intestinal tract, which contains trillions of microbes thus, the formation of the gut microbiota. These organisms comprise thousands of various bacterial species, the bacteria detected in the gut are almost similar to the total number of human body cells. Thus, although human gut microbiota is rather heterogeneous and is influenced by heredity, food intake, age, and the person's geographical position (Pulipati et al., 2020) the typical bacterial phyla in healthy individuals involve Firmicuties, Bacteroidetes, Actinobacteria, and Proteobacteria. This diversity is very essential for establishing a proper microbiota, which has the capability of synthesizing many products relevant to human beings (Table 1).

Table 1: Microbiome Composition in Health and Disease

Bacterial Group	Healthy Gut	Inflammatory Bowel Disease (IBD)	Diabetes	References
Firmicutes	Abundant	Reduced	Increased	(Stojanov et al., 2020)
Bacteroidetes	Abundant	Reduced	Reduced	(Labbé et al., 2014)
Actinobacteria	Present	Variable	Variable	(Xu et al., 2022)
Proteobacteria	Present	Increased	Increased	(Salem et al., 2019)
Bifidobacterium	Abundant	Reduced	Reduced	(Das et al., 2021)
Lactobacillus	Abundant	Reduced	Reduced	(Salem et al., 2019)
Faecalibacteriumprausnitzii	Abundant	Reduced	Reduced	(Remely et al., 2016)
Akkermansia muciniphila	Present	Reduced	Reduced	(Zheng et al., 2023)

2.2 Role of Microbiota in Health and Disease

The microbiome could not be regarded as just being there in the human (and organs of the human body) but is rather a sort of co-participant that, in a way, defines human health or disease. Healthy and balanced gut microbiotas are today established as a component of the physiological stability of the body and aspects such as digestion, immune system, and protection against diseases (Hajiagha et al., 2022).

Digestion and Metabolism: The microbes that exist in each of us are, at the very least, capable of helping with the digestion of complex carbohydrates, absorption of vitamins, and metabolism of several nutrients (Ofoedu et al., 2021). They also are involved in strengthening the most critical line of defense, namely the barrier that has formed in the intestine, which many pathogenic substances must not penetrate.

Immune Function: This is because the immunity of any organism depends on the digestive system, and therefore, due to this, the connection between the two is great. This, in turn, helps to enhance the immunity of the persons to be treated to be able to differentiate between and reject non-pathogenic substances and organisms. Immunomodulation relates to the alteration within the normal function of the immune system due to dysbiosis, bringing about continual inflammation leading to autoimmune diseases (Balakrishnan & Taneja, 2018).

Neurological Function: For the sake of clarity, the gut microbiota has been shown to have an interaction with the central nervous system with the help of the gut-brain axis that acts as a moderator of mood, behavior, and cognition. Some of the neurological conditions that they have linked to shifts in the gut microbiome include Parkinsonism, Alzheimers, and autism, according to some of the literature available (Stopińska et al., 2021).

2.3 Factors Influencing Microbiome Composition

The composition and function of the microbiome are not fixed but are constantly shaped by a multitude of intrinsic and extrinsic factors: It is urgent to realize that microbiome composition, as well as its functioning, can be continuously influenced by numerous intrinsic and extrinsic factors:

Diet: It should be noted that consumption patterns are one of the most significant factors determining the features of the composition of the gut microbiota. Consumption of fiber, fruits, vegetables, and whole grains gives the Microbiome in one's stool a healthy, diversified eating plan (Jawhara, 2023). However, a diet that complements processed food, refined sugars, and unhealthy fats increases dysbiosis, which is characterized by significantly low rates of beneficial bacteria and high rates of risk bacteria.

Antibiotics: Antibiotics are strong agents that change the balance of the population in the gut. They are good at cleaning out bacterial infections; however, they are potent on all bacteria, and their use destroys the many beneficial bacteria that may have future benefits for a person's health (Bloomfield et al., 2006).

Age: Considering this fact the gut microbiome is not a constant system during people's lifetime as it is ecosystems that are home to trillions of microbes (Fasano & Flaherty, 2021). There are relatively few kinds of microorganisms in the body of a baby at birth, but as the age of the baby the variety and the complicated nature of microorganisms increases. However, with time, the variety of the microbiota and its stability are in danger, and it has something to do with some of the troubles that are associated with age.

Genetics: Host genetics are also necessary for regulating the sensibility of the gut microbiome; however, this factor remains, to some extent, undefined (Patrignani et al., 2014). SNP is valuable as it influences the functions of genes, which in turn manage to turn on the immune reactivity, nutrients, and microbiome, among other functions.

Environmental Factors: Different kinds of negative influences, such as toxins, pollutants, stress, and others, alter the concentration of the gut microbiota and its action (Bhardwaj et al., 2024). These factors alter the homeostasis of the microbial community, which, if disrupted, leads to dysbiosis and the development of disease. These aspects must be understood to develop specific approaches towards manipulating the microbiota for a therapeutic end.

3. Basics of Regenerative Medicine

Regenerative medicine is defined as the new direction in healthcare management. The main goal of this field is to restore damaged or failed tissues and organs by activating the organism's self-change processes. This field involves a wide range of strategies, and despite its different mechanisms of operation and general functions, it is mostly aimed at enhancing the wound-healing process (Figure 1).

Tissue Engineering: In this case, tissue engineering is a broad area of study that is concerned with the development of functional tissues or organs using cells, scaffolds, and signals (Abdollahiyan et al., 2021). These cells are then harvested directly from the patient, which is then cultured on the scaffold that also defines the formation of the tissues. At first, a positive effect on cell metabolism is applied with basic proteins; later, for cell proliferation and formation of functional tissues, growth factors, and cytokines are used (Deuel & Chang, 2014).

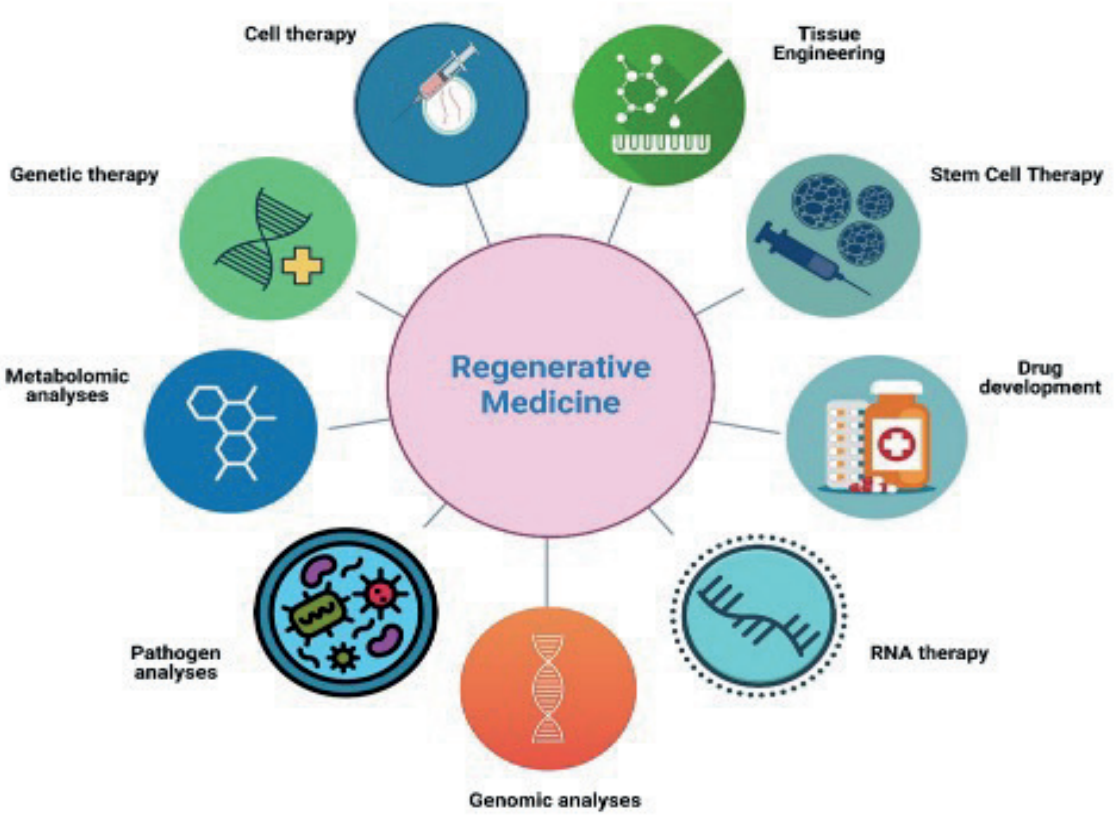


Figure 1. Basics of Regenerative Medicine

Stem Cell Therapy: Stem cells are the cells that still retain the ability to divide and produce more stem cells and other specialized cell types; they constitute part of the foundation of regenerative medicine (Suman et al., 2019). They can be derived directly from embryonic stem cells; they can also be derived from adult stem cells and also from the creation of human somatic cells to pluripotent stem cells known as iPSC. Stem cell therapy involves the master donor of these cells and infusing them into tissues where they can differentiate into such kinds of cells, plug up the gaps in tissues,

and help in the repair of damaged tissues (Mafruchati, 2023). The experimental application of stem cells is widely implemented in the treatment of various illnesses: Cardiovascular and vascular, neurological and neurosensory, and musculoskeletal diseases and injuries.

Biomaterials: Biomaterials can be described as the biological or synthetic components that are laid down with the specific task of performing a particular function in the body of a living organism (Lakes & Park, 2012). They are essential in all segments of tissue engineering, drug delivery systems, and implantation materials that substitute damaged tissues. The NBM and any other components of regenerative medicine must comprise biocompatibility and bioactivity in order not to cause negative impacts in the human body but at the same time, they should be able to offer the desired effect. In light of the structure of the composite biomaterials, at least one of the components in the composite material replicates the extracellular matrix, which is the natural environment of cells and tissues and directs their formation (De Santis et al., 2019).

3.2 Current Application and Case Studies

Regenerative medicine has already achieved remarkable success in various clinical applications, demonstrating its potential to transform healthcare: This young branch of medicine has already provided numerous outstanding results in numerous clinical uses, proving the viability of applying regenerative medicine for the improvement of healthcare services:

Skin Regeneration: Cultured skin cells and biomaterials have also been used to manage burns and chronic ulcers and improve wound healing rates with minimum keloid scar formation (Elfawy et al., 2023). The mentioned grafts can serve as either the temporary or definitive layer of the wound, promoting tissue repair and preventing infection.

Cartilage Repair: MSC therapy seems to hold impressive expectations in regenerating the impaired cartilage in joints thereby reducing the frequency of total joint replacement surgeries (Vigano, 2017). This therapy involves the use of the patient's cartilage cells or MSCs harvesting and expansion, and reconstructed cells are implanted, leading to cartilage restoration of the arthritic joint.

Bone Regeneration: Since time immemorial, bone grafts, whether autografts where the graft is derived from the recipient's body or allografts where the donor is different from the recipient have been employed to improve bone fracture and nonunion healing. New ones are bone tissue engineering, which employs the use of autografts combined with growth factors and stem cells in bone regeneration and remodeling (Nassif & El Sabban, 2011).

Corneal Regeneration: One of the procedures that has been used successfully to treat patients with corneal blindness due to limbal stem cell deficiency has emerged as autologous limbal stem cell transplantation (Selver et al., 2017). This involves moving normal stem cells from another donor or the patient's healthy eye or affected eye to encourage the growth of the cornea.

3.3 Challenges and Limitations in Regenerative Medicine

Despite the significant progress and promising results, regenerative medicine still faces several challenges and limitations: There are many drawbacks and limitations in the development of regenerative medicine, but it continues to show promising results and a lot of progress The biggest challenges are the following:

Complexity of Tissue and Organ Regeneration: Despite all these advances, tissue engineering is still in front of several major technical issues. In creating the methodologies for the formation of the tissues and organs containing several types of cells and organized in the multi-functional 3D constructs. It is thus crucial to be able to control the differentiation process of the cells in space and time, tissue organization, and vascularization for tissue biomimicry (Carotenuto et al., 2022).

Immune Rejection: Immunological rejection of the transplanted tissue is always an increasing factor and can be more emphasized in the case of allogeneic tissue (González-Molina et al., 2016). The presumption regarding the risk of GvHD is still a mystery, but immunosuppressive medications or a generation of hypoallergenic cell sources are possibilities.

Long-Term Efficacy and Safety: The helpful and safe effects of regenerative medicine cannot skip the research review of clinical trials and literature. This entails assessing the capacity of cell therapy to revive tumorigenicity, differentiate abnormally, and any other effect that might develop after some time (Carvalho, 2020).

Regulatory and Ethical Considerations: The realization and advancement of regenerative medicine therapies entail qualities or matters that relate to regulation and ethical standards (Yamada et al., 2021). For example, matters concerning the safety and quality of cell and tissue products and issues regarding the use of hESC and avoiding unethical stem cell research and clinical application. Thus, it is possible to overcome these challenges and limitations and continue regenerative medicine's development with its incredible opportunities for creating a new future for medicine and the lives of many patients.

4. Mechanisms of Microbiome Influence on Regeneration

Therefore, relating microbes with their host and the host's tissues is a process, and the use of the microbiome in regenerative medicine is analogous to a well-coordinated ballet. These interactions include direct and indirect communication, altering the immune response, regulation of inflammation, and biosynthesis of bioactive compounds (Caffaratti et al., 2021). Understanding these mechanisms is necessary to evaluate and enhance the microbiome's potential in the therapeutic process and tissue regeneration.

4.1 Microbiome-Host Interactions

The microbiome and its host are two entities continually sending signals to each other, and each can impact the other's function through infinitely many molecular messengers.

Direct Cell-to-Cell Communication: According to parts of the microbiota, they may directly come into contact with the host cells or release compounds capable of binding to host cell receptors (Krasulova & Illes, 2021). For example, certain bacteria in this place are known to adhere to the mucosa of the small bowels through intricate intracellular signaling, frequently used in the stimulation of cell division and differentiation required in tissue healing.

Indirect Signaling via Metabolites: These are propionate, acetate, and butyrate of SCFAs, cobalamin, niacin, and folate of vitamins, tryptophan, histidine, and cysteine of amino acids, and u bowel of secondary bile acids. These metabolites can act as soluble mediators of the host and gene system's state or modulate the corresponding system (McCarville et al., 2020). For instance, SCFAs can bind to GPCRs on the surface of the host cells to modulate the immune response, promote angiogenesis, and regain the integrity of the intestinal barrier (Fock & Parnova, 2023).

Immune System Modulation: In the immune system the gut microbiome plays a crucial role in both the innate and adaptive immune system since they are part of the body's development. This interaction is relevant to help avoid a constant inflammatory status that does not allow tissues to heal (Wilson et al., 2001).

4.2 Role of Microbiota in Immune Modulation

The microbiome impact on immune modulation is multifaceted and involves several key mechanisms: Thus, immune modulation is just one of the microbiome functions, and there are several ways it is realized:

Promotion of Immune Tolerance: From these points of view, a capacity to stimulate the immune or hosting system's tolerance to harmless antigens such as a food particle and environmental allergens relates largely to commensal bacteria as the most crucial element or resident as a component of the host gut habitat. This tolerance is very crucial in preventing over-activation of the immune cells that are likely to destroy tissues while arresting their healing process (Tu & Li, 2023).

Regulation of Inflammation: The SCFAs and PSA are some of the inflammation inhibitory spectra that gut bacteria produce. They act to block the pro-inflammatory processes in the body and, at the same time, promote the differentiation of Treg cells (Dwivedi et al., 2016). Treg cells are also involved in shifting the equilibrium of immune responses and implementing the anti-inflammatory processes, resulting in tissue repair and regeneration.

Protection Against Pathogens: Symbiotic microorganisms are present to counter the colonization of tissues by the pathogens of the host and to envelop them (Ganesan et al., 2022). This protective function is achieved through competitive exclusion, the production of antibiotics, and the role of giving signals to the host's immune system.

4.3 Impact on Inflammation and Healing Processes

Inflammation is a biological process and can be described as being multistage and its major function is to help repair tissue. Hence, acute inflammation is vital in initiating the healing process. However, chronic inflammation is dreadful in tissue healing since it upregulates fibrosis and scarring reactions. The targets of the microbiome suggest its capacity to reduce inflammation and tissue healing (Laing et al., 2018). Stereochemical fecal acids, which are products of the gut microbes, can, exhibit efficient anti-inflammatory qualities. Consequently, SCFAs can act as ligands of certain receptors on immune cells: Thus, they can inhibit the production of pro-inflammatory cytokines and stimulate the production of anti-inflammatory Treg cells (Rasouli-Saravani et al., 2023). All that has been said and depicted above indicates the anti-inflammatory property of the adipose tissue-derived stem cells that could facilitate tissue repair and regeneration by minimizing the degree of tissue inflammation, providing the formation of new blood vessels (or angiogenesis), and activating the stem cells for proliferation and differentiation.

4.4 Production of Bioactive Compounds and Metabolites

There are many papers on bioactive compounds and metabolites of gut bacteria that impact host physiology and tissue regeneration. These include:

Short-chain fatty acids (SCFAs): Dietary fibers are fermented in the gut by bacteria, and SCFAs are produced, where butyrate, propionate, and a minor amount of acetate are obtained (Vinelli et al., 2022). SCFAs were related to the up-regulated proliferation genes and anti-tissue repair actions in neovascularization, reformation of the epithelial barrier, decreasing inflammation, and providing energy to intestinal cells.

Vitamins: Gut bacteria can also synthesize some vitamins, including vitamin K and vitamin B, which are involved in cell metabolism, DNA synthesis, energy generation, and cellular redox state regulation (Hossain et al., 2022). These vitamins play essential roles in the healing process or even the regrowth of tissues in the body.

Bile Acids: The bacterial flora in the gut can convert the first bile from the liver to the secondary bile, which has many activities. Some secondary bile acids enhance the TGF-β and Smad signaling pathway involved in tissue remodeling and enhance stem cell differentiation to maturation besides stimulating angiogenesis (Wiercinska, 2005).

Neurotransmitters: Microbiota can produce some neurotransmitters, such as serotonin and dopamine, which impact the brain and its functions and behavior (Ignatova, 2019). These neurotransmitters can also act on the gut and regulate the transport of nutrients and the immune

status of the intestinal tissues.

5. The Microbiome in Wound Healing and Tissue Repair

The relations between skin microbiota and wound healing are considered a relatively new field of knowledge (Canesso et al., 2014). Although studies coming to the very center of the concept regarding the microbial societies living symbiotically with us play a complex role in regulating the sequence of events that make up the process of wound healing. Such knowledge could build therapies that would boost the capacity of the microbiome to restore sinuses and, therefore, the patient's state.

5.1 Skin Regeneration Impact

The epidermis or skin, which is the largest organ of the human body and acts as the primary barrier against pathogens, has a complex and constantly changing population of microorganisms that reside there, collectively referred to as the skin microbiota (Pistone et al., 2021). This skin microbiome plays many roles in the health of the skin, control of pathogens, regulation of the immune system, and healing of skin injury. Recent studies have shed light on the specific mechanisms by which the skin microbiome impacts skin regeneration (Figure 2). Recent studies have helped identify how the skin microbiome influences skin regeneration through skin biology's various mechanisms (Patel et al., 2022).

Inflammation Modulation: The skin microbiome plays a role in the intention of inflammation, particularly due to skin injury (Nørreslet et al., 2020). On a similar note, Staphylococcus epidermidis, a blow-seen bacterium responsible for human skin, acts against pathogenic bacteria and additionally produces antimicrobial peptides that hinder the intrusion of pathogenic organisms and can prevent infections. In addition, these bacteria can regulate the functions of inflammatory and anti-inflammatory cytokines that define the level of inflammation and cell tissue repair (Steen et al., 2020).

Re-epithelialization Enhancement: Re-epithelialization refers to the process of movement and replication of tissues that results in the wound bed being covered and is considered a standard component of the phases of healing. For instance, Staphylococcus epidermidis is regarded as a healing-promoting bacteria and should enhance cutaneous wound healing and the pan of the keratinocyte to form the scar faster (Stoica et al., 2020). Also, these bacteria stimulate the synthesis of growth factors, including KGF, which aids the re-epithelialization processes in addition.

Angiogenesis Stimulation: An example of the latter is angiogenesis. New blood vessels are formed to support the formation of blood vessels to heal a given wound. Angiogenesis can also be affected by chemicals released from the skin microbiome, among them being the vascular endothelial growth factor (VEGF) and the platelet-derived growth factor (PDGF), among others (Zielińska et al., 2023). They produce positive effects that enhance the motility of the endothelial cells; thus, the formation of blood vessels and improved blood flow in the tissues is enhanced.

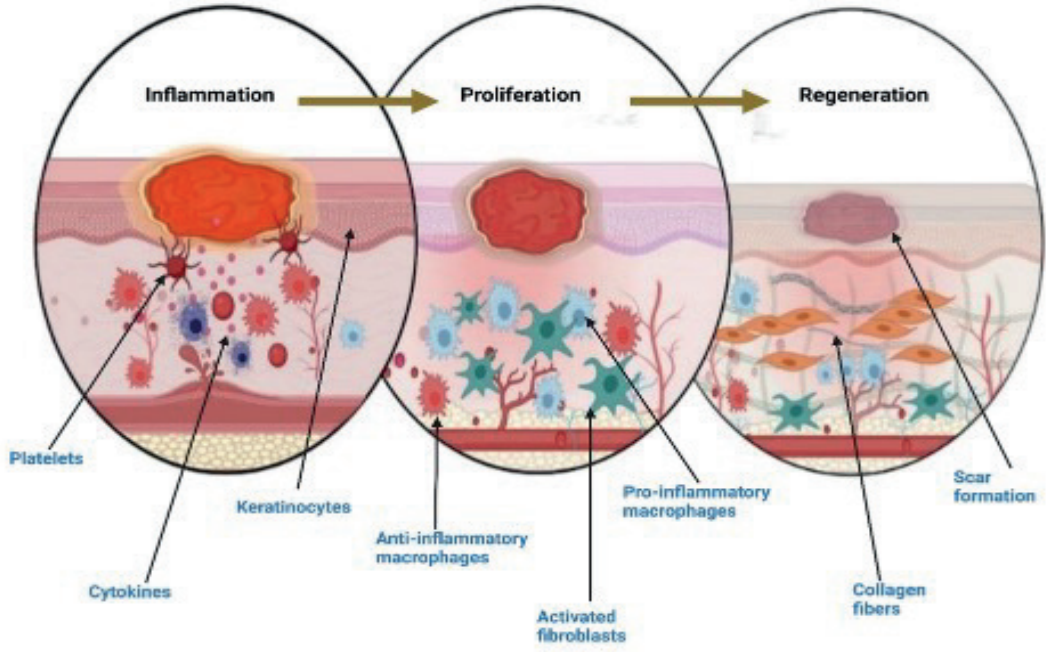


Figure 2. Stages of Wound Healing: A Dynamic Journey of Repair and Regeneration

Scar Formation Modulation: It also plays a role in scar tissue formation, the last process in wound healing, which is a complicated pathological process. Skin dysbiosis describes the skin microbial imbalance and is linked with hypertrophic scarring, which entails the accumulation of collagen and other ECM proteins (Fernandes et al., 2023). Conversely, an appropriately functioning microbial community will encourage scarless healing by regulating the activity of the fibroblasts, the cells that synthesize collagen.

5.2 Microbiome in Chronic Wound and Ulcer

It affects mid and elderly-aged masses; a special type of lesions is chronic non-healing ulcers; diabetic foot ulcers, pressure ulcers, and venous leg ulcers. These are significant health burdens worldwide characterized by long-healing time, recurrent infection, and impaired quality of life (Probst et al., 2022). The composition of the microbiome contributes significantly to the development and treatment process of chronic wounds. Thus, chronic wounds, the majority of the time, can be associated with dysbiosis indicated by a decrease in microbial richness and an increase in pathogenic load (Tang et al., 2023). This imbalance continues inflammation within the chronic wound, limits the body's ability to heal damaged tissues, and sets the optimal stage for biofilm development, a bacterial colony protected by a slimy matrix that eludes conventional treatments and the body's defenses. Another issue that aggravates chronic wound healing is the formation of biofilms because they reduce the ability of topical agents, including antibiotics, to penetrate through the wound site and may contribute to the delay in the healing process (Razdan et al., 2022).

5.3 Probiotics and Prebiotics Applied in Therapy

The health-related uses of probiotics and prebiotics, especially in wound healing and tissue repair, have been considered for further studies. Among nutraceuticals, probiotics are live microorganisms that possess health benefits, and prebiotics are non-digestible food ingredients (Table 2). It stimulates the growth of beneficial bacteria, which have been considered to effectively alter the skin microbiome as well as improve the healing rate of the skin (Canchy et al., 2023). Some of the beneficial effects demonstrated by the use of topical probiotics are the decrease in inflammation, acceleration of the re-epithelialization process, angiogenesis in the granulation

issues, and the inhibition of biofilm formation, although these effects were studied in animals only (Bădăluță et al., 2024).

Table 2: Therapeutic Interventions for Wound Healing Using Probiotics and Prebiotics

Intervention	Mechanism of Action	Effectiveness	Potential Applications	References
Probiotics	Introduce beneficial bacteria to restore microbial balance and promote healing.	Varies depending on strain and application	Chronic wounds, burns, diabetic ulcers, pressure sores	(Fijan et al., 2019)
Prebiotics	Provide nourishment for beneficial bacteria, promoting their growth and activity.	It is promising, but more research is needed	Same as probiotics, also in preventive skincare	(França, 2021)
Synbiotics	Combination of probiotics and prebiotics for synergistic effects.	Potentially enhanced effectiveness	It is the same as probiotics and prebiotics	(Simon et al., 2021)
Topical Probiotics	Direct application of beneficial bacteria to the wound site.	Limited evidence	Minor cuts, abrasions, skin infections	(Mohammedsaeed, 2015)

Thus, probiotics can cause these effects through the direct production of bacteriocins and other antimicrobial peptides, alteration in cytokine secretion, or the activation of growth factors. FOS and GOS used in the diet can also reduce bacterial infection and enhance their positive effect on bacterial metabolites, such as SCFAs (Zhang et al., 2022). These metabolites can improve wound healing by increasing new blood vessel formation, regulating the immune system, and preventing bacterial growth. The findings of existing studies regarding probiotics and prebiotics in wound healing have not been well researched and, therefore, are promising. The mentioned therapies are considered as a potential organic solution to regular measures taken while treating the wound, thus minimizing the probability of receiving adverse effects.

6. Effects of Microbiome and Stem Cell Therapy

The correlation between the microbiome and stem cell therapy has recently become an extensive and complex field of study, the findings of which open a fresh world of possibilities for stem cell therapy in regenerative medicine (Tu et al., 2022). The specific interest are the roles of the gut microbiome in stem cell biology and its relation with stem cell function and differentiation, as well as the interaction between stem cells and the surrounding microenvironment, locally referred to as the stem cell niche.

6.1 Enhancing Stem Cell Function and Differentiation

Recent findings indicate that the gut microbiota affects the function and differentiation of stem cells both directly at the site of the gut microbiota niche and indirectly to other tissues. This modulation is regulated by several processes, chiefly through the synthesis of active metabolites by the gut microbiome.

Short-Chain Fatty Acids (SCFAs): Gut microbiota-derived metabolites, SCFAs, are the most significant modulators of stem cells' properties generated from dietary fiber fermentation. The role played by Butyrate, an SCFA, as one of the most effective factors was to increase the number of intestinal stem cells (ISCs), which are important in maintaining acceptable levels of Epithelial layer integrity. That occurs through activating G protein-coupled receptor 43 (GPR43) on ISCs, promoting Wnt signaling, a critical pathway for stem cell division (Ma et al., 2022). Butyrate has also been reported to affect the regulation of colonic Tregs, which is important for immune regulation and the overall health status in the gut (Silva et al., 2018).

Microbiome-Derived Factors and Stem Cell Migration: The gut microbiome can synthesize numerous factors that affect stem cell migration and homing. For instance, some bacteria are in a position to release chemoattractants that direct stem cells to areas of damaged tissue or inflammation (Ratajczak et al., 2013). This can promote tissue repair by producing a pool of cells that will replace the damaged or dying tissues.

Regulation of Epigenetic Modifications: Microbiota can affect gene regulation by altering the epigenetic marks like DNA methylation and histone acetylation of stem cells, thus changing their fate (Lorzadeh et al., 2021). The described epigenetic changes can be brought by microbial metabolites or through the microbiome's interaction with immune systems and may affect stem cells' ability to differentiate and tissues to regenerate.

6.2 Modulation of Stem Cell Niches by Microbiota

Stem cells are located in a specific structure known as a niche, which is responsible for their quiescence, renewal, and distinction. The availability and function of SCNs involved in stem cells are highly influenced by the gut microbiome, which alters the functions of various stem cells and tissue repair.

Gut Microbiome and Intestinal Stem Cell Niche: Gut microbiota is also known for its important function in protecting the stem cells of the small intestine situated in the crypt base (Nigro & Sansonetti, 2015). Dysbiosis can be defined as the adjustment of this niche, which contributes to the decline in the functionality of stem cells, changes in the differentiation patterns, as well as to compromised tissue regeneration. For instance, antibiotics' action on dysbiosis restrains the proliferation of the normal cellular parts, which are Lgr5 + stem cells and Paneth cells that are vital in the regulation of intestinal epithelium's homeostasis (Wallaeys et al., 2023).

Microbiome and Bone Marrow Stem Cell Niche: Among the current research works that have been conducted, it is possible to point out such a correlation that was not expected between the gut microbiome and the BMSC niche that enabled it to be determined (Gavin, 2019). It has also been noted that the relative signals of the gut microbiota can control the formation and productivity of hematopoietic stem cells (HSCs) that are believed to be liable for the production of all kindsblood cells. This will logically lead to the fact that SCFAs that stem from gut metabolism either enhance or decrease the functional ability of the HSCs residing in the bone marrow. It is mainly responsible for the general immunological capacity and the general potential of the marrow on which a second layer of coating can be applied (Li et al., 2021).

6.3 Case Studies: Gut Microbiota and Bone Marrow Transplantation

The gut microbiota's influence on MSC-based treatment is most pronounced in the context of bone marrow transplantation (BMT), which is a lifesaving intervention for patients with hematologic cancers and other blood dyscrasias. However, BMT is often complicated by various side effects such as graft versus host disease, infection, and immune reconstitution disorders (Barrett, 1987).

It was also identified that obesity also affects the complexity of the gut microbiome and the risk of development and severity of these complications. It has also been observed that the gut microbiota of patients with low Bacterial and fungal diversity with pathogenic bacteria overgrowth are at a higher risk of getting GVHDs and infections (Kumari et al., 2019). On the other hand, a pathogenic and imbalanced gut microbiota has been associated with the above-mentioned complications and hinders the engraftment of the transplanted stem cells. Recent studies indicate that manipulating gut microbiota via the administration of probiotics, prebiotics, or FMT might enhance the treatment results in patients receiving BMT (Yu et al., 2020). The guidelines for these interventions are as follows: interventions that can assist in reconstructing a microbiome, decrease inflammation, improve immune reconstitution, and lower the risk of developing GVHD.

7. Gut Microbiota and Organ Regeneration

Though mostly associated with the intestines, the gut microbiome critically impacts the renewal of different organs in the human body. Recent studies have elaborated on the relationship between microbiota and organ regeneration and are thus in a position to explore the microbiome's regenerative capabilities for acting as a therapeutic tool.

7.1 Liver Regeneration and Microbiome

The organ most sensitive to gut microbiota is the liver, which is recognized for its excellent ability to regenerate. The gut-liver axis, as a two-way communication channel, consists of the metabolites, bacteria, immune cells, and signaling molecules that influence liver performance and regeneration (Huang et al., 2024).

Gut Microbiota and Liver Injury: Pro-inflammatory dysbiosis involving disruption of the gut microbiota is posited to be involved in NAFLD, ALD, and cirrhosis patients, respectively (Giraud & Saleh, 2021). These conditions are defined as chronic inflammation, high levels of oxidants, and defective hepatocyte proliferation. Both basic studies and clinical trials have demonstrated that the changes in the gut microbiome by using probiotics, prebiotics, or FMT can decrease hepatotoxicity and inflammation and enhance liver regeneration in animal experiments and clinical research (Xue et al., 2019).

Microbiome-Derived Metabolites and Liver Regeneration: Liver regeneration is mainly regulated by gut bacteria metabolites that directly impact this body's function. The fermentation products of proteins and fibrous constituents of diet, referred to as SCFAs, have been demonstrated to induce the proliferation of liver cells, referred to as hepatocytes, as well as stimulate the metabolic activity of those cells (Visekruna & Luu, 2021). Also, SCFAs regulate immune responses, decrease inflammation, and enhance the gut barrier function, which is significant for the liver and its regeneration process.

Gut Microbiota and Liver Transplantation: Therefore, the gut microbiota significantly influences liver transplantation outcomes. Studies has revealed that McMaster has adverse effects on the recipient, such as infection, rejection, and GVHD, whereas, on the other hand, a healthy, diverse MAC increases the chances of graft survival and immunological acceptance (Yao, 2022). Hence, interventions aimed at altering the gut microbiota through prebiotics, probiotics, or FMT might help to enhance the prognosis among liver transplant patients.

7.2 Role in Intestinal and Colonic repair

The gut microbiome plays critical functions for the remodeling and healing of the epithelium which is a monolayer of cells that forms a layer of protection in our gut from certain compounds. Intestinal epithelium is self-renewable due to the presence of a small nutrient supply containing Isc associated with the bottom of the crypts (De Francesco et al., 2016).

Microbiome-Derived Factors and ISC Proliferation: These bacteria generate several metabolites that can impact ISC proliferation and IEF directly or without any interference. For example, butyrate, which is a kind of SCFAs that derive from some host bacteria, has been verified to facilitate the expansion of ISC and defend against intestinal injury (Sphyris et al., 2021). Other microbial metabolites affect ISC functionality, the differentiation of ISC, and the overall epithelial homeostasis of the intestine. This is through tryptophan metabolites and bile acids.

Microbiome and Inflammatory Bowel Disease: Crohn's disease and ulcerative colitis are subtypes of IBD; it is defined by the presence of chronic inflammation and compromised mucosal healing of the gut (Zonderman & Vender, 2009). The imbalance of gut microbiota, commonly described as dysbiosis, is a characteristic feature of IBD associated with the decrease in anti-inflammatory and the increase in pro-inflammatory bacteria. Fecal microbiota transplantation, as well as the use

of probiotics, have been advocated in the amelioration of IBD and have demonstrated the ability to induce remission and heal the mucosa in such patients (Imdad et al., 2023).

7.3 Cardiac Regeneration: Insights from the Gut-Heart Axis

As bidirectional communication, the gut-heart axis showed that the aim of the microbiome can be concerned with cardiac regeneration. Some observations made recently are the findings that gut microbiota seems to lead to a lifelong change in the functional properties of the cardiac tissue (Lippi et al., 2017). It also the adaptation and repair of the tissue by influencing the process of inflammation, production of reactive oxygen species, and metabolic engineering of cardiac muscle (Figure 3).

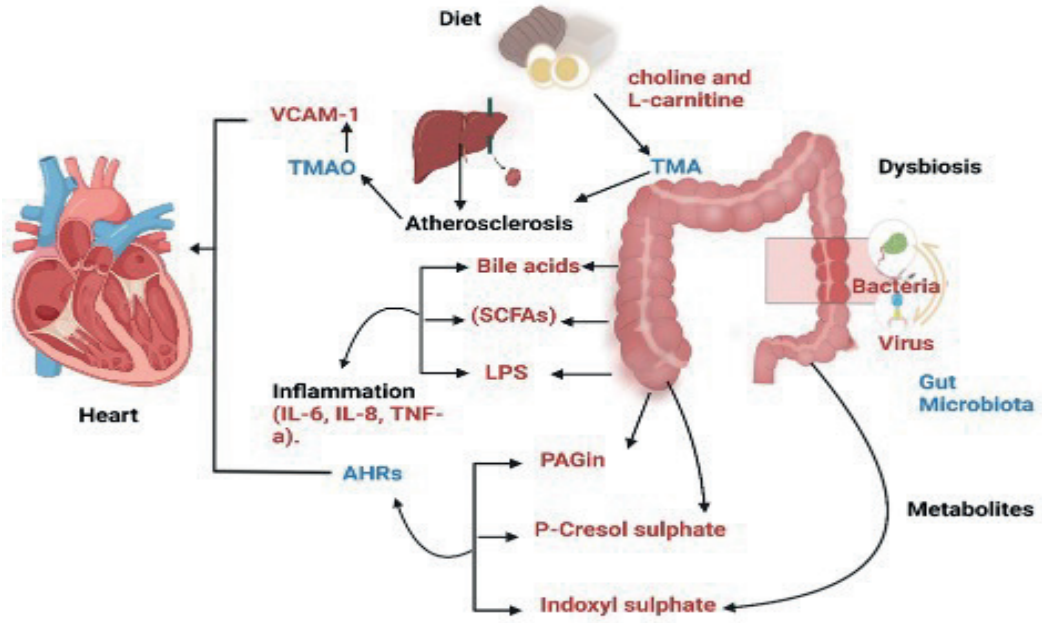


Figure 3. Gut-Heart Axis: Microbiota's Influence on Cardiac Regeneration

Microbiome and Myocardial Infarction: An example of an Acute condition is an acute myocardial infarction, also known as heart attack, in which there is death of cardiac muscles. The specific type of bacteria within the GI tract may also affect inflammation and tissue healing after an MI, which may affect the heart's performance and self-repair (Zhu et al., 2020). Several studies showed that the change in the gut microbial composition that was induced by the probiotics leads to a reduction of the range of cardiac damage. It also has protective effects on the worsening of the contractile dysfunction of the myocardial cells in animal models of MI (Chen et al., 2019).

Microbiome-Derived Metabolites and Cardiac Repair: What is clear to all of us is that there are gut bacteria that produce certain metabolites, and all these metabolites can influence the state and the recovery of the heart. Among the newly identified human gut metabolites termed Trimethylamine N-oxide or TMAO, the cardiovascular consequences were unfavorable (Wang et al., 2021). But other metabolites have, for instance, been classified under SCFAs, which Scientific studies claim have the potential to offer cardioprotection through the processes that assist in combating inflammation and enhancing endothelial function and angiogenesis.

8. Microbiome-Based Therapies in Regenerative Medicine

The symbiotic relationship between bacteria and their host regarding the host's ability to regenerate its tissues has created new horizons in treatment; microbiome therapies might serve as supplements for the body's inherent ability to fix itself. These advanced strategies utilize microbial interactions to influence immune reactions, blood vessel formation, and stem cell activity and, as a result, improve tissue healing and regeneration processes.

8.1 Fecal Microbiota Transplantation (FMT) and Tissue Repair

FMT, a procedure in which stool from a healthy individual is introduced into the gastrointestinal system of a disorder recipient with pathological gut microbiota, has been identified as a strong technique for re-establishing the relation and complexity of the gut microbiome. Although it was initially applied to patients with recurrent C. difficile infection, FMT has derived a positive result for various diseases, such as IBD and IBS (Borody et al., 2019). However, the potential roles of this effect have recently expanded over and above the newly discovered inflammatory diseases and encompassed tissue repair and regeneration.

FMT and Wound Healing: Diabetic foot ulcers, pressure ulcers, and venous ulcers are some common types of CRWs that affect the healthcare systems globally. Some of these injuries are qualified as dysbiosis, which means that there are disruptions in the composition of the microbial community, which can cause the wound not to heal. There are indications that FMT can be applied in chronic wound infection; researchers have found that it can alter, dampen, increase, and expedite wound healing in the GI microbiota, inflammation, and angiogenesis, respectively (Bangs, 2020).

FMT and Organ Regeneration: The studies that were carried out earlier in the recent indicated that FMT might be used in the regenerative medicine of vital organs. For instance, certain techniques, such as Fecal Microbiota Transplantation, have been identified to help regain liver function and further assist in the regeneration of liver tissues in patients with cirrhosis, a severe liver disease. The introduced microbiome is believed to suppress inflammation and/or directly alter the gut microbiota to facilitate organ regeneration. Further, FMT has been considered for application in stem cell transplantation, where it would help improve their engraftment and functioning by shaping up the gut microbiota (Zama et al., 2020).

8.2 Development of Microbiome Derived Bioactive Molecules

The microbiota synthesizes numerous bioactive metabolites, of which SCFAs, vitamins, amino acids, and secondary bile acids can be expected to have tissue repair activities (Debnath et al., 2021). To present these molecules from the microbiome to treat the above-said person is now the field of regenerative medicine.

SCFAs as Therapeutic Agents: Therefore, SCFAs, especially butyrate, have been disclosed to be the promoters of the tissue repair and regeneration process (Hajjar et al., 2021). These metabolites can affect stem cell division and differentiation and may participate in forming new blood vessels, regulating immune cells, and reducing inflammation. While butyrate is supplied for IBD, it is also used in such experimentations to elicit the formation of genes required for wound healing, any process associated with necrosis stated, or any impaired tissue repair.

Microbiome-derived Antimicrobial Peptides (AMPs): AMPs are small molecules produced by bacteria inhabitant the intestinal tract that has a direct impact on pathogens by killing them (Furci & Secchi, 2018). They can kill or restrict the growth of pathogenic bacteria, thus showing prospects of being used in the treatment of infections and the promotion of wound healing. Emergent work has been done to discover and classify the new AMPs from the gut microbiome and their additional role in regenerative therapy.

8.3 Synthetic Biology and Engineered Microbes

Biologically inspired engineering and system techniques within synthetic biology pave the way for microbiome-based therapeutic approaches. In creating the microbial solution, the scientists hope for the achievement of site-specific therapies that will address the regenerative processes.

Engineered Probiotics: Thus, researchers are selecting and modifying probiotic strains to have various custom features, including the synthesis of certain metabolites or the expression of therapeutic proteins (Singh et al., 2018). These purposefully constructed bacteria could be utilized

to carry therapeutic compounds directly to the particular area of tissue damage or disease, thus improving tissue remodeling and regeneration.

Microbial Consortia: Another promising strategy in synthetic biology is the construction of microbial communities and multiple bacterial strains (Rodríguez Amor & Dal Bello, 2019). These consortia could also work harmoniously to enhance the yield of specific desirable metabolites and have a greater impact on tissues than a single strain.

Targeted Drug Delivery: The engineered microbes can thus be used as carriers of drugs or any other therapeutic molecules, with a preference towards a particular tissue or organ (Wu & Liu, 2022). They can also increase the efficiency of the drugs and diminish the overall toxicity of the system; they can also help increase the regenerative capacity of the established remedies.

9. Challenges and Future Directions

The prospectus of microbiome-based therapies in regenerative medicine is profound. However, multiple complexities and concerns have to be met to effectively and safely transport these promising treatments into the clinic.

9.1 Technical and Scientific Problems

The microbiome is a multifaceted and constantly changing system, and the involvement of the microbiome in regenerative medicine is an area of distinctive study. Several technical and scientific challenges remain to be addressed:

Identifying Key Microbial Players: The microbiome contains an incredible number of microorganisms, and it is difficult to pinpoint the exact species or even strains that are so important for tissue regeneration (DeSalle & Perkins, 2015). Novel sequencing and computational biology techniques are being discovered to catalog the microbiome and discover possible drugs for treatment.

Understanding Mechanisms of Action: Although it is clear that the microbiome does indeed dictate the means of tissue regeneration, the exact ways in which this process is regulated are still not quite understood. More work should be conducted on the various parts and pathways of bacterial metabolites, the signaling of bacteria with host tissues, and the immune response to bacterial repair of injured tissues (Yang & Chiu, 2017).

Developing Standardized Therapies: The challenge then emerges as to how to standardize and reproduce post-rigor microbiome-based therapies like probiotics and Fecal Microbiota Transplant. Microbial communities also have different structures and functions in different people, which makes it impossible to talk about individual universals in the use of therapies (Moran et al., 2019). Dietary recommendations and the intensity of treatments may have to be chosen depending on the results of an individual's microbiota analysis for optimized therapeutic outcomes.

9. 2 Policy and Process Implications

The use of microbiome-based therapies raises several ethical, legal, and social considerations that need to be carefully addressed: The use of microbiome-based therapies raises several ethical, legal, and social considerations that need to be carefully addressed:

Safety and Long-Term Effects: The consequences of adjusting this microbiome, especially from sanitation or pharmacologic research, including FMT, are not the subject to good comprehension today (König et al., 2017). However, these therapies must be proven safe and effective with the applicable double-blind studies first.

Informed Consent and Autonomy: Patients' conditions must be explained to ensure that they understand the consequences such as the probability of contracting other diseases, side effects, and the long-term impact of microbiome therapies (Ribeiro et al., 2020). Although it may be impossible

to avoid conflicts of interest in healthcare, the patient's right to decide and be protected must be upheld by acquiring informed consent.

Access and Equity: Some micro-biome-based treatments, like FMT, are expensive and, therefore, not affordable to all people. It remains a major ethical issue to ensure that people in need and who could benefit from these types of interventions get equal chances and opportunities (Hoggett et al., 2008).

Regulatory Oversight: The existing legal framework of microbiome-based therapies is also continuously shifting (Manrique et al., 2024). Therefore, measures, requirements, policies, and objectives regarding the production and use of these therapies need to be developed and established.

9.3 Regulatory Factor and Approval Process

Approving these microbiome-based therapies requires particular concern because the microbiome is large and variable.

Classification of Microbiome-Based Products: It is, therefore, possible to categorize microbiome-based therapies as drugs, biologics, or medical devices depending on their intended usage and composition, creating more regulatory issues (Manrique et al., 2024). More specific regulations are missing or lacking details that could help in launching and approving these treatments.

Clinical Trial Design: Considering important aspects like the microbiome's complexity, the inter-individual response, or the outcomes of microbiota-targeted therapies, clinical trials for microbiota-based approaches should be specifically designed (Favaron et al., 2023). The study designs should be strong, following globally established guidelines to produce evidence that fits the acceptance criteria of regulatory agencies.

Post-Market Surveillance: Due to the immense process of constant change of the microbiome, after-approval monitoring or post-market surveillance becomes a necessity to assess the safety and effectiveness of microbiome-based therapies. This can help identify an adverse effect, follow the evolution of the microbiome, and estimate the impact of these therapies in patient management (Vázquez-Baeza et al., 2018).

9.4 The Possibility of Patient-Specific Regenerative Medicine

The convergence of microbiome with regenerative medicine can be seen as the key to the future of the field because it makes it possible to create the individual's regenerative approach (Williams et al., 2023).

Microbiome Profiling: It has been found that by looking at an individual's microbiome, which is the microorganisms living in the body, clinicians can determine if there is dysbiosis or imbalances in the body that would prevent essential tissue repair. These details can help to design individual treatment plans; for example, the client can take probiotics, prebiotics, or receive an FMT to restore a healthy microbiota and achieve the best regenerative result (Ugwu et al., 2024).

Targeted Therapies: Microbiome-based therapies can be designed to modulate the pathways contributing to tissue healing and regeneration (Lee, 2021). This specific procedure can improve the effectiveness of regenerative treatments while reducing side effects.

Predictive Biomarkers: Thus, expanding the understanding of the relationship between microbiome and an individual's response to regenerative therapies offers the potential for treatment optimization and better patient outcomes (Van Lier et al., 2021).

9.5 Directions for Collaboration Between Microbiome and Regenerative Medicine Investigators

It is here important to link microbiome investigators with regenerative medicine to hasten the possibility of a cure undertaking. This collaborative approach can be facilitated through several key strategies. Thus, several strategies may be employed to enhance this kind of collaborative approach:

Joint Research Projects: Therefore, the representatives of the microbiome and regenerative medicine can produce a positive interaction that will offer an opportunity to develop and perform intricate investigations. That will help in conceiving and displaying the processes, which would improve knowledge of the microbiome and the niches of tissue regeneration. Such projects can focus on such objectives as the identification of microbial genera or bioactive compounds that are engaged in the healing process, the identification of the signaling networks of such processes, or the new therapeutic approaches that regulate the interaction with host microbiota (Pires et al., 2024).

Data Sharing and Integration: Clinicians and microbiome-inspired researchers need to share data so that new knowledge that is created needs to be applied (Tomasulo et al., 2024). Microbiome collections might be merged with clinical data to identify correlations and connections that are hard to ascertain in studies involving individuals at given time points. Thus, it helps define new biomarkers for the potential assessment of the patient's response to therapies, identification of potential beneficiaries of certain treatments, and, all in all, the assessment of the long-term outcomes driven by microbiome interventions (Elhag et al., 2022).

Multidisciplinary Teams: It is important to identify various teams containing particular specially microbiome researchers' immunologists, senior bioinformaticians, and other special individuals belonging to a similar subject treatment. Such teams could advise their specialist and provide the required knowledge on the aspects concerning the growth of microbial consortia and the development of the delivery system to achieve the goal the paper aims for, namely, standardization of FMT (Fitzpatrick et al., 2024).

9.6 Empirical Process and Clinical Trails

Many healthcare providers want microbiome-based therapies to become standard clinical practice. However, this is only possible if well controlled trials are conducted.

Well-Designed Studies: Clinical trials must be designed according to certain research questions and appropriate endpoints and methodological stringency (Provencher et al., 2018). Due to the complexity of the microbiome and persons' responses to the administered treatments, this position is understandable. For example, the current level of the microbiome characterization means that patients need to be segmented based on characteristics of the microbiome to identify the population that will benefit based on the changes to be made to its structure through various interventions.

Standardized Protocols: Therefore, there is a need to capture the comparability of the various Microbiome interventions; Fecal Microbiota Transplantation FMT, Probiotics, and Prebiotics for repeatability of the studies involved (Yadegar et al., 2024). Proselytization of such protocols should include information about the choice of the donors, preparation of the material, its delivery, the doses to be used, and the length of the treatment. Standardization is also necessary, especially when it comes to the safety and quality of the products developed from microbiomes such as FMT.

Long-Term Follow-Up: Due to the described consequences and the complexity, one should control the patients' outcomes after microbiota manipulation by using microbiome-based therapies with definite prolonged intervals (Abdul Rahman et al., 2021). It can assist in assessing the sustainability of the therapeutic interventions' gains for side effects and other factors that may influence the treatment outcome. In addition, with the help of long-term research, it is possible to define the effectiveness of microbiome interventions in preventing cancer relapse or progression.

Continuing Medical Education: Thus, it might be advisable for healthcare providers to engage in relevant CME programs to familiarize themselves with the existing state of the studies and clinical guidelines regarding the utilization of the microbiome in treatment. This can furnish them with the knowledge and skills that they need to practice these therapies and also handle patients in the same (Gonzalez et al., 1990).

Patient Education: The patients that have to be administered the microbiome treatment would have to understand what the microbiome is, how it works, and such things as the microbiome therapy is beneficial or hazardous to the human body (Nayak & Turnbaugh, 2016). This may help them make proper decisions on their health and make them participate in their treatment. Referral materials, including brochures, sources of information on the internet, and support groups from the patients, could be vital in the general process of educating the patients.

10. Conclusion

Microbiome or microbial symbionts, which are a prolonged identity of people, are at the forefront of new regenerative medicine. It plays some appreciable role in the process of tissue repair and regeneration, involving in part the regulation of immune cells and angiogenesis, influence on the stem cells, and last but not least, the process of differentiation. Now that the role of the concept of the microbiome was viewed from other points as the support of the healing process of different tissues together with the Bioluminescent technology a new area was opened in the treatment of many illnesses and injuries. Some of the existing and known treatments cover FMT, the combination of probiotics with prebiotics, and producing active molecules originating from microorganisms that efficiently accelerate the regeneration and skin repair process. The ability to build functional and controlled communities or from certain residents who ensure the right environment for tissue renovation is a new approach that addresses the challenges of chronic ulcers, biomatrix damage, and degeneration among the population. However, there are several problems related to using microbiome research in regenerative medicine. Difficulties in isolation and delineation of such microorganisms and their niches and ways of operation, as well as logical, juridical, and ethically considerate problems, demand additional research and passingly navigated paths. Therefore, the task of building a common and personal, at the same time, highly effective and reproducible microbiota-directed therapy remains a tough one, and, accordingly, it is hoped that it will be solved by people of various fields only. However, microbiome-based regenerative medicine has a great future based on the following factors. Novel techniques, including single-cell sequencing, and new insights into the bioinformatics tools, are helping them expand the horizon for the perspective of deciphering the trends of the microbiota and the host tissues. For such reasons, in light of opportunities to use genetic manipulations of microbial cells and targeted delivery systems, the prospects of the application of microbes in the treatment of diseases are much broader. As researchers study further the microbiome's roles in aiding the regeneration of tissue, improved therapies should be developed because of this energy source for healing. It is a new overcoming paradigm in the field of regenerative medicine that possesses an excellent opportunity to revolutionize the present system of health care by offering new concepts, ideas, and strategies in the management of chronic non-healing ulcer wounds, organ failure and degenerative diseases with the overall improvement in the quality of life of the patients.

11. References

Abdollahiyan, P., Oroojalian, F., & Mokhtarzadeh, A. (2021). The triad of nanotechnology, cell signalling, and scaffold implantation for the successful repair of damaged organs: An overview on soft-tissue engineering. Journal of Controlled Release, 332, 460-492.

Abdul Rahman, R., Lamarca, A., Hubner, R. A., Valle, J. W., & McNamara, M. G. (2021). The microbiome as a potential target for therapeutic manipulation in pancreatic cancer. Cancers, 13(15), 3779.

Bădăluță, V. A., Curuțiu, C., Dițu, L. M., Holban, A. M., & Lazăr, V. (2024). Probiotics in Wound Healing. International journal of molecular sciences, 25(11), 5723.

Balakrishnan, B., & Taneja, V. (2018). Microbial modulation of the gut microbiome for treating autoimmune diseases. Expert Review of Gastroenterology & Hepatology, 12(10), 985-996.

Bangs, K. (2020). A Small Answer to a Big Problem: How re-establishing homeostasis in the human gut microbiome after solid organ transplantation can improve transplant success

Barrett, A. (1987). Graft-versus-host disease: a review. Journal of the Royal Society of Medicine, 80(6), 368-373.

Bhardwaj, G., Riadi, Y., Afzal, M., Bansal, P., Kaur, H., Deorari, M., Tonk, R. K., Kazmi, I., Alzarea, S. I., & Kukreti, N. (2024). The hidden threat: environmental toxins and their effects on gut microbiota. Pathology-Research and Practice, 255, 155173.

Bloomfield, S. F., Stanwell-Smith, R., Crevel, R., & Pickup, J. (2006). Too clean, or not too clean: the hygiene hypothesis and home hygiene. Clinical & Experimental Allergy, 36(4), 402-425.

Borody, T. J., Eslick, G. D., & Clancy, R. L. (2019). Fecal microbiota transplantation as a new therapy: from Clostridioides difficile infection to inflammatory bowel disease, irritable bowel syndrome, and colon cancer. Current Opinion in Pharmacology, 49, 43-51.

Caffaratti, C., Plazy, C., Mery, G., Tidjani, A.-R., Fiorini, F., Thiroux, S., Toussaint, B., Hannani, D., & Le Gouellec, A. (2021). What we know so far about the metabolite-mediated microbiota-intestinal immunity dialogue and how to hear the sound of this crosstalk. Metabolites, 11(6), 406.

Canchy, L., Kerob, D., Demessant, A. L., & Amici, J. M. (2023). Wound healing and microbiome, an unexpected relationship. Journal of the European Academy of Dermatology and Venereology, 37, 7-15.

Canesso, M. C., Vieira, A. T., Castro, T. B., Schirmer, B. G., Cisalpino, D., Martins, F. S., Rachid, M. A., Nicoli, J. R., Teixeira, M. M., & Barcelos, L. S. (2014). Skin wound healing is accelerated and scarless in the absence of commensal microbiota. The Journal of Immunology, 193(10), 5171-5180.

Carotenuto, F., Politi, S., Ul Haq, A., De Matteis, F., Tamburri, E., Terranova, M. L., Teodori, L., Pasquo, A., & Di Nardo, P. (2022). From soft to hard biomimetic materials: Tuning micro/nano-architecture of scaffolds for tissue regeneration. Micromachines, 13(5), 780.

Carvalho, J. (2020). Cell reversal from a differentiated to a stem-like state at cancer initiation. Frontiers in oncology, 10, 541.

Chen, X., Li, H.-Y., Hu, X.-M., Zhang, Y., & Zhang, S.-Y. (2019). Current understanding of gut microbiota alterations and related therapeutic intervention strategies in heart failure. Chinese medical journal, 132(15), 1843-1855.

Das, T., Jayasudha, R., Chakravarthy, S., Prashanthi, G. S., Bhargava, A., Tyagi, M., Rani, P. K., Pappuru, R. R., Sharma, S., & Shivaji, S. (2021). Alterations in the gut bacterial microbiome in people with type 2 diabetes mellitus and diabetic retinopathy. Scientific reports, 11(1), 2738.

De Francesco, F., Romano, M., Zarantonello, L., Ruffolo, C., Neri, D., Bassi, N., Giordano, A., Zanus, G., Ferraro, G. A., & Cillo, U. (2016). The role of adipose stem cells in inflammatory bowel disease: From biology to novel therapeutic strategies. Cancer biology & therapy, 17(9), 889-898.

De Santis, R., Guarino, V., & Ambrosio, L. (2019). Composite biomaterials for bone repair. In Bone repair biomaterials (pp. 273-299). Elsevier.

Debnath, N., Kumar, R., Kumar, A., Mehta, P. K., & Yadav, A. K. (2021). Gut-microbiota derived bioactive metabolites and their functions in host physiology. Biotechnology and Genetic Engineering Reviews, 37(2), 105-153.

DeSalle, R., & Perkins, S. L. (2015). Welcome to the microbiome: getting to know the trillions of bacteria and other microbes in, on, and around you. Yale University Press.

Deuel, T. F., & Chang, Y. (2014). Growth factors. In Principles of Tissue Engineering (pp. 291-308). Elsevier.

Dwivedi, M., Kumar, P., Laddha, N. C., & Kemp, E. H. (2016). Induction of regulatory T cells: a role for probiotics and prebiotics to suppress autoimmunity. Autoimmunity Reviews, 15(4), 379-392.

Elfawy, L. A., Ng, C. Y., Amirrah, I. N., Mazlan, Z., Wen, A. P. Y., Fadilah, N. I. M., Maarof, M., Lokanathan, Y., & Fauzi, M. B. (2023). Sustainable approach of functional biomaterials–tissue engineering for skin burn treatment: a comprehensive review. Pharmaceuticals, 16(5), 701.

Elhag, D. A., Kumar, M., Saadaoui, M., Akobeng, A. K., Al-Mudahka, F., Elawad, M., & Al Khodor, S. (2022). Inflammatory bowel disease treatments and predictive biomarkers of therapeutic response. International journal of molecular sciences, 23(13), 6966.

Fasano, A., & Flaherty, S. (2021). Gut feelings: The microbiome and our health. MIT Press.

Favaron, A., McCoubrey, L. E., Elbadawi, M., Basit, A. W., & Orlu, M. (2023). The Ageing Microbiome, Pharmaceutical Considerations, and Therapeutic Opportunities. In Pharmaceutical Formulations for Older Patients (pp. 191-230). Springer.

Fernandes, A., Rodrigues, P., Pintado, M., & Tavaria, F. (2023). A systematic review of natural products for skin applications: Targeting inflammation, wound healing, and photo-aging. Phytomedicine, 115, 154824.

Fijan, S., Frauwallner, A., Langerholc, T., Krebs, B., ter Haar, J. A., Heschl, A., Mičetić Turk, D., & Rogelj, I. (2019). Efficacy of using probiotics with antagonistic activity against pathogens of wound infections: an integrative review of literature. BioMed research international, 2019(1), 7585486.

Fitzpatrick, F., Brennan, R., van Prehn, J., Skally, M., Brady, M., Burns, K., Rooney, C., & Wilcox, M. H. (2024). European Practice for CDI Treatment. In Updates on Clostridioides difficile in Europe: Advances in Microbiology, Infectious Diseases and Public Health Volume 18 (pp. 57-84). Springer.

Fock, E., & Parnova, R. (2023). Mechanisms of blood–brain barrier protection by microbiota-derived short-chain fatty acids. Cells, 12(4), 657.

França, K. (2021). Topical probiotics in dermatological therapy and skincare: a concise review. Dermatology and therapy, 11(1), 71-77.

Furci, L., & Secchi, M. (2018). AMPs and mechanisms of antimicrobial action. In Antimicrobial Peptides in Gastrointestinal Diseases (pp. 97-131). Elsevier.

Ganesan, R., Wierz, J. C., Kaltenpoth, M., & Flórez, L. V. (2022). How it all begins: bacterial factors mediating the colonization of invertebrate hosts by beneficial symbionts. Microbiology and Molecular Biology Reviews, 86(4), e00126-00121.

Gavin, C. (2019). Mesenchymal Stromal Cell Crosstalk with the Immune System Karolinska Institutet (Sweden)].

Giraud, J., & Saleh, M. (2021). Host–Microbiota Interactions in Liver Inflammation and Cancer. Cancers, 13(17), 4342.

Gomes, S., Rodrigues, A. C., Pazienza, V., & Preto, A. (2023). Modulation of the tumor Microenvironment by Microbiota-derived short-chain fatty acids: impact in colorectal cancer therapy. International journal of molecular sciences, 24(6), 5069.

González-Molina, M., Ruiz-Esteban, P., Caballero, A., Burgos, D., Cabello, M., Leon, M., Fuentes, L., & Hernandez, D. (2016). Immune response and histology of humoral rejection in kidney transplantation. nefrologia, 36(4), 354-367.

Gonzalez, V. M., Goeppinger, J., & Lorig, K. (1990). Four psychosocial theories and their application to patient education and clinical practice. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology, 3(3), 132-143.

Hajiagha, M. N., Taghizadeh, S., Asgharzadeh, M., Dao, S., Ganbarov, K., Köse, Ş., & Kafil, H. S. (2022). Gut microbiota and human body interactions; its impact on health: a review. Current pharmaceutical biotechnology, 23(1), 4-14.

Hajjar, R., Richard, C. S., & Santos, M. M. (2021). The role of butyrate in surgical and oncological outcomes in colorectal cancer. American Journal of Physiology-Gastrointestinal and Liver Physiology, 320(4), G601-G608.

Hoggett, P., Mayo, M., & Miller, C. (2008). The dilemmas of development work: Ethical challenges in regeneration. Policy Press.

Hossain, K. S., Amarasena, S., & Mayengbam, S. (2022). B vitamins and their roles in gut health. Microorganisms, 10(6), 1168.

Huang, J., Huang, T., & Li, J. (2024). Regulation Mechanism and Potential Value of Active Substances in Spices in Alcohol–Liver–Intestine Axis Health. International journal of molecular sciences, 25(7), 3728.

Ignatova, V. (2019). Influence of gut microbiota on behavior and its disturbances. Behavioral Neuroscience, 17-43.

Imdad, A., Pandit, N. G., Zaman, M., Minkoff, N. Z., Tanner-Smith, E. E., Gomez-Duarte, O. G., Acra, S., & Nicholson, M. R. (2023). Fecal transplantation for treatment of inflammatory bowel disease. Cochrane Database of Systematic Reviews(4).

Jawhara, S. (2023). Healthy diet and lifestyle improve the gut microbiota and help combat fungal infection. Microorganisms, 11(6), 1556.

König, J., Siebenhaar, A., Högenauer, C., Arkkila, P., Nieuwdorp, M., Norén, T., Ponsioen, C., Rosien, U., Rossen, N., & Satokari, R. (2017). Consensus report: faecal microbiota transfer–clinical applications and procedures. Alimentary pharmacology & therapeutics, 45(2), 222-239.

Krasulova, K., & Illes, P. (2021). Intestinal interplay of quorum sensing molecules and human receptors. Biochimie, 189, 108-119.

Kumari, R., Palaniyandi, S., & Hildebrandt, G. C. (2019). Microbiome: an emerging new frontier in graft-versus-host disease. Digestive diseases and sciences, 64, 669-677.

Labbé, A., Ganopolsky, J. G., Martoni, C. J., Prakash, S., & Jones, M. L. (2014). Bacterial bile metabolising gene abundance in Crohn's, ulcerative colitis and type 2 diabetes metagenomes. PloS one, 9(12), e115175.

Laing, B., Barnett, M. P., Marlow, G., Nasef, N. A., & Ferguson, L. R. (2018). An update

on the role of gut microbiota in chronic inflammatory diseases, and potential therapeutic targets. Expert Review of Gastroenterology & Hepatology, 12(10), 969-983.

Lakes, R. S., & Park, J. B. (2012). Biomaterials: an introduction. Springer Science & Business Media.

Lee, M. H. (2021). Harness the functions of gut microbiome in tumorigenesis for cancer treatment. Cancer Communications, 41(10), 937-967.

Li, R., Mao, Z., Ye, X., & Zuo, T. (2021). Human gut microbiome and liver diseases: from correlation to causation. Microorganisms, 9(5), 1017.

Lippi, G., Danese, E., Mattiuzzi, C., & Favaloro, E. J. (2017). The intriguing link between the intestinal microbiota and cardiovascular disease. Seminars in thrombosis and hemostasis,

Lorzadeh, A., Romero-Wolf, M., Goel, A., & Jadhav, U. (2021). Epigenetic regulation of intestinal stem cells and disease: a balancing act of DNA and histone methylation. Gastroenterology, 160(7), 2267-2282.

Ma, N., Chen, X., Johnston, L. J., & Ma, X. (2022). Gut microbiota-stem cell niche crosstalk: A new territory for maintaining intestinal homeostasis. iMeta, 1(4), e54.

Mafruchati, M. (2023). Basic Concepts in Stem Cell Therapy Stem Cell Therapy Strategy Development for Embryo. Zifatama Jawara.

Malaviya, A., Krishna, K. V., Malviya, S., & Nimisha Das, T. (2022). Gut-skin axis: role in health and disease. Probiotic Research in Therapeutics: Volume 3: Probiotics and Gut Skin Axis–Inside Out and Outside In, 1-26.

Manrique, P., Montero, I., Fernandez-Gosende, M., Martinez, N., Cantabrana, C. H., & Rios-Covian, D. (2024). Past, present, and future of microbiome-based therapies. Microbiome Research Reports, 3(2).

McCarville, J. L., Chen, G. Y., Cuevas, V. D., Troha, K., & Ayres, J. S. (2020). Microbiota metabolites in health and disease. Annual review of immunology, 38(1), 147-170.

Mohammedsaeed, W. (2015). Characterisation of the potential of probiotics or their extracts as therapy for skin. The University of Manchester (United Kingdom).

Moran, N. A., Ochman, H., & Hammer, T. J. (2019). Evolutionary and ecological consequences of gut microbial communities. Annual Review of Ecology, Evolution, and Systematics, 50(1), 451-475.

Nassif, L., & El Sabban, M. (2011). Mesenchymal stem cells in combination with scaffolds for bone tissue engineering. Materials, 4(10), 1793-1804.

Nayak, R. R., & Turnbaugh, P. J. (2016). Mirror, mirror on the wall: which microbiomes will help heal them all? BMC medicine, 14, 1-8.

Nazir, A., Farooq, B., Farooq, M., Anjum, S., Yousuf, S., Shafi, N., & Parray, J. A. (2024). Concept and dynamics of earth microbiome. In Microbiome Drivers of Ecosystem Function (pp. 1-15). Elsevier.

Nigro, G., & Sansonetti, P. J. (2015). Microbiota and gut stem cells cross-talks: a new view of epithelial homeostasis. Current stem cell reports, 1(1), 48-52.

Nørreslet, L. B., Agner, T., & Clausen, M.-L. (2020). The skin microbiome in inflammatory skin diseases. Current Dermatology Reports, 9, 141-151.

Ofoedu, C. E., Iwouno, J. O., Ofoedu, E. O., Ogueke, C. C., Igwe, V. S., Agunwah, I. M., Ofoedum, A. F., Chacha, J. S., Muobike, O. P., & Agunbiade, A. O. (2021). Revisiting food-sourced vitamins for consumer diet and health needs: A perspective review, from vitamin classification, metabolic functions, absorption, utilization, to balancing nutritional requirements. PeerJ, 9, e11940.

Oncel, S., & Basson, M. D. (2022). Gut homeostasis, injury, and healing: New therapeutic targets. World Journal of Gastroenterology, 28(17), 1725.

Patel, B. K., Patel, K. H., Huang, R. Y., Lee, C. N., & Moochhala, S. M. (2022). The gut-skin microbiota axis and its role in diabetic wound healing—a review based on current literature. International journal of molecular sciences, 23(4), 2375.

Patrignani, P., Tacconelli, S., & Bruno, A. (2014). Gut microbiota, host gene expression, and aging. Journal of Clinical Gastroenterology, 48, S28-S31.

Pires, L., González-Paramás, A. M., Heleno, S. A., & Calhelha, R. C. (2024). Exploring Therapeutic Advances: A Comprehensive Review of Intestinal Microbiota Modulators. Antibiotics, 13(8), 720.

Pistone, D., Meroni, G., Panelli, S., D'Auria, E., Acunzo, M., Pasala, A. R., Zuccotti, G. V., Bandi, C., & Drago, L. (2021). A journey on the skin microbiome: pitfalls and opportunities. International journal of molecular sciences, 22(18), 9846.

Probst, S., Apelqvist, J., Bjarnsholt, T., Lipsky, B. A., Ousey, K., & Peters, E. (2022). Antimicrobials and non-healing wounds: an uptdate: including a concise approach to treating potentially infected wounds. Journal of wound management, 1.

Provencher, S., Archer, S. L., Ramirez, F. D., Hibbert, B., Paulin, R., Boucherat, O., Lacasse, Y., & Bonnet, S. (2018). Standards and methodological rigor in pulmonary arterial hypertension preclinical and translational research. Circulation research, 122(7), 1021-1032.

Pulipati, P., Sarkar, P., Jakkampudi, A., Kaila, V., Sarkar, S., Unnisa, M., Reddy, D. N., Khan, M., & Talukdar, R. (2020). The Indian gut microbiota—Is it unique? Indian Journal of Gastroenterology, 39, 133-140.

Rasouli-Saravani, A., Jahankhani, K., Moradi, S., Gorgani, M., Shafaghat, Z., Mirsanei, Z., Mehmandar, A., & Mirzaei, R. (2023). Role of microbiota short-chain fatty acids in the pathogenesis of autoimmune diseases. Biomedicine & Pharmacotherapy, 162, 114620.

Ratajczak, M. Z., Serwin, K., & Schneider, G. (2013). Innate immunity derived factors as external modulators of the CXCL12-CXCR4 axis and their role in stem cell homing and mobilization. Theranostics, 3(1), 3.

Razdan, K., Garcia-Lara, J., Sinha, V., & Singh, K. K. (2022). Pharmaceutical strategies for the treatment of bacterial biofilms in chronic wounds. Drug Discovery Today, 27(8), 2137-2150.

Remely, M., Hippe, B., Zanner, J., Aumueller, E., Brath, H., & G Haslberger, A. (2016). Gut microbiota of obese, type 2 diabetic individuals is enriched in Faecalibacterium prausnitzii, Akkermansia muciniphila and Peptostreptococcus anaerobius after weight loss. Endocrine, Metabolic & Immune Disorders-Drug Targets (Formerly Current Drug Targets-Immune, Endocrine & Metabolic Disorders), 16(2), 99-106.

Ribeiro, C. F. A., Silveira, G. G. d. O. S., Candido, E. d. S., Cardoso, M. H., Espinola Carvalho, C. M., & Franco, O. L. (2020). Effects of antibiotic treatment on gut microbiota and how to overcome its negative impacts on human health. ACS Infectious Diseases, 6(10), 2544-2559.

Rodríguez Amor, D., & Dal Bello, M. (2019). Bottom-up approaches to synthetic cooperation

in microbial communities. Life, 9(1), 22.

Salem, F., Kindt, N., Marchesi, J. R., Netter, P., Lopez, A., Kokten, T., Danese, S., Jouzeau, J.-Y., Peyrin-Biroulet, L., & Moulin, D. (2019). Gut microbiome in chronic rheumatic and inflammatory bowel diseases: Similarities and differences. United European gastroenterology journal, 7(8), 1008-1032.

Selver, Ö. B., Yağcı, A., Eğrilmez, S., Gürdal, M., Palamar, M., Çavuşoğlu, T., Ateş, U., Veral, A., Güven, Ç., & Wolosin, J. M. (2017). Limbal stem cell deficiency and treatment with stem cell transplantation. Turkish Journal of Ophthalmology, 47(5), 285.

Shavandi, A., Saeedi, P., Gérard, P., Jalalvandi, E., Cannella, D., & Bekhit, A. E. D. (2020). The role of microbiota in tissue repair and regeneration. Journal of Tissue Engineering and Regenerative Medicine, 14(3), 539-555.

Silva, J. P., Navegantes-Lima, K. C., Oliveira, A. L., Rodrigues, D. V., Gaspar, S. L., Monteiro, V. V., Moura, D. P., & Monteiro, M. C. (2018). Protective mechanisms of butyrate on inflammatory bowel disease. Current Pharmaceutical Design, 24(35), 4154-4166.

Simon, E., Călinoiu, L. F., Mitrea, L., & Vodnar, D. C. (2021). Probiotics, prebiotics, and synbiotics: Implications and beneficial effects against irritable bowel syndrome. Nutrients, 13(6), 2112.

Singh, A., Vishwakarma, V., & Singhal, B. (2018). Metabiotics: the functional metabolic signatures of probiotics: current state-of-art and future research priorities—metabiotics: probiotics effector molecules. Advances in Bioscience and Biotechnology, 9(04), 147-189.

Sipe, J. D. (2002). Tissue engineering and reparative medicine. Annals of the New York Academy of Sciences, 961(1), 1-9.

Sphyris, N., Hodder, M. C., & Sansom, O. J. (2021). Subversion of niche-signalling pathways in colorectal cancer: what makes and breaks the intestinal stem cell. Cancers, 13(5), 1000.

Steen, E. H., Wang, X., Balaji, S., Butte, M. J., Bollyky, P. L., & Keswani, S. G. (2020). The role of the anti-inflammatory cytokine interleukin-10 in tissue fibrosis. Advances in wound care, 9(4), 184-198.

Stoica, A. E., Grumezescu, A. M., Hermenean, A. O., Andronescu, E., & Vasile, B. S. (2020). Scar-free healing: current concepts and future perspectives. Nanomaterials, 10(11), 2179.

Stojanov, S., Berlec, A., & Štrukelj, B. (2020). The influence of probiotics on the firmicutes/bacteroidetes ratio in the treatment of obesity and inflammatory bowel disease. Microorganisms, 8(11), 1715.

Stopińska, K., Radziwoń-Zaleska, M., & Domitrz, I. (2021). The microbiota-gut-brain axis as a key to neuropsychiatric disorders: a mini review. Journal of Clinical Medicine, 10(20), 4640.

Suman, S., Domingues, A., Ratajczak, J., & Ratajczak, M. Z. (2019). Potential clinical applications of stem cells in regenerative medicine. Stem Cells: Therapeutic Applications, 1-22.

Tandon, V., Kondapurkar, U., Chowda, H. K., & Kumar, A. (2024). Regenerative Medicine and Stem Cell Therapy: An Evolving Paradigm in Modern Healthcare. European Journal of Cardiovascular Medicine, 14(2).

Tang, Q., Xue, N., Ding, X., Tsai, K. H.-Y., Hew, J. J., Jiang, R., Huang, R., Cheng, X., Ding, X., & Cheng, Y. Y. (2023). Role of wound microbiome, strategies of microbiota delivery system and clinical management. Advanced Drug Delivery Reviews, 192, 114671.

Tomasulo, A., Simionati, B., & Facchin, S. (2024). Microbiome One Health Model for a Healthy Ecosystem. Science in One Health, 100065.

Tu, H., & Li, Y.-L. (2023). Inflammation balance in skeletal muscle damage and repair. Frontiers in immunology, 14, 1133355.

Tu, H., Xiao, E., & Liu, O. (2022). Taking microbiota into consideration in mesenchymal stem cell research. Journal of Dental Research, 101(8), 880-886.

Ugwu, O. P.-C., Alum, E. U., Okon, M. B., & Obeagu, E. I. (2024). Mechanisms of microbiota modulation: Implications for health, disease, and therapeutic interventions. Medicine, 103(19), e38088.

Van Lier, Y. F., Van den Brink, M. R., Hazenberg, M. D., & Markey, K. A. (2021). The post-hematopoietic cell transplantation microbiome: relationships with transplant outcome and potential therapeutic targets. Haematologica, 106(8), 2042.

Vázquez-Baeza, Y., Callewaert, C., Debelius, J., Hyde, E., Marotz, C., Morton, J. T., Swafford, A., Vrbanac, A., Dorrestein, P. C., & Knight, R. (2018). Impacts of the human gut microbiome on therapeutics. Annual review of pharmacology and toxicology, 58(1), 253-270.

Vigano, M. (2017). Mesenchymal Stem Cells for the treatment of osteoarthritis and tendinopathy.

Vinelli, V., Biscotti, P., Martini, D., Del Bo', C., Marino, M., Meroño, T., Nikoloudaki, O., Calabrese, F. M., Turroni, S., & Taverniti, V. (2022). Effects of dietary fibers on short-chain fatty acids and gut microbiota composition in healthy adults: a systematic review. Nutrients, 14(13), 2559.

Visekruna, A., & Luu, M. (2021). The role of short-chain fatty acids and bile acids in intestinal and liver function, inflammation, and carcinogenesis. Frontiers in Cell and Developmental Biology, 9, 703218.

Wallaeys, C., Garcia-Gonzalez, N., & Libert, C. (2023). Paneth cells as the cornerstones of intestinal and organismal health: a primer. EMBO Molecular Medicine, 15(2), e16427.

Wang, B., Qiu, J., Lian, J., Yang, X., & Zhou, J. (2021). Gut metabolite trimethylamine-N-oxide in atherosclerosis: from mechanism to therapy. Frontiers in cardiovascular medicine, 8, 723886.

Wiercinska, E. (2005). TGF-β, Smad [TGF-beta, Smad] signaling in hepatic stellate cells and during liver fibrogenesis Aachen, Techn. Hochsch., Diss., 2005].

Williams, K. L., Enslow, R., Suresh, S., Beaton, C., Hodge, M., & Brooks, A. E. (2023). Using the microbiome as a regenerative medicine strategy for autoimmune diseases. Biomedicines, 11(6), 1582.

Wilson, M. (2018). The Human Microbiota in Health and Disease: An Ecological and Community-Based Approach. Garland Science.

Wilson, S. E., Mohan, R. R., Mohan, R. R., Ambrosio Jr, R., Hong, J., & Lee, J. (2001). The corneal wound healing response:: cytokine-mediated interaction of the epithelium, stroma, and inflammatory cells. Progress in retinal and eye research, 20(5), 625-637.

Wu, F., & Liu, J. (2022). Decorated bacteria and the application in drug delivery. Advanced Drug Delivery Reviews, 188, 114443.

Xu, X., Ocansey, D. K. W., Hang, S., Wang, B., Amoah, S., Yi, C., Zhang, X., Liu, L., & Mao, F. (2022). The gut metagenomics and metabolomics signature in patients with inflammatory bowel disease. Gut Pathogens, 14(1), 26.

Xu, Z., & Hsia, H. C. (2018). The impact of microbial communities on wound healing: a

review. Annals of plastic surgery, 81(1), 113-123.

Xue, L.-F., Luo, W.-H., Wu, L.-H., He, X.-X., Xia, H. H.-X., & Chen, Y. (2019). Fecal microbiota transplantation for the treatment of nonalcoholic fatty liver disease. Exploratory Research and Hypothesis in Medicine, 4(1), 12-18.

Yadegar, A., Bar-Yoseph, H., Monaghan, T. M., Pakpour, S., Severino, A., Kuijper, E. J., Smits, W. K., Terveer, E. M., Neupane, S., & Nabavi-Rad, A. (2024). Fecal microbiota transplantation: current challenges and future landscapes. Clinical microbiology reviews, e00060-00022.

Yamada, S., Behfar, A., & Terzic, A. (2021). Regenerative medicine clinical readiness. Regenerative medicine, 16(3), 309-322.

Yang, N. J., & Chiu, I. M. (2017). Bacterial signaling to the nervous system through toxins and metabolites. Journal of molecular biology, 429(5), 587-605.

Yao, M. H. (2022). Targeting Innate and Adaptive Immune Responses to Achieve Long-term Allograft Acceptance Following Transplantation Karolinska Institutet (Sweden)].

Yu, J., Sun, H., Cao, W., Han, L., Song, Y., Wan, D., & Jiang, Z. (2020). Applications of gut microbiota in patients with hematopoietic stem-cell transplantation. Experimental Hematology & Oncology, 9, 1-13.

Zama, D., Bossù, G., Leardini, D., Muratore, E., Biagi, E., Prete, A., Pession, A., & Masetti, R. (2020). Insights into the role of intestinal microbiota in hematopoietic stem-cell transplantation. Therapeutic advances in hematology, 11, 2040620719896961.

Zhang, N., Jin, M., Wang, K., Zhang, Z., Shah, N. P., & Wei, H. (2022). Functional oligosaccharide fermentation in the gut: Improving intestinal health and its determinant factors-A review. Carbohydrate Polymers, 284, 119043.

Zheng, M., Han, R., Yuan, Y., Xing, Y., Zhang, W., Sun, Z., Liu, Y., Li, J., & Mao, T. (2023). The role of Akkermansia muciniphila in inflammatory bowel disease: Current knowledge and perspectives. Frontiers in immunology, 13, 1089600.

Zhu, Y., Shui, X., Liang, Z., Huang, Z., Qi, Y., He, Y., Chen, C., Luo, H., & Lei, W. (2020). Gut microbiota metabolites as integral mediators in cardiovascular diseases. International journal of molecular medicine, 46(3), 936-948.

Zielińska, M., Pawłowska, A., Orzeł, A., Sulej, L., Muzyka-Placzyńska, K., Baran, A., Filipecka-Tyczka, D., Pawłowska, P., Nowińska, A., & Bogusławska, J. (2023). Wound Microbiota and Its Impact on Wound Healing. International journal of molecular sciences, 24(24), 17318.

Zonderman, J., & Vender, R. S. (2009). Understanding Crohn disease and ulcerative colitis. Univ. Press of Mississippi.

About The Authors

Maria Nazir is an MPhil Scholar of Microbiology at the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur, Pakistan. She is involved in a National Research Program for Universities (NRPU) Project, with research interests in Molecular Characterization. She has submitted abstracts to various conferences and authored and coauthored of several book chapters. Her research focuses on the isolation and Molecular characterization of Corynebacterium pseudotuberculosis and their applications in promoting animal health. Her interested research criteria are based on genetics, molecular biology, and bioinformatics.

Email: nazirmaria545@gmail.com ORCID 0009-0004-6714-6212

Dr. Zubia Rashid received her PhD in 2020 from the University of Karachi, Pakistan. She is serving as Manager of Laboratory/Officer-Quality and Safety at PureHealth, Abu Dhabi, United Arab Emirates. Her research interests include infectious diseases, biotechnology, antimicrobial resistance, virology, computational biology, and bioinformatics. She is a recognized people manager; published twenty research articles in several international peer-reviewed journals in areas linking biotechnology, bioinformatics, microbiology, molecular biology, and pharmaceuticals.

Email: zubia.rashid@purelab.com ORCID: 0000-0002-8753-8385

Dr. Amina Farrukh Alavi is currently doing her PhD studies at Quaid-i-Azam University, Pakistan. She is studying Environmental Microbiology and has done a Masters from LUMS in Biology. Her research interests include molecular biology, cancer genetics and therapeutics, and environmental and applied microbiology. She has published six research articles in well-reputed international and national journals.

Email: afalavi94@gmail.com ORCID: 0009-0002-1558-1533

Muhammad Mudussair Khan received his bachelor in 2023 from Cholistan university of veterinary and animal science Bahawalpur, Pakistan. He is MPhil microbiology scholar at the Islamia University of Bahawalpur, Pakistan. His research interests include predictive breeding models, Genetic selection, Genomics, reproductive biotechnology and selection and judging of animals for beauty attributes. He also has written book chapters.

Email : muhammadmudussairkhan@gmail.com ORCID:0009-0005-9491-2442

Muhammad Ejaz earned Bachelor's in applied microbiology from Cholistan university of veterinary and animal sciences (CUVAS) Bahawalpur Pakistan. His research interest in Microbial genetics, Molecular biology, and food quality and its application.

Email: ijazrasheed334@gmail.com ORCID: 0009-0006-1709-6653

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as "Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone". His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

Dr. Muhammad SAFDAR earned his PhD in Molecular Biology and Genetics from Gaziantep University, Turkey. He is Lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 70 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

E-mail: msafdar@cuvas.edu.pk ORCID: 0000 0002 3720 2090

To Cite This Chapter

NAZIR M et al., (2024). The role of microbiome in regenerative medicine: a new frontier. In Current Studies in Health and Life Sciences 2024 (pp.265-190). ISRES Publishing.

An Evaluatıon Of The 112 Emergency Medıcal System And The Mısuse Of The 112 Emergency Call Center In Turkey

Ali SERT

Introduction

The spread of common values in political, social, economic, and cultural areas between countries in an unbounded global manner has affected our present and will inevitably influence the future of all nations. This transformation has become a continuous and persistent part of our lives. The foundation of this change lies in various economic and social factors such as the transition from an industrial society to an information society, rapid developments in information technology, changes in bureaucratic management models, increasing population, migration movements, search for quality of life, and efforts to improve efficiency. It is the primary responsibility of states to ensure public safety, prevent emergencies that may harm society, produce services that meet societal needs, and deliver essential public services swiftly and efficiently to citizens in life-threatening situations. Particularly, for the management of emergencies, all public resources and services are mobilized, and significant budgets are allocated to ensure success (Ekşi, 2016).

Looking at the fundamental definition of health, it was provided by the World Health Organization in 1948. According to this, health is not merely the absence of disease or disability but a state of complete physical, social, and mental well-being (Bölükbaşı, 2007). Health, in a negative sense, can be defined as "the absence of illness," while, in a positive sense, it refers to the individual's ability to participate in life, cope with stressful situations, their level of psychological well-being and physical harmony, and their ability to form good relationships with society (Çelikli, 2007). Physical health is defined as being inseparable from an individual's psychological state and social environment (Özden, 2016). To assess changes in community health and health issues over time and to compare the health level of one society with another, basic health indicators are examined to evaluate the effectiveness of health services. In this regard, Turkey has, especially in recent years, developed a perspective that emphasizes quality and accreditation in the health sector. Concepts like patient rights and the right to choose a doctor, which put the patient in the forefront as the service recipient, have become important, and this health reform has been confirmed by various data.

The primary goal of public service delivery is undoubtedly to bring the beneficiary of the service together with public resources as soon as possible, without losing time, and to provide the necessary service promptly. Undoubtedly, one of these areas is Emergency Health Services. In emergency aid services, where societal needs operate 24 hours a day, seven days a week, it is essential to ensure that services are sustained continuously and systematically. Emergency Health Services (EHS) are a discipline that involves the rapid intervention and decision-making for urgent cases such as sudden illnesses, accidents, and injuries. These services are provided by a healthcare team specialized in the field and supported by medical equipment (Atilla, 2016). In other words, it is a vital public health service that helps individuals maintain their vital functions during transport in situations requiring urgent medical care and ensures their rapid access to emergency services (Şimşek et al., 2019).

Turkey is a country where emergencies, accidents, and injuries are frequently encountered, alongside extraordinary situations and disasters that occur intensely. For these reasons, the organizational structure and practices of emergency health services on a national level are of great importance (İnan et al., 2006). Pre-hospital emergency health services in Turkey first began in 1986 in Ankara, İzmir, and Istanbul under the name "077 Hızır Emergency Service" and could be reached by calling the number 077. In 1994, with a project initiated by the Ministry of Health, these services were developed under the name "112 Emergency Aid and Rescue Services," accessed by the number

112. Problems encountered during any stage of delivering pre-hospital emergency health services negatively affect other stages, thereby reducing the efficiency of emergency medical services. Emergency health services begin with a call for emergency medical assistance made through the toll-free number "112." The command and control center, which receives the call, quickly evaluates whether the request requires emergency health services based on the information gathered. In cases that do not require an emergency response, the service has the authority to refuse the request. The operation of emergency health services is as follows: in situations that require urgent attention, the command center assigns the nearest and most appropriate 112 emergency team to the request as quickly as possible. The 112 emergency teams reach the scene in the shortest time possible, provide emergency medical assistance, and conduct primary and secondary assessments of the case. If the patient requires advanced medical intervention, they are stabilized and then transported to the most suitable secondary or tertiary healthcare facility (Göcen & Ateş, 2013).

A significant issue is the use of these units, which are primarily intended to serve individuals in need of emergency health services, by patients who do not have urgent health problems, could be treated at the primary care level, or whose conditions could be postponed. The unnecessary use of emergency health services by individuals for non-emergency reasons is a global problem (Aktaş, 2009; Özyaral, 2005). The Emergency Health Services system is composed of a comprehensive network of personnel, equipment, and resources created to provide assistance and emergency medical care to society. These services also ensure that emergency medical care is provided swiftly, efficiently, and with high-quality assurance. The continuity of emergency aid services means that they are available 24/7 whenever needed. Emergency aid services are provided quickly and effectively to anyone in need, regardless of geographic or climatic conditions, at the beneficiary's location. The provision of ambulance services and the usage rates of ambulances vary depending on local, socioeconomic, and cultural conditions in developed and developing countries. Worldwide, emergency ambulance services are provided on a provincial or regional scale, under the direction and management of command and control centers, 24 hours a day, without interruption (Kıdak, 2009).

When evaluating the criteria for the effectiveness of emergency aid services, they can be listed as primarily accessibility, early and rapid intervention, and accurate and timely diagnosis and treatment. In Turkey, in order to fulfill these objectives, emergency call services have been established in every province to ensure that the service is effective, fast, and manageable. These centers use a short and memorable emergency call number (112) so that citizens can quickly request emergency assistance and receive immediate responses to their requests. By unifying emergency call lines under a single number, the need for citizens and foreigners in Turkey to know multiple numbers for emergency calls has been eliminated.

• Cost savings and service efficiency have been achieved.

• Coordination and cooperation between relevant institutions have been established.

• All emergency calls have been recorded. By employing staff who speak foreign languages, it has become possible for foreigners to benefit from the service.

• Uniformity in practice has been ensured across provinces.

• The technical system used in call centers has been standardized and maintained at the same quality across all provinces.

• Through the geographical information systems used in call centers, it has become easier to locate the scene of an incident.

• Thanks to the vehicle tracking system, the dispatch and management of vehicles and teams have become more efficient.

• Since all data from call reception to team arrival at the scene is recorded in the system, it

is possible to statistically measure efficiency. International standards and developments have been tracked and integrated into our country's system.

112 Emergency Call Centers play a critical role in emergency situations by offering much-needed assistance, producing quick solutions to relevant problems, and determining which team is most suitable to respond. These centers ensure the flow of services through clear communication and by following specific steps. The first step begins with evaluating the incoming call within 30 seconds and dispatching the relevant team to the scene within 180 seconds. In the following steps, healthcare, security, and other teams focus on securing the scene and addressing the case. The most important aspect of the first step is the communication between the 112 Emergency Call Center personnel and the caller. It is vital to identify the problem quickly and provide an accurate address and case description. The fact that these services are provided to citizens within seconds is undoubtedly due to the clear and understandable communication established between personnel and citizens. In 2023, a total of 105,618,984 calls were made to 112 Emergency Call Centers, and 36,756,785 incidents were responded to. Coordination between institutions was ensured in 4,331,757 of these incidents. The 112 Emergency Call Centers handled 6,065 emergency calls from disabled citizens via the "Engelsiz 112" and "Engelsiz CİMER" applications. To assist foreigners living in Turkey, 106,059 emergency calls were answered in German, Arabic, English, and Russian. Additionally, 147,139 emergency calls were received from vehicles equipped with the E-Call system, which automatically contacts 112 Emergency Call Centers via sensors or manually through the emergency call button in case of traffic accidents. The 112 Emergency Call Centers provide uninterrupted emergency call and aid services 24/7 in 81 provinces, with 13,000 employees.

Accessible 112 Project

The Engelsiz 112 application has been developed to enable disabled citizens to quickly connect with the relevant 112 unit during emergencies and to easily report the emergencies they experience or witness. Disabled citizens can use the mobile application, which they can download for free on their personal phones, to instantly notify the 112 Emergency Call Center. They can initiate a video call with the qualified 112 personnel or report their problems (such as health, safety, fire, etc.) via instant messaging through the application. If they wish, disabled citizens can also record their existing health problems in the app, and they can enter the contact information of their emergency contacts, allowing 112 personnel to see this information at the time of the emergency call. This will enable more efficient and faster service during the process. Location information can be used in emergencies to reach the user as quickly and effectively as possible. Access to the camera and microphone is necessary to communicate with the user.

When Should 112 Be Called?

112 Emergency should be called in any situation that threatens health (chest pain, fainting, drowning, traffic accidents, poisoning, injuries, suspected fractures, etc.), any situation that threatens your safety (theft, assault, injury, smuggling, etc.), in the event of fires (house, vehicle, stubble, forest fires, etc.), or in extraordinary circumstances (earthquakes, floods, collapses, disappearances, etc.). The usage rate of ambulances varies based on factors such as age, the severity of trauma or illness, geographic factors, time of day, socioeconomic status, and insurance coverage. Today, the strength of public administrations is evaluated by their ability to reach individuals in need of urgent assistance in a timely manner. In recent years, motorcycle ambulances to overcome traffic congestion, snow-tracked ambulances for harsh winter conditions, and air ambulances such as planes and helicopters, as well as various vehicles of institutions working in a multidisciplinary manner in this field, have been frequently used to reduce response times. Fast and effective emergency services increase citizens' trust and loyalty to the state, while any negative developments in this regard lead to the questioning of public authority by citizens. If continuity in the effective and efficient delivery of services cannot be ensured, public order may be adversely affected, and social costs may arise (Özata et al., 2011).

The delivery of ambulance services and the rate of ambulance use in developed and developing countries vary based on local, socio-economic, and cultural conditions (Langhelle, 2004). In recent years, the demand for emergency ambulance services has been steadily increasing (Zenginol, 2011). The fact that the 112 emergency number can be called for free also leads to some abuses. Common situations include some malicious adults or children continuously calling the emergency center to occupy the lines, or phone repair technicians calling the emergency number to test phones without inserting a SIM card. Abuse cases like these can result in unnecessary calls, and for the 112 Emergency Number, the rate of such misuse can reach as high as 95%. This negatively affects the effective and efficient delivery of services. The unnecessary use of ambulance services is one of the major problems in today's modern healthcare systems. This situation increases the workload of emergency services and negatively impacts the economy of the country (Yaylacı et al., 2013).

Today, the misuse of emergency call services is considered one of the most significant issues in the delivery of emergency aid services. The misuse of emergency call services can be divided into two categories: unintentional, meaning unconscious, and intentional false calls. A large portion of misuse falls under the group of unintentional calls, where individuals who do not have the right to use the service for non-emergency situations still request help. These calls include requests for emergency aid for situations that do not actually meet the definition of an emergency, such as asking for assistance with an ongoing complaint of abdominal pain that has lasted for days. The use of these units, which are designed to serve individuals in need of emergency medical care, by patients whose condition is not urgent and could be treated at primary care or whose treatment could be delayed, is a significant issue. The unnecessary use of emergency medical services by individuals for non-emergency reasons is a global problem (Aktaş, 2009; Özyaral, 2005). A large portion of the calls made to the 112 Emergency Call Center are unnecessary, unfounded, frivolous, false, or made for the purposes of seeking information or consultation. Such calls cause public personnel, vehicles, and equipment to be needlessly occupied, prevent citizens with genuine emergencies from rapidly accessing the service, and delay timely intervention. It is observed that those who behave irresponsibly in this manner put public safety, public order, and public health at risk. During the provision of these services, the ease and free access to the service offers certain privileges to the service beneficiaries.

These privileges, in some cases, lead to the misuse of the emergency call line by the beneficiaries. This situation can lead to delays in providing services to those who genuinely need emergency assistance, thus unfairly victimizing these individuals. The potential for such unconscious misuse of emergency call services has recently emerged as a significant issue (Ekşi, 2016). False reports refer to calls where, upon the arrival of teams at the scene, it is determined that the report was not real.

Unnecessary calls are defined as those in which the call center is contacted without any actual report being made, with the intent to harass or verbally abuse the call-taker or dispatcher, play music, leave silent calls, or otherwise hinder the work of personnel, reduce work efficiency, and waste time and resources in the provision of emergency services. The fact that false reports and unnecessary calls occupy a large portion of the total calls, and that personnel are unnecessarily occupied, decreases the productivity of the staff answering such calls, wastes state resources, and causes delays in the ability of individuals in need of emergency assistance to reach the "112" service, resulting in both material and moral losses. To ensure that citizens with genuine emergencies and needs can benefit from the 112 Emergency Call Line in a timely manner, it is important to discourage those who occupy the lines with unfounded and false issues. Imposing legal sanctions on individuals who engage in these negative behaviors would serve as a deterrent. This is also important for the timely, effective, and efficient delivery of critical public services such as emergency health, safety, and fire response. In Turkey, according to Law No. 5326 on Misdemeanors, administrative fines are imposed by provincial governors on individuals who are found to have occupied the 112 Emergency Call Center with false reports. In the case of repeat offenses, the penalty is doubled.

CONCLUSION

It is of great importance to raise awareness in society and explain the significance of systems established with the aim of benefiting people through proper education. Educating the public on when and under what circumstances to call the 112 Emergency line, as well as ensuring that the situation is described briefly and clearly with effective communication techniques, must be emphasized. The public should understand that the unnecessary use of the Emergency Call Center may delay the delivery of services to someone else, possibly even a family member, in the case of a real emergency. In Turkey, the country has been successful in various aspects such as the number of ambulances, response times, quick interventions by institutions, ensuring scene safety, and the coordinated efforts of institutions. However, the rate of unnecessary calls to the 112 Emergency line remains high. To prevent the potential social costs that could arise from the loss of the efficiency of this 24/7 service, as well as to prevent individual rights violations, technical, administrative, and punitive measures must be implemented to address unconscious misuse. Awareness-raising activities are crucial in making citizens understand the consequences of unnecessarily occupying the 112 Emergency Call Center, including the possible victimization of others.

REFERENCES

2023 Year Call Statistics. Retrieved from: https://www.112.gov.tr/2023-yili-cagri-istatistikleri (Access Date: 01.10.2024)

Accesible-Free 112 Project. Retrieved from: https://www.112.gov.tr/engelsiz-112-projesi (Access Date: 09.09.2024)

Aktaş, C. & Sarıkaya, S. (2009). Emergency Care in the Field. T.C. Yeditepe University Publications: Istanbul; 2009, pp. 13-20.

Atilla, R., Özel, G., Özel, B.A., & Özcan, C. (2016). Emergency Medical System and Its History. Ankara; Ayrıntı Publishing and Printing Services Ltd., pp. 3-9.

Bölükbaşı, N. et al. (2007). Knowledge Levels of the Final Year Students of the Ordu Girls' Vocational High School in First Aid Applications for Children. AÜ Nursing School Journal; 10(3), 52-59.

Çelikli, S. (2007). Ambulance and Emergency Care Technician (Paramedic) Program. Proceedings of the 3rd International Ambulance Rally and Emergency Health Services Congress, Ankara. 2007, pp. 33-37.

Ekşi, A. (2016). Evaluation of the Incident Management System in Mass Casualty Situations

in Terms of Coordination in Public Administration. Journal of Dicle University Institute of Social Sciences, (16), 105-118.

Kıdak, L., Keskinoğlu, P., Sofuoğlu, T., & Ölmezoğlu, Z. (2009). Evaluation of the Use of 112 Emergency Ambulance Services in İzmir Province. Journal of General Medicine/Genel Tıp Dergisi, 19(3).

Langhelle, A., Lossius, H.M., Silfvast, T., Björnsson, H.M., Lippert, F.K., & Ersson, A. (2004). International EMS Systems: The Nordic Countries. Resuscitation, 61:9-21.

Özata, M., Toygar, Ş.A., & Yorulmaz, M. (2011). Comparative Analysis of 112 Emergency Ambulance Services on the Example of Turkey–Konya. European Journal of General Medicine, 8(4), 262-267.

Özden, A. (2016). Psychosocial Health and Exercise. Türkiye Klinikleri J Physiotherapy-Rehabilitation-Special Topics, 2(1), 122-126.

Özyaral, O. (2005). Sterilization and Disinfection in Ambulance and First Response. Proceedings of the 4th National Sterilization and Disinfection Congress, pp. 344-374. Antalya.

Regulation on the Establishment, Duties, and Work of 112 Emergency Call Centers. Official Gazette: 16.05.2014-29002.

Sert, A., & Polat, M. (2021). Retrospective Evaluation of Emergency Health Services in Burdur Province (2013-2017). Journal of Adnan Menderes University Faculty of Health Sciences, 5(1), 61-71.

Sert, A., Köksoy, S., & Polat, M. (2022). Pilot Study on the Use of Wearable Technologies by Emergency Health Workers. TOGÜ Journal of Health Sciences, 2(3), 290-299.

Şimşek, P., Günaydın, M., Gündüz, A. (2019). Pre-Hospital Emergency Health Services: The Example of Turkey. GÜSBD, 8(1), 120-127.

Yaylacı, S., Yılmazer Çelik, S., & Öztürk Cimilli, T. (2013). Retrospective Evaluation of the Urgency of Patients Admitted to the Emergency Department by Ambulance. ACU Health Sci, 4(2), 64-67.

Zenginol, M., Al, B., Genç, S., Deveci, İ., Yarbil, P., Yilmaz, D.A., ... & Yildirim, C. (2011). Three-Year Study Results of 112 Emergency Ambulances in Gaziantep Province. Eurasian Journal of Emergency Medicine, 10(1), 27.

About The Authors

Ali SERT: I am a lecturer at Burdur Mehmet Akif Ersoy University. I am currently a doctoral thesis student in the CBRN Department in the organic chemistry laboratory. I have been working for 3 years

E mail: alisert@mehmetakif.edu.tr. ORCID: 0000-0003-1780-9458

Similarity Index: The similarity index obtained from the plagiarism software for this book chapter is 5%.

To Cite This Chapter:

Sert A., (2024). An Evaluatıon Of The 112 Emergency Medıcal System And The Mısuse Of The 112 Emergency Call Center In Turkey. In Current Studies in Health and Life Sciences 2024 (pp.293-298 ISRES Publishing.

The Importance Of Interdisciplinary Communication In Dısaster Management

Mümin Polat

Eda Arıcı

Introduction

Disasters are unexpected events that cause significant loss of life and material damage. Managing natural or man-made disasters such as earthquakes, floods, fires, and pandemics is a complex process. In this process, collaboration between experts from different disciplines is essential. Professional groups such as healthcare workers, engineers, firefighters, psychologists, and law enforcement play a crucial role in the success of post-disaster interventions through effective communication. However, this collaboration process often encounters various communication barriers and challenges. Disasters, whether natural or man-made, present significant challenges to societies worldwide. Effective disaster management requires coordination across various sectors and disciplines, each bringing unique expertise to tackle the multifaceted nature of emergencies. Interdisciplinary communication refers to the collaboration between experts from different fields to ensure a comprehensive and coordinated response to disasters. In this essay, we will explore the importance of interdisciplinary communication in disaster management, examining the various phases of disaster response, the challenges in ensuring effective communication, and examples of successful interdisciplinary efforts in real-life disaster scenarios.

Understanding Disaster Management; Phases of Disaster Management

Disaster management encompasses a range of activities that occur before, during, and after a disaster event. It is often divided into four main phases:

Prevention and Mitigation: This phase focuses on reducing the risks and impacts of potential disasters through proactive measures such as hazard mapping, building regulations, and public education.

Preparedness: This involves the development of plans, protocols, and training exercises that ensure readiness for potential disasters. This phase is crucial for fostering collaboration among different disciplines, such as medical teams, emergency responders, engineers, and local governments.

Response: When a disaster occurs, the immediate priority is to save lives, alleviate suffering, and prevent further damage. This phase requires quick and effective communication between multiple disciplines, including emergency medical services, law enforcement, and humanitarian organizations.

Recovery: This phase focuses on restoring the affected community to its pre-disaster state or better. Interdisciplinary communication is essential in the recovery phase, as it requires long-term planning and collaboration between engineers, environmental scientists, mental health professionals, and local authorities.

The Role of Different Disciplines in Disaster Management

In each phase of disaster management, various professionals contribute their expertise:

Public Health and Medical Professionals: Provide life-saving care and prevent disease outbreaks.

Engineers and Urban Planners: Work on rebuilding infrastructure and ensuring future resilience.

Environmental Scientists: Monitor environmental impacts and help in the recovery of ecosystems.

Sociologists and Psychologists: Address the social and psychological impacts of disasters on communities.

Communication Specialists: Ensure clear and timely dissemination of information to the public and coordination among different agencies.

The aim of this study is to emphasize the importance of interdisciplinary communication in disaster management, analyze the communication problems encountered, and present suggestions for overcoming these challenges.

The Importance of Interdisciplinary Communication

Enhancing Collaboration and Efficiency

Interdisciplinary communication ensures that all stakeholders are working towards the same goals and that their efforts are complementary rather than duplicative. For example, in a disaster, emergency medical teams must coordinate with law enforcement to secure affected areas before delivering care, while engineers work alongside public health experts to ensure the safety of water and sanitation systems. Without clear communication, these efforts could be misaligned, resulting in inefficient use of resources or even endangering lives.

Facilitating Accurate and Timely Information Sharing

One of the greatest challenges in disaster response is the need for accurate, real-time information. Different disciplines often have access to varying types of data, all of which are crucial to creating a comprehensive picture of the disaster scenario. For example, meteorologists can provide weather forecasts, geologists may offer insights on aftershocks following an earthquake, and medical teams can report on the number and severity of injuries. Timely communication between these disciplines allows decision-makers to make informed choices and adapt their strategies as situations evolve.

Breaking Down Silos and Bridging Cultural Gaps

In many disaster management situations, communication barriers exist due to organizational silos or cultural differences between agencies and disciplines. For instance, the language and priorities of the medical community may differ from those of emergency responders or environmental scientists. Effective interdisciplinary communication helps break down these silos and encourages professionals to appreciate the perspectives of their colleagues from other fields. In international disaster scenarios, cultural differences between organizations from different countries can also present challenges that need to be overcome through communication training and collaboration exercises.

Challenges in Interdisciplinary Communication in Disaster Management

Language and Terminology Barriers

Each discipline involved in disaster management has its own specific terminology and jargon. While engineers might discuss structural integrity, medical professionals may focus on triage and epidemiology, and law enforcement may be concerned with security and evacuation logistics. Misunderstandings stemming from these differences in language can slow down disaster response efforts or lead to mistakes. For example, the word “critical” might have different connotations in a medical context versus a structural engineering context. Clear communication protocols and training that bridge these terminological gaps are essential.

Institutional and Bureaucratic Challenges

Different agencies and organizations involved in disaster management often have their own protocols, hierarchical structures, and decision-making processes. This can create bottlenecks in communication, as agencies may be reluctant to share information or coordinate their efforts due to internal politics or concerns about jurisdiction. These challenges are particularly pronounced in large-scale disasters involving multiple governmental agencies, international organizations, and non-governmental organizations (NGOs). Overcoming institutional barriers requires fostering a culture of collaboration, establishing clear lines of communication, and ensuring that all agencies are aligned with the common goal of disaster mitigation and response.

Technological and Logistical Barriers

Technological barriers can also hinder effective interdisciplinary communication. In many disaster scenarios, communication infrastructure may be damaged or overwhelmed, making it difficult for agencies to share information. While modern communication technologies like satellite phones, radio systems, and internet-based platforms can facilitate interdisciplinary communication, their effectiveness depends on the availability of reliable infrastructure and trained personnel. Furthermore, logistical barriers such as time zone differences in international collaborations or the sheer physical distance between different response teams can complicate coordination efforts.

Interdisciplinary Communication in Disaster Management; Disaster management is a multi-dimensional process, encompassing preparation, response, and recovery phases. In each phase, different professional groups must communicate with one another. During the preparation phase, engineers, planners, and risk management specialists coordinate efforts. In the response phase, emergency teams, healthcare workers, and security forces are at the forefront. Finally, during the recovery phase, professionals such as social workers and psychologists take on significant roles.

Effective communication throughout this process facilitates rapid decision-making, coordination, and collaboration. However, the unique jargon of each profession and the use of different communication techniques can sometimes lead to misunderstandings and delays. Hierarchical structures may also negatively impact communication flow.

Communication Challenges; One of the most common challenges in disaster management is the inconsistency in terminology and concepts used by different professional groups. For instance, an engineer and a healthcare worker might approach the same disaster scenario from different angles, leading to misunderstandings. Additionally, the organizational cultures of different professions can cause communication breakdowns during crises.

Another significant challenge is the lack or insufficient use of technological communication tools. Particularly in rural or underdeveloped areas, the damage to communication infrastructure during disasters can disrupt information sharing. This hinders the ability of response teams to act promptly.

Strategies for Improving Interdisciplinary Communication

Joint Training and Simulation Exercises

One of the most effective ways to improve interdisciplinary communication in disaster management is through joint training and simulation exercises. By practicing disaster response scenarios together, professionals from different disciplines can become familiar with each other's priorities, terminologies, and workflows. This not only improves communication but also builds trust between agencies, which is critical in high-stress disaster situations. For example, large-scale disaster drills often involve medical teams, firefighters, police, and government officials working together to simulate an earthquake response. These exercises help identify communication breakdowns and allow for the development of strategies to improve coordination.

Leveraging Technology to Facilitate Communication

Advances in technology have provided new tools for enhancing interdisciplinary communication. For instance, geographic information systems (GIS) can provide a common platform for sharing real-time data on the locations of affected populations, damage assessments, and resource availability. Similarly, mobile applications designed for disaster management can facilitate rapid communication between teams in the field. Cloud-based platforms that enable remote collaboration are also becoming increasingly important, especially in international disaster responses where agencies are spread across different regions. The key to successfully leveraging technology is ensuring that all agencies involved are trained in its use and that systems are interoperable between different organizations.

Establishing Clear Communication Protocols

Effective interdisciplinary communication requires clear protocols that define how information should be shared, who is responsible for decision-making, and what channels of communication will be used. These protocols should be developed in advance of a disaster and should be regularly updated based on lessons learned from previous events. In many countries, incident command systems (ICS) are used to establish a standardized approach to disaster management that facilitates coordination between different agencies and disciplines. ICS provides a common framework for organizing resources, personnel, and communication during a disaster response, which helps prevent confusion and ensures that all teams are working towards the same objectives.

Successful Communication Strategies; To improve interdisciplinary communication in disaster management, several strategies are recommended. First, developing a common language and organizing continuous training for professional groups can reduce communication errors during crises. Crisis simulations can also help teams gain practice in working together.

Technological solutions play a critical role in this process. Specifically, commonly used digital platforms and systems that enable real-time data sharing can speed up information flow among teams. These platforms allow different professional groups to quickly access the information they need at different phases of the disaster, ensuring timely interventions.

Case Studies of Successful Interdisciplinary Communication in Disaster Management

2004 Indian Ocean Tsunami

The response to the 2004 Indian Ocean Tsunami demonstrated the importance of interdisciplinary communication in disaster management. Following the devastating earthquake and subsequent tsunami, international aid organizations, governments, and local communities worked together to coordinate relief efforts. Medical teams collaborated with engineers to rebuild infrastructure, while environmental scientists assessed the long-term impacts on coastal ecosystems. Despite the complexity of the disaster, effective communication between disciplines helped save lives and lay the foundation for recovery.

2010 Haiti Earthquake

Another example of successful interdisciplinary communication can be seen in the response to the 2010 Haiti earthquake. In the aftermath of the quake, humanitarian organizations, the United Nations, and local government agencies worked together to provide emergency relief and coordinate the distribution of aid. Interdisciplinary teams of engineers, medical professionals, and logistics experts collaborated to restore critical infrastructure, establish field hospitals, and provide clean water and sanitation services to displaced populations. While the response was not without its challenges, the coordination between different disciplines helped mitigate the worst effects of the disaster.

2020 COVID-19 Pandemic

The COVID-19 pandemic underscored the importance of interdisciplinary communication in managing global health crises. Public health officials, epidemiologists, economists, and policymakers worked together to devise strategies for containing the virus, while medical professionals collaborated with supply chain experts to distribute vaccines and medical supplies. The pandemic also highlighted the role of technology in facilitating interdisciplinary communication, as virtual meetings and data-sharing platforms enabled collaboration across borders despite travel restrictions. While the pandemic response exposed gaps in global disaster preparedness, it also demonstrated the potential for interdisciplinary communication to drive more effective disaster management in the future.

Discussion

The nature and scale of disasters influence interdisciplinary communication in disaster management. While communication may be easier during smaller-scale incidents, coordination becomes more challenging in large-scale disasters. This highlights the importance of pre-established communication protocols for each disaster scenario. Moreover, the development of joint training programs to promote interdisciplinary collaboration can enable accurate and timely interventions during crises.

Another crucial aspect is the role of leadership in disaster management. Leaders should foster an environment that supports interdisciplinary communication and implement policies that enhance collaboration between teams.

Conclusion

Disaster management is a complex and multifaceted process, and its effectiveness is largely dependent on the success of interdisciplinary communication. During crises caused by disasters, professionals from various disciplines must work in coordination and effectively communicate to ensure successful intervention and recovery efforts. Thus, reducing the communication challenges faced by professionals in disaster management processes is of vital importance.

In this context, strategies aimed at strengthening interdisciplinary communication should be developed. First, a common language between professional groups should be established to enable effective interventions. This involves standardizing technical terms and jargon and understanding the perspectives of different disciplines. Regular training exercises and simulations can also enhance communication skills and improve collaboration between teams.

The importance of utilizing technological tools cannot be ignored. Real-time data sharing during crises allows for rapid and accurate decision-making. Digital platforms play a crucial role in speeding up information flow and mobilizing the necessary resources in a timely manner. These technological systems should be accessible, easy to use, and effective for all professional groups involved in disaster management.

Leadership is another vital element in ensuring successful interdisciplinary communication in disaster management. Leaders must create a secure environment during crises, fostering trust and supporting information sharing among different professional groups. Strong leadership facilitates effective coordination and communication networks, enabling timely and accurate interventions. Furthermore, preparations made before a disaster also play a critical role in interdisciplinary communication. Joint exercises and simulations conducted during the pre-disaster phase help teams learn how to respond during crises, increasing harmony and coordination between groups. These simulations allow for the identification and resolution of potential communication issues, minimizing chaos and coordination problems during a disaster.

In conclusion, interdisciplinary communication is crucial for effective disaster management. Disasters are complex events that require input and collaboration from a wide range of disciplines,

from medical professionals and engineers to environmental scientists and communication specialists. By enhancing collaboration, facilitating information sharing, and breaking down silos between disciplines, interdisciplinary communication ensures that disaster response efforts are more efficient, effective, and adaptive. While challenges such as language barriers, institutional obstacles, and technological limitations must be overcome, strategies such as joint training

In conclusion, interdisciplinary communication is essential for a successful response and recovery process in disaster management. The success of communication not only affects coordination during the crisis but also has a direct impact on reducing the effects of the disaster. Overcoming communication challenges requires both technological solutions and strategies aimed at increasing trust between professions. Training, efforts to develop a common language, leadership, and the integration of technological systems can strengthen interdisciplinary communication and make disaster management processes more effective. Continued work on interdisciplinary communication in disaster management will enable better preparedness for future crises.

References

Arıcı, E., Polat M. (2024). Determination of Major Heavy Metal Levels in Pepper Gas Used as Chemical Agents in CBRN Field. Suleyman Demirel University Journal of Health Sciences Volume 15, Issue 2, 226-35.

Comfort, L. K. (2007). Crisis Management in Hindsight: Cognition, Communication, Coordination, and Control. Public Administration Review, 67(S1), 189-197.

Comfort, L. K., Ko, K., & Zagorecki, A. (2004). Coordination in Rapidly Evolving Disaster Response Systems: The Role of Information. American Behavioral Scientist, 48(3), 295-313.

Kapucu, N. (2012). Disaster Resilience and Adaptive Capacity in Central Florida: Multilevel Network in Emergency Management. Natural Hazards, 58(3), 863-886.

Kapucu, N., & Van Wart, M. (2008). The Evolving Role of the Public Sector in Managing Catastrophic Disasters. Public Administration Review, 68(4), 745-757.

Lindell, M. K., Prater, C. S., & Perry, R. W. (2006). Fundamentals of Emergency Management. Federal Emergency Management Agency.

McEntire, D. A. (2002). Coordinating Multi-Organizational Responses to Disaster: Lessons from the March 28, 2000 Fort Worth Tornado. Disaster Prevention and Management: An International Journal, 11(5), 369-379.

Sert, A., & Polat, M. (2021). Burdur ili acil sağlık hizmetlerinin retrospektif olarak değerlendirilmesi (2013-2017 yılları arası). Adnan menderes üniversitesi sağlık bilimleri fakültesi dergisi, 5(1), 61-71

Sert, A., Polat, M., & Erdemir, S. (2022). Kimyasal Biyolojik Radyolojik Nükleer (Kbrn) Ajanlardan Kan Zehirleyici Gazların (Hcn, Co, As) Önemi. Uluslararası Sağlık Bilimlerinde Disiplinler Arası Etkileşim Dergisi,1(1),42-51.

Sert, A., Köksoy, S., & Polat, M. (2022). Acil Sağlık Hizmetlerinde Çalışanların Giyilebilir Teknolojileri

About The Authors

Eda ARICI: She works as a lecturer at Antalya Bilim University. Her undergraduate and graduate degrees are in emergency aid and disaster management. She is also a paramedic and has worked actively in the field in the past.

E-mail: eda.arici@antalya.edu.tr

ORCID: 0009-0000-5057-6313

Mümin POLAT: He works as an associate professor at Burdur Mehmet Akif Ersoy University. His doctoral field is microbiliology. In addition to being the head of the emergency aid and disaster management department, he is also the director of Burdur Vocational School of Health Services. He has been working at the university for 23 years.

E mail: mpolat@mehmetakif.edu.tr. ORCID: 0000-0001-8082-0735

Similarity Index: The similarity index obtained from the plagiarism software for this book chapter is 5%.

To Cite This Chapter:

Arıcı E., Polat M., (2024). The Importance Of Interdıscıplınary Communıcatıon In Dısaster Management. In Current Studies in Health and Life Sciences 2024 (pp.300-305). ISRES Publishing.

Chapter II: Dentistry

ISRES Publishing

Hard Tissue Renegation Techniques

Saim YANIK

Mehmet Turhan TEKE

Ömer Faruk KAYGISIZ

Introduction

Bone is a unique structure of mineralized hard tissue, unlike any other part of the body. The ability of bone to continuously remodel itself has created different clinical approaches to the treatment of damaged bone. Large bone defects are rehabilitated with dental implants placement in the jaw after rehabilitation. Revolutionized the field of dentistry and improved patients' quality of life by rehabilitating edentulous patients with osseointegrated implants. Nevertheless, bone depletion or inadequacy resulting from diverse systemic and periodontal illnesses, injuries, and lesions persists as a significant hurdle for implant fabrication. To ensure a favorable long-term outlook for osseointegrated implants, ample and high-quality bone must be present at the sites of implantation.". Different techniques such as bone grafting techniques, alveolar distraction and guided bone regeneration (GBR) have been applied to replace lost bone to ensure that the implant is osseointegrated and maintained during functional loading (Chiapasco et al., 2006).

Following tooth loss, resorption of alveolar bone typically transpires within the initial 6 months, commencing horizontally and subsequently progressing vertically. Numerous methods exist to ameliorate deficiencies in alveolar bone, encompassing guided bone regeneration (GBR), onlay and inlay grafting, distraction osteogenesis, crest splitting, free vascularized autografts, and maxillary sinus grafting. The severity of bone depletion and the configuration of defects dictate the type, scope, and prognosis of bone grafting interventions. Despite clinical evidence indicating a high implant survival rate in augmented bone, extensive long-term clinical data for many techniques are lacking.(Aghaloo & Moy, 2007).

Although many techniques have been presented in the literature, there are basically five techniques. These are GBR, distraction osteogenesis, alveolar crest split, sinus floor elevation, and onlay block grafting. We present current literature data on surgical techniques for hard tissue regeneration.

1.Guided Bone Regenaration (GBR)

The GBR method involves isolating non-osteogenic cells, such as rapidly proliferating epithelial and connective tissue cells, from the grafted region using a barrier membrane. This setup enables osteoprogenitor cells to generate bone within the defective area. GBR is commonly employed in conjunction with bone grafting procedures. (Figure 1) (Dimitriou et al., 2012).

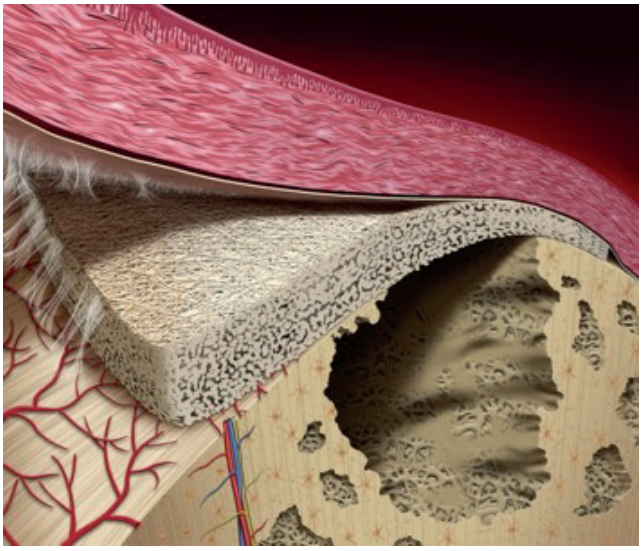


Figure 1. GBR procedure (Elgali et al., 2017)

The use of membranes in GBR technique is the most important component of the treatment. Desirable properties of membranes include biocompatibility, ease of application, adequate mechanical strength, and integration into the grafted area. If membranes are used in combination with bone grafts, they stabilize the graft materials. This reduces the resorption rate of the graft. There are resorbable and non-resorbable membranes used in periodontal tissue and bone regeneration (Bottino et al., 2012).

Membranes Used in GBR Technique

Non-Resorbable Barrier Membranes

They are biocompatible and have physical properties such as not disrupting their structural integrity, protecting the defect cavity better, not collapsing and shrinking towards the defect area compared to resorbable membranes. One of their disadvantages is that they cause bone resorption due to the exposure of the membrane due to its rigid structure. They do not have the ability to integrate with the tissue and their removal requires a second surgical intervention because they do not resorb. These membranes are divided into two groups (Rakhmatia et al., 2013).

Politetrafloroetilen (PTFE) Membrane: The clinical efficacy of PTFE membranes depends on the surgical placement technique and the preservation of soft tissue coverage over the membrane. It is critical that the keratinized gingiva over the membrane is thick for optimal healing (Retzepi & Donos, 2010).

Expanded/e-PTFE membranes:

It has a porous structure and a flexible form. It is a chemically stable and inert polymer. It resists microbiological and enzymatic damage and does not cause immunological reactions. After placement of the membrane, bone formation on radiographs occurs after six months and can continue for a year. Clinical studies have shown that ePTFE membranes used in the GBR procedure are effective in correcting defects (Retzepi & Donos, 2010).

High density/ d-PTFE mambranes:

Although e-PTFE is commonly used in dentistry, high-density teflon (d-PTFE) membranes have been used in recent years instead of e-PTFE depending on the patient and defect. The reason for this choice is that the high-density teflon membrane has a smaller pore size, which minimizes the risk of infection by minimizing bacterial infiltration. High-density PTFE membranes protect

the cavity and provide adequate stabilization of the incision, allowing sufficient time for bone regeneration. In addition, the fact that the membrane is not adhered to the tissue allows it to be removed using a mucosal flap without disrupting and traumatizing the mucosal tissue. The limited number of pores of dense PTFE membranes also limits blood flow to the area, so the blood flow required for bone regeneration is provided through holes created in the cortical bone (Soldatos et al., 2017).

Titanium Reinforced-PTFE :

Titanium-reinforced PTFE membranes are preferred when the defect morphology fails to create an adequate gap. Creation and maintenance of the gap have been recognized as important pre-requisites for achieving the desired regeneration. Cavity formation also depends on the mechanical ability of the membrane to resist collapse. Titanium-supported PTFE membranes have been produced for situations where more space is needed to preserve the volume of the graft placed in the defect and for the desired regeneration. They are designed in configurations similar to conventional PTFE membranes. Several studies have shown that titanium-reinforced PTFE membranes have significant biological potential in alveolar bone regeneration. The cavity created is more predictable and more resistant to collapse due to mucosal overlying tissue than non-titanium-reinforced membranes (Soldatos et al., 2017).

Titanium Mesh Membran: It has good mechanical properties and biocompatibility. It provides a barrier for osteogenesis with its high strength and stiffness. The formable titanium mesh adapts to bone defects by flexion. These properties ensure that GBR with titanium mesh has a stable osteogenesis effect and bone augmentation in horizontal and vertical directions. Thickness and porosity are the main factors affecting its mechanical properties. Commonly used titanium mesh thicknesses range from 0.1 to 0.6 mm. Usually, titanium mesh with a thickness of 0.2 mm is used. Thick titanium mesh should be used in GBR to protect the bone regeneration area (Xie et al., 2020).

Resorbable Barrier Membranes

Resorbable barrier membranes have been developed to avoid the possibility of membrane exposure and a second surgical procedure. In the area where they are placed, they are resorbed by enzymatic reaction or hydrolysis. These membranes are biocompatible, flexible and formable. They are easier to shape clinically than non-resorbable membranes. The inadequate barrier of resorbable membranes due to their flexible structure may result in failure in preventing the migration of fibrous tissue forming cells to the area. Due to the low mechanical resistance of these membranes, they may be insufficient to protect the defect cavity, which must be protected for bone formation, against external forces. There is also a risk of triggering an immune response as they are resorbed by enzymatic reaction (Strietzel et al., 2006).

There are basically three types of resorbable membranes:

- polymeric centetic polyglycocytes (i.e., polylactic acite, polylactate/polygalactate co-polymers);
- collagen
- calcium sulfate

The synthetic ones exist as polymers of glycolic acid and lactic acid. The ester bonds between these membranes dissolve between 30-60 days and an inflammatory reaction may occur due to the free acids released as a result of this dissolution (Duskova et al., 2006).

Collagen, acellular dermal matrix, fascia lata, pericardium and laminar bone are naturally resorbable membranes.

Collagen-based membranes produced from human skin, pig skin and bovine tendon have

started to be used instead of synthetic membranes due to their higher biocompatibility. Collagen membranes are resorbable without foreign body reaction, exhibit rapid vascularization and good tissue compatibility. The adhesion of connective tissue cells to the collagen membrane supports periodontal regeneration and provides hemostasis by helping to fill the defect with clot. Because of these properties, collagen membranes are an ideal choice for resorbable GBR barriers (Bunyaratavej & Wang, 2001).

GBR studies comparing the use of resorbable membranes with ePTFE membranes have shown that both membranes are equally effective. This has resulted in most clinicians using resorbable membranes in GBR procedures. In addition to collagen membranes, a wide variety of polyester-containing membranes such as polylactic acid (PLA) and its copolymers have been used. Many types of membranes combined with other polymers have been developed to improve their properties and clinical results are promising. The bio-resorbable GBR barrier membrane was constructed with PLA/poly(glycolide-co-lactide) copolymer (PLGA) membrane with polyglycolic acid network. PLGA is easy to handle and elastic at room or body temperature, but swells and hardens to prevent epithelial and gingival connective tissue displacement apically. Membrane destruction occurs over a period of 2-6 months. Furthermore, compared to PTFE membranes, polyester-containing membranes are bio-resorbable and easier to use. These membranes need to remain physically and mechanically intact for at least 4-6 weeks for regenerative therapy to be successful (Bottino et al., 2012).

Grafts Used in GBR Technique

Autogenous Grafts

Autogenous grafts; It is a type of graft that contains osteoprogenitor cells and live osteoblasts taken from a region of the same living creature and transplanted to the operated area. In the maxillofacial region, the mental region, mandibular ramus area, maxillary tuber area are considered intraoral autogenous graft sources, while iliac bone, rib and tibial bone are extraoral autogenous graft sources. Autogenous grafts are advantageous in terms of preference in GBR surgery due to early revascularization, no antigenic properties in the recipient site, high biocompatibility, osteoinductive effect and high osteogenic potential (Albrektsson & Tjellström, 2019).

Autogenous bone graft shows osteogenic effect in the first 2 weeks after placement. The osteoinductive effect starts 2-6 weeks after grafting and lasts up to 6 months. Finally, appositional bone formation occurs with osteoconductive effect. Collagen, the organic component of the graft, provides flexibility, strength and stability to the graft, while hydroxy apatite, the inorganic component, contributes to the rigidity of the graft (Albrektsson & Tjellström, 2019).

Allografts

It is a graft material that is transferred between individuals of the same species with different genotypes. Allografts do not contain osteogenic cells and their osteoinductive effect is considerably reduced as a result of demineralization. The fact that it does not require a donor site during sourcing and therefore does not require a secondary operation provides an advantage in terms of preference in maxillary GBR surgery (Albrektsson & Tjellström, 2019).

Freeze-dried bone allografts (FDBA) or demineralized freeze-dried bone allografts (DFDBA) can be categorized as cortical or trabecular. The benefits of using allografts include their ready-to-use nature, sparing patients from extensive autogenous graft harvesting, reducing surgical duration, and lowering complication risks. However, they are not as effective as autogenous bone grafts in promoting new bone formation. (Misch & Dietsh, 1993).

Xenografts

Xenografts, in which the donor type and recipient type are different for the graft source, have the ability to form a suitable scaffold for bone tissue. In cases where xenograft alone is used,

bone formation occurs from the source bone to the graft site. In surgical operations, deproteinized bovine bone is the most commonly used xenograft, either alone or mixed with autogenous bone or platelet rich plasma (PRP) (Rivara et al., 2017).

Alloplastics grafts

Hydroxyapatite is the most widely used alloplastic graft material that does not cause immune reactions, non-cytotoxic, resistant to masticatory forces, does not deteriorate by maintaining its stable structure before and after application, and meets the definition of ideal synthetic graft with its osteophilic and osteoconductive effects. Another alloplastic material approved for the regeneration of all bone tissue defects in the skeletal system is β-TCP. This graft material is completely absorbed at the site of implantation and is replaced by living and natural bone tissue after 3 months to 2 years. The blood vessels and collagen structure localized at the insertion site cover the porous particulate system of the material and form the matrix structure for new bone tissue formation. It has been reported to be a mechanically stable material without causing infection or immune reactions (Rivara et al., 2017).

Horizontal alveolar grafting typically yields a more predictable outcome compared to vertical alveolar grafting. However, studies in the literature have demonstrated successful results when vertical alveolar grafting is conducted in conjunction with non-resorbable PTFE membranes and bone grafts (Canullo & Malagnino, 2008). While non-resorbable membranes have traditionally been the go-to choice for vertical alveolar grafting, recent clinical studies suggest that the utilization of resorbable collagen membranes holds promise. The most important complication in the use of non-resorbable membranes is the opening of the flap and infection of the site. This is a common complication especially in vertical alveolar grafting applications due to the limiting effect of soft tissue (Canullo & Malagnino, 2008).

In cases where the defect is large, bioactive regenerative therapies such as the administration of recombinant growth factors in combination with GBR have been applied to achieve acceptable bone regeneration as a result of GBR application. In a clinical study, it was shown that when recombinant human platelet-derived growth factor (rhPDGF-BB) was applied by GBR technique with bone graft and resorbable membrane, the vertical dimension of the bone was preserved after implant treatment in the relevant region. However, further studies are required to clinically prove the mechanism of action of the growth factor (R. E. Jung et al., 2008).

Platelet concentrates such as platelet-rich plasma and platelet-rich fibrin have been proposed as additional stimulators for bone remodeling. Platelet concentrates were initially used as autologous scaffolds in GBR and maxillofacial surgery. Platelet concentrates contain wound healing promoting factors such as growth factors, platelets with the potential to secrete cytokines, leukocytes and are derived from the patient's own blood Despite claims of platelet-rich fibrin being a bioactive membrane for guided bone regeneration (GBR), there have been relatively few published clinical reports in this area. (Chen et al., 2014). Concerns regarding the low mechanical strength and rapid resorption of this membrane have arisen in its application. Kawase et al. managed to mitigate these issues by employing a heat compression technique, which effectively reduced the biodegradation rate of the platelet-rich fibrin membrane without compromising its biocompatibility (Kawase et al., 2015).

2. Alveolar Crest Expansion

The alveolar crest-split procedure is the division and horizontal expansion of the existing narrow alveolar crest to accommodate the placement of implants. Since grafts and membranes are not used in this technique, treatment is less expensive, implant rehabilitation requires less time and complications, especially postoperative infections, occur less frequently. However, this procedure can also be performed as interpositional grafting by placing bone graft between the buccal and lingual bone walls of the surgically expanded alveolar crest. Systematic reviews and meta-analyses

in the literature have shown that horizontal reconstruction of the knife-edge alveolar crest with the crest-split technique is an effective surgical technique with a high implant success rate, low complication rate, increased horizontal alveolar crest width and an effective surgical technique (Figure 3) (Starch-Jensen & Becktor, 2019).

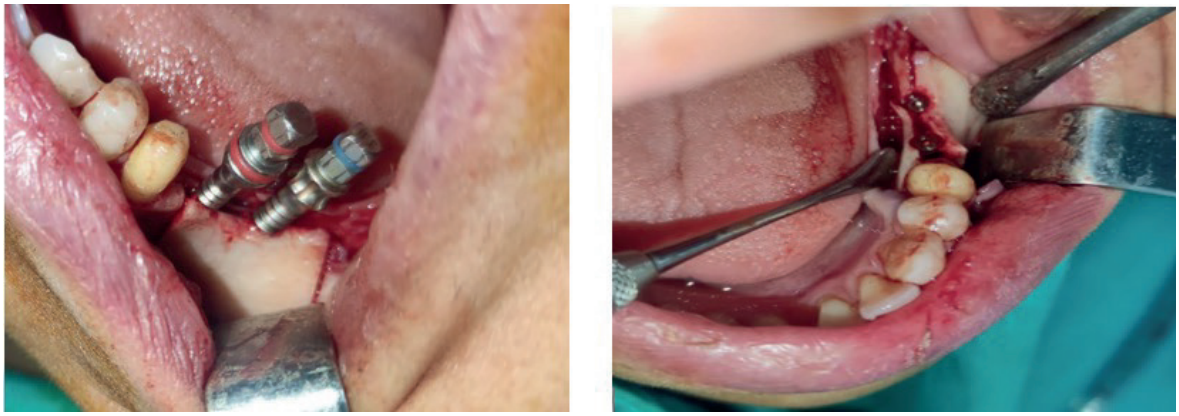


Figure 3. Crest split operation

In implant treatments, there should be 1 mm of bone around the implant in the buccal/lingual direction after implant treatment. Therefore, the average buccolingual width should be 6 mm. In the crest split technique, cortical and spongiose bone layers should be present in the buccal and lingual bone plates in the split of the knife-edge alveolar crest. Considering this available information, the alveolar crest should be 3-5 mm thick for crest split application. Preoperative clinical and radiologic evaluation of the patients is of great importance (Artzi, 2023).

In classical crest splitting procedures, osteotomes, hammers, rotating instruments and bone saws are used. Osteotome operations require more careful and atraumatic work during osteotomy, which prolongs the operation time. Rotating instruments work faster, but soft tissues may be damaged and bone loss may occur depending on the thickness of the burs used. In addition, when working with rotating instruments, neighboring teeth may prevent access to the area. The piezosurgery method, on the other hand, causes less damage to the soft tissue, minimal bone loss and less risk of damage to neighboring tissues. In addition, piezosurgery provides a more comfortable field of vision in the operation compared to other methods. In addition, piezosurgery is superior to conventional rotary devices in cases where the area to be operated is close to the nerves, such as cutting in mineralized tissue, impacted wisdom teeth very close to the inferior alveolar nerve, osteotomies to be applied close to the mental foramen and nerve repositions (Blus & Szmukler-Moncler, 2006).

Autogenous block bone grafting from the mandibular ramus or iliac crest to the knife-edge alveolar crest is generally considered the treatment of choice for horizontal reconstruction of the alveolar crest. The high survival rate of implants placed at the grafted site has been documented in systematic reviews and meta-analyses (Waechter et al., 2017). However, the use of block bone graft has disadvantages such as donor site morbidity, unexpected resorption of the grafting material, and long healing time of the grafted area. Therefore, alveolar crest split treatment technique has been proposed for horizontal reconstruction of the alveolar crest in patients with knife-edge alveolar crest due to less surgical morbidity and short treatment time (Waechter et al., 2017).

Since the preparation of the bone cavity for implant placement in the crest split procedure differs from routine implant treatment, it is important to evaluate the neck resorption of the implant after the application of this technique. In a retrospective study of 22 patients, a mean crestal bone loss of 0.8 mm was observed after 6 months. The mean crestal bone loss at 6 months after function was 1.0 mm. However, the authors noted that implant neck resorption increased as the compact bone ratio increased. Therefore, bone quality seems to be a determining factor in cases with indication for crest split (Strietzel et al., 2002).

In contrast, Bruschi et al. evaluated crestal bone loss in 71 cases of crest split with 137 implants with a mean radiographic follow-up of 6.5 years. While an average of 1.1 mm of crestal bone loss was recorded after the first year, an average of 0.89 mm of bone gain was observed after 3 years and remained stable after that (Bruschi et al., 2017).

In a recent short-term evaluation of 13 crest split and 42 implant-treated patients, crestal bone loss was measured by periapical radiography. For both jaws, a mean bone loss of 1.26 mm was observed after a 6-month healing period, which was significantly reduced to 0.5 mm at the end of the first year (Sharaf et al., 2022).

In the meta-analysis of Chiapasco et al. 374 articles were reviewed and 392 crest split operations and 733 implant treatments were followed up for 6-68 months and the surgical success rate was found to be 98%-100%. Implant survival rates were found to be between 91% and 97.3%. Fracture of the buccal plate during crest split was reported as the most important complication, although rare (Chiapasco et al., 2006).

Donos et al. performed a similar systematic clinical evaluation on 435 articles they reviewed. They placed 1090 implants in a total of 279 patients who underwent crest split treatment and reported implant survival rates ranging from 86.2% to 100% during the 18-60 month follow-up period. Again, fracture of the buccal bone plate during crest split was the most common complication, while loss of osseointegration was rare (Donos et al., 2008).

Milinkovic and Cordaro's systematic review included six studies, two prospective and four retrospective. The mean increase in bone width ranged from 3.37-6.33 mm, with a mean gain of 2.96 mm and a mean implant survival rate of 97.4%. Reported complications included infection, non-integration of the implant and buccal bone plate fractures, with a mean complication rate of 6.8% (Milinkovic & Cordaro, 2014).

Bassetti et al. used two databases, Medline and EMBASE, to further expand their systematic review of the crest split procedure. Their data included 18 human and 6 animal studies followed by histologic interpretation, with implant survival ranging from 91.7% to 100% and surgical success ranging from 88.2% to 100% after an average follow-up of 1-10 years. They observed crestal bone loss after the first year of loading, especially in the buccal bone plate, and these authors suggested that additional horizontal grafting of the alveolar crest with directed bone regeneration would reduce buccal crestal bone loss (Bassetti et al., 2016).

Santagata et al. reported 13 cases of combined subepithelial connective tissue grafting to improve soft tissue management in crest split procedures. These authors measured a mean alveolar crest width gain of 3.5 mm and an implant survival rate of 97% (Santagata et al., 2015).

In conclusion, the alveolar crest split method allows the implant to be placed in the same session in cases of insufficient bone width. By applying bone graft materials to the cavity obtained in the same operation, support for the separated bone layers is created and relapse is prevented.

3. Distraction Osteogenesis

Distraction osteogenesis is the process of forming new bone in the space between two separated bone fragments by applying a graded and controlled stretching force to the new bone. Alveolar distraction osteogenesis is a method used to elevate or widen the mandible and maxilla and its success depends on the appropriate mechanical tensile force applied to the osteotomy site (Figure 4) (Mohanty et al., 2015).

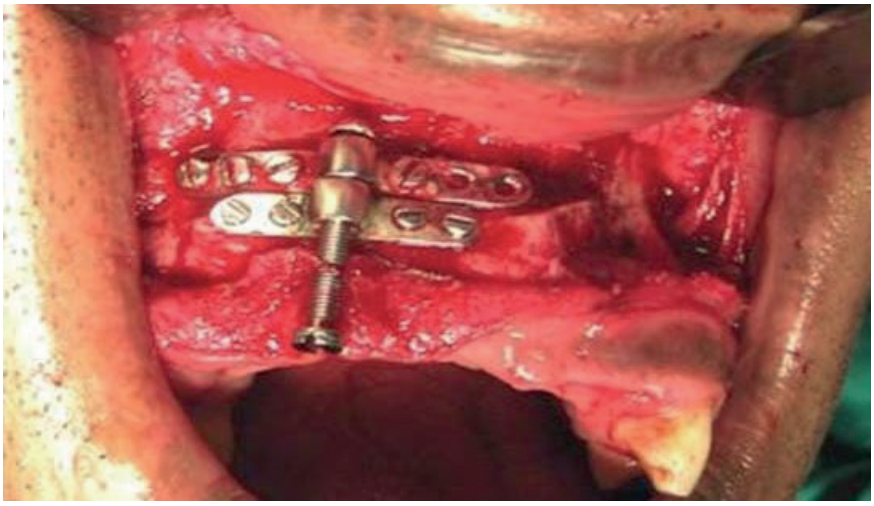


Figure 4. Alveolar distraction osteogenesis (Mohanty et al., 2015)

Alveolar distraction osteogenesis was first applied on dogs by Block et al. in 1996. In the same year, the investigators made the first application in humans using an alveolar distractor in alveolar defects caused by traumatic tooth loss. Since then, promising results have increased its popularity, but this treatment modality is still in the early stages of development (Mohanty et al., 2015).

Severe atrophy of the edentulous crest (insufficiencies greater than 4 mm), segmental alveolar crest insufficiencies that aesthetically and functionally compromise implant placement (inappropriate crown-implant relationship), narrow alveolar crests where horizontal distraction can be applied, Alveolar distraction osteogenesis can be used in cases where orthodontic displacement is not feasible or fails, such as the gradual vertical movement of ankylosed teeth and the gradual vertical displacement of an osseointegrated implant with the surrounding alveolar bone, edentulous spaces between 2-4 teeth, tissue loss due to traumatic injuries, restoration of teeth lost as a result of periodontal disease, congenital malformations, after grafting. Alveolar distraction osteogenesis is contraindicated in patients who have undergone radiotherapy, in patients with osteoporosis and in patients with general systemic diseases (Garcia-Garcia et al., 2004).

Distraction osteogenesis is used in maxilla and midface deformities, hypoplastic mandible, mandibular defects after temporomandibular joint ankylosis and pre-implant alveolar bone correction. This method is based on the tension-stress principle described by Dr. Ilizarov. The principle of operation is that after corticotomy is performed on the bone segments to be separated, the distraction apparatus is placed. The gradual removal of bone segments (0.5-1 mm per day) by the distraction apparatus creates a tension that stimulates bone formation and induces a biological response. Subsequently, pluripotent cell differentiation, angiogenesis, osteogenesis and bone mineralization occur. Compared to augmentation with autogenous bone grafts, the advantage of this technique is that new bone is formed in the intervening space as a result of the gradual removal of bone, the movement of bone segments can be controlled and the amount of soft tissue increases in adaptation to this situation. There is no donor site morbidity because grafting is not performed (Tolstunov et al., 2019).

Alveolar distraction osteogenesis no morbidity at the donor site, simultaneous changes in both hard and soft tissues, less likelihood of exposure of hard tissues and less likelihood of resorption of grafts, more predictable volume of hard and soft tissue gained, teeth or implants can be present in the transferred fragment and thus occlusal or aesthetic defects can be corrected, consolidation time and total treatment time are short, It has advantages such as allowing the use of complementary regeneration techniques in cases where the results are insufficient, minimal

bone resorption following distraction, the new bone to be formed as a result of distraction in the maxilla and mandible is predictable and stable, it is the technique that provides the most vertical gain among the techniques of crest elevation or expansion, the possibility of infection is low, the transferred part is always fed from the original sources of the body (M.Miloro GEG, P.E.Larsen, P.D. Waite. Peterson's Principles of Oral and Maxillofacial Surgery. Second Edition Ed. London: BC Decker Inc; 2004., n.d.).

In addition to the advantages of alveolar distraction osteogenesis; The disadvantages of veolar distraction osteogenesis include the need for daily activation of the distractor, intraoral appliances making speech and eating difficult, inability to apply in highly atrophied mandibles, risk of losing the position of the distracted part, risk of bleeding at the osteotomy site, fracture of the part during large movements of the thin alveolus, difficult adaptation of microplates, need for patient cooperation, high number of controls, expensive application, difficulties in cooperation with the patient or family members for activation of the appliance (McAllister & Gaffaney, 2003).

In a meta-analysis study, all authors agreed that the frequency of distraction should not exceed 1 mm per day, and since 2007, almost all authors have used a distraction force of 1 mm per day. In addition, the mean bone gain with alveolar distraction osteogenesis was 7.55 mm, while extraosseous distraction devices reported higher bone gains ranging from 8.13-6.97 mm (Pérez-Sayáns et al., 2018). Researchers agree that alveolar distraction osteogenesis is the technique with the greatest potential for bone gain in the vercical direction (Pérez-Sayáns et al., 2018).

Milinkovic and Cordaro revised 351 implants placed after alveolar distraction osteogenesis and found success rates of 98.8% and 92.3%, respectively (Milinkovic & Cordaro, 2014). The longest follow-up period after implant placement was developed by Kim et al. who observed a 92.7% success rate and 97.3% survival rate in implants followed for 85 months (Kim et al., 2013).

Perez-Sayans et al. compared 50 implants placed in a group of patients undergoing alveolar distraction osteogenesis with 50 patients without alveolar distraction osteogenesis. They analyzed peri-implant loss at the time of loading and after 1 and 3 years. They found that there were significant differences in loading time, more resorption in the alveolar distraction osteogenesis group (0.5 mm in the alveolar distraction osteogenesis group and 0.25 mm in the control group), and no difference in peri-implant bone after one year of follow-up (loss 0.66 mm in both groups). However, at 3-year follow-up, bone loss was significantly higher in the alveolar distraction osteogenesis group (1.03 mm vs. 0.68 mm) (Perez-Sayans et al., 2013). According to Saulacic et al., the effect of previous bone defects in the alveolar distraction osteogenesis group on these results corresponded to 51% and 58% of cases (Saulacic et al., 2008).

Chiapasco et al. conducted an analysis of 138 implants subsequent to alveolar distraction osteogenesis over a four-year period. Their findings indicated an initial loss of 0.8 mm during the first year post-functional loading. Subsequently, resorption rates were recorded at 0.1 mm in the second and third years, and 0.2 mm in the fourth year. Impressively, they achieved a survival rate of 100% and a success rate of 94.2% for the implants. (Chiapasco et al., 2004).

Polo et al. observed a 1.9 mm resorption one year after loading in a total of 34 implants inserted following alveolar distraction osteogenesis in the posterior maxillary region. (Polo et al., 2005). In a subsequent study, Chiapasco et al. compared the outcomes of 19 implants inserted following alveolar distraction osteogenesis with 21 implants placed after augmenting the graft with autogenous block. They reported comparable results between the two techniques regarding success and survival rates, as well as surgical and postoperative complications (Polo et al., 2005).

Alveolar Distraction Osteogenesis Protocol

Latent Phase: This is the period from the time the osteotomy is performed until the start of traction. During this period, soft new bone is formed. The latent period applied in maxillofacial

distraction varies between 4-10 days. Adequate blood supply in the maxillofacial region reduces or eliminates the latent period. In the studies, no significant difference was observed between those with and without a latent period. In clinical alveolar distraction, a latent period of 4-7 days is indicated to prevent premature exposure of the bone (Saulacic et al., 2004).

Distraction Phase: It is the period when the tensile force is applied to the transferred bone fragment and new immature tissue is formed. During the distraction phase, the values of three variables must be determined. These are: the rate and rhythm of distraction and the total time required for distraction. In alveolar distraction, this period usually ends in 1-2 weeks. A daily distraction rate of less than 0.3 mm is insufficient for cell proliferation and premature union may occur. A daily distraction rate of 0.3-0.7 mm increases cell proliferation. A daily rate of 0.8-1 mm is optimal for cell proliferation. Distractions performed too fast cause fibrous nonunion. It has been reported that distraction can be applied 3 times a day at 0.3 mm or 2 times a day at 0.4 mm. (McAllister & Gaffaney, 2003).

Consolidation Phase: This is the period that allows the newly formed bone to mature. After the end of distraction, the central fibrous and osteoid areas of the facial bones begin to ossify and mineralize largely intramembranously. After this period, implants can be placed in the area. If implants are placed after 4 weeks, the displacement of the cortical bone and deformation of the callus will be above physiologic limits. After eight weeks, the distribution of forces becomes more homogeneous and the displacement of the distracted cortical fragment decreases. Studies show that 16 weeks is optimal for consolidation; however, values obtained after 8 weeks are sufficient for implant placement. After 8 weeks is considered to be the appropriate time for implant placement, earlier applications may result in failure (Enislidis et al., 2005).

Since the beginning of distraction applications, problems related to the activation of distraction devices have caused interruptions and delays in the treatment. Failure to achieve the intended success in treatments where the activation of the device is not performed by the physician causes the treatment to last longer than the targeted time. Accordingly, researchers are trying to make improvements on automatic distractors. The conclusion drawn from a study comparing automatic distractors is that although automatic distractors have advantages, studies need to continue before they can be put into general use, especially due to their size and problems with their systems (Huang et al., 1999).

In another study on distractors, especially external distractors were organized by calculating the comfort of use of external distractors on the patient and sleep patterns, and distractors that can provide bilateral distraction and whose extemal extension is unilateral were used (Shang et al., 2012).

The use of distraction osteogenesis in the early treatment of children with the syndrome is increasing in several western countries, especially in patients with Pierre Robin syndrome, early distraction can be used to treat patients without the need for tracheosteomy (Hönig et al., 2002).

Bone lengthening procedures have started to be performed by taking autogenous grafts from the patient (tibia, etc.) and distracting this graft after callus formation in the recipient area in the latent period, especially in cases with excessive hard tissue loss and requiring reconstructive surgery (Block et al., 1996).

The aim of orthodontic treatments is the manipulation of teeth and bone. Distraction osteogenesis method, which is used in the treatment of dentofacial deformities, can be used for many orthodontic treatments. In addition to its use for palatal expansion for many years, its use for distalization of the canine tooth has become widespread in recent years. The time required for this treatment is considerably reduced (Kisnisci & Iseri, 2011).

In an animal study investigating the effect of hyperbaric oxygen therapy on consolidation time, the effects of hyperbaric oxygen on the blood supply of tissues, which is also an important part

of Ilizarov principles, were investigated. In this study, it was also observed in histological sections that oxygen accelerated healing and it was demonstrated that the treatment could be completed with less consolidation time than normal (Ilizarov, 1990).

In an animal study investigating the latent period, new bone density and quality were compared in the group that started distraction immediately after the surgical phase and in the group that started treatment after the latent period. The results of this study showed that the latent period had little or no effect on bone quality and quantity (Okcu et al., 2009).

4. Sinus Floor Elevation

The maxillary bone is atrophied at the level of the second premolar in more than half of the patients and at the level of the molars in 80-90% of the patients. In this region, advanced surgical techniques are needed to place dental implants due to the proximity to the maxillary sinus and decreased bone height. One of these techniques is sinus floor elevation. The first prosthetic filling of the maxillary sinus with bone graft was performed by Boyne in 1960. With the development of titanium implants in root form, alveolar crest augmentation for implant placement in the maxillary posterior region with insufficient vertical bone height was sometimes sufficient to overcome this deficiency, but it became necessary to place a graft in the sinus floor in most cases. Boyne and James first reported sinus floor grafting for metallic implant placement in 1980. Before this report, Tatum presented the clinical application of this procedure but did not publish the results in the literature (J.-H. Jung et al., 2007).

Today, sinus floor elevation can be performed in two ways: open (lateral window method) and crestal technique (osteotome). In the lateral technique, a bone window is opened in the maxillary sinus wall and the bone height is increased by applying graft material under the exposed sinus floor. This technique requires a large working area. The lateral sinus lift technique is shown in Figure 5. The crestal technique is less invasive than the lateral technique because it can be performed with osteotomes over the crest. Crestal sinus lift technique is shown in Figure 6 (J.-H. Jung et al., 2007). Another method applied in the crestal sinus lift technique is the antral membrane balloon elevation (AMBE) technique. The minimally invasive antral membrane balloon elevation technique is based on the elimination of the Schneiderian membrane by means of a latex mini balloon. The AMBE technique allows the operation to be performed with a limited mucosal incision and a small entry window in the residual bone (Soltan & Smiler, 2005).

Both techniques are known to be an effective and safe method for dental implant placement in the posterior maxilla. During or after sinus floor elevation, complications such as patient-related complications, perforation of Schneider's membrane, bleeding, pushing the implants into the sinus and infection may occur. Depending on the source of the complication, the treatment may vary from palliative treatment to surgical intervention (J.-H. Jung et al., 2007).

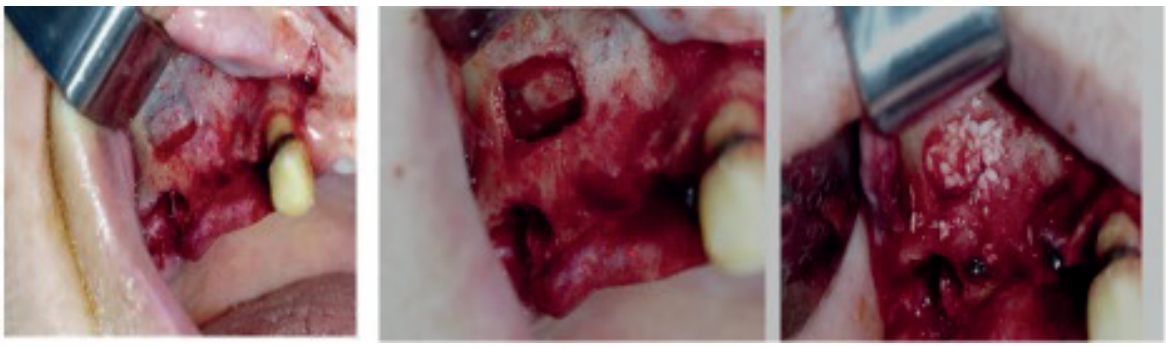


Figure 5. Lateral sinus lift technique

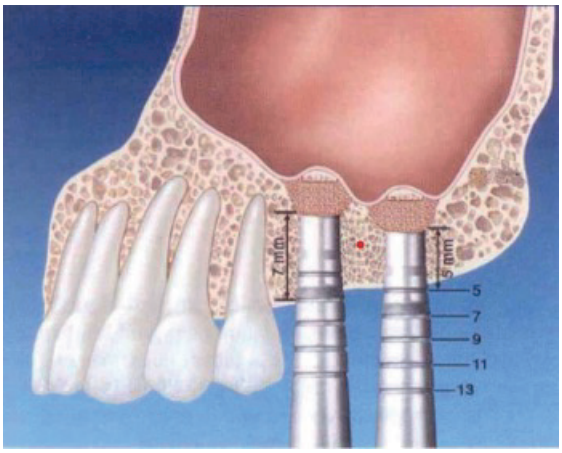


Figure 6. Crestal sinus lift technique (Dergisi & Cilt, 2009)

For many years, the use of autogenous allogeneic bone grafts and alloplasts in sinus augmentation in single or combined single or double stage has been mentioned. However, there is still no definitive conclusion as to which material is superior. Although autogenous grafts with osteogenic, osteoconductive and osteoinductive properties are considered the gold standard for sinus augmentation, their use in sinus augmentation has been questioned due to disadvantages such as the need for extra donor site and general anesthesia, high cost and rapid resorption of the graft. It has been reported that successful results have been obtained in maxillary sinus elevation with allografts, which are preferred because of their advantages over autografts, such as ease of application, no need for a second operation site, and no need for quantity limitation as in autografts (FINDIK & ŞENTÜRK, 2015).

Schneider's membrane is a 0.13-0.5 mm thick mucous membrane containing multilayered cylindrical epithelium lining the maxillary sinus. Perforation of the membrane is the most common complication during sinus floor elevation with a rate of 12% to 44%. Infection, chronic sinusitis, graft and implant loss may occur as a result of direct contact between the graft material and the sinus cavity due to perforation of the membrane during the operation. Factors that may cause membrane perforation include thin membrane, presence of septum in the sinus, sharp protrusion of the bone, and malpractice during osteotomy or membrane elevation. Vlassis and Fugazzotto reported that perforation occurred during osteotomy rather than membrane elevation (Vlassis & Fugazzotto, 1999).

Thick membranes are membranes with a thickness of 1.5 mm or more and thin membranes are membranes with a thickness of less than 1.5 mm. The rate of perforation in thick membranes is 16.6%, while this rate increases to 41.0% in thin membranes. In the literature review, it was found that the most commonly used perforation repair method was the use of resorbable membranes. However, there are also studies in which fibrin glue and cyanoacrylate adhesive were used (Choi et al., 2006).

Becker et al. In their study of 41 patients in which they evaluated the prognosis of sinus membrane perforation, defects smaller than 5 mm were repaired with resorbable collagen membrane and defects larger than 5 mm were repaired with 6.0 resorbable suture material. For defects larger than 1 cm, the operation was stopped. Based on the findings of the study, it was reported that membrane perforations did not show adverse effects as long as they were repaired during the operation (Becker et al., 2008).

There is no consensus on the effect of membrane perforations on implant success. Proussaefs et al. reported implant success of 69.5% in sinus floor elevation procedures in which perforation occurred and 100% in sinus floor elevation procedures in which the membrane remained intact; based on these results, they revealed that sinus membrane perforation decreases implant success.

(Proussaefs et al., 2004).

The maxillary sinus is supplied by the posterior superior alveolar, infraorbital and posterior lateral nasal arteries, which are branches of the maxillary arteries. Although these arteries are relatively small, serious bleeding may occur if they are damaged during surgery. However, bleeding has not been reported to be life-threatening. The most common arteries that can be exposed in the lateral window technique are the posterior superior alveolar artery and the infraorbital arteries. Elian et al. performed CT examination to determine the presence of the maxillary artery in the lateral sinus wall and detected the artery in 52.9% of cases. The average distance of 80% of the arteries to the alveolar crest was found to be 16 mm. Since this distance is sufficient for the preparation of the osteotomy and implant application, the risk of encountering the artery during the operation was reported to be 20%, and it was recommended to determine the localization of the artery with CT examination before the operation. In case of intraoperative bleeding, it has been reported that elevating the patient's head to an upright position reduces nasal mucosal blood flow by 38%. Other precautions include tampon compression, use of electrocautery, suturing, and placement of particulate bone graft into the artery (Katranji et al., 2008).

In studies, Schneiderian membrane perforation was measured as 6.76% in sinus lift operations performed using the AMBE technique. Sinus elevation and bone gain success rates were observed between 91.6% and 71.4%. Approximately 6.96 mm bone gain was achieved with the AMBE technique (Asmael, 2018).

Implant thrust into the sinus is caused by a lack of primary stabilization when the crest thickness is minimal. In this case, the implants are removed by Caldwell Luc technique or endoscopic approach. Although both methods are effective, the endoscopic approach is known to be more advantageous in terms of postoperative comfort (Felisati et al., 2007).

Excessive filling of the sinus cavity with graft material during sinus floor elevation may cause sinusitis by obstructing the ostium and a second surgical procedure may be required to remove the excess material. During the operation, contamination of the surgical field or graft material with saliva and lack of aseptic conditions may cause infection. Entry of the graft into the sinus as a result of membrane perforation during the operation is also an important factor. The incidence of infection is between 10% and 20%. This rate can be reduced with careful surgical practice and antibiotic prophylaxis. It is also recommended to add antibiotics to the graft during the operation (Katranji et al., 2008).

Lundgren et al. In 2004, Lundgren et al. described the graftless lifting procedure by stating that the space to be left between the antral wall and the schneiderian membrane would result in new bone formation around the implants in the maxillary sinus, even without the use of bone graft, and applied 19 implants in 10 patients with maxillary sinus elevation in a single stage. The reason for the formation of new bone obtained with this method is still not fully understood, it is thought that mesenchymal cells originating from the bone walls of the sinus and the osteogenic capacity of the membrane are effective in new bone formation. (Lundgren et al., 2004).

Altıntaş et al. reported that the new bone formed in the sinus lifting procedure performed without graft was denser than the bone formed in the procedure performed with graft. (Altintas et al., 2013).

The PRF clot developed by Choukrun et al. consists of platelets, leukocytes, cytokines and stem cells surrounded by a fibrin matrix network. Ali et al. stated that PRF can be used in combination with bone grafts or alone to fill the sinus cavity and reported that immediate implant placement following PRF application yielded successful results. (Ali et al., 2015).

5. Onlay Block Grafting

Onlay block bone grafts enable the acquisition of sufficient bone volume and appropriate morphology, facilitating the correction of abnormal intermaxillary relationships and the secure fixation of implants for both aesthetic and functional purposes. However, a significant challenge associated with alveolar reconstruction using appositional block grafts (onlay grafts) is the elevated occurrence of superficial resorption over the medium to long term. This resorption is particularly pronounced during vertical augmentation, as the forces exerted on the graft can lead to increased surface resorption when the soft tissue is vertically expanded (Chiapasco et al., 2006).

The process of neovascularization following bone placement in the recipient site is crucial for the long-term viability of the graft. This revascularization, which needs to be both rapid and thorough, can be challenging to achieve completely in bone blocks with a significant cortical component, such as onlay grafts. The infiltration of macrophage cells before the newly formed vessels penetrate the interior of the graft has been documented to induce necrosis in central areas, ultimately leading to resorption. The prognosis of the graft is determined by the quality and intensity of revascularization. The faster the revascularization, the more favorable the regeneration and graft survival. Graft revascularization does not normally start in the first hours after surgery. Osteoblasts and osteocytes can be nourished by fluid in their reserves and by diffusion for up to 4 days. They can survive longer if blood supply is available in the early period. Grafts from the iliac crest are one of the best graft types in terms of regeneration due to their morphologic structure containing a large proportion of cancellous bone. Bone marrow contains a large number of bone cells and has a high capacity for revascularization. Although excellent in terms of regeneration, the same cannot be said for the osseointegration quality of the dental implant. Biopsies taken from the bone 6 months after surgery showed bone of poor quality in terms of density. On the other hand, mandibular bone grafts, consisting mainly of cortical bone and a low proportion of cancellous bone, are resistant to revascularization and have poor regeneration potential. However, they have excellent bone quality for osseointegration (Figure 7) (Khoury, F., Antoun, H., & Missika, 2007).

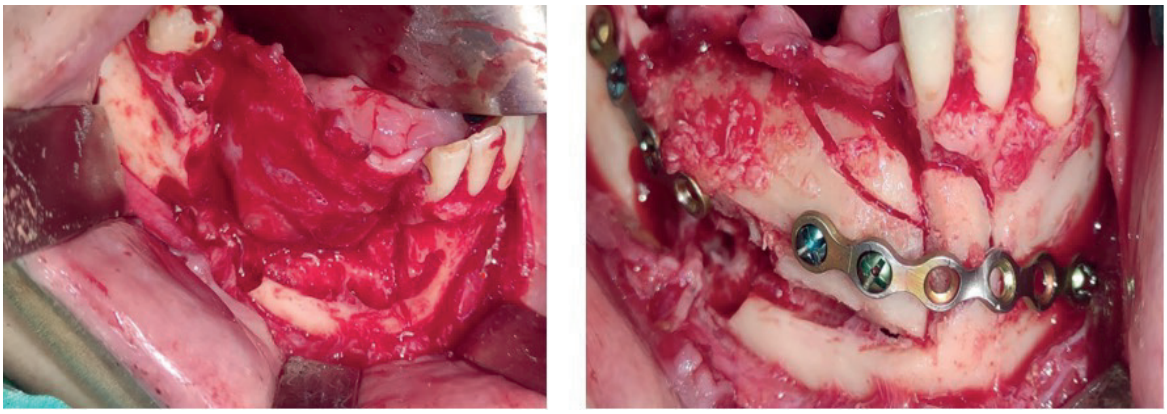


Figure 7. Iliac bone graft

To combine the advantages of the low resorption rate of cortical bone with the osteoconductive properties of cancellous bone, Khoury developed a bone block grafting method in which a thin block of cortical bone is fixed to the alveolar crest at a distance with osteosynthesis screws. The space between the crest and the graft is then filled with bone particles (Khoury & Hanser, 2015).

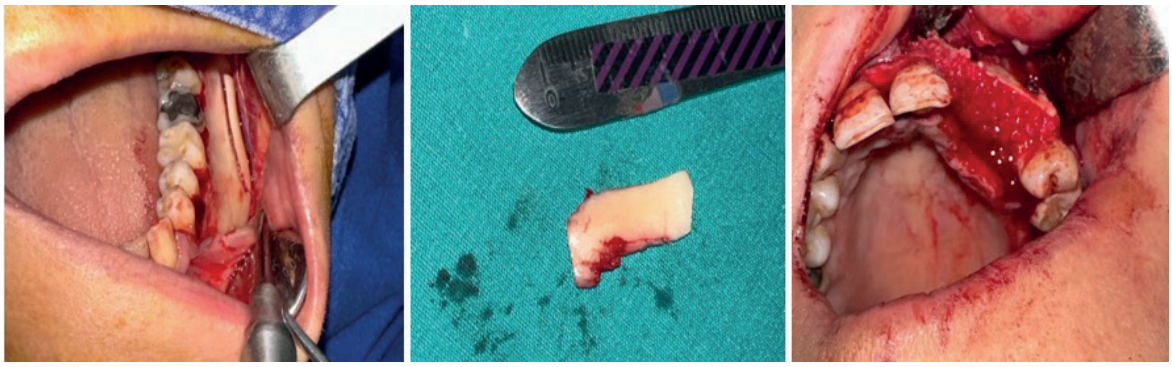


Figure 8. Khoury Technique

Autogenous bone block grafting has been associated with a high survival rate of superstructures and implants, minimal marginal bone loss, adequate width gain in alveolar bone, and few complications. However, harvesting an autogenous bone block graft presents drawbacks such as donor site morbidity, unpredictable graft resorption, and the risk of injury to adjacent vital structures. Consequently, various allogeneic, xenogeneic, and alloplastic bone block materials have been utilized for reconstructing alveolar crest deficiencies, aiming to simplify the surgical procedure and avoid the need for a second operative field required for harvesting autogenous bone block grafts. Nevertheless, these materials are linked to a significantly higher incidence of complications, including infection due to immunologic reactions, wound dehiscence, implant loss, and partial or complete loss of graft material, when compared to autogenous bone block grafts.

The use of autogenous tooth grafts in the reconstruction of alveolar deficiencies has also been proposed. In addition to their high biocompatibility and convenient acquisition, they do not require high temperature or other processing procedures to alter their internal structure; therefore, they retain a large amount of organic matter to enhance bone regeneration. They have osteoinductive effects and dental tissue can serve as a scaffold for bone repair. Therefore, autogenous dental materials are classified as a new type of bone substitute that can be used as bone grafts and are expected to have broad development prospects. However, the difficulty in obtaining them from each patient as needed is one of their major disadvantages (Zhang et al., 2018).

Obtaining the Graft

Extraoral and intraoral sites are utilized to obtain autogenous bone in areas where the amount of bone is insufficient. The techniques used to obtain bone extraorally require hospitalization under general anesthesia. This increases the risk of complications and cost. Since the graft material obtained will show endochondral healing, the possibility of resorption was also found to be higher. Iliac, costochondral, calvarium, proximal tibia and vascularized fibula grafts are commonly used extraoral autogenous graft sources (Saruhan, N., Ertaş, 2012).

In the mouth, block grafts can be obtained from the ramus, symphysis, tuber and zygoma. The most commonly used intraoral sites are the ramus and symphysis. A cone beam computed tomography scan is recommended before graft harvesting. One of the advantages of using a mandibular donor site for bone grafting is that the recipient site improves bone quality and volume. When the dense symphysis or ramus with a denser structure is preferred for graft harvesting, it has been found that bone resorption is less than in other regions and the amount of densities in the recipient area is higher (Alfaro, 2006).

The symphysis is a suitable donor site that can be easily accessed and bone blocks can be obtained without weakening the mandible. Although the morbidity of the donor site is much lower than extraoral sites, it has been reported to have disadvantages such as pain, functional limitations, swelling and paresthesia in the mental and lower lip region. In one study, transient paresthesia

was observed between 10% and 50%. During graft harvesting from the symphysis, a vestibular incision is made 5 mm below the gingival line to expose the mental muscle. Then the muscle and periosteum are passed and the bone is reached. The graft is obtained by maintaining a distance of 5 mm from the mental nerve, 5 mm from the apical teeth and 5 mm from the lower border of the jaw (Hunt & Jovanovic, 1999).

The mandibular symphysis contains cortical and cancellous bone, so that a corticocancellous block graft of approximately 1.5 x 6 cm^2 can be taken from the midline. This amount is usually sufficient to place 4 implants. However, in cases where more height and width gain is required, this amount is insufficient. The limited amount of bone available for reconstruction is the biggest disadvantage of intraoral donor sites. The symphysis shows more bone resorption than the ramus, but less resorption is observed in intraoral grafts compared to grafts obtained from the iliac crest, proximal tibia and costa. Disadvantages include sensory disturbances to the teeth, mucosa or skin and altered jaw profile. To avoid neurologic problems or to reduce the risk of damage, it is recommended that the donor site be 5 mm more apical to the tooth roots (Herford & Nguyen, 2015).

The mandibular ramus is a dense, cortical structure used for the reconstruction of small and medium alveolar defects of the maxilla and mandible. With autogenous grafts prepared from the ramus, sufficient bone volume and sufficient stability for implant placement can be obtained. It shows minimal resorption, postoperative graft failure has been reported at low rates. The close proximity of the recipient and donor sites shortens the duration of surgery and anesthesia. It has disadvantages such as the risk of damage to the inferior alveolar and lingual nerve, hematoma, infection and fracture risk. If more graft is needed, it can also be taken bilaterally. Evaluation of the ramus as a donor site is done by panoramic radiography and clinical examination of the external oblique margin. Attention should be paid if there is an impacted 3rd molar in the area (Yates et al., 2013).

Inferior alveolar block anesthesia or local infiltrative anesthesia can be used to obtain a block graft from the ramus. Local infiltrative anesthesia is recommended because the complete loss of sensation alerts the operating physician when the canal is approached. A trapezoidal incision is made and the ascending ramus is exposed. A graft 2-3 cm in length and width can be obtained from the external oblique ridge. Khoury divided this graft into two thin laminae with disks, fixed it with screws and filled the gaps with autogenous bone particles (Fouad Khoury et al., 2007). The mandibular ramus donor site shows fewer postoperative complications than the symphysis site. However, patients may experience swelling and difficulty opening the mouth and chewing. Sensory change is lower (in the range of 0% to 5%) and usually not permanent compared to the symphysis (Brugnami et al., 2009).

The zygomatic region has good bone quality (D1-D2) and is relatively easy to access. The amount of bone that can be obtained from the zygomatic arch is limited. It can usually only be used to obtain sufficient bone for the repair of a few edentulous defects. In the operations performed to obtain bone from the donor area, care should be taken to avoid perforation of the sinus membrane and damage to the infraorbital nerve adjacent to the relevant area. There are disadvantages such as bleeding and trismus as postoperative complications (Sittitavornwong & Gutta, 2010).

Calvarial bone grafts are taken from the parietal bone, the thickest part of the outer layer of the skull. Due to its dense cortical structure, it can be rigidly fixed as a block. Osseointegration and blood supply are successful and resorption rate is low. Postoperative morbidity is minimal when a drain is placed to prevent hematoma formation. Low complication rate, painless healing process compared to other donor sites and scar tissue remains under the scalp are among its advantages (Smolka et al., 2005).

Costochondral grafts, which contain both bone and cartilage tissue, are used as an ideal graft in pediatric patients and in temporomandibular joint reconstruction. The fact that costochondral bone

is covered with cartilage and has a rounded surface makes it histologically and morphologically similar to the normal mandibular condyle. In surgery, the right side is generally preferred because of the location of the heart and the 5th to 8th costae are chosen as donors. It has a low morbidity rate. Pain, postoperative pulmonary complications and scar tissue are among its disadvantages (Thapliyal, 2006).

A large amount of cannellous graft can be obtained from the proximal part of the tibia by medial or lateral approach. It is used for alveolar crest and maxillary sinus augmentation. The advantages of this donor site are that general anesthesia and hospitalization are not required, the patient can walk immediately after the operation, pain complaints are less common and the risk of complications is low. However, tibial bone graft should not be used in young and growing patients because of the risk of damage to the growth centers (Thapliyal, 2006).

The iliac bone is an easily accessible site with rapid revascularization and integration, partially abundant (approximately 50 cm3 corticocancellous) and high quality bone. The presence of a second surgical site (donor site) in the patient may lead to increased morbidity, which is a disadvantage, but studies have reported low complication rates and high long-term success rates. However, there is a risk of morbidity at the donor site and some surgical complications in autogenous graft harvest from the anterior iliac crest.

The iliac crest is the most commonly preferred extraoral donor site for augmentation of large bone defects. It contains a higher volume of cannelline bone than other donor sites and has the highest cannelline/cortical bone ratio. The graft can be harvested from anterior or posterior iliac crest sites (Nguyen et al., 2019).

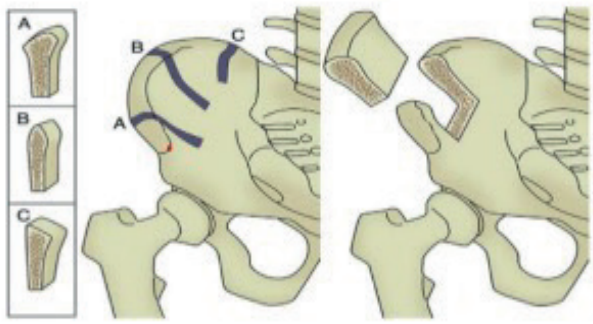


Figure 9. A. anterior iliak krest B. Orta iliak krest C. Posterior iliak krest (Misch, 2007)

From the posterior iliac crest, 2-2.5 times more grafts can be obtained than from the anterior iliac crest; therefore, it is preferred when larger graft volumes are required. It has advantages such as less postoperative morbidity, pain and gait disturbance. However, it has disadvantages such as additional intraoperative time for patient positioning, risk of displacement of the endotracheal tube, and inability to perform graft harvesting and grafting procedures simultaneously. Infection, hematoma, nerve injury, persistent pain, gait disturbance, iliac crest fracture, ileus, sacroiliac instability, abdominal hernia and cosmetic deformity are some of the complications seen after iliac crest grafting (Joshi & Kostakis, 2004).

Although studies have shown that autogenous grafts are the best graft material, an additional surgical field is required to obtain the bone. The optimal donor site should be chosen depending on the volume and type of bone required. The largest volume of bone graft is obtained from the posterior iliac crest (~140 mL), followed by the anterior iliac crest (~70 mL), calvarium (~40 mL) and tibia (~20-40 mL). However, graft preparation from extraoral donor sites has the disadvantages of higher cost, the need for general anesthesia and hospitalization. Another disadvantage is the increased resorption potential of the graft if simultaneous dental implant placement cannot be

performed. The limited amount of bone available for reconstruction is the biggest disadvantage of intraoral donor sites. Up to 5-10 mL of bone can be obtained from the ascending ramus and up to 5 mL from the symphysis. The advantages of intraoral grafts are the proximity of the donor and recipient sites, practical surgical access to the site, prevention of a surgical scar and short duration of surgery and anesthesia (Herford & Nguyen, 2015).

In the period immediately after autogenous bone graft placement, healing begins with remodeling and resorption stages. This loss of autogenous graft volume in the future depends on the size and quality of the bone graft, bone quality at the recipient site, biomechanical properties and the degree of fixation of the graft to the surrounding bone. During the first phase of bone regeneration, the transplanted cells in the graft proliferate and form new osteoid for several weeks. The cells within the graft are nourished by plasmatic diffusion for the first 3-5 days. From the fifth day onwards, capillary growth from the surrounding soft tissue and bone into the graft occurs (Thapliyal, 2006).

The healing of grafts differs according to the type of graft (cannellous, coticocancellous or cortical). Following surgical trauma, hemorrhage occurs in and around the graft. Various mediators released from the tissue and cellular components of the blood stimulate the migration of inflammatory cells, phagocytes and mesenchymal pluripotent cells by chemotaxis. Depending on the type of stimulus, mesenchymal cells differentiate into endothelial cells, fibroblasts and osteoblasts and proliferate to form new blood vessels and connective tissues. As a result of anastomosis of the vessels in the graft and the recipient bed, revascularization begins within a few hours after grafting. Completion of revascularization of the cancellous bone graft occurs within a few weeks. Unlike cortical bone graft, bone formation occurs without resorption caused by osteoclasts. Osteoblasts line up on the surface of the old trabeculae and initiate osteoid formation. This tissue is then mineralized and immature bone is formed. During the final remodeling stage, osteoclasts resorb newly formed immature bone and necrotic bone, which are then replaced by mature lamellar bone (Thapliyal, 2006).

Interpositional (Inlay) Grafting

Inlay grafting is the process of increasing bone volume by applying graft between bone osteotomy incisions. Inlay grafting is applied especially in the reconstruction of vertical deficiencies of the maxilla and mandible. This method, which is mostly indicated in the maxillary anterior region, can be used in most regions of the maxilla and mandibular arch. It is preferred in cases where vertical bone is required in moderately atrophic areas such as 3-8 mm. The alveolar segment is moved and fixed in the required vertical dimension. Since the periosteal blood supply of the separated part continues, its dimensional stability will be preserved. A maximum vertical movement of 5 mm can be made in the anterior region of the maxilla. In more than 5 mm movement, blood support will decrease and slippage of the segment and aesthetic problems will occur. The interpositional graft technique is a simpler technique compared to block graft methods due to the need for less flap lifting. In order to be applied in the posterior areas of the mandible, there must be a minimum of 4 mm of bone tissue above the nerve. Otherwise, there is a risk of iatrogenic nerve injury. Successful results have been obtained in cases of moderate atrophy in the posterior mandible. The inlay technique is also used synonymously with the sandwich technique. In the inlay technique, there are also cases where Le Fort I osteotomy should be performed in the maxilla (Figure 10) (T., 2007).

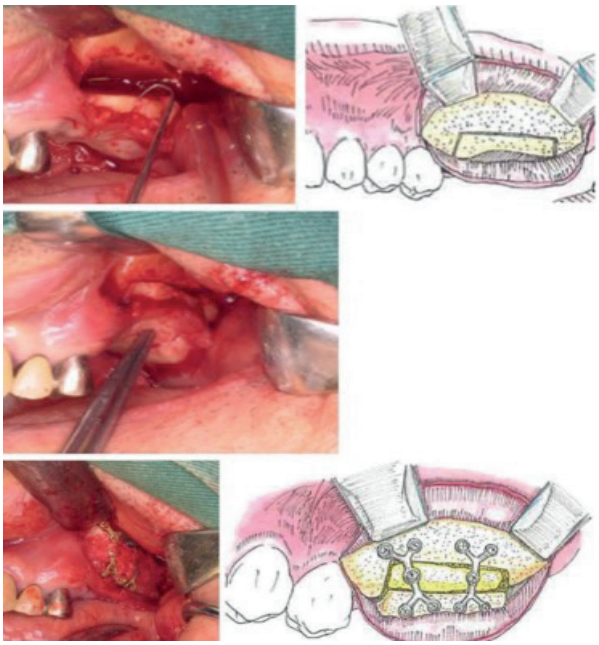


Figure 10. Interpositional (Inlay) Grafting (Tanaka et al., 2017)

Le fort I osteotomy used in interpositional grafting is an effective technique for positioning the maxilla inferiorly and anteriorly in patients with severe maxillary resorption and block graft from the iliac crest is preferred because of its corticocancellous structure.

The interpositional grafting procedure is based on the theory that biomaterial placed between cancellous bone in 2 pieces of pedicled bone will provide rapid and complete healing and fuse with the graft with a lower percentage of resorption. The sandwich osteotomy allows the graft to be positioned in a well-demarcated area as well as providing adequate blood supply to sustain new bone growth (Figure 10). This procedure allows simultaneous correction of the sagittal intermaxillary relationship and vertical dimension. This technique has been applied to both the mandible and maxilla. In the case of performing a sandwich osteotomy in the posterior mandible, significant surgical precision is essential to prevent injury to the inferior alveolar nerve. Given these considerations and the limited available data in the literature, further research is necessary to validate the predictability of this regenerative technique (Figure 11) (Laino et al., 2014).

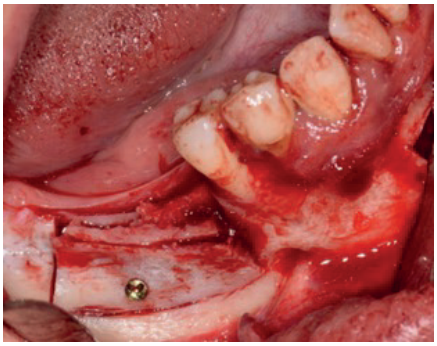


Figure 11. Sandwich osteotomy (Atef et al., 2019)

In 1976, Epker and Wolford reported that grafting should be performed in all cases of maxillary advancement if more than 10 mm of posterior maxillary grafting was to be performed. This guideline stated by Epker and Wolford was later revised and it was reported that grafting must be performed if more than 0.5 cm advancement is to be performed. In surgeries where the maxilla is positioned downward, the use of interpositional bone graft serves to prevent soft tissue migration into the osteotomy gaps, accelerate bone healing, and create a physical barrier against

occlusal forces (Epker et al., 1976).

Rosen et al. 1989 and 1991 reported that the use of autogenous bone (iliac graft) as an interpositional bone graft is the gold standard. The main reason why iliac bone graft is the gold standard is that it has a high osteogenic potential and no immunologic reaction is observed. However, it also has disadvantages such as the need to create a second surgical field for iliac bone grafting and lower extremity limitation (Rosen, 1989).

In their study, Egbert and Waite reported that while a relapse rate of 10-26% was observed in maxillary advancement surgery without interpositional graft placement, this rate decreased to 6-7% with graft use (Waite et al., 1996).

Araujo et al. In their 1978 study, they found a great difference between the two groups in terms of the potential for relapse after maxillary advancement surgery in a study between two study groups with and without graft application. The mean amount of advancement of the study groups was determined as 6 mm. The amount of relapse observed in the study group using grafts was between 0-5%, while the amount of relapse observed in the study group not using grafts was between 31% and 68%. In addition, as a result of the study, it was stated that the routine use of interpositional bone grafts after maxillary advancement surgeries is not indicated if surgical stability and plate fixation are adequate, skeletal maxillomandibular fixation can be achieved, ideal occlusion is achieved postoperatively and the amount of movement is less than 5 mm. If one or more of these parameters cannot be achieved, the use of interpositional bone grafts has been reported to be necessary to achieve postoperative stability (Araujo et al., 1978).

Yang et al. In their 2012 article, they reported a modified Le Fort I osteotomy study in which inferior positioning of the maxilla was known to be the minimum stable movement in terms of stability and therefore they aimed to increase postoperative stability by increasing the bone contact points. In the study, the maxilla should be positioned inferiorly in cases with vertical insufficiency, but as Proffit et al. 2007, they mentioned that inferior positioning is the least stable movement known. Some of the factors that are effective in decreasing stability are increased masticatory forces, the presence of inadequately applied or never applied bone grafts, and inadequate stabilization. In the article, the use of plates to increase mouth opening before surgery for the adaptation of the muscular system, bilateral coronoidotomy or pterigomasseteric myotomy applications during the operation were mentioned and it was mentioned that these applications facilitate adaptation to the increased facial height after the operation. In addition, rigid fixation of the maxilla with a miniplate, the use of interpositional bone grafts and simultaneous mandibular surgery will help to increase stability by reducing occlusal forces (Wardrop & Wolford, 1989).

Interpositional grafts are grafts placed in the 3, 4 or 5-walled cannellous bone compartment. These grafts are placed in defects where the borders are alveol, sinus membrane and medial wall as in the sinus floor elevation technique. Thus, the graft is stabilized and blood supply is provided. Another interpositional graft application is the cortical split technique applied in alveolar bone. The cortical bone is separated vertically and the cannellous bone compartment is exposed. The graft is then inserted into the cavity. A similar technique is the sandwich graft technique applied in the mandible. In this technique, the cortical bone is removed, the graft is placed in the kansellous compartment and the removed cortical bone is placed on the graft with the help of screws and stabilized (Smiler & Soltan, 2006).

References

Aghaloo, T. L., & Moy, P. K. (2007). Which hard tissue augmentation techniques are the most successful in furnishing bony support for implant placement? The International Journal of Oral & Maxillofacial Implants, 22 Suppl, 49–70.

Albrektsson, T., & Tjellström, A. (2019). Bone Healing Concepts in Craniomaxillofacial

Reconstructive and Corrective Bone Surgery. Craniomaxillofacial Reconstructive and Corrective Bone Surgery: Second Edition, 129–142. https://doi.org/10.1007/978-1-4939-1529-3_13

Alfaro, F. (2006). Bone grafting in oral implantology. Quintessence Pub.

Ali, S., Bakry, S. A., & Abd-Elhakam, H. (2015). Platelet-Rich Fibrin in Maxillary Sinus Augmentation: A Systematic Review. Journal of Oral Implantology, 41(6), 746–753. https://doi.org/10.1563/AAID-JOI-D-14-00167

Altintas, N. Y., Senel, F. C., Kayıpmaz, S., Taskesen, F., & Pampu, A. A. (2013). Comparative Radiologic Analyses of Newly Formed Bone After Maxillary Sinus Augmentation With and Without Bone Grafting. Journal of Oral and Maxillofacial Surgery, 71(9), 1520–1530. https://doi.org/10.1016/j.joms.2013.04.036

Araujo, A., Schendel, S. A., Wolford, L. M., & Epker, B. N. (1978). Total maxillary advancement with and without bone grafting. Journal of Oral Surgery (American Dental Association : 1965), 36(11), 849–858.

Artzi, Z. (2023). Lateral augmentation of the jaw by the split expansion ridge technique. A critical review. Periodontology 2000, 93(1), 205–220. https://doi.org/10.1111/prd.12527

Asmael, H. M. (2018). Is antral membrane balloon elevation truly minimally invasive technique in sinus floor elevation surgery? A systematic review. International Journal of Implant Dentistry, 4(1), 12. https://doi.org/10.1186/s40729-018-0123-9

Atef, M., Osman, A. H., & Hakam, M. (2019). Autogenous interpositional block graft vs onlay graft for horizontal ridge augmentation in the mandible. Clinical Implant Dentistry and Related Research, 21(4), 678–685. https://doi.org/10.1111/cid.12809

Bassetti, M. A., Bassetti, R. G., & Bosshardt, D. D. (2016). The alveolar ridge splitting/expansion technique: a systematic review. Clinical Oral Implants Research, 27(3), 310–324. https://doi.org/10.1111/clr.12537

Becker, S. T., Terheyden, H., Steinriede, A., Behrens, E., Springer, I., & Wiltfang, J. (2008). Prospective observation of 41 perforations of the Schneiderian membrane during sinus floor elevation. Clinical Oral Implants Research, 19(12), 1285–1289. https://doi.org/10.1111/j.1600-0501.2008.01612.x

Block, M. S., Otten, J., McLaurin, D., & Zoldds, J. (1996). Bifocal distraction osteogenesis for mandibular defect healing: Case reports. Journal of Oral and Maxillofacial Surgery, 54(11), 1365–1370. https://doi.org/10.1016/S0278-2391(96)90499-1

Blus, C., & Szmukler-Moncler, S. (2006). Split-crest and immediate implant placement with ultra-sonic bone surgery: a 3-year life-table analysis with 230 treated sites. Clinical Oral Implants Research, 17(6), 700–707. https://doi.org/10.1111/j.1600-0501.2006.01206.x

Bottino, M. C., Thomas, V., Schmidt, G., Vohra, Y. K., Chu, T.-M. G., Kowolik, M. J., & Janowski, G. M. (2012). Recent advances in the development of GTR/GBR membranes for periodontal regeneration—A materials perspective. Dental Materials, 28(7), 703–721. https://doi.org/10.1016/j.dental.2012.04.022

Brugnami, F., Caiazzo, A., & Leone, C. (2009). Local Intraoral Autologous Bone Harvesting for Dental Implant Treatment: Alternative Sources and Criteria of Choice. The Keio Journal of Medicine, 58(1), 24–28. https://doi.org/10.2302/kjm.58.24

Bruschi, G., Capparé, P., Bravi, F., Grande, N., Gherlone, E., Gastaldi, G., & Crespi, R. (2017). Radiographic Evaluation of Crestal Bone Level in Split-Crest and Immediate Implant Placement:

Minimum 5-Year Follow-up. The International Journal of Oral & Maxillofacial Implants, 32(1), 114–120. https://doi.org/10.11607/jomi.4203

Bunyaratavej, P., & Wang, H. (2001). Collagen Membranes: A Review. Journal of Periodontology, 72(2), 215–229. https://doi.org/10.1902/jop.2001.72.2.215

Canullo, L., & Malagnino, V. A. (2008). Vertical ridge augmentation around implants by e-PTFE titanium-reinforced membrane and bovine bone matrix: a 24- to 54-month study of 10 consecutive cases. The International Journal of Oral & Maxillofacial Implants, 23(5), 858–866.

Chen, T.-L., Lu, H.-J., Liu, G., Tang, D.-H., Zhang, X., Pan, Z.-L., Wang, S.-F., & Zhang, Q. (2014). Effect of Autologous Platelet-Rich Plasma in Combination With Bovine Porous Bone Mineral and Bio-Guide Membrane on Bone Regeneration in Mandible Bicortical Bony Defects. Journal of Craniofacial Surgery, 25(1), 215–223. https://doi.org/10.1097/SCS.0000000000000420

Chiapasco, M., Consolo, U., Bianchi, A., & Ronchi, P. (2004). Alveolar distraction osteogenesis for the correction of vertically deficient edentulous ridges: a multicenter prospective study on humans. The International Journal of Oral & Maxillofacial Implants, 19(3), 399–407.

Chiapasco, M., Zaniboni, M., & Boisco, M. (2006). Augmentation procedures for the rehabilitation of deficient edentulous ridges with oral implants. Clinical Oral Implants Research, 17(S2), 136–159. https://doi.org/10.1111/j.1600-0501.2006.01357.x

Choi, B.-H., Kim, B.-Y., Huh, J.-Y., Lee, S.-H., Zhu, S.-J., Jung, J.-H., & Li, J. (2006). Cyanoacrylate adhesive for closing sinus membrane perforations during sinus lifts. Journal of Cranio-Maxillofacial Surgery, 34(8), 505–509. https://doi.org/10.1016/j.jcms.2006.07.859

Dergisi, İ. Ü. D. H. F., & Cilt, D. (2009). Complications of Sinus Floor Augmentation and Treatment Options. 133–139.

Dimitriou, R., Mataliotakis, G. I., Calori, G. M., & Giannoudis, P. V. (2012). The role of barrier membranes for guided bone regeneration and restoration of large bone defects: current experimental and clinical evidence. BMC Medicine, 10(1), 81. https://doi.org/10.1186/1741-7015-10-81

Donos, N., Mardas, N., & Chadha, V. (2008). Clinical outcomes of implants following lateral bone augmentation: systematic assessment of available options (barrier membranes, bone grafts, split osteotomy). Journal of Clinical Periodontology, 35(s8), 173–202. https://doi.org/10.1111/j.1600-051X.2008.01269.x

Duskova, M., Leamerova, E., Sosna, B., & Gojis, O. (2006). Guided Tissue Regeneration, Barrier Membranes and Reconstruction of the Cleft Maxillary Alveolus. Journal of Craniofacial Surgery, 17(6), 1153–1160. https://doi.org/10.1097/01.scs.0000236435.90097.7b

Elgali, I., Omar, O., Dahlin, C., & Thomsen, P. (2017). Guided bone regeneration: materials and biological mechanisms revisited. European Journal of Oral Sciences, 125(5), 315–337. https://doi.org/10.1111/eos.12364

Enislidis, G., Fock, N., Millesi-Schobel, G., Klug, C., Wittwer, G., Yerit, K., & Ewers, R. (2005). Analysis of complications following alveolar distraction osteogenesis and implant placement in the partially edentulous mandible. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology, 100(1), 25–30. https://doi.org/10.1016/j.tripleo.2004.11.021

Epker, B. N., Friedlaender, G., Wolford, L. M., & West, R. A. (1976). The use of freeze-dried bone in middle-third face advancements. Oral Surgery, Oral Medicine, Oral Pathology, 42(3), 278–289. https://doi.org/10.1016/0030-4220(76)90161-4

Felisati, G., Lozza, P., Chiapasco, M., & Borloni, R. (2007). Endoscopic removal of an

unusual foreign body in the sphenoid sinus: an oral implant. Clinical Oral Implants Research, 18(6), 776–780. https://doi.org/10.1111/j.1600-0501.2007.01409.x

FINDIK, Y., & ŞENTÜRK, M. F. (2015). GREFTSIZ SINÜS YÜKSELTME TEKNIĞINDE YENI BIR YAKLAŞIM. Atatürk Üniversitesi Diş Hekimliği Fakültesi Dergisi, 25(1). https://doi.org/10.17567/dfd.50272

Garcia-Garcia, A., Somoza-Martin, M., Gandara-Vila, P., Saulacic, N., & Gandara-Rey, J. M. (2004). Horizontal alveolar distraction: A surgical technique with the transport segment pedicled to the mucoperiosteum. Journal of Oral and Maxillofacial Surgery, 62(11), 1408–1412. https://doi.org/10.1016/j.joms.2004.07.004

Herford, A. S., & Nguyen, K. (2015). Complex Bone Augmentation in Alveolar Ridge Defects. Oral and Maxillofacial Surgery Clinics of North America, 27(2), 227–244. https://doi.org/10.1016/j.coms.2015.01.003

Hönig, J. F., Grohmann, U. A., & Merten, H. A. (2002). Facial Bone Distraction Osteogenesis for Correction of Malocclusion. Plastic and Reconstructive Surgery, 109(1), 41–44. https://doi.org/10.1097/00006534-200201000-00007

Huang, C.-S., Ko, W.-C., Lin, W.-Y., Liou, E. J.-W., Hong, K.-F., & Chen, Y.-R. (1999). Mandibular Lengthening by Distraction Osteogenesis in Children—A One-Year Follow-Up Study. The Cleft Palate-Craniofacial Journal, 36(3), 269–274. https://doi.org/10.1597/1545-1569_1999_036_0269_mlbdoi_2.3.co_2

Hunt, D. R., & Jovanovic, S. A. (1999). Autogenous bone harvesting: a chin graft technique for particulate and monocortical bone blocks. The International Journal of Periodontics & Restorative Dentistry, 19(2), 165–173.

Ilizarov, G. A. (1990). Clinical application of the tension-stress effect for limb lengthening. Clinical Orthopaedics and Related Research, 250, 8–26.

Joshi, A., & Kostakis, G. C. (2004). An investigation of post-operative morbidity following iliac crest graft harvesting. British Dental Journal, 196(3), 167–171. https://doi.org/10.1038/sj.bdj.4810945

Jung, J.-H., Choi, B.-H., Jeong, S.-M., Li, J., Lee, S.-H., & Lee, H.-J. (2007). A retrospective study of the effects on sinus complications of exposing dental implants to the maxillary sinus cavity. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology, 103(5), 623–625. https://doi.org/10.1016/j.tripleo.2006.09.024

Jung, R. E., Thoma, D. S., & Hammerle, C. H. F. (2008). Assessment of the potential of growth factors for localized alveolar ridge augmentation: a systematic review. Journal of Clinical Periodontology, 35(s8), 255–281. https://doi.org/10.1111/j.1600-051X.2008.01270.x

Katranji, A., Fotek, P., & Wang, H.-L. (2008). Sinus Augmentation Complications: Etiology and Treatment. Implant Dentistry, 17(3), 339–349. https://doi.org/10.1097/ID.0b013e3181815660

Kawase, T., Kamiya, M., Kobayashi, M., Tanaka, T., Okuda, K., Wolff, L. F., & Yoshie, H. (2015). The heat-compression technique for the conversion of platelet-rich fibrin preparation to a barrier membrane with a reduced rate of biodegradation. Journal of Biomedical Materials Research Part B: Applied Biomaterials, 103(4), 825–831. https://doi.org/10.1002/jbm.b.33262

Khoury, F., Antoun, H., & Missika, P. (2007). Bone augmentation in oral implantology: Quintessence Publishing Hanover Park.

Khoury, F., & Hanser, T. (2015). Mandibular Bone Block Harvesting from the Retromolar

Region: A 10-Year Prospective Clinical Study. The International Journal of Oral & Maxillofacial Implants, 30(3), 688–697. https://doi.org/10.11607/jomi.4117

Kim, J.-W., Cho, M.-H., Kim, S.-J., & Kim, M.-R. (2013). Alveolar distraction osteogenesis versus autogenous onlay bone graft for vertical augmentation of severely atrophied alveolar ridges after 12 years of long-term follow-up. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology, 116(5), 540–549. https://doi.org/10.1016/j.oooo.2013.06.037

Kisnisci, R. S., & Iseri, H. (2011). Dentoalveolar Transport Osteodistraction and Canine Distalization. Journal of Oral and Maxillofacial Surgery, 69(3), 763–770. https://doi.org/10.1016/j.joms.2010.11.035

Laino, L., Iezzi, G., Piattelli, A., Lo Muzio, L., & Cicciù, M. (2014). Vertical Ridge Augmentation of the Atrophic Posterior Mandible with Sandwich Technique: Bone Block from the Chin Area versus Corticocancellous Bone Block Allograft—Clinical and Histological Prospective Randomized Controlled Study. BioMed Research International, 2014, 1–7. https://doi.org/10.1155/2014/982104

Lundgren, S., Andersson, S., Gualini, F., & Sennerby, L. (2004). Bone reformation with sinus membrane elevation: a new surgical technique for maxillary sinus floor augmentation. Clinical Implant Dentistry and Related Research, 6(3), 165–173.

M.Miloro GEG, P.E.Larsen, P.D. Waite. Peterson's Principles of Oral and Maxillofacial Surgery. Second Edition ed. London: BC Decker Inc; 2004. (n.d.).

McAllister, B. S., & Gaffaney, T. E. (2003). Distraction osteogenesis for vertical bone augmentation prior to oral implant reconstruction. Periodontology 2000, 33(1), 54–66. https://doi.org/10.1046/j.0906-6713.2002.03305.x

Milinkovic, I., & Cordaro, L. (2014). Are there specific indications for the different alveolar bone augmentation procedures for implant placement? A systematic review. International Journal of Oral and Maxillofacial Surgery, 43(5), 606–625. https://doi.org/10.1016/j.ijom.2013.12.004

Misch, C. E. (2007). Contemporary implant dentistry-E-Book. Elsevier Health Sciences.

Misch, C. E., & Dietsh, F. (1993). BONE-GRAFTING MATERIALS IN IMPLANT DENTISTRY. Implant Dentistry, 2(3), 158–166. https://doi.org/10.1097/00008505-199309000-00003

Mohanty, R., Kumar, N. N., & Ravindran, C. (2015). Vertical Alveolar Ridge Augmentation by Distraction Osteogenesis. Journal of Clinical and Diagnostic Research : JCDR, 9(12), ZC43-6. https://doi.org/10.7860/JCDR/2015/15976.6993

Nguyen, T. T. H., Eo, M. Y., Kuk, T. S., Myoung, H., & Kim, S. M. (2019). Rehabilitation of atrophic jaw using iliac onlay bone graft combined with dental implants. International Journal of Implant Dentistry, 5(1), 11. https://doi.org/10.1186/s40729-019-0163-9

Okcu, K. M., Sencimen, M., Karacay, S., Bengi, A. O., Örs, F., Dogan, N., & Gokce, H. S. (2009). Anterior segmental distraction of the hypoplastic maxilla by a tooth borne device: a study on the movement of the segment. International Journal of Oral and Maxillofacial Surgery, 38(8), 817–822. https://doi.org/10.1016/j.ijom.2009.04.005

Perez-Sayans, M., Leon-Camacho, M., Somoza-Martin, J., Fernandez-Gonzalez, B., Blanes-Vazquez-Gundin, S., Gandara-Rey, J., & Garcia-Garcia, A. (2013). Dental implants placed on bone subjected to vertical alveolar distraction show the same performance as those placed on primitive bone. Medicina Oral Patología Oral y Cirugia Bucal, e686–e692. https://doi.org/10.4317/medoral.18545

Pérez-Sayáns, M., Martínez-Martín, J.-M., Chamorro-Petronacci, C., Gallas-Torreira, M., Marichalar-Mendía, X., & García-García, A. (2018). 20 years of alveolar distraction: A systematic

review of the literature. Medicina Oral, Patologia Oral y Cirugia Bucal, 23(6), e742–e751. https://doi.org/10.4317/medoral.22645

Polo, W. C. K., Cury, P. R., Sendyk, W. R., & Gromatzky, A. (2005). Posterior Mandibular Alveolar Distraction Osteogenesis Utilizing an Extraosseous Distractor: A Prospective Study. Journal of Periodontology, 76(9), 1463–1468. https://doi.org/10.1902/jop.2005.76.9.1463

Proussaefs, P., Lozada, J., Kim, J., & Rohrer, M. D. (2004). Repair of the perforated sinus membrane with a resorbable collagen membrane: a human study. The International Journal of Oral & Maxillofacial Implants, 19(3), 413–420. https://doi.org/15214227

Rakhmatia, Y. D., Ayukawa, Y., Furuhashi, A., & Koyano, K. (2013). Current barrier membranes: Titanium mesh and other membranes for guided bone regeneration in dental applications. Journal of Prosthodontic Research, 57(1), 3–14. https://doi.org/10.1016/j.jpor.2012.12.001

Retzepi, M., & Donos, N. (2010). Guided Bone Regeneration: biological principle and therapeutic applications. Clinical Oral Implants Research, 21(6), 567–576. https://doi.org/10.1111/j.1600-0501.2010.01922.x

Rivara, F., Negri, M., Lumetti, S., Parisi, L., Toffoli, A., Calciolari, E., Manfredi, E., & Macaluso, G. M. (2017). Maxillary Sinus Floor Augmentation Using an Equine-Derived Graft Material: Preliminary Results in 17 Patients. BioMed Research International, 2017, 1–6. https://doi.org/10.1155/2017/9164156

Rosen, H. M. (1989). Porous, block hydroxyapatite as an interpositional bone graft substitute in orthognathic surgery. Plastic and Reconstructive Surgery, 83(6), 985–990; discussion 991-3.

Santagata, M., Guariniello, L., & Tartaro, G. (2015). Modified Edentulous Ridge Expansion Technique and Immediate Implant Placement: A 3-Year Follow-Up. Journal of Oral Implantology, 41(2), 184–187. https://doi.org/10.1563/AAID-JOI-D-12-00308

Saruhan, N., Ertaş, Ü. (2012). Atrofik Alveolar Kretlerin Ogmentasyonunda Ekstraoral Otojen Kemik Grefti Uygulamaları. Turkiye Klinikleri Journal of Dental Sciences Special Topics, 3(3), 18–28.

Saulacic, N., Gándara-Vila, P., Somoza-Martín, M., & García-García, A. (2004). Distraction osteogenesis of the alveolar ridge: a review of the literature. Medicina Oral : Organo Oficial de La Sociedad Espanola de Medicina Oral y de La Academia Iberoamericana de Patologia y Medicina Bucal, 9(4), 321–327.

Saulacic, N., Iizuka, T., Martin, M. S., & Garcia, A. G. (2008). Alveolar distraction osteogenesis: a systematic review. International Journal of Oral and Maxillofacial Surgery, 37(1), 1–7. https://doi.org/10.1016/j.ijom.2007.07.020

Shang, H., Lin, X., Du, J., He, L., & Liu, Y. (2012). Use of a new curvilinear distractor to repair mandibular defects in dogs. British Journal of Oral and Maxillofacial Surgery, 50(2), 166–170. https://doi.org/10.1016/j.bjoms.2011.02.003

Sharaf, M. Y., Eskander, A. E., & Elbakery, A. I. (2022). Short-Term Evaluation of Prosthetic Rehabilitation of Thin Wiry Ridge by Ridge Splitting and Simultaneous Implants Placement: Non-randomized Control Trial. European Journal of Dentistry, 16(02), 414–423. https://doi.org/10.1055/s-0041-1736292

Sittitavornwong, S., & Gutta, R. (2010). Bone Graft Harvesting from Regional Sites. Oral and Maxillofacial Surgery Clinics of North America, 22(3), 317–330. https://doi.org/10.1016/j.coms.2010.04.006

Smiler, D., & Soltan, M. (2006). The Bone-Grafting Decision Tree: A Systematic Methodology for Achieving New Bone. Implant Dentistry, 15(2), 122–128. https://doi.org/10.1097/01.id.0000217780.69637.cc

Smolka, W., Eggensperger, N., Kollar, A., & Iizuka, T. (2005). Midfacial Reconstruction Using Calvarial Split Bone Grafts. Archives of Otolaryngology–Head & Neck Surgery, 131(2), 131. https://doi.org/10.1001/archotol.131.2.131

Soldatos, N. K., Stylianou, P., Koidou, V. P., Angelov, N., Yukna, R., & Romanos, G. E. (2017). Limitations and options using resorbable versus nonresorbable membranes for successful guided bone regeneration. Quintessence International (Berlin, Germany : 1985), 48(2), 131–147. https://doi.org/10.3290/j.qi.a37133

Soltan, M., & Smiler, D. G. (2005). Antral Membrane Balloon Elevation. Journal of Oral Implantology, 31(2), 85–90. https://doi.org/10.1563/0-773.1

Starch-Jensen, T., & Becktor, J. P. (2019). Maxillary Alveolar Ridge Expansion with Split-Crest Technique Compared with Lateral Ridge Augmentation with Autogenous Bone Block Graft: a Systematic Review. Journal of Oral and Maxillofacial Research, 10(4). https://doi.org/10.5037/jomr.2019.10402

Strietzel, F. P., Khongkhunthian, P., Khattiya, R., Patchanee, P., & Reichart, P. A. (2006). Healing pattern of bone defects covered by different membrane types—A histologic study in the porcine mandible. Journal of Biomedical Materials Research Part B: Applied Biomaterials, 78B(1), 35–46. https://doi.org/10.1002/jbm.b.30452

Strietzel, F. P., Nowak, M., Küchler, I., & Friedmann, A. (2002). Peri-implant alveolar bone loss with respect to bone quality after use of the osteotome technique. Clinical Oral Implants Research, 13(5), 508–513. https://doi.org/10.1034/j.1600-0501.2002.130510.x

T., A. (2007). Vertikal Kemik Ogmentasyonu. Turkiye Klin Dent Sci.

Tanaka, K., Sailer, I., Kataoka, Y., Nogami, S., & Takahashi, T. (2017). Sandwich bone graft for vertical augmentation of the posterior maxillary region: a case report with 9-year follow-up. International Journal of Implant Dentistry, 3(1), 20. https://doi.org/10.1186/s40729-017-0063-9

Thapliyal, G. (2006). Peterson's Principles of Oral & Maxillofacial Surgery. Medical Journal Armed Forces India, 62(1), 89. https://doi.org/10.1016/S0377-1237(06)80173-5

Tolstunov, L., Hamrick, J. F. E., Broumand, V., Shilo, D., & Rachmiel, A. (2019). Bone Augmentation Techniques for Horizontal and Vertical Alveolar Ridge Deficiency in Oral Implantology. Oral and Maxillofacial Surgery Clinics of North America, 31(2), 163–191. https://doi.org/10.1016/j.coms.2019.01.005

Vlassis, J. M., & Fugazzotto, P. A. (1999). A Classification System for Sinus Membrane Perforations During Augmentation Procedures With Options for Repair. Journal of Periodontology, 70(6), 692–699. https://doi.org/10.1902/jop.1999.70.6.692

Waechter, J., Leite, F. R., Nascimento, G. G., Carmo Filho, L. C., & Faot, F. (2017). The split crest technique and dental implants: a systematic review and meta-analysis. International Journal of Oral and Maxillofacial Surgery, 46(1), 116–128. https://doi.org/10.1016/j.ijom.2016.08.017

Waite, P. D., Tejera, T. J., & Anucul, B. (1996). The stability of maxillary advancement using Le Fort I osteotomy with and without genial bone grafting. International Journal of Oral and Maxillofacial Surgery, 25(4), 264–267. https://doi.org/10.1016/S0901-5027(06)80052-4

Wardrop, R. W., & Wolford, L. M. (1989). Maxillary stability following downgraft and/or

advancement procedures with stabilization using rigid fixation and porous block hydroxyapatite implants. Journal of Oral and Maxillofacial Surgery, 47(4), 336–342. https://doi.org/10.1016/0278-2391(89)90333-9

Xie, Y., Li, S., Zhang, T., Wang, C., & Cai, X. (2020). Titanium mesh for bone augmentation in oral implantology: current application and progress. International Journal of Oral Science, 12(1), 37. https://doi.org/10.1038/s41368-020-00107-z

Yates, D. M., Brockhoff, H. C., Finn, R., & Phillips, C. (2013). Comparison of Intraoral Harvest Sites for Corticocancellous Bone Grafts. Journal of Oral and Maxillofacial Surgery, 71(3), 497–504. https://doi.org/10.1016/j.joms.2012.10.014

Zhang, Y., Zhang, C., Han, X.-R., Li, W., & Wang, Y. (2018). Determinants of compassion satisfaction, compassion fatigue and burn out in nursing. Medicine, 97(26), e11086. https://doi.org/10.1097/MD.0000000000011086

About The Authors

Dr. Saim YANIK is an Associate Professor of Oral and Maxillofacial Surgery at Gaziantep University Faculty of Dentistry. He graduated from Atatürk University Faculty of Dentistry in 2004 and received the title of dentist. He graduated from Gaziantep University Faculty of Dentistry, Department of Oral and Maxillofacial Surgery in 2014 and received the title of Specialist. His main areas of interest are ortognatic surgery, TMJ disorders and surgery, maxillofacial trauma, oral pathology and implantology.

Orcid number: ORCID: 0000-0002-1229-2982

E-mail: saimyanik@hotmail.com

Mehmet Turhan TEKE graduated from Ege University Faculty of Dentistry in 2016 and received the title of dentist. He graduated from Gaziantep University Faculty of Dentistry, Department of Oral and Maxillofacial Surgery in 2024 and received the title of Specialist. He continues to work on kinesio tape applications in jaw surgery. He regularly attends training to improve himself.

Orcid number: 0009-0006-7153-7261

E-mail: turhanteke@hotmail.com

Ömer Faruk KAYGISIZ graduated from Ankara University Faculty of Dentistry in 2019 and received the title of dentist. In 2024, he graduated from Gaziantep University Faculty of Dentistry, Department of Oral and Maxillofacial Surgery and received the title of Specialist. He has studies such as artificial intelligence and bibliometric analysis in maxillofacial surgery. He participates in short-term education abroad to improve himself.

Orcid number: 0009-0003-7935-1144

E-mail: dtkaygisiz@gmail.com

To Cite This Chapter

YANIK S et al., (2024). Hard tıssue regeneratıon technıques. In Current Studies in Health and Life Sciences 2024 (pp.307-333). ISRES Publishing.

Evalution of The Effect of The Covid-19 Pandemic on The Educational Concerns of Destistry Students and Cilinical Practices

Büşra TOSUN

Merve Nur YILMAZ

Pınar GÜL

1. INTRODUCTION

In December 2019, a coronavirus that had never been seen before in humans was identified in Wuhan, China's Hubei province (Lu et al., 2020). The World Health Organization (WHO) named this pneumonia-causing virus the novel coronavirus (2019-nCoV), and it was later named SARS-CoV-2 due to its taxonomic similarity to the virus that causes Severe Acute Respiratory Syndrome (SARS) (Cascella et al., 2023). As new coronavirus cases increased rapidly and spread across continents, this situation was declared a pandemic by WHO on March 11, 2020. (Who et al., 2020). The first case of COVID 19 diagnosed in our country was officially announced by the Ministry of Health on March 10, 2020.

With the increase in cases, research examining the clinical and epidemiological features of the disease has accelerated. Clinical symptoms and radiographic examinations are similar to the symptoms of infection caused by other respiratory viruses, making it difficult to diagnose COVID 19 cases at an early stage. The fact that the majority of detected cases are in people in the advanced stages of the disease causes the case incidence-fatality rate to be higher than expected. As the number of tests performed increases and data on mild/asymptomatic infections is obtained, the case incidence-fatality rate is expected to decrease further. However, the low mortality rate should not cause one to ignore the fact that the risk of widespread transmission of the disease is serious (Wang et al., 2020).

Current observations show that people of all ages are likely to contract this new infectious disease, and although symptomatic COVID 19 patients are the main source of transmission, asymptomatic patients and those in their incubation period are also carriers of the virüs (Chan et al., 2020; Rothe et al., 2020).

Information about the transmission routes, incubation period, and clinical course of the disease is interpreted based on the first data obtained, and research will continue to clarify the COVID 19 process (Cascella et al., 2023). Considering transmission through droplets and aerosols, dentists constitute a high risk group. During the COVID 19 pandemic, necessary precautions should be taken to control the risk of cross-infection that may occur between dentists and patients in dental practice environments and emergency treatment application protocols should be determined.

Since dentists are in the primary risk group in terms of encountering infectious diseases, it is extremely important to provide training to undergraduate dentistry students about the risks of infectious diseases and the use of personal protective equipment (PPE) (Coulthard et al., 2020). The US Occupational Safety and Health Administration has similarly reported that dentists are at very high risk of contracting COVID 19 (Deery et al., 2020). For this reason, during the pandemic period, authorities recommended postponing procedures other than emergency dental treatments. However, during this period, undergraduate education continued online (Deery et al., 2020; Prati et al., 2020).

Studies reporting the impact of the pandemic on undergraduate dental education are limited (Shacham et al., 2020; Iyer at al., 2020; Desai et al., 2020; Bellini et al., 2020). There is no official information regarding the continuity of dental education to protect students, faculty and patients

(Bellini et al., 2020). Therefore, new studies are needed to evaluate the quality of online education during the pandemic period and make suggestions for improvement. This study aims to examine the COVID 19 knowledge levels of 4th and 5th grade students of Abant İzzet Baysal University and Atatürk University Faculty of Dentistry and to obtain information about the educational concerns of the pandemic and its impact on clinical practices.

2. MATERIALS AND METHODS

2.1. Survey and Study Design

This study was approved by the Ethics Committee of Bolu Abant Izzet Baysal University and Erzurum Atatürk University (2022/25, 2022/35). First of all, Turkish and English literature review was conducted. Articles related to the study were collected by typing the keywords 'COVID 19', 'Dentistry' and 'Survey'. A total of 35 questions were prepared online via Google forms from the references obtained. The study material consists of Term 4 and Term 5 students studying at Abant İzzet Baysal University and Atatürk University Faculty of Dentistry, 4 of whom are over the age of 32 and 12 of whom are between the ages of 25-32, the majority of whom are between the ages of 21-25. The faculty of dentistry in Turkey lasts 5 years and consists of a training program in the last 2 years of which students look at patients in the clinic and perform appropriate examination and treatment. Therefore, 4th and 5th year undergraduate dentistry students were included in this study.

The survey was prepared to evaluate the level of knowledge of dental students about COVID 19 and the impact of the pandemic on education and clinical practices. The questions of the study were prepared by compiling from the literature in the field and were presented to the opinion of 20 expert academicians (Boukhobza et al., 2021; Aragao et al., 2022; Mutluay et al., 2022). In this way, the appropriateness of the questions in terms of features such as language, scope and understandability was ensured. In addition, to ensure the validity of the questions, the Content Validity Ratio was calculated for each question with the data obtained from the relevant expert group and these values were found to be within acceptable limits (Table 1) (Yurdugül et al., 2005).

Table 1. Content validity ratio (CVR) and index

Questions	**Necessary**	**Useful but not**	**Unnecessary**	**CVR**
What do you think about COVID 19?	20	-	-	1.00
Do you consider COVID 19 infection fatal?	19	1	-	0.90
What is the name of the virus responsible for the pandemic?	17	2	1	0.70
What is the incubation period of the virus?	19	1	-	0.90
What are the main ways of transmission of COVID 19?	18	2	-	080
What are the main symptoms of the disease?	20	-	-	1.00
What are your sources of information about COVID 19?	20	-	-	1.00
Are you worried about getting infected with COVID 19?	20		-	1.00
Have you ever been diagnosed with COVID 19 or suspected of having COVID 19?	20	-	-	1.00
How would you classify the risk of contracting COVID 19 infection in clinical practices at the Faculty of Dentistry?	20	-	-	1.00
Have you been forced to work under conditions that could jeopardize your personal safety?	19	1	-	0.90
What are personal protective equipment?	20	-	-	1.00
In what order should personal protective equipment be worn?	20	-	-	1.00

Questions	Necessary	Useful but not	Unnecessary	CVR
In what order should personal protective equipment be removed?	19	1	-	0.90
Which mask is included in the N95 mask?	18	1	1	0.80
Do you believe that personal protective equipment will protect against COVID 19?	20	-	-	1.00
Do you think you might be infected with COVID-19 while performing dental procedures?	20	-	-	1.00
What do you think about the return to clinical activities in dentistry?	20	-	-	1.00
What precautions should be taken to reduce the risk of spreading COVID 19?	19	-	1	0.90
Have you ever received training on biosecurity measures to prevent the spread of COVID 19 in dentistry?	19	1	-	0.90
Do you have sufficient knowledge about infection control during the pandemic?	20	-	-	1.00
Which of the following precautions do you apply to your patients against Covid-19 in your professional life?	19	1	-	0.90
As a dentist, do you inform your patients about Covid-19?	20	-	-	1.00
Has the institution you work for changed its patient admission policy due to Covid-19?	20	-	-	1.00
What are the problems you encountered in the workplace during the Covid-19 outbreak?	18	2	-	0.80
How should undergraduate education be implemented during the pandemic period?	19	1	-	0.90
Do you think face-to-face education is risky during the pandemic?	20	-	-	1.00
Do you find clinical internship training risky during the pandemic period?	20	-	-	1.00
How was the quality of the undergraduate education you received affected during the pandemic period?	20	-	-	1.00
Are you worried about the pandemic continuing after you graduate?	20	-	-	1.00
Do you plan to continue doing your job if the pandemic continues after graduation?	20	-	-	1.00

Before the study, power analysis (G*Power 3.1.9.4 software (Heinrich-Heine Dusseldorf University, Dusseldorf, Germany) was applied to determine the number of volunteers to be surveyed. According to the results of the analysis, it was determined that the number of volunteers in each group should be a minimum of 191 people in order for the study to be conducted at 95% power with an effect size of 0.3 and a margin of error of 0.05.

The prepared questions were sent to the dentistry students to whom the survey would be applied via the online survey, WhatsApp social network platform, and the voluntary consent of each participant was obtained. The number of dental students surveyed was greater than the required sample size calculated for this study. A total of 429 responses were obtained. Survey data was collected between 26.01.2022-16.03.2022.

The survey questions were categorized into 3 groups: questions containing sociodemographic characteristics, questions measuring the level of knowledge about COVID 19, and questions measuring the impact of the pandemic on clinical practices. Questions containing sociodemographic characteristics include information about the person's age, gender, the university he/she studied at

and the grade in which he/she studied. Questions measuring the level of knowledge about COVID 19; It includes what he thinks about COVID 19, whether he considers it fatal or not, the name of the responsible virus, the incubation period, the main ways of transmission, the main symptoms of the disease, where he got the information about COVID 19, whether he is worried about being infected, and whether he has previously encountered the COVID 19 virus. Questions measuring the impact of the pandemic on clinical practices are; It covers a number of questions such as how it classifies the risk of contracting COVID 19 infection in clinical practices at the faculty of dentistry, the situation of being forced to work under conditions that may endanger personal safety, the personal protective equipment used when examining patients and the order in which they put on and take off these equipment, and N95 mask information.

2.2. Statistical analysis

The obtained data were analyzed using SPSS 20 (IBM, Chicago, IL, USA) statistical package program. The collected data were taken from Google Forms and converted into Excel (Microsoft, USA) sheets. The frequency distribution of data, were compared using Chi-square or Fisher's exact tests by institution type (two separate universities). The statistical significance level was taken as 5%.

3. RESULTS

A total of 429 valid responses were received from participants at Bolu Abant Izzet Baysal and Atatürk University Faculty of Dentistry within 60 days. Demographic characteristics of dentistry students are given in Table 2. Participants were mostly female (58%) and aged between 21 and 25 (96.3%). 54.1% of the participants were from Atatürk University, 45.9% were from Abant Izzet Baysal University, 62.2% were in the 4th grade and 37.8% were in the 5th grade.

Table 2. Demographic characteristics of dentistry students, (n = 429)

Variables	**n**	**%**
Gender		
Female	249	58.0
Male	180	42.0
Age		
21-25	413	96.3
25-32	12	2.8
>32	4	0.9
University		
Abant Izzet Baysal	197	45.9
Ataturk	232	54.1
Class		
Class 4	267	62.2
Class 5	162	37.8

Results and statistical comparison results regarding students' general knowledge and perceptions about COVID-19 according to university types were given in Table 3. While 40.6% of the respondents see COVID 19 as a serious disease, 4.9% did not consider it as a serious disease. 44.5% of the participants see this disease as fatal, and 11.4% did not see it as a fatal disease. Participants often know the name of the virus responsible for the pandemic as COVID 19 and SARS COV 2, and there was also a segment of 1.9% who do not have any knowledge about it. While 56.2% stated the incubation period of the virus as 1-7 days, 2.3% stated it as 14-21 days. 3% stated that they did not have any information on this subject. While 85.1% of the participants stated the main transmission routes of COVID 19 as air droplets from the infected person, 28.2% stated that it was transmitted

as a result of contact with the blood of the infected person. While the three symptoms known as the main symptoms of the disease, namely fever, dry cough and fatigue, were selected at a higher rate, diarrhea, nausea and vomiting and runny nose were selected at the lowest rates. While a high percentage (80%) of the participants obtained information through the websites and/or social media accounts of official organizations and professional organizations such as the Ministry of Health, DSO, and television, 1.6% stated that they had not received any information about COVID 19 so far.

Table 3. General knowledge and perceptions of students about COVID-19 by university types

Variables	University		
	Abant n (%)	Ataturk n (%)	p
What do you think about COVID 19?			
It is not a serious disease.	12 (6.1)	9 (3.9)	0.764a
It is a moderately serious disease.	56 (28.4)	66 (28.4)	
It is a serious disease.	78 (39.6)	96 (41.4)	
It is a serious disease only in people in the risk group.	51 (25.9)	61 (26.3)	
Do you consider COVID 19 infection fatal?			
Yes	90 (45.7)	101 (43.5)	0.862a
No	23 (11.7)	26 (11.2)	
Partially	84 (42.6)	105 (45.3)	
What is the name of the virus responsible for the pandemic?			
2019 nCoV	20 (10.2)	28 (12.1)	0.835a
Coronavirus	40 (20.3)	53 (22.8)	
COVID-19	68 (34.5)	69 (29.7)	
SARS COV-2	66 (33.5)	78 (33.6)	
I don't know	3 (1.5)	4 (1.7)	
What is the incubation period of the virus?			
1-7 days	135 (68.5)	106 (45.7)	0.000a*
7-14 days	55 (27.9)	110 (47.4)	
14-21 days	2 (1.0)	8 (3.4)	
I don't know	5 (2.5)	8 (3.4)	
What are the main ways of transmission of COVID 19?			
Shaking hands with an infected person	87 (12.6)	81 (13.6)	0.075a
Through air droplets from an infected person	181 (26.1)	184 (31.0)	
Contact with infected surfaces	96 (13.9)	54 (9.1)	
Exposure to aerosol (a mixture of air, water and solid particles)	192 (27.7)	158 (26.6)	
Contact with the blood of an infected person	62 (8.9)	59 (9.9)	
Injury from contaminated sharp objects	75 (10.8)	58 (9.8)	
What are the main symptoms of the disease?			
Fire	185 (18.4)	210 (17.8)	0.727a
Dry cough	172 (17.1)	201 (17.1)	

Variables	University		
	Abant n (%)	**Ataturk n (%)**	**p**
Diarrhea	55 (5.5)	79 (6.7)	
Tiredness	145 (14.4)	165 (14)	
Sore throat	135 (13.4)	146 (12.4)	
Nausea and vomiting	38 (3.8)	52 (4.4)	
Difficulty breathing	142 (14.1)	152 (12.9)	
Headache	99 (9.8)	114 (9.7)	
Runny nose	37 (3.7)	59 (5)	
What are your sources of information about COVID 19?			
Television	139 (23.2)	158 (23.3)	0.398a
from circle of friends	83 (13.9)	82 (12.1)	
Websites and/or social media accounts of official organizations and professional organizations such as the Ministry of Health and the World Health Organization	164 (27.4)	179 (26.4)	
Physicians' personal websites/social media accounts	97 (16.2)	109 (16.1)	
From medical books, magazines and articles	38 (6.3)	56 (8.2)	
From events such as seminars/meetings/congresses organized by institutions	30 (5)	44 (6.5)	
From communication groups such as WhatsApp and Viber	47 (7.8)	45 (6.6)	
I have not received any information so far	1 (0.2)	6 (0.9)	
Are you worried about getting infected with COVID 19?			
Yes	63 (32)	71 (30.6)	0.890a
No	62 (31.5)	71 (30.6)	
Partially	72 (36.5)	90 (38.8)	
Have you ever been diagnosed with COVID 19 or suspected of having COVID 19?			
Just suspected	66 (33.5)	84 (36.2)	0.077a
It was suspected. The test result came back negative.	69 (35)	97 (41.8)	
It was suspected. The test result came back positive.	62 (31.5)	51 (22)	
How would you classify the risk of contracting COVID 19 infection in clinical practices at the Faculty of Dentistry?			
Low	5 (2.5)	11 (4.7)	0.233a
Middle	42 (21.3)	35 (15.1)	
High	84 (42.6)	98 (42.2)	
Very high	66 (33.5)	88 (37.9)	
Have you been forced to work under conditions that could jeopardize your personal safety?			
Yes	35 (17.8)	82 (35.3)	0.000a*
No	105 (53.3)	98 (42.2)	

Variables	University		
	Abant n (%)	**Ataturk n (%)**	**p**
Partially	57 (28.9)	52 (22.4)	
What personal protective equipment do you use when examining patients?			
Mask	191 (23.5)	224 (23.9)	0.915a
Glove	192 (23.6)	223 (23.8)	
Goggles	62 (7.6)	80 (8.5)	
Visor	188 (23.1)	202 (21.6)	
Apron/ overalls	181 (22.2)	207 (22.1)	
In what order should personal protective equipment be worn?			
Mask-glasses-apron-gloves	39 (19.8)	57 (24.6)	0.008a*
Mask-apron-glasses-gloves	97 (49.2)	78 (33.6)	
Apron-mask-glasses-gloves	53 (26.9)	78 (33.6)	
Apron-glasses-mask-gloves	8 (4.1)	19 (8.2)	
In what order should personal protective equipment be removed?			
Gloves-apron-glasses-mask	36 (18.3)	63 (27.2)	0.024a*
Gloves-glasses-apron-mask	104 (52.8)	90 (38.8)	
Gloves-glasses-mask-apron	43 (21.8)	56 (24.1)	
Gloves-mask-glasses-apron	14 (7.1)	23 (9.9)	
Which mask is included in the N95 mask?			
surgical mask	35 (17.8)	39 (16.8)	0.002a*
FFP1	16 (8.1)	11 (4.7)	
FFP2	73 (37.1)	56 (24.1)	
FFP3	12 (6.1)	32 (13.8)	
I don't know	61 (31)	94 (40.5)	
Do you believe that personal protective equipment will protect from COVID 19?			
Yes	107 (54.3)	120 (51.7)	0.831a
No	15 (7.6)	17 (7.3)	
Partially	75 (38.1)	95 (40.9)	
Do you think you might be infected with COVID-19 while performing dental procedures?			
Yes	133 (67.5)	147 (63.4)	0.632a
No	15 (7.6)	18 (7.8)	
Partially	49 (24.9)	67 (28.9)	
What do you think about the return to clinical activities in dentistry?			
I'm not worried	132 (67)	132 (56.9)	0.044a*
I'm worried	54 (27.4)	90 (38.8)	
I'm very worried	11 (5.6)	10 (4.3)	

Variables	University		
	Abant n (%)	Ataturk n (%)	p
What precautions should be taken to reduce the risk of spreading COVID 19?			
Hand washing before and after treatment	182 (17.4)	191 (17.7)	0.435a
Use of barriers to prevent mucosal contamination	143 (13.7)	158 (14.7)	
Use of disposable aprons	158 (15.1)	191 (17.7)	
Rubber dam use	136 (13)	143 (13.3)	
Rinsing the patient's mouth with mouthwash before the clinical examination	138 (13.2)	119 (11)	
Use of high vacuum suction (saliva and water absorber)	159 (15.2)	145 (13.5)	
Checking patients' body temperatures	131 (12.5)	130 (12.1)	
Have you ever received training on biosecurity measures to prevent the spread of COVID 19 in dentistry?			
I've never had any training.	132 (67)	132 (56.9)	0.044a*
I received general information training without application.	54 (27.4)	90 (38.8)	
I received practical training.	11 (5.6)	10 (4.3)	
Do you have sufficient knowledge about infection control during the pandemic?			
Yes	79 (40.1)	81 (34.9)	0.534a
No	24 (12.2)	32 (13.8)	
Partially	94 (47.7)	119 (51.3)	
Which of the following precautions do you apply to your patients against COVID 19 in your professional life?			
Before the dental procedure, I ask patients if they have complaints such as fever and cough and apply a rubber dam.	105 (22.5)	114 (25.6)	0.003a*
Before a dental procedure, I have patients rinse their mouths with an antiseptic mouthwash containing chlorhexidine.	65 (13.9)	43 (9.7)	
Before a dental procedure, I have patients rinse their mouths with an antiseptic mouthwash containing 1% hydrogen peroxide.	22 (4.7)	25 (5.6)	
I use a powerful saliva and water absorbing system (suction) during the procedure.	142 (30.4)	127 (28.5)	
I follow the 14-day waiting rule for potentially infected patients.	122 (26.1)	103 (23.1)	
None	11 (2.4)	33 (7.4)	
As a dentist, do you inform your patients about COVID 19?			
Yes	44 (22.3)	50 (21.6)	0.525a
No	73 (37.1)	98 (42.2)	

Variables	University		
	Abant n (%)	**Ataturk n (%)**	**p**
Partially	80 (40.6)	84 (36.2)	
Has the institution you work for changed its patient admission policy due to COVID 19?			
Change has been made.	130 (66)	177 (76.3)	0.024b*
No changes were made.	67 (34)	55 (23.7)	
What problems are you facing in the workplace during the COVID 19 pandemic?			
I have difficulty accessing protective equipment (mask, visor, etc.).	68 (21.2)	62 (15.5)	0.008a*
I do not think that my doctor friends' awareness on this issue has reached a sufficient level yet.	44 (13.8)	81 (20.3)	
I think the level of awareness on this issue among healthcare professionals is low.	45 (14.1)	81 (20.3)	
I think patients' awareness of this issue is low.	126 (39.4)	140 (35.1)	
I did not encounter any problems	37 (11.6)	35 (8.8)	
How should undergraduate education be implemented during the pandemic period?			
Online	38 (19.3)	77 (33.2)	0.004a*
Written document	6 (3)	4 (1.7)	
Clinical internship (face to face)	153 (77.7)	151 (65.1)	
Do you think face-to-face education is risky during the pandemic?			
Yes	70 (35.5)	95 (40.9)	0.484a
No	40 (20.3)	46 (19.8)	
Partially	87 (44.2)	91 (39.2)	
Do you find clinical internship training risky during the pandemic period?			
Yes	39 (19.8)	69 (29.7)	0.055a
No	58 (29.4)	64 (27.6)	
Partially	100 (50.8)	99 (42.7)	
How was the quality of the undergraduate education you received affected during the pandemic period?			
Positive	24 (12.2)	20 (8.6)	0.010a*
Negative	107 (54.3)	159 (68.5)	
I am not sure	66 (33.5)	53 (22.8)	
Are you worried about the pandemic continuing after you graduate?			
Yes	92 (46.7)	107 (46.1)	0.773a
No	48 (24.4)	63 (27.2)	
Partially	57 (28.9)	62 (26.7)	
Do you plan to continue doing your job if the pandemic continues after graduation?			
Yes	176 (89.3)	200 (86.2)	0.389a

Variables	University		
	Abant n (%)	Ataturk n (%)	p
No	7 (3.6)	15 (6.5)	
Partially	14 (7.1)	17 (7.3)	

While 37.8% of the participants feel somewhat worried about being infected with COVID 19, there is only 1 difference between the participants who preferred yes and no options. 38.7% of the respondents were suspected of having COVID 19 but the test result was negative, 35% were only suspected but not tested, and 26.3% were suspected of COVID 19 and the test result was positive. While the majority of students classified the risk of contracting COVID 19 infection in clinical practices at the faculty of dentistry as high (42.4%), 3.7% stated this risk as low. A large percentage of students were not forced to work under conditions that would endanger their personal safety (47.3%), while a group of students stated that they were forced (27.3%).

Among the personal protective equipment, the most used equipment was mask, gloves, visor, apron/overall, and the least used equipment was marked as protective glasses (33.1%). While 30.5% of the participants correctly marked the option of apron-mask-glasses-gloves, which was the correct order of wearing personal protective equipment, 23.1% of the participants correctly marked the option of glove-glasses-mask-apron, which was the correct order of removing personal protective equipment. Although the majority of students did not know which mask group the N95 mask belongs to (36.1%), 30.1% selected the correct option, FFP2. While the majority believe that personal protective equipment will protect from COVID 19 (52.9%), 7.5% do not believe that personal protective equipment will protect from COVID 19. 65.3% of the students think that you could be infected with COVID 19 while performing dental procedures, while 7.7% do not think that you could be infected with COVID 19. While the majority did not feel worried about returning to clinical activities in dentistry (61.5%), 4.9% feel very worried about it.

Among the precautions that should be taken to reduce the risk of spreading COVID 19, the most marked ones were hand washing before and after treatment, use of disposable aprons and use of high vacuum suction (saliva and water absorber). However, the option of rinsing the patient's mouth with mouthwash before the clinical examination was the least marked option. While 49.7% of the participants stated that they received general information training on biosecurity measures to prevent the spread of COVID 19, 47.1% stated that they did not receive any training. While 49.7% of the students think that they have partially sufficient knowledge about infection control, 13.1% do not think that they have sufficient knowledge.

62.7% of the participants chose to use a powerful saliva and water absorber system during dental procedures, while 10.3% of the participants chose not to take any extra precautions. While 39.9% of the students did not inform their patients about COVID 19, 38.2% partially inform their patients and 21.9% inform their patients in detail. 63.6% of the participants stated that patient admissions were partially reduced in the institution where they worked. While 28.4% of the participants considered low awareness of the COVID 19 epidemic to be one of the problems they encountered while working at work during this period, 16.8% stated that they did not encounter any problems at work. While 70.9% of the students wanted their undergraduate education to continue in the form of clinical internships (face-to-face) during the pandemic period, 41.5% thought that partially and 38.5% thought that completely face-to-face education was risky. While 46.4% find clinical internship training partially risky, 25.2% consider it completely risky. In addition, 62% of the participants stated that the quality of the undergraduate education they received during the pandemic period was negatively affected by this process. While 46.4% of the students were worried about the pandemic continuing after graduation, 25.9% stated that they did not have any concerns. At the same time, 87.6% of students stated that they would continue to do their jobs after graduation, even if the pandemic continues, while 5.1% stated that they would prefer not to do their jobs.

4. DISCUSSION

Dental professionals worldwide were concerned about the safety and well-being of themselves and their patients during the pandemic. COVID 19 has severely impacted the continuity of education worldwide (Boukhobza et al., 2021). Healthcare workers and students have been greatly affected by social distancing and university quarantines (Aragao et al., 2022). Given the high exposure to aerosols and the potential risk of spreading SARS-CoV-2 (Li et al., 2020), the dental school has moved to online education, creating difficulty in delivering practical training (Prati et al., 2020; Wu et al., 2020; Quinn et al., 2020). Some universities have attempted a partial return to face-to-face activities. Addressing students' basic understanding of the disease can be a starting point for dental schools to plan their return (Ataş et al., 2020; Esmaeelinejad et al., 2020). Therefore, in this study, the COVID 19 knowledge levels of 4th and 5th grade students of the Faculty of Dentistry and the impact of the pandemic on educational concerns and clinical practices were examined. Web-based surveys are very advantageous in terms of their low cost and the ability to access large groups of people and collect data easily and at large amounts (Couper et al., 2001). In this regard, in the current study, survey questions were prepared via Google forms.

The results regarding dentistry students' general knowledge about COVID 19 show that the majority of students know the incubation period and main symptoms of the disease, but they have insufficient knowledge about the ways of transmission. 28.2% of the participants stated that contamination occurred as a result of contact with the blood of an infected person. This result is consistent with the study results of Aragao et al (Aragao et al., 2022). For this reason, it has become necessary for schools to prepare educational materials to provide reliable information to students.

Since students are exposed to intense amounts of aerosol during dentistry practices, they need to pay more attention to protective measures, especially since they have less clinical experience (Peng et al., 2020). Although most of the participants in the current study are knowledgeable about protective equipment, they have insufficient knowledge about the order of wearing and removing the equipment. This situation poses a problem in terms of transmission of the disease. It is recommended that patients use mouthwash (1% hydrogen peroxide or 0.2% povidone iodine) and rubber dam during treatment procedures (Samaranayake et al., 20024). In this study, the use of high vacuum suction (saliva and water absorber) was the most frequently marked precaution to reduce the risk of spread, and the option of rinsing the patient's mouth with mouthwash before the clinical examination was the least marked option. In this regard, students should be encouraged to use rubber dam and rinse the patient's mouth with mouthwash before the procedure.

The current study, like other studies in the literature, revealed gaps in dental students' knowledge about COVID 19 (Aragao et al., 2022; Almulhim et al., 2021). 47.1% of the participants stated that they did not receive practical general information training on biosecurity measures to prevent the spread of COVID 19.

Although the theoretical parts of the Dentistry education curriculum were successfully carried out through online distance learning, there were deficiencies in the parts that required clinical experience. In the current study, it was observed that 70.9% of the students wanted their undergraduate education to continue in the form of clinical internships (face-to-face) during the pandemic period. For this reason, after the epidemic, it became necessary for school administrations to organize lessons and/or information meetings for students. 62% of the participants stated that the quality of the undergraduate education they received during the pandemic period was negatively affected by this process. Our results are consistent with previous reports that the COVID 19 pandemic is a major challenge for dental practice and dental education.11, 20

5. CONCLUSION

The impact of the COVID 19 pandemic has greatly affected dental education. To face future challenges, dental educators must be careful, not panic, be flexible and open to changes. The dentistry education model should be renewed to suit different situations and dental education should be open to changes. Although the COVID 19 epidemic has had a devastating impact all over the world, this epidemic should mobilize healthcare professionals to be better prepared for any epidemic that may arise in the future.

REFERENCES

Almulhim B, Alassaf A, Alghamdi S, Alroomy R, Aldhuwayhi S, Aljabr A, Mallineni SK (2021) Dentistry amidst the COVID-19 pandemic: knowledge, attitude, and practices among the Saudi Arabian dental students. Frontiers in Medicine 8:654524.

Aragão MGB, Gomes FIF, Pinho Maia Paixão-de-Melo L, Corona SAM (2022) Brazilian dental students and COVID-19: A survey on knowledge and perceptions. European Journal of Dental Education 26(1):93-105.

Ataş O, Yildirim TT (2020) Evaluation of knowledge, attitudes, and clinical education of dental students about COVID-19 pandemic. PeerJ 8:e9575.

Bellini P, Iani C, Zucchelli G, Franchi M, Mattioli AV, Consolo U (2020) Impact of the COVID-19 pandemic on dental hygiene students in the Italian region of Emilia-Romagna. Minerva Dental and Oral Science 71(3):180-191.

Boukhobza S, Ritschl V, Stamm T, Bekes K (2021) The COVID-19 pandemic and its impact on knowledge, perception and attitudes of dentistry students in Austria: A Cross-Sectional Survey. Journal of Multidisciplinary Healthcare 1413-1422.

Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R (2023) Features, evaluation, and treatment of coronavirus (COVID-19). Statpearls [internet].

Chan JF-W, Yuan S, Kok K-H, To KK-W, Chu H, Yang J, Xing F, Liu J, Yip CC-Y, Poon RW-S, Tsoi H-W, Lo SK-F, Chan K-H, Poon WK-M, Chan W-M, Ip JD, Cai J-P, Cheng VC-C, Chen PH, Hui CK-M, Yuen PK-Y (2020) A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. The lancet 395(10223):514-523.

Coulthard P (2020) Dentistry and coronavirus (COVID-19)-moral decision-making. British Dental Journal 228(7):503-505.

Couper MP, Traugott MW, Lamias MJ (2001) Web survey design and administration. Public opinion quarterly 65(2):230-253.

Deery C (2020) The COVID-19 pandemic: implications for dental education. Evidence-based dentistry 21(2):46-47.

Desai BK (2020) Clinical implications of the COVID-19 pandemic on dental education. Journal of dental education 84(5):512.

Esmaeelinejad M, Mirmohammadkhani M, Naghipour A, Hasanian S, Khorasanian S (2020) Knowledge and attitudes of Iranian dental students regarding infection control during the COVID-19 pandemic. Brazilian oral research 34:e121.

Iyer P, Aziz K, Ojcius DM (2020) Impact of COVID-19 on dental education in the United States. Journal of dental education 84(6):718-722.

Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KSM, Lau EHY, Wong JY, Xing X, Xiang N, Wu Y, Li C, Chen, Q, Li D, Liu T, Zhao J, Liu M, Tu W, Chen C, Jin L, Yang R, Wang Q, Zhou S, Wang R, Liu H, Luo Y, Liu Y, Shao G, Li H, Tao Z, Yang Y, Deng Z, Liu B, Ma Z, Zhang Y, Shi G, Lam TTY, Wu JT, Gao GF, Cowling BJ (2020) Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. New England journal of medicine 382(13):1199-1207.

Lu H, Stratton CW, Tang YW (2020) Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. Journal of medical virology 92(4):401.

Mutluay AT, Mutluay M (2022) Educational concerns and awareness level among dental hygiene students during the COVID-19 pandemic. International Journal of Dental Hygiene 20(2):273-281.

Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B (2020) Transmission routes of 2019-nCoV and controls in dental practice. International journal of oral science 12(1):1-6.

Prati C, Pelliccioni G, Sambri V, Chersoni S, Gandolfi M (2020) COVID-19: its impact on dental schools in Italy, clinical problems in endodontic therapy and general considerations. International endodontic journal 53(5):723.

Quinn B, Field J, Gorter R, Akota I, Manzanares M-C, Paganelli C, Davies J, Dixon J, Gabor G, Mendes RA, Hahn P, Vital S, O'Brien J, Murphy D, Tubert-Jeannin S (2020) COVID-19: The immediate response of european academic dental institutions and future implications for dental education. European Journal of Dental Education 24(4):811-814.

Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, Zimmer T, Thiel V, Janke C, Guggemos W, Seilmaier M, Drosten C, Vollmar P, Zwirglmaier K, Zange S, Wölfel R, Hoelscher M (2020) Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. New England journal of medicine 382(10):970-971.

Samaranayake LP, Peiris M (2004) Severe acute respiratory syndrome and dentistry: a retrospective view. The Journal of the American Dental Association 135(9):1292-1302.

Shacham M, Hamama-Raz Y, Kolerman R, Mijiritsky O, Ben-Ezra M, Mijiritsky E (2020) COVID-19 factors and psychological factors associated with elevated psychological distress among dentists and dental hygienists in Israel. International journal of environmental research and public health 17(8):2900.

Wang C, Horby PW, Hayden FG, Gao GF (2020) A novel coronavirus outbreak of global health concern. The lancet 395(10223):470-473.

Who C (2020) World health organization. Responding to the Community Spread of COVID-19. Reference WHO/COVID-19/Community _ Transmission/2020.

Wu DT, Wu KY, Nguyen TT, Tran SD (2020) The impact of COVID-19 on dental education in North America—Where do we go next? European Journal of Dental Education 24(4):825-827.

Yurdugül H (2005) Ölçek geliştirme çalışmalarında kapsam geçerliği için kapsam geçerlik indekslerinin kullanılması. XIV. Ulusal Eğitim Bilimleri Kongresi 1:771-774.

About The Authors

About The Authors

Büşra TOSUN has completed her specialization in Prosthetic Dentistry, Ataturk University, Turkey. Her research interests are included mechanic and optic property of prosthetic materials, surface modification methods etc. Research articles have been published in many national and international journals. She also has written book chapters.

E-mail: dtbusra86@hotmail.com, ORCID: 0000-0003-3145-4454

Merve Nur YILMAZ has completed her specialization in Restorative Dentistry, Ataturk University, Turkey. She is a researcher specializing in dental materials, unreacted monomers and color stability. Merve Nur YILMAZ has submitted one research paper as the first author, which is currently under review.

E-mail: mervenurylmz91@hotmail.com, ORCID: 0000-0002-8037-6408

Prof. Dr. Pinar GUL received her PhD in 2012 Institute of Health Sciences at Atatürk University, Turkey. She is a Professor in Restorative Dentistry. Her research interests are included Restorative Materials, Bleaching, Residual Monomer etc. She has published more than 50 research articles in national and international well reputed journals. She also has written book chapters.

E-mail: opinargul@gmail.com, ORCID: 0000-0003-3714-4991

To Cite This Chapter

Tosun B et al., (2024). Evaluation of the Effect of the Covid-19 Pandemic on the Educational Concerns of Dentistry Students and Clinical Practices. In Current Studies in Health and Life Sciences 2024 (pp.35-347). ISRES Publishing.

Chapter III: Animal Sciences

ISRES Publishing

Potential and Challenges of Catfish Aquaculture in Pakistan

Shahid SHERZADA

Khadija SHOUKAT

Talib HUSSAIN

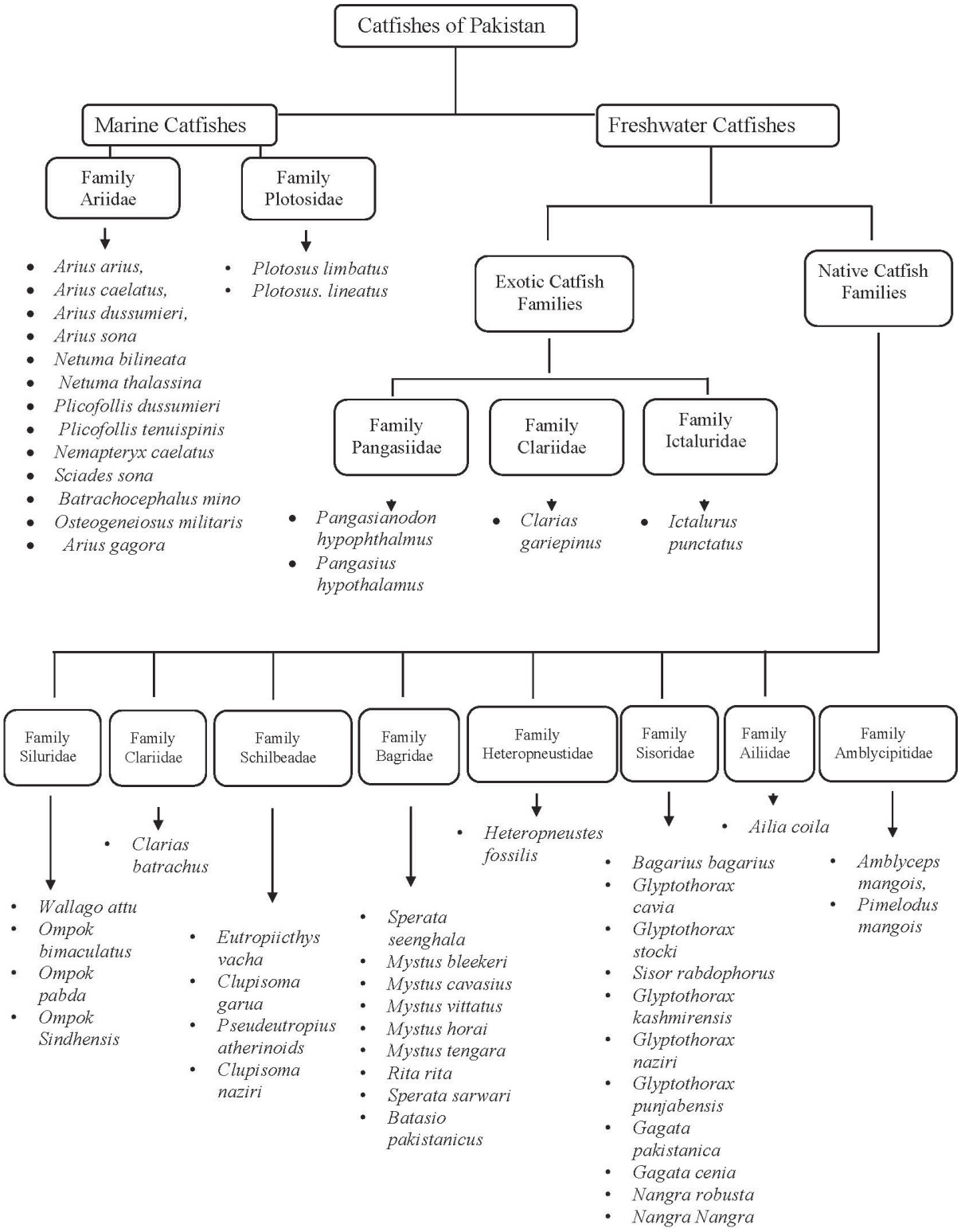
Nimra HUSSAIN

Introduction

Aquaculture has emerged as the fastest growing food source in an effort to meet the demands of a growing population (FAO, 2006). The global population is rapidly increasing, resulting in an alarmingly high hunger ratio that necessitates the provision of shelter, clothing, and food. Poverty is major threat to global food security and can only be achieved by the inland fisheries and aquaculture sectors. Additionally, fisheries resources also contribute in GDP of any country (FAO 2004). In this perspective, aquaculture can meet the needs of developing countries in terms of livelihood, food security, social development and a source of income (Nowsad et al. 2015). It can contribute in reducing hunger by the production of aquatic protein and through the generation of income sources (Garcia-Rodriguez and Cruz-Aguero 2011). From past two decades, the overall consumption of fish and fisheries products have increased due to the rapid growth of aquaculture production (FAO, 2004). Globally, carp, tilapia, salmon, and catfish are prevalent choices for fish farming activities. By the year 2030, freshwater species, including carp and catfish, are estimated to dominate global aquaculture production, making up the majority at 62% (FAO, 2020).

Among Ostariophysi, the second largest superorder of fishes, order siluriformes is considered to be rich in diversity including 477 genera, 39 families and approximately 4000 species (Senthilkumaran and Kar 2021; Fricke et al. 2019; Ferraris, 2007). It includes major groups of catfishes that are commercially and economically important throughout the world. Majority of these catfish are cultivated in Asia as they can bear temperate environment (Punhal et al. 2018). About 107 species of catfishes are present in Asia and Europe (Ditcharoen et al. 2019). Catfishes, belongs to the order Siluriformes, are a diverse group of fishes characterized by their whisker-like barbells around the mouth, just like cat's whiskers which helps in sensory perception. They possess scaleless skin and a distinctive adipose fin lacking fin rays. Additionally, their dorsal and pectoral fins are armed with sharp spines, serving a defensive purpose (Muhammad et al. 2017; Wang et al. 2016). They are preferred for food, due to high protein content, hardy nature, high fecundity and resilience nature (Senthilkumaran and Kar 2021). Besides this, they possess relatively high adaptability to artificial spawning, hatchability, culturing and resistance to diseases. These characteristics also make them excellent model organism in valuable research regarding evolutionary biology, fisheries, parasitology, economics etc. particularly in toxicology experiments, where their tolerance to environmental stressors like low dissolved oxygen and adaptability nature proves advantageous (Rejab et al. 2020; Turan et al. 2020; Senthilkumaran and Kar 2021; Tripathi et al. 2023). Notable catfish species, includes the Amur catfish (Silurus asotus), Channel catfish (Ictalurus puncuatus), Striped catfish (Pangasius hypophthalmus), and African catfish (Clarias gariepinus) having approximately -0.62%, 0.53%, 0.52% and 0.33% contribution in total fish production by the end of 2014 and 0.49%, 0.91%, 4.3%, 5.1% respectively by the end of 2018 (FAO 2014, 2018).

In the United States, catfish are regarded as a key species for aquaculture. In late 18s and early 19s Bull heads were cultured on a large scale for the purpose of sport fishing (leary, 1910). To increase aquaculture production and recreational fishing, the channel catfish, Ictalurus punctatus, has been introduced into more than 32 nations, including the UK, Brazil, China, India, Thailand, and Russia (Welcomme, 1988; FAO, 2006). Fishes are introduced to almost all parts of North America where the suitable water resources are available (Moyle, 1976). The private hatcheries and the government have propagated about 7 species of the catfishes for recreational fishing and



stocking purposes. These species include the blue catfish, white catfish channel catfish, flathead catfish, yellow bullhead catfish, and black bullhead catfish. Among them, the second most cultured catfish is the blue catfish (Dunham et al 2008). On the other hand, the channel catfish is a fish that has been cultured worldwide and brought into more than 32 nations, including China, India, Thailand, and Russia, in order to increase aquaculture production (FAO, 2006). Channel catfish has significance performance in freshwater and its production is moving toward sustainability (Engle, 2003). Besides this, it also made a hybrid with the blue catfish. This combination proved to be efficient for pond culture (Dunham et al. 2008). Because it shows a high growth level and resistance

to the bacterial diseases. Moreover, this new hybrid species tolerates low level of oxygen (Arias et al 2012). Another fact that makes it culture friendly is that both the blue catfish and the channel catfish have a low survival rate in high density and have higher chances of disease when cultured separately, however their hybrid has remarkably high rate of survival even in high stocking densities.

Additionally, African catfish has recently gained the attention of fish sector all over the world because of its advantages. It can tolerate the high temperature and low DO that make them more resistant to the stress (Olaleye, 2005). In addition to that it has the ability to show resistance against diseases and their breeding can be done under captivity. These species can even survive at the highest stocking density (Van der Waal, 1998).

Potential of Catfish Culture in Pakistan

Pakistan is enriched with a great variety of fishes along with streams, rivers, dams and oceans (Ahmad et al. 2020). It has 1120 kilometers of coastline and 3,102,408 hectares of inland water reserves (Samuel et al, 2011). It has 225 wetlands, among which 74% are freshwater while rest are marine water wetlands (Muhammad et al. 2019). In addition to that, it has world-class fish wharf, with Karachi Fisheries Harbor being the most significant since it handles 90% of the nation's fish and seafood imports as well as 95% of its fish exports. Moreover, Sindh and Baluchistan coastlines are also noteworthy for their abundant natural fish fauna reserves (Pirarat et al. 2017).

Pakistan has 233 freshwater and 800 marine water species, among which 31 freshwater species and 120 marine water species are of commercial importance (Altaf et al. 2015; Laghari, 2018). Pakistan's Indus River is habitat to more than 180 different fish species. The world's largest land and rock filled dam, Tarbela dam with six barrages (Jinnah, Guddu, Kotri, Chasma, Taunsa and Sukkur) are constructed on Indus River in Pakistan (Mirza and Mirza 2011). Despite of all these resources, there are only few fish species and water resources that are been explored for culturing. Many researchers reported that there are many continental areas in Sindh and Baluchistan, Pakistan that have high capability for fish production but unfortunately these are untouched until now. The effective use of these unutilized areas for fish farming needs careful planning. The data deficiency is another element in the sector of aquaculture. The data validity is questionable or sometimes the data is insufficient. There may be hundreds of fish farms which are not registered so they cannot be surveyed by the fisheries department because of their poor power resources and insufficient operational funds (Nazir et al, 2016). To meet the increasing demand for fish, food security, employment opportunities and for strengthening the national GDP, the fish production sector is making progress. However, still there remains a crucial need to further develop and expand the aquaculture sector (Shah et al. 2018). By paying more attention to fisheries, the economy of the country can be boosted (Mohsin et al. 2015).

In Pakistan, only few species like Labeo rohita, Cirrhinus mrigala, Catla catla, Cyprinus carpio, Hypophthalmichthys molitrix, Ctenopharyngodon idellus, and Hypophthalmichthys nobilis are frequently cultured. Among them, Catla catla, Labeo rohita, and Cirrhinus mrigala command higher market value due to consumer preferences. However, the culturing of Catfishes, Snakeheads and tilapia are in developmental phases (Laghari, 2018). In a recent study done by Rossignoli et al. 2023 on challenges of saline aquaculture in Pakistan, they found that Rohu is the most commonly stocked fish species among farmers, followed by Catla, Mirgal, Common Carp, and Grass Carp, with varying percentages. On the other hand, Catfish and Tilapia are stocked by only a small percentage of farmers (medium and large-scale farmers), with more than 90% preferring carp species and about one-tenth (12%) of farmers harvest species other than Carp, like Tilapia or Singhari (catfish) (Rossignoli et al. 2023). Although, catfish cultivation has its perks when compared to carp farming as it can endure low-oxygen environments, handle crowded conditions well, and support high stocking densities with artificial feeds (Ali et al. 2015). Despite of that, here most of the catfish production relies on wild resources as these are easily accessible and affordable sources for freshwater food. Consequently, these fishes are predominantly consumed by the local communities

in the area which results in overexploitation and thus risk of the loss of these valuable fishes (Ali et al. 2015). In addition to that, many researchers reported climatic change, water pollution and other anthropogenic aspects as contributing factor in decline of these fishes in both freshwater and marine water sources of Pakistan (Noman et al. 2018; Gilani et al. 2020; Afreen et al. 2022; Malik et al. 2023). Such kind of circumstances reflects the consumer interest and thus need of proper culturing of catfishes. There are many cultivable and economical important catfish species in Pakistan. The data regarding the exact number of catfish species in present in Pakistan is scarce but on the basis of previous documentation it can be concluded that there are approximately thirty plus freshwater indigenous catfish species belonging to 7 different families (Siluridae, Schilbeadae, Bagridae, Sisoridae, Heteropneustidaeare, Claridae and Amblycipitidae) that are being reported in freshwater resources of Pakistan (Ferraris, 2007; Rafique and khan 2012; Muhammad et al. 2017). On the other hand, about 15 seawater catfish species belonging to 2 different families i.e. Ariidae (sea catfishes) and Plotosidae (eel catfishes) are documented by various researchers (Farooq et al. 2016; Sattar et al. 2016). Among these, there are many species that are commercially important for food and ornamental purposes throughout the world. But in Pakistan none of these are preferred by farmers. However, the wild sources are these species are heavily under the pressure of overfishing which leads to the decline in the population of these commercially important species. Furthermore, among freshwater catfish species of Pakistan 31 species have special IUCN status indicating 17 % species as near threatened, 14% as endangered and 6% as vulnerable (Figure 1).

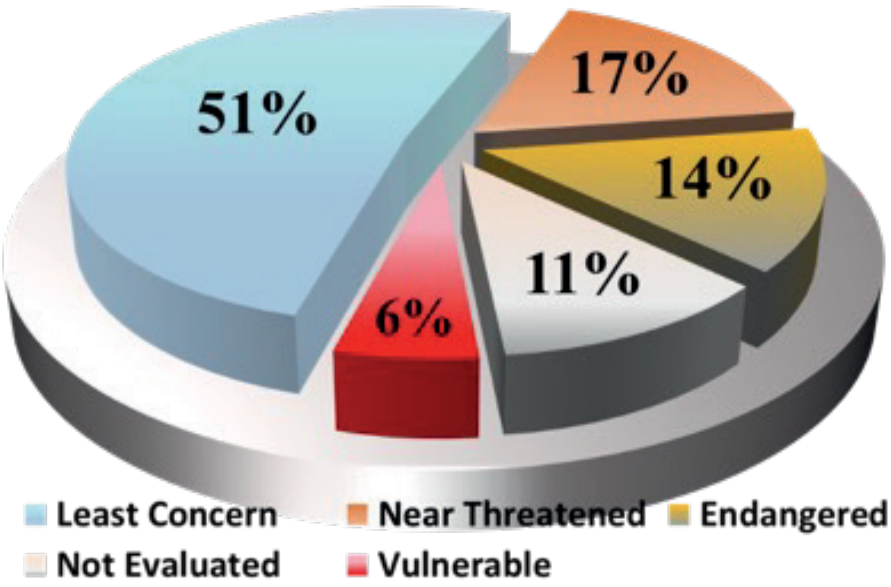


Figure 1. IUCN status of freshwater fishes of Pakistan

Table 1. Indigenous Freshwater Species of Pakistan

Family	Species	Distribution	IUCN status	Commercial value	Reference
Siluridae	*Wallago attu*	AJK, Balochistan, KP, Punjab, Sindh	Vulnerable	Very high	Rafique and khan 2012; Ferraris, 2007; IUCN 2020
	Ompok bimaculatus	KP, Punjab, Sindh	Near Threatened		
	Ompok pabda	AJK, Balochistan, KP, Punjab, Sindh	Near Threatened		
	Ompok Sindhensis	Sindh	Not evaluated		
Schilbeadae	*Eutropiicthys vacha*	KP, Punjab, Sindh	Least concern		Mirza 2003; IUCN 2009; Ferraris, 2007
	Clupisoma garua	AJK, Punjab, Sindh	Least Concern	Very high	
	Pseudeutropius atherinoids	Punjab, Sindh	Least concern		
	Clupisoma naziri	AJK, KP, Punjab	Near Threatened	Very high	IUCN 2019; Rafique and khan 2012; Ferraris, 2007
Bagridae	*Sperata seenghala*	AJK, Balochistan, KP, Punjab, Sindh	Least Concern	Very high	Rafique and khan 2012; Ferraris, 2007, Mirza 2003, IUCN 2009
	Sperata sarwari	Balochistan, KP, Punjab, Sindh, AJK	Not evaluated		
	Mystus bleekeri	KP, Punjab, Sindh	Least concern		
	Mystus cavasius	KP, Punjab, Sindh	Least concern		
	Mystus vittatus	KP, Punjab, Sindh	Least concern		
	Mystus tengara	KP, Punjab, Sindh	Least concern		
	Rita rita	Balochistan, KP, Punjab, Sindh	Least Concern	Very high	
	Mystus gulio	Balochistan, Sindh	Least Concern		IUCN 2019; Mirza 2003
	Mystus horai	Punjab	Vulnerable		IUCN 2020; Rafique and khan 2012; Ferraris, 2007
	Batasio pakistanicus	Punjab	Endangered		

Family	Species	Distribution	IUCN status	Commercial value	Reference
Sisoridae	*Bagarius bagarius*	Punjab, Sindh	Near threatened	high	
	Glyptothorax cavia	AJK, KP, Punjab	Least concern		IUCN 2009; Ferraris, 2007; Mirza 2003
	Glyptothorax stocki	AJK, KP, Punjab	Endangered		Rafique and khan 2012; Ferraris, 2007; IUCN 2020
	Sisor rabdophorus	Punjab and Sindh	Least Concern/ Very rare		
	Glyptothorax kashmirensis	AJK	"Critically Endangered"		
	Glyptothorax naziri	AJK, Balochistan, KP, Punjab	Near threatened		
	Glyptothorax punjabensis	AJK, Balochistan, KP, Punjab	Endangered		
	Nangra robusta	Punjab	Endangered		
	Gagata pakistanica	KP, Punjab	Least concern		
	Gagata cenia	KP, Punjab, Sindh	Least concern		Mirza 2003; Ferraris, 2007; IUCN 2009
	Glyptothorax pectinopterus	AJK, KP	Least concern		
	Nangra Nangra	Punjab	Least concern		Mirza 2003; Ferraris, 2007; IUCN 2007
Amblycipitidae	*Amblyceps mangois*	AJK, Sindh, Balochistan, Punjab	Not evaluated		Ferraris, 2007; Mirza 2003
	Pimelodus mangois	AJK, Sindh, Balochistan, Punjab	Not evaluated		
Ailiidae	*Ailia coila*	Punjab, Sindh	Near threatened		Ferraris, 2007; Rafique and khan 2012; IUCN 2020
Heteropneustidae	*Heteropneustes fossilis*	KP, Punjab, Sindh	Least Concern		Muhammad et al. 2017; Ferraris, 2007; IUCN 2019
Clariidae	*Clarias batrachus*	Restricted areas of Punjab	Least Concern	High	Rafique and khan 2012; Ferraris, 2007; IUCN 2019

Besides this, a few exotic species, due to their commercial and economic importance worldwide, have also been introduced into the natural resources of Pakistan. These include African Catfish (Clarias gariepinus) (Basharat et al. 2020), Channel Catfish (Ictalurus punctatus) (Abdul et al. 2007), Asian Catfish (Pangasianodon hypophthalmus) (Shah et al. 2014) and stripped Catfish (Pangasius hypothalamus) (Mehboob et al. 2017). In 2007 about 2000 fingerlings of Channel Catfish were imported from Thailand by national agriculture research center of Pakistan as a pioneer step to promote catfish culturing (Abdul et al. 2007). Earlier Asian Catfish was also introduced to Pakistan in early 2000s to diversify aquaculture production, however the exact documented introduction of this species was not reported. Likewise, in 2017 stripped Catfish fry was imported from Thailand by group of progressive researchers and analyzed the effect of fenugreek as a feed additive on its survival, growth and body composition (Mehboob et al. 2017) which is followed by its culturing in earthen ponds having HAPAS by Khan et al. 2018. Recently, in 2020 another group of researchers in association with national agriculture research center of Pakistan imported African catfish from Thailand and successfully adapted it in the environment of Pakistan (Basharat et al. 2020). In order to expand the fisheries industry in Pakistan there is dire need of introduction of new species having high export potential. Currently there are about 64 different kinds of exotic species in water bodies of Pakistan. On the other hand, ill effect of these alien species is also being reported by many researchers (Imran et al. 2021; Bilal and Khan 2023). That is why, proper management and control policies must be formulated for such introductions, otherwise it can lead to long-lasting ecological damages to native diversity of Pakistan (Bilal and Khan 2023).

Major challenges of catfish culture in Pakistan

The major factors that affect the culturing of the catfish in Pakistan include the fish feed, breeding, water, climatic conditions, and antibiotics resistant genes. These are listed below:

Fish feed

The prosperity of aquaculture businesses is directly tied to nutritional excellence. Developing topsider feed formulations demand comprehensive insights into the unique biology and dietary needs of various fish species (Khan et al. 2018). Most of the commercial aquaculture practices in Pakistan are of extensive while some are of semi-intensive nature which is far behind other countries (Basharat et al. 2020). In order to promote aquaculture industry, there is a dire need to go for intensive culture system with artificial feeding. Artificial feed includes many ingredients that have high market price. The increasing cost of feed ingredients resisting the effective production of catfish in developing countries as it indulges farmers towards the culturing of those species that can give efficient output in extensive and semi-intensive culture system. Feed Cost in the aquaculture account for about 50% of the production cost (Barrows et al., 2007). It is rising day by day because of the lack of attention of aquacultrist in calculating the exact relationship between the feed cost and the weight gain by the fish. Extrusion method is a technology that is used for the fish feed production. In this, high temperature, moisture and high pressure are required and different dies are used to attain desirable size pellet size (Watanabe and Pongmaneerat, 1993).

Catfishes required 40 cp feed for better growth (Pourjafar, 2007). These are mainly omnivores and carnivores in nature and possess simple digestive system having limited carbohydrases, thus there is requirement of artificial feed that have high protein contents (Ogello et al., 2014; Khalil et al. 2017). This can be fulfilled by adding fish meal or other kind of live feed in diet which made this practice a bit expensive. Nutritionists across the world are continuously in search for other plant-based protein replacements that can cut down overall feed cost. Usually, Small-scale farmers lacks knowledge about advances in fish culture and they exhibit reluctance toward adopting new technologies. But it is the time to drive the system towards the intensive aquaculture of the highest stocking density by the introduction of the high value fish species that have the high growth potential (Faheem et al., 2019; Mahmoud et al., 2019). For this aquaculturists must be aware about the selection of efficient feed that can give good FCR at minimum amount. This can lead to cut down

the cost of feed which in turn will be responsible for better output for farmers. As recently, Basharat et al. (2023) found that the highest weight gain for newly introduced African catfish occurred at an 8% feeding level. However, a comprehensive cost-benefit analysis revealed that feeding at a 4% rate yielded the most favorable outcomes for African catfish culture in Pakistan's earthen pond system. Such kind of practices by researchers can encourage farmers to go for intensive culture system that is more advantageous.

Water

Water is the primary element, which is crucial in maintaining a healthy aquatic environment and producing abundant fish food organisms. The change in physiochemical parameters of water can directly affect the growth of fish. The distribution of species in rivers is significantly influenced by temperature and turbidity, as these factors shows a stronger correlation with dissolved oxygen (DO) and pH (Arino et al. 2013). Now a days many factors i.e. climate condition, habitat fragmentation, water pollution by industrial and municipal wastes deteriorated the water quality of natural waterbodies. A study by Malik et al. 2023 found the abundance of heavy metal accumulation in Wallago attu from Pat Feeder Canal, Pakistan which resulted in prevalence of Pseudomonas aeruginosa, a normal microbiota in digestive tract of fish which becomes pathogenic during adverse condition. These conditions had impact on the survival chances of aquatic organism. Just like freshwater sources, our marine sources (Arabian Sea at Karachi coast) are also facing same issues of climatic changes and water pollution (Afreen et al. 2022). Data compiled by Noman et al. 2018 found that the marine catfish stock at Sindh coastline is continuously declining. Again, prevailing overexploited and adverse environmental and water condition in sea water are responsible for loss in biodiversity. On the other hand, Catfish farming in environments having low salinity levels, up to 10%, creates conditions inhospitable to catfish diseases, thereby it can be a viable strategy for disease control. In contrast, freshwater environments with 0% salinity provide favorable environment for the growth of catfish diseases (Fiess et al., 2007). These circumstances showed the need of intensive farming of catfish, where proper check and balance on water quality parameter can be maintained.

Temperature

All metabolic, physiological, and biological functions, including feeding, reproduction, migration, and distribution of aquatic organisms, are influenced by temperature. Catfish's temperature is only 1 °C above or below the water temperature. The metabolic activity of the warm water fishes is higher at the high temperature however the cold-water fishes such as salmonids show the best activity at the low temperature. These cold-water fishes including salmonids and the white fishes slow down their growth and consumption of food at high temperature. The water temperature also linked with the initiation of certain diseases. The immune system of the majority of the fishes shows their best activity at 15 °C (Sapkota et al. 2008). Under the natural conditions fishes can easily tolerate the seasonal changes in the water temperature but these changes should not be abrupt because this can lead to the death of the fishes. If fishes are put into the poor water temperature alterations, then it can show cardiac and muscle paralysis. Their digestion process slows down and their food remains undigested or partially digested which can result in the blotting of the fish. Moreover, the transfer of the fish to too much cold water can cause ammonia autointoxication (Bohl, 1989).

In Pakistan, under the prevailing extensive culture system having no check and balance on physiochemical parameters, there are high risk of disease outbreak. The wild sources of Pakistan are also being reported as victim of climate change and anthropogenic activities. This may cause the loss of catfish diversity along with other aquatic fauna and flora, as catfish production mainly relies on these wild resources (Ali et al. 2015). A study at the Taunsa Barrage of Indus River revealed that catfishes are stressed due to certain anthropogenic factors i.e. natural habitat disturbance, overfishing, water pollution etc. (Muhammad et al. 2017). Such conditions provide favorable environments for pathogens to grow. Furthermore, changes in average water temperature as a result of climate change can indirectly affect the catfish sector by increasing pathogen load along with reduction

in host sensitivity, transmission rates, and survival probabilities (Kumar et al., 2018). Likewise, another study by Gilani et al. 2020 claimed that the distribution of Glyptothorax kashmirensis in AJK, Pakistan was impacted by environmental variations and found that during summer months, rising temperatures significantly alter fish distribution in both Jhelum and Poonch Rivers of Azad Jammu and Kashmir. Moreover, increased turbidity is also associated with higher relative fish abundance in these river systems.

Impact of Anthropogenic activities on water quality

Anthropogenic activities are also responsible for poor water composition.

These activities include:

• Enhancement of suspended particles in the water after cutting and Logging of commercial forestry.

• Increase in the concentration of the metals in the drainage water by the metal mining by the men that exposed rocks surface area to the rainfall.

• Discharged of large volumes of organic waste in water in the forms of sewage

• Embryo Larval toxicity test with organic compounds.

pH

The hydrogen ion (H+) concentration in soil and water is measured using the pH scale. When pH below is 7 it become acidic and when rise from 7 become basic. The ideal pH for catfish growth is 6.5-8-5 and the optimum value for best growth is 7.5-8.5. However, it varies from species to species and aquatic ecosystem (Assefa et al., 2019). In fish pond the pH rise during day time due to the start of photosynthesis because phytoplankton utilize CO2 and it declines during night as a result of the process of respiration and aquatic flora and fauna dissipate CO2 into water. When pH fluctuate it causes the stress for fish and in results the production of mucus increases on body as well as gills. Fish eyes become opaque and diverge inside and disturb byuoncy of catfish.

Dissolved oxygen

One of the most important factors in aquaculture is dissolved oxygen (DO). Maintaining adequate DO levels in the water is critical for effective production since oxygen has a direct impact on feed intake, illness resistance, and metabolism. As a result, it is important to maintain dissolved oxygen levels in aquaculture systems above 4 parts per million (ppm). Ponds' dynamic oxygen cycle changes during the day as a result of phytoplankton respiration and photosynthesis. The significant element in a farmer's daily work is controlling the balance of photosynthesis and respiration as well as the growth of algae. (Alexander et al. 2010). Due to the accumulation of oxygen (O2) from photosynthesis during the day, maximum DO will happen in the late afternoon. DO levels decrease because phytoplankton (microscopic algae) typically consumes the most O2 and because photosynthesis does not occur at night. Ponds experience critically low DO when algae blooms dissipate. Besides this, a lot of oxygen is required for subsequent bacterial breakdown of the dead algal cells. It is vital to remember that water's DO content rises as temperature falls and falls as salinity rises (Khan and Thulin 1991). Even in the summer, the level of oxygen is sufficient and the growth of the plant is high, while the level of oxygen can decline in the autumn and the plants may die. Low oxygen levels enhance the eutrophication process. Hence the declining level of the dissolved oxygen is a major challenge for the fish culture.

Ammonia

The breakdown of decaying organic materials, including algae, plants, animals, and uneaten food, results in the production of ammonia in ponds. In water, ammonia can be found in two different

states: as the gas NH-3 or as the ion ammonium (N 1-14+). The gaseous form of ammonia is risky to cultural animals and can irritate the gills and cause respiratory issues (Koteswar et al 2017). The pH and water temperature of the pond affect the ammonia levels. There are several actions that can be taken if the water in the pond contains high amounts of ammonia. It can be compensated by filling the pond with fresh water, reduce the stocking density, and aerate the pond during emergencies as precautions and it will decrease the pH (Koskivaara et al. 1991).

Stocking density

The production of catfish and the profitability of the farms is determined by a major factor called as this stocking density because stocked in density affect the growth, health, water quality and the feeding of the fish. Aquaculture utilizes the natural aquatic resources more efficiently due to which it provides food security and increases the family incomes especially for the underdeveloped countries because of the supply of high-quality nutrition. This causes the reduction in poverty (Kubtiza and Ono 2010). Because stocking density directly influences fish growth and survival, it plays a significant role in determining the aquaculture system's profitability (Gibtan et al. 2008). Fish can be addressed by the highest stocking density which in result causes the decrease in the growth rate of the fish and their final weight (Kamstra, 1993). High stocking density can also affect the survival rate and the feeding of the fish (Stankus, 2021)). A high stocking density, however, also contributes to the producing a large number of fishes, which enhances the biomass production. Because of these relationships between fish growth and stocking density it is compulsory to find out the stocking density of the production system.

Fastest growth ability, ease of cultivation and ability to resist disease are some of the characteristics of the catfish due to which the catfish culture has been increasing (Jamabo and Keremah 2009). The cultivation of the catfish can be done in the high stocking density technology, Biofloc technology (Yusuf et al, 2015). According to the recent research cultivation of the catfish in high density by the use of the Biofloc system allow the cultivation of 50 catfishes in hundred liters of water (Ogunji et al 2008).

Breeding techniques

Breeding techniques for catfish in Pakistan comprise a range of methods that are aimed of boosting aquaculture. Here primarily, emphasizes was given to carp species, but it is now delving into catfish species in order to enhance their production. Usually, catfishes undergo breeding in natural water resources thus they face survival pressure due to water pollution and other prevailing conditions (Khan and Khan 2018). Keeping this fact in mind, induced breeding of few catfishes has been carried out but still these efforts are not enough. In 2014, under Aquaculture and Fisheries Program, NARC, Pakistan, Khan et al. 2014 for the first time undergo induced breeding of Giant Catfish, Sperata seenghala by using different hormonal analogues (ovaprim, HcG, LHRH and ovatide). They reported best performance with HcG with 2 doses at 10 µg/kg. Likewise in 2020, induced breeding of Rita rita was performed by Hayat et al. 2020 at Fish Biodiversity Hatchery Punjab Fisheries Department, Chashma, Mianwali as an initiative for the conservation and domestication of this endangered species. Recently, the acclimatization of Clarias gariepinus has been carried out which leads Ameer et al. 2021 to undergo Comparative study of the efficacy of two different hormones Ovaprim and hMG (menotropin) to induce breeding in exotic Clarias gariepinus at Muzafargarh Fish Hatchery Punjab, Pakistan.

Culture systems

In Pakistan different type of culture systems are used which includes the cage cultures system, pond culture system, recirculating culture system and Biofloc Technology. However, catfish production mainly based on the wild sources, which causes their over exploitation due to high consumer demand. Despite of this fact, very limited work is being carried out on catfish culturing. In 2019, Jalbani et al. 2019 first time undergo rearing of Catfish, Rita rita with Live

and Prepared Feeds in Cemented Cisterns and found that chopped chicken viscera could be good option for its culturing (Jalbani et al. 2019). Likewise, currently Parveen et al. 2022 successfully tried polyculture of P. hypophthalmus with Indian and Chinese carp to achieve sustainable higher production in Pakistan. Besides these, there are many other commercial and economically important catfishes that are present in Pakistan but no published information is available at the moment on their culturing from Pakistan. If culturing of these species could develop, Pakistan would be able to earn a lot of foreign exchange by exporting these fish in future.

• Cage Culture

Globally, the production of the catfishes in different culture system is also increasing day by day. In Europe Asia and Africa, the culturing of the catfishes in the cages have been done successfully (Bardach et al.1972). Previously, in Bangladesh, there is focus on the pond culture for catfish production. (Karim, 1987). But now because of large number of the water bodies the aquaculture industry is focusing on catfish production through cages culture.

Besides this, by using the combination of the catfishes and tilapia many of the integrated systems are being practiced and developed (Marshall and Levy 2011). Stocking of species with different feeding habitats is done in the polyculture because there targeting the high valued species is not possible. In most intense culture systems, the nutrient utilization efficiency is 30% (Beveridge and Phillips, 1993). However, with the integrated cage cum pond system, the nutrient consumption efficiency is 50%, resulting in significantly less odor emission into the surrounding area (Yi, 2001).

• Recirculating culture system

An enclosed system known as a recirculating aquaculture system simply replaces the water that is lost during evaporation and cleaning processes. Management of the waste and the recycling of the nutrients are the opportunities provided by the recirculating culture system (Piedrahita, 2003). This method also improves hygiene and disease management (Summerfelt et al., 2005). In this, a wide variety of organisms can be raised, including a wide range of species from freshwater to seafood products and fingerlings to grow-out production (Davis and Arnold, 1998). Recirculating aquaculture systems are primarily concerned with nutrient recycling through integrated farming and technological advancement (Martins et al., 2010a). The aquaculture community in the United States and other countries are very interested in recirculating systems in aquaculture (Xie et al, 2007). Beginners can learn how to manage and keep the system in good working order so that fish or other aquaculture plants and animals can be raised in a healthy environment. Regarding quantity, China produces around 67% of the world's aquaculture products while accounting for 49% of the total value in 2006 (FAO, 2008). A number of significant issues related to this industry have recently arisen in China, including the country's limited land and water resources along with the ongoing degradation of the aquatic ecosystem, various disease outbreaks, and challenges with wastewater and sediment treatment (El-Olemy et al. 2014). New culture methods are being preferred in order to reduce waste production, meet fuel demands, and optimize water usage. A recirculating aquaculture system is an aquatic system built on land in which the water is partially reused following mechanical and biological treatments in order to reduce water and energy usage, as well as the release of nutrients into the environment (Martins et al., 2011).

• Pond raceway system

In 2008 a large number of the channel catfish production was reported (USDA, 2009). The production was 92% in Alabama, Mississippi and Texas. In Alabama the channel catfish production sector is the most important sector in the aquaculture industry (USDA, 2009). Primarily the production of the channel catfishes is done in the watershed ponds or in the embankment ponds. After culturing the catfishes are harvested by seining. The production of channel catfishes in ponds can be significantly increased if it is raised through various ways that maintain water quality (Boyd and Tucker, 1998). Traditionally, production of the channel catfish in the ponds produces 5000 kg/

ha of catfish and the maximum production is about 7000 kg/ha. The production increases to 10,000 kg /ha in Alabama but there is lack of proper aeration for maintaining dissolved oxygen (Boyd and Hanson, 2010). An optimum value of the feed Conversion ratio is required for the proper ponds management. The average value of FCR is 1.6-1.8 which is considered to be the best value for pond management (Boyd and Tucker, 1998). For more profit and sustainability, the catfish farming should be well managed and efficient. So, in addition to the improvement in the fish production in the ponds there is the high need of using different efficient techniques for catfish productions.

The pond raceway culture consisted of the raceways which had the highest stocks of the catfish fingerlings. Water circulation is facilitated through the cultural unit, and an airlift pump is also utilized in the process. A good waste management system is used to remove the body solid fish waste from the raceway ends (Hawcroft et al 1994). In addition to that this system was successful in the research setting but this system also had some disadvantages due to unequal water flow and poor solid waste removal system (Tucker and Kingsburg, 2009). In Pakistan in 2015, an important catfish species Sperata seenghala was first time introduced in culture system by utilizing both indoor fiberglass circular tanks and outdoor concrete raceways (Ali et al. 2015).

• Biofloc system

The production of the catfish can be increased by the use of a Biofloc system in close containers. These systems allow the cultivation of the catfish in high density thus increasing the production of catfish (Kareem et al 2015). Basically, the Biofloc system is the collection of various organisms that includes the algae fungi bacteria protozoa. The cultivation of the catfish in high density produces more waste so a regular stirring is to be done for the removal of the waste. The Biofloc systems increase the ratio of carbon and nitrogen by the addition of organic carbohydrate which stimulates the growth of heterotrophic bacteria. By using probiotics in Biofloc, you may improve the water's quality, increase the amount of nutrients for feed, and prevent harmful bacteria (Yusuf et al 2015).

It is a successful enterprise to cultivate catfish in high density using a Biofloc method. For small-scale or domestic industries, this may be a good option. More research has revealed that in such systems, it is simple to determine the survival rate of the fish, food conservation ratio, total revenue, and profit. Additionally, studies also inferred that the business's R/C ratio runs from 1.47 to 1.68, demonstrating its high profitability (Hilge, 1981).

Diseases

Any disorder that affects an aquatic animal's regular physiological processes is considered a disease. Fish illness outbreaks raise production costs due to the investment in dead fish, treatment expenditures and reduction in development during restoration (Khalil et al., 2001). We are less aware of fish disease concerns in nature because predators quickly remove unhealthy species from the community. Under natural circumstances, parasites and bacteria might not be significant, but in captivity, where animals are overpopulated and stressed, they can cause serious issues (Locke, 2010).

Protective Barriers against Infection

Fish have four infection-resistance mechanisms:

• Mucus

• Scales and skin

• Inflammation

• Antibodies

A physical barrier known as mucus (slime coat) prevents disease-causing organisms from entering fish from the environment. It also functions as a chemical barrier since it has lysozymes

and immunoglobulins, which can destroy pathogens (Elsherief et al, 2014). In addition to lubricating the fish and facilitating movement through the water, mucus is crucial for osmoregulation. The fish's skin and scales serve as a physical barrier to prevent harm. A window gets opened for bacteria and other organisms to begin an infection when this barrier got damaged.

A biological, non-specific response to an invasive protein is inflammation (Hien, 2008). An invasive protein could manifest as a bacterium, virus, parasite, fungus, or toxin. Pain, bloating, redness, heat, and loss of function are all signs of inflammation. It is the body's protective response and an effort to wall off and eliminate the invader. A particular cellular response, antibodies are molecules created to defend against invasive proteins or organisms (Dung 2008). When a fish is exposed to an invader for the first time, antigen antibodies develop to prevent the fish from infection by the same organism in the future. Additionally, for a fish to develop an effective immune system, exposure to sub-lethal levels of pathogens is crucial. A sterile environment will provide little immunity to disease in an animal (Elsherief et al, 2014).

Disease Types

Fish are susceptible to both infectious and noninfectious diseases. Pathogenic organisms may be found in the environment or transported by other fish (Olatoye and Basiru, 2013). They are infectious, and some type of treatment may be needed to control the disease outbreak. Noninfectious diseases, on the other hand, are brought on by environmental issues, nutritional deficits, or genetic defects. Noninfectious diseases are not transmissible and may not have any treatment options available.

Infectious Diseases

• Parasitic Disease

Most often, minute creatures called "protozoa" that exist in the aquatic environment are the cause behind parasitic infections in fish. Fish that have protozoan infestations in their gills and skin experience itching, weight loss, and eventually death (Young and Blenden, 2011). The majority of protozoan infections can be effectively treated with common fisheries chemicals like copper sulphate, formalin, or potassium permanganate (Plumb, 1997).

As fishes act as the host for various tapeworm species so it becomes source of nourishment for parasites. As a result, the host gets worse and develops other illnesses. Large numbers of eggs are produced by parasites, and many of them go through different stages of their life cycle in several hosts.

Tapeworms

The catfish tapeworm (Corallobothrium fimbriatum and Ligula intestinalis), the Asian tapeworm (Bothriocephalus opsarichthydis), the bass tapeworm (Proteocephalus ambloplitis), and others are among the causative organisms. The type of tapeworm varies with the species of host fish. All fish are vulnerable, but black basses, Chinese carps, catfishes, sunfishes, and golden shiners are particularly sensitive (Serrano, 2005). Fish frequently not show any visible symptoms, but they may become sluggish lose weight, or become sterile. In rare cases, such as severe Asian tapeworm infections in grass carp, the abdomen swells and the intestines get blocked. Tapeworm presence is determined by microscopic examination (Burridge 2006).

The use of tapeworm-infected broodfish, purchasing infected fry and fingerlings, or exposure to surface water containing hosts for tapeworms all increase the risk of infection. Tapeworms may also be introduced via the droppings of fish-eating birds in and around the pond. Aquaculturalists avoid keeping or purchasing contaminated fry, fingerlings, and broodfish. They drain, dry, and disinfect ponds between fish crops, eliminating or reducing exposure to intermediate hosts. Currently, no treatment drugs are available. (Lillehaug et al, 2003).

• Bacterial Disease

Internal infections caused by bacteria are frequently bacterial diseases that need to be treated with medicated diets containing antibiotics that have been approved for use in fish by the Food and Drug Administration (Saad et al., 2014). Fish with bacterial infections frequently develop hemorrhagic spots or ulcers along the body wall and in the vicinity of their eyes and mouths. Additionally, they could have bulging eyes and an inflated, fluid-filled belly. External bacterial infections are also possible; they can cause skin erosion and ulceration. Rough treatment has been linked to external bacterial infections like Columnaris (Singh and Lakra, 2011).

Besides this, certain antibiotics are in use but due to certain factor such as development of disease resistance in microbe, this method is not much appreciated by researchers. A recent study was reported by Mahmood et al. 2023 revealed that Aeromonas hydrophila that infected Sperata sarwari (Singharee) of different wild sites i.e. Head Baloki, Head Trimmu, Head Taunsa and Head Chashma got resistance against different antimicrobials i.e. sulfamethoxazole, ampicillin, neomycin, and norfloxacin. To get rid of this, currently other methods i.e. vaccines and probiotics, herbal treatments etc are being preferred globally for disease prevention.

• Viral Disease

Without specialized laboratory tests, it is hard to differentiate between bacterial and viral diseases. There are no specific treatments for fish viral infections, and they are challenging to diagnose. Although not all viral diseases have vaccines, immunization can shield fish against them.

• Fungal Disease

The fourth category of infectious diseases includes fungi. Although they are prevalent in the aquatic environment, healthy fish are usually unaffected by fungus spores. Fungi may infect sick tissue on the outer layer of fish when the fish are infected with an external parasite or bacterial infection or have been hurt during handling (Uedeme-Naa and Nwafili, 2017). When the fish is removed from the water, these areas may appear as brown matted areas or to have a cottony growth. For the majority of fungal infections, potassium permanganate is beneficial. Fungi are frequently a secondary problem, thus it's critical to identify and address the primary issues (Lumanlan-Mayo et al, 1996).

Table 2. Prevalence of catfish infectious diseases in Pakistan

Species	**Locality**	**Pathogen**	**Prevalence (%)**	**Reference**
Sperata sarwari (Singharee)	Lahore, Punjab	Copepod parasites (Lernaea)	26.66%	Batool et al. 2022
Sperata sarwari (Singharee)	Punjab (Head Baloki, Head Trimmu, Head Taunsa, Head Chashma)	Aeromonas hydrophila (bacteria)	6.25%	Mahmood et al. 2023
Arius arius, Arius caelatus, Arius dussumieri, Arius sona	Karachi coast, Sindh	Nematode parasites (Raphidascaris acus larvae, Metabronema magnum, Haplonema immutatum and Hedruris bryttosi)	22.22%	Sattar et al. 2016

Species	Locality	Pathogen	Prevalence (%)	Reference
Rita rita	River Punjkorha, KPK	Ectoparasite (Rhobdocorna magna, Camallanus, Senga taunsaensis and Helicometra fasciata)	33.4%	Ayaz et al. 2013
Mystus vittatus	River Punjkorha, KPK	Ectoparasite (Rhobdocorna magna, Camallanus, Senga taunsaensis and Helicometra fasciata)	22.2%	Ayaz et al. 2013

Non-Infectious Diseases

Environmental, dietary, and genetic factors can largely be categorized as noninfectious disorders. The most significant environmental diseases are major threat to commercial aquaculture. Low dissolved oxygen, high ammonia, high nitrite, or natural or man-made contaminates in the aquatic environment are examples of environmental diseases. Producers can stop the majority of environmental diseases with the right methods for regulating water quality (FDA, 2016).

To mitigate the disease frequency, it is necessary to understand the epidemiology of diseases along with the implementation of their risk analysis procedures. In intensive farming, keeping a good balance between the environment, the fish being raised, and disease-causing agents is tough but really important.

Environment sustainability

The external aquatic environment is directly linked with the sustainability of catfish farming. The main source of the pollution that degrades the water quality is said to be the immense amount of effluent that comes from catfish ponds that cannot be handled. The high seed mortality in many of the places is correlated with the low water quality. Therefore, for the sustainability of the catfishes, control of these effluent and thus water quality is necessary. Different efforts have been adapted for reducing the environmental pollution which include registration of new farms, establishment of new farms, demonstration and encouragement for supply of good agricultural practices. In addition to that reduction in stocking density are also suggested for in order to reduce the pollution.

High economic returns

The farming of the catfishes required a high level of investment for the infrastructural building operating cost that includes the feed and seed cost and the investment for the land. In the case of fishes, the production cost and the net profit are relatively lower than that of production cost and net profit of other species but still total net profit of the fishes per hectare is much higher than the other species because of the high productivity. The cost for the production is increasing day by day. In 2006 the production cost for the catfishes farming was reported to be 0.59 dollar per kg but in 2008 (Hien 2008) the production cost for the catfish was 0.70 kg per hectare.

Availability of the markets

The fast expansion of the catfish farming industry is linked with the accessibility of the export market. Over time, the markets for catfish fillets expected to continue to expand. White flesh fish are being replaced by striped catfish (Lin CK 1990). Before 2003 there were much limitations in the export markets of the striped catfishes, among which the US exporters was the most important one. Now the export of catfish was done to over 80 countries worldwide. In these 80 countries the markets shared about 48 percent in the European countries 9.2% in the Russia and 6.9% in US (Dung 2008). By improving the product quality with expansion of the export market the production

can be increased at a high rate.

Conclusion

Pakistan has high potential for catfish aquaculture as it is enriched with the resources that can assist in the aquaculture sector. Current article recommended some strategies that need to be adopted for the successful expansion of this sector. Advanced farming technologies should be adopted instead of traditional methods for expanding this sector at global level. The intensive farming systems should be the priority of the farmers which will lessen the deterioration caused by climatic change, pollution and overfishing etc. Furthermore, Farmers training and education should be utmost priority for promotion and strengthening of this sector.

Recommendation

To promote catfish culturing, following strategies are suggested for Research, farmers and government sectors regarding aquaculture in Pakistan

• Focusing on propagating catfish culture and their breeding techniques just like carp culture that can been standardized or transferred to fish farmers.

• Established breeding and rearing techniques for economically important exotic catfish species.

• The development and use of high-quality, catfish-specific feeds with alternative protein sources.

• Exploring the use of vaccines, herbal treatments and probiotics for disease prevention.

• Improving infrastructure and developing effective marketing channels to connect catfish farmers with domestic and international markets.

• Establishment of the stocking and conservation programs for the production of those catfishes whose stock is continuously declining.

Besides this, it is also necessary to organize aquaculture extension leadership and training programs in Pakistan to create awareness on substantial fluctuations in climatic variables. One proposed solution is to establish a more inclusive framework by training trainers from neighboring countries renowned for their innovative aquaculture industries, thus fostering increased capabilities and resilience in the face of environmental challenges.

REFERENCES

Abdul, R., Muhammad, A., Asim, A., Ali, M.R., Khan, S.U., Khan, M.F., Sultan, M. and Mazhar, Q., 2007. Introduction of channel catfish Ictalurus punctatus (Rafinesque) in Pakistan and its performance during acclimatization and pond culture. Pakistan Journal of Zoology, 39(4), pp.239-244.

Afreen, M., Ucak, İ. and Bagdatli, M.C., 2022. The analysis of climate variability on aquaculture production in Karachi of Pakistan. International Journal of Engineering Technologies and Management Research, 9(8), pp.16-23.

Ahmad M, Shah AH, Maqbool Z, Khalid A, Khan KR, Farooq M. 2020. Ichthyofaunal diversity and conservation status in rivers of Khyber Pakhtunkhwa, Pakistan. Proceedings of the Int. j. ecol. environ. sci. 10(4): 131-143.

Alexander, T.W., Inglis, G.D., Yanke, L.J., Topp, E., Read, R.R., Reuter, T. and McAllister, T.A., 2010. Farm-to-fork characterization of Escherichia coli associated with feedlot cattle with a known history of antimicrobial use. International journal of food microbiology, 137(1), pp.40-48.

Ali, M.R., Muhammad Afzal, M.A. and Shamim Akhter, S.A., 2015. Transportation and

acclimatization of giant river catfish Sperata seenghala (Sykes): an attempt for its induction in culture system.

Altaf M, Javid A, Khan AM, Hussain A, Umair M, Ali Z. 2015. The status of fish diversity of river Chenab, Pakistan. J Animal Plant Sci. 25(3): 564-569. Analysis version 7.0 for bigger data sets. Molec. Biol. Evol. 33: 1870–1874.

Ameer, M.W., Jabeen, F., Asad, M., Kaukab, G., Bashir, A., Rasheed, M., Younis, H., Munir, N., Nawaz, J., Zainab, R. and Akram, M., 2021. Comparative efficacy of Ovaprim and hMG (menotropin) to induce breeding in African catfish (Clarias gariepinus). Fish Physiology and Biochemistry, 47(5), pp.1559-1564.

Arias, C.R., Cai, W., Peatman, E. and Bullard, S.A., 2012. Catfish hybrid Ictalurus punctatus× I. furcatus exhibits higher resistance to columnaris disease than the parental species. Diseases of aquatic organisms, 100(1), pp.77-81.

Ariño, A., Beltrán, J.A., Herrera, A. and Roncalés, P., 2013. Fish and seafood: Nutritional Value Encyclopedia of Human Nutrition (pp. 254-261).

Assefa, A., Regassa, F., Ayana, D., Amenu, K. and Abunna, F., 2019. Prevalence and antibiotic susceptibility pattern of Escherichia coli O157: H7 isolated from harvested fish at Lake Hayq and Tekeze dam, Northern Ethiopia. Heliyon, 5(12).

Ayaz, S., Khan, M.A., Rehman, I.U., Anwar, M., Saeed, S. and Zarin, S., 2013. Prevalence of endoparasites in fresh water fishes in River Punjkorha, Khyber Pukhtunkhwa Pakistan. International Journal of Biology, Pharmacy and Allied Sciences, 2(1), pp.111-115.

Bardach, J.E., Ryther, J.H. and McLarney, W.O., 1972. Aquaculture: the farming and husbandry of freshwater and marine organisms. (No Title).

Barrows, F.T., Stone, D.A. and Hardy, R.W., 2007. The effects of extrusion conditions on the nutritional value of soybean meal for rainbow trout (Oncorhynchus mykiss). Aquaculture, 265(1-4), pp.244-252.

Basharat, H., Ali, M.R., Ahmed, A., Kausar, R. and Akhter, S., 2023. Effects of feeding levels on production characteristics of pond-raised African catfish in pond culture system of Pakistan. Sarhad Journal of Agriculture, 39(1), pp.166-173.

Basharat, H., M.R. Ali, M.M. Shahid, A. Ahmed and S. Akhter. 2020. Introduction of African catfish (Clarias gariepinus) in aquaculture system of Pakistan: Its transportation, acclimatization and cannibalism study. Pak. J. Agric. Sci., 56(6): 1645-1652.

Batool, T., Latif, A.A. and Sarwar, S., 2022. Study of Various Ectoparasites from Sperata Sarwari (Singharee) Obtained from Various Areas of Lahore, Pakistan: Ectoparasites From Sperata sarwari (Singharee) Obtained From Lahore. MARKHOR (The Journal of Zoology), pp.16-19.

Beveridge MCM, and MJ Phillips, 1993. Environmental impacts of tropical inland aquaculture. In:Pullin R. S. V., H. Rosenthal and J L Maclean, Editors.

Bilal, W. and Khan, A.M., Pros and cons of alien fish introductions: a case scenario from Pakistan. VOLUME 19 ISSUE 03 MARCH 2023

Bohl, M., 1989. Optimal water quality-basis of fish health and economical production. Current trends in fish therapy, pp.18-32.

Boyd CE and Hanson TR. 2010. Dissolved-oxygen concentration in pond aquaculture. Glob Aqua. Advocate 13 (1), 40–41.

Boyd CE andTucker CS. 1998. Pond Aquaculture Water Quality Management. Kluwer Academic Publishers, Boston, MA.

Burridge. 2006. Chemical use in salmon aquaculture: a review of current practices and possible environmental effects. Heavy use of prophylactic antibiotics in aquaculture: a growing problems for human and animal health and for the environment. Environ Microbiol. 2006; 8(7):1137–44.

Das, S., Mondal, K. and Haque, S., 2017. A review on application of probiotic, prebiotic and synbiotic for sustainable development of aquaculture. J. Ent. Zool. Stud., 5: 422-429.

Davis D and Arnold C. 1998. The design, management and production of a recirculating raceway system for the production of marine shrimp. Aqua Eng. 17,193–211.

Ditcharoen S, Antonio Carlos Bertollo L, Rab P, Hnatkova E, Franco Molina W, Liehr T, Pengseng, P. 2019. Genomic Organization of Repetitive DNA Elements and Extensive Karyotype Diversity of Silurid Catfishes (Teleostei: Siluriformes): A Comparative Cytogenetic Approach. Int. J. Mol. Sci. 20(14): 3545

Dung NH. 2008. Achieving a sustainable future for the Vietnamese seafood industry. Keynote Speech at the IIFET 2008 Conference, Nha Trang, Vietnam, July 22–25.

Dunham, R.A., Umali, G.M., Beam, R., Kristanto, A.H. and Trask, M., 2008. Comparison of production traits of NWAC103 channel catfish, NWAC103 channel catfish× blue catfish hybrids, Kansas Select 21 channel catfish, and blue catfish grown at commercial densities and exposed to natural bacterial epizootics. North American Journal of Aquaculture, 70(1), pp.98-106.

El-olemy, G.M.; Lobna, M.A.; Salem, N.;Khalifa, O. and Abd el wahab, M.S.2014. Detection of some bacterialzoonosis in market fish in Qalyoubiaprovince and their control.BenhaVeterinary Medical Journal,26(2):126-136.

Elsherief MF, Mousa MM, Abd El-Galil H, El-Bahy EF. 2014. Enterobacteriaceae associated with farm fish and retailed ones. Alex J Vet Sci. 42: 99-104.

Faheem, M., S. Khaliq and K.P. Lone. 2019. Effect of Bisphenol-A on serum biochemistry and Liver Function in the freshwater Fish, Catla catla. Pak. Vet. J. 39:71-75.

FAO (2004). Fisheries in irrigation systems of arid Asia. FAO Fisheries Technical Paper 430, Rome, 150pp.

FAO (2014) FAO year book, Fishery and Aquaculture Statistics, Food and Agriculture Organization of the United Nations, Rome.

FAO (2020) The State of World Fisheries and Aquaculture-Contributing to food security and nutrition for all. Fisheries and Aquaculture Department, Food and Agriculture Organization of the United Nations, Rome pp: 200.

FAO (Food and Agriculture Organization). State of World Fisheries and Aquaculture 2020. Rome: FAO; 2020

FAO, Food and Agriculture Organization of the United Nations, 2020. The state of world fisheries and aquaculture. Sustainability in action. Food and Agriculture Organization of the United Nations. Rome.

FAO. 2006. Introduced species database. FIGIS. 1-3. www.fao.org/figis.

FAO. 2014. The State Of World Fisheries and Aquaculture. http://www.fao.org /docrep/009/af000e/af000e00.HTM

FAO. 2018. The state of world fisheries and aquaculture.

FDA. NADA number: 038-439. 2016 [cited 2016 2 January]; Available from: FDA. NADA number: 141-246. 2016. [cited 2016 2 January]; Available from: http://www.accessdata.fda.gov/scripts/animaldrugsatfda/details.cfm?d=141-24 6.

Ferraris CJ. 2007. Checklist of catfishes, recent and fossil (Osteichthyes: Siluriformes), and catalogue of siluriformes primary types. Zootaxa. 1418(1): 1-628.

Ferraris, C.J., 2007. Checklist of catfishes, recent and fossil (Osteichthyes: Siluriformes), and catalogue of siluriform primary types. Zootaxa, 1418(1), pp.1-628.

Fiess, J. C., Kunkel-Patterson, A., Mathias, L., Riley, L. G., Yancey, P. H., Hirano, T. and Grau, E. G. (2007).Effects of environmental salinity and temperature on osmoregulatory ability, organic osmolytes, and plasma hormone profiles in the Mozambique tilapia (Oreochromis mossambicus). Comparative Biochemistry and Physiology Part A: Molecular and Integrative Physiology, 146(2): 252-264.

Fricke R, Eschmeyer WN, Fong JD. 2019. Species by family/subfamily. Eschmeyer's catalog of fishesRafique, M. and Khan, N.U.H., 2012. Distribution and status of significant freshwater fishes of Pakistan. Rec. Zool. Surv. Pakistan, 21, pp.90-95.

Garcia-Rodríguez, F.G. and De La Cruz-Aguero, J., 2011. Review on post-harvest losses in artisanal fisheries of some African countries. Fish. Aquat. Sci, 6(2), pp.186-193.

Gibtan, A., Getahun, A. and Mengistou, S., 2008. Effect of stocking density on the growth performance and yield of Nile tilapia [Oreochromis niloticus (L., 1758)] in a cage culture system in Lake Kuriftu, Ethiopia. Aquaculture Research, 39(13), pp.1450-1460.

Gilani, N., Rafique, M., Akhter, S., Qureshi, H., Shoaib, A. and Ahmad, S., 2020. Studies on the impact of key environmental variables on kashmir catfish (Glyptothorax kashmirensis Hora, 1923) distribution and abundance in Azad Jammu and Kashmir, Pakistan. Kuwait Journal of Science, 47(4).

Hawcroft BA. 1994. Development and evaluation of an in-pond raceway and waste removal system. MS. Thesis, Department of Fisheries and Allied Aquacultures, Auburn University, Alabama

Hayat, S., Ramzan, M., Zafarullaf, M., Ahmad, I., Ali, Q. and Malik, A., 2020. Conservation of an endangered carnivorous fish rita rita through induced breeding. Biological and Clinical Sciences Research Journal, 2020(1).

Hien LL. 2008. Analysis of the supply and demand of striped catfish (Pangasianodon hypophthalmus) in the Mekong river delta. Master Thesis in Department of Fisheries and Allied Aquacultures, Auburn University, Alabama.

Hilge V. 1981. Some aspects of recent developments in the research on fish reproduction. In: Intensive Aquaculture European Mariculture Society, Bredene, Belgium, Special Publication No. 6, 229p.

Hossain, M.J., Sun, D., McGarey, D.J., Wrenn, S., Alexander, L.M., Martino, M.E., Xing, Y., Terhune, J.S. and Liles, M.R., 2014. An Asian origin of virulent Aeromonas hydrophila responsible for disease epidemics in United States-farmed catfish. MBio, 5(3), pp.10-1128.

Imran, M., Khan, A.M., Altaf, M., Ameen, M., Ahmad, R.M., Waseem, M.T. and Sarwar, G., 2021. Impact of alien fishes on the distribution pattern of indigenous freshwater fishes of Punjab, Pakistan. Brazilian Journal of Biology, 82, p.e238096.

IUCN. 2007. The IUCN Red List of Threatened Species. Version 2007-1. Available at: www.iucnredlist.org.

IUCN. 2009. The IUCN Red List of Threatened Species. Version 2009-1. Available at: www.iucnredlist.org.

IUCN. 2019. The IUCN Red List of Threatened Species. Version 2019-1. Available at: www.iucnredlist.org.

IUCN. 2020. The IUCN Red List of Threatened Species. Version 2020-1. Available at: www.iucnredlist.org.

Jalbani, S., Narejo, N.T. and Khan, P., 2019. Rearing of Catfish, Rita rita with Live and Prepared Feeds in Cemented Cisterns. Pakistan Journal of Zoology, 51(6), p.2397.

Jamabo, N.A. and Keremah, R.I., 2009. Effects of stocking density on the growth and survival of the fingerlings of Clarias gariepinus (Burchell, 1822). Journal of fisheries international, 4(4), pp.55-57.

Kamstra, A., 1993. The effect of size grading on individual growth in eel, Anguilla anguilla, measured by individual marking. Aquaculture, 112(1), pp.67-77.

Kareem, O.K. and Olanrewaju, A.N., 2015. Effect of different stocking density on nutrient utilization, growth performance and survival of African Catfish (Clarias gariepinus, Burchell, 1822) fry in recirculatory System. Journal of Fisheries and Aquatic Science, 10(5), p.400.

Karim M, 1987. Pen and cage culture prospective in Bangladesh. ICLARM report, 58 p.

Khalil RH, ST Atallah, MK Soliman, SG Ismail and N Mahfouz. 2001. Economic losses due to fish diseases at the farm level. Aquaculture Europe. [New Species, New Technologies] Trondheim, Norway, August 3-7.

Khalil, M., Azmat, H., Khan, N., Javid, A., Hussain, A., Hussain, S.M., Ullah, A. and Abbas, S., 2018. Growth responses of striped catfish Pangasianodon hypophthalmus (Sauvage, 1878) to exogenous enzyme added feed. Pakistan J. Zool, 50(2), pp.685-693.

Khan RA and Thulin J. 1991. Influence of pollution on parasites of aquatic animals. Advances in Parasitology; 30:202-238.

Khan, I.A. and Khan, M.S., 2018. Developing sustainable agriculture in Pakistan. CRC press.

Khan, M.F., Ali, M.R., Muhammad Afzal, M.A., Abdul Rab, A.R., Awan, M.A. and Aziz Ahmed, A.A., 2014. Induced breeding of giant catfish, Sperata seenghala using hormonal analogues.

Khan, N., Atique, U., Ashraf, M., Mustafa, A., Mughal, M.S., Rasool, F., Azmat, H., Tayyab, M. and Iqbal, K.J., 2019. Effect of various protein feeds on the growth, body composition, hematology and endogenous enzymes of catfish (Pangasius hypophthalmus).

Koskivaara, M., Valtonen, E.T. and Prost, M., 1991. Seasonal occurrence of gyrodactylid monogeneans on the roach (Rutilus rutilus) and variations between four lakes of differing water quality in Finland.

Koteswar, B., Reddy, A.D., Ravi, G. and Karunasagar, I., 2017. Occurrence of pathotypes of Escherichia coli in aquatic environment. Int J Curr Microbiol App Sci, 6, pp.3266-75.

Kubtiza, F. and Ono, E.A., 2010. Family fish farming as a tool for development and food security in rural areas. Aquaculture Overview, 20, pp.14-23.

Kumar, N., Krishnani, K. K., Brahmane, M. P., Gupta, S. K., Kumar, P. and Singh, N. P. (2018). Temperature induces lead toxicity in P. hypophthalmus: an acute test, antioxidative status and cellular metabolic stress. International Journal of Environmental Science and Technology, 15(1): 57-68.

Laghari MY. 2018. Aquaculture in Pakistan: Challenges and opportunities. International Journal of Fisheries and Aquatic Studies. 6(2): 56-59.

Laghari, M.Y., 2018. Aquaculture in Pakistan: Challenges and opportunities. International Journal of Fisheries and Aquatic Studies, 6(2), pp.56-59.

Leary, J.L., 1910. Propagation of crappie and catfish. Transactions of the American Fisheries Society, 39(1), pp.143-148.

Lillehaug A, Lunestad BT and Grave K. 2003. Epidemiology of bacterial diseases in Norwegian aquaculture a description based on antibiotic prescription data for the ten-year period 1991 to 2000. Dis Aquat Org; 53(2):115–25

Lin CK. 1990. Integrated culture of walking catfish (Clarias macrocephalus) and tilapia (Oreochromis niloticus). Int J Curr Micro App Sci.. 4(9):pp. 209–212.

Locke JB. 2010. Evaluation of Streptococcus iniae killed bacterin and live attenuated vaccines in hybrid striped bass through injectionand bath immersion. Dis Aquat Org. 89(2):117–23.

Lumanlan-Mayo SC, Cruz-Lacierda ER and De la Peña LD. 1996. The use of chemicals in aquaculture in the Philippines. Tigbauan. p. 155–184.

Mahmood, S., Rasool, F., Hafeez-ur-Rehman, M. and Anjum, K.M., 2024. Molecular characterization of Aeromonas hydrophila detected in Channa marulius and Sperata sarwari sampled from rivers of Punjab in Pakistan. Plos one, 19(3), p.e0297979.

Mahmoud, N.E., M.M. Fahmy, M.M. Abuowarda, M.M. Zaki, E. Ismael and E.M. Ismail. 2019. Influence of water quality parameters on the prevalence of Livoneca redmanii (Isopoda; Cymothoidae) infestation of Mediterranean sea fishes, Egypt. Inter. J. Vet. Sci. 8:174-181.

Malik, Y., Ackakzai, W.M., Mustafa, S., Saddozai, S. and Akbar, A., 2023. Accumulation of heavy metals and detection of resistant-associated genes in Pseudomonas aeruginosa in an edible catfish (Wallago attu) from Pat Feeder Canal, Pakistan. Iranian Journal of Fisheries Sciences, 22(3), pp.602-614.

Marshall, B.M. and Levy, S.B., 2011. Food animals and antimicrobials: impacts on human health. Clinical microbiology reviews, 24(4), pp.718-733.

Martins, C.I., Eding, E.H. and Verreth, J.A., 2011. The effect of recirculating aquaculture systems on the concentrations of heavy metals in culture water and tissues of Nile tilapia Oreochromis niloticus. Food Chemistry, 126(3), pp.1001-1005.

Martins, C.I.M., Eding, E.H., Verdegem, M.C., Heinsbroek, L.T., Schneider, O., Blancheton, J.P., d'Orbcastel, E.R. and Verreth, J.A.J., 2010. New developments in recirculating aquaculture systems in Europe: A perspective on environmental sustainability. Aquacultural engineering, 43(3), pp.83-93.

Mehboob, A., Khan, N., Atiq, U., Iqbal, K.J., Tayyab, R., Batool, S.S., Batool, H.S., Amjad, S. and Tanveer, M., 2017. Effect of fenugreek as a feed additive on the growth, body composition and apparent nutrients digestibility of striped catfish Pangasius hypophthalmus fry. Pakistan Journal of Zoology, 49(6).

Mirza ZS, Mirza MR, Mirza MA and Sulehria AQK. 2011. Ichthyofaunal Diversity

Mirza, M.R., 2003. Checklist of freshwater fishes of Pakistan.

Mohsin M, Yongtong M, Hussain K, Mahmood A, Zhaoqun S, Nazir K, Wei W. 2015. Contribution of fish production and trade to the economy of Pakistan. Mar Sci Technol. 5.

Moyle, P.B., 1976. Inland fishes of California. Univ of California Press.

Muhammad N, Umair M, Khan AM, Yaqoob M, Ashraf S, Haider MS, Iqbal KJ. 2019. Statistical analysis of freshwater fishes of head Khanki, Punjab, Pakistan. Journal of Wildlife and Ecology. 3(1): 1-9.

Muhammad, H., Iqbal, Z., Bashir, Q. and Hanif, M.A., 2017. Length-weight relationship and condition factor of cat fish species from Indus River, Pakistan. Punjab University Journal of Zoology, 32(1), pp.35-38.

Natl. 2012. Catfish processing. Agric.Stat. Serv., Washington, DC. 02- 21-2012.pdf.

Nazir K, Mu Y, Hussain K, Kalhoro MA, Kartika S and Mohsin M. 2016. A study on the assessment of fisheries resources in Pakistan and its potential to support marine ecology. Ind J Geo-Mar Sci; 45(9):1181-1187.

Noman, M., Mu, Y.T., Abbas, S., Mohsin, M. and Mehak, A., 2018. Estimation of maximum sustainable harvest levels of sea catfishes in Sindh, Pakistan. JAPS: Journal of Animal & Plant Sciences, 28(5).

Nowsad, A.A., Hossain, M.M., Hassan, M.N., Sayem, S.M. and Polanco, J.F., 2015. Assessment of post harvest loss of wet fish: a novel approach based on sensory indicator assessment.

Ogello, E.O., Munguti, J.M., Sakakura, Y. and Hagiwara, A., 2014. Complete replacement of fish meal in the diet of Nile tilapia (Oreochromis niloticus L.) grow out with alternative protein sources: A review. Int. J. Adv. Res., 2: 962-978.

Ogunji, J., Schulz, C. and Kloas, W., 2008. Growth performance, nutrient utilization of Nile tilapia Oreochromis niloticus fed housefly maggot meal (magmeal) diets. Turkish Journal of Fisheries and Aquatic Sciences, 8(1), pp.141-147.

Olaleye, V.F., 2005. A review of reproduction and gamete management in the African catfish Clarias gariepinus (Burchell). Ife journal of Science, 7(1), pp.63-70.

Olatoye IO and A Basiru. 2013. Antibiotic usage and oxyteracycline residue in African catfish (Clarias gariepinus in Ibadan, Nigeria), W J Fish and Mari Sci. 5 (3): 302-309.

Perveen, S., Khan, N., Yin, F., Rasool, F., Wang, C., Butt, M. and Irm, M., 2023. Development of Pangasius hypophthalmus polyculture production in Pakistan when cultured with freshwater and Chinese carps. Aquaculture International, 31(5), pp.2727-2741.

Piedrahita RH. 2003. Reducing the potential environmental impact of tank aquaculture effluents through intensification and recirculation. Aquaculture 226, 35–44.

Pirarat K, Khunrae T, Rattanapong R, Vanichviriyakit and S Senapin. 2017. Emergence of tilapia lake virus in Thailand and an alternative semi-nested RT-PCR for detection. Int J Aqua. 476: 111-118.

Plumb JA. 1997. Infectious diseases of tilapia. J Life Sci. 476: 111-118.

Pourjafar, A., 2007. A comprehensive guide to grow rainbow trout. Parto Vaghe'eh publications. Tehran. Iran. P, 106.

Punhal L, Laghari MY, Waryani B, Hussain I, Khooharo AR, Sun X, Zhang Y. 2018. Genetic diversity and phylogenetic relationship of catfish Order Siluriformes inferred from mitochondrial gene sequence variation. Acta. Sci. Agri. (ISSN: 2581-365X). 2(5).

Rejab, M.R.M., Manam, N.K.A., Fauzi, N.S., Mohamed, S. and Ngah, N., 2020. Ecotoxicity of Furcraea gigantae leaves on nontarget organism. Biosci. Res., 17, pp.64-70.

Rossignoli, C.M., Obi, C., Ali, S.A., Ullah, N., Khalid, S., Hafeez, M. and Shah, S.M.H., 2023. Production system and challenges of saline aquaculture in Punjab and Sindh provinces of Pakistan. Frontiers in Aquaculture, 2, p.1302571.

Saad TT, SAA Ketkat and FA Mohamed. 2014. Changes associated with pseudomonas infection in cultured Oreochromis species and its relations to economic losses of fish production farms. J Life Sci research, 2:184-190

Samuel L, Marian MM, Apun K, Lesley MB and Son R. 2011. Characterization of Escherichia coli isolated from cultured catfish by antibiotic resistance and RAPD analysis. Int F R J. 18(3):971-976.

Sapkota, A., Sapkota, A.R., Kucharski, M., Burke, J., McKenzie, S., Walker, P. and Lawrence, R., 2008. Aquaculture practices and potential human health risks: current knowledge and future priorities. Environment international, 34(8), pp.1215-1226.

Sattar, A., Khan, A., Khatoon, N. and Mujahid, A., 2016. Occurrence of some nematode parasites in the gastrointestinal tract of Ariidae (Teleostei: Siluriformes) catfish, Arius arius (Hamilton, 1822) from Karachi coast. Sarhad Journal of Agriculture, 32(4).

Senthilkumaran, B. and Kar, S., 2021. Advances in reproductive endocrinology and neuroendocrine research using catfish models. Cells, 10(11), p.2807.

Serrano PH. 2005. Responsible use of antibiotics in aquaculture. FAO. Fish Tech Pap. 2005; 469:21–4.

Shah SBH, Mu Y, Abbas G, Pavase TR, Mohsin M, Malik A, Soomro M A. 2018. An economic analysis of the fisheries sector of Pakistan (1950-2017): Challenges, opportunities and development strategies. International Journal of Fisheries and Aquatic Studies. 6(2): 515-524.

Shah, S.A., Malik, A., Kalhoro, H., Kalhoro, I.B., Wadhar, G.M. and Maher, G.M., 2014. Growth performance of exotic catfish Pangas, Pangasius hypophthalmus (Sauvage, 1878) at Fish Hatchery ChilyaThatta, Sindh, Pakistan. Sindh University Research Journal-SURJ (Science Series), 46(2).

Singh AK and WS Lakra. 2011. Risk and benefit assessment of alien fish species of the aquaculture and aquarium trade into India. Reviews in Aquaculture, 3: 3–18.

Stankus, A., 2021. State of world aquaculture 2020 and regional reviews: FAO webinar series. FAO aquaculture newsletter, (63), pp.17-18.

Summerfelt, R.C. and Penne, C.R., 2005. Solids removal in a recirculating aquaculture system where the majority of flow bypasses the microscreen filter. Aquacultural Engineering, 33(3), pp.214-224.

Tripathi, S., Purchase, D., Chandra, R., Nadda, A.K. and Chaturvedi, P., 2023. Emerging pollutants characterization, mitigation and toxicity assessment of sewage wastewater treatment plant-India: a case study. Journal of Contaminant Hydrology, 254, p.104139.

Tucker CS and Kingsburg S. 2009. A split-pond aquaculture system for growing catfish: Catfish Farmers of America Meeting, March 5–7.

Turan, F., Eken, M., Ozyilmaz, G., Karan, S. and Uluca, H., 2020. Heavy metal bioaccumulation, oxidative stress and genotoxicity in African catfish Clarias gariepinus from Orontes river. Ecotoxicology, 29, pp.1522-1537.

Uedeme-Naa B and SA Nwafili. 2017. Influence of African catfish (Clarias gariepinus) size on fingerlings growth rate. App. Sci. Report., 19 (3): 85-88.

USDA and NASS. 2009. Production and Inventory of Channel Catfish. United States Department of Agriculture, Washington, DC.

Van der Waal, B.C.W., 1998. Survival strategies of sharptooth catfish Clarias gariepinus in desiccating pans in the northern Kruger National Park. Koedoe, 41(2), pp.131-138.

Wang, J., Lu, B., Zan, R., Chai, J., Ma, W., Jin, W., Duan, R., Luo, J., Murphy, R.W., Xiao, H. and Chen, Z. 2016: Phylogenetic Relationships of Five Asian Schilbid Genera Including Clupisoma (Siluriformes: Schilbeidae). PLoS ONE, 11(1): e0145675. doi: 10.1371

Watanabe T and Pongmaneerat J. 1993. Potential of Soybean Meal as a Protein Source in Extruded Pellets for Rainbow Trout. Noppon Suisan Gakkaishi, 59(8), 1415-1423.

Welcomme, R.L. ed., 1988. International introductions of inland aquatic species (Vol. 294). Food & Agriculture Org..

Xie B, and Yu KJ. 2007. Shrimp farming in China: Operating characteristics, environmental impact and perspectives. Ocean Coast. Manage. 50, 538–550.

Yi Y and CK Lin, 2001. Effects of biomass caged Nile tilapia (Oreochromis niloticus) and aeration on the growth and yields in an integrated cage-cum-pond system. Aquaculture, 195: 253–267.

Young WP and M Blenden. 2011. Chinook salmon (Oncorhynchus tshawytscha) spawning ground surveys in the South Fork Salmon River and Big Creek, 1996–2008.

Yusuf MW, Utomo NBP, Yuhana M, Widanarni. Growth performance of catfish (Clarias gariepinus) in biofloc-based super intensive culture added with Bacillus sp. Journal of Fisheries and Aquatic Science. 2015;10(6):523–532.

About The Authors

Dr. Shahid Sherzada is currently working as Assistant Professor, Department of Zoology Government College University Lahore. Previously he served as Lecture in two well known institutions, UVAS and Virtual University of Pakistan. He has earned is PhD degree in Zoology from University of the Punjab Lahore Pakistan. His field of interest is Aquatic Ecology and Biotechnology. He has published 32 research articles in well reputed National and International impact factor journals. He has supervised and co-supervised 40 Graduate/Postgraduate students in field of Zoology/Fisheries and Aquaculture. His future goals are to work for management and conservation of sustainable aquatic resources.

Email: shahid.sherzada@gcu.edu.pk

ORCID: 0000-0003-0431-7294

Ms. Khadija Shoukat is doing M.Phil. degree from Government College University Lahore, Pakistan (2023-2025). She has completed her BS (Hons.) Zoology from Government College University, Lahore, Pakistan. She is very keen to work for sustainable culture of commercially important fish species of Pakistan.

Email: khadijashoukat29@gmail.com

ORCID: 0009-0005-7541-8641

I am Talib Hussain currently perusing M.Phil. degree in Freshwater Biology, Fisheries and Aquaculture from Government College University Lahore, Pakistan. I completed my Bachelor degree in Fisheries and Aquaculture from University of Veterinary and Animal Sciences, Lahore, Pakistan with good grades. My area of interest is Fish Biotechnology. I have wide experience of fisheries field work as well as lab work.

Email: talibhussaintalib45@gmail.com

ORCID: 0009-0009-1352-0068

Ms. Nimra Hussain holds an M.Phil. degree from prestigious University of Veterinary and Animal Sciences Lahore, Pakistan (2022). Her research interests include fisheries management and conservation Genetics. She has published 1 research articles in well-reputed international journal.

Email: nimrahussain281@gmail.com

ORCID: 0009-0000-7479-5748

To Cite This Chapter

Sherzada S et al., (2024). Potential and challenges of catfish aquaculture in pakistan. In Current Studies in Health and Life Sciences 2024 (pp.349-372). ISRES Publishing.

Diseases of Ornamental Fishes and Their Management

Farkhanda ASAD

Rafia JAMAL

Aiman NADEEM

Basim. S. A. Al SULIVANY

1. Introduction

Because of their beautiful colours, shapes, and behaviours, ornamental fish are often called living jewels and kept in aquaria or garden pools for entertainment and decorative purposes. In aquaculture, ornamental fish culture is an economically important aspect that enhances its worldwide eminence (Hoseinifar et al., 2023). Globally, ornamental fish prices are based on their colour. Fish farmers must enhance/improve the colouration of ornamental fish skin to meet their high demand and profit, as this determines their market value and commercial acceptance (Das, 2023). Carotenoids, as a natural pigment source serving as the main contributors to the pigmentation of fish skin, lead to various colours (red, orange, yellow, and brown) (Kaur & Shah, 2017).

Figure 1. Ornamental fish with brilliant colors

To understand the evolution of ornamental fish, they are systematically classified according to their genetic and morphological characteristics (Pouil et al., 2020).

Table 1: lists some ornamental fish with distinctive features

Sr.#	Common name	Scientific name	Features
1.	Angelfish	Pterophyllum scalare	Anal and dorsal fins elongated, body triangular
2.	Neon Tetra	Paracheirodon innesi	Lustrous blue and red stripes, schooling behavior
3.	Guppy	Poecillia reticulata	Diverse and colorful patterns, live-bearing reproduction
4.	Goldfish	Carassius auratus	Varieties of color, unique body shapes
5.	Zebrafish	Danio rerio	Horizontal stripes, active behavior
6.	Clownfish	Amphiprion ocellaris	Variations in color, symbiotic with anemones
7.	Discus	Symphysodon spp.	Body disc-shaped, vivid colors, complicated social behavior
8.	Siamese Fighting	Betta spendens	Flowing fins, brilliant colors, territorial behavior
9.	Demasoni chichlid	Pseudotropheus demasoni	Coloration is blue and black, nature is territorial and social

© Alam et al., (2024). Genetic Advancement, Global Trade Dynamics, Persistent Challenges and Future Prospects in Ornamental Fish Culture. Asian Journal of Research in Zoology, 7(1), 32-46.

A freshwater fish called the goldfish, domesticated more than 1000 years ago in China, considered the first ornamental fish. Marine ornamental fish refers to coral reefs with brilliant colours and distinctive patterns. As a result of coral reefs for aquariums, Sri Lanka became a major maritime trading centre in the 1930s, with an estimated 1.5 billion ornamental fish traded each year (Biondo & Burki, 2019). Among the world's largest ornamental fish exporters, Singapore stands out as the hub; Betta fish, a popular species symbolic of beauty and resiliency, falls into this category (Ahilan & Kamalii, 2022). Ornamental fish are reared and marketed in more than 7000 species in the present day. They are divided into 5000 freshwater species and 1800 marine species (Chen et al., 2020). The diversity of coastal and marine life, such as ornamental fish, shellfish, and coral reefs, contributes to an especially stunning natural scene. Mangrove forests, seagrass meadows, and coral reefs are other characteristic coastal environments (Kasmi et al., 2022; Sulkifli et al., 2023).

Economic Aspects of Ornamental Fish Trade

The ornamental fish industry was valued at an astounding USD 5.4 billion in 2021, and analyst's project that it will continue to rise at an annual pace of 8.5% until 2030, when it will have a 51.7% revenue share. A lot of freshwater decorative plants may be purchased for as little as $1–$6. Over 15% of all traded fish are marine ornamental species, which are prized for their eye-catching coloration and mannerisms (Satam et al., 2018). Over half of the commerce is with Asian nations, with a total export value of USD 130 million. Following North America (3.98%), Africa (2.2%), Oceania (1.4%), South America (7.5%), and the Middle East (0.5%), Europe accounted for 27.6% of the total (Figure 1). With 20% of the total USD 69.32 million in ornamental fish exports, Singapore was the leading exporter (Dey, 2016). Japan ranked second in terms of Koi carp output, with USD 41.34 million (Pinnegar & Murray, 2019).

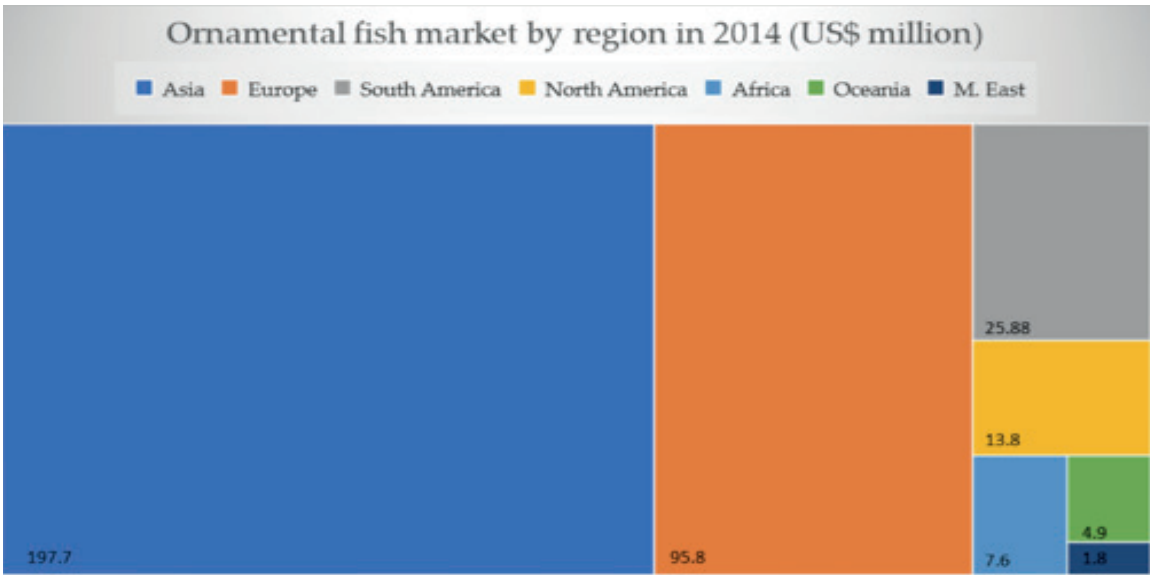


Figure 2. "The distribution of exports across key markets by region in 2014, measured in millions of US dollars."

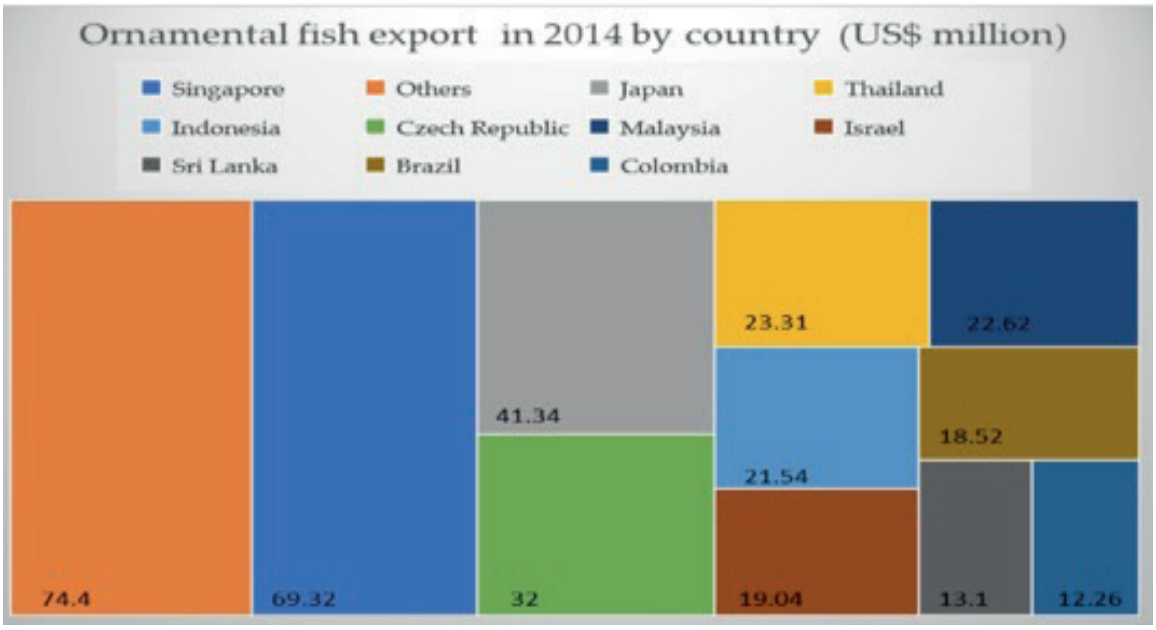


Figure 3. "The distribution of exports across major markets by country in 2014, expressed in millions of US dollars."

Europe, the US, and Japan are the top three importers of marine ornamental fishes or regions, whereas Indonesia, the Philippines, and Sri Lanka are the top exporters (Biondo & Burki, 2020). Worldwide exports and imports were used to calculate the worldwide market share for each year (Figure 4). The total exports for 1992, 1994, and 1998 were either much less than or equal to the total imports of the three main importing nations (Figure 4). Figure 5 shows the proportion of marine ornamental fishes from the major exporting nations to the worldwide market; a single-digit percentage figure primarily represents marine ornamental fishes.

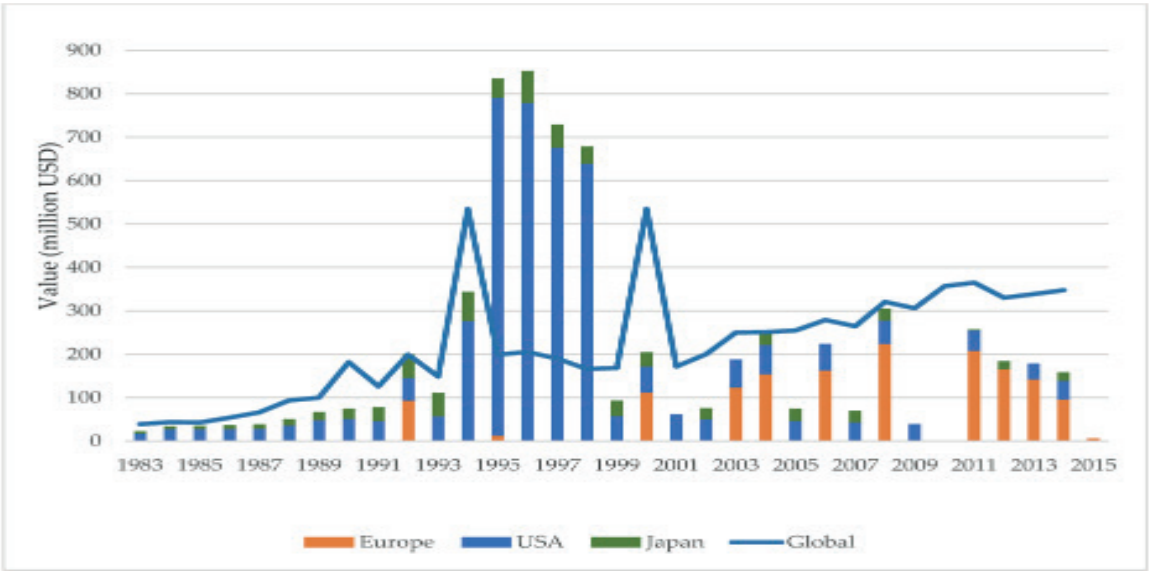


Figure 4. "The average wholesale value, in millions of US dollars, of both freshwater and marine fish for worldwide export, compared to their import values in Europe, the United States, and Japan."

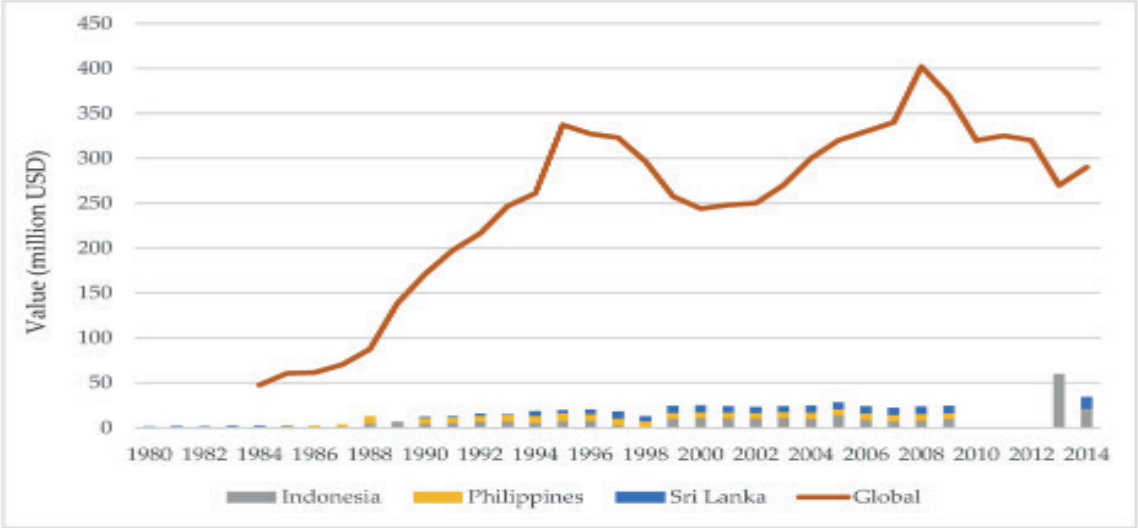


Figure 5. "The wholesale value, in millions of US dollars, of freshwater and marine fish exports by region in 2014, compared to the total exports from individual countries for the same year or the nearest year with available data."

2. Types of Ornamental Fish

2.1. Freshwater Ornamental Fish:

There are many diverse habitats for ornamental fish. They live in freshwater habitats, including rivers, lakes, ponds, swamps, and saltwater environments. Freshwater ornamental fish are valuable commercially and possess an esthetic quality due to their remarkable colors, shape and health. Ornamental fish, in high demand by the public, are traded as commodities because they can fulfil the market at all price points (Prasetya et al., 2021). According to UN-Comtrade data, the global trade in ornamental fish export in 2021 was worth $379.1 million. The export of freshwater ornamental fish generated $279.6 million, while marine ornamental fish generated $99.5 million (Tarihoran et al., 2023).

2.1.1. Tropical Freshwater Fishes

Tetra fish have brilliantly colourful skin that changes appearance depending on the perspective. These rich hues are produced by special cells known as chromatophores, which include layers that reflect light in a way that produces vivid colours when viewed from different angles (ke et al., 2022). The Neon Tetra fish's stripes change colour from blue-green in light to indigo in darkness by reflecting light off layers of guanine crystals, generating customizable patterns (Setiyowati et al., 2022).

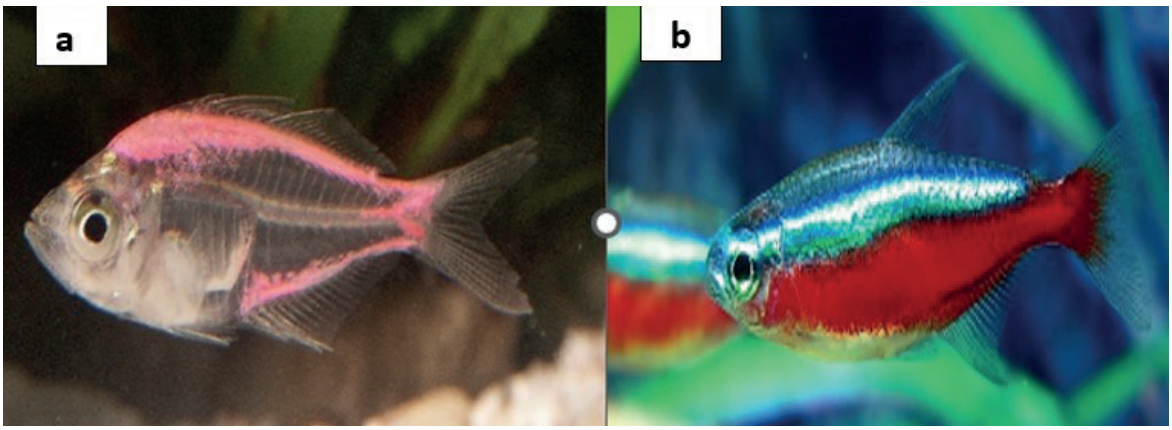


Figure 6. a) Tetra fishes b) Neon Tetra fish

Originating in Central and South America, guppies and mollies are well known for their vivid colours and low maintenance requirements (Tuckett et al., 2021). Guppies have various colours and tail forms and are highly prized in aquariums (Sinha & Pandey, 2023). The beautiful and intelligent angelfish can withstand salinities up to 4 g/LnaCl (Eiras et al., 2019).

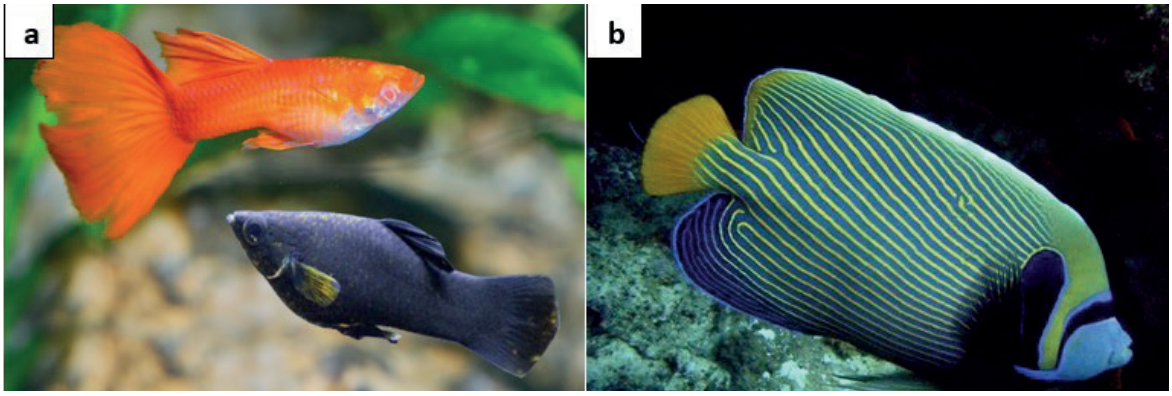


Figure 7. a) Guppy and Molly b) Angle-fish

The diverse shapes, colours, and patterns of dicus fish, "the king of Aquarium Fish," make them highly valuable. Sidi and Sungkowo (2022) stated that discus fish enthral enthusiasts with their unique patterns and elegance. Anglefish thrive in recirculating aquaculture systems. Oros et al. (2022) described betta splendens as a popular ornamental fish with distinctive qualities and high market value.

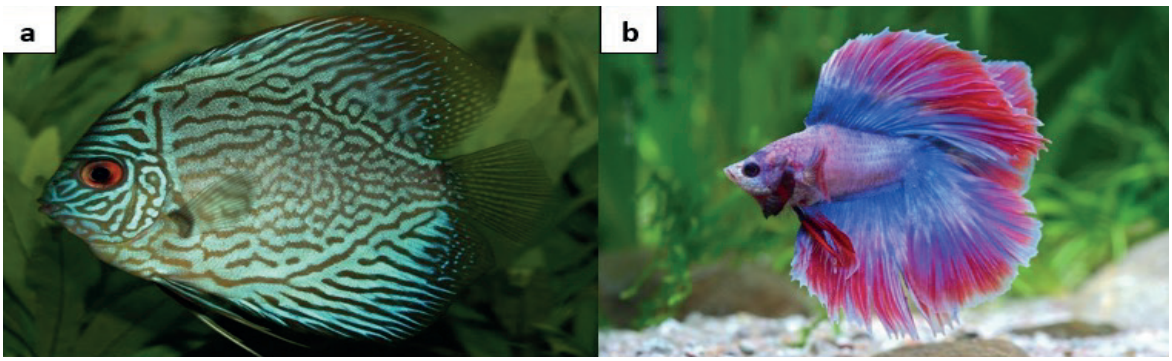


Figure 8. a) Discus fish b) Betta splendens

2.1.2. Cold Freshwater Ornamental Fish

A popular choice in the ornamental fish industry, goldfish come in both common and fancy varieties. Their economic value remains steady due to their consistent demand (Shukla et al., 2022). Koi, Prized for their stunning colours and captivating forms, hold significant economic importance within the ornamental fish trade (Daud et al., 2023). Rosy Red Minnows, Prized for their stunning colours and captivating forms, koi hold significant economic importance within the ornamental fish trade. (Horne et al., 2010).

Figure 9. a) Goldfish b) koi fish c) Rosy Red Minnows

2.2. Types of Saltwater Ornamental Fish

Marine decorative fish, a part of the marine aquarium industry, are mainly obtained from natural habitats because the trade heavily relies on capturing them from the wild (Chen et al., 2023). Clownfish, a beloved species in aquariums, encounter difficulties in breeding. Enhancing their colours, they are widely cherished as pets (Santikawati et al., 2023). Butterflyfish play a role in the Indo-Pacific Ocean ecosystem, acting as health indicators and being sought after in the ornamental fish market (Mahadevan et al., 2023). Damselfishes, crucial for coral reefs, are important as marine ornamental species. Their presence is vital for aquaculture practices aimed at conservation efforts and improving transportation methods (Roberts et al., 2023).

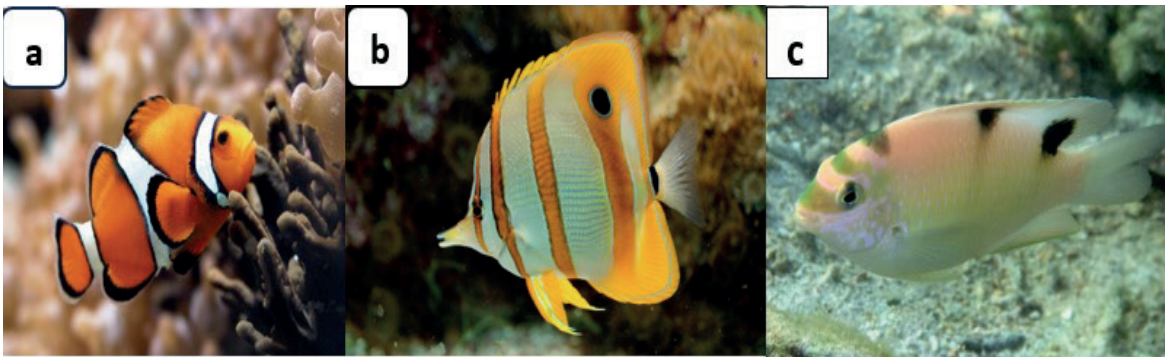


Figure 10. Saltwater ornamental fish a) Clownfish b) Butterflyfish c) Damselfish

2.3. Brackish water ornamental fish:

For sustainable aquaculture, brackishwater ornamental fish production offers a bright future. Freshwater and tropical fish make up the majority of the ornamental fish trade, with brackishwater fish making up a minor portion (Hossain & Heo, 2021). For sustainable aquaculture, brackishwater ornamental fish production offers a bright future. Freshwater and tropical fish make up most of the ornamental fish trade, with brackishwater fish making up a minor portion (Hossain & Heo, 2021).

The silver moony is a native species to the Western Pacific region, and fish is highly prized as a species that can adapt to water environments, including freshwater, brackish water and seawater. The aquaculture of fishes, such as the silver moony, has increased due to their popularity and economic value (Vasantharajan, 2023). The Green Scat, also called Spotted Scat, inhabits the western Pacific oceans, including the Sundarbans in Bangladesh. Its unique ability to tolerate changes in salinity makes it a fascinating subject for studying how animals adapt to salt levels in their surroundings (Washim et al., 2022). The Silver Molly, a true freshwater fish, can surprisingly adapt to slightly salty brackish waters. They play an important role in keeping their environment healthy by what they eat and how they reproduce (Hussein et al., 2023). On the other hand, the Mono Sebae, also known as the Mono angel, thrives in brackish water but can adjust to a range of saltiness, from freshwater to even the ocean. This makes them popular ornamental fish, prized for their beauty and economic value in the aquarium trade (yue et al., 2022).

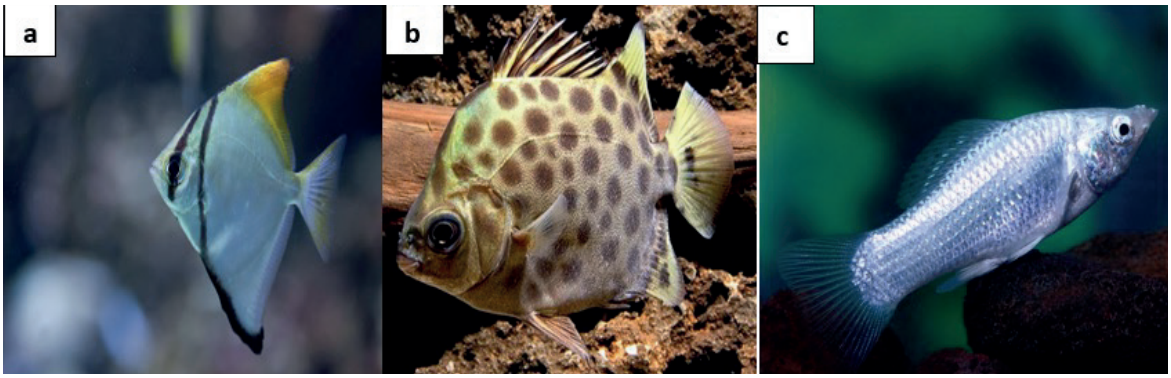


Figure 11. a) Silver moony b) green scat c) silver molly

3. Common Diseases and their Causative Factors

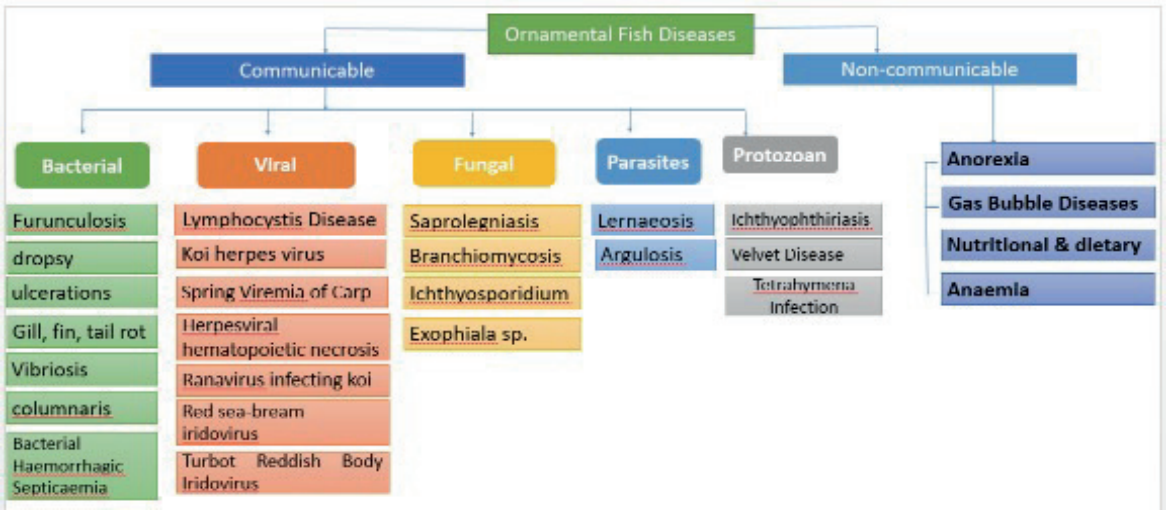


Figure 12: Common diseases in Ornamental fish

3.1 Communicable diseases

Pathogens, /Co-existing organisms (biological entities) are Bacteria, Viruses, Fungi and Parasites

3.1.1 Bacterial diseases

The most prevalent infectious issue affecting ornamental fish is bacterial illness. Numerous bacteria are the cause of bacterial illnesses in ornamental fish. These microorganisms can lead to diseases including dropsy, red pests, ulcerations, fin and tail rot and red sores (Walczak et al., 2017). Environmental factors such as stress and poor water quality can lead to bacterial infections in ornamental fish, both gram-positive and gram-negative. Pet fish mortality and morbidity can be significantly increased by these illnesses, which are impacted by dietary, environmental, and genetic variables. Gram-positive infections spread more slowly and are more difficult to identify in the early stages, whereas gram-negative infections act quickly and can be fatal within 24 hours. Stress plays a major role in developing bacterial illnesses in fish (Irshath et al., 2023). Bacterial pathogens are classified into two major groups: Gram-positive and Gram-negative (Ziarati et al., 2022).

A. Gram negative diseases

Table 2: Gram negative bacterial diseases

Family	Pathogens	Diseases	Symptoms	Prevention & control	Treatments/ Medication
Aeromonadaceae	"A. hydrophila A. salmonicida A. veronii A. jandaei A. Punctata"	Furunculosis, ulcer disease, dropsy, Bacterial Haemorrhagic Septicaemia, Tail and fin rot	Fin rot, skin ulcers, enlarged eyes, renal dropsy, abdominal distension, and reddening of the body with hemorrhagic patches on the body wall, internal organs, tail, fins, and gills.	Maintain good water quality, reduce stress, avoid overcrowding	"Medicated feed, Terrramycin, Antibiotic drug (chloramphenicol), Apply lime"
Vibrionaceae	"V. anguillarum V. salmonicida V. vulnificus, V. parahaemolyticus V. alginolyticus V. Harveyi"	vibriosis, Tail and fin rot	hemorrhagic septicemia, skin ulcers, fin rot and internal organ damage	Proper management practices, including maintaining excellent water quality, hygiene, and nutrition	Suplhamerazine
Pseudomondaceae	Pseudomonas	Bacterial Haemorrhagic Septicaemia, Tail and fin rot	red sores on the body, ragged fins, lethargy, loss of appetite, and rapid mouth movement	Maintain good water quality, reduce stress, avoid overcrowding	Terrancyin, Chloromycetin
Enterobacteriaceae	Salmonellosis		internal organ haemorrhages, skin lesions, lack of appetite, and lethargy	Maintain good water quality, reduce stress, avoid overcrowding	Terrancyin
Flavobacteriaceae	Flavobacterium columnare	columnaris disease	skin ulcers, fin rot, and internal organ damage in ornamental fish, resulting in high mortality rates	Proper management practices, including biosecurity measures, monitoring water quality, and implementing vaccination strategies	Bath of copper sulphate or potassium permanganate Terrancyin

I. Aeromonadaceae

(Furunculosis, ulcer disease, dropsy, Bacterial Haemorrhagic Septicaemia, Tail and fin rot)

Aeromonas is a Gram-negative bacterium that infects fish and causes illnesses such as ulcer disease, red-sore illness, hemorrhagic septicemia, and motile Aeromonas septicemia. Antibiotics are often used to treat infected fish. Aeromoniasis is a bacterial infection caused by Aeromonas species, widely seen in ornamental fish (Hossain & Heo, 2021). Aeromoniasis can infect a large number of fish species. Aeromonas and Vibrio infect fish similarly, although Aeromonas is more common in freshwater fish, whereas Vibrio species may be found in freshwater, brackish water, estuaries, and the ocean. Aeromonas pathogens can cause bacterial infections in ornamental fish, including A. hydrophila, A. salmonicida, A. veronii, and A. jandaei (Walczak et al., 2017).

Aeromonas hydrophila is a bacterial infection that have serious consequences for ornamental fish. This bacteria is known to induce septicemia in ornamental fish, which results in high death rates and huge economic losses for the industry (Smith et al., 2009; Anjur et al., 2021). Fish diseased with A. hydrophila demonstration a variety of clinical indicators, including abrupt mortality in otherwise healthy fish and symptoms including inappetence, swimming irregularities, pale gills, bloat, and skin ulcerations. A. hydrophila illness, also known as Hemorrhagic Septicemia, Motile A. Septicemia, Ulcer illness, or Red-Sore Disease, mostly affects freshwater fish and many tropical and ornamental fish species. A. hydrophila can induce opportunistic illness in weakfish as a subordinate infection. There have been seen histological changes in the stomach, spleen, gills, liver, and kidney (AlYahya et al., 2018).

Furunculosis caused by *A. salmonicida* usually called koi ulcer disease or ulcer disease, is a common condition in ornamental fish. Most warm-water and freshwater fish, including koi (Cyprinus carpio) and goldfish, are susceptible to the sickness identified by the red sores covering the creature. Ecchymosis, enlarged belly, and exophthalmia are other symptoms. The skin bleeds and necrosses in the ulcerative type, exposing the muscle and bone (Lewbart et al., 2001). Secondary infections are brought on by bacteria, fungi, and metazoa or protozoa through these sores. Usually, primary or secondary infections and a fluid imbalance cause these fish to perish (Hossain et al., 2021).

The bacterial infection of Aeromonas veronii and Aeromonas jandaei can seriously harm ornamental fish. A. veronii infection in ornamental fish can cause a variety of clinical symptoms such as skin ulcers, enlarged eyes and fluid buildup in the abdomen, renal dropsy, ragged fins and body wall, internal organs, gills, tail, and fins all have hemorrhagic patches and are reddened (Walczak et al., 2017). When fish are infected, these signs may result in serious health problems and perhaps significant mortality rates. One of the most prevalent bacterial illnesses affecting ornamental fish is A. veronii and A. jandaei which can result in large losses for the ornamental fish culture sector (Soni et al., 2021). Stress factors that can contribute ornamental fish to infections include poor water quality, insufficient nourishment, handling, transportation, and overcrowding of fish (Walczak et al., 2017).

A bacterial pathogen called Aeromonas punctata may infect ornamental fish and cause various illnesses. A. punctate is known to cause illnesses in fish and other aquatic creatures, especially ornamental fish. These microorganisms are common in many aquatic habitats, including freshwater, brackish, and marine water. Motile Aeromonas species are recognized as the causative agents of motile aeromonad infections in ornamental fish. These infections can result in notable fish mortality and financial losses for the ornamental fish trade. When fish are contaminated, these clinical symptoms may cause serious health problems and perhaps significant mortality rates (Hossain & Heo, 2021).

II. Vibrionaceae

(vibriosis, Tail and fin rot)

Vibriosis is a potentially fatal illness that affects fish, and the excessive usage of antibiotics in cultured systems has made the bacterium more resistant to them (Helmi et al., 2020). There are plenty of vibrio species in both fresh and brackish water. Vibrio species are Gram-negative bacteria that cause vibriosis. Pathogens such as V. anguliforme, V. salmonicida, V. vulnificus, V. parahaemolyticus, V. alginolyticus and V. harveyi can infect ornamental fish and cause illnesses. It is well recognized that these Vibrio species are important fish infections, resulting in a range of clinical symptoms and health problems in ornamental fish. They can cause internal organ damage, fin rot, hemorrhagic septicemia and skin ulcers, among other ailments that result in significant mortality rates and financial losses for the ornamental fish business (Saad & Elkamel, 2015).

III. Pseudomonadaceae

(Bacterial Haemorrhagic Septicaemia, Tail and fin rot)

A bacterial disease called pseudomonas can harm ornamental fish, resulting in various symptoms, including ragged fins, red lesions on the body, lethargy, loss of appetite, and fast jaw movement. Most warm-water and freshwater fish, including koi and goldfish, are susceptible to the sickness identified by the red sores covering the creature. Pseudomonas bacterium is the source of the sickness. However, other factors such as seasonal changes, injuries, abrupt changes in water temperature, and inadequate nutrition or cleanliness might make the fish more vulnerable to the bacteria. The opportunistic Gram-negative bacillus Pseudomonas. It is a hazard to fish in stressed conditions since it is a part of their natural microbiota (Algammal et al., 2020).

IV. Enterobacteriaceae

Salmonella species bring on a Gram-negative bacterial illness called salmonellosis. A bacterial illness known as salmonellosis is brought on by Salmonella species (Bibi et al., 2015). Fish can pick up the bacterium and become carriers through polluted water or food sources. The bacterium can be spread by direct contact with sick fish or exposure to polluted water or equipment (Antunes et al., 2018; Gazal et al., 2018). Fish may show symptoms of a systemic illness, such as internal organ haemorrhages, skin lesions, lack of appetite, and lethargy (Mawa et al., 2021). Sick fish can be treated with antibiotics, but prevention is the key.

V. Flavobacteriaceae

(columnaris disease)

Fish kept as ornaments may suffer greatly from the bacterial disease Flavobacterium columnare. This bacteria causes columnaris disease, affecting several fish species and ornamental fish. F. columnare is the source of the illness columnaris, which can cause fin rot, skin ulcers, and internal organ damage in ornamental fish. These symptoms can result in significant death rates and financial losses for the ornamental fish business. The prevention and control of the spread of columnaris disease in ornamental fish depend on good management practices, including biosecurity precautions, water quality monitoring, and vaccination programs (Declercq et al., 2013).

B. Gram positive diseases

Table 3: Gram positive bacterial diseases

Family	Pathogens	Symptoms	Prevention & Control
Streptococcaceae	Streptococcus	exophthalmia, distention of the abdomen, confusion, abnormal swimming, anorexia, opacity in the eyes, skin darkening and bleeding, and finally death	Maintain good water quality, reduce stress, avoid overcrowding
Mycobacteriaceae	Mycobacterium	pigmentation, exophthalmia, stomach distention, lethargy, skin lesions, and mortality	Maintain good water quality, reduce stress, avoid overcrowding
Erysipelotrichaceae	Erysipelothrix	fish may not show any obvious symptoms	Maintain good water quality, reduce stress, avoid overcrowding

VI. Streptococcaceae

Streptococcaceae (gram-positive bacterial family) is responsible for systemic streptococcosis, which harms fish populations globally, causes financial losses and raises health issues for the general public (Iregui et al., 2016). For the ornamental fish sector, the illness is a major threat. In addition, the bacteria have increased the morbidity and death rates in freshwater and marine fish. The disease's clinical indicators vary depending on the type of fish. Nonetheless, exophthalmia, abdominal distention, loss of direction, irregular swimming, and opacity in the eyes, darkening and bleeding of the skin, anorexia and ultimately death are the most common symptoms (Leal et al., 2019). Due to its neurotropic properties, streptococcus is thought to cause imbalanced swimming behaviour in fish. The bacteria are present in the tissues needed by fish for pathogen defence and the liver, gills, kidneys, and spleen. The Streptococcosis species that cause diseases in ornamental fish include *S. agalactiae, S. iniae, S. dysgalactiae* and *S. parauberis* (Ziarati et al., 2022).

VII. Mycobacteriaceae

Mycobacterium spp. are pleomorphic, aerobic, acid-fast, Gram-positive bacteria that are associated with fish. They are members of the Mycobacteriaceae family of hazardous bacteria (Delghandi et al., 2020). Fish that live in freshwater, brackish water and the ocean frequently contract mycotuberculosis, which is thought to be a primary cause of death for both farmed and wild fish (Hashish et al., 2018). It has also been documented that ornamental fish can harbor Mycobacterium spp. (Puk & Guz, 2020). Due to the large variety of host species and the many distinct kinds of bacteria that may infect fish, the clinical symptoms of infection vary. Fish infected with Mycobacterium species might exhibit unique symptoms such as pigmentation, exophthalmia, stomach distention, lethargy, skin lesions, and mortality. But through the circulatory and lymphatic systems, the virus has made its way to the eyes, gills, liver, kidneys and spleen, among other fish organs. Furthermore, fish infections may manifest as enlarged liver, kidney, spleen, and internal organ nodules (Delghandi et al., 2020). Fish may show signs including fin rot, emaciation, lethargy, and skin sores. Granulomas and caseous necrosis can be seen in internal organs (El-Amrani et al., 2010). Isolating sick fish and administering the proper antibiotic medication is part of the treatment.

VIII. Erysipelotrichaceae

A Gram-positive bacteria linked to fish is called Erysipelothrix. Erysipelothrix rhusiopathiae is the bacterium that causes erysipeloid (Rostamian et al., 2022). Before 2014, it was believed that E. rhusiopathiae was a common fish bacterium; nevertheless, reports of Erysipelothrix-associated mortality have come from several nations. Fish have been shown to harbor E. piscisicarius, a recently found species of ornamental fish (Pomaranski et al., 2020). Although fish may not show obvious symptoms, they can still carry and release the bacterium into the surrounding water.

3.1.2 Viral diseases

Diseases that spread among ornamental fish due to viruses are a concern, as viral pathogens can harm these fish. Such diseases can lead to illness and death within affected fish populations, threatening the aquaculture industry. While more common in marine and brackish water fish, certain freshwater species like the terror are also susceptible. Some diseases found in fish include Lymphocystis disease, Koi Herpesvirus Disease, Infectious Spleen and Kidney Necrosis Virus (ISKNV) and Red Sea Bream Iridovirus (RSIV. Numerous viral illnesses, such as carp pox, koi herpesvirus, herpesviral hematopoietic necrosis, angelfish herpesvirus, and herpesvirus, iridoviruses, megalocytivirus, and koi sleepy disease, impact ornamental fish populations, leading to significant illness and death. These diseases, caused by different viruses like poxvirus and herpesviruses, pose a serious threat to the aquaculture industry due to their potential to cause high morbidity and mortality among affected fish populations (Su & Su, 2018).

I. Lymphocystis disease

Lymphocystis disease is caused by an iridovirus that infects tissue cells, resulting in hypertrophy and visible lumps in the fish. Outbreaks of this disease often follow events like the capturing and shipping of fish (Borrego et al., 2017). Symptoms include granular lesions on the skin and fins, which sometimes affect the mouth and gills. Infected fish may develop white or grey nodules of varying sizes that alter their appearance. Although lymphocytes usually resolve on their own without causing health problems, they can affect the appearance of the infected fish. Infected fish tend to develop bumps or abnormal growths on their skin, fins, and gills. These growths can come in sizes and quantities potentially leading to infections (Harikrishnan et al., 2010). Prompt veterinary consultation is crucial for an accurate diagnosis and suitable treatment. In the case of Lymphocystis disease in ornamental fish, there is no proven chemotherapeutic treatment, and it often resolves on its own with proper water quality and nutrition (Yanong, 2013). Surgical removal of hyperplastic fibroblasts, followed by topical antibiotics, can be a treatment option. A microscopic examination of the affected areas will reveal circular, clustered, light orange-hued enlarged cells to diagnose the disease. Preventive measures include quarantining new fish arrivals, maintaining excellent water quality, and avoiding overcrowding (Volpatti & Ciulli, 2022).

The Lymphocystis viral disease is more prevalent in marine and brackish water fish. However, it can also impact certain freshwater species like the green terror (Aequidens rivulatus), blue gouramis (Trichogaster trichopterus), and angelfish (Pterophyllum scalare). In Asia, examples of ornamental fish affected by Lymphocystis disease include the Scatophagus argus. These fish species have been linked to systemic diseases caused by iridoviruses, including Lymphocystis, resulting in illness and death in freshwater tropical fish populations (Yanong et al., 2003; Hoseinifar et al., 2023). Stress, particularly after fish capture and shipping, plays a role in developing this disease.

II. Ranavirus infecting koi (KIRV)

The ranavirus infecting koi (KIRV) in ornamental fish is a highly contagious viral pathogen first reported in India in 2015. This virus, isolated and characterized by moribund koi (Cyprinus carpio), causes severe clinical signs such as skin darkening, loss of scales, uncoordinated swimming, and other abnormalities, leading to significant mortality in infected fish populations. KIRV belongs

to the family Iridoviridae and seriously threatens ornamental fish health and aquaculture practices (George et al., 2015).

III. Megalocytivirus

Megalocytivirus is a group of iridoviruses that impact ornamental fish, including Red Sea Bream Iridovirus (RSIV), Infectious Spleen, and Kidney Necrosis Virus (ISKNV). RSIV primarily affects marine fish, while ISKNV and Turbot Reddish Body Iridovirus (TRBIV) are also significant (Sumithra et al., 2022). RSIV and ISKNV can lead to high mortality in infected fish, showing non-specific clinical signs. RSIV primarily affects marine fish, while ISKNV and TRBIV are more common in freshwater species. These viruses threaten marine and freshwater ornamental fish populations, emphasizing the importance of disease management and prevention in aquaculture. (Yanong & Waltzek, 2010).

IV. Spring Viremia of Carp (SVC)

A highly infectious viral illness that predominantly affects carp species is called spring viremia of carp (SVC), including koi and goldfish. The disease is caused by Rhabdovirus carpio, which can infect fish and potentially pose a risk to humans (Jia et al., 2020). Fish with SVC infection may exhibit a range of clinical symptoms, including lethargy, haemorrhages, swollen abdomen, and gill abnormalities. Mortality rates can vary depending on the severity of the infection (Zhang et al., 2019). In fish, post-mortem examination may reveal haemorrhages, congestion, and abnormalities in the internal organs, particularly the liver and spleen (Liang et al., 2022). The virus that causes SVC is the Spring Viremia of Carp Virus (SVCV), a member of the Vesiculovirus family with a bullet-shaped, encased virion. SVC was once exclusively found in Eastern and Western Europe, but with to improved surveillance and the global trade in ornamental fish, it has since spread to North America, Asia, and Europe. Four main genetic clades linked to the virus's expansion in China, where common carp are grown for consumption and koi for export, have been identified by the genotyping of SVCV isolates and pike fry rhabdovirus from Europe (Meng et al., 2021). Currently, there are no vaccines for SVC. Fish hobbyists should keep their fish in separate tanks at events, and anglers must avoid moving fish between water bodies to prevent disease spread. Reporting unusual fish deaths to local fish and game authorities is important.

V. Koi Herpesvirus Disease

The extremely infectious virus known as koi herpesvirus (KHV) infects ornamental carp kinds including koi and ghost koi as well as ordinary carp. The virus, commonly known as cyprinid herpesvirus-3, can cause carps to develop interstitial nephritis and gill necrosis. Infected fish populations can experience up to 100% mortality (Rathore, 2012). The virus is a DNA virus that is closely linked to the goldfish hematopoietic necrosis virus and the carp pox virus. It is a member of the Herpesviridae family. As KHV may live in infected fish for a lifetime, fish that have been exposed to the virus or have recovered from it should be treated as carriers. KHV frequently causes non-specific clinical symptoms, and in infected populations, mortality can start very quickly—deaths can occur 24 to 48 hours following the onset of clinical symptoms. Fish of all ages are affected by the virus, however cohabitation studies indicate that fry are more vulnerable than older fish (Hartman et al., 2013).

VI. Herpesviral hematopoietic necrosis (HVHN)

Herpesviral hematopoietic necrosis (HVHN) is a severe disease affecting ornamental fish like goldfish and crucian carp, caused by Cyprinid herpesvirus 2. This viral infection leads to noticeable symptoms such as gill bleeding, body swelling, abdominal haemorrhages, and pale skin. HVHN results in necrosis in the kidney and spleen's hematopoietic tissue, causing extensive damage and mortality rates of up to 100% in goldfish populations. The virus has been identified in various countries worldwide, affecting goldfish and other cyprinid species like Prussian carp

and crucian carp. Early detection through PCR testing is crucial due to the challenges in isolating and diagnosing this disease, emphasizing the importance of disease surveillance and prevention in ornamental fish (Giovannini et al., 2016; Goodwin et al., 2006).

VII. Viral haemorrhagic septicaemia (VHS) and Infectious haematopoietic necrosis (IHN)

These are not typically associated with ornamental fish. These diseases primarily affect salmonid fish species and are not commonly found in ornamental fish.

3.1.3 Fungal disease

Fungal diseases in ornamental fish can be caused by various types of fungi commonly found in aquariums, such as Saprolegnia and Achyla. These infections typically affect fish that are stressed, injured, or ill, with poor water quality worsening the situation. Fungal infections in fish, also known as mycoses, are common in freshwater and marine species. These infections are often caused by poor water quality, hygiene, injuries, other diseases, or dead fish or decomposing organic material in the pond. Fungal spores are widespread in aquatic environments and can quickly colonize stressed, injured, or diseased fish, leading to external fungal infections known as 'cotton wool disease' due to their white, fluffy appearance (Verma, 2008).

Figure 13: Fungal Diseases

The visible sign of these fungal infections is often a white fluffy appearance known as 'cotton wool disease. Freshwater aquarium salt baths or commercially available antifungal medications made especially for aquarium usage are two ways to treat fungal diseases like cotton wool disease in freshwater fish. In cases where individual fish are infected, treating them in a separate hospital tank is preferable. Additionally, applying Gentian Violet, which has antifungal and antibacterial properties, can be an effective treatment method (Ozcan & Arserim, 2021). Fish with dermal lesions from African sharp-tooth catfish (Clarias gariepinus), snakeskin gourami (Trichogaster pectoralis), gold gourami (Trichopodus trichopterus), angelfish (Pterophyllum scalare), and red hybrid tilapia (Oreochromis spp.) were examined in a study on fungal infections in common ornamental and edible fish species (Routh & Solanki, 2023).

I. Cotton Wool Fungus (Saprolegniasis)

Cotton wool fungus, also known as Saprolegniasis, is a common fungal infection in freshwater fish, particularly ornamental fish (Vajargah & Majidiyan, 2022). This disease is caused by water moulds, specifically in the genus Saprolegnia, which are filamentous protists with specific characteristics like oospores, diploid chromosomes, and cell walls made of beta-glucans and cellulose. Saprolegnia species typically infect fish with prior injuries on their external tissues, often caused by mechanical abrasion or other primary pathogens. Saprolegniasis manifests as grey or white patches on fish, primarily on the external tissues and gills, and is temperature-dependent, often occurring at low temperatures. The infection manifests as white or brown cotton-like growths on the skin or gills, with early signs showing pale areas that may ulcerate, exposing underlying musculature. In severe cases, systemic infections can lead to mycelial masses in the gut and viscera,

causing peritonitis and extensive tissue damage. The disease is usually transmitted through water or by ingesting contaminated food. Environmental stress, minor injuries, and suboptimal water quality contribute to outbreaks of Saprolegniasis. Treatment involves managing the environment, providing supportive care, and using chemicals like potassium permanganate, formalin, malachite green, and salt to control the infection. Wet mount examinations are crucial for diagnosis, revealing characteristic structures like aseptate hyphae and zoosporangia.

II. Gill Rot Disease (Branchiomycosis)

It is an acute infection of the gills that primarily affects various ornamental and freshwater fish species, including Koi, eels, bass, and perch. This disease is caused by two species of the genus Branchiomyces, namely B. sanguinis and B. denigrans, which produce branched and non-septate hyphae. The infection is transmitted through water, where fungal spores adhere to the gills, germinate, and produce hyphae that penetrate the gill tissue and damage the blood supply to the area (Ozcan & Arserim, 2021). Branchiomycosis, a fungal infection in fish, spreads through water, where fungal spores attach to the gills and grow hyphae that invade the gill tissue. The disease progresses rapidly within 2-4 days under suitable conditions, with clinical signs like weakened movement, fish gathering at water inlets, respiratory distress, and the presence of fungus on or in the gill tissue, leading to obstruction and necrosis. Reddened gills indicate impaired circulation, highlighting the severity of this fungal infection in fish.

Treatment for Branchiomycosis involves using malachite green, formalin baths, copper sulfate, benzalkonium chloride dips, and oral methylene blue. It is crucial to address factors like overcrowding, ammonia levels, algal blooms, organic material levels, water temperature, and hygiene to control the condition. Prompt removal of infected or dead fish and proper quarantine measures are essential to prevent the spread of the disease and maintain a healthy aquatic environment.

III. Ichthyosporidium

Ichthyosporidium is a fungal infection that primarily affects the kidneys and liver of fish, leading to sluggishness, balance loss, and external cysts or sores. This disease is present in ornamental fish and is caused by a fungus that manifests internally, spreading throughout the body after attacking the kidneys and liver. The disease is often associated with poor water quality, poor hygiene, fish injuries, dead fish or large amounts of decomposing organic material in the tank. Treatment options for Ichthyosporidium include a 1% Phenoxethol solution, or Chloromycetin added to the food. Reducing ammonia levels, algal blooms, amounts of organic material, water temperature, and enhancing cleanliness are some of the factors that assist regulate the disease. Fish that are dead or infected should be removed from the tank right away, and new fish should first be given enough time to recover in a proper quarantine.

IV. Exophiala sp.

Exophiala sp. is a group of fungal organisms that can cause darkening, lethargy, and abnormal swimming behavior in fish, along with yellow to white granulomas in visceral organs like the liver, kidney, and spleen. These infections can occur in ornamental fish and are associated with poor water quality, poor hygiene, fish injuries, or dead fish or large amounts of decomposing organic material in the tank. While prevention and therapy are not yet available for some of these infections, maintaining optimal water quality and hygiene can help control their spread. Fish with fungal infections can be treated with formalin baths, copper sulphate or benzalkonium chloride dips, and antifungal medicines like malachite green. Fish should be properly quarantined before being reintroduced to the tank, and any dead or infected fish should be removed right away (Verma, 2008).

3.1.4 Parasitic diseases

Many organisms, including protozoa, trematodes, cestodes, nematodes, acanthocephalans, crustaceans, and arthropods, cause parasitic diseases in ornamental fish. These organisms can infest various host tissues, including the skin, gills, and internal organs, leading to various clinical signs and pathological changes. Various organisms, including metazoan parasites, protozoan parasites, copepod arthropods and digenean trematodes can cause parasitic diseases in ornamental fish. Examples of these parasites include nine species of monogenean trematodes, seven protozoan species, three species of copepod arthropods, one metacercarial stage of a digenean trematode (Centrocestus spp.) and one nematode (Capillaria spp.).

These parasites can cause various symptoms in ornamental fish, such as irritation, injury, tissue atrophy, occlusions of the alimentary canal, and deprivation of normal feeding. In some cases, parasitic infections can lead to high mortality rates in fish populations . Prevention is the best method of control for many of these parasitic diseases, although some parasites may be susceptible to various parasiticides. Good husbandry practices are essential for reducing further parasite infestations (Thilakaratne et al., 2003; Florindo et al., 2017).

I. Argulosis

Argulosis is a disease in ornamental fish caused by the ectoparasite Argulus spp. Because it is common in carp culture, trout farming, and the ornamental fish business and causes large economic losses, this parasite is extensively researched. Using maxillary suckers and hooks, the parasite clings to the host's integument and feeds on its blood and outer tissues. Dermal ulceration, physiological stress, immunological suppression, secondary infections, decreased fish development, and death are among the harms brought on by feeding activities (Steckler & Yanong, 2013). The current strategies for controlling argulosis rely on veterinary medicines, including vaccines. However, the parasite's resistance to anti-parasitic drugs and the significant losses experienced globally necessitate further research and development in vaccination technology.

II. Lernaeosis

Lernaeosis, also known as Lernaeasis, is a disease in ornamental fish caused by the copepod ectoparasite Lernaea spp., commonly called anchor worms. These parasites attach to the exterior parts of the fish, including the gills, fins, and scales, leading to various health issues and potential mortality in infected fish. The disease is prevalent in freshwater ornamental fish and can cause significant economic losses in aquaculture due to high mortality rates in cultured fish populations. Proper identification and treatment of Lernaeosis are essential to prevent the spread of the disease and maintain the health of ornamental fish populations (Steckler & Yanong, 2013).

3.1.5 Protozoans diseases

Protozoan diseases can have varying impacts on the health of ornamental fish (Martins et al., 2015)

I. Ichthyophthiriasis (white spot disease)

Ichthyophthiriasis, commonly known as white spot disease, is caused by Ichthyophthirius multifiliis and affects freshwater fish. Ichthyophthiriasis, commonly known as white spot disease, is a significant protozoan disease affecting ornamental fish. It is caused by the ciliated parasite Ichthyophthirius multifiliis, which infects the skin and gills of freshwater fish. The disease is characterized by white spots on the skin and gills, which are visible macroscopic manifestations of the trophont stage of the parasite. Ichthyophthiriasis can lead to significant economic losses in the aquaculture sector due to high mortality rates during epidemics. The disease is often associated with low water temperature, affecting health and making fish more susceptible to parasitic infections. During an outbreak, fish are stressed, and their immune reactions are compromised, which enables

aquatic bacterial pathogens to infect the host and increase the severity of the disease (Wei & Yu, 2013) (Dickerson & Dawe, 2006)

II. Piscinoodinium pillulare (Velvet Disease):

Velvet disease in ornamental fish is caused by the dinoflagellate parasites Piscinoodinium pillulare in freshwater fish and Amyloodinium ocellatum in saltwater fish, leading to yellowish spots on the skin and gills. This parasitic infestation can quickly lead to the death of fish if not diagnosed and treated promptly. The disease is also known as "rust" or "gold dust" disease, characterized by yellow, rust, or gold-dust-colored spots or film on the fish's body, giving it a velvet-like appearance. The treatment for velvet disease in ornamental fish involves specific medications like copper formulations for marine fish and freshwater dips for three to five minutes, along with commercial fish medications containing formalin or malachite green for freshwater fish. Proper quarantine protocols for new fish additions, regular water testing, and excellent water conditions are essential preventive measures to protect ornamental fish from velvet disease (Saha & Bandyopadhyay, 2017).

III. Tetrahymena Infection (Guppy Killer Disease)

Tetrahymena pyriformis is the cause of Tetrahymena Infection, also referred to as Guppy Killer Disease. It mostly affects a variety of tropical aquarium fish species, especially guppies (Poecilia reticulata). Infection leads to parasite invasion of internal organs, skin, and muscle in all fish species; the illness is prevalent in crowded environments. The most vulnerable species to Tetrahymena infection are guppies, which in two different tests showed fatality rates of 87% and 100%. Additionally, platyfish have high death rates (77%), whereas molly and angelfish have far lower mortality rates (23% and 33%, respectively). Tetrahymena infection has a lower death rate in goldfish and koi carp (24% and 59%, respectively). Because the parasite is immunogenic, three weeks after infection, koi carp that have been infected have an almost three-fold increased Tetrahymena immobilisation response. Fish that are infected display signs such internal organ, skin, and muscle parasite invasion; guppies are the most vulnerable species (Sharon et al., 2014) (Thilakaratne et al., 2003).

IV. Pleistophora hyphessobryconis:

The cause of neon tetra disease, infecting a wide variety of aquarium fish, including tetras, barbs, and goldfish.

3.2 Non-communicable diseases

Non-infectious or non-communicable diseases in ornamental fish are caused by environmental problems, nutritional deficiencies, or genetic conditions and are not contagious. These diseases can lead to direct mortalities, productivity losses due to reduced growth, fecundity, product quality, and social factors, and the costs of control measures (Shefat & Karim, 2018; Admasu & Wakjira, 2021).

I. Anorexia

Anoxia in ornamental fish refers to a state of oxygen deprivation in which fish are exposed to low or no oxygen levels, leading to a shift in their metabolic processes towards anaerobic respiration. A concentration of 5mg/l oxygen is considered to be sufficient for most fish. Concentration less than 3mg/l may prove fatal for many species of fish. Goldfish and crucian carp are natural models of anoxia tolerance, with crucian carp being able to survive in oxygen-depleted waters for extended periods due to their ability to produce ethanol as a byproduct of anaerobic metabolism (Fagernes et al., 2017). To prevent anoxia in ornamental fish, proper water conditions, including adequate oxygen levels, temperature, and pH, must be maintained. This can be achieved through regular water changes, aeration, and filtration, as well as the use of air pumps and protein skimmers.

II. Gas Bubble Diseases

Gas bubble disease can affect ornamental fish. It is a condition in which bubbles form within a fish's body due to water supersaturated with dissolved gas. These bubbles can lead to various symptoms like disorientation, visible bubbles in the eyes, skin, or fins, and tissue degeneration. The causes include sudden temperature or pressure changes, faulty filter equipment, and gas influx from an outside source. Prevention involves maintaining proper water conditions and monitoring for excess gas bubbles.

I. Nutritional and dietary diseases

Malnutrition or dietary diseases in ornamental fish can occur due to inadequate nutrition, poor diet, or certain diseases such as heavy tapeworm infestation. Affected fish may refuse to feed, leading to a gradual loss of body mass and muscle wastage. Malnourished fish can become emaciated and develop a pinched-in 'hollow' belly, with their heads appearing disproportionately more significant than their bodies (Admasu & Wakjira, 2021).

Anemia in ornamental fish is characterized by a deficiency of hemoglobin, packed cell volume, or erythrocytes in the blood. It can be caused by various factors, including bacterial, fungal, viral, and parasitic infections, folic acid deficiency, exposure to high levels of nitrates, and infestation of blood-sucking parasites such as leeches. Anemia can lead to severe symptoms such as lethargy, weight loss, and abnormally pale gills in fish.

4. Prevention Measures and Control of Diseases

4.1 Importance of maintaining stable aquarium/environmental conditions

These decorative fish "pets" have seen a sharp rise in commerce worldwide in recent years. There is an urgent need to grow this industry by adding more new ornamental species, as evidenced by recent studies that found that over 20 million marine ornamental fish are thought to be taken from the wild and sold to over 2 million aquarium hobbyists worldwide (Chen et al., 2020). The debate over whether fish can feel pain, discomfort, misery, anxiety, or discomfort has persisted for several decades and is a crucial first step towards comprehending fish welfare. A viewpoint posits that fish lack the requisite anatomical features and cognitive understanding to identify pain (Rose et al., 2014). Because the ornamental fish market is a component of the pet industry, which is sometimes referred to be a multibillion dollar sector with a trade value between $15 and $30 billion, aquarium maintenance is crucial (Tarihoran et al., 2023). Because ornamental fish are a popular and simple hobby that relieves tension, they also aid in import and export operations and foreign exchange. There are already 3.2 million aquariums in the EU and 7.2 million in the USA, and the number is rising every day globally. To meet the need, ornamental fish aquaculture is being developed. The biggest markets for ornamental fish worldwide are the USA, Europe, and Japan, while over 65% of shipments are from Asia. This will promote economic growth (Pouil et al., 2020).

4.2 Strategies to maintain a stable aquarium

Maintenance of water quality

The importance of water quality in fish exhibits and habitats cannot be overstated; water composition is essential to the health and well-being of all fish species. However, different species and life stages may require similar or extremely different water quality parameters to provide appropriate environmental conditions for optimal health and welfare. Water quality parameters outside the tolerant range of the species can cause significant changes in several physiological and biochemical properties of a fish, resulting in abnormalities of blood chemistry and hematology, changes in the cellular permeability, and changes in the osmoregulatory needs of the fish. The resulting “stress response”, or disturbance in the balance of the physiological homeostasis, initiates various adaptive responses to help return the fish to a stable homeostatic state (Iwama et al., 2005).

Nutrition

The majority of fish species kept in captivity have distinct dietary needs that are currently unknown. Commercially available formulated meals for fish raised in aquaculture, such carp, salmonids, and catfish, are frequently unsuitable for the variety of fish kept in public aquariums. Therefore, it is often advised to offer a tasty food that satisfies the species' daily needs for nutrition and behavior (Council et al., 2010).

Habitat Design

Any physical environment that fish occupy should be constructed from materials that are safe, non-toxic, and devoid of pathogens, such as crushed coral, gravel, or sterilized sand. Fish behavior and wellbeing are significantly influenced by substrates, and research has revealed that different species—and even individual members of the same species—have distinct preferences. For example, to support their natural foraging habit, corydoras catfish (Corydoras spp.) prefer sand over bigger pebbles. Additionally, it has been demonstrated that Nile tilapia exhibit unique preferences for various substrate sizes (Maia & Volpato, 2018).

4.3 Strategies to avoid infected fish or plant in ornamental fish

Introduced plants or fish that are infected might spread the disease to other species in the aquarium, affecting the entire fish population. Different tactics are used to steer clear of these circumstances. The risk of contaminating the primary stock of fish with unknown health statuses must be reduced by enacting stricter quarantine regulations and treatment or mitigation measures for microorganisms that are prohibited from entering the EU.

4.4 Notifiable diseases—Check local and national regulations.

The intergovernmental organization in charge of enhancing animal health globally is the World Organization for Animal Health (OIE). One of the official responsibilities of an OIE Member State is to provide data as soon as possible and transparently on any relevant animal illness situation, including the existence of any zoonosis. The OIE provides a list of fish infections to be taken into account for international commerce as well as further details concerning associated illnesses, diagnostic procedures to detect them, and management strategies (Mocho et al., 2022).

4.5 Assess risk before importation

Before agreeing to accept a shipment of fish, the responsible representative of the receiving facility should review the health reports and facility description of the exporting facility (Mocho et al., 2022).

4.6 Mitigate risk according to fish developmental stage.

The developing stage, which will be approved for shipping, is a crucial control point early in the import process. The lifecycle (length), reproduction mode (oviparous or ovoviviparous), and other reproductive parameters (such seasonal fertility and the capacity to reproduce in captivity) are among the species' features to take into account. Importing embryos is not possible in many fish research institutions (for example, because of the features of the species or the capacity to undertake egg surface cleaning). In quarantine, adult immigrants may undergo nonlethal screening and postmortem examination following spawning or cryopreserved sperm. To create new colonies, germplasm such as frozen gametes can also be transplanted. Because freezing kills some particular germs, it may lower the risk of contamination. But since many microorganisms are resistant to cryopreservation, frozen biological. However, many microbes resist cryopreservation so that frozen biological material can remain a biosecurity hazard (Norris, Watral, & Kent, 2018)

4.7 Biocontain imported fish in quarantine.

All fish should be brought into a quarantine chamber that is physically segregated and controlled once the introduction of additional fish has been permitted. The EU's main building and the quarantine chamber ought to be apart. In addition to being spread by vectors like fish, birds, air, water, or biological materials, infections can also arise via unintentional surface contact. As a result, the primary holding systems and the quarantine area need to share a separate room, washbasin, bench, water system or other piece of furniture. Aside from being separate from other EUs, the quarantine area should include all the equipment required (refrigerators, incubators, feeding devices, microscopes, water testing kits, maintenance tools, etc.).

4.8 Provide ample time for quarantine and acclimatization

Upon arrival, fish should be observed in quarantine for a minimum of two weeks (Aleström et al., 2020). Depending on the estimated risks of the shipment and local regulations (Arthur et al., 2008), this observation period may require an extension for up to or over six weeks. The recommended minimum duration of quarantine in public aquaria is 30 days; in aquaculture, it is 30 to 60 days (Hadfield, 2012; Mocho et al., 2022).

4.9 Screen imported fish for pathogens.

Fish placed in quarantine should be checked for infections and kept an eye out for any overt symptoms of illness or higher mortality. Testing can be done for excluded microorganisms in quarantine system water and some imported fish. The conditions of the existing facility (number of imports present, size of quarantine, phases of development upon arrival, and exclusion of infections) should be taken into account while monitoring the health of imported fish. Screening the system environment, analyzing each import group in-person, and reviewing clinical cases are additional helpful activities (Kent et al., 2011).

5. Treatments

5.1 For bacterial diseases

Bacterial infections are very common in ornamental fish and can be caused by various Gram-negative and Gram-positive bacteria. Treatments often involve antibiotics and disinfecting the water.

5.2 For viral diseases

Lymphocystis is a common viral disease that causes white, cauliflower-like growths on the fish's body and fins. There is no proven treatment, but the infected fish can be separated and the disease is often self-limiting if water quality and nutrition are good

5.3 For fungal diseases

Saprolegniosis is a common fungal disease that causes white, cotton-like growths. It can be treated with antifungal compounds like formaldehyde, malachite green, or salt.

5.4 For parasitic diseases

External parasites like Lernaea (anchor worms) can be removed manually or treated with chemical dips.

5.5 For non-infectious diseases

Environmental factors like water quality, temperature, and nutrition play a big role in fish health. Addressing these underlying issues is important for prevention and treatment. Physical injuries from handling or transport can also predispose fish to secondary infections and should be avoided.

A combination of good husbandry, quarantine, and targeted treatments are recommended to control diseases in ornamental fish (Verma, 2008; Lipton, 2006).

Conclusion

Ornamental fish keeping is a significant global industry that relies heavily on ensuring the health and well-being of the fish. These beautiful fish are vulnerable to a variety of diseases, both infectious and non-infectious, which can have a profound impact on their survival and overall health. When it comes to diseases, ornamental fish can suffer from viral infections like lymphocystis, which leads to distinctive white, cauliflower-like growths. Unfortunately, there is no established treatment for this viral disease. Bacterial infections, such as fin and tail rot, dropsy, and ulcerations, are commonly managed with antibiotics. Fungal diseases like saprolegniosis can be addressed with antifungal compounds, while parasitic diseases, including external parasites like anchor worms, may require manual removal or chemical treatments. Apart from infectious diseases, ornamental fish can also be affected by non-infectious conditions triggered by environmental factors like poor water quality, inadequate nutrition, and physical injuries. To safeguard the health of ornamental fish, it is crucial to focus on disease prevention and effective management strategies. This involves maintaining optimal water quality, isolating new fish in quarantine, and administering targeted treatments when needed. By combining good husbandry practices with the appropriate use of medications, the impact of diseases on ornamental fish can be effectively controlled.

References

Admasu, F., & Wakjira, M. (2021). Non-Infectious diseases and biosecurity management practices of fishes health in aquaculture. Journal of FisheriesSciences. com, 15(6), 1-6.

Ahilan, B., & Kamalii, A. (2022). Ornamental Livebearers: CRC Press.

Alam et al., (2024). Genetic Advancement, Global Trade Dynamics, Persistent Challenges and Future Prospects in Ornamental Fish Culture. Asian Journal of Research in Zoology, 7(1), 32-46.

Aleström, P., D'Angelo, L., Midtlyng, P. J., Schorderet, D. F., Schulte-Merker, S., Sohm, F., & Warner, S. (2020). Zebrafish: Housing and husbandry recommendations. Laboratory animals, 54(3), 213-224.

Algammal AM, Mabrok M, Sivaramasamy E, Youssef FM, Atwa MH, El-Kholy AW, Hetta HF, Hozzein WN. 2020. Emerging MDR Pseudomonas aeruginosa in fish commonly harbor oprL and toxA virulence genes and blaTEM, blaCTX M, and tetA antibiotic resistance genes. Sci Rep. 10(1):15961.

AlYahya S, Ameen F, Al-Niaeem K, Al-Sa'adi BA, Hadi S, Mostafa AA. 2018. Histopathological studies of experimental Aeromonas hydrophila infection in blue tilapia, Oreochromis aureus. Saudi J Biol Sci. 25(1):182–185.

Anjur, N., Sabran, S. F., Daud, H. M., & Othman, N. Z. (2021). An update on the ornamental fish industry in Malaysia: Aeromonas hydrophila-associated disease and its treatment control. Veterinary World, 14(5), 1143.

Antunes P et al., 2018. Inflow water is a major source of trout farming contamination with Salmonella and multidrug resistant bacteria. Science of the Total Environment 642: 1163-1171.

Arthur, J. R., Bondad-Reantaso, M. G., & Subasinghe, R. P. (2008). Procedures for the quarantine of live aquatic animals: a manual.

Bibi F et al., 2015. Occurrence of Salmonella in freshwater fishes: A review. Journal of Animal and Plant Sciences 25: 303-310

Biondo, M. V., & Burki, R. P. (2019). Monitoring the trade in marine ornamental fishes through the European Trade Control and Expert System TRACES: Challenges and possibilities. Marine Policy, 108, 103620.

Borrego JJ et al., 2017. Lymphocystis disease virus: its importance in aquaculture. Reviews in Aquaculture 9: 179- 193.

Cardoso, P. H. M., Moreno, A. M., Moreno, L. Z., Oliveira, C. H. D., Baroni, F. D. A., Maganha, S. R. D. L., ... & Balian, S. D. C. (2019). Infectious diseases in aquarium ornamental pet fish: prevention and control measures. Brazilian Journal of Veterinary Research and Animal Science, 56(2), 1-16.

Chen, J. Y., Zeng, C., Jerry, D. R., & Cobcroft, J. M. (2020). Recent advances of marine ornamental fish larviculture: broodstock reproduction, live prey and feeding regimes, and comparison between demersal and pelagic spawners. Reviews in Aquaculture, 12(3), 1518-154.

Council, N. R., Earth, D. o., Studies, L., Research, I. f. L. A., Care, C. f. t. U. o. t. G. f. t., & Animals, U. o. L. (2010). Guide for the care and use of laboratory animals.

D'souza CA et al., 2011. Genome variation in Cryptococcus gattii, an emerging pathogen of immunocompetent hosts. Molecular Biosystems 2: 10-1128.

Das, M. (2023). Effect of Insect Meals on the Growth Efficiency, SurvivalandTotalCarotenoid Content of an Ornamental Fish Xiphophorus maculatus (Gunther, 1866). Asian J. Fish. Aqu. Res, 22(3), 1-9.

Daud, M., Fachroji, R., Hasibuan, A., Putri, R., Nratha, I. M. A., & Isa, M. (2023). Design of Automatic Pond Water Quality Control in Koi Fish Farm. Journal of Renewable Energy, Electrical, and Computer Engineering, 3(1), 6-11.

Declercq, A. M., Haesebrouck, F., Van den Broeck, W., Bossier, P., & Decostere, A. (2013). Columnaris disease in fish: a review with emphasis on bacterium-host interactions. Veterinary research, 44, 1-17.

Delghandi MR, El-Matbouli M, Menanteau-Ledouble S. (2020). Mycobacteriosis and infections with nontuberculous mycobacteria in aquatic organisms: a review. Microorganisms. 8(9):1368.

Dey, V. (2016). The global trade in ornamental fish. Infofish International, 4(16), 23-29.

Dickerson, H. W., & Dawe, D. L. (2006). Ichthyophthirius multifiliis and Cryptocaryon irritans (phylum Ciliophora). Fish diseases and disorders, 1, 116-153.

Eiras, B. J., Veras, G. C., Alves, A. X., & Da Costa, R. M. (2019). Effect of artificial seawater and feeding frequency on the larval culture of freshwater Amazonian ornamental fish banded cichlid Heros severus (Heckel, 1840) and angelfish Pterophyllum scalare (Schultze, 1823). Spanish journal of agricultural research, 17(2), 604.

El Amrani et al., 2010. Upper extremity Mycobacterium marinum infection. Orthopaedics & Traumatology: Surgery & Research, 96: 706-711.

Fagernes, C. E., Stensløkken, K. O., Røhr, Å. K., Berenbrink, M., Ellefsen, S., & Nilsson, G. E. (2017). Extreme anoxia tolerance in crucian carp and goldfish through neofunctionalization of duplicated genes creating a new ethanol-producing pyruvate decarboxylase pathway. Scientific reports, 7(1), 7884.

Florindo, M. C., Jerônimo, G. T., Steckert, L. D., Acchile, M., Figueredo, A. B., Gonçalves, E. L. T., & Martins, M. L. (2017). Metazoan parasites of freshwater ornamental fishes. Latin american journal of aquatic research, 45(5), 992-998.

G SAAD EL-DEEN, A. Y. A., & A ELKAMEL, A. H. M. A. D. (2015). Clinical and experimental study on vibriosis in ornamental fish. Assiut Veterinary Medical Journal, 61(146), 147-153.

Gazal LES et al., 2018. Salmonella sp. in fish—What is the importance for health in fish farm. Pesqui Agropecuária Gaúcha 24: 55-64.

George MR, John KR, Mansoor MM, Saravanakumar R, Sundar P, Pradeep V. Isolation and characterization of a ranavirus from koi, Cyprinus carpio L., experiencing mass mortalities in India. Journal of Fish Diseases. 2015;38:389-403. DOI: 10.1111/jfd.12246

Giovannini, S., Bergmann, S. M., Keeling, C., Lany, C., Schütze, H., & Schmidt-Posthaus, H. (2016). Herpesviral hematopoietic necrosis in goldfish in Switzerland: early lesions in clinically normal goldfish (Carassius auratus). Veterinary pathology, 53(4), 847-852.

Goodwin, A. E., Khoo, L., LaPatra, S. E., Bonar, C., Key, D. W., Garner, M., ... & Hanson, L. (2006). Goldfish hematopoietic necrosis herpesvirus (cyprinid herpesvirus 2) in the USA: molecular confirmation of isolates from diseased fish. Journal of Aquatic Animal Health, 18(1), 11-18.

Greg Lewbart, M. S. Important Infectious Diseases of Ornamental Fish Atlantic Coast Veterinary Conference 2001.

Hadfield, C. (2012). Quarantine of fish and aquatic invertebrates in public display aquaria. In Fowler's Zoo and Wild Animal Medicine (pp. 202-209). Elsevier.

Harikrishnan R et al., 2010. Effect of probiotics enriched diet on Paralichthys olivaceus infected with lymphocystis disease virus (LCDV). Fish & Shellfish Immunology 29: 868-874.

Hartman, K. H., Yanong, R. P., Pouder, D. B., Petty, B. D., Francis-Floyd, R., Riggs, A. C., & Waltzek, T. B. (2013). Koi Herpesvirus Disease (KHVD). Extension Factsheet VM-149.

Hashish E, Merwad AMA, ElgamiSh A, Amer A, Kamal H, Elsadek A, Marei A, Sitohy M. 2018. Mycobacterium marinum infection in fish and man: epidemiology, pathophysiology and management; a review. Vet Q. 38(1):01–34.

Helmi M, Mukti AT, Soegianto A, Effendi MH. 2020. A review of vibriosis in fisheries: public health importance. Sys Rev Pharm. 11(8):51–58.

Horne, A. N., Stone, N., & Engle, C. R. (2010). Development of new intensive hatchery methods for rosy red fathead minnow. North American Journal of Aquaculture, 72(3), 237-251.

Hoseinifar, S. H., Maradonna, F., Faheem, M., Harikrishnan, R., Devi, G., Ringø, E., & Carnevali, O. (2023). Sustainable ornamental fish aquaculture: the implication of microbial feed additives. Animals, 13(10), 1583.

Hossain S and Heo GJ, 2021. Ornamental fish: a potential source of pathogenic and multidrug-resistant motile Aeromonas spp. Letters in Applied Microbiology 72: 2-12.

Hussein, M. M., Sayed, R. K., & Mokhtar, D. M. (2023). Structural and immunohistochemical analysis of the cellular compositions of the liver of molly fish (Poecilia sphenops), focusing on its immune role. Zoological Letters, 9(1), 1.

Iregui CA, Comas J, Vasquez GMV, Verjan N. 2016. Experimental early pathogenesis of Streptococcus agalactiae infection in red tilapia Oreochromis spp. J Fish Dis. 39(2):205–215.

Irshath, A. A., Rajan, A. P., Vimal, S., Prabhakaran, V. S., & Ganesan, R. (2023). Bacterial pathogenesis in various fish diseases: recent advances and specific challenges in vaccine development. Vaccines, 11(2), 470.

Iwama, G., Afonso, L., & Vijayan, M. (2005). Stress in fishes.

Jia S et al., 2020. Oral immunization of carps with chitosan–alginate microcapsule containing probiotic expressing spring viremia of carp virus (SVCV) G protein provides effective protection against SVCV infection. Fish & Shellfish Immunology 105: 327-329.

Kasmi, M., Sulkifli, S., & Asriany, A. (2022). Status tingkat pemanfaatan ikan hias Injel (Angel fish) untuk ekspor. Paper presented at the Prosiding Seminar Nasional Politeknik Pertanian Negeri Pangkajene Kepulauan.

Kaur, R., & Shah, T. K. (2017). Role of feed additives in pigmentation of ornamental fishes. International Journal of Fisheries and Aquatic Studies, 5(2), 684-686.

Ke, Y., Tan, Y., Feng, C., Chen, C., Lu, Q., Xu, Q., & Long, Y. (2022). Tetra-Fish-Inspired aesthetic thermochromic windows toward Energy-Saving buildings. Applied Energy, 315, 119053.

Kent, M. L., Buchner, C., Watral, V. G., Sanders, J. L., LaDu, J., Peterson, T. S., & Tanguay, R. L. (2011). Development and maintenance of a specific pathogen-free (SPF) zebrafish research facility for Pseudoloma neurophilia. Diseases of aquatic organisms, 95(1), 73-79.

Kwon-Chung et al., 2017. The case for adopting the "species complex" nomenclature for the etiologic agents of cryptococcosis. MSphere 2: 10-1128.

Leal CAG, Queiroz GA, Pereira FL, Tavares GC, Figueiredo HCP. 2019. Streptococcus agalactiae sequence type 283 in farmed fish, Brazil. Emerg Infect Dis. 25(4):776–779.

Lewbart, G. (2001) Bacteria and ornamental fish. Semin Avian Exot Pet Med 10, 48–56

Liang H et al., 2022. The effect and underlying mechanism of yeast β-glucan on antiviral resistance of zebrafish against spring viremia of carp virus infection. Frontiers in Immunology 13: 1031962.

Lipton, A. P. (2006). Diseases of ornamental fishes and their control.

Mahadevan, G., Gosavi, S. M., Murugesan, P., & Arumugam, A. (2021). Demographics of butterfly fish, Heniochus acuminatus (Perciformes, Chaetodontidae) from the Gulf of Mannar, India. Thalassas: An International Journal of Marine Sciences, 37, 81-91.

Maia, C. M., & Volpato, G. L. (2018). Individuality matters for substrate-size preference in the Nile tilapia juveniles. Journal of applied animal welfare science, 21(4), 316-324.

Martins, M. L., Cardoso, L., Marchiori, N., & Benites de Pádua, S. (2015). Protozoan infections in farmed fish from Brazil: diagnosis and pathogenesis. Revista Brasileira de Parasitologia Veterinária, 24, 1-20.

Matthews, J.L., A.M.V. Brown, K. Larison,J.K. Bishop-Stewart, J.K., P. Rogers, and M.L. Kent. 2001. Pseudoloma neurophilia n.g., n.sp., a new genus and species of Microsporidia from the central nervous system of the zebrafish (Danio rerio). J. Euk. Microbiol. 48:229-235

Mawa J et al., 2021. Physicochemical and bacteriological screening of pathogenic microorganisms from aquarium water collected from katabon area in Dhaka city. Stamford Journal of Microbiology 11: 20-23

Meng, K. F., Ding, L. G., Wu, S., Wu, Z. B., Cheng, G. F., Zhai, X., & Xu, Z. (2021). Interactions between commensal microbiota and mucosal immunity in teleost fish during viral infection with SVCV. Frontiers in immunology, 12, 654758.

Mocho, J.-P., Collymore, C., Farmer, S. C., Leguay, E., Murray, K. N., & Pereira, N. (2022a). FELASA-AALAS recommendations for biosecurity in an aquatic facility, including prevention of zoonosis, introduction of new fish colonies, and quarantine. Comparative Medicine, 72(3), 149-168.

Mocho, J.-P., Collymore, C., Farmer, S. C., Leguay, E., Murray, K. N., & Pereira, N. (2022b). FELASA-AALAS recommendations for monitoring and reporting of laboratory fish diseases and health status, with an emphasis on zebrafish (Danio rerio). Comparative Medicine, 72(3), 127-148.

Norris, L. J., Watral, V., & Kent, M. L. (2018). Survival of bacterial and parasitic pathogens from zebrafish (Danio rerio) after cryopreservation and thawing. Zebrafish, 15(2), 188-201.

Orós, J., Priestnall, S. L., & Suárez-Bonnet, A. (2022). Histopathological description of iridophoromas resembling skin nodule syndrome in Siamese fighting fish Betta splendens. Diseases of Aquatic Organisms, 151, 23-27.

Ozcan, F., & Arserim, N. B. (2021). Fungal Diseases in Fish. Black Sea Journal of Agriculture, 5(1), 48-52.

Pinnegar, J. K., & Murray, J. M. (2019). Understanding the United Kingdom marine aquarium trade–a mystery shopper study of species on sale. Journal of Fish Biology, 94(6), 917-924.

Pomaranski EK, Griffin MJ, Camus AC, Armwood AR, Shelley J, Waldbieser GC, LaFrentz BR, García JC, Yanong R, Soto E. 2020. Description of Erysipelothrix piscisicarius sp. nov., an emergent fish pathogen, and assessment of virulence using a tiger barb (Puntigrus tetrazona) infection model. Int J Syst Evol Microbiol. 70(2):857–867.

Pouil, S., Tlusty, M. F., Rhyne, A. L., & Metian, M. (2020). Aquaculture of marine ornamental fish: overview of the production trends and the role of academia in research progress. Reviews in Aquaculture, 12(2), 1217-1230.

Prasetya, B., Nurhayati, A., Suryadi, I. B. B., & Gumilar, I. (2021). Mapping of Ornamental Fish Farming Cultivation Production Areas in Bogor Regency. Asian Journal of Fisheries and Aquatic Research, 15(6), 71-77.

Puk K, Guz L. 2020. Occurrence of Mycobacterium spp. in ornamental fish. Ann Agric Environ Med. 27(4):535–539.

Rathore, G., Kumar, G., Raja Swaminathan, T., & Swain, P. (2012). Koi herpes virus: a review and risk assessment of Indian aquaculture. Indian Journal of Virology, 23, 124-133.

Roberts, M. B., Schultz, D. T., Gatins, R., Escalona, M., & Bernardi, G. (2023). Chromosome-level genome of the three-spot damselfish, Dascyllus trimaculatus. G3: Genes, Genomes, Genetics, 13(4), jkac339.

Rose, J. D., Arlinghaus, R., Cooke, S. J., Diggles, B. K., Sawynok, W., Stevens, E. D., & Wynne, C. D. (2014). Can fish really feel pain? Fish and Fisheries, 15(1), 97-133.

Rostamian M et al., 2022. Clinical manifestations, associated diseases, diagnosis, and treatment of human infections caused by j: a systematic review. Germs 12: 16.

Routh, S., & Solanki, M. (2023). Analysis of Invasion of Fungal Infection in Some Species of Fish. Journal of Advanced Zoology, 44.

Saha, M., & Bandyopadhyay, P. K. (2017). Seasonal incidence of protozoan parasitic infestation in ornamental fishes of West Bengal, India. Journal of Parasitic Diseases, 41, 523-526.

Santikawati, S., Syafriadiman, S., & Syawal, H. (2023). Water quality improvement and analysis for clown fish (Amphiprion ocellaris) cultivation in a recirculation system. Asian Journal of Aquatic Sciences, 6(1), 136-141.

Satam, S., Sawant, N., Ghughuskar, M., Sahastrabuddhe, V., Naik, V., Pagarkar, A., Sadawarte, V. (2018). Ornamental fisheries: a new avenue to supplement farm income. Advanced Agricultural

Research and Technology Journal, 2(2), 193-197.

Setiyowati, H., Nugroho, M., & Halik, A. (2022). Developing a blue economy in Depok West Java, Indonesia: Opportunities and challenges of neon tetra fish cultivation. Sustainability, 14(20), 13028.

Sharon, G., Leibowitz, M. P., Chettri, J. K., Isakov, N., & Zilberg, D. (2014). Comparative study of infection with Tetrahymena of different ornamental fish species. Journal of Comparative Pathology, 150(2-3), 316-324.

Shefat, S. H. T., & Karim, M. A. (2018). Nutritional diseases of fish in aquaculture and their management: A review. Acta Scientific Pharmaceutical Sciences, 2(12), 50-58.

Sidi, F. P., & Sungkowo, A. B. (2022). Potensi Pertumbuhan Usaha Budidaya Ikan Hias Discus Sja. Prosiding Working Papers Series In Management, 14(1), 340-357.

Smith, J., Fratamico, P. M., & Uhlich, G. (2009). Molecular mechanisms involved in biofilm formation by food-associated bacteria. In Biofilms in the food and beverage industries (pp. 42-98). Woodhead Publishing.

Soni, M., Qureshi, Q. A., Mishra, M., Nishad, C. S., Chhaba, B., & Das, S. A. (2021). Common Aeromonas infections in ornamental fishes: a review. In Biol. Forum (Vol. 13, pp. 433-439).

Steckler, N., & Yanong, R. P. (2012). Lernaea (anchorworm) Infestations in fish. Florida: University of Florida.

Steckler, N., & Yanong, R. P. (2013). Argulus (Fish Louse) infections in fish: FA184, 11/2012. Edis, 2013(2).

Su, H., & Su, J. (2018). Cyprinid viral diseases and vaccine development. Fish & shellfish immunology, 83, 84-95.

Sulkifli, S., Kasmi, M., & Yusuf, Y. M. (2023). Size Structure, Long-Weight Relations And Growth Angel Ornamental Fish (Pomacanthus Imperator) In Spermonde Waters, South Sulawesi, Indonesia. International Journal of Technology and Education Research, 1(02), 51-64.

Sumithra, T. G., Sharma, S. K., Neelima, L., Dhanutha, N. R., Joshy, A., Anusree, V. N., ... & Rajesh, K. M. (2022). Red sea bream iridovirus infection in cage farmed Asian sea bass (Lates calcarifer): Insights into the pathology, epizootiology, and genetic diversity. Aquaculture, 548, 737571.

Tarihoran, A. D. B., Hubeis, M., Jahroh, S., & Zulbainarni, N. (2023). Competitiveness of and Barriers to Indonesia's Exports of Ornamental Fish. Sustainability 2023, 15, 8711.

Tarihoran, A. D. B., Hubeis, M., Jahroh, S., & Zulbainarni, N. (2023). Competitiveness of and Barriers to Indonesia's Exports of Ornamental Fish. Sustainability, 15(11), 8711.

Thilakaratne, I. D. S. I. P., Rajapaksha, G., Hewakopara, A., Rajapakse, R. P. V. J., & Faizal, A. C. M. (2003). Parasitic infections in freshwater ornamental fish in Sri Lanka. Diseases of Aquatic Organisms, 54(2), 157-162.

Tuckett, Q. M., Ressel, K. N., Ritch, J. L., Lawson, K. M., & Hill, J. E. (2021). Domestication and feralization influence the distribution and phenotypes of escaped ornamental fish. Biological Invasions, 23, 1033-1047.

Vajargah, M. F., & Majidiyan, N. (2022). A review of Saprolegniosis. J Aquac Mar Biol, 11(1), 17-19.

Vasantharajan, M. (2023). A Brief Note on Important Freshwater Ornamental Fishes.

Verma, V. (2008). Fungus disease in fish, diagnosis and treatment. Veterinary World, 1(2), 62.

Volpatti D and Ciulli S, 2022. Lymphocystis virus disease. Aquaculture Pathophysiology 201-216

Walczak, N., Puk, K., & Guz, L. (2017). Bacterial flora associated with diseased freshwater ornamental fish. Journal of veterinary research, 61(4), 445.

Washim, M. R., Ahmmed, S., Rube, A. K. M., Mondal, D. K., Begum, N., & Islam, M. L. (2022). The effects of Synthetic gonadotropin releasing hormone analogue (SGnRHa) on artificial propagation of spotted scat, Scatophagus argus (Linnaeus, 1766). South Asian Journal of Experimental Biology, 12(2).

Wei, J. Z., Li, H., & Yu, H. (2013). Ichthyophthiriasis: emphases on the epizootiology. Letters in Applied Microbiology, 57(2), 91-101.

Yanong, R. P. (2003). Use of antibiotics in ornamental fish aquaculture.

Yanong, R. P. (2013). Lymphocystis disease in fish. UNIVERSITY of Florida. Institute of Food and Agricultural Sciences. Florida Cooperative Extension Service. School of Forest Resources and Conservation. Program in Fisheries and Aquatic Sciences.[Document FA181]. Florida: University of Florida, 1-4.

Yanong, R. P. E., & Terrell, S. (2003). Iridoviral-associated disease in oscars (Astronotus ocellatus). In Proceedings of the 34th Annual Conference, International Association for Aquatic Animal Medicine, Waikoloa, Hawaii, May (pp. 9-14).

Yanong, R. P., & Waltzek, T. B. (2010). Megalocytivirus infections in fish, with emphasis on ornamental species. Retrieved November, 29, 2018.

Yue, G. H., Wang, L., Sun, F., Yang, Z., Shen, Y., Meng, Z., & Alfiko, Y. (2022). The ornamental fighting fish is the next model organism for genetic studies. Reviews in Aquaculture, 14(4), 1966-1977.

Zhang C et al., 2019. Evaluation of immune response and protection against spring viremia of carp virus induced by a single-walled carbon nanotubes-based immersion DNA vaccine. Virology 537: 216-225.

Ziarati, M., Zorriehzahra, M. J., Hassantabar, F., Mehrabi, Z., Dhawan, M., Sharun, K., & Shamsi, S. (2022). Zoonotic diseases of fish and their prevention and control. Veterinary Quarterly, 42(1), 95-118.

About The Authors

Dr. Farkhanda Asad, Zoology Department, Government College University Faisalabad, Faisalabad, Punjab, Pakistan

E-mail: farkhanda.asad@gcuf.edu.pk ORCID: 0000-0002-5729-085X

Dr. Aiman Nadeem, Zoology Department, Government College University Faisalabad, Faisalabad, Punjab, Pakistan

Email: aimannadeem77@gmail.com ORCID: 0000-0003-1391-8913

Dr. Rafia Jamal, Zoology Department, Government College University Faisalabad, Faisalabad, Punjab, Pakistan

Email: rafiajamal734@gmail.com ORCID: 0009-0007-2156-850X

Basim. S. A. Al SULIVANY

To Cite This Chapter

Asad F et al., (2024). Diseases of Ornamental Fishes and Their Management. In Current Studies in Health and Life Sciences 2024 (pp.374-401). ISRES Publishing.

Impact of Antibiotics onAquatic Life

Qurat-ul-Ane GILLANI

Ayesha RIAZ

Arifa MEHREEN

Muhammad SAFDAR

1. Introduction

The use of antibiotics has increased over the years to enhance human and animal well-being since these infections are now easily controlled (Singer et al., 2003). However, their widespread use and improper disposal have led to a significant environmental crisis: Antibiotic resistance and the presence of antibiotics in water. This contamination is dangerous as it disrupts the natural distribution of life in water bodies beginning with microscopic organisms, fish, other water animals, and even man. Most of these antibiotics end up in water systems through agricultural drained water, treated sewage effluents, and discarded unused or expired medicines. Subsequently, these drugs remain and concentrate in water, thus causing a biochemical impact on every biological life stage of the aquatic life forms. The ecological importance of microorganisms in aquatic ecosystems makes them sensitive to antibiotics. They are involved in such important processes as nutrient cycling, decomposition of organic matter, and forming a source of food for organisms in higher trophic levels. Antibiotics affect microbial LM communities, decrease their diversity, and modify key biogeochemical processes (Grenni et al., 2018). Furthermore, utilization of water sources with antibiotics has been associated with the genesis of antibiotic-resistant bacteria, a notable concern in today's world. These resistant bacteria can spread resistance genes to human pathogens and hence directly affect the health of people. Antibiotics are not limited to humans and livestock only but also impact fish and other water animals. The use of these drugs can hurt height, fecundity, and character (Lee et al., 2007). In certain situations, antibiotics can be directly deadly to the fauna in the aquatic ecosystem, and lead to death. Interference with these species could result in detrimental effects on food chains and the general health of the water bodies. Antibiotics can potentially affect whole aquatic systems due to the contamination of water bodies. It was established that any imbalance in the water affects fish and other organisms; therefore, the use of antibiotics has ripple effects. This can bring about a reduction in the overall population of some species, an increase in the population density of other species, and an overall reduction in species diversity. It is established that human health is inextricably connected to the condition of the aquatic biome. Water can also affect the health of people directly if they drink the infected water and indirectly if they consume the fish and seafood obtained from such water (Iwamoto et al., 2010). Another great concern is the spread of antibiotic-resistant bacteria in the surrounding environment thereby increasing the risk of certain antibiotics being deficient in combating infections.

Due to the consequential impact of antibiotic contamination, the search for possible solutions and measures that could be taken is crucial. Some specific measures that need to be taken to combat this problem include better sanitation, higher regulatory standards, and the creation of environmentally friendly substitutes for antibiotics. Furthermore, public awareness and education on the proper utilization and disposal of antibiotics help minimize this environmental and epidemic health challenge (Manyi-Loh et al., 2018).

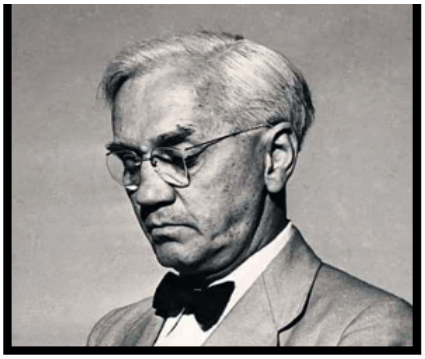
2. The Rising Tide of Antibiotic Pollution

Antibiotics, which many people consider to be one of the greatest discoveries of the past century, have contributed to the removal of bacterial diseases including millions of people's lives. However, the widespread and often indiscriminate use of these powerful drugs has led to an unforeseen and growing environmental crisis: the contamination of antibiotics. In preliminary to

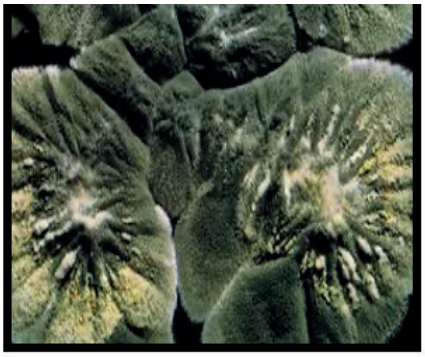
this chapter, this chapter discusses the background, concern, and impact of antibiotic pollution on the aquatic environment (Penesyan et al., 2015).

2.1. Historical context and development

The general use of antibiotics started with the world's first antibiotic, penicillin, discovered by Alexander Fleming in 1928 (Kourkouta et al., 2018). Since then, antibiotics have found a wide application in the national health care system, livestock, and fish farming. Antibiotics became widely produced and used after World War II not only for human treatment but also to increase meat production in livestock and to avoid infections in fish farming.



Alexander Fleming



Penicillin (world's

This exponential growth in antibiotic use has however come at the expense of the environment in the following ways:

2.2. Extent of Antibiotic Pollution

Antibiotic pollution may be described as the occurrence of these pharmaceuticals in ecosystems, specifically in water systems including rivers, lakes, and seas (Gothwal & Shashidhar, 2015). This pollution is on a very large scale. Research has established the presence of antibiotics in water systems worldwide, ranging from urban environments to rural wilderness.

Human Waste: Through urine excretion and fecal elimination, antibiotics taken by humans are not completely assimilated but instead are released into the sewerage system and water bodies.

Agricultural Runoff: From this kind of farming, antibiotics are washed downstream into rivers and streams.

Aquaculture: Aquaculture often treats fish with antibiotics to reduce the risk of disease, which is released directly into the aquatic environment.

Pharmaceutical Manufacturing: Manufacturers of antibiotics can emit large amounts of such compounds into the environment.

Improper Disposal: Flushing of unused medications into toilets is one common way through which high levels of antibiotics are found in water systems due to poor disposal methods.

3. Pathways of Antibiotic Entry into Aquatic Systems

Focusing on the major sources by which antibiotic contaminants are released into the environment including wastewater treatment plants, agricultural drainage, fish farming operations, medication disposal, industrial effluent, and dust. (Danner et al., 2019).

3.1. Wastewater Treatment Plants (WWTPs)

WWTPs are processing facilities that have been established to achieve the main goal of purifying sewage in a bid to discharge the water into water bodies (Qasim, 2017). However, most

WWTPs were reported to be lacking in the capacity to remove the pharmaceuticals, including antibiotics. These facilities can become major sources of antibiotic pollution due to inefficiency in the elimination of these compounds (conventional treatment processes remove only a small fraction of antibiotics and thus, effluent antibodies are often released into the treated water) and concentration in sewage sludge (antibiotics have been observed to concentrate in the sludge, which is frequently applied as a fertilizer and may infiltrate water resources). Fluctuations in removal efficiencies the case of European WWTPs pointed out that antibiotics are discharged into rivers with concentrations measurable and have impacts on aquatic life in the lower reaches. In one way or the other, the mentioned deficiencies greatly affect the ability of the mentioned nations to contain and combat communicable diseases hence there is a need to improve on the treatment technologies and enhance the implementation of better regulation measures.

3.2. Agricultural Runoff

Antibiotics are used in animal production for therapeutic purposes, disease prevention and treatment, and growth promotion of these animals. They lead to the accumulation of antibiotics in manure, which is spread on farms as a type of manure. These residues can readily reach water bodies through surface runoff (the ability of rainwater to transport antibiotics from fields into streams, rivers, and lakes) and leaching (water solubility and carrying capacity to transport antibiotics through the soil depths and pollute water wells). For instance, over-prescribed antibiotics in feeding cattle in the United States have been reported to pollute the River Mississippi with high levels of water pollution through agricultural runoff (McEwen & Fedorka-Cray, 2002).

3.3 Aquaculture

Another related practice that leads to the release of antibiotics in the environment is the aquaculture or fish farming industry. To safeguard fish from more prevalent diseases, especially in crowded fish farming establishments, antibiotics are given through the feed or water dip. This results in a direct discharge in which many antibiotics not taken by the fish are expelled into the water and sedimentation because they are water soluble and may sink to the bottom affecting the benthic organisms and may sometimes be resuspended into the body of water (Hossain et al., 2022). It was established that intensive shrimp farming released high levels of antibiotics into coastal waters of Southeast Asia as well as posing a great danger to marine life and humans who consume such seafood products.

3.4. Improper Disposal of Medications

Some individuals have the practice of flushing toilet facilities and disposing of unused or expired drugs by washing them down the drain, thereby contaminating the environment. High flushing of medications causes the antibiotics to get into the sewage system, and then without adequate treatment, the water gets into the water bodies. Drugs that are disposed of into the sewers through the sink find their way into the system through sewerage systems and treatment plant discharges. For example, surveys of occupant behavior in the UK reveal that many households throw medications in the trash, resulting in detectable levels of antibiotics entering rivers and lakes (Marwa et al., 2021). All pathways are shown in Fig 1.

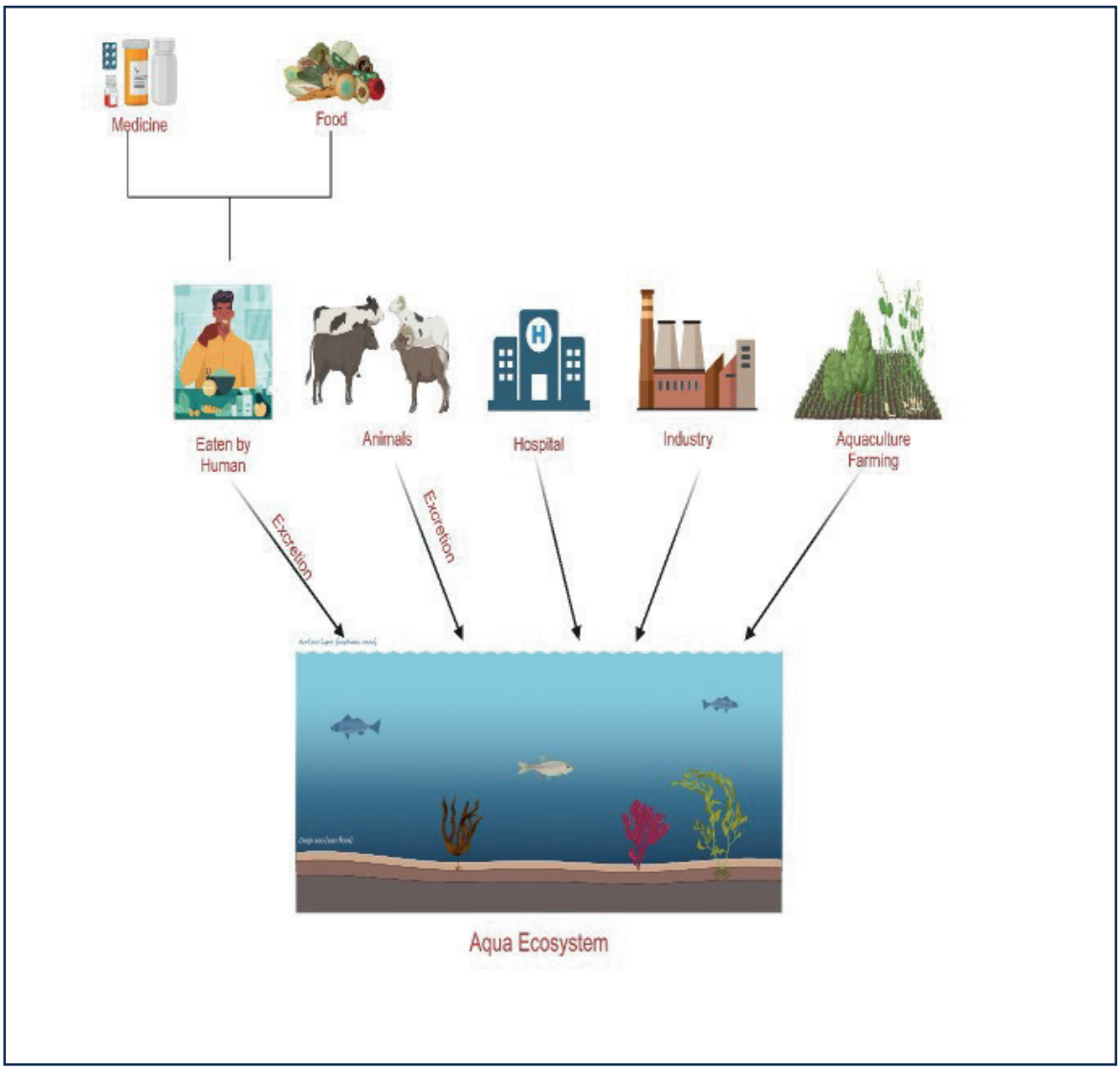


Figure 1: Pathways of Antibiotic Entry into Aquatic Systems

4. Effects of Aquatic Microorganisms

Bacteria, algae, fungi, and other microorganisms are the chief components of aquatic structures. They are important in cycling nutrients, breaking down organic matter throughout the water systems, and the health of water bodies (Sigee, 2005). Low concentrations of antibiotics, formulated to act against bacteria, are inevitably disruptive to these microbial ecosystems.

4.1. Impact on Bacterial Communities

Diversity and Abundance: Ampicillin significantly reduces species richness and density of bacteria in aquatic systems in a dose-dependent manner. In this case, sensitive bacterial species may be eradicated or substantially reduced in population thereby reducing the overall microbial diversity and leading to the emergence of resistant types.

Functional Impact: There are potential consequences for ecosystem functioning where bacterial communities undergo shifts. Some processes, such as nitrogen fixation and decomposition, are known to play crucial roles in bacteria. These functions are also negatively affected by disruptions caused by antibiotics, which in turn alter nutrient availability and rates of decomposition with potential ramifications for the structure of food webs and energy flows (Ambrosini et al., 2016).

4.2. Effects on Algal Populations

Growth and photosynthesis: Specifically, antibacterials can affect algal density, a key component in the primary producers of aquatic habitats (Sharma et al., 2021). It is important in oxygen-making and forms the basic component of the food chain. Some of the antibiotics can prevent algal growth, decrease primary production, and consequently decrease energy flow by preventing photosynthetic processes in aquatic habitats.

4.3. Fungal Communities

Role in Decomposition: Aquatic fungi are essential in breaking down organic material and cycling the nutrients within the water body. Antibiotics can interact with fungi where the fungal growth is suppressed and this will lead to changes in the microbial community which in turn can impact nutrient cycling (Sharma et al., 2021).

The effects of ampicillin on aquatic microorganisms are described in Table 1.

Table 1: Effects of Ampicillin on Aquatic Microorganisms (Singh et al., 2019)

Microorganisms	**Key Roles in Ecosystem**	**Observed Impact Due to Ampicillin Exposure**	**Potential Ecosystem Consequences**
Bacteria	Nutrient cycling, decomposition, and maintaining water health	Reduced species diversity and abundance, potential emergence of resistant strains	Disrupted nitrogen fixation, altered decomposition rates, impacts on food webs and energy flow
Algae	Primary producers: oxygen generation, the base of the food chain	Decreased algal density, inhibited growth and photosynthesis	Reduced primary production, decreased oxygen availability, disrupted energy flow
Fungi	Decomposition and nutrient cycling	Suppressed fungal growth and altered microbial community composition	Disrupted nutrient cycle, potential accumulation of organic matter

4.4. Antibiotic Resistance Development

Mechanisms of Resistance: Thus, the investigated antibiotics are introduced into the aquatic environment, which leads to the development and proliferation of antibiotic resistance among microorganisms by a process referred to as horizontal gene transfer and selective pressure (Shao et al., 2018).

Ecological and Health Implications: It is estimated that a high number of antibiotic-resistant bacteria are present in water bodies which in turn; brings about ecological consequences as well as a direct threat to human health through water recreation and consumption.

Impact on Biofilms: Biofilms on the other hand can be described as structured microbial populations that are attached to the surfaces within the aquatic systems (Donlan, 2002). Some antibiotics can affect the formation and structure of a biofilm and also change its susceptibilities to other antibiotics.

5. Antibiotic Resistance in Aquatic Environments

It was observed that antibiotic-resistant bacteria are on the rise within the clinical and environmental scenarios (Pepi & Focardi, 2021). As existing literature shows that antibiotic resistance in aquatic environments results from various origins, water bodies are sources of ARB and ARG.

5.1. Mechanisms of Antibiotic Resistance

Genetic Basis of Resistance: This occurs during a process known as mutational mechanisms which may include changes in genes or the structure of bacteria in antibiotic presence. These changes could include mutation which is heritable variation and is a genetic change that occurs without opportunity for modification; and horizontal gene transfer (HGT); the transmission of genetic material between organisms (Giedraitienė et al., 2011). HGT is the process of gene transmission through one or more bacteria through conjugation, transformation, or transduction.

Types of Resistance Mechanisms: It is, therefore, essential to understand the following strategies employed by bacteria as a response to the antagonizing effect of the antibiotics:

Efflux Pumps: Sometimes, bacteria can pump antibiotics out of their body through effluxed pumps, a mechanism that makes it hard for the antibiotic to function.

Target Modification: Another form of bacterial resistance is by altering the structure of the area in the bacterium that the antibiotic acts on, hence failing to bind to it properly.

Reduced Permeability: These can change the cell membrane permeability, and in this way, reduce the amounts of the antibiotics that can be incorporated.

WWTP Effluents: According to the research done by Barnett et al. (2017), this information reveals that when treated wastewater is discharged into natural water sources, both ARB and ARGs can be conveyed.

Agricultural Runoff: In farm areas, concentration enhances the distribution of ARB and ARGs through rivers and streams, and in industrial areas, the focus enhances the distribution of ARB and ARG in industrial waterways.

Aquaculture: Intensive fish farming practices have also been cited by studies that can result in the development of resistance.

Industrial Discharges: ARB and ARGs can be accumulated from entities that are in the business of manufacturing; for example, pharmaceutical manufacturers.

Water Flow: The movement of ARB and ARGs can also be attributed to water currents in the rivers and streams; such currents often create turbulence which may enhance the mobility of the bacterial species.

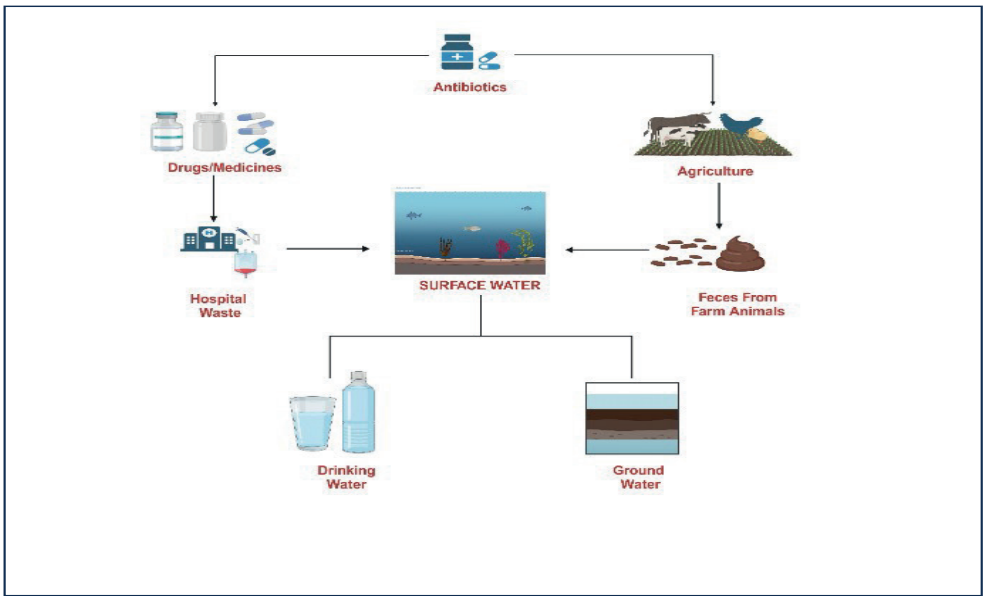


Figure 2: Antibiotic Resistance in Aquatic Environments

6. Impact on Fish and Other Aquatic Fauna

Pollution by antibiotics in the water bodies has numerous risks to the fish and many other water-dwelling creatures. These organisms are likely to come into direct contact with the antibiotics through the water they occupy, resulting in a range of physiological, behavioral, and ecological impacts (Amarasiri et al., 2020).

6.1. Physiological Effects on Fish

Health and Growth: Antibiotics have various physiological impacts on the life of fish their health and growth. If applied for a long period, antibiotics lower fish immunity and increase their vulnerability to diseases and infections. Apart from that, antibiotics affect the liver, kidneys, and gills and reduce their ability to perform their functions optimally and remain healthy. Conversely, low and environmentally safe doses of antibiotics can limit the rate of growth and the total biomass of fish (Yang et al., 2020).

6.2. Reproductive Impacts

Fertility and Development: Industrialized fish may be exposed to antibiotic substances that alter their reproductive mechanism and stunt the growth of their young ones (Manyi-Loh et al., 2018). Some types of antibiotics can cause hormonal dysfunction in the endocrine system hence affecting reproduction. Antibiotics have been found to decrease the rate of sperm production as well as the quality of the eggs, thus less chance of reproduction. Further, treating animals with antibiotics can also cause embryonic and larval malformation and mortality.

6.3. Behavioral Changes

Feeding and Predation: Chemicals such as antibiotics can interfere with fish by changing their feeding and predator/prey relationship patterns. Antibiotic agents can decrease the feed intake and feed conversion in animals, resulting in stunted growth and malnutrition. Both sensory and motor losses can negatively affect a fish's ability to evade predators hence increasing its chances of being preyed upon (Danner et al., 2019).

6.4. Effects on Other Water Biodiversity

Invertebrates: Antibiotics can affect the ability to grow, reproduce, and survive in water organisms of crustaceans, mollusks, and insects (Romero et al., 2012). Such organisms are involved in nutrient cycling and many of them are consumed by organisms at higher trophic levels.

Amphibians: Among these sensitive groups, frogs and salamanders are the most affected by antibiotic pollution because their skin is permeable. They lead to developmental malformations, immunosuppression, and higher risks of infections (Magalhães, 2016).

This pollution has dangerous implications for fish and other aquatic fauna in environments that are contaminated with antibiotics. Through the water they occupy, these organisms are directly subjected to antibiotics, which in turn, cause different physiological, behavioral, and ecological alterations.

6.5. Physiological Effects on Fish

Health and Growth: Physicochemical properties of antibiotics affect fish physiology and have a significant impact on fish health and growth. Long-term administration of antibiotics is dangerous for fish in that it compromises their immune systems, and they become more vulnerable to diseases and infections (Limbu et al., 2018). Antibiotics also affect the organs such as the liver, kidney, and gill in fish by damaging them and consequently reducing their health. Also, low levels of antibiotics can decrease the growth rates and the biomass of fish populations significantly.

6.6. Effects on Other Water Wildlife

Invertebrates: Chemicals like antibiotics can have undesirable effects on the growth, reproduction capacity, and mortality of water organisms such as crustacea, Mollusca, and insects (Gräslund & Bengtsson, 2001). These organisms are involved in the decomposition and recycling of nutrients and act as a base for higher trophic levels.

Amphibians: Frogs and salamanders are especially sensitive to antibiotic pollution because their skin is porous. Such developmental defects, as well as immune suppression and raised susceptibility to infections, are caused by antibiotics (Magalhães, 2016).

The impact of Antibiotic Pollution on Aquatic Life is described in Table 2:

Table 2: Impacts of Antibiotic Pollution on Aquatic Life

	Specific Impact	**Physiological Consequences**	**Behavioral Consequences**	**Reproductive Consequences**	**Ecological Consequences**
Fish	Reduced immunity, organ damage (liver, kidney, gills)	Increased disease susceptibility, impaired detoxification, reduced respiratory function			
	Decreased growth rates	Reduced body size, lower energy reserves	Altered feeding patterns		Reduced population size, disrupted food webs
	Hormonal imbalances	Disrupted metabolism, impaired stress response		Reduced fertility, developmental abnormalities in offspring	
	Neurological effects	Impaired sensory perception, motor dysfunction	Altered predator avoidance, decreased foraging success		Increased predation risk
Invertebrates	Impaired growth and development	Reduced body size, delayed maturity		Reduced reproductive output	Disrupted nutrient cycling, decreased food availability for higher trophic levels
	Increased mortality				Reduced biodiversity, altered community composition
Amphibians	Developmental abnormalities	Malformed limbs, organ dysfunction		Reduced reproductive success	Increased mortality, population declines
	Immunosuppression	Increased susceptibility to infections			
	Disrupted metamorphosis	Delayed or incomplete transformation			Reduced recruitment, ecological imbalances

7. Disruption of Aquatic Ecosystems

This pollution leads to changes in the properties of water; impacts prokaryotes, macroinvertebrates, and fish; and alters the structure of an ecosystem.

7.1. Changes in Microbial Dynamics

Microbial Community Shifts: Antibiotics can shift the structure of microbial soil, where most of the susceptible species become non-competitive, while antibiotic-resistant strains can grow in the soil. It leads to a general reduction in microbial diversity and alters the architecture and dynamics of microbial communities (Topcu & Taşkan, 2021).

Functional Consequences: Such alterations may impact the fundamental activities of such ecosystems such as nutrient biogeochemical cycling, nitrogen and phosphorus, and decomposition of organic matter. Such occurs when nutrient cycling is inhibited, bacterial activity impacts primary production, or when reduced bacterial turnover rate impacts the sinking of organic matters which in turn affects the detrital food web and nutrient cycling (Bärlocher & Rennenberg, 2014).

7.2. Impacts on Primary Producers

Algae and Phytoplankton: From this list, algae and phytoplankton may be considered as the first trophic level, or raw producers, in the water food chain. Because of the increased microbial load, antibiotics can suppress the growth and photosynthetic activity of these primary producers (Taşkan, 2016). Changes in microbial composition also affect other producers in a manner that will allow them to access nutrients in forms or with different microorganisms that they have not experienced before.

7.3. Disruption of Food Webs

Trophic Interactions: The effects of antibiotic pollution include the disruption of the traditional food chain by the conversion of various trophic levels. Changes in prey abundance and distribution ultimately impact predator structures and feeding habits. Alterations at one trophic level may cascade up and down the food chain altering the distribution of energy and redox state (Danner et al., 2019).

7.4. Habitat and Biodiversity Loss

Habitat Degradation: Antibiotic pollution can also lead to changes in physical and chemical properties at the depositional site of the environment. Water pollution affects the quality of water and also, and the level of antibiotics that are bound to sediments has implications on space use among species which has textbook implications on biological diversity (Lyautey et al., 2021).

Biodiversity Impacts: Endangered species are likely to reduce in population or even go extinct, thus reducing the additive level of species diversity. That is, with the decline in the number of species, the ecosystems become less able to tolerate the changes and loads that occur in the environment and receive.

7.5. Ecosystem Services

Provisioning Services: The major ecosystem services include the provision of fish and approval as the water quality controller. The discovery is that antibiotics contaminate the fish environment, which affects the condition of fisheries for maintaining fish supply. It can also hemo natural filtration and nutrient cycling processes that influence the water filtration rating.

Regulating Services: Another function that is sustained in aquatic environments is the regulation of temperature because they are carbon sinks. If the balance of these ecosystems is disrupted, then these functions can be affected. Disruption of one of these ecosystems automatically

leads to the disruption of these functions. Moreover, the presence of antibiotic compounds in the water body disrupts disease dynamics and distribution by transferring antibiotic-resistant bacteria into the aquatic food chain (Schulze, 2006).

8. Human Health Implications

Antibiotic pollution in water bodies is said to pose various risks of exposure to man and animals through the sequences (Gothwal & Shashidhar, 2015). More specifically, specific environmental, contagion, and direct exposure to contaminated water.

Recreational Water Use: Food consumed from seeds that are washed with polluted water or even prepared with water from sources containing antibiotics also exposes the consumer to direct antibiotics and antibiotic-resistant bacteria responsible for skin infections, gastrointestinal diseases, and other related diseases.

Drinking Water Contamination: A large number of antibiotic compounds can enter water, primarily through raw and inadequately treated water and effluence, as well as livestock farming. This directly exposes the consumers to the possible risks of infection, allergic reactions, and health complications due to the consumption of toxic substances in the form of antibiotic residues and antibiotic-resistant bacteria through drinking water containing antibiotics (Khan et al., 2020).

Food Chain Transmission The virus can also spread through contact with foods that have been in contact with an infected individual.

Contaminated Seafood: These fish and prawns contain antibiotics in their meat that when consumed enter the body making the body adapt to the new antibiotics thus making it resistant to them.

Agricultural Products: Consumption of food crops produced using water that has been contaminated with antibiotics is also a threat to human beings.

Environmental Reservoirs: Antibiotic-contaminated effluent could increase the release and dissemination of ARB and horizontal transfer of antibiotic-resistance genes in microbes.

Health Implications: This is due to the ease of infections with highly resistant characteristics which are a threat to public health since ARB-associated infections are more difficult to treat, cause more severe and longer illness, involve considerably higher costs of medicines, and produce more deaths.

8.1. Broader Public Health Implications

Increased Healthcare Costs: The social cost can also be incurred through healthcare costs since antibiotic-resistant infections are treated using expensive and more complex procedures.

Global Health Threat: Environmental pollution is another well-known factor that leads to the development of antibiotic resistance, which is one of the biggest challenges facing the healthcare system. The spread of antibiotic-resistant bacteria is through water, trade, and human movements meaning more effort has to be made to address this issue.

Improving Water Treatment: By incorporating new technologies in the treatment of water and establishing strict bureaucratic standards, the consumption of antibiotics in water can be prevented.

Promoting Responsible Antibiotic Use: The cases of polluting the environment with antibiotics only require a change in the daily rate of using antibiotics in healthcare, livestock, and farm fish production.

Public Awareness and Education: For instance, in the case of antibiotic pollution, educating the people on the consequences of polluting the environment with antibiotics and the right process

of discarding any unused antibiotics is very useful for the mitigation measures.

9. Conclusion

The quest to always strive to reduce antibiotic pollution in water bodies and the impacts it has on wildlife and human beings is always a challenging task. It will involve enhancing the laws for the usage of water resources, the issue and dissemination of effective water treatment techniques, bringing in effective techniques in farming, and coming up with the best techniques for communicating ideas to the people. Hence, by promoting a better code of antibiotic disposal and use both at the domestic and cross-national level, it is possible to reduce, if not eradicate, environmental pollution. The number of interventions laid for the removal of antibiotics from water strings at wastewater treatment plants has been augmented with technologies such as membrane filtration and advanced oxidation processes. In addition, enhancing quality nutrition by increasing the production of quality crops and animals, and advice on the right practices such as integrated pest management instead of resorting to antibiotic circulation in the first place would also be an avenue to minimize the use of antibiotics. Public awareness of the potential consequences of antibiotic pollution to the environment and human health should be observed. Members of the public should also ensure that they dispose of their waste adequately and even take a section on the usage of antibiotics as this can decrease the contamination of pollinators. This challenge can be partly addressed within the context of international cooperation and therefore ensuring and encouraging research and innovation activities. This paper has highlighted that, despite most of the aquatic habitats being on the brink of destruction, the protection of the few remaining ones, the health of the nation/province, and the sustainability of water resources can only be achieved through cooperation among the stakeholders.

References

Amarasiri, M., Sano, D., & Suzuki, S. (2020). Understanding human health risks caused by antibiotic resistant bacteria (ARB) and antibiotic resistance genes (ARG) in water environments: Current knowledge and questions to be answered. Critical Reviews in Environmental Science and Technology, 50(19), 2016-2059.

Ambrosini, A., de Souza, R., & Passaglia, L. M. (2016). Ecological role of bacterial inoculants and their potential impact on soil microbial diversity. Plant and Soil, 400, 193-207.

Bärlocher, F., & Rennenberg, H. (2014). Food chains and nutrient cycles. Ecological Biochemistry: Environmental and Interspecies Interactions, 92-122.

Danner, M.-C., Robertson, A., Behrends, V., & Reiss, J. (2019). Antibiotic pollution in surface fresh waters: Occurrence and effects. Science of the Total Environment, 664, 793-804.

Donlan, R. M. (2002). Biofilms: microbial life on surfaces. Emerging infectious diseases, 8(9), 881.

Giedraitienė, A., Vitkauskienė, A., Naginienė, R., & Pavilonis, A. (2011). Antibiotic resistance mechanisms of clinically important bacteria. Medicina, 47(3), 19.

Gothwal, R., & Shashidhar, T. (2015). Antibiotic pollution in the environment: a review. Clean–Soil, Air, Water, 43(4), 479-489.

Gräslund, S., & Bengtsson, B.-E. (2001). Chemicals and biological products used in south-east Asian shrimp farming, and their potential impact on the environment—a review. Science of the Total Environment, 280(1-3), 93-131.

Grenni, P., Ancona, V., & Caracciolo, A. B. (2018). Ecological effects of antibiotics on natural ecosystems: A review. Microchemical Journal, 136, 25-39.

Hossain, A., Habibullah-Al-Mamun, M., Nagano, I., Masunaga, S., Kitazawa, D., & Matsuda, H. (2022). Antibiotics, antibiotic-resistant bacteria, and resistance genes in aquaculture: risks, current concern, and future thinking. Environmental Science and Pollution Research, 1-22.

Iwamoto, M., Ayers, T., Mahon, B. E., & Swerdlow, D. L. (2010). Epidemiology of seafood-associated infections in the United States. Clinical microbiology reviews, 23(2), 399-411.

Khan, N. A., Ahmed, S., Farooqi, I. H., Ali, I., Vambol, V., Changani, F., Yousefi, M., Vambol, S., Khan, S. U., & Khan, A. H. (2020). Occurrence, sources and conventional treatment techniques for various antibiotics present in hospital wastewaters: a critical review. TrAC Trends in Analytical Chemistry, 129, 115921.

Kourkouta, L., Koukourikos, K., Iliadis, C., Plati, P., & Dimitriadou, A. (2018). History of antibiotics. Sumerian J Med Healthcare, 1, 51-55.

Lee, L. S., Carmosini, N., Sassman, S. A., Dion, H. M., & Sepulveda, M. S. (2007). Agricultural contributions of antimicrobials and hormones on soil and water quality. Advances in agronomy, 93, 1-68.

Limbu, S. M., Zhou, L., Sun, S.-X., Zhang, M.-L., & Du, Z.-Y. (2018). Chronic exposure to low environmental concentrations and legal aquaculture doses of antibiotics cause systemic adverse effects in Nile tilapia and provoke differential human health risk. Environment international, 115, 205-219.

Lyautey, E., Bonnineau, C., Billard, P., Loizeau, J.-L., Naffrechoux, E., Tlili, A., Topp, E., Ferrari, B. J., & Pesce, S. (2021). Diversity, functions and antibiotic resistance of sediment microbial communities from Lake Geneva are driven by the spatial distribution of anthropogenic contamination. Frontiers in microbiology, 12, 738629.

Magalhães, A. F. A. (2016). Assessment of the Antimicrobial Activity of Bacterial Isolates from Frogs' Skins From Urban Zones Universidade de Aveiro (Portugal)].

Manyi-Loh, C., Mamphweli, S., Meyer, E., & Okoh, A. (2018). Antibiotic use in agriculture and its consequential resistance in environmental sources: potential public health implications. Molecules, 23(4), 795.

Marwa, K. J., Mcharo, G., Mwita, S., Katabalo, D., Ruganuza, D., & Kapesa, A. (2021). Disposal practices of expired and unused medications among households in Mwanza, Tanzania. PloS one, 16(2), e0246418.

McEwen, S. A., & Fedorka-Cray, P. J. (2002). Antimicrobial use and resistance in animals. Clinical infectious diseases, 34(Supplement_3), S93-S106.

Penesyan, A., Gillings, M., & Paulsen, I. T. (2015). Antibiotic discovery: combatting bacterial resistance in cells and in biofilm communities. Molecules, 20(4), 5286-5298.

Pepi, M., & Focardi, S. (2021). Antibiotic-resistant bacteria in aquaculture and climate change: A challenge for health in the Mediterranean area. International journal of environmental research and public health, 18(11), 5723.

Qasim, S. R. (2017). Wastewater treatment plants: planning, design, and operation. Routledge.

Romero, J., Feijoó, C. G., & Navarrete, P. (2012). Antibiotics in aquaculture–use, abuse and alternatives. Health and environment in aquaculture, 159(1), 159-198.

Schulze, E.-D. (2006). Biological control of the terrestrial carbon sink. Biogeosciences, 3(2), 147-166.

Shao, S., Hu, Y., Cheng, J., & Chen, Y. (2018). Research progress on distribution, migration, transformation of antibiotics and antibiotic resistance genes (ARGs) in aquatic environment. Critical reviews in biotechnology, 38(8), 1195-1208.

Sharma, L., Siedlewicz, G., & Pazdro, K. (2021). The toxic effects of antibiotics on freshwater and marine photosynthetic microorganisms: State of the art. Plants, 10(3), 591.

Sigee, D. C. (2005). Freshwater microbiology: biodiversity and dynamic interactions of microorganisms in the aquatic environment. John Wiley & Sons.

Singer, R. S., Finch, R., Wegener, H. C., Bywater, R., Walters, J., & Lipsitch, M. (2003). Antibiotic resistance—the interplay between antibiotic use in animals and human beings. The Lancet infectious diseases, 3(1), 47-51.

Singh, A. K., Sisodia, A., Sisodia, V., & Padhi, M. (2019). Role of microbes in restoration ecology and ecosystem services. In New and future developments in microbial biotechnology and bioengineering (pp. 57-68). Elsevier.

Taşkan, E. (2016). Effect of tetracycline antibiotics on performance and microbial community of algal photo-bioreactor. Applied biochemistry and biotechnology, 179, 947-958.

Topcu, Ş., & Taşkan, E. (2021). Effect of the tetracycline antibiotics on performance and microbial community of microbial fuel cell. Bioprocess and Biosystems Engineering, 44, 595-605.

Yang, C., Song, G., & Lim, W. (2020). A review of the toxicity in fish exposed to antibiotics. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 237, 108840.

About The Authors

Dr. Qurat-ul-Ane Gillani is an Assistant Professor of Zoology at Women University Multan. Her research primarily focuses on the effects of various substances on animal physiology and behavior, particularly in mice. She has investigated the impact of nickel chloride on fish, plant extracts on mice, and the neurological mechanisms of COVID-19. Additionally, her work has explored the role of GABAB receptor antagonists on behavior, hematology, and biochemistry in mice models, sometimes with a focus on neonatal brain damage. She has also conducted research on detecting blood parasites in cattle.

E-mail: anneegillani@wum.edu.pk ORCID: 0000-0002-1068-4472

Dr. Ayesha Riaz serves as Assistant Professor at the Institute of Molecular Biology and Biotechnology (IMBB) at the University of Lahore. She holds a Ph.D. in Zoology from the University of Punjab. Her research focuses on the isolation and characterization of probiotic strains and their applications in promoting animals and human health.

Email: ayesha@imbb.uol.edu.pk ORCID: 0000-0003-1868-2073

Dr. Arifa Mehreen is an Assistant Professor of Zoology at the University of Agriculture Faisalabad (UAF). Her research focuses on antimicrobial properties of natural products, drug formulation and pharmacokinetics, and characterization of bacterial pathogens. She has studied the antimicrobial and toxicological effects of Origanum vulgare, developed a fixed-dose combination drug for cardiovascular disease, and investigated the characteristics of Staphylococcus aureus strains.

E-mail: arifa.mehreen@uaf.edu.pk ORCID: 0000-0001-5899-8027

Dr. Muhammad SAFDAR earned his PhD in Molecular Biology and Genetics from Gaziantep University, Turkey. He is Lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 70 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

E-mail: msafdar@cuvas.edu.pk ORCID: 0000 0002 3720 2090

To Cite This Chapter

Gillani A et al., (2024). Impact of Antibiotics on Aquatic Life. In Current Studies in Health and Life Sciences 2024 (pp.403-415). ISRES Publishing.

Future Frontiers: Emerging Trends and Applications in Animal Biotechnology

Shumaila BATOOL Hareem FAYYAZ

Urwa SHEIKH

Anam SHEHZADI

Fatima AMIN

1. Introduction

Animal biotechnology is a sub-discipline of biotechnology that involves the use of molecular biology tools to modify animals genetically. The main aim is to enhance the stability for usage in agriculture, industry, or medicine. Biotechnologies have played an important role in enhancing livestock production, especially in developed countries, and can potentially eradicate poverty, hunger, diseases, and environmental degradation in developing countries. Many biotechnologies are available, and some have already been applied in the main areas of animal science in developing countries, such as animal reproduction, genetics and breeding, animal nutrition and production, and animal health (Estrada et al., 2017). In addition to their role in characterizing and conserving animal genetic resources, molecular DNA markers can also be utilized for genetic improvement through marker-assisted selection. Microorganisms, including those created using recombinant DNA technology, are extensively used in animal feeding and production biotechnologies. Biotechnologies in animal health are utilized to improve the precision of complications diagnosis, disease control, and therapy. So, there is a need for specific advice that can assist developing countries in making advancements through the utilization of appropriate animal biotechnologies in the future (Mekonnen, 2021). This chapter aims to highlight the recent advances in the field of animal biotechnology and to explore the biotechnological applications in animals.

1.1 Historical Overview Of Animal Biotechnology

The utilization of animal biotechnology originated about 8000 years ago, coinciding with the commencement of humans domesticating and selectively breeding animals (Aerni, 2021). In 1917, Karl Ereky introduced the phrase "beet diet" to describe a feeding method employed to raise many pigs (Wu-Pong, 1999). Subsequent historical findings have spurred biotechnology to emerge as a highly active industry and scientific field during the latter part of the twentieth century. Biotechnology has been increasingly important in manipulating organisms' DNA at the molecular level, particularly after the discovery of the structure of DNA in 1933 and the invention of ways to modify DNA in 1970. The transition from animal production as a means of subsistence and extraction to a commercial enterprise occurred during the twentieth century. During that period, there was an increasing need for animals that exhibited superior performance and increased adaptability to various environmental conditions (Greenfield, 2010).

As a result, efforts were made to start breeding programs for a variety of animal species, including sheep, goats, pigs, cattle, and poultry. These programs were developed using domesticated breeds' genetic makeup as a foundation. They were implemented intuitively, considering the desirable features related to production and aesthetics found in animals with superior phenotypes. As a result, this selection process resulted in more advantageous alleles that help in livestock improvement, disease diagnosis, and treatment (Gowane et al., 2019).

1.2 Current State of Animal Biotechnology

Animal biotechnology has experienced significant advancements throughout the last two decades. The advent of animal biotechnology in the contemporary period occurred after the

identification of the genetic code in the mid-1930s (Rasmussen, 2014). Currently, there are over 230 Biotechnology Health Care Products and Vaccines accessible to patients, primarily for diseases that were previously incurable. Over 13.3 million farmers worldwide employ agricultural biotechnology to increase crop yields, minimize pest-related harm, and mitigate the environmental impact of farming (Kesik-Brodacka, 2018). Recent progress spans multiple fields, such as genetic editing methods like CRISPR-Cas9, which enable accurate genetic alterations to enhance animal well-being and product excellence. Cloning and reproductive technologies provide chances to save uncommon genetic characteristics and improve cattle productivity, yet they come with ethical and genetic diversity dilemmas. Advancements in technology, such as enhanced computational capabilities, genomic sequencing, cloning, regenerative medicine, and direct gene manipulation, have allowed individuals to significantly modify animals for various purposes, such as food production, medical applications, and scientific research. Modern biotechnology is the result of humans manipulating the environment and the development of molecular and computational technologies. Modern biotechnology offers advanced solutions and techniques to address severe and uncommon illnesses, minimize our impact on the environment, alleviate hunger, promote cleaner and more sustainable energy sources, and enhance the safety, cleanliness, and efficiency of industrial manufacturing processes. Transgenic animals, genetically modified with other organisms' genes, are used for many goals, such as enhancing production and studying diseases (Khan, 2020). Recent developments and progress in biotechnology equip us to prepare for and address society's most pressing concerns. However, the use of these animals raises ethical and regulatory issues.

2. Emerging Trends in Animal Biotechnology

Global livelihoods depend significantly on livestock agriculture for financial stability, draught power, and offering non-food items in addition to food. It is anticipated to rise in value and now represents roughly 43% of the gross value of agricultural output (Pingault et al., 2016). Over one-third of the agricultural GDP in developing nations comes from the livestock production industry, one of the world's most rapidly evolving sectors. By 2030, it's expected that the market for animal products will have almost doubled, with developing nations accounting for most of this growth (Yitbarek, 2019).

Sustainable animal production is confronting obstacles, including livestock-mediated waste, genetic resource loss, global warming, severe water scarcity, and the risk of developing infectious illnesses. A restricted natural resource such as water and land is the main problem in finding sustainable ways to increase cattle output. Modern scientific and technological developments will be crucial in advancing the livestock industry. Due to the rapid population growth, there are opportunities, in addition to problems, that increase the demand for animal products (Liu et al., 2020).

Biotechnology can increase animal productivity by improving growth, health, reproduction, nutrition, welfare, and waste management. Livestock production is expected to expand rapidly and overtake all other agricultural sectors by 2020 (Yitbarek, 2019). Current advancements in biotechnology have created new avenues for increasing the productivity of domestic animals in various ways, including the potential to improve animal growth, rates of reproduction, and nutrient efficacy. Developing nations, however, need to prepare for these economic and technological advancements, and their decisions may be influenced by social objectives and commercial concerns to meet global demand and promote genetic variety among animals (Sharma et al., 2021).

Animal biotechnology has recently advanced to the point where it has transformed several sectors, including environmental management, medicine, and agriculture. The ability to precisely modify animal genomes with CRISPR-Cas9 gene editing has changed the game. Food security has increased, and agricultural losses have decreased as a result of the development of disease-resistant livestock, such as swine resistant to Porcine Reproductive and Respiratory Syndrome Virus, which is made possible by this technology. Furthermore, with the successful cloning of species like the black-footed ferret, advances in stem cell research and cloning have aided the protection

of endangered species. To solve the severe lack of transplant organs, genetically modified animals are employed in medicine to create organs compatible with humans. Moreover, developments in synthetic biology have produced animals that have been bioengineered to create drugs, like goats that can make spider silk proteins in their milk for medical sutures. These innovations underscore the transformative potential of biotechnology in addressing global challenges (Laible et al., 2015).

2.1 Gene Editing and CRISPR Technology

Animal biotechnology relies heavily on CRISPR technology to create genetically engineered animals with desired characteristics like disease resistance. This method directs the Cas9 enzyme to a specific place in the genome, causing breakage in double-strand DNA. The cell then uses either homology-directed repair, which requires the presence of a DNA template, or non-homologous end joining to fix this break. In animal biotechnology, CRISPR is useful for many reasons (Singh & Ali, 2021). The first advantage is that it enables creation of genetically modified animals with desired characteristics, such as disease resistance, which can improve animal welfare and agricultural output (Figure 1). Second, by creating animals that can create organs compatible with humans, CRISPR helps progress in biomedical research. Finally, CRISPR contributes to conservation by enabling the genetic rescue of endangered species by introducing desirable characteristics or correcting deleterious mutations. CRISPR is an essential technique in animal biotechnology because of its accuracy, effectiveness, and adaptability (Wang & Doudna, 2023).

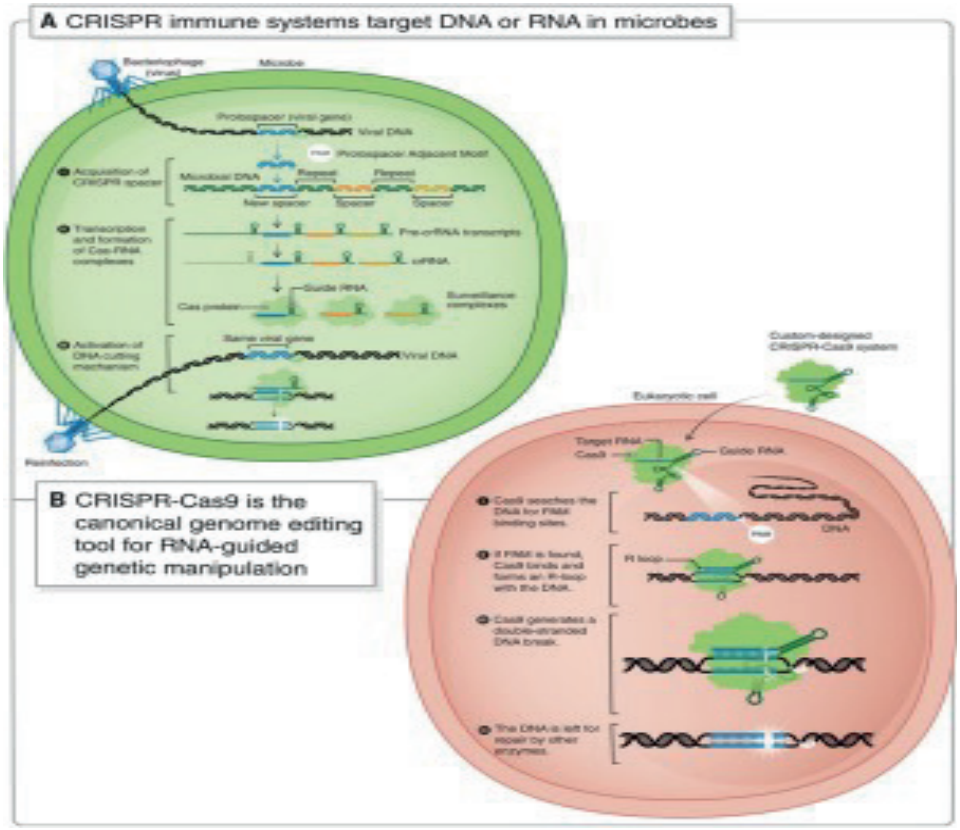


Figure 1. CRISPR-based editing of nuclear material for developing immunity (Wang & Doudna, 2023)

CRISPR is naturally found in archaea and bacteria, and their nuclear material is protected against foreign DNA (Munawar & Ahmad, 2021). In the field of genetic engineering, the CRISPR-associated system type II employs CRISPR-RNA to guide the CRISPR-associated nuclease to particular locations. This is accomplished through a CRISPR-RNA and transactivating CRISPR-RNA duplex, which is combined to form sgRNA (Single Guide RNA) to facilitate the process of DNA cleavage. Upon introduction into the cell or zygote, these constituents generate a double-strand break (DSB) by pointing Cas9 to the corresponding loci in DNA (Figure 2) (Menchaca et al., 2020).

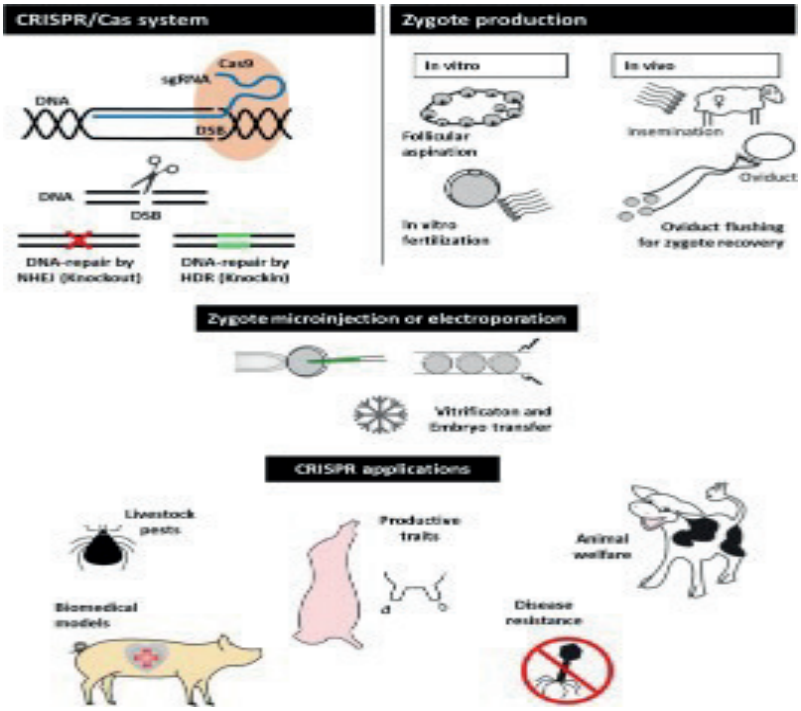


Figure 2. CRISPR-Cas system formation, zygote production and its implantation (Menchaca et al., 2020).

The CRISPR-associated system has been used to repair DSBs in livestock via NHEJ (Non-Homologous End Joining) and HDR (Homology Directed Repair). The former causes small deletions or insertions, disrupting open reading frames and creating knockouts of a few genes, and this method has been successful in generating genes in cows, goats, sheep, and pigs (HASAN et al., 2022; Park et al., 2019). In contrast, HDR uses a homologous-repair template to fix DSBs allowing specific changes in DNA, and this method has been successful in generating knock-in large animals in goats, sheep, and pigs (McLean et al., 2021). Recently, a new CRISPR tool called base editors was developed in which a combination of Cas 9 (inactive) and cytidine deaminase enzyme was used, which is cytidine with thymine (Kantor et al., 2020).

2.1.1 Applications in Livestock Improvement

The CRISPR technology is being utilized to reduce pest species, increase animal productivity and health, and improve animal comfort and disease resistance. Reports have been of this technology used for commercial usage, research, or proof of concept.

In 2014, MSTN mutation was introduced in the Merino breed, enhancing protein production and leading to the birth of the first animals modified using CRISPR. Superfine Merino is renowned for yielding the finest wool, but farmers endure reduced growth rates and smaller lambs. Traditional genetics, like selective breeding, has increased meat yield at the expense of decreased wool quality. At the embryonic stage, Merino was modified using CRISPR to break MSTN gene, resulting in twofold muscular lambs with faster development rates and higher body weights. In addition to being 23% heavier, the knockout lambs had the same characteristics of wool quality as Merino lambs (Crispo et al., 2015).

Pigs and Cashmere goats from China are two examples of additional species whose fitness or productive qualities have been enhanced through the application of CRISPR, and CRISPR has been utilized to enhance carcass qualities in pigs (Wang et al., 2015). Innovative approaches to using CRISPR to modify the male-to-female ratio in cattle have been put forth; these approaches are especially useful when only one sex can provide the desired result. To increase productivity

and prevent female culling, for instance, male offspring tactics have been suggested for beef cattle. Another strategy to prevent male-specific boar taint and induce a female phenotype in pigs is limiting testicle development in fetal genital ridges (Kurtz & Petersen, 2019).

Animals frequently experience acute or long-term pain during routine operations such as male castration, dehorning, tail docking, and abortion, and editing the genome can help prevent these actions. Calves often get their horns removed, but it hurts and stresses them out. Due to a polled feature, some cattle breeds, such as Angus, are naturally hornless. To reduce physical dehorning in Holstein cattle without sacrificing production, TALENs were employed to introduce the causal mutation (Carlson et al., 2016). It has also been suggested that CRISPR can create male pigs with germline ablations (Kurtz & Petersen, 2019), opening up new possibilities for pig surgical castration (Lee et al., 2020).

2.1.2 Potential for Disease Resistance

Cattle diseases can majorly affect public health, outbreaks, business, and productivity. The worldwide livestock and agriculture sectors are affected by some pandemics, such as the African swine disease that struck Asia. Animal welfare should be considered, as healthy animals are the first to experience sickness and death. An unusual increase in new and resurfacing animal illnesses, as well as infectious diseases, is being caused by this intensification of livestock production (Rohr et al., 2019).

An international animal illness called African swine fever is endangering neighboring areas and inflicting substantial losses in the Asian pig business. The virus infects domestic and wild pigs, although warthogs do not show any symptoms. The Rosen Institute's researchers suggest genetically modifying domestic pigs to provide the virus resistance to illness (Bisimwa et al., 2024). In China, coronavirus-resistant pigs and modified cows with heightened resistance to TB have also been created with CRISPR, which has promise as a cutting-edge approach to managing infectious illnesses in cattle (Menchaca et al., 2020).

2.2 Cloning and Transgenesis

Cloning is the process of making identical copies of DNA using advanced reproductive techniques such as embryo culture microsurgery and then transfer into surrogate mothers. The procedure creates embryos that can give rise to living, genetically identical individuals by inserting a nucleus into an oocyte with its nuclear DNA removed (Figure 3) (Keefer, 2015). In nature, clones like armadillos and identical twins exist. Artificial cloning requires embryo splitting, which splits blastomeres to generate smaller embryos

Transgenic animals are necessary for researching disease progression, analyzing strategies for treatment, and examining gene activity during development, organogenesis, and aging. Recombinant protein preparation, preventing illnesses for animals, and the introduction of unique genetic traits are among their commercial uses. Invertebrate species such as Drosophila melanogaster and Caenorhabditis elegans are commonly employed, whereas fish, amphibians, birds, and mammals are among the transgenic vertebrates. Nevertheless, their potential for portraying human illnesses may be limited due to their distant evolutionary link with humans (Christapher et al., 2022).

2.2.1 Cloning via Transfer of Nuclear Material

The most common methods for transferring donor cell nuclei into enucleated oocytes include injection, virus, and electrofusion. Oocytes in which the nucleus is transplanted require artificial activation because, in contrast to spermatozoa, embryonic and adult somatic cells cannot activate oocytes. Commonly utilized stimuli include chemical, electric pulses, or a mix of the two (Srirattana et al., 2022). Due to differences in the properties of donor cells and oocytes, there is no universal cloning procedure for all mammalian species. Every species requires a different set of technical

requirements.

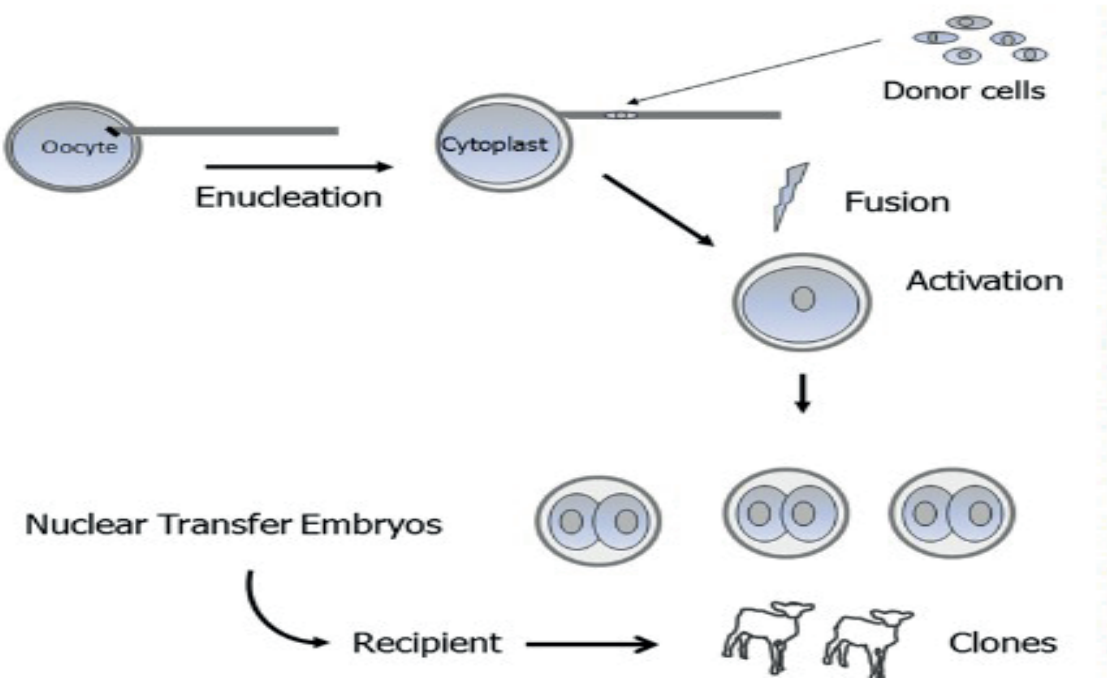


Figure 3. Cloning via transfer of nuclear material (Keefer, 2015).

2.2.2 Cloning via Early Embryonic Cell Nuclei

It is anticipated that every nucleus in early embryos, including those with two to eight cells, would possess the ability to grow into new organs. Although it is possible for an enucleated oocyte united with one of the eight blastomeres of an eight-cell (sheep) embryo to grow into a normal progeny (Hosseini et al., 2016), it has never been possible to produce eight offspring utilizing the blastomeres of a single eight-cell embryo. Still, the same applies for two- and four-cell embryos. The donor cell nuclei may become incapable of participating in normal embryonic development if the cytoplasm and nucleus are slightly damaged. Cloning has been attempted using fewer than 3% of the enlarged blastocyst cell mass and trophectoderm cells. Both cultured embryonic germ (EG) and embryonic stem (ES) cells have a 3 percent success rate (Rahbaran et al., 2021).

2.2.3 Cloning via somatic cell nuclei

The cloning success is just 3 percent, irrespective of the kind and age of the cells. This indicates the proportion of developmentally totipotent cells in any given tissue is less than 3% (Suzuki et al., 2016). Pre-selecting cells may help boost the success rates of cloning, perhaps preserving developmental totipotency in some tissues. Nevertheless, the majority of cloned embryos die before and after implantation, suffering from breathing issues, numerous systemic dysfunctions, and malformed placentas. The exception was cloned infants who lived to adulthood and could be borne again as 90% of mouse embryos cloned using cumulus cells had normal chromosomal composition. It's more likely that defective epigenetic reprogramming in contrast to genetic issues caused the majority of cloned embryos or babies to pass away (Hino et al., 2016).

2.2.4 Transgenic Animal Models for Research

Transgenes are being introduced in various non-mammalian invertebrates and vertebrates, such as fruit flies and nematodes. In fruitfly (Bachmann and Knust, 2008), transposable vector systems are used to inject the transgene into the cytoplasm, while in nematode (Caldwell et al., 2020), DNA via injection is introduced in syncytial gonad or maturing oocytes, targeting its germline which is

hermaphrodite. The suppressor tRNA (gene sup-7) can be included to prevent high-copy number transgenic lines.

In fish, the vitelline membrane is surrounded by a tough chorionic membrane, which means that microinjection can only occur through the micropyle. In Xenopus, an effective method is to incubate sperm nuclei that have been permeabilized with linearized DNA and then decondense the resultant mixture using an enzyme-restricted egg extract. It allows the integration of DNA before its fertilization, forming an embryo having non-mosaic transgenes (Hino et al., 2016).

Transgenes have been successfully inserted into huge numbers of sperm or eggs of fish by electroporation to create transgenic invertebrates or chordates. It has also been possible to introduce DNA in the fertilized eggs of loach, zebrafish, and a few other species via particle bombardment using metallic beads coated in DNA (de Siqueira-Silva et al., 2018).

2.3 Stem Cell Research in Animals

After the isolation of stem cells from mice in the embryonic stage in the 1980s, stem cell biology has revolutionized the field and opened the door to a variety of pluripotent or multipotent cell types for use in preclinical or clinical investigations; however, the lack of animal models for target diseases has forced some researchers to forego traditional preclinical animal testing; choosing appropriate model for the pre-clinical studies demands an understanding of species-specific aspects of stem cell biology, further progress demands research on different animals to form principle and evaluate safety of possible treatments.

Stem cells can proliferate and differentiate into specialized cells throughout fetal development and adult tissues. In the lab, they are modified by adding genes, which modify their behavior. Inner cell mass at the early embryonic stage is obtained from donor females, where embryonic stem cells originate. After that, the inner cell mass of these embryos is cultured in vitro until it takes the shape of an egg cylinder (Figure 4) (Kumari et al., 2023).

Mice have been among the preferred species for studying stem cell biology in mammals due to their low cost, rapid reproduction, and ease of genetic manipulation. However, their ability to predict therapies based on stem cell effectiveness is still controversial. Several models fail to accurately mimic phenotypes of specific human diseases, prompting researchers to explore other species that could provide better predictions for human outcomes. Animals, including dogs, goats, pigs, rabbits, sheep, and primates, excluding humans, often serve as superior models due to their long lifespans facilitating critical studies for applications of stem cells. Moreover, their physiological parameters, such as the working of the immune system, closely resemble those of humans, influencing the host's reaction to cell transplantation. Another advantage of large animals is they provide a quantity and variety of stem cells that can be consistently extracted and manipulated from a single specimen for analysis and various applications (Rubessa et al., 2017).

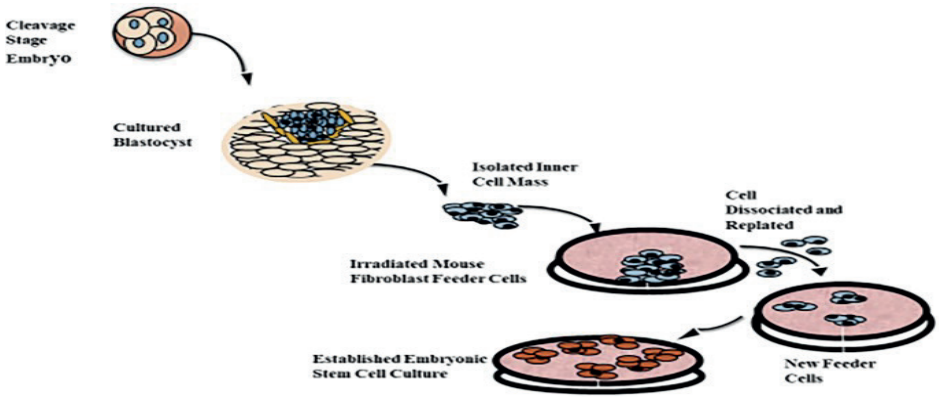


Figure 4. Method of Stem Cell Culturing (Kumari et al., 2023).

3. Applications of Animal Biotechnology

3.1 Improved Livestock Breeding

The livestock industry is anticipated to expand significantly to meet the rising demand for animal products, necessitating a shift in production methods to enhance efficiency and productivity. Biotechnological research becomes crucial in addressing the challenge of increasing animal food production to meet the needs of a growing human population (Henchion et al., 2021). Consequently, there is a pressing need to adopt biotechnological advancements to improve livestock breeding and management practices, ensuring sustainable food production while meeting the increasing demands of a rapidly expanding global population.

3.1.1 Selective Breeding Strategies

Selective livestock breeding refers to the systematic breeding of animals to enhance productivity and other important traits. There are many different approaches to this type of breeding, ranging from expensive and high-tech procedures like genetic engineering or in-vitro fertilization to simpler, low-cost approaches that rely on the controlled breeding of animals based on observable traits (Brito et al., 2020). Important traits linked to resilience and adaptation to climate change include animal morphology, low-quality feed, high survival rates, thermal tolerance, and disease resistance. Selective breeding can be done in three main ways:

3.1.1.1 Outcrossing

An outcross occurs when two animals have not mated for at least four or six generations. This approach functions best when a trait's genetic variation is high. Outcrossing is ideal when dominant genes are the desired ones. The ability of outcrossing to keep harmful traits recessive is one of its greatest benefits. Fitness traits like longevity, milk production, survivability, and reproductive ability are all enhanced by outcrossing (Wolfe et al., 2021).

3.1.1.2 Linebreeding

Linebreeding is the practice of mating related animals, such as cousins, aunts and nephews, half-brothers and half-sisters, and other more distant relationships. The usual reason for doing this is to profit from a shared exceptional ancestor that showed up in more recent pedigree generations. With linebreeding, there is less chance of detrimental genetic defects than with inbreeding and a higher degree of uniformity.

3.1.1.3 Inbreeding

This method of breeding involved mating animals that were directly related to each other, such as full siblings, father, and daughter. By using this technique, latent weaknesses are typically driven out of the gene pool, and uniformity and prepotency are created. Nonetheless, there is a greater chance of producing children with issues because recessive genes contribute more to genetic defects than dominant genes do. The number of genes available is decreased by inbreeding, which can potentially wipe out certain genelines (Hieber, 2020).

3.1.2 Genomic Selection in Livestock

Animal breeding has played a significant role in improving livestock productivity. Improvements in genetics have been crucial in raising the efficiency of desired traits in cattle, sheep, pigs, and poultry (Friggens et al., 2017). With the development of gene technology, producers of commercial livestock products and livestock breeders can now base breeding decisions on gene marker technology. Genomic selection is one of the gene marker technologies in which an animal's breeding value can be precisely calculated without knowledge of the animal's phenotype or that of close relatives using a dense chromosomal map. Genomic selection has increased animal productivity by lowering the generation interval and costs of animals (Ibtisham et al., 2017).

3.2 Disease Resistance in Animals

The prevalence of the disease hurts the welfare and productivity of livestock, as well as the production of food from animals and human health. To produce healthy and strong animals, farmers, veterinarians, and animal scientists have been combining their efforts to investigate efficient disease control strategies. Traditional approaches to the management of disease involve administering vaccines and antibiotics. The optimal approach is cultivating disease-resistant livestock, achieved through immune response genes.

3.2.1 Genetic Modification for Disease Resistance

The production of disease-resistant animals can be achieved through genome editing and immunogenomics. Disease severity and pathogenesis are influenced by the interaction between the host immune system and invading pathogens, with host genetics playing a crucial role. Immunogenomics employs integrated bioinformatics tools to explore how host genetics impact this interaction, identifying candidate genes contributing to disease resistance. Using CRISPR/Cas9 genome editing technology, these identified genes can be precisely targeted and modified in the host genome to produce animals with enhanced disease resistance, as illustrated in Figure 5 (Islam et al., 2020).

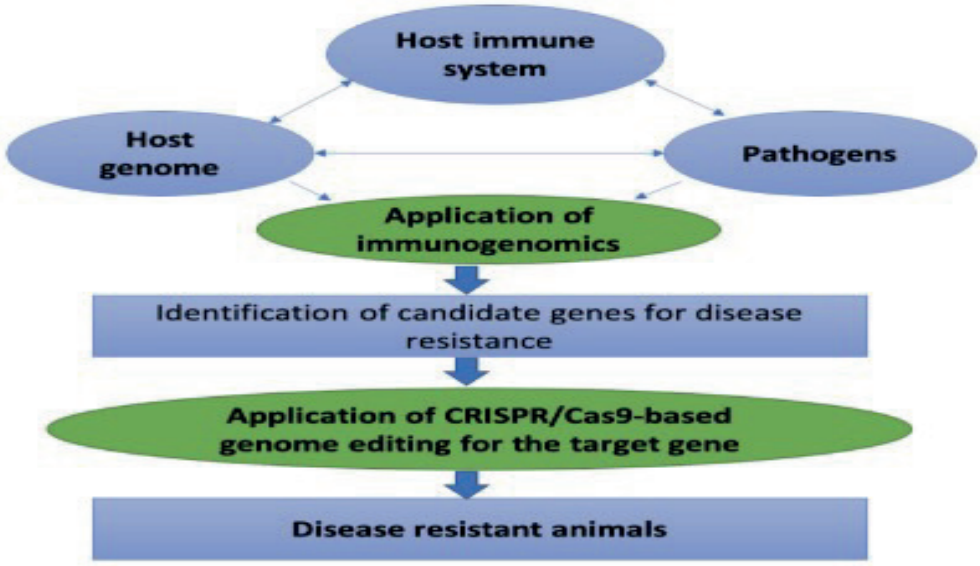


Figure 5. Diagrammatic representation illustrating the use of genome editing and immunogenomics for producing disease-resistant animals (Islam et al., 2020).

3.2.2 Vaccine Development in Livestock

Animal diseases can be effectively prevented by vaccinations against a variety of ailments. Several successful vaccinations have greatly lessened the impact of serious diseases in livestock. Live attenuated, killed/inactivated, cell membrane compounds or toxoids make up most veterinary vaccines approved for use in medicine. Live attenuated vaccines induce immune responses but risk virulence. Killed/inactivated vaccines are safer but less effective. Toxoids require complex culture medium. The limitations of these vaccine types and the lack of efficient disease treatments necessitate the development of recombinant vaccines (Jansen et al., 2018).

Recombinant vaccines are a promising approach to getting around the drawbacks of conventional vaccines. International initiatives are underway to use recombinant DNA technology to create more effective vaccines against a wide range of diseases. Recombinant vaccines are created by strategically selecting and purifying specific antigens using methods informed by the vaccine's structure or genome, enhancing efficacy and safety through targeted antigen design. These vaccines harness molecular techniques to engineer immunogenic components precisely, optimizing immune

response and minimizing adverse reactions (Pollet et al., 2021).

3.3 Biomedical Research and Therapeutics

The use of animal models in scientific research is a topic of debate, but their selection based on functional and genetic qualities has significantly contributed to the evolution of medicine from an art to a science. Animal models have been instrumental in advancing the understanding of biological and pathological processes, providing invaluable insights that inform biomedical research. These contributions are crucial, enabling the development and testing of medications, vaccines, and surgical techniques applicable in human and veterinary medicine. Consequently, animal models play a vital role in bridging the gap between basic research and clinical applications, fostering medical progress and innovation (Vashishat et al., 2024).

3.3.1 Animal Models for Human Diseases

Animal models play a crucial role in biomedical research by enabling the study of pathogenesis and various diseases. Livestock, including goats, cattle, pigs, and sheep, share common anatomy and physiology with humans, making them well-established models for studying genetic disorders. Whole genome sequencing and genetically engineered livestock have made them more significant in biomedical studies. Advances in genomics, therapeutic cloning, stem cell research, biotechnology, and surgical techniques offer potential solutions for non-treatable infectious diseases. Animal models also help toxicologists develop knowledge about chemical toxicity and protect humans, animals, and the environment from toxic exposures (Singh & Seed, 2021).

3.3.2 Gene Therapy in Veterinary Medicine

Gene therapy involves transferring target genes into specific cells within an organism, a principle that drives advancements in biomedicine by introducing novel, genetically engineered medications into clinical practice. These gene drugs are primarily used to treat rare, life-threatening genetic, oncological, and other diseases that lack conventional treatments. Additionally, gene therapy can promote regenerative processes in cases of chronic non-fused bone fractures and severe muscle and tendon injuries that do not respond to traditional therapies. Large animals are often employed as models for developing and testing these innovative gene therapy techniques. In modern veterinary practice, human-specific drugs are frequently used, but gene technologies also allow the creation of species-specific gene drugs. This ensures treatments are tailored to particular animal species, minimizing side effects and enhancing efficacy (Nóbrega et al., 2020).

4. Future Prospects and Challenges

Although the future of biotechnology is promising, it faces challenges stemming from the development and use of methods like cloning, transgenic organisms, CRISPR, stem cell research, selective breeding, and disease resistance. Transgenic organisms and animal clones raise significant ethical issues, including concerns about biodiversity and animal welfare and possibly creating species with unforeseen negative traits (Seidel, 2020). The precision of genome editing, especially in germline modifications that can be inherited, also brings ethical boundaries into question. Comprehensive regulatory frameworks are necessary to ensure the safe use of biotechnological advances, but varying regulations across countries can complicate global collaboration and commercialization.

Genetically modified organisms should be safe for human consumption, and their impact on the environment remains a critical challenge, with long-term effects still not fully understood. Techniques like CRISPR, although revolutionary, are not flawless; off-target effects and mosaicism can lead to unintended genetic changes. Cloning success rates are relatively low, and cloned animals often suffer health problems. Public fear and misinformation about biotechnological methods can hinder scientific progress and acceptance, making transparent communication and education essential. Releasing transgenic organisms into the wild can disrupt natural ecosystems and affect

biodiversity, with long-term ecological impacts still uncertain (Shah et al., 2018).

On the positive side, stem cell research can revolutionize medicine by aiding the replacement or repair of impaired tissues and organs. CRISPR and other gene-editing technologies can create disease-resistant animals, reducing reliance on antibiotics and improving animal welfare. Selective breeding and genetic modification can produce crops and livestock with enhanced traits, such as improved nutritional content, increased yield, and pest resistance.

Cloning and genetic engineering can aid in the conservation of endangered species by increasing diversity and restoring their populations. Transgenic animals and plants can be engineered cost-effectively to produce biopharmaceuticals, such as vaccines, hormones, and antibodies. Biotechnology can also help meet the growing global demand for food by increasing the efficiency and productivity of agricultural systems (Massa et al., 2019).

In conclusion, while the prospects of biotechnology are vast and transformative, addressing the ethical, regulatory, safety, and public perception challenges will be crucial for its sustainable and responsible advancement.

5. Conclusion

Agriculture, medicine, and environmental conservation are all being revolutionized by animal biotechnology by using methods such as cloning, CRISPR-Cas9 gene editing, and developing transgenic organisms that have produced disease-resistant livestock, increasing agricultural productivity and protecting endangered species. Genetically modified animals are used to produce human-compatible organs and biopharmaceuticals, which address shortages in healthcare and improve healthcare. Stem cell research provides new treatments for various conditions, and selective breeding encourages sustainability and food security. Nevertheless, obstacles to progress include ethical considerations, regulatory complexity, safety concerns, and public perception.

References

Aerni, P. (2021). The Ethics of Farm Animal Biotechnology from an Anthropological Perspective. Sustainability, 13(7), 3674.

Bisimwa, P. N., Ongus, J. R., Tonui, R., Bisimwa, E. B., & Steinaa, L. (2024). Resistance to African swine fever virus among African domestic pigs appears to be associated with a distinct polymorphic signature in the RelA gene and upregulation of RelA transcription. Virology Journal, 21(1), 93.

Brito, L. F., Oliveira, H. R., McConn, B. R., Schinckel, A. P., Arrazola, A., Marchant-Forde, J. N., & Johnson, J. S. (2020). Large-scale phenotyping of livestock welfare in commercial production systems: a new frontier in animal breeding. Frontiers in genetics, 11, 793.

Caldwell, K. A., Willicott, C. W., & Caldwell, G. A. (2020). Modeling neurodegeneration in Caenorhabditis elegans. Disease Models & Mechanisms, 13(10), dmm046110.

Carlson, D. F., Lancto, C. A., Zang, B., Kim, E.-S., Walton, M., Oldeschulte, D., Seabury, C., Sonstegard, T. S., & Fahrenkrug, S. C. (2016). Production of hornless dairy cattle from genome-edited cell lines. Nature biotechnology, 34(5), 479-481.

Christapher, P. V., Ganeson, T., Chinni, S. V., & Parasuraman, S. (2022). Transgenic Rodent Models in Toxicological and Environmental Research: Future Perspectives. Journal of Pharmacology and Pharmacotherapeutics, 13(3), 258-265.

Crispo, M., Mulet, A., Tesson, L., Barrera, N., Cuadro, F., dos Santos-Neto, P., Nguyen, T., Crénéguy, A., Brusselle, L., & Anegón, I. (2015). Efficient generation of myostatin knock-out sheep using CRISPR/Cas9 technology and microinjection into zygotes. PLoS One, 10(8), e0136690.

de Siqueira-Silva, D. H., Saito, T., dos Santos-Silva, A. P., da Silva Costa, R., Psenicka, M., & Yasui, G. S. (2018). Biotechnology applied to fish reproduction: tools for conservation. Fish Physiology and Biochemistry, 44(6), 1469-1485.

Estrada, A. C., Díaz, D. V., & Hernández, C. A. M. (2017). The role of biotechnology in agricultural production and food supply. Ciencia e investigación agraria: Revista Latinoamericana de Ciencias de la Agricultura, 44(1), 1-11.

Friggens, N., Blanc, F., Berry, D., & Puillet, L. (2017). Deciphering animal robustness. A synthesis to facilitate its use in livestock breeding and management. Animal, 11(12), 2237-2251.

Gowane, G. R., Kumar, A., & Nimbkar, C. (2019). Challenges and opportunities to livestock breeding programmes in India. Journal of Animal Breeding and Genetics, 136(5), 329-338.

Greenfield, H. J. (2010). The Secondary Products Revolution: the past, the present and the future. World Archaeology, 42(1), 29-54.

HASAN, M. U., KOZAKLI, Ö., & CEYHAN, A. (2022). Possibilities of using CRISPR-based genome editing Technologies in Livestock. Journal of Agriculture, Food, Environment and Animal Sciences, 3(1), 56-68.

Henchion, M., Moloney, A., Hyland, J., Zimmermann, J., & McCarthy, S. (2021). Trends for meat, milk and egg consumption for the next decades and the role played by livestock systems in the global production of proteins. Animal, 15, 100287.

Hieber, J. K. (2020). Inbreeding and inbreeding depression in linebred beef cattle Montana State University].

Hino, T., Muro, Y., Tamura-Nakano, M., Okabe, M., Tateno, H., & Yanagimachi, R. (2016). The behavior and acrosomal status of mouse spermatozoa in vitro, and within the oviduct during fertilization after natural mating. Biology of reproduction, 95(3), 50, 51-11.

Hosseini, S.-M., Moulavi, F., Tanhaie-Vash, N., Asgari, V., Ghanaei, H.-R., Abedi-Dorche, M., Jafarzadeh, N., Gourabi, H., Shahverdi, A.-H., & Dizaj, A. V. (2016). The principal forces of oocyte polarity are evolutionary conserved but may not affect the contribution of the first two blastomeres to the blastocyst development in mammals. PLoS One, 11(3), e0148382.

Ibtisham, F., Zhang, L., Xiao, M., An, L., Ramzan, M. B., Nawab, A., Zhao, Y., Li, G., & Xu, Y. (2017). Genomic selection and its application in animal breeding. The Thai Journal of Veterinary Medicine, 47(3), 301-310.

Islam, M. A., Rony, S. A., Rahman, M. B., Cinar, M. U., Villena, J., Uddin, M. J., & Kitazawa, H. (2020). Improvement of disease resistance in livestock: application of immunogenomics and CRISPR/Cas9 technology. Animals, 10(12), 2236.

Jansen, K. U., Knirsch, C., & Anderson, A. S. (2018). The role of vaccines in preventing bacterial antimicrobial resistance. Nature medicine, 24(1), 10-19.

Kantor, A., McClements, M. E., & MacLaren, R. E. (2020). CRISPR-Cas9 DNA base-editing and prime-editing. International journal of molecular sciences, 21(17), 6240.

Keefer, C. L. (2015). Artificial cloning of domestic animals. Proceedings of the National Academy of Sciences, 112(29), 8874-8878.

Kesik-Brodacka, M. (2018). Progress in biopharmaceutical development. Biotechnology and applied biochemistry, 65(3), 306-322.

Khan, F. A. (2020). Biotechnology Fundamentals Third Edition. CRC Press.

Kumari, R., Rani, M., Nigam, A., & Kumar, A. (2023). Stem cell culture techniques. In Animal Cell Culture: Principles and Practice (pp. 213-234). Springer.

Kurtz, S., & Petersen, B. (2019). Pre-determination of sex in pigs by application of CRISPR/Cas system for genome editing. Theriogenology, 137, 67-74.

Laible, G., Wei, J., & Wagner, S. (2015). Improving livestock for agriculture–technological progress from random transgenesis to precision genome editing heralds a new era. Biotechnology journal, 10(1), 109-120.

Lee, K., Farrell, K., & Uh, K. (2020). Application of genome-editing systems to enhance available pig resources for agriculture and biomedicine. Reproduction, Fertility and Development, 32(2), 40-49.

Liu, Y., Ma, X., Shu, L., Hancke, G. P., & Abu-Mahfouz, A. M. (2020). From industry 4.0 to agriculture 4.0: Current status, enabling technologies, and research challenges. IEEE transactions on industrial informatics, 17(6), 4322-4334.

Massa, S., Presenti, O., & Benvenuto, E. (2019). Engineering plants for the future: farming with value-added harvest. Progress in Botany Vol. 80, 65-108.

McLean, Z., Oback, B., & Laible, G. (2021). Embryo-mediated genome editing for accelerated genetic improvement of livestock.

Mekonnen, G. (2021). Review on application of nanotechnology in animal health and production. J. Nanomed. Nanotechnol, 12, 559.

Menchaca, A., Dos Santos-Neto, P., Mulet, A., & Crispo, M. (2020). CRISPR in livestock: From editing to printing. Theriogenology, 150, 247-254.

Munawar, N., & Ahmad, A. (2021). CRISPR/Cas system: an introduction. CRISPR Crops: The Future of Food Security, 1-35.

Nóbrega, C., Mendonça, L., & Matos, C. A. (2020). A handbook of gene and cell therapy (Vol. 3). Springer.

Park, J. S., Han, S. T., Lee, K. H., Kim, Y. M., Lee, H. J., & Han, J. Y. (2019). Targeted genome modification mediated by homology-directed repair and non-homologous end joining and its application. J. Anim. Breed. Genet, 3(3).

Pingault, N., Caron, P., Kalafatic, C., Allahoury, A., Fresco, L. O., Kennedy, E., Khan, M., Kliksberg, B., Mei, F., & Murphy, S. (2016). Sustainable agricultural development for food security and nutrition: what roles for livestock? A report by the High Level Panel of Experts on Food Security and Nutrition of the Committee on World Food Security.

Pollet, J., Chen, W.-H., & Strych, U. (2021). Recombinant protein vaccines, a proven approach against coronavirus pandemics. Advanced drug delivery reviews, 170, 71-82.

Rahbaran, M., Razeghian, E., Maashi, M. S., Jalil, A. T., Widjaja, G., Thangavelu, L., Kuznetsova, M. Y., Nasirmoghadas, P., Heidari, F., & Marofi, F. (2021). Cloning and embryo splitting in mammalians: brief history, methods, and achievements. Stem Cells International, 2021(1), 2347506.

Rasmussen, N. (2014). Gene jockeys: Life science and the rise of biotech enterprise. JHU Press.

Rohr, J. R., Barrett, C. B., Civitello, D. J., Craft, M. E., Delius, B., DeLeo, G. A., Hudson, P. J., Jouanard, N., Nguyen, K. H., & Ostfeld, R. S. (2019). Emerging human infectious diseases

and the links to global food production. Nature Sustainability, 2(6), 445-456.

Rubessa, M., Polkoff, K., Bionaz, M., Monaco, E., Milner, D. J., Holllister, S. J., Goldwasser, M. S., & Wheeler, M. B. (2017). Use of pig as a model for mesenchymal stem cell therapies for bone regeneration. Animal biotechnology, 28(4), 275-287.

Seidel, G. E. (2020). GM farm animals: potential impact on biodiversity including ethical concerns. GMOs: Implications for Biodiversity Conservation and Ecological Processes, 277-285.

Shah, S. Z., Rehman, A., Nasir, H., Asif, A., Tufail, B., Usama, M., & Jabbar, B. (2018). Advances in research on genome editing CRISPR-Cas9 technology. Journal of Ayub Medical College Abbottabad, 31(1), 108-122.

Sharma, B., Chettri, D., & Verma, A. K. (2021). Biotechnological advancements in livestock production. Sustainable Agriculture Reviews 54: Animal Biotechnology for Livestock Production 1, 107-130.

Singh, P., & Ali, S. A. (2021). Impact of CRISPR-Cas9-based genome engineering in farm animals. Veterinary Sciences, 8(7), 122.

Singh, V. K., & Seed, T. M. (2021). How necessary are animal models for modern drug discovery? Expert opinion on drug discovery, 16(12), 1391-1397.

Srirattana, K., Kaneda, M., & Parnpai, R. (2022). Strategies to improve the efficiency of somatic cell nuclear transfer. International journal of molecular sciences, 23(4), 1969.

Suzuki, S., Iwamoto, M., Hashimoto, M., Suzuki, M., Nakai, M., Fuchimoto, D., Sembon, S., Eguchi-Ogawa, T., Uenishi, H., & Onishi, A. (2016). Generation and characterization of RAG2 knockout pigs as animal model for severe combined immunodeficiency. Veterinary immunology and immunopathology, 178, 37-49.

Vashishat, A., Patel, P., Das Gupta, G., & Das Kurmi, B. (2024). Alternatives of animal models for biomedical research: a comprehensive review of modern approaches. Stem Cell Reviews and Reports, 20(4), 881-899.

Wang, J. Y., & Doudna, J. A. (2023). CRISPR technology: A decade of genome editing is only the beginning. Science, 379(6629), eadd8643.

Wang, X., Yu, H., Lei, A., Zhou, J., Zeng, W., Zhu, H., Dong, Z., Niu, Y., Shi, B., & Cai, B. (2015). Generation of gene-modified goats targeting MSTN and FGF5 via zygote injection of CRISPR/Cas9 system. Scientific reports, 5(1), 13878.

Wolfe, M. D., Chan, A. W., Kulakow, P., Rabbi, I., & Jannink, J.-L. (2021). Genomic mating in outbred species: predicting cross usefulness with additive and total genetic covariance matrices. Genetics, 219(3), iyab122.

Wu-Pong, S. (1999). An overview of biotechnology. Biopharmaceutical Drug Design and Development, 1-19.

Yitbarek, M. B. (2019). Livestock and livestock product trends by 2050. IJAR, 4, 30.

About The Authors

Miss Shumaila Batool is an MPhil scholar in Zoology at the University of Agriculture Faisalabad, Pakistan. Her research focuses on Fisheries, specifically fish nutrition and toxicology, as well as conservation biology with an emphasis on wildlife and biodiversity. She is actively investigating the impacts of climate change on various species. Her two articles as a first author are under review in international journals and has also contributed to several interdisciplinary book chapters published by Springer and Elsevier.

Email: Shumailabatool262@gmail.com

Urwah Sheikh is an M Phil scholar at University of agriculture Faisalabad, Pakistan. Her research area is aquaculture and primarily focuses on how micronutrient supplementation can make aquaculture sustainable by improving health and enhancing immunity of fish.

Email: urwahsheikh77@gmail.com

Hareem Fayyaz is an MPhil Zoology student at the University of Agriculture, Faisalabad, Pakistan. Her research focuses on fish genetics, specifically examining how inbreeding in introduced fish species impacts genetic diversity in riverine populations and affects breeding patterns, potentially threatening the survival of these species. She has also written two book chapters.

Email: hfayyazahmed391@gmail.com

Anam Shehzadi is an MPhil scholar in Zoology, Wildlife and Fisheries Department of the University of Agriculture Faisalabad. She has impressively submitted 4 chapters and 1 review article at the international level, along with another chapter at the national level. Her research focus is on tackling critical animal-related issues and their solutions. Her research explores innovative technologies that enhance the well-being of animals in the context of climate change, alongside effective water management strategies aimed at ensuring the sustainability of aquatic life.

Email: shehzadianam2121@gmail.com

Fatima Ameen is an MPhil scholar in Zoology, Wildlife and Fisheries Department of the University of Agriculture, Faisalabad.

Email: arooggoraya@gmail.com

To Cite This Chapter

Batool S et al., (2024). Future Frontiers: Emerging Trends and Applications in Animal Biotechnology. In Current Studies in Health and Life Sciences 2024 (pp.424-437). ISRES Publishing.

Potential of Microsatellites DNA Markes in Monitoring The Genetic Diversity of Fishes

Tanveer AHMED Ayesha YASEEN

Aqsa PERVAIZ

Beenish SHAKIR

Laiba HANIF

Areeb JAVED

Huma NAZ

Khalid ABBAS Muhammad ARSHAD

Hira ASAD

Zainab BASHIR

Muhammad Sarfraz AHMAD

Shahbaz AHMAD

.

1. Introduction

Microsatellite DNA markers or simple sequence repeats (SSRs) (Tautz 1989), or short tandem repeat (STR) (Tautz, 1989; Edward et al., 1991) are known as the versatile, very popular and most desired genetic markers that found multiple applications in conservation genetics, genetic composition of biological populations, molecular ecology, developmental and evolutionary biology. The phenotypic characteristics of any organism are determined by the genes. Genetic variation results in the production of individuals that are distinct from one another at the organismic as well as molecular level. Stock is a panmictic population within a species that has related individuals and is genetically different from other such populations. Fishery biologists began dealing with economically significant marine organisms by utilizing these intra-specific groups, whom they were referred to as "stocks" (Shaklee et al., 1990). The crucial component in any management regime is the detection of distinct stocks (Ihseen et al., 1981; & Fetterolf et al., 1981). Genetic variety in the form of various alleles of many genes exists in the majority of natural populations. Population that is sexually reproducing, there aren't any two organisms that can be believed to have identical genotypes for every gene (Hartle and Clark1989). A genetic marker is one whose genotype can be derived from the phenotype through genetic screening and it is a variant that is inherited genetically. DNA (molecular) and protein are the two major types of genetic markers. Nuclear DNA markers are now the most familiar markers to identify the genetic variation within the population of organisms such as in fishes. They are molecular genetic markers with short segments of about 1- base pairs in length, (Beckmann and Weber 1992). DNA is composed of di, tri, and tetra nucleotide repeats sequence. They are highly short, abundant, co-dominant, and hyper-variable with frequencies of 10, 20, and 100 bases and are widely spread in the genome of eukaryotes and they have multiple alleles in them (Mojekwu et al., 2013). Microsatellites have been classified into various categories concerning the type of repeated sequence present. Microsatellites in the population of fish provide critical information for example demographic bottleneck detection, genome, pedigree and parental analysis detection, genetic variation identification within and between stocks, genetic conservation, and QTL (quantitative trait loci) detection (Fjalestad et al., 2003; Olubunmi, 2019 & Chistiakov et al., 2005). Microsatellites have developed as the ideal marker due to their ease of assaying, accuracy, and high variability, and that's the reason they are used in research for populations

with high resolution (Tripathy, 2018). The primers designed in a species for the amplification of microsatellites also in adjacent species offer cross-amplification for homologous loci, which proves helpful in assessing populations that are on the edge of extinction or are small (Estoup 1998). Comprising the changes and interactions of countless genes has also been made possible by genomic research, and including certain biological phenomena has been made possible by genome analysis (Venkatesh et al., 2007& Hudson et al., 1980). The procedure that is used to identify the genotype of the DNA marker of the fish is known as microsatellite genotyping. There are three basic steps in this procedure firstly microsatellite amplification, secondly specific design of the primer, and lastly the testing of Polymorphism. As primer is designed then amplification of such marker takes place. Currently, the amplification of the tiny DNA fragments is made possible via advanced thermo-cyclers by Polymerase chain reaction (PCR). In fisheries, microsatellite DNA markers contribute lots of necessary information such as genomic markers as well as diagnostics markers for diseases in fish (Duran et al. 2009). Although microsatellite markers provide multiple benefits, but they also have various disadvantages, and limitations and present several challenges that can severely suppress their application such as by complicating data analysis. Because of microsatellite flexibility to tackle a wide range of ecological queries overcome their disadvantages in many cases, even though all types of markers have their pitfalls. Luckily, through the procedure of isolation, many problems that are related to microsatellite markers can be condemned by selecting loci carefully. In this review, we will discuss the potential of microsatellite DNA markers in monitoring the genetic diversity in fish through their functioning, working, role in genetic diversity, genetic structure, microsatellite genotyping, advantages, and role in fish conservation, as well as it's limitations.

2. Microsatellite DNA markers

A short DNA sequence that appears numerous times at various locations across an organism's DNA is referred to as a molecular DNA marker. These repeats are highly variable making them useful as markers or tags for specific locations (polymorphic locus or loci) (Okumus & Ciftci, 2004). The molecular markers based on DNA sequence polymorphisms play a significant role in the measurement of genetic variation and genetic analysis in fish. (Olubunmi et al., 2019). Based on the current scientific understanding as stated in Deepak et al. (2017), molecular markers can be grouped into three categories. The first category involves nucleic acid hybridization which relies on complementary base pairing and includes techniques such as restriction fragment length polymorphisms (RFLPs). The second category comprises techniques such as microsatellites, or SSRs, AFLP (amplified fragment length polymorphisms) RAPD (random amplification of polymorphic DNA), that use PCR-based DNA amplification methods. The third category is single nucleotide polymorphisms (SNPs) as described by Duran et al. (2009). The non-coding and neutral markers are microsatellites and AFLPs (Brown et al., 2003).

The modern DNA structural model was developed in 1950 by F. Crick, J. Watson, and M. Wilkins, who also introduced the idea of molecular genetics (Hallerman et al., 2003). Since then, advancements in the understanding of DNA and gene structure and function have led to their use in determining genetic diversity. Different types of DNA markers were developed during the 1980s. However, the first investigation into population genetics based on mitochondrial DNA was carried out in the early 1980s (Avise et al., 1979). Later, the development of PCR technology facilitated the emergence of various methodologies for studying population genetics. These approaches encompassed not only DNA sequencing of the target regions but also techniques that examined length polymorphisms, including microsatellite DNA markers (Hansen, 2003).

Microsatellite DNA markers are molecular genetic markers with short sequences of around 1-6 base pairs in length (Beckmann et al., 1992). They are referred to as SSRs (Tautz et al. 1989) and STR (short tandem repeat) (Jeffreys et al., 1988; Edwards et al., 1991, & Weber et al., 1990) and broadly distributed over the genome of eukaryotes. They are highly abundant, small, and co-dominant with frequencies of 10 to 10 copies, 20 and 100 bases, and are widely distributed in the genome of eukaryotes and they have multiple alleles in them (Mojekwu et al., 2013). They are

hyper-variable, nuclear-encoded genetic markers that can be amplified by polymerase chain reaction or DNA sequencing markers (Phumichai et al., 2015 & Deepak et al., 2017). Microsatellite DNA markers have two main techniques to analyze (Okumus & Ciftci, 2004). Tautz (Tautz et al., 1989) and Weber and May first explained the polymorphism loci at microsatellite markers (Weber et al., 1989).

PCR plays a crucial role in amplifying alleles at microsatellite loci (Saiki et al., 1988). This technique enables the amplification of small samples of genomic DNA, allowing for the precise separation and sizing of alleles on a polyacrylamide gel or agarose gel. The resulting bands, typically appearing as one or two distinct bands, can then be utilized to quantify genetic variations within and between populations of a species. (Connel et al., 1997). Microsatellites allow for accurate differentiation based on electrophoresis (Muneer et al., 2009). Every locus is distinguished by a recognized DNA sequence that comprises both unique DNA segments and repetitive DNA motifs (Tautz et al., 1984). Simple sequence repeats, often made up of two to four nucleotides like (AC) n or (GATA) n, where n is between five and fifty, make up the repeating elements (Dewoody et al., 2000). Di-nucleotide repeats -GT and CA- are considered to be the most common microsatellites in vertebrates (Zardoya et al., 1996). To analyze single locus microsatellites specific primers flanking the repeat units are required and these sequences are obtained from genomic DNA libraries or are readily available in gene banks. These techniques are often used for developing microsatellite markers (Zane et al., 2002). Genetic markers serve as valuable tools for studying fish populations, offering valuable insights such as identifying genetic variations between and within stocks, monitoring genetic changes in stocks through gene tagging, detecting quantitative trait loci, and identifying demographic bottlenecks.(Chistiakov et al., 2005).

3. Functions of Microsatellite DNA Markers

For inscribing questions in evolution and population genetics microsatellite is one of the most adaptable and conventional markers (Flajoulot et al., 2005). Microsatellite marker is highly used in the correlated field of life sciences due to their fast detection protocol, high volume of polymorphism, and comparatively small size (Coe et al., 2009). Microsatellite has a wide variety of functions which include;

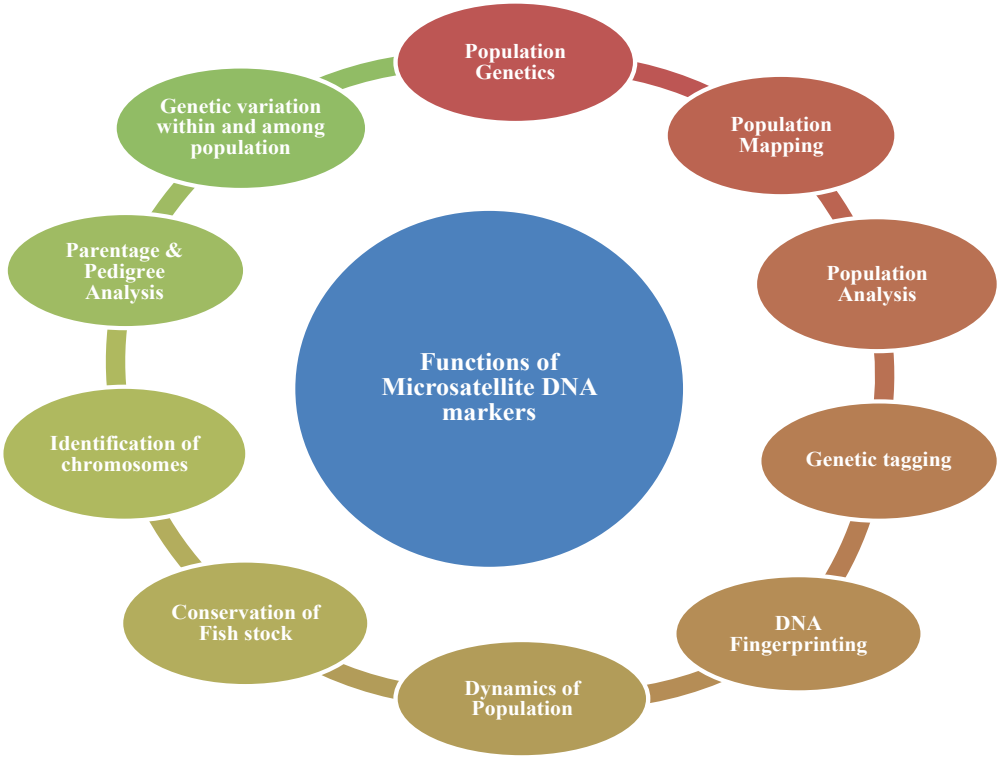


Fig.1. Showing functions of Microsatellite DNA markers

3.1. Parentage and Pedigree Analysis:

Microsatellite has mostly come out as a type of marker that is selected for pedigree analysis. In the task of a parent, microsatellites act as an effective instrument such as there are always hereditary alleles from both parents by each progeny. Broad genetic constitution details on the trait of examined discrete can be acquired with the use of multiple panel microsatellite markers (Duran et al., 2009; Olubunmi et al., 2019 & Sundaray et al., 2016). Microsatellite loci are used to rebuild pedigree in fish populations conceived from joint families (Norris et al., 1999; Morelli et al., 2007; Teng et al., 2020 & Olivatti et al., 2011). Microsatellite has modified applications such as assignment testing of population (Glover et al., 2010). In selective breeding, microsatellites provide us with various details in aquaculture for pedigree and parentage analysis such as genome mapping, regulating the genetic mutation in stock, observation of quantitative trait loci (QTL), an association of genetic variability among and within stock (Fjalestad et al., 2003; Subasinghe et al., 2003; Volckaert et al., 2008 & Olubunmi et al., 2019).

By using just two microsatellite loci and demonstrating the offspring accomplishment of mature males (cuckolders), Colbourne et al. (1996) conducted a parental analysis on eggs laid in a natural nest of bluegill sunfish (Lepomis macrochirus, Centrarchidae). Paternity in offspring from seven species of lekking cichlids is analyzed by (Kellogg et al., 1995) in a similar study. In the majority of the cases, these analyses circulate multiple paternity and in one exceptional condition, it divulged the offspring from one young was extracted from not less than six males. This level of study was not possible in the past due to the sharing of high levels of alleles recognized with less volatile markers. This kind of research will enable the proficiency of various living-history models in fish, which show a significant divergence in the phylogenetic perspectives among vertebrates to be calculated. In confined care schemes, the pedigree information is highly beneficial for farm management (O'Connell et al., 1997). In broad-scale pedigree analysis, the production of any path will increase with the amount of available molecular information. For example, for a higher number of alleles per locus we will use an increased number of loci that will increase the possibility of successful parentage assignments (Slate et al., 2000) and it will also increase both the correctness and accuracy of relatedness evaluation (Ritland, 1996). Microsatellites have been used to distinguish joint family groups and also to evaluate family/parentage locating in many species (Tripathy et al., 2018; Duran et al., 2009; & Al-Atiyat et al., 2012). Fractional allocation is another method for parentage analysis. Rather than regulating the single similar parent from a set of applicants, the fractional allocation method tries to fractionally allocate the offspring among non-excluded parents based on their likelihood parentage (Neff et al., 2001).

3.2. Genetics Variation of Closely Related Species:

Tautz (Powell et al., 1995) and Weber and May (Ma et al., 2010) first displayed the polymorphism at microsatellite loci. The polymerase chain reaction (Saiki et al., 1988) can increase the symbol of alleles at microsatellite loci from small genomic DNA specimens. These alleles segregate and correctly sort as one or two bands on a polyacrylamide gel, and these bands are used for evaluating genetic variation within and among individuals or species (Abdul-Muneer et al., 2014). Microsatellite is a dominant genetic indicator for evaluating the hereditary variation between and within individuals or species according to (Muneer, et al., 2011). For genetics population and stock isolation microsatellites is a precious marker (O'Connell et al., 1997, & Abdul Muneer et al., 2012). As stated by (Barbara et al., 2007) the triumph of assignable microsatellite loci was straightly associated with evolutionary relationships among groups are associated and transferable for the fish breed can be almost 70 percent in relative and 60% lowering between groups of similar families (Abdul Muneer et al., 2012 & Gopalakrishnan et al., 2009). Microsatellites use evaluation directly from DNA and are modified to survey the genetic diversity within and among the population (Ekerette et al., 2017).

3.3. Population Genetics:

According to Beckmann and Soller (Beckmann et al., 1990) the microsatellite markers are used in the population genetics of fish. Microsatellites as genetic molecular markers are dominant instruments to perceive the hereditary rareness of individuals, groups of populations, or breeds as stated by (Duncan et al., 2001; Amos et al., 2001; Avise, 1986; & Avise, 1994) and Linda and Paul (Askari et al., 2013). These are necessary for the analysis of the genetic diversity of various population groups (Collevatti et al., 1999). These molecular markers could give a powerful basis for the genetic diversity of fish assessment and locating of populations or species from various model and non-model organisms (Tripathy et al., 2018). Microsatellites having one locus in which both of the alleles express co-dominance declaration in heterozygotes have been extensively utilized for population studies (Abdul Muneer et al., 2009). With microsatellites only a few alleles are rigorously adapted for studies of population genetics, while for genome mapping the more changeable loci are ideal and to determine taxonomic vagueness in different taxa the stable or fewer polymorphic microsatellite loci and pedigree analysis are used (Carvalho et al., 1994). The variation in the microsatellite and sequence of freshwater and saltwater fishes for demographic genetics is described by (Chauhan, et al., 2007; Mandal, et al., 2018; & Xu, et al., 2020) and (Sinama et al., 2011; Abdul Muneer et al., 2012; & Muneer et al., 2011). Microsatellite shows the markers to select for genetic monitoring of farmed stock (Davis et al., 1998, & Hulata, 2001).

3.4. Genome Mapping:

By using various types of polymorphic markers the genetic linkage map has been established for several water-based species(Moen et al., 2008; Jiang et al., 2013; Liu et al., 2013; Wu et al., 2023; Zhu et al., 2019; Keong et al., 2014; & Hollenbeck et al., 2015). For genome mapping, divergence of population, pedigree and parentage analysis, and recognition of stock microsatellites as genetic markers have been used (Wright et al., 1995; Hansen et al., 2001; Liu et al., 2004; Webster et al., 2005; & Sanetra et al., 2009). Microsatellite markers have been utilized to develop the genetic maps by analyzing the reinterpretation and alleles separation via genotyping in common carp, cichlids, trout, zebrafish, and many other species. (O'Reilly et al., 1995) who recommend that microsatellites would be more useful for genomic identification. For establishing a genetic structure microsatellites have a strong use of various mapping tactics (comparative genetic, physical mapping, linkage mapping, and genomic tools) to include additional genes and markers. To locate the map the controlling of important features economically and finally cloned to classify the candidate gene.

3.5. Population Analysis:

Microsatellites have become the markers of option for population analysis of high constancy due to their high variance, facileness, and correctness of assaying according to (Estoup, et al., 1993). For isolation of stock and population genetics microsatellite markers are an effective instrument (Wright et al., 1995, & Abdul Muneer et al., 2012). Microsatellite loci are expensive instruments to examine genetic variability with application to management and population genetics (Oliveira et al., 2006).

3.6. Genetic Tagging:

Microsatellite markers are developing for a selected species providing several benefits, the genetic tags are the physical markers for parentage projects in assigning offspring to their birth parents. This process allows many families to be bred in a common aquarium from propagation to reaping size, an exercise that can crucially lower the amount and grind involved while removing any problem with common environmental results (Gjedrem, 2005). All of the progeny of bloodstock are essentially "tagged" by the genotyping of their DNA. A non-lethal tissue sample can be used to genetically recognize this youngster (for example, tag recovery), and parentage assessment can be used to determine an offspring's parents. This determines the age and hatchery stock of the tested offspring.

3.7. DNA Fingerprinting:

However, in-stock uses of DNA fingerprinting recognition and observing possible interchange in brood fish (Fjalestad et al., 2003; Sekino et al., 2001; & Alam et al., 2005). Microsatellite and mtDNA sequencing have been employed to evaluate the wild population and breeding of Japanese flounder (Paralichthysolivaceus) in contrast to French and Czech breeding populations of common carp (Cyprinus carpio) implementing allozymes and microsatellite analysis of the data of genetic diversity perceive a huge distinction among spot of two countries by Microsatellite marker.

3.8. Dynamics of Population:

By using microsatellite markers we can manage the genetic variability and vast diversity of innovational studies. Microsatellites are more fragile than allozymes for the advancement of population dynamics which include statistics bottleneck (Olubunmi et al., 2019). A method to reduce the population of brown trout in Denmark and to give gap microsatellite has been used (Zeng et al., 2017). Microsatellite loci are a benefit due to their high mutation rate that is used in genetic studies of population dynamics.

3.9. Conservation of Fish Stock:

With the help of microsatellite markers, polymorphism is achieved which supplies strong information that is used in the conservation of fish stock (Aida, 1921). For feasible yield and in the conservation of genetic variability molecular markers have informative applications which provide information on the molecular structure of fish species that will help locate distinctive stock and improvement of stock (Tripathi et al., 2011 & Ude et al., 2020). In examining inbreeding desolation microsatellites have essential approaches by detecting particular chromosomal regions that are answerable for inbreeding stress (Zhan et al., 2008). However, microsatellites would become the most suitable with cultivated species within a closed system where parents and their offspring can be controlled and traced. Microsatellite plays a remarkable role in the maintenance of fisheries and the conservation of species in their native populations.

3.10. Identification of Chromosomes:

Microsatellites have been verified successfully in the identification of various chromosome regions consisting of recognized quantitative traits loci gene which impact the capacity of rainbow trout to bear the infection-induced pancreatic Necrosis (IPN), determination of sex regions in channel catfish and also in the identification of relationship with stress-related plasma cortisol level and Basal plasma glucose volume in common carp (Waldbieser et al., 2001; Ozaki et al., 2001; & Tanck et al., 2001).

4. Genetic Diversity in Fishes & DNA Markers Potential

The genetic diversity among species is crucial in their ability to persist and adapt to their changing environments (Soule & Wilcox, 1980). Fish from freshwater and marine environments have more genetic variety than fish from freshwater environments (McCusker & Bentzen, 2010). Mitochondrial DNA (mtDNA) is a key DNA marker in phylogeography and population genetics. The recombination gap and rise in mutation particularly help to signal speciation, highlight the geographical separation of populations by a barrier that is often physical, and indicate whether there is a decrease or increase in population diversity (Avise, 1994). Since there are so many different species of fish, especially marine ones, it is possible to identify genetic hitchhiking in them. Most fish species are monitored using DNA markers for conservation, preservation, and organization (Avise, 1998; Moritz, 1994; Grant & Waples, 2000; Shaklee & Bentzen, 1998; Hauser et al., 2002). Fish have the greatest species diversity among vertebrates. The fish family has more than 32,000 species, and their number is enormous and incalculable. They may be found in various aquatic environments, including deep ocean bottoms at 6000 to 7000 meters and ecosystems in

the mountains at 2000 meters (Fishbase, 2014).

The IUCN Red List of 2014 revealed that 2172 varieties of fish are on the edge of disappearing due to overfishing, the degradation of natural ecosystems, which includes pollution, dam building, and the removal of water bodies for the benefit of humans (IUCN, 2014). Mutations are mostly responsible for the genetic diversity. The pace of evolution will eventually be very low if the mutation rate is low. Genetic diversity across organisms cannot exist if there are no mutations. Point mutations at certain DNA locations identify the genetic diversity. The use of DNA markers has been used to demonstrate these alterations. SNPs are recognized by sequencing genetic material, while mutations are most easily detected by electrophoresis on an agarose gel (Liu & Cordes, 2004). Using molecular markers makes it possible to keep track of and benefit from genetic variation throughout the whole genome. Because of this, the use of molecular markers in fish has made it possible to quickly track advancements in the exploration of inherited traits and closely related species, antecedent establishment, recognition of variety, construction of relationships in genes of fishes that are important for aquaculture, and identification of multi-factorial Loci associated with particular characteristics for marker aided selection.

Genetic indicators of Type 1 were formerly regarded as unsuitable to use for fish genetic research. Still, it is now proven that these indicators or markers have critical significance when dealing with natural populations as well as fish farming. These markers are now essential for comprehending linkage phenomena and for QTL mapping. They are useful for comparative research in genomes and also for the recognition of potentially suitable genes for quantitative characteristics in a variety of fish types used for the aquaculture industry. Numerous studies have looked at the molecular bases of many salmonid species' traits that are important commercially. For instance, when it encounters Atlantic salmon, QTL analysis was done for loci related to resistance to viral infections (Houston et al., 2008), flesh color and growth aspects (Baranski et al., 2010), salt tolerance (Norman et al., 2012), late sexual maturity (Gutierrez et al., 2014), etc. The first set of molecules includes those found in repetitive genomic sequences, PASA (PCR Amplification of Specific Alleles), PCR-RFLP, and SNP (Liu & Cordes, 2004). Only morphological descriptions of Romania's natural Salmonid varieties are known (Emil et al., 2011), and molecular-based research on these species is still in its early stages. Using the 16SrRNA and 12SrRNA sequences of genomes, Romanian salmonid varieties were separated phylogenetically. (Dudu et al., 2011) was one of the rare studies that looked at the genetic differentiation of salmonid fishes using the PCR-RFLP method. Even though the phylogeny and evolution of the salmonid fish family have been extensively studied, many questions remain. As a consequence, despite several investigations employing both morphological (Stearley & Smith, 1993) and genomic data (Kitano et al., 1997; Oohara et al., 1997; Crespi & Fulton, 2004), considering relationships on the genus stage, there persistently exist conflicting views (Dudu et al., 2011). The Coregoninae and Thymallinae subgroups came out of a common origin earlier than Salmoninae (including various genera such as Hucho, Salmo, Oncorhynchus, Salvelinus & Brachymystax), depending on the evolutionary study of early salmonid varieties. According to morphology and genetic proof, Coregoninae and Thymallinae had been believed to be the Salmonidae family's first extensions (Crespi & Fulton, 2004).

5. Microsatellite DNA marker Working

Microsatellites are ranging from 1 to 6 base pairs in size and are unitedly organized (Tautz et al., 1984 & Tautz et al. 1989). Regions that are gene-coded, non-gene sequences, and introns all have shown them (Liu et al., 2001). Microsatellites are the fastest evolving markers, as compared to point mutations they are 10 times faster, per generation mutation rate is 10^{-3} to 10-□(Goldstein et al., 1995), and recent investigation found that in all fish species, they exist usually every 10 kb (Wright, 1993). PIC (Polymorphic Information Content) value of microsatellite markers is high i.e., PIC regards the marker value for determining population polymorphism. Microsatellite gives this benefit besides their excess, high Q polymorphism, small locus size, and even genomic distribution. SSRs are constructed reproducible and highly polymorphic by the processes of uneven chromosomal

recombination and/or slippage of DNA polymerase. Null allele's presence is the main limitation, in spite of the benefits of microsatellite markers. When the SSRs locus acquires mutations at the primer binding regions null alleles arise, but the microsatellite DNA itself not gets mutated. The locus presenting null alleles is usually eliminated.

Shutter or shadow bands are a significant drawback of microsatellite markers, which can result from PCR errors generated by slipped strands (Tautz et al. 1989) or amplification products' incomplete denaturation (Reilly et al., 1999). By radioactive marking of either of the two primers, SSRs are usually studied this way, both primers have a sequence that is complementary on both sides of the repeat unit array. In PCR reaction the repeat unit array is amplified by using these primers. The amplification products are streamed on a sequencing gel to resolve the length difference that results from samples that have a variable number of repeats among themselves. Then the gel is dried and developed overnight usually after X-ray film exposure. In order to determine allele size reference to standards and allelic ladder is used generally such as the M13 sequence. In the genome, these loci are distributed all over and seem to be highly abundant, contrary to some reports considering mini-satellites that in chromosomes telomeric regions tend to be clustered (Jeffreys et al., 1987& 1991; Royle et al., 1988). In DNA extraction of an elementary configuration, PCR analysis largely utilizes micro-tissue quantities, and the chloroform/ phenol steps that are laborious are usually eradicated, therefore in contrast to mini-satellites, SSRs is proportionally facile to isolate (e.g. McGregor et al., 1996). Furthermore, by using imaging systems (e.g. the Hitachi FMBIO system or Molecular Dynamic's STORMTM)and automated fluorescent sequencers per day a significant number of samples can be genotyped (maintaining accuracy and quality), which gives microsatellites the potential to increase the number of samples (O'Reilly & Wright 1995and O'Reilly et al., 1996). The PCR technology was first developed in 1985, and during the past 100 years, the progress of amplification of DNA by employing the PCR technique has made it possible to study the genetic changes in fish populations during the past century (Ferguson & Denman 1988).

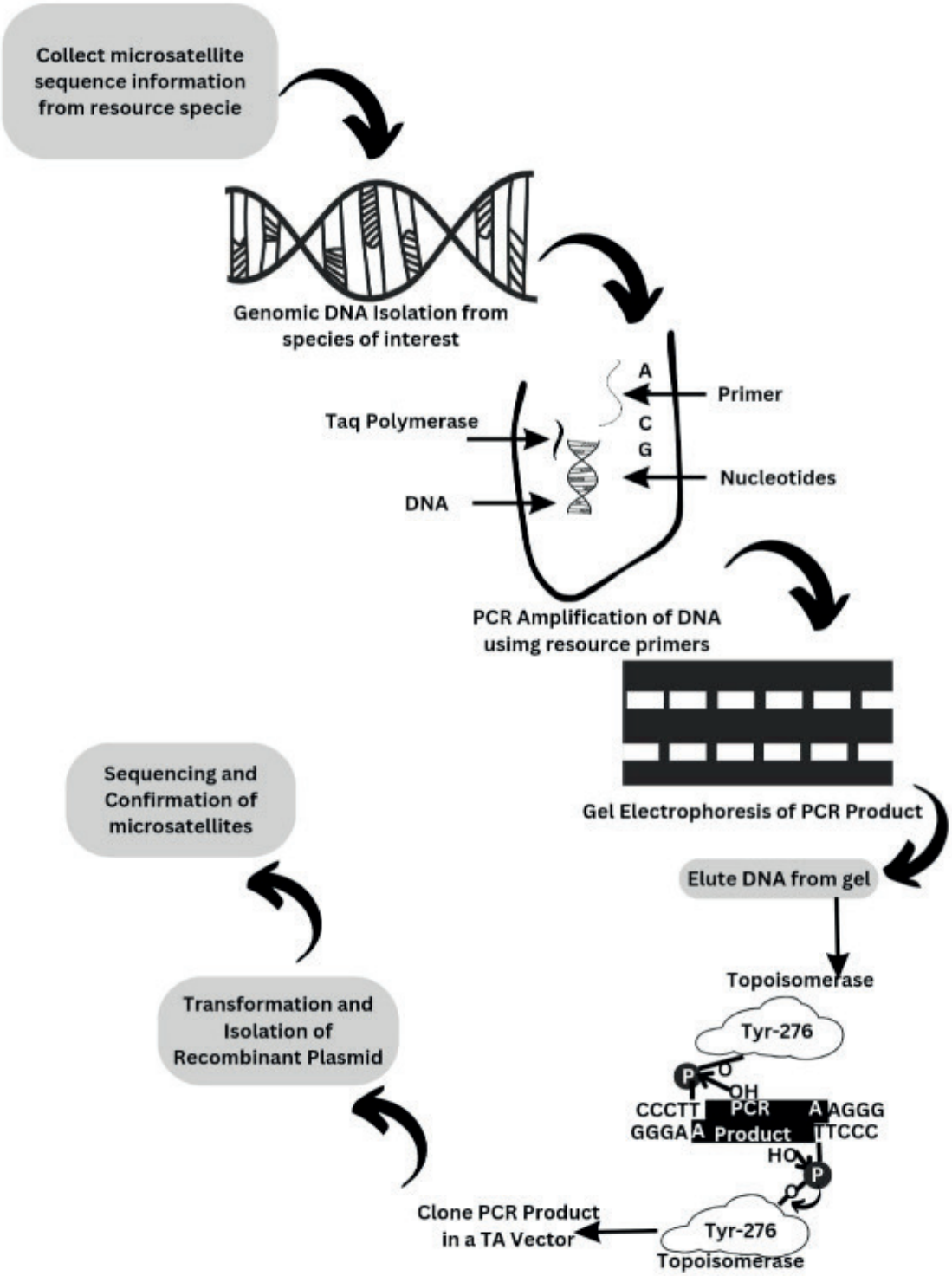


Fig.2. Showing Development of Microsatellite DNA Marker

5.1. Isolation:

Practice explanation is commonly used in the identification of repeat di-nucleotide loci and isolation (O'Reilly & Wright 1995). Shortly after, the DNA is broken down by enzymes, sorted by size on an agarose gel, and by cutting from the gel a particular size range (often it ranges between 300 to 600 bp) is eliminated. A vector such as pUC18 is used to link retrieved DNA. This procedure can be used to produce a partial genomic library and for cell transformation. Then a probe that contains repeating units, such as GT (n), is used to screen the library. The clones that efficiently hybridize with the GT (n) probe are then sequenced, and primers are developed to match unique sequences flanking the array. In spite of its simplicity, some significant moves are there to take,

that can considerably enhance the microsatellite numbers separated from a library.

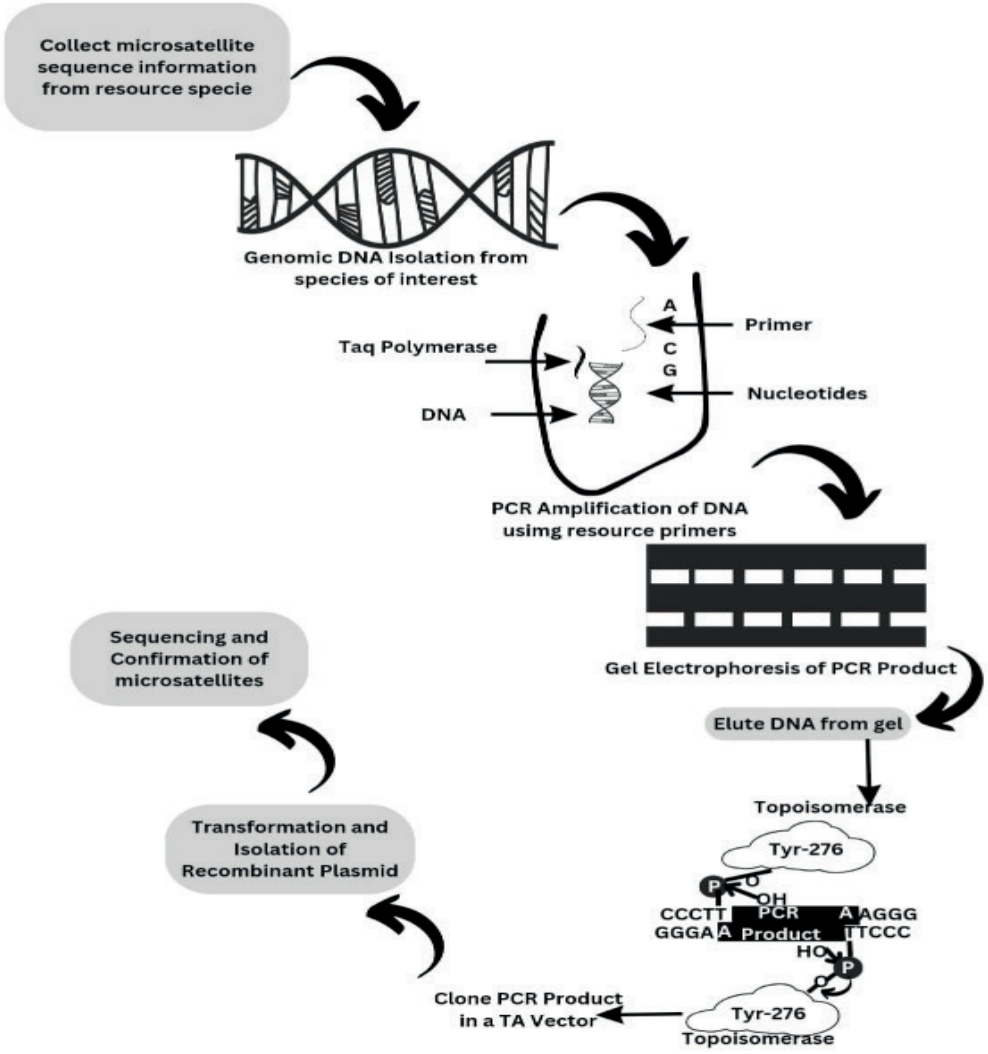


Fig.3. Traditional Method for Development Microsatellite DNA Marker

5.2. Technical Analysis & Potential Problems:

Beneath are technical aspects to consideration and troubles that may arise during microsatellite library creation.

1. It is suggested that during the library construction process DNA of high quality that has undergone purification via an organic extraction protocol.

2. If workable, focus on making a library with a colony including 20,000 or more. Mark down those libraries that can be constructed with less than 50 micrograms of DNA. Nevertheless, the time taken for microsatellite loci primers development can be lowered appreciably by increasing this quantity twofold (specifically if only one enzyme such as Mbot has been digested with the genomic DNA).

3. Prior to progressing with screening and cloning, it is important to examine the genomic digest to be utilized for multiplex copy elements such as Alut elements, accompanied by the single enzymes.

4. It is recommended to retain the size of the PCR product to less than 220 bp to avoid indefinite and vague alleles. If dealing with deteriorated or aged tissue such as scales or otolithor this is specifically significant, as amplification of products larger than 120 bp generally evinces unsuccessful.

5. Except for working on mapping, it is suggested to emphasize the isolation of tri- and tetra-nucleotide primers in various implementations.

6. More critically primer synthesis standard is the base on which the loci amplification capability is dependent than signature (stuttering) patterns. Consequently, it is serious to recognize an authentic supplier and keep away from making changes unless utterly mandatory.

7. To identify the consistent amplification of loci, it is suggested to allot enough resources and time through the development stage. The urge to utilize the first identified polymorphic markers must be ignored.

Progressively workers are shifting to loci that feature longer repeat units to make PCR products that can be examined effortlessly by exercising an automated scoring system and to lower the scoring error. In contrast to dinucleotide-based loci, these loci exhibit notably less stuttering, enabling more precise allele typing. Microsatellite alleles that are dinucleotide are exceedingly seen as a series of bands rather than individual discrete bands.

The phenomenon that is considered to emerge from slipped-strand miss-pairing is called stuttering (O'Reilly and Wright, 1995). Various protocols for enrichment have been set up that give instructions on the isolation of loci based on tri- and tetra nucleotides (Armour et al., 1995; Edwards et al., 1995; Karagyozov et al., 1993; Ostrander et al., 1992; Kijas et al., 1994 & Waldbieser, 1995). Contrasting to the ordinary "shotgun cloning" a technique that is used for the isolation of di-nucleotide repeat loci, additional time is significantly needed for employing tri and tetra nucleotide loci, however, utilizing tri and tetra nucleotide loci facilitates remarkably by overcoming any starting developmental problems.

6. Microsatellite genotyping

In Fish Genome, the procedure for determining the individual genetic makeup for each microsatellite locus or Simple sequence repeat is known as genotyping (Guichoux et al., 2011). First, the fish species are collected and the caudal fin from each fish is taken and preserved in -20°C and 70% ethanol solution for further DNA extraction process (Wattanadilokchatkun et al., 2022). As the total genomic DNA of fish is isolated, 1% agarose gel electrophoresis and spectro-photometry vice verses used to identify the quality and quantity of the DNA (Zhang et al., 2016). Due to low DNA quantity, the PCR of stomach specimens failed and Microsatellite genotyping is only successful for dorsal fin, caudal fin, or muscle tissue samples of fish (Choi et al., 2021). For microsatellite genotyping, you need to design specific primers, amplify the microsatellite regions, and test for Polymorphism (Vieira et al., 2016).

6.1. Specific primer design:

Microsatellite markers are used for testing genotyping of fish. In order to fulfill this purpose first SSRs primers are designed for a closely related species. In SSRs primer it is mandatory to have nucleotides sequence first (Vieira et al., 2016). By the application of the Microsatellite identification (MISA) tool, SSRs motifs can be determined. SSRsL locator v1.0 is used to design the locus-specific primers. The primers can be forward primer or Reverse primer. They can be formed manually or automated (Vieira et al., 2016). A fluorescent dye marks the 5-end of the forward primer in each primer pair (Choi et al., 2021).

6.2. Amplification of microsatellite:

To confirm the effectiveness of the SSRs primers, it is necessary to perform PCR amplification. The SSRs-PCR reaction mixture, which has a volume of 20 uL, contains DNA polymerase, a reaction buffer with a concentration of 1x, a forward primer with a concentration of 0.5 umol L^1, dNTP mix with a concentration of 40 umol L^1, MgCl2 with a concentration of 2 mmol L^1, a reverse primer with a concentration of 0.5 umol L^1, and 50 ng of genomic DNA. The PCR instrument runs

the thermal cycling with these steps: 5 min of initial denaturation at about 94°C, 36 cycles of 50s denaturation at 94°C, 1 min annealing at optimal temperature, and 1 min extension at 72°C, and a final extension of 7 min at 72°C (Chowdhry et al., 2021).On a 1% agarose gel, the products of PCR were separated by electrophoresis. To ensure accuracy, the PCR amplification process is repeated at least three times for each sample, which helps to minimize the impact of any erroneous alleles. Once the PCR amplification products are fluorescently labeled, they are genotyped using an automated sequencer such as the ABI 3730XL from Applied Biosystems (Applied Biosystems, Foster City, CA, USA). This is typically done at the DNA sequencing service of a specialized laboratory such as Macrogen, Inc. The data obtained from the sequencer is then analyzed to determine the particular sequence of alleles present in the sample being tested. The determination of allelic size was carried out through the utilization of Peak Scanner version 1.0 software from Applied Biosystems, based in Foster City, California, USA. The genotypic data resulting from this process has been archived in the Dryad Digital Repository (Wattandilokchatkun et al., 2022).

6.3. Polymorphism testing:

By using PAGE (polyacrylamide gel electrophoresis) or agarose gel electrophoresis, the PCR results are visualized. PAGE genotyping provides good resolution however it is labor intensive. For conducting finely detailed analyses, specific SSRs primers that have been labeled with a fluorescence dye can be produced. These primers facilitate genotyping via capillary electrophoresis, which can be carried out using specialized instruments such as the ABI 3730 DNA Analyzer (Saha et al., 2017). In this scenario, the amplified DNA fragments obtained through PCR are introduced into capillaries filled with a polyacrylamide matrix. Subsequently, electrophoresis takes place within these capillaries, during which the emitted fluorescence is detected. This fluorescence data is utilized to determine the molecular weight of each PCR product. A visual representation called an electropherogram is created, displaying distinct peaks of luminescence that correspond to the amplified alleles (Saha et al.,2017). Microsatellite Genotyping helps to figure out the polymorphism of fishes by identifying the genetic diversity in fishes such as Siamese fighting fish as well as freshwater fishes and marine fishes (Wattanadilokchatkun et al., 2022).

7. Genome mapping

Genome mapping is used to record the synchrony, sequence, and spacing of genes or genetic markers present on chromosomes. The genome maps provide homologous regions in one species to be observed with mapped genes in another, in addition to this they also make it simpler to map genes and markers which are undetermined in their placement. The position of markers or genes is offered by genome mapping with reliable proof. Thus, it is possible to identify quantitative genes that have value for commerce using genetic markers, and this is exactly what has been done. These genes can be recognized being single genes that are transmitted according to the Mendelian manner. Other than that, they might refer to sections within a genome that have been identified as most responsible for the quantitative variability in a gene. Certain physical attributes and resistance to diseases may be regulated by only one gene, but numerous traits with commercial significance are influenced by several genes with modest combined effects.

AFLPs are an additional popular genetic marker for gene mapping. Although it is challenging to construct microsatellite markers, AFLP has in fact been chosen for certain crustaceans (Moore et al., 1999; Davis and Hetzel, 2000). One of the reasons AFLPs are so attractive is because a genetic map can be developed in a couple of months, instead of years. According to Young et al. (1998), a rainbow trout linkage map of roughly 500 markers has been made available, with most of the markers belonging to the AFLP category (Young et al., 1998). For lineage analysis and QTL mapping, AFLP markers might have some disadvantages because many of them seem to be expressed dominantly. The quantification technique of PCR known as densitometric PCR will be required to differentiate between homozygous and heterozygous genotypes due to the absence of co-dominant allelic expression for these areas (Ferguson and Danzmann, 1998). Microsatellite

loci are considered to be better than AFLPs and RAPDs also, for genome mapping as well as when looking for QTL (Sakamoto et al., 1999), despite being utilized more time and technically challenging to develop. This is because the first kind is co-dominantly inherited, while the second type inherits itself as recessives and dominants also (Okumuş et al., 2003).

7.1. QTL Mapping:

QTLs (Quantitative Trait Loci) are identified by evaluating phenotypes via linked marker maps. The process to detect markers associated with QTLs can yield notable advantages for traits that can be costly or challenging to quantify (such as feed conversion), are quantified only for one sex (like fecundity), can solely be calculated after the time of choice (reproductive traits), can solely be calculated after homicide the specimen (flesh quality), or might just be calculated on fish that are raised in an environment apart from the primary breeding stock (disease resistance) (Davis and Hetzel, 2000). Monitoring of genetic diversity and proximity among individuals, strains, and families is the goal of QTL mapping, and the results are used to inform marker-assisted operations aimed at improving production-related traits (Fjalestad et al., 2003). Genetic map construction enables the recognition of QTLs as well as the identification of markers for QTLs. Numerous technologies are accessible (Park and Moran, 1995) and might be implemented (Poompuang and Hallerman, 1997). By extracting a significant number (often more than 100 loci) of extremely diverse markers (typically microsatellite loci, AFLPs, or RAPDs), this method looks for the association among numerous production traits in each allele separately and in combination. Hypervariable microsatellite regions are perhaps the most potential way to generate molecular markers. Depending on known mapping studies, they seem to be extensively distributed in fish genomes and various in the majority of fish species.

8. DNA Markers Potential in Conservation of Fish Diversity

The research of microsatellite markers will allow the administration of fisheries and the preservation of organisms in their native populations, which offers helpful knowledge on fish species' genetic diversity and stock organization. Differentiating a species into genetically distinct populations is an important phase in evolution. This process is affected by biological, physical, and geographic hurdles as well as migration, selection, and genetic drift. Small and declining populations of endangered species make inbreeding and genetic diversity loss inevitable. Because genetic diversity is being lost and inbreeding is increasing, populations' capacity to adapt to environmental change is being lowered; Frankham (Kounnamasa, 2021) hypothesized that these genetic traits would increase the danger of extinction, particularly in vulnerable species with tiny populations. The low diversity of genes (hybrid deficit and divergence from Hardy-Weinberg equilibrium) and hereditary (positive value of FIS) in population genetic analysis demonstrates the effects of a genetic bottleneck brought on by overexploitation and habitat destruction. (Ranjan, 1997) "Supportive breeding" may increase an endangered species' natural numbers. A portion of the wild parents are used in this program to breed in captivity, and the offspring are then returned to the wild.

• In the holding facility, fish species progeny from various rivers must be recognized and stored in separate pools.

• Additionally, there shouldn't be a cap on the size of an effective breeding population or the sex ratio. A wide variety of courses in different lengths or decades provided at various times are preferable to a single class in a single size and year.

• To enhance the quantity of high-yielding communities and aid in the improvement of fish populations that are at risk of becoming extinct, cryo-preserved milt which was previously collected from multiple males and pooled could be applied. Gene banking using sperm cryopreservation is significantly more affordable, simple to operate, and less susceptible to the risk imposed by system failure or death related to illness than the captive breeding program. As a result, it ought to be a helpful addition to the captive breeding effort.

• The same rivers from which the genetic stocks are gathered should be used for independent breeding and ranching of the various genetic stocks.

• River segments with a resident population or those potentially acting as a sanctuary may be chosen for fish population ranching.

• For evaluating the effects of ranching, experimental fishing should be utilized from tracking parameters like catch per unit effort/area.

It is important to monitor the abnormalities in the genetic code or rate of alleles, particularly the incidence of uncommon allelomorphs throughout time (Willi et al., 2022, & O'Connell et al., 197). The basic genetic profiles of representative fish stock samples from the holding facility and the ranching zones should be preserved. To more fully evaluate the influence of genetic diversity, the baseline information obtained in this research by utilizing microsatellite markers may be beneficial. Because of their special qualities, including their high polymorphism, reproducibility, co-dominance, strong discriminatory power, specificity in PCR-based assays, wide distribution in the genome, and extraordinarily high allelic variation, microsatellite markers are extremely helpful. They are quickly becoming indispensable in fish biotechnology (Chao et al., 2022, & Olubunmi, 2019). Fish biotechnology uses it for various purposes, including genetic fingerprinting (Schlötterer, 2000). Using microsatellite markers will improve the management of wild fish populations (Agbebi et al., 2013). Managing wild fish populations, including trout and salmon, would benefit tremendously from approaches based on DNA markers at scale emerging from genetics of population and conservation. SSRs are the preferred markers in aquaculture for genetic management of cultured livestock in light of breeding projects, as they allow for the design of good crosses, the selection of genetically improved stocks, the reduction of inbreeding, and an increase in selection response (León-Bernabeu et al., 2021).

9. Expediency in Monitoring Fish Diversity

Microsatellite markers offer lots of advantages over other molecular markers like allozymes and mitochondrial DNA (mtDNA) and also provide more effective information than mtDNA or allozymes-type markers. These Mendelian inherited microsatellite molecular markers have a codominant nature (can distinguish heterozygotes from homozygotes), have high variability, are easy to isolate, and are highly polymorphic. All these properties make them very preferable, highly valued, and ideal for studying pedigree analysis, population composition, and stock structure determination in fisheries (Grover et al., 2016). These markers have the capability of observing the genetic variations and differences among very closely related species and can distinguish between genotypes (Gowrimanohari Rakkannan 2022). Thus, they provide an effective substitute for other markers in determining the sources of hybrid populations of migratory fish specimens. For QTL (Quantitative Trait Loci) identification and genome mapping, where lots of loci are needed (Okumus et al., 2003).

In the past decade, the use of DNA satellites to diagnose genetic mutations and deletions has increased. These markers are effective for genetic stick characterization, gene mapping, broodstock selection, mapping metric traits, and mapping the genetic loci associated with these traits in the fields of aquaculture and fisheries. (Xiao-Gu et al., 2006). These microsatellite markers provide very useful and effective information for developing efficient strategies for population analysis, fisheries stock management, and biodiversity conservation (Gowrimanohari & Rakkannan, 2022). The unique features of microsatellites have resulted in improvements in the fields of digital information retention and the development of automated detection and diagnostic mechanisms like fluorescence imaging equipment (O'Connell et al., 1997). Simple sequence repeats loci containing a huge number of alleles are very effective for the identification of population genetics, phylogeny, and mixed population parent-offspring (Gowrimanohari Rakkannan, 2022).

In short, microsatellite DNA markers can be used for identifying and monitoring genetic

variations within and between stocks, for pedigree analysis, parentage determination, and examining potential genetic changes in fish stocks (Mojekwu et al., 2020) and provide effective information for developing strategies for fisheries stock conservation and management.

10. Microsatellite Limitations

Despite the certain capability of microsatellites in fish biotechnology, they have several limitations in their application. Chance of error is one of the principal considerations in all data sets, involving genotyping errors that in population genetics possibly can prejudice the ultimate conclusions (Bonin et al., 2004). Several variables are reviewed that might produce microsatellite genotyping errors, such as contamination or Taq polymerase error, and reagent quality. Misinterpretation of banding patterns of alleles is the major outcome of those errors (Pompano et al., 2005).

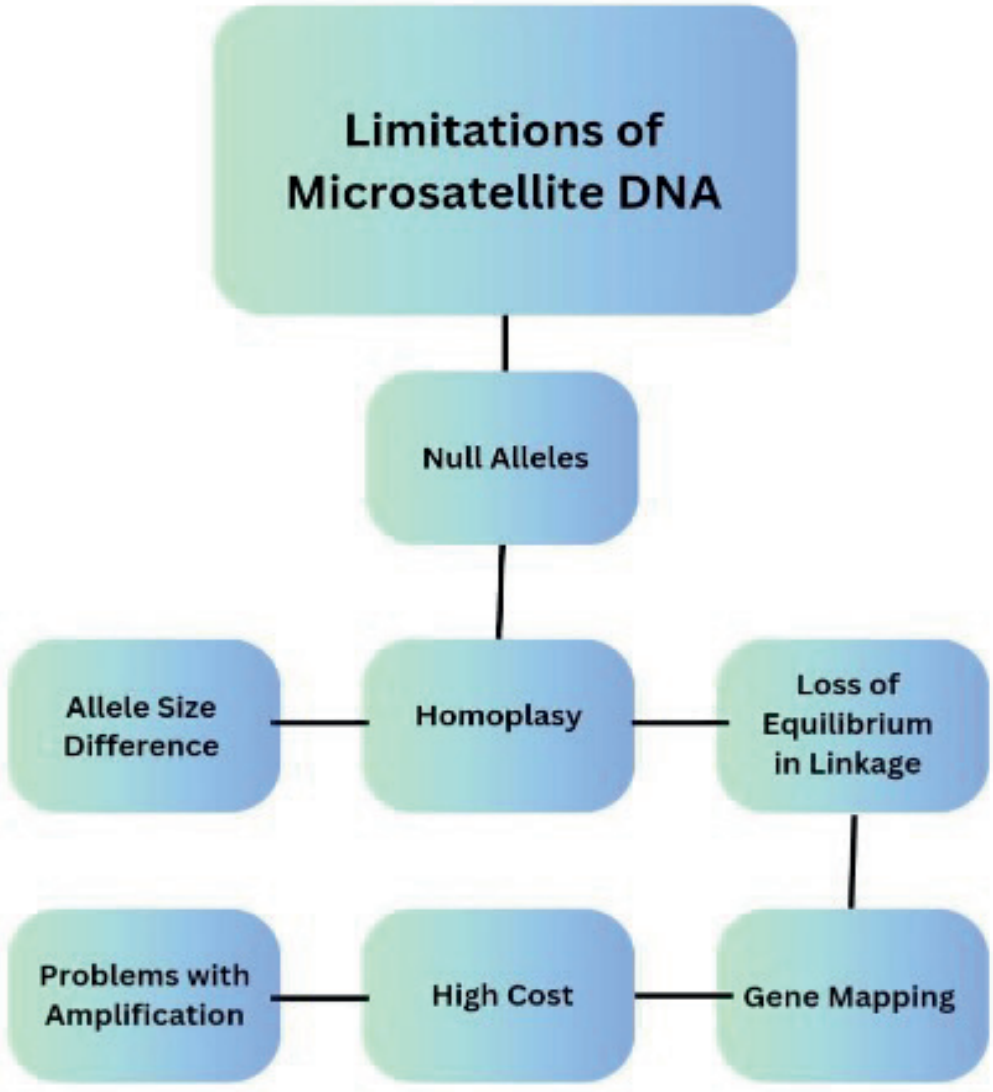


Fig.4. Flow- Sheet diagram showing Microsatellite DNA Markers Limitation

Limitations of Microsatellite Markers:

10.1. Null alleles:

Recognition of heterozygotes and amplification of locus can be prohibited by mutation or deletions of the locus in the annealing primer site and conduct to incorrect assessment of segregation rates and frequency of allele. This issue can probably be settled by primer redesign.

•An additional main barrier in the employment of microsatellite markers is null allele's

presence, which are alleles that fail to amplify during PCR reactions (O'Reilly et al., 1995).

10.2. Allele Size Difference:

Provided with alleles of a microsatellite locus that have slight dissimilarities in size between them (like a locus that is constituted by repeats of di-nucleotide as small as 2 base pair) can appear as a outcome of slippage of polymerase in the time of replication.

10.3. Homoplasy:

Jarne & Lagoda described the homoplasic alleles as alleles that don't share the same ancestral origin but share the same length (Jarne & Lagoda 1996). Furthermore homoplasic alleles can share both sequence and same length, yet have divergent evolutionary histories (Anmarkrud et al., 2008). Unfortunately; homoplasy can direct the true genetic divergence to underestimations in between the populations, because it is overlooked. The identification of evolutionary history difference may only possible by the use of pedigree that is documented mutations, while sequence difference can be detected by sequencing.

• The existence of homoplasy can generate bias into genetic analyses of natural populations; consequently impediment is produced in efforts to identify conservation units (Curtu et al., 2004).

10.4. Loss of Equilibrium in Linkage:

Extensive breeding and sub-structuring of population mainly results in non-random distribution of alleles in a population (Weising et al., 2005). Particularly for paternal exclusion and population studies it is significantly causing troublesome. The issues can be identified using several techniques such as offspring analysis and computer programs.

10.5. Gene mapping:

The presence of fragments of unknown DNA makes the use of microsatellite detrimental in gene mapping (Mojekwu et al., 2012). Moreover, when utilizing primers produced from one taxon to investigate phylogeny, they may not be useful on all the taxa whose genotype is being analyzed.

10.6. High cost:

Furthermore pitfall of microsatellites usage involve high cost that is associated with species-specific primers production, as well as the labor-intensive procedure that demands considerable personnel time for primer development (Telles et al., 2010).

10.7. Problems with amplification:

Portion of the genome with an adequately prominent mutation rate that multiple versions (alleles) occurs in a designated population, must be determined in order to discover a functional DNA marker locus. Furthermore, this area should be located next to a low mutation rate, extend of DNA that can tie up PCR primers in nearly all individuals of the species, approaching nearly 100%. Few individuals have alleles that maybe unsuccessful to amplify at all or few individuals have one amplified allele only (Paetkau & Strobeck 1995).

The effect of the error fluctuates following the usage of the data. Usually, homoplasy is not an important issue in population genetic analyses (Estoup et al., 2002), with the exclusion of markers that are hyper-mutable and the slippage rate they exhibit is high (Anmarkrud et al., 2008). The rate of inaccurate paternity restriction surpasses 20% even with error rates per allele as minimal as 0.01, demonstrating that even little errors can have a significant impact (Hoffman & Amos2005).For genotyping errors there are a great deal of informatics tool that have been listed, are considered for such errors (listed by Pompanon et al., 2005).The error rates are analyzed by a protocol that is proposed by these authors, which should be employed to ensure the dependability

of published genotyping research.

Conclusion:

Taking everything into account, this review provides comprehensive details on the role & potential of microsatellite DNA markers for monitoring genetic diversity in fishes using. Measuring genetic diversity helps in the understanding and effective management of fish stock. Microsatellite markers are based on DNA sequence polymorphisms and are pivotal in determining the genetic variation/diversity in fishes. Microsatellite loci are widely distributed in eukaryotic genomes, and each locus has a unique DNA sequence consisting of single DNA and DNA repeat motifs. Microsatellites are reliable, cost-effective and easy to isolate and these attributes make them valuable and suitable genetic markers for performing various functions, including Parentage and Pedigree Analysis, Conservation of Fish Stocks, Gene Tagging/mapping, determination of genetic diversity within and among population, DNA Fingerprinting, population genetics, and developing efficient strategies for fish conservation. These markers can provide essential information and are more efficient than mtDNA or allozymes type markers. Thus, provide an effective alternative over other markers for keeping track of the sources of mixed populations of migrating fish specimens, identifying Quantitative Trait Loci and genome mapping, which necessitate a large number of loci.

Preserving genetic diversity is essential to ensure that the stocked fish attain their maximum potential, making the species to get adapted to their changing environment. Genetic Variation results from mutational changes, migration, selection and breeding strategies. Both genetic variants intraspecific and interspecific exist. Genetic markers monitor and manage the genetic diversity of an organism. In addition, PCR products must be limited to 220 bp to reduce selectivity and vague alleles. Working of microsatellites involves Polymerase chain Reaction amplification of loci flanking repetitive sequences by using fluorescent primers. The microsatellite genotyping system mostly involves developing primer sequences that are specific to the targeted microsatellites, amplifying the microsatellites to generate enough material for analysis, and confirming the presence of polymorphism by conducting assays to detect variations between samples.

The main limitation of microsatellites is the presence of null alleles that fail to amplify. Non-random allele distribution in a population and presence of unknown DNA fragments can cause troublesome. Furthermore, species-specific primers production associated with high cost is another limitation. Microsatellite markers provide opportunities for different types of research to identify and track genetic variation within and among fish species and provide better information for conservation strategies. Simple sequence repeats are the most preferred markers in fisheries and aquaculture for monitoring the genetic diversity of stocks breeding programs, as they along with other genetic tools and technologies can be integrated for developing efficient strategies for the conservation and rehabilitation of genetic diversity in fish. Microsatellites can be the most unusual candidates for novel and unique marker systems that may be useful and can potentially replace allozymes markers for monitoring genetic diversity in fish.

References

Abdul Muneer, P. M., Gopalakrishnan, A., Musammilu, K. K., Basheer, V. S., Mohindra, V., Lal, K. K., … & Ponniah, A. G. (2012). Comparative assessment of genetic variability in the populations of endemic and endangered Yellow Catfish, Horabagrus brachysoma (Teleostei: Horabagridae), based on allozyme, RAPD, and microsatellite markers. Biochemical genetics, 50, 192-212.

Abdul Muneer, P. M., Gopalakrishnan, A., Musammilu, K. K., Mohindra, V., Lal, K. K., Basheer, V. S., & Lakra, W. S. (2009). Genetic variation and population structure of endemic yellow catfish, Horabagrus brachysoma (Bagridae) among three populations of Western Ghat region using RAPD and microsatellite markers. Molecular biology reports, 36, 1779-1791.

Abdul-Muneer P. M. (2014). Application of microsatellite markers in conservation genetics and fisheries management: recent advances in population structure analysis and conservation strategies. Genetics research international, 2014, 691759. https://doi.org/10.1155/2014/691759

Agbebi, O. T., Ilaboya, D. E., & Adebambo, A. O. (2013). Preliminary characterization of genetic strains in clariid species, Clarias gariepinus and Heterobranchus bidorsalis using microsatellite markers. African journal of Biotechnology, 12(4), 364.

Aida, T. (1921). On the inheritance of color in a fresh-water fish, Aplocheilus latipes Temmick and Schlegel, with special reference to sex-linked inheritance. Genetics, 6(6), 554.

Alam, M. S., & Islam, M. S. (2005). Population genetic structure of Catla catla (Hamilton) revealed by microsatellite DNA markers. Aquaculture, 246(1-4), 151-160.

Al-Atiyat, R. M., Tabbaa, M. J., Salameh, N. M., Tarawneh, K. A., Al-Shmayla, L., & Al-Tamimie, H. J. (2012). Analysis of genetic variation of fat tailed-sheep in southern region of Jordan. Asian Journal of Animal and Veterinary Advances, 7(5), 376-389.

Anmarkrud, J. A., Kleven, O., Bachmann, L., & Lifjeld, J. T. (2008). Microsatellite evolution: Mutations, sequence variation, and homoplasy in the hypervariable avian microsatellite locus HrU10. BMC Evolutionary Biology, 8(1), 1-10.

Armour, J. A., Neumann, R., Gobert, S., & Jeffreys, A. J. (1994). Isolation of human simple repeat loci by hybridization selection. Human molecular genetics, 3(4), 599-605.

Askari, G. H., Shabani, A., & Kolangi Miandare, H. (2013). Application of molecular markers in fisheries and aquaculture. Scientific Journal of Animal Science, 2(4), 82-88.

Avise JC (1994) Molecular Markers, Natural History, and Evolution. Chapman & Hall, New York; London.

Avise, J. C. (1986). Mitochondrial DNA and the evolutionary genetics of higher animals. Philosophical Transactions of the Royal Society of London. B, Biological Sciences, 312(1154), 325-342.

Avise, J. C. (1998). Conservation genetics in the marine realm. Journal of Heredity, 89(5), 377-382.

Avise, J. C., Lansman, R. A., & Shade, R. O. (1979). The use of restriction endonucleases to measure mitochondrial DNA sequence relatedness in natural populations. I. Population structure and evolution in the genus Peromyscus. Genetics, 92(1), 279-295.

Baranski, M., Moen, T., & Våge, D. I. (2010). Mapping of quantitative trait loci for flesh colour and growth traits in Atlantic salmon (Salmo salar). Genetics Selection Evolution, 42(1), 1-14.

Barbara, T., PALMA-SILVA, C. L. A. R. I. S. S. E., Paggi, G. M., Bered, F., Fay, M. F., & Lexer, C. (2007). Cross-species transfer of nuclear microsatellite markers: potential and limitations. Molecular ecology, 16(18), 3759-3767.

Beckmann, J. S., & Soller, M. (1990). Toward a unified approach to genetic mapping of eukaryotes based on sequence tagged microsatellite sites. Bio/technology, 8(10), 930-932.

Beckmann, J. S., & Weber, J. L. (1992). Survey of human and rat microsatellites. Genomics, 12(4), 627-631.

Bonin, A., Bellemain, E., Bronken Eidesen, P., Pompanon, F., Brochmann, C., & Taberlet, P. (2004). How to track and assess genotyping errors in population genetics studies. Molecular ecology, 13(11), 3261-3273.

Brown, B., & Epifanio, J. (2003). Nuclear DNA. Population Genetics: Principles and Applications for Fisheries Scientists. American Fisheries Society, Bethesda, MD, 458.

Carvalho, G. R., & Hauser, L. (1994). Molecular genetics and the stock concept in fisheries. Reviews in fish biology and fisheries, 4, 326-350.

Chao, C. H., Yeh, Y. H., Chen, Y. M., Lee, K. H., Wang, S. H., & Lin, T. Y. (2022). Sire pedigree error estimation and sire verification of the Taiwan dairy cattle population by using SNP markers. Polish Journal of Veterinary Sciences, 25(1), 61-65.Boriss B., Xenia C. O., Marcel S. VGenetic diversity of six populations of red hybrid tilapia, using Microsatellite genetic markers. Revised, MVZ Cordoba, 2011: 16 (2): 2491-2498.

Chauhan, T., Lal, K. K., Mohindra, V., Singh, R. K., Punia, P., Gopalakrishnan, A., … & Lakra, W. S. (2007). Evaluating genetic differentiation in wild populations of the Indian major carp, Cirrhinus mrigala (Hamilton–Buchanan, 1882): evidence from allozyme and microsatellite markers. Aquaculture, 269(1-4), 135-149.

Chistiakov, D. A., Hellemans, B., Haley, C. S., Law, A. S., Tsigenopoulos, C. S., Kotoulas, G., ... & Volckaert, F. A. (2005). A microsatellite linkage map of the European sea bass Dicentrarchus labrax L. Genetics, 170(4), 1821-1826.

Choi, H. K., Jang, J. E., Byeon, S. Y., Kim, Y. R., Maschette, D., Chung, S., … & Lee, H. J. (2021). Genetic diversity and population structure of the Antarctic toothfish, Dissostichus mawsoni, using mitochondrial and microsatellite DNA markers. Frontiers in Marine Science, 8, 666417.

Çiftci, Y., & Okumuş, İ. (2002). Fish population genetics and applications of molecular markers to fisheries and aquaculture: I-Basic principles of fish population genetics. Turkish Journal of Fisheries and Aquatic Sciences, 2(2).

Coe, T. S., Hamilton, P. B., Griffiths, A. M., Hodgson, D. J., Wahab, M. A., & Tyler, C. R. (2009). Genetic variation in strains of zebrafish (Danio rerio) and the implications for ecotoxicology studies. Ecotoxicology, 18, 144-150.

Colbourne, J. K., Neff, B. D., Wright, J. M., & Gross, M. R. (1996). DNA fingerprinting of bluegill sunfish (Lepomis macrochirus) using (GT) n microsatellites and its potential for assessment of mating success. Canadian Journal of Fisheries and Aquatic Sciences, 53(2), 342-349.

Collevatti, R. G., Brondani, R. V., and Grattapaglia, D., 1999. "Development and characterization of microsatellite markers for genetic analysis of a Brazilian endangered tree species." Hered, vol. 83, pp. 748-756.

Crespi, B. J., & Fulton, M. J. (2004). Molecular systematics of Salmonidae: combined nuclear data yields a robust phylogeny. Molecular phylogenetics and evolution, 31(2), 658-679.

Curtu, A. L., Finkeldey, R., & Gailing, O. (2004). Comparative sequencing of a microsatellite locus reveals size homoplasy within and between European oak species (Quercus spp.). Plant Molecular Biology Reporter, 22(4).

D PAETKAU, C. S. (1995). The molecular basis and evolutionary history of a microsatellite null allele in bears. Molecular ecology, 4(4), 519-520.

Davis, G. P., & DeNise, S. K. (1998). The impact of genetic markers on selection. Journal of Animal Science, 76(9), 2331-2339.

Davis, G. P., & Hetzel, D. S. (2000). Integrating molecular genetic technology with traditional approaches for genetic improvement in aquaculture species. Aquaculture research, 31(1), 3-10.

Deepak J., Ram R. N and Pushpa L (2017). Microsatellite markers and their application in

fisheries. International Journal of Advances in Agricultural Science and Technology, 4 (10), 67-104.

DeWoody, J. A., & Avise, J. C. (2000). Microsatellite variation in marine, freshwater and anadromous fishes compared with other animals. Journal of fish biology, 56(3), 461-473.

Dudu, A., Georgescu, S. E., Popa, O., Dinischiotu, A., & Costache, M. (2011). Mitochondrial 16s and 12srRNA sequence analysis in four salmonid species from Romania. Acta Zoologica Academiae Scientiarum Hungaricae, 57(3), 233-246.

Duncan, K. M., Martin, A. P., Bowen, B. W., & de Couet, H. G. (2008). Amos, W. & Balmford, A.(2001). When does conservation genetics matter? Heredity 87: 257-265. Applied Biosystems, Incorporated (2001). Seq Ed version 1.0. 3. Avise, JC (1986). Mitochondrial DNA and the evolutionary genetics of higher animals. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences 312: 325–342. Avise, JC (1994). Molecular Markers, Natural History and Evolution. Chapman & Hall, New York, NY. Records of the Western Australian Museum, 23, 307-308.

Duran, C., Appleby, N., Edwards, D., & Batley, J. (2009). Molecular genetic markers: discovery, applications, data storage and visualisation. Current bioinformatics, 4(1), 16-27.

Edwards, A., Civitello, A., Hammond, H. A., & Caskey, C. T. (1991). DNA typing and genetic mapping with trimeric and tetrameric tandem repeats. American journal of human genetics, 49(4), 746.

Edwards, K. J., Barker, J. H. A., Daly, A., Jones, C., & Karp, A. (1996). Microsatellite libraries enriched for several microsatellite sequences in plants. Biotechniques, 20(5), 758-760.

Ekerette, E. E., Kineme, E. V., Utensil, O. U., Ozone, M. O., Etukudo, O. M., Umoyen, A. J., … & Wheto, M. (2017). Phylogenetics and molecular divergence of tilapia fish (Oreochromis species) using mitochondrial D-loop and cytochrome b regions. American Journal of Molecular Biology, 8(01), 39.

Emil, G. S., Andreea, D., Radu, S., Ionuţ, V., Ovidiu, I., & Marieta, C. 2011, Evaluarea şi caracterizarea genetică a salmonidelor din România.

Estoup, A. (1998). Microsatellites and minisatellites for molecular ecology: theoretical and experimental considerations. Advances in molecular ecology.

Estoup, A., Jarne, P., & Cornuet, J. M. (2002). Homoplasy and mutation model at microsatellite loci and their consequences for population genetics analysis. Molecular ecology, 11(9), 1591-1604.

Estoup, A., Presa, P., Krieg, F., Vaiman, D., & Guyomard, R. (1993). n and (GT) n microsatellites: a new class of genetic markers for Salmo trutta L.(brown trout). Heredity, 71(5), 488-496.

Ferguson, M. M., & Danzmann, R. G. (1998). Role of genetic markers in fisheries and aquaculture: useful tools or stamp collecting?. Canadian Journal of Fisheries and Aquatic Sciences, 55(7), 1553-1563.

Ferguson, M. M., & Danzmann, R. G. (1998). Role of genetic markers in fisheries and aquaculture: useful tools or stamp collecting?. Canadian Journal of Fisheries and Aquatic Sciences, 55(7), 1553-1563.

Fetterolf Jr, C. M. (1981). Foreword to the stock concept symposium. Canadian Journal of Fisheries and Aquatic Sciences, 38, 4-5.

FishBase http://www.fishbase.org/search.php, accessed on 23 July 2014.

Fjalestad, K. T., Moen, T., & Gomez-Raya, L. (2003). Prospects for genetic technology in

salmon breeding programmes. Aquaculture Research, 34(5), 397-406.

Fjalestad, K. T., Moen, T., & Gomez-Raya, L. (2003). Prospects for genetic technology in salmon breeding programmes. Aquaculture Research, 34(5), 397-406.

Flajoulot, S., Ron fort, J., Bedouin, P., Barre, P., Hogue, T., Huyghe, C., & Julie, B. (2005). Genetic diversity among alfalfa (Medicago sativa) cultivars coming from a breeding program, using SSRS markers. Theoretical and Applied Genetics, 111, 1420-1429.

Gjedrem, T. (2005). Status and scope of aquaculture. Selection and Breeding Programs in Aquaculture, 1-8.

Glover, K. A. (2010). Forensic identification of fish farm escapees: the Norwegian experience. Aquaculture Environment Interactions, 1(1), 1-10.

Goldstein, D. B., Ruiz Linares, A., Cavalli-Sforza, L. L., & Feldman, M. W. (1995). An evaluation of genetic distances for use with microsatellite loci. Genetics, 139(1), 463-471.

Gopalakrishnan, A., Musammilu, K. K., Basheer, V. S., Lijo, J., Padmakumar, K. G., Lal, K. K., … & Lakra, W. S. (2009). Low genetic differentiation in the populations of the Malabar carp Labeo dussumieri as revealed by allozymes, microsatellites and RAPD. Asian Fisheries Science, 22(2), 359-391.

Gowrimanohari Rakkannan (2022) Microsatellite Markers in FisheriesActa Scientific Veterinary Sciences (ISSN: 2582-3183) Volume 4 Issue 7 July 2022.

Grant, W. S., & Waples, R. S. (2000). Spatial and temporal scales of genetic variability in marine and anadromous species: implications for fisheries oceanography. Fisheries oceanography: an integrative approach to fisheries ecology and management, 61-93.

Grover, A., & Sharma, P. C. (2016). Development and use of molecular markers: past and present. Critical reviews in biotechnology, 36(2), 290–302.

Guichoux, E., Lagache, L., Wagner, S., Chaumeil, P., Léger, P., Lepais, O., ... & Petit, R. J. (2011). Current trends in microsatellite genotyping. Molecular ecology resources, 11(4), 591-611.

Gutierrez, A. P., Lubieniecki, K. P., Fukui, S., Withler, R. E., Swift, B., & Davidson, W. S. (2014). Detection of quantitative trait loci (QTL) related to grilsing and late sexual maturation in Atlantic salmon (Salmo salar). Marine Biotechnology, 16, 103-110.

Hallerman, E., Brown, B., & Epifanio, J. (2003). An overview of classical and molecular genetics. Population genetics: Principles and applications for fisheries scientists, 3-20.

Hansen, M. M. (2003). Application of molecular markers in population and conservation genetics, with special emphasis on fishes.

Hansen, M. M., Kenchington, E., & Nielsen, E. E. (2001). Assigning individual fish to populations using microsatellite DNA markers. Fish and Fisheries, 2(2), 93-112.

Hartl, D. L., & Clark, A. G. (1989). Principles of population genetics. Sinauer Assoc. Inc, Sunderland, Massachusetts.

Hauser, L., Adcock, G. J., Smith, P. J., Bernal Ramírez, J. H., & Carvalho, G. R. (2002). Loss of microsatellite diversity and low effective population size in an overexploited population of New Zealand snapper (Pagrus auratus). Proceedings of the National Academy of Sciences, 99(18), 11742-11747.

Hollenbeck, C. M., Portnoy, D. S., & Gold, J. R. (2015). A genetic linkage map of red drum (Sciaenops ocellatus) and comparison of chromosomal syntenies with four other fish species.

Aquaculture, 435, 265-274.

Houston, R. D., Haley, C. S., Hamilton, A., Guy, D. R., Tinch, A. E., Taggart, J. B., … & Bishop, S. C. (2008). Major quantitative trait loci affect resistance to infectious pancreatic necrosis in Atlantic salmon (Salmo salar). Genetics, 178(2), 1109-1115.

HUDSON, A. P., CUNY, G., CORTADAS, J., HASCHEMEYER, A. E., & BERNARDI, G. (1980). An analysis of fish genomes by density gradient centrifugation. European Journal of Biochemistry, 112(2), 203-210.

Hulata, G. (2001). Genetic manipulations in aquaculture: a review of stock improvement by classical and modern technologies. Genetica, 111, 155-173.

Jarne, P., & Lagoda, P. J. (1996). Microsatellites, from molecules to populations and back. Trends in ecology & evolution, 11(10), 424-429.

Jeffreys, A. J., Royle, N. J., Patel, I., Armour, J. A. L., MacLeod, A., Collick, A., … & Monckton, D. (1991). Principles and recent advances in human DNA fingerprinting. DNA fingerprinting: approaches and applications, 1-19.

Jeffreys, A. J., Royle, N. J., Wilson, V., & Wong, Z. (1988). Spontaneous mutation rates to new length alleles at tandem-repetitive hypervariable loci in human DNA. Nature, 332(6161), 278-281.

Jeffreys, A. J., Wilson, V., Kelly, R., Taylor, B. A., & Bulfied, G. (1987). Mouse DNA 'fingerprints': analysis of chromosome localization and germ-line stability of hypervariable loci in recombinant inbred strains. Nucleic Acids Research, 15(7), 2823-2836.

Jiang, L., Chu, G., Zhang, Q., Wang, Z., Wang, X., Zhai, J., & Yu, H. (2013). A microsatellite genetic linkage map of half smooth tongue sole (Cynoglossus semilaevis). Marine genomics, 9, 17-23.

Karagyozov, L., Kalcheva, I. D., & Chapman, V. M. (1993). Construction of random small-insert genomic libraries highly enriched for simple sequence repeats. Nucleic acids research, 21(16), 3911.

Kellogg, K. A., Markert, J. A., Stauffer, J. R., & Kocher, T. D. (1995). Microsatellite variation demonstrates multiple paternity in lekking cichlid fishes from Lake Malawi, Africa. Proceedings of the Royal Society of London. Series B: Biological Sciences, 260(1357), 79-84.

Keong, B. P., Siraj, S. S., Daud, S. K., Panandam, J. M., & Rahman, A. N. A. (2014). Identification of quantitative trait locus (QTL) linked to dorsal fin length from preliminary linkage map of molly fish, Poecilia sp. Gene, 536(1), 114-117.

Kijas, J. M. H., Thomas, M. R., Fowler, J. C. S., Roose, M. L., Primmer, C. R., Raudsepp, T., ... & Moller, A. P. (1997). H. Andersson. Biotechniques, 16, 657-662.

Kitano, T., Matsuoka, N., & Saitou, N. (1997). Phylogenetic relationship of the genus Oncorhynchus species inferred from nuclear and mitochondrial markers. Genes & genetic systems, 72(1), 25-34.

León-Bernabeu, S., Shin, H. S., Lorenzo-Felipe, Á., García-Pérez, C., Berbel, C., Elalfy, I. S., … & Afonso, J. M. (2021). Genetic parameter estimations of new traits of morphological quality on gilthead seabream (Sparus aurata) by using IMAFISH_ML software. Aquaculture Reports, 21, 100883.

Liu, F., Sun, F., Li, J., Xia, J. H., Lin, G., Tu, R. J., & Yue, G. H. (2013). A microsatellite-based linkage map of salt tolerant tilapia (Oreochromis mossambicus x Oreochromis spp.) and mapping of sex-determining loci. BMC genomics, 14(1), 1-14.

Liu, Z. J., & Cordes, J. F. (2004). DNA marker technologies and their applications in aquaculture genetics. Aquaculture, 238(1-4), 1-37.

Liu, Z., Li, P., Kocabas, A., Karsi, A., & Ju, Z. (2001). Microsatellite-containing genes from the channel catfish brain: evidence of trinucleotide repeat expansion in the coding region of nucleotide excision repair gene RAD23B. Biochemical and Biophysical Research Communications, 289(2), 317-324.

Ma, H., Ma, C., Ma, L., & Cui, H. (2010). Novel polymorphic microsatellite markers in Scylla paramamosain and cross-species amplification in related crab species. Journal of Crustacean Biology, 30(3), 441-444.

McCusker, M. R., & Bentzen, P. (2010). Positive relationships between genetic diversity and abundance in fishes. Molecular Ecology, 19(22), 4852-4862.

McGregor, D., Galvin, P., Sadusky, T., & Cross, T. (1996). PCR amplification of a polymorphic minisatellite VNTR locus in whiting [Merlangiusmerlangus L. Animal genetics, 27(1), 49-51.

Moen, T., Hayes, B., Baranski, M., Berg, P. R., Kjøglum, S., Koop, B. F., ... & Lien, S. (2008). A linkage map of the Atlantic salmon (Salmo salar) based on EST-derived SNP markers. BMC genomics, 9(1), 1-14.

Mojekwu, T. O, Oguntade, O. R, Oketoki. T. O and Usman A. B Genetic variability of Tilapia in different water bodies using RAPD markers, Proceedings of the 25th Annual Conference Of the Biotechnology Society of Nigeria held at National Open University, Abuja. 26th – 31st August, 2012.

Mojekwu, T. O., & Anumudu, C. I. (2013). Microsatellite markers in Aquaculture: Application in Fish population genetics.

Mojekwu, Tonna. (2020). Microsatellite markers in Aquaculture: Application in Fish population genetics. IOSR Journal of Environmental Science Toxicology and Food Technology. 5. 43-48.

Moore, S. S., Whan, V., Davis, G. P., Byrne, K., Hetzel, D. J., & Preston, N. (1999). The development and application of genetic markers for the Kuruma prawn Penaeus japonicus. Aquaculture, 173(1-4), 19-32.

Morelli, K. A., Revaldaves, E., Oliveira, C., & Foresti, F. (2007). Isolation and characterization of eight microsatellite loci in Leporinus macrocephalus (Characiformes: Anostomidae) and cross-species amplification. Molecular Ecology Notes, 7(1), 32-34.

Moritz, C. (1994). Applications of mitochondrial DNA analysis in conservation: a critical review. Molecular Ecology, 3(4), 401-411.

Muneer, P. A., Gopalakrishnan, A., Shivanandan, R., Basheer, V. S., & Ponniah, A. G. (2011). Genetic variation and phylogenetic relationship between two species of yellow catfish, Horabagrus brachysoma and H. nigricollaris (Teleostei: Horabagridae) based on RAPD and microsatellite markers. Molecular biology reports, 38, 2225-2232.

Muneer, P. A., Sivanandan, R., Gopalakrishnan, A., Basheer, V. S., Musammilu, K. K., & Ponniah, A. G. (2011). Development and characterization of RAPD and microsatellite markers for genetic variation analysis in the critically endangered yellow catfish Horabagrus nigricollaris (Teleostei: Horabagridae). Biochemical genetics, 49, 83-95.

Neff, B. D., Repka, J., & Gross, M. R. (2001). A Bayesian framework for parentage analysis: the value of genetic and other biological data. Theoretical Population Biology, 59(4), 315-331.

Norman, J. D., Robinson, M., Glebe, B., Ferguson, M. M., & Danzmann, R. G. (2012). Genomic arrangement of salinity tolerance QTLs in salmonids: a comparative analysis of Atlantic

salmon (Salmo salar) with Arctic charr (Salvelinus alpinus) and rainbow trout (Oncorhynchus mykiss). BMC genomics, 13(1), 1-15.

Norris, A. T., Bradley, D. G., & Cunningham, E. P. (1999). Microsatellite genetic variation between and within farmed and wild Atlantic salmon (Salmo salar) populations. Aquaculture, 180(3-4), 247-264.

O'connell, M., & Wright, J. M. (1997). Microsatellite DNA in fishes. Reviews in fish biology and fisheries, 7, 331-363.

O'Connell, M., Danzmann, R. G., Cornuet, J. M., Wright, J. M., & Ferguson, M. M. (1997). Differentiation of rainbow trout (Oncorhynchus mykiss) populations in Lake Ontario and the evaluation of the stepwise mutation and infinite allele mutation models using microsatellite variability. Canadian Journal of Fisheries and Aquatic Sciences, 54(6), 1391-1399.

Okumus, I. & Ciftci, Yilmaz. (2003). Fish population genetics and molecular markers: II. Molecular markers and their applications in fisheries and aquaculture. Journal of Fisheries and Aquatic Science. 3. 51-79.

Okumuş, İ., & Çiftci, Y. (2003). Fish population genetics and molecular markers: II-molecular markers and their applications in fisheries and aquaculture. Turkish Journal of Fisheries and Aquatic Sciences, 3(1).

Olivatti, A. M., Boni, T. A., Silva Júnior, N. J. D., Resende, L. V., Gouveia, F. O., & Telles, M. P. D. C. (2011). Heterologous amplification and characterization of microsatellite markers in the Neotropical fish Leporinus friderici.

Oliveira, E. J., Pádua, J. G., Zucchi, M. I., Vencovsky, R., & Vieira, M. L. C. (2006). Origin, evolution, and genome distribution of microsatellites. Genetics and Molecular Biology, 29, 294-307.

Olubunmi, O. O. (2019). Application of microsatellite in fish biotechnology: Prospects and drawback–review. International Journal of Bioengineering and Biotechnology, 4(3), 37-43.

Oohara, I., Sawano, K., & Okazaki, T. (1997). Mitochondrial DNA sequence analysis of the Masu salmon—phylogeny in the genusOncorhynchus. Molecular Phylogenetics and Evolution, 7(1), 71-78.

O'Reilly, P. T., Hamilton, L. C., McConnell, S. K., & Wright, J. M. (1996). Rapid analysis of genetic variation in Atlantic salmon (Salmo salar) by PCR multiplexing of dinucleotide and tetranucleotide microsatellites. Canadian Journal of Fisheries and Aquatic Sciences, 53(10), 2292-2298.

O'reilly, P., & Wright, J. M. (1995). The evolving technology of DNA fingerprinting and its application to fisheries and aquaculture. Journal of Fish Biology, 47, 29-55.

Ostrander, E. A., Jong, P. M., Rine, J., & Duyk, G. (1992). Construction of small-insert genomic DNA libraries highly enriched for microsatellite repeat sequences. Proceedings of the National Academy of Sciences, 89(8), 3419-3423.

Otel, V. (2007). Atlasul pestilor din rezervatia biosferei Delta Dunarii.

Ozaki, A., Sakamoto, T., Khoo, S., Nakamura, K., Coimbra, M. R., Akutsu, T., & Okamoto, N. (2001). Quantitative trait loci (QTLs) associated with resistance/susceptibility to infectious pancreatic necrosis virus (IPNV) in rainbow trout (Oncorhynchus mykiss). Molecular Genetics and Genomics, 265(1), 23-31.

P. E. Ihssen, H. E. Booked, J. M. Cassel man, J. M. Clade, N. R. Payne, and F. M. Utter, "Stock identification: materials and methods," Canadian Journal of Fisheries and Aquatic Sciences,

vol. 38, pp. 7838-7855, 1981.

Park, L. K., & Moran, P. (1994). Developments in molecular genetic techniques in fisheries. Reviews in fish biology and fisheries, 4, 272-299.

Phumichai, C., Phumichai, T., & Wonkier, A. (2015). Novel chloroplast microsatellite (cpSSRS) markers for genetic diversity assessment of cultivated and wild Hevea rubber. Plant molecular biology reporter, 33, 1486-1498.

Pompanon, F., Bonin, A., Bellemain, E., & Taberlet, P. (2005). Genotyping errors: causes, consequences and solutions. Nature Reviews Genetics, 6(11), 847-859.

Poompuang, S., & Hallerman, E. M. (1997). Toward detection of quantitative trait loci and marker-assisted selection in fish. Reviews in Fisheries Science, 5(3), 253-277.

Powell, W., Morgante, M., Andre, C., McNicol, J. W., Machray, G. C., Doyle, J. J., … & Rafalski, J. A. (1995). Hypervariable microsatellites provide a general source of polymorphic DNA markers for the chloroplast genome. Current Biology, 5(9), 1023-1029.

Ranjan, P. The Biodiversity of Fish Fauna in GobardhanDas Pond (Saran District), North Bihar. International Journal on Orange Technologies, 2(9), 22-25.

Reilly, A., Elliott, N. G., Grewe, P. M., Clabby, C., Powell, R., & Ward, R. D. (1999). Genetic differentiation between Tasmanian cultured Atlantic salmon (Salmo salar L.) and their ancestral Canadian population: comparison of microsatellite DNA and allozyme and mitochondrial DNA variation. Aquaculture, 173(1-4), 459-469.

Ritland, K. (1996). Estimators for pairwise relatedness and individual inbreeding coefficients. Genetics Research, 67(2), 175-185.

Royle, N. J., Clarkson, R. E., Wong, Z., & Jeffreys, A. J. (1988). Clustering of hypervariable minisatellites in the proterminal regions of human autosomes. Genomics, 3(4), 352-360.

Saha, D., Rana, R. S., Chakraborty, S., Datta, S., Kumar, A. A., Chakraborty, A. K., & Karmakar, P. G. (2017). Development of a set of SSRS markers for genetic polymorphism detection and interspecific hybrid jute breeding. The Crop Journal, 5(5), 416-429.

Saiki, R. K., Gelfand, D. H., Stoffel, S., Scharf, S. J., Higuchi, R., Horn, G. T., ... & Erlich, H. A. (1988). Primer-directed enzymatic amplification of DNA with a thermo Stable DNA polymerase. Science, 239(4839), 487-491.

Sakamoto, T., Danzmann, R. G., Okamoto, N., Ferguson, M. M., & Ihssen, P. E. (1999). Linkage analysis of quantitative trait loci associated with spawning time in rainbow trout (Oncorhynchus mykiss). Aquaculture, 173(1-4), 33-43.

Sanetra, M., Henning, F., Fukamachi, S., & Meyer, A. (2009). A microsatellite-based genetic linkage map of the cichlid fish, Astatotilapia burtoni (Teleostei): a comparison of genomic architectures among rapidly speciating cichlids. Genetics, 182(1), 387-397.

Schlötterer, C. (2000). Evolutionary dynamics of microsatellite DNA. Chromosoma, 109(6).

Sekino, M., Hara, M., & Taniguchi, N. (2001). Genetic Diversity Within and Between Hatchery Strains of Japanese Flounder Paralichthys olivaceus Assessed by Means of Microsatellite and Mitochondrial DNA Sequencing Analysisδ. Ecology of Aquaculture Species And Enhancement of Stocks, 43.

Shaklee, J. B., & Bentzen, P. (1998). Genetic identification of stocks of marine fish and shellfish. Bulletin of Marine Science, 62(2), 589-621.

Shaklee, J. B., Allendorf, F. W., Morizot, D. C., & Whitt, G. S. (1990). Gene nomenclature for protein-coding loci in fish. Transactions of the American Fisheries Society, 119(1), 2-15.

Sinama, M., Dubut, V., Costedoat, C., Gilles, A., Junker, M., Malausa, T., ... & Meglécz, E. (2011). Challenges of microsatellite development in Lepidoptera: Euphydryas aurinia (Nymphalidae) as a case study. European Journal of Entomology, 108(108), 261-266.

Slate, J., Marshall, T., & Pemberton, J. (2000). A retrospective assessment of the accuracy of the paternity inference program CERVUS. Molecular Ecology, 9(6), 801-808.

Soulé, M. E., & Wilcox, B. A. (1980). Conservation biology: an evolutionary-ecological perspective. Sinauer Associates.

Stearley, R. F., & Smith, G. R. (1993). Phylogeny of the Pacific trouts and salmons (Oncorhynchus) and genera of the family Salmonidae. Transactions of the American Fisheries Society, 122(1), 1-33.

Subasinghe, R. P., Curry, D., McGladdery, S. E., & Bartley, D. (2003). Recent technological innovations in aquaculture. FAO Fisheries circular, 886.

Sundaray, J. K., Rasal, K. D., Chakrapani, V., Swain, P., Kumar, D., Ninawe, A. S., ... & Jayasankar, P. (2016). Simple sequence repeats (SSRs) markers in fish genomic research and their acceleration via next-generation sequencing and computational approaches. Aquaculture international, 24, 1089-1102.

Tanck, M. W., Palstra, A. P., Weerd, M. V. D., Leffering, C. P., Poel, J. V. D., Bovenhuis, H., & Komen, J. (2001). Segregation of microsatellite alleles and residual heterozygosity at single loci in homozygous androgenetic common carp (Cyprinus carpio L.). Genome, 44(5), 743-751.

Tautz, D. (1989). Hypervariability of simple sequences as a general source for polymorphic DNA markers. Nucleic acids research, 17(16), 6463-6471.

Tautz, D., & Renz, M. (1984). Simple sequences are ubiquitous repetitive components of eukaryotic genomes. Nucleic acids research, 12(10), 4127-4138.

Telles, M. P. D. C., Resende, L. V., Brondani, R. P. V., Collevatti, R. G., Costa, M. C. D., & Silva Júnior, N. J. D. (2010). Isolation and characterization of microsatellite markers in the armored catfish Hypostomus gymnorhynchus (Loricariidae).

Teng, T., Zhao, X., Li, C., Guo, J., Wang, Y., Pan, C., ... & Ling, Q. (2020). Cloning and expression of IGF-I, IGF-II, and GHR genes and the role of their single-nucleotide polymorphisms in the growth of pikeperch (Sander lucioperca). Aquaculture International, 28, 1547-1561.

The IUCN Red List of Threatened Species http://www.iucnredlist.org/about/summary-statistics#Tables_1_2 accessed at 23 July 2014.

Tripathi, S. D. (2011). Aquaculture: a panacea for the future. Fishing Chimes, 31, 12-15.

Tripathy, S. K. (2018). Broad Spectrum Utilities of Microsatellite in Fish and Fisheries. Journal of Biotechnology Research, 4(6), 29-45.

Ude, G. N., Igwe, D. O., Brown, C., Jackson, M., Bangura, A., Ozokonkwo-Alor, O., … & Das, A. (2020). DNA barcoding for identification of fish species from freshwater in Enugu and Anambra States of Nigeria. Conservation Genetics Resources, 12, 643-658.

Venkatesh, B., Kirkness, E. F., Loh, Y. H., Halpern, A. L., Lee, A. P., Johnson, J., … & Brenner, S. (2007). Survey sequencing and comparative analysis of the elephant shark (Callorhinchus milii) genome. PLoS biology, 5(4), e101.

Vieira, M. L. C., Santini, L., Diniz, A. L., & Munhoz, C. D. F. (2016). Microsatellite markers: what they mean and why they are so useful. Genetics and molecular biology, 39, 312-328.

Volckaert, F. A. M., Batargias, C., Canario, A., Chatziplis, D., Chistiakov, D., Haley, C., ... & Tsigenopoulos, C. (2008). European sea bass. Genome mapping and Genomics in Fishes and Aquatic Animals, 117-133.

Waldbieser, G. C. (1995). PCR-based identification of AT-rich tri-and tetranucleotide repeat loci in an enriched plasmid library. Biotechniques, 19(5), 742-744.

Waldbieser, G. C., Bosworth, B. G., Nonneman, D. J., & Wolters, W. R. (2001). A microsatellite-based genetic linkage map for channel catfish, Ictalurus punctatus. Genetics, 158(2), 727-734.

Wattanadilokchatkun, P., Panthum, T., Jaisamut, K., Ahmad, S. F., Dokkaew, S., Muangmai, N., … & Srikulnath, K. (2022). Characterization of Microsatellite Distribution in Siamese Fighting Fish Genome to Promote Conservation and Genetic Diversity. Fishes, 7(5), 251.

Weber, J. L. (1990). Informativeness of human (dC-dA) n·(dG-dT) n polymorphisms. Genomics, 7(4), 524-530.

Weber, J. L., & May, P. E. (1989). Abundant class of human DNA polymorphisms which can be typed using the polymerase chain reaction. American journal of human genetics, 44(3), 388.

Webster, M. S., & Reichart, L. (2005). Use of microsatellites for parentage and kinship analyses in animals. In Methods in enzymology (Vol. 395, pp. 222-238). Academic Press.

Weising, K., Nybom, H., Pfenninger, M., Wolff, K., & Kahl, G. (2005). DNA fingerprinting in plants: principles, methods, and applications. CRC press.

Willi, Y., Kristensen, T. N., Sgrò, C. M., Weeks, A. R., Ørsted, M., & Hoffmann, A. A. (2022). Conservation genetics as a management tool: The five best-supported paradigms to assist the management of threatened species. Proceedings of the National Academy of Sciences, 119(1), e2105076119.

Wright, J. M. (1993). DNA fingerprinting of fishes. Biochemistry and molecular biology of fishes, 2, 57-91.

Wright, J. M., & Bentzen, P. (1995). Microsatellites: genetic markers for the future. Molecular genetics in fisheries, 117-121.

Wu, L., Yang, Y., Wang, X., Weng, Z., Hua, S., Li, D., ... & Meng, Z. (2023). Genome-wide QTL mapping and RNA-seq reveal the genetic variation influencing growth traits in giant grouper (Epinephelus lanceolatus). Aquaculture, 563, 738944.

Xiao-Gu, Z., Jin-Gou, T., & Bang-Xi, X. (2006). Applications of microsatellite markers in studies of genetics and breeding of fish. Chinese Journal of Agricultural Biotechnology, 3(2), 83-87.

Xu, S. Y., Song, N., Xiao, S. J., & Gao, T. X. (2020). Whole genome survey analysis and microsatellite motif identification of Sebastiscus marmoratus. Bioscience Reports, 40(2).

Young, W. P., Wheeler, P. A., Coryell, V. H., Keim, P., & Thorgaard, G. H. (1998). A detailed linkage map of rainbow trout produced using doubled haploids. Genetics, 148(2), 839-850.

Zane, L., Bargelloni, L., & Patarnello, T. (2002). Strategies for microsatellite isolation: a review. Molecular ecology, 11(1), 1-16.

Zardoya, R., Vollmer, D. M., Craddock, C., Streelman, J. T., Karl, S., & Meyer, A. (1996). Evolutionary conservation of microsatellite flanking regions and their use in resolving the phylogeny of cichlid fishes (Pisces: Perciformes). Proceedings of the Royal Society of London. Series B:

Biological Sciences, 263(1376), 1589-1598.

Zeng, Q., Sun, C., Dong, J., Tian, Y., & Ye, X. (2017). Comparison of the crossbreeding effects of three Mandarin fish populations and analyses of the microsatellite loci associated with the growth traits of F1 progenies. Comparison of the Crossbreeding Effects of Three Mandarin Fish Populations and Analyses of the Microsatellite Loci Associated with the Growth Traits of F1 Progenies.

Zhan, A., Wang, Y., Brown, B., & Wang, H. P. (2008). Isolation and characterization of novel microsatellite markers for yellow perch (Perca flavescens). International Journal of Molecular Sciences, 10(1), 18-27.

Zhang, J., Ma, W., Wang, W., Gui, J. F., & Mei, J. (2016). Parentage determination of yellow catfish (Pelteobagrus Fulvidraco) based on microsatellite DNA markers. Aquaculture international, 24, 567-576.

Zhu, C., Liu, H., Pan, Z., Chang, G., Wang, H., Wu, N., … & Yu, X. (2019). Construction of a high-density genetic linkage map and QTL mapping for growth traits in Pseudobagrus ussuriensis. Aquaculture, 511, 734213.

Kounnamasa, C. (2021). International and European Legislation for Forest Management. Handbook for the sustainable management and long-term conservation of a narrow endemic habitat type in a limited area of occupancy-The case of the habitat type 9590* Cedrus brevifolia forests (Cedrosetum brevifoliae). LIFE-KEDROS, 9590, 225.

About The Authors

Dr. Tanveer Ahmed completed his Doctorate degree in Zoology (Specialization in Fish Population Genetics) from the University of Agriculture, Faisalabad, Pakistan in January 2019. Currently, he is serving as an Assistant Professor in the Department of Life Sciences, Khwaja Fareed University of Engineering and Information Technology, Rahim Yar Khan, since October 2019.

Email: tanvirahmeduaf@gmail.com ORCID: 0000-0001-9346-2500

Dr. Huma Naz earned her PhD degree in Zoology from the University of Agriculture, Faisalabad, Pakistan in July 2017. Currently, she is serving as an Assistant Professor in the Department of Zoology, Cholistan University of Veterinary and Animal Sciences, Bahawalpur, Pakistan since November 2018.

Email: dr.humanaz98@gmail.com ORCID: 0000-0003-3465-0960

Dr. Khalid Abbas is an esteemed professor in the Department of Zoology, Wildlife & Fisheries at the University of Agriculture, Faisalabad, Pakistan. Dr. Abbas has successfully completed five research projects and has an impressive publication record, including 83 articles in impact factor journals, 26 non-impact factor publications, and over 100 conference papers.

Email: dr.abbas@uaf.edu.pk ORCID: 0000-0002-3146-7792

Ayesha Yaseen earned her BS in zoology from the Khawaja Fareed University of Engineering and Information Technology Rahim Yar Khan, Punjab, Pakistan.

Email: jz33892@gmail.com ORCID: 0009-0009-2807-9367

Aqsa Pervaiz completed her Graduation in Zoology from Khwaja Fareed University of Engineering and Information Technology, Rahim Yar Khan, Pakistan.

Email: aqsap7422@gmail.com ORCID: 0009-0006-9511-0385

Beenish Shakir got her Graduation in Zoology from Khwaja Fareed University of Engineering and Information Technology, Rahim Yar Khan, Pakistan.

Email: beenishshakir090@gmail.com ORCID: 0009-0005-5988-0676

Laiba Hanif earned her Graduation in Zoology from khawaja Fareed University of Engineering and Information Technology, RYK, Pakistan.

Email: laibahanif157p@gmail.com ORCID: 0009-0009-8091-3742

Areeb Javed got his Graduation in Zoology from Khwaja Fareed University of Engineering and Information Technology, RYK, Pakistan.

Email: areebjaved721@gmail.com ORCID: 0009-0002-6482-049X

Muhammad Arshad earned his M.Phil. in Zoology from the Department of Zoology, Government College University Lahore, Pakistan. Currently, his research interests focus on human genetics, gene polymorphisms, molecular biology, and nanotechnology.

Email: arshadmuhammad0876@gmail.com ORCID: 0000-0001-8696-3788

Hira Asad has recently completed her Master of Science (MS) in Zoology, with a specialization in Fisheries.

Email: heerasad105@gmail.com ORCID: 0009-0007-4828-9084

Zainab Bashir has completed her BS in Physics from University of Agriculture, Faisalabad, Pakistan. She is interested in the field of Nanotechnology.

Email: zainabbashir@gmail.com ORCID: 0009-0004-2585-3664

Muhammad Sarfraz Ahmed is a Ph.D. scholar in Zoology at the University of Agriculture Faisalabad, focusing on the hybridization of Silver Carp and Bighead Carp. His areas of interest include molecular ecology, conservation genetics, and fish genetic resource management. Email: Email: sarfrazahmed1920@gmail.com ORCID: 0000-0003-3654-7369

Shahbaz Ahmad is an Assistant Director of Fisheries at the Fish Seed Hatchery in Faisalabad and a Ph.D. candidate in Zoology at the University of Agriculture Faisalabad.

Email: shahbazjnw@gmail.com ORCID: 0009-0006-2270-318X

To Cite This Chapter

Ahmed T et al., (2024). Potential of microsatellites DNA markers in monitoring the genetic diversity of fishes. In Current Studies in Health and Life Sciences 2024 (pp.436-463). ISRES Publishing.

Dynamics of Animal Pathogens

Ghanwa MARYAM

Nazish FATIMA

Hamna SHAHID

Muhammad EJAZ

Minahal FATIMA

Aansa TAHREEM

Shafeeq Ur REHMAN

Introduction:

The intricate interplay between animals and the viruses they host is a fascinating ballet that has significant effects on ecosystem stability as well as human health (Marchesini & De Sanctis, 2021). Animal pathogens, which include bacteria, fungi, viruses, and parasites, have a substantial impact on wildlife populations, livestock productivity, and human health. It is essential to comprehend the dynamics of these viruses, including how they adapt, spread, and engage with their hosts, to protect animal health and stop disease outbreaks. Explores the many variables that control the distribution and effects of animal diseases, providing an in-depth look at this complicated realm. The ways in which variables such as environmental influences influence disease dynamics, host vulnerability, and the existence of intermediary hosts (vectors) Look at the ongoing evolutionary arms race between diseases and their hosts, in which both parties constantly modify their strategies to get past the protections of the other. By comprehending these processes, we can develop effective solutions for disease control. This chapter will cover the significance of comprehending pathogen dynamics, transmission dynamics, host-pathogen interaction, evolutionary dynamics, immunization programs, enhanced biosecurity protocols, and focused interventions to break the cycle of transmission. All ecosystems naturally contain pathogens. Co-evolutionary responses that lessen the infections' severity or increase the host's capacity to fend off or recover from infection are the outcome of their long-term connection with their vertebrate hosts (Shillcock, 2022). Human-induced environmental changes frequently disrupt these natural pathogen-host connections, often resulting in unfavorable outcomes. Pathogens have been present on Earth since the beginning of time, and many of them have caused serious illness and death in people. Many of the illnesses that these agents induce are known to spread between different animal species as well as between animals and people. Smallpox is one such disease that exemplifies this, having developed from infections that were circulating in wildlife. Wildlife serves as a host or vector for around 70% of all newly discovered infectious diseases that affect humans (Tomassone et al., 2018). The presence of various hosts, vectors, or infectious agents in complex biological systems is a common factor contributing to the establishment of infectious illnesses. This can impede control and mitigation efforts aimed at specific hosts of management. Even though infections can affect multiple hosts, complicated interactions between the agents co-infecting the same host can still affect pathology, transmission, and virulence. HIV is one example of this, as it has favored the reemergence of drug-resistant forms of tuberculosis, and helminthiasis, like hookworm, can worsen the effects of malaria(de las Heras, 2011). In addition, ecological shifts can occasionally spur evolution and alter the intricate interactions between diseases, hosts, and environments, which will ultimately favor transmission. Changes in temperature or environment can also affect the biogeographic distribution of animal pathogen hosts and vectors, leading to the invasion (or re-invasion) of diseases that had previously been eradicated. Epidemiological investigations can only identify the source of infection in cases of localized illness outbreaks. In some cases, this can be done by identifying the contaminated

vegetable source contaminated coleslaw, or by determining the source of infection through infected manure used for fertilization. Another method of transmission is inhaling aerosolized excreta from infected animals. For example, spelunkers who explore bat-infested caverns contaminated with Histoplasma capsulatum spores may develop "cave disease," or there may be occasional cases of hantavirus pulmonary disease from inadvertently inhaling dust-borne rat excreta. Infected animal excretions can potentially spread disease by contaminating drinking or bathing water or by unintentionally exposing skin to puddles of rat urine, which can lead to leptospirosis (Tanga et al., 2022). A common way for animal viruses to infect humans is by intermediary transfer via vectors. Humans are typically incidental hosts and do not play a critical role in the parasite or pathogen's life cycle. Since ancient times, human societies have been plagued by vector-transmitted zoonoses, which will likely continue to do so in the future. Humans were plagued with Chagas disease as early as 9000 years ago, which was spread by the "kissing bug" (triatomine). Trypanosoma cruzi, the causal parasite, was identified in 1909 and is present in at least 150 species of domestic and wild animals. Paleoparasitologists have also found T. cruzi DNA in human mummies from prehistoric times. A common way for animal viruses to infect humans is by intermediary transfer via vectors. Humans are typically incidental hosts and do not play a critical role in the parasite or pathogen's life cycle. Since ancient times, human societies have been plagued by vector-transmitted zoonoses, which will likely continue to do so in the future.

Humans were plagued with Chagas disease as early as 9000 years ago, which was spread by the "kissing bug" (triatomine). Trypanosoma cruzi, the causal parasite, was identified in 1909 and is present in at least 150 species of domestic and wild animals. Paleoparasitologists have also found T. cruzi DNA in human mummies from prehistoric times. Dengue fever and West Nile virus disease are two examples of vector-borne zoonoses that are spreading globally and continuing to arise in the modern period (Biswas et al., 2023). Other vector-borne zoonoses are Lyme disease. Collectively, these kinds of outbreaks are referred to as emerging infectious diseases (EIDs), which are defined as infections that are newly discovered in a community or that are expanding fast in frequency or geographic scope. The majority of illnesses known as zoonoses which affect humans are brought on by infections that were previously spread by other animal species. Flaviviruses like West Nile virus and certain types of avian influenza are examples of zoonoses. Natural alterations in their genetic makeup can lead animal diseases to become invasive, resulting in new strains with higher rates of pathogenicity or transmission. One such example is the novel calicivirus which first appeared in Chinese rabbits in 1984 and spread to other countries via the trade of farmed rabbits. This virus was closely related to the virus that causes European brown hare illness (Kerr et al., 2021). Unvaccinated European rabbits were extremely susceptible to the highly fatal epidemics of rabbit hemorrhagic illness that ensued. Reservoirs of bacterial communities, including some resistant to widely used antibiotics, can be found in humans, animals, and environmental settings. There is growing fear that greater microbial resistance will trigger future disease outbreaks since our agricultural practices are creating more and more conditions for these resistant bacteria to develop and proliferate. Nonetheless, the majority of animal pathogen introductions are brought about by human and animal migration or as a result of environmental changes brought about by people (Skočajić & Nešić, 2021).

A well-established (and constantly expanding) set of theories is used by mathematical models of the population dynamics of infectious diseases to provide condensed representations of epidemiological systems (Karpatne et al., 2022). Most importantly, the central processes of epidemic dissemination and the important demographic groups are explicitly represented by dynamic models. Unlike chronic disorders like cancer or heart disease, infectious diseases are uncommon in that the population's overall health affects the likelihood of infection in addition to an individual's particular risk factors. This causes a population's subgroups to interact non-linearly, which can produce complicated and perhaps illogical epidemic behavior. Groups of people within the host population are categorized as "susceptible" to infection, "infected" and able to spread the disease, or "recovered" and immune to reinfection in the basic susceptible-infected-recovered

(SIR) paradigm. Transmission of infection to recent cases is driven by contacts between susceptible and infectious individuals. Although crude, this model reproduces the classical epidemic curve and has been remarkably successful in elucidating fundamental principles; including the "tipping point" threshold for epidemics to take off if is greater than 1, and the potential to achieve "herd immunity" through vaccination programs. Because of the emphasis on mechanism, dynamical models can address questions outside the scope of statistical and geospatial analyses. Modelers can conduct "what if" experiments by changing parameter values or reformulating mechanisms to investigate issues that are impractical or unethical to investigate in the real world. Through the use of cross-scale synthesis, researchers can also extract important features of epidemics, such as shifts in the value of the "effective" reproductive number (Re) in response to the implementation of control measures or the depletion of susceptible host populations. Rabies transmission models have anticipated the disease's geographic spread, influenced vaccination policies, and offered biological understanding (Layan et al., 2021).

Models were used to assess the transmissibility of the SARS coronavirus (SARS-CoV) and to improve strategies for infection management and case isolation used to contain the outbreak after it first surfaced. Unlike the last influenza pandemic in 1968, when models were utterly ignored, dynamical models are now crucial for anticipating and combating pandemic influenza strains (Méthot & Alizon, 2015). For instance, school closures were instituted in American cities hit by the new H1N1 influenza, sometimes known as the "swine flu," in the spring of 2009 and have been recognized as a crucial control tool early on in the pandemic's propagation. Travel restrictions are pointless when a pathogen is already spreading within a region, as demonstrated by models of both SARS and influenza. As disease-dynamic models can integrate and analyze several complicated processes at the same time while accounting for the uncertainty inherent in animal diseases, they are an effective way to provide information for management decisions (Hill et al., 2022). In order to inform disease management and modeling at the interface of domestic animals and wildlife, we describe here the paths and processes of disease introduction and transmission. Managing diseases that can spread from domestic animals to wildlife poses unique challenges (Shapiro et al., 2022).

Importance of understanding the dynamics of the animal pathogen:

Understanding pathogen dynamics is crucial in various aspects of public health, epidemiology, and medicine. Pathogens, such as viruses, bacteria, fungi, and parasites, continuously develop and adapt, posing significant challenges to human health. By studying the dynamics of these microorganisms, researchers can better comprehend their transmission, spread, evolution, and the effectiveness of interventions, leading to improved strategies for prevention, control, and treatment (Peng et al., 2020). This essay will explore the importance of understanding pathogen dynamics, focusing on the transmission dynamics, evolution, and implications for public health.

• Transmission Dynamics:

A crucial aspect of pathogen dynamics involves comprehending the mechanisms through which pathogens move from one host to another. Various pathogens employ different modes of transmission, including direct contact, airborne transmission, ingestion of contaminated substances, vector-borne transmission, and vertical transmission from mother to child (Ganter, 2015). Analyzing transmission dynamics aids in pinpointing the primary routes of transmission and devising targeted interventions to halt the spread of infections. For instance, in the context of respiratory viruses such as influenza and COVID-19, grasping the dynamics of droplet transmission is vital for implementing efficient methods of preventing infections, such as wearing masks, physically separating oneself, and improving indoor ventilation (Yashavarddhan et al., 2023). Likewise, for vector-borne diseases like malaria and dengue fever, understanding the dynamics of vector populations and their interactions

with human hosts is crucial for crafting strategies for vector control such as indoor residual spraying and insecticide-treated bed nets (Mack, 2016).

• Evolutionary Dynamics:

Pathogens continually undergo evolutionary shifts fueled by factors such as host immunity, environmental alterations, and the introduction of antimicrobial treatments. Evolutionary dynamics significantly influence the virulence, transmission capabilities, and resistance patterns of pathogens (Andersson et al., 2020). Analyzing the evolutionary patterns of pathogens enables researchers to monitor shifts in their genetic composition over time and predict future trends in disease emergence and dissemination. For example, the swift development of antibiotic resistance in bacteria poses a grave threat to global public health. By comprehending the mechanisms behind antibiotic resistance and tracking the evolutionary paths of resistant strains, scientists can devise strategies to safeguard the effectiveness of existing antibiotics and identify novel antimicrobial agents (Muteeb et al., 2023).

• Implications for Public Health:

Policy and practice in public health are significantly impacted by our growing understanding of pathogen dynamics. It helps decision-makers use resources wisely and make evidence-based choices about disease surveillance, outbreak response, immunization campaigns, and more (Montibeller, 2022). Researchers can estimate the possible effects of interventions and evaluate their cost-effectiveness in managing infectious diseases by combining mathematical models with empirical data. Furthermore, knowledge of pathogen dynamics is crucial for responding to and preparing for pandemics. The importance of prompt and well-coordinated action to monitor the spread of newly emerging infectious diseases, produce vaccines, therapies, and diagnostic tools, and implement non-pharmaceutical interventions to reduce transmission has been brought to light by the COVID-19 pandemic (Chen et al., 2023). Plans for pandemic preparedness in the future can be guided by the insightful information gained from the COVID-19 pandemic. These include early detection and containment of novel viruses and improving the capacity of health systems to respond to epidemics.

To sum up, successful prevention, control, and treatment of infectious diseases depend on an understanding of pathogen dynamics. By clarifying the mechanisms of pathogen transmission and their evolutionary patterns, scientists can create focused interventions, foresee obstacles in the future, and influence public health policy and practice. It is imperative to maintain funding for pathogen dynamics research to ensure the security of global health and lessen the effects of infectious disease outbreaks.

• Transmission Dynamics of Animal Pathogen:

Infectious illnesses sometimes referred to as transmissible or communicable diseases, are brought on by the presence and dissemination of pathogenic biological organisms, or pathogens, within a single host organism (Sarmah et al., 2018). Bacteria, fungi, viruses, protozoa, multicellular parasites, and prions are examples of pathogens that cause disease. Since the pathogen inhibits infectious breakouts when it is absent, they are the main causes of disease epidemics. The host is the organism that a pathogen infects (Pontier et al., 2009). Pathogens cause disease in the human host by interfering with vital physiological activities or inducing immunological responses. Based on how frequently they occur, infectious diseases can be divided into four categories: endemic (constantly present in a population), pandemic (global epidemic), sporadic (occurring sporadically), and epidemic (a sudden rise of cases in a localized place within a short time frame).

Modes of Transmission

Humans can contract infectious organisms from animals in a number of ways. Animals can transmit infectious agents to humans in a number of ways, including direct contact with live

animals or their corpses, indirect contact through animal products like milk or eggs, intermediate transmission through vectors (mosquitoes, mites, ticks, etc.), and remote contact through exposure to contaminated waters, soil, or air. Diseases can spread through direct contact with animals or carcasses in a number of ways, but the two most common are by oral ingestion (foodborne zoonoses) and accidental pet handling without proper hand sanitization. Animal bites, scratches, or mucosal contact with contaminated fluids can very rarely spread disease, as in the cases of rabies and animal-related wound infections (Tsikalas et al., 2023). Animal infections can also be contracted by inhaling droplets of contaminated secretions. This is thought to have happened in China, where local epidemics of avian influenza were caused by exposure to sick ducks or fowls in open marketplaces. Anthrax infections can occasionally be brought on by inhaling microbiological spores or contaminating torn or abraded skin from contact with tainted animal hide. Animal excretions are frequently the source of animal infectious diseases that are not suspected, and in the rare instances when they are, the source is typically not found (Schantz., 1991).

• Animal Disease via the Food Chain

The global incidence of foodborne infectious infections is notoriously difficult to assess, even in countries with extensive surveillance. In developing nations, where healthcare infrastructure and facilities are weak and foodborne zoonoses are the most common worldwide, estimating foodborne illnesses is much more challenging (Godwin et al., 2022). It is estimated that a significant portion of animal pathogens and at least one-third of foodborne diseases affect people worldwide annually. According to earlier estimates from the Centers for Disease Control and Prevention [CDC] in 2011, there may be more than 48 million cases of foodborne disease annually, with at least 9.4 million episodes of illness being caused by 31 main pathogens acquired in the US. According to Clemmons et al. (2021), animal-derived infections that are commonly transmitted through food are assumed to be the cause of 30% of all newly found infectious disorders during the preceding 60 years. There are over 250 different types of foodborne illnesses, with the majority caused by chemicals and poisons and the remainder by transmissible microorganisms such as viruses, bacteria, prions, and parasites.

• Bacterial Foodborne Zoonoses:

In the US and the EU, Campylobacter sp. and Salmonella Sp. are the two most prevalent domestically acquired bacterial foodborne zoonoses. Most of the ensuing ailments are typically self-limited gastroenteritis, but infrequently, chronic side effects such as reactive arthritis/spondylitis and irritable bowel syndrome might occur. In the natural environment, these bacteria are widely dispersed and often become established in the intestines of wild and domestic animals, such as sheep, cattle, poultry, and pigs. The 10 pathogen-food combinations included in recent US research that ranked the illness burden of food source infections included five pathogens: Campylobacter, Salmonella, norovirus, Listeria monocytogenes, and T. gondii. The researchers included five pathogens in their recent US research that ranked the illness burden of food source infections: Campylobacter, Salmonella, norovirus, Listeria monocytogenes, and T. gondii. Mostly produced by lysogenic bacteriophages inserted into chromosomes to encode the genes for six or more STXs, strong cytotoxins referred to as "shiga toxins" (STXs) or "verotoxins" are produced (Lucchesi et al., 2023). These bacteriophages are primarily found in zoonotic pathogenic E. coli. STX1 or STX2 is the cause of the majority of STEC diseases. Due to the bacteria's resistance to stomach acid and low infectious dosage (10–100 colony-forming units), STEC spreads easily. Goats, sheep, and cattle are the main STEC hosts, however, other species may also harbor the infection. The most frequent source of foodborne illness is Vibrio parahaemolyticus, which primarily manifests as self-limited gastroenteritis. Vibrios are naturally occurring commensals in marine and estuarine saltwater. Seldom is Vibrio vulnificus foodborne, however, it is linked to septicemia and soft tissue infections. Q-fever and brucellosis are two other bacterial foodborne zoonoses that are more prevalent in the Mediterranean region and poor nations than they are in North America (Asante et al., 2019). The continued presence of these infections in these areas can mostly be attributed to uncontrolled animal husbandry. Different bacterial foodborne zones are summarized in Table 1.

Table 1. Bacterial foodborne zones (Asante et al., 2019).

Microbes	Distribution	Animals	Frequency
Salmonella spp.	Worldwide	"Poultry, cattle, rabbits, sheep, pigs, and pets"	>1 million/year in US
Campylobacter spp.	Worldwide	Pets, livestock, pigs, sheep, bunnies, and poultry	>1 million annually in the US
E. coli—STEC	Worldwide	sheep, goats, and cattle	>265,600 annually in the US
Listeria monocytogenes	Globally/worldwide	Ruminants, Cattle	>16,000 annually in the US
Yersinia enterocolitica	Worldwide	Farm animals, including pigs	N/A
Vibrio spp.			
Vibrio parahaemolyticus	"Eastern Coast US, Southeast Asia"	oysters, Sea crabs	N/A
B. mellitensis	Mediterranean, worldwide	Sheep &goats	N/A
Bacillus suis	Asia, Africa, S. America	Pigs, cattle	N/A
Brucella abortus	Western Europe	Cattle	500,000/year
Mycobacteria bovis	Worldwide	Cattle, buffaloes	N/A
Coxiella burnetii	"Worldwide except New Zealand"	Sheep, goats	N/A

• Vector-Borne Zoonoses:

Worldwide zoonotic disease transmission from companion animals is mostly dependent on vectors. The major worldwide vectors of companion animal zoonoses are listed in the table. In this category, visceral leishmaniosis is the most important illness globally. It is caused by Leishmania infantum [L. chagasi] and is transmitted by sandflies from the primary reservoir of domestic dogs. There are several countries in southern Europe, South and Central America, northern Africa, and Asia where the disease is prevalent, and a significant number of dogs in these areas are affected (Vilas-Boas et al., 2024). The WHO estimated in 2007 that there were around 12 million HIV-positive individuals globally, with 2 million new cases reported annually. Additionally, individuals living with HIV had a higher chance of developing serious illness. Because pets are traveling across borders more frequently, controlling leishmaniosis in endemic places is extremely difficult, and spreading the disease to non-endemic areas is quite concerning. The implementation of control measures in Brazil involved serological testing of dogs and the culling of positive animals. Additionally, the commercial vaccine Leishmune, when administered to dogs, led to a drop in the prevalence of both human and canine leishmaniosis due to a reduced rate of transmission (França-Silva et al., 2023). Cat scratch disease is the zoonotic infection caused by the Bartonella bacteria that is most commonly found. Although it is found throughout the world, temperate regions with indoor pets seem to have higher populations of it. Even though they don't show any symptoms, cats can harbor a lot of human Bartonella henselae, clarridgeiae, and Koehlerae infections (França-Silva et al., 2023). Cat scratch disease primarily affects youngsters and is spread by infected flea excrement that kittens scrape with their claws. Therefore, it is a vector-borne infection that is spread by fleas

from cats that have bacteremia to humans and other cats. Fever and localized lymphadenopathy are the typical symptoms of the infection; however, in rare cases, more serious side effects such encephalitis, granulomatous hepatitis, retinitis, choroiditis, arthritis, and osteomyelitis might appear. Cats in impoverished nations often have a 27% seropositivity rate for Bartonella and a 10% bacteremia rate. Regarding increasing transmission and diseases in human societies, there are a number of tick-borne illnesses that are common to companion animals as well as humans. These include tick-borne encephalitis, which is widespread in Europe and Northwestern Asia, borreliosis [Lyme disease], ehrlichiosis, babesiosis, rickettsiosis, anaplasmosis, Q-fever, and tularemia. Only a small number of these illnesses, nevertheless, have been proven to be spread by pet interaction. Pets (dogs and cats) may help humans become exposed to diseases including ehrlichiosis, babesiosis, anaplasmosis, and Lyme disease that is transmitted through outdoor activities, even though the diseases' natural hosts are black-legged deer ticks. In endemic areas, having a dog raises the risk of rickettsiosis infection in people due to the spread of the disease by dog ticks (Stanley & Rhodes, 2021). In many US states, Rocky Mountain spotted fever (RMSF) is endemic; nevertheless, it is more common in the mid-south Atlantic states and the west-south-central region than in the Rocky Mountain states. Northern South America (Brazil and Columbia) and Central America (Mexico, Costa Rica, and Panama) also have it. Therefore, there is little chance that owning a pet will increase a person's risk of developing these illnesses. Different parasitic food borne pathogens are summarized in Table 2.

Table 2. Parasitic foodborne pathogens (Stanley & Rhodes, 2021).

Microbes	**Distribution**	**Animals**	**Frequency**
Clonorchis sinensis	35 million worldwide	pigs, Freshwater fish, rats	Asia
Toxoplasma gondii	Worldwide	cats, sheep, pigs, and rabbits	½ billion globally
Opisthorchis sp.	SE. Asia, SE. Europe, Northern, Thailand, Siberia,	Cats, Canines, fish from freshwater	Variable
Fasciola hepatica	Globally, elevated figures in Asia, Northern Europe, South America, and the Nile Delta.	Domestic and wild ruminants	N/A, variable
Diphyllobothrium latum [fish tapeworm]	China, America Baltic region, Northern Japan, N. hemisphere,	Freshwater fish	N/A
Taenia solium [pork tapeworm]	Southeast Asia, Africa, Central America, South America, and Eastern Europe	Undercooked pork, Pigs	Not at all
Taenia saginata [beef tapeworm]	Worldwide, SE. Asia, high in E. Africa, China, cosmopolitan	Cattle, rarely in Beef, deer	4 million global
Paragonimus westermani [lung fluke]	South and Central America, Asia. Africa.	Pigs, crabs, Freshwater shellfish	20 million globally
Angiostrongylus cantonensis	Southern US, Australia, India, SE. Asia, Caribbean	rats—lung worm, crab fish Freshwater crabs,	N/A
Visceral cysticercosis	SE. Asia, Africa, South and Eastern Europe, South and Central America.	Fecal-oral route	10–20% of the population in endemic areas
Gnathostoma spinigerum [Gnathostomiasis]	Japan, France, Spain, rarely in the US, Cosmopolitan, Netherlands	cats, snails, dogs, Freshwater fish, frogs, chickens	N/A
Anisakis simplex [Herring worm]	Australia, Central America, SE. Asia,	squids, Sea—fish, marine mammals	N/A

Factors influencing transmission rates:

The effects of industrialization and community growth to accommodate the world population increase are examples of human-related issues. The ecology of wildlife is impacted by the development of new roads, homes, towns, and farms, which results in the removal of forests (Fong & Fong, 2017). Furthermore, changes in farming and food chain practices, increased hunting and pet ownership, ecotourism, and the growth of the culinary industry all contribute to human encroachment on animal ecology. The exposure of humans to animals and wildlife can be impacted by political regime shifts, armed conflicts, starvation, mass migration, lax border restrictions, and the collapse of public health infrastructure. Moreover, malnourishment and inadequate nutrition typically leave a population particularly vulnerable to a range of illnesses, including infections that are either directly or indirectly spread by animals.

Genetic variability, selection pressures for the development of increased microbial resistance and virulence, and changes in the ecosystem and biodiversity all have an impact on pathogen-related factors. These changes can also have an impact on the composition and quantity of the local fauna, which can lead to an increase in the number of vectors and disease reservoirs/hosts. In recent times, there has been a growing concern regarding climatic and environmental variables. This is because abnormal changes in the climate pattern in the north and south hemispheres due to global climate change might impact the life cycles of host vectors and affect the fauna and ecology of these animals.

Host-Pathogen interaction:

The symbiotic relationship between hosts and their microbiota is a complex network that influences host physiology, immunomodulation, and overall health. A variety of factors influence this dynamic connection, including dietary components, microbiota-derived metabolites, and a wide spectrum of antimicrobial drugs (Kogut et al., 2020). By acting as a physical barrier, the maternal-fetal interface protects the developing fetus from dangerous diseases and medications that are present in the mother's bloodstream. Nonetheless, certain infectious agents, including viruses, have the potential to penetrate this protective barrier by exploiting their small size or replicating within maternal and fetus placenta cells. Notable instances include T. gondii, N. caninum, Brucella abortus, and Chlamydia abortus, among other contributing factors, inducing tissue damage and boosting the likelihood of abortion (Pastor-Fernández et al., 2021). Newborn calves must make a number of difficult adjustments in their early years as they adapt to a new, highly pathogen-filled environment. They have to learn to control their body temperature on their own, go from eating through the umbilical cord to drinking milk from bottles or buckets, and change from having a pre-ruminant digestive system to a ruminant digestive system. The calf experiences an immense amount of stress as a result of these numerous changes, which frequently put its immune system to the test in the first three weeks of life. At the same time, dangerous pathogens such as coronavirus, Cryptosporidium spp., and enterotoxigenic Escherichia coli (ETEC) colonize the digestive tract during this critical time, highlighting the transition from passive immunity derived from colostrum to the development of active immunity (Osorio, 2020). In order to start replication, the virus transfers its genetic material into the host cell. To accomplish this, the viral capsid fuses with the phagosome of the host cell or the viral or cellular machinery creates pores in the capsid (Kellermann, Scharte, & Hensel, 2021). During this sequence, pathogen-associated molecular patterns (PAMPs) contained in the virus are selectively engaged with by pattern recognition receptors (PRRs), which help the host immune system recognize the virus. This recognition event triggered a sequence of innate immune responses, leading to the release of interferons and cytokines as well as the mobilization of immune cells (Rajput & Thakur, 2023). As innate immune cells, NK cells have the amazing ability to respond quickly and destroy cells that a virus has altered or infected without the need for prior sensitization (Mikelez-Alonso et al., 2021). Even though NK cells are innate immune cells, they can exhibit characteristics similar to the adaptive immune response. Like T cells, NK cells

express antigen-specific receptors, go through clonal proliferation when they come into contact with pathogens and mature into self-tolerance. Additionally, they are able to produce long-lasting memory cells that self-renew continuously and provide powerful effector responses against pathogens that they have already encountered (Sharrock & Sun, 2020). The outcome of this virus-host interaction relies on a number of variables related to either the virus or the host (Correa et al., 2021). These outcomes could result in the virus being eliminated by the host's immune system, the virus evading the host's immune system, or acute, chronic, persistent, or latent infections established (Hoffman et al., 2020). Research suggests that viruses with a high rate of mutation have an advantage when it comes to evolving, surviving, and evading the host's immune response. The host range of the virus may also change as a result of these modifications (Tenthorey et al., 2022). Prebiotics and phytonutrients are particularly important dietary components for enhancing immunity and fortifying chickens against disease (Islam et al., 2022). Furthermore, during the past 10 years, a great deal of research has been done on the supplementation of yeast-derived products with the goal of improving innate immunity. The foundation for investigating nutrigenomic strategies to advance the profitability and well-being of chicken production. As of right now, 10 TLR (Toll-like receptor) genes in chickens have been fully characterized. Variations in TLR sequences affect how the recognition patterns of Pathogen-Associated Molecular Patterns (PAMPs), thereby altering the host's defenses against pathogenic diseases. TLR polymorphism has significant potential as a genetic marker in selective breeding programs meant to enhance chicken breeds (Rehman et al., 2021). Globally, gastrointestinal nematodes (GIN) provide significant threats to sheep health and the economy. Haemonchus contortus, Nematodirus battus, Teladorsagia circumcincta, and several species of Trichostrongylus (such as T. colubriformis and T. vitrinus) are the primary GIN that harm sheep. These parasites are usually spread by the fecal-oral route, wherein infectious larvae grow in the abomasum or small intestine, causing severe mucosal damage and inciting the host's immune system to become inflamed (Smith et al., 2021). Additionally, sheep can serve as hosts for enteric pathogens of significant worldwide importance, including Salmonella enterica and Escherichia coli (STEC), which produce Shiga toxin (van den Brom et al., 2020). Furthermore, due to their physiological, genetic, and immunological resemblances to human virus outbreaks, pigs are becoming more and more popular in xenotransplantation and as models for human diseases and conditions. In addition to causing disease transmission and fatalities, these epidemics force the culling of swine herds, which results in significant economic losses (Marrana, 2022). Forecasting newly emerging infectious diseases (EIDs) in pigs and people is a major issue. Viral dynamics are heavily driven by selection mechanisms, leading to fast variations in viral landscapes, even if viral zoonoses are scarce in humans in comparison to the enormous viral diversity seen in the animal kingdom. In an EID scenario, the introduction of a novel host can act as a new found viral reservoir, allowing the virus to spread to other vulnerable species. For example, the SARS-CoV-2 transmission chain started with horseshoe bats, moved to an unidentified mammalian intermediate, later to humans, then to minks, and back to humans (Glud et al., 2021).

Evolutionary Dynamics of Animal Pathogen

Because metagenomics offers a more comprehensive viewpoint, it has greatly increased our understanding of the diversity of the animal virome. Animal viruses are currently classified into 5 out of 6 realms, 5 out of 10 kingdoms, 11 out of 17 phyla, 26 out of 39 classes, 36 out of 59 orders, and 99 out of 189 families according to the most recent update to the International Committee on Taxonomy of Viruses (ICTV) classification system, which was released in July 2021. The great diversity of animal viruses is brought to light by this new classification scheme, underscoring the significance of metagenomics in revealing this diversity (Walker et al., 2021). One intriguing finding from metagenomics studies of animal viromes is that, in line with their large species diversity, invertebrates usually contain a much greater diversity and ample of viruses than vertebrates. Specifically, a thorough metagenomics study of invertebrates has revealed new viral lineages and families, as well as those that were previously thought to be unique to vertebrates. These investigations have also demonstrated that invertebrate viruses exhibit a broad variety of

novel genome structures, demonstrating that viral genome evolution is more flexible and dynamic than previously thought (Harvey & Holmes, 2022). Meanwhile, a variety of stressors, such as the scarcity of vital nutrients, frequently confront free-living bacteria in the environment (Marmion et al., 2022). A host that can provide a stable and nutrient-rich habitat through an autotrophic or heterotrophic lifestyle is one of the many strategies that bacteria can use to lessen or avoid environmental stressors. It may be significantly more advantageous for a variety of bacteria to evolve chemotaxis abilities and adaptations that make it easier for them to colonize a host because carbon and nitrogen are scarce in the environment. Novel bacterial traits and behaviors that improve the bacteria's capacity to thrive in an environment associated with their host could emerge as a result of this selective pressure (Wiesmann et al., 2023). Both commensal and pathogenic organisms possess a variety of adaptations that improve their capacity to exploit resources. For example, they can secrete siderophores to scavenge iron or form biofilms to secure a space. However, because they involve harming the host directly, pathogens have evolved unique mechanisms to obtain resources that are unavailable to commensals (McLaren & Callahan, 2020). Microbes use a combination of active and passive interference strategies to outcompete one another. Frequently harboring prophage capable of initiating viral outbreaks and possessing mechanisms to release toxins into the surroundings or target cells, these organisms are equipped with defensive tools to eliminate rival organisms. Because of these adaptations, microbes can more successfully compete for resources and ensure their survival in a variety of ecological niches (Brüssow, 2021; Hernandez et al., 2020). Secreting chemicals that interfere with competitors' biofilms or cell-to-cell communication are two more active interference tactics. In addition to being widely utilized by pathogens, these mechanisms are also frequently employed by commensals against them. These tactics help organisms better exploit resources in a variety of ecological niches by impeding the growth and survival of their competitors (Kern et al., 2021).

- **Genetic variation and adaption in pathogens**

Genetic variation has largely influenced the evolution of animals and plants resulting from microbial acquisition (Ma et al., 2022; Perreau & Moran, 2022). In contrast to mutations, which result in minor alterations to preexisting genomes, the holobiont gains hundreds of new functional gene sets in a single step in acquiring a microbe. Microbes play a crucial role in the evolution of life forms by supplying a diverse array of genetic material that can be integrated into the host's genome. They existed on Earth for two billion one hundred million years before animals and plants appeared (Rosenberg, 2022). The concept of holobiont recognizes the interdependence of the host and its associated microbiome, emphasizing their co-evolutionary relationship. It views these entities as a single, cohesive entity. This viewpoint encourages a broader understanding of inheritance and the quick evolution of organisms as a result of the inheritance of acquired characteristics (Huitzil et al., 2023). It is therefore advisable to consider that these animal and plant holobionts obtained their genetic materials in the form of microbes. The next processes dictated and implemented were the mutations and selection processes, both in the microbe and the host for optimized performance. This process showcases how the HGT plays a critical role in the co-evolutional relationship between the host and the microbes and how the host's genetic makeup is shaped (Zilber-Rosenberg & Rosenberg, 2021). Research is currently being done to determine how much host genetics affect the gut microbiota. But an increasing amount of research from studies on a variety of animal species, including humans, mice, chickens, cattle, and swine, indicates that host genetics may have an impact on the makeup of the gut microbiota. Since the introduction of cutting-edge technologies, like genome-wide association studies (GWAS), a great deal of correlations have been found between the abundance of commensal bacteria and the genotypes of single nucleotide polymorphisms (SNPs), which are primarily found in genes linked to immune disease and host metabolic syndrome. These results demonstrate the intricate relationship between gut microbiota and host genetics, which can have implications for understanding the occurrence of various diseases (Fan et al., 2020). Despite the statistical significance of the relationship between host SNPs and individual bacterial taxa, recent studies have challenged this finding, suggesting that environmental factors may have a

more profound impact on shaping the gut microbiota than host genetics. (Cahana & Iraqi, 2020; Sanna et al., 2022). Population variation, genetic distance, age, and environmental variables may all contribute to the differences in understanding the roles of host genetics and environmental factors (De Kort et al., 2021). Furthermore, host genetic influences on the gut microbiota may be masked by the interplay between environmental variables and host genetics. To fully comprehend the intricate interactions that exist between host genetics, environmental variables, and the gut microbiota, more research is required (Cai et al., 2020).

Ticks are an obligate bloodsucking arthropod that is found all over the world. They frequently parasitize humans and other animals and act as intermediates or vectors for a diversity of infections, such as bacteria, viruses, and protozoa (Jia et al., 2022). Across many tick species, the GC content is comparably constant, I. Persulcatus has the lowest conserved synteny among the six tick genomes that have been sequenced, indicating a high degree of genetic divergence from other tick species. Orthologous protein sequences from six tick species, including I. scapularis, and two outgroup species, P. tepidariorum, and C. sculpturatus, in order to evaluate the evolutionary relationships between these species and arachnids. After constructing a maximum likelihood tree with these sequences, the evolutionary distances between the species will be calculated.In addition, using the coding sequences of 464 single-copy orthologous genes, we calculated the divergence period of these species. Identifying the genetic diversity and evolutionary links between tick species and their arachnid relatives is made possible by this analysis (Jia et al., 2020). Influenza Antigenic drift and shift cause viruses (IAVs) to exhibit a high degree of variety. The process known as "antigenic drift" refers to the slow buildup of minor genetic changes in the genome, particularly in the hemagglutinin (HA) and neuraminidase (NA) proteins, aiding influenza A viruses (IAVs) in evading host immune responses. This phenomenon is attributed, at least in part, to the limited proofreading capability of the viral RNA polymerase as shown in Figure 1 (Varghese et al., 2022).

When multiple subtypes of Influenza A virus infect a cell simultaneously, a process known as antigenic shift occurs, as shown in figure 2. This phenomenon involves a substantial change where viral segments are exchanged, leading to the emergence of new viral subtypes. Antigenic shift represents a distinct immunological event from the existing Influenza A viruses and occurs in a host lacking prior immunity.

New viral subtypes that arise via the genetic reassortment of IAVs have the potential to trigger epidemics or pandemics in humans since there is a lack of pre-existing immunity against the new antigens (Huang & Wang, 2020).

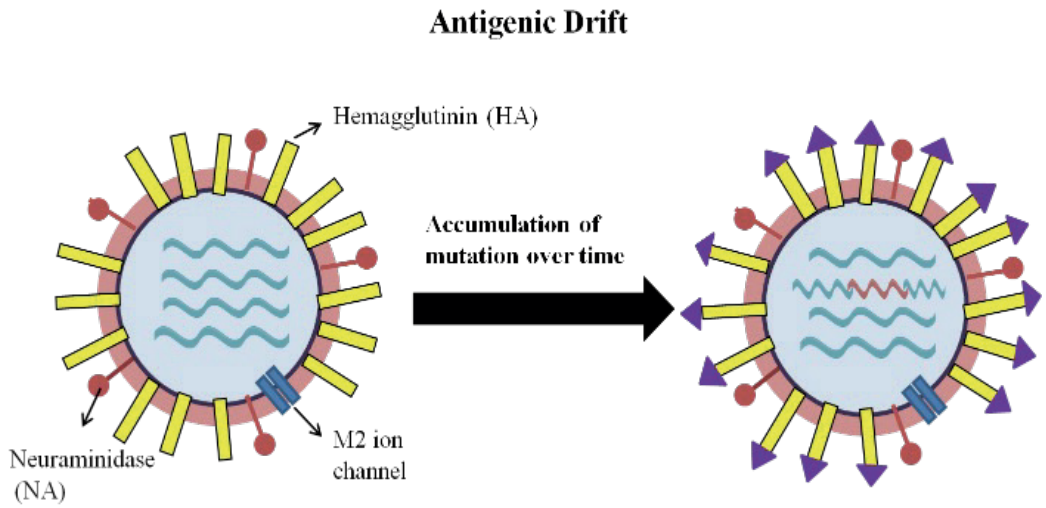


Figure 1. Antigenic drift

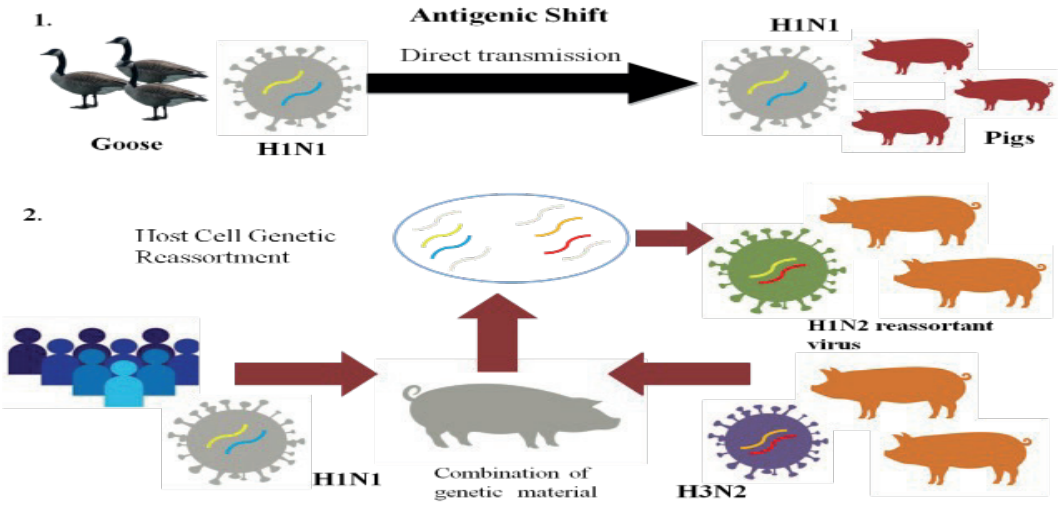


Figure 2 Antigenic shift

Disease control and management strategies

Animal disease control programs (CPs) have various advantages, including as better animal welfare and health, reducing the need for antibiotics, and increasing the safety of animal products in the event of zoonotic disease outbreaks. CPs also help to reduce direct and indirect disease losses (Hodnik et al., 2021). For ages, indigenous communities have relied on medicinal herbs as their main source of disease prevention and management for livestock. The local plants are a useful resource for illness prevention and management since the villagers are aware of their medicinal properties. Because it is easily accessible in remote locations and has the capability to cure an inclusive livestock illnesses, ethnoveterinary medicine is a highly adaptable and dynamic field that offers a more affordable option than synthetic medications (Rafique Khan et al., 2021). A few benefits of using medicinal plants to control animal disease are its affordability, convenience of usage, and little environmental effect. These plants are also a great resource for illness prevention and control since they frequently contain a variety of bioactive chemicals with antibacterial, anti-inflammatory, and immunomodulatory properties (El-Saadony et al., 2023). To effectively manage these challenges, specialized strategy plans must be developed for the prevention and control of exotic and transboundary animal diseases (TADs) (Singh, 2021). In the context of India, examples of such viral diseases include African swine fever (ASF), transmissible gastroenteritis (TGE), and swine vesicular disease in pigs, as well as Rift Valley fever, African horse sickness (AHS), West Nile fever, Eastern equine encephalomyelitis (EEE), Western equine encephalomyelitis (WEE), and Venezuelan equine encephalomyelitis (VEE). Furthermore, prion diseases such as bovine spongiform encephalopathy (BSE) and scrapie, Nipah virus, Hendra virus, SARS coronavirus, and FMD virus types 'C', 'SAT I', 'SAT II', and 'SAT III' are serious issues that need for focused prevention and control measures. Because of the distinctive dangers and challenges posed by each of these illnesses, specific strategies that are adapted to their particular traits and possible effects on agriculture, public health, and animal health are required. Through individualized strategic plans, nations can better protect their livestock, agricultural sectors, and overall biosecurity by tackling these illnesses (Yadav et al., 2020).

- **Vaccination and immunization programs**

With vaccinations available for over four hundred diseases affecting fish, birds, and mammals, vaccination is an essential approach to treating infectious diseases in livestock. Vaccines are particularly important to the livestock production businesses because they help prevent diseases like Marek's disease in poultry, Porcine Reproductive and Respiratory Syndrome (PRRS) in pigs, and

Foot-and-Mouth Disease (FMD) in cattle, sheep, goats, and pigs. Vaccinations improve livestock strength against disease by lowering or eliminating the dangerous effects of infections on their health, survival, and production. Essentially, vaccinations are essential to maintaining the health and welfare of animals, which in turn ensures the livestock sector's feasibility and profitability. Lumpy Skin disease (LSD) can be effectively controlled when there is a regional commitment to coordinate efforts aimed at limiting its spread, as demonstrated by the Balkans' successful eradication of the disease. These precautions consist of vaccinations, vaccine campaigns, trade and limited action for cattle, a feasible stamping-out program, decontamination, and vector control. The experience of the Balkans shows that eradicating LSD on a regional level is difficult but possible (Tuppurainen et al., 2021).

Vaccines containing Clostridium novyi can be used to help prevent economic losses in animals in cases of black disease, but controlling fascioliasis is just as crucial to the overall control strategy. Vaccination is the most effective way to stop the spread of LSD in both endemic and newly affected places. In both locations where the disease is already common and in areas where outbreaks have recently occurred, immunization is the major method of preventing the spread of LSD. The effectiveness of LSD control depends on the vaccination approach chosen, and there are differences in the value, cost, safety, and response of the vaccines that are now on the market (Ahmed, Yehia, & Ahmed, 2022; Caravedo & Cabada, 2020). To minimize the risk of an LSD outbreak, it is essential to implement biosecurity measures, enhance tracing and surveillance, conduct awareness campaigns, and administer inactivated vaccines. Since LSD is a transboundary disease, its constant appearance and reemergence in different nations raises serious concerns for animal health (Tuppurainen et al., 2021). It is crucial to maintain stringent control and prevention methods to prevent the spread of LSD, as outbreaks can have severe consequences for both animal health and the economy. Lactobacillus casei cells have been used to synthesize and produce ETX, a non-toxic mutant vaccine (toxoid). A vaccine made up of a bacterial suspension that expresses the recombinant protein has shown promise as an effective candidate for preventing enterotoxaemia in mice (Alimolaei, Golchin, & Baluch-Akbari, 2021). A wide range of clostridial toxoid, bacterin-toxoid, or whole culture vaccines protect against a variety of diseases worldwide animals. However, successfully arousing the host's immune system is a substantial problem in the forming of an ideal vaccination. The generation of mutants by the identification of clostridial target genes and the production of DNA vaccines are recent developments in the field of clostridial vaccines. Additionally, animal immune responses can be enhanced by novel vaccination formulations that contain suitable adjuvants, especially for toxoid vaccines. These advancements in vaccine technology have the potential to significantly improve the effectiveness of clostridial vaccines and provide better protection for animals against various diseases (Abdolmohammadi Khiav & Zahmatkesh, 2021). Canine coronavirus vaccines offer protection to young puppies, even though the disease itself is typically mild and tends to resolve on its own without intervention. In contrast, feline coronavirus infections can manifest as either mild symptoms or progress to a severe, potentially fatal immune-mediated condition known as feline infectious peritonitis. As a result, the goal of vaccinating domestic cats is to incite a protective immunological response without inducing an immune-mediated disease. Vaccines targeting bovine coronavirus are extensively utilized in cattle populations to guard against enteric and respiratory ailments in young calves (Tizard, 2020). Different vaccines used against pathogens are given in Table 3.

Table 3. Vaccines Against Various Pathogens in Different Species (Tizard, 2020).

Species	Pathogen	Vaccines	Types	References
Salmonid	Infectious Hematopoietic Necrosis	Apex IHN®	DNA vaccines	(Marsella et al., 2022)
Canine	Canine distemper virus	Recombitek® CDV	Viral vector (canarypox)	(Gong et al., 2020)
	Leishmania	Leish-Tech®	Recombinant protein	(Yasmin et al., 2022)
	Borrelia burgdorferi	Vanguard® crL-yme	Chimeric Protein	(Izac et al., 2020)
	Leishmania	Lentifend®	Chimeric Protein	(Aida et al., 2021)
Feline	Feline Leukemia virus	PureVax® Recombinant FeLV	Viral vector (canarypox)	(Tizard, 2021)
Equine	West Nile Virus	ALVAC® -WNC	Viral vector (canarypox)	(Vrba et al., 2020)
	Classical swine fever virus	Suvaxyn® CSF Marker	Chimeric viral vector (BVDV)	(Li et al., 2022)
Swine	A.pleuropneumoniae	Porcilis® APP	Subunit	(Hugo Dunlop, 2021)
	Porcine Circovirus Type 2	Ingelvac CircoFLEX®	Subunit (BEVS)	(Madapong et al., 2022)
	Porcine Circovirus Type 2	Circumvent® PCV-M G2	Subunit (BEVS)	(Aida et al., 2021)
Rabbits	Rabbit hemorrhagic disease virus	Novibac® Myxo-RHD	Chimeric viral vector (myxoma virus)	(Mears, 2022)
Bovine	Bovine Herpesvirus-1	Bovilis® IBR Marker Live	DIVA vaccines/ marker vaccines	(Petrini et al., 2021)
	Foot and Mouth Disease	Adt. A24 FMD	DIVA vaccines/ marker vaccines	(Singh et al., 2024).

• Surveillance and early detection methods

The most effective strategy for managing AKAV (Akabane virus) involves vaccinating susceptible animals before the onset of the disease season. In Japan, a live attenuated virus vaccine has been used, while in Australia, Japan, and Korea, an inactivated virus vaccine suitable for emergency vaccination of pregnant animals has been employed. Additionally, implementing vector control measures like safeguarding breeding areas from flies, using insect repellents, and administering pesticide treatments can also be beneficial in controlling the spread of the virus.

Output-focused standards specify the desired outcomes of surveillance, rather than specifying the specific activities that must be carried out, as is the case with input-based surveillance. When applied correctly, output-based techniques can produce surveillance standards that are uniform and cross-nationally comparable. This can result in disease control programs (CPs) that are customized for each country, taking into account their specific risk factors, such as herd density, contact structure, and disease occurrence. This may result in CPs that are socially acceptable, financially feasible, and optimally designed. Because of this, output-based management can increase the security of the animal trade while enabling nations to select the best control strategies by their particular epidemiological conditions (Costa et al., 2020). The fundamental guidelines for disease management, which involve providing therapy to impacted individuals, immunizing healthy individuals and animals, restricting

animal mobility, managing animal populations, and executing test-and-cull tactics (for illnesses like anthrax, glanders, and Rift Valley fever), can likewise be utilized in the handling of zoonotic diseases (Rao & Sharma, 2023). (Rao & Sharma, 2023). It is essential to decontaminate infected materials to minimize the risk of contracting new infections (Pandey et al., 2020). Appropriate disposal of terminated pregnancies can help reduce the frequency of brucellosis. Maintaining cleanliness and utilizing protective equipment like gloves, masks, lab coats, helmets, and goggles is critical. When suitable, comprehensive disinfection of polluted materials and locations should be carried out to aid in preventing the spread of diseases such as brucellosis, salmonellosis, and tuberculosis. Addressing emerging and re-emerging zoonotic diseases necessitates collaborative and interdisciplinary efforts. Efficient monitoring depends on well-supplied laboratories, sufficient diagnostic capacities, skilled staff, and adequate funding (Rahman et al., 2020).To effectively handle extremely dangerous transboundary disease agents, BSL III and BSL IV facilities are essential to guarantee biosafety, biosecurity, and biocontainment (Brake et al., 2020).

It is essential to put into practice strict zoo hygiene protocols, such as isolating new arrivals, controlling rodents and disease-carrying insects, cleaning and disinfecting animal enclosures and the entire facility, disposing of waste properly, and managing the remains of deceased animals, to successfully regulate and restrict the spread of newly identified infectious diseases and diseases that can spread across borders between countries (Collett et al., 2020; Gongal et al., 2022).

Prompt, fast, and exact disease reporting based on diagnostic tests approved by the World Organization for Animal Health (OIE) is crucial for early identification and reaction to pathogens, stopping further transmission. To fight new foreign diseases, it is suggested to set up standard operating protocols (SOPs) and technical instructions, together with defined decision-making levels, sufficient financing, and legal backing (Yadav et al., 2020). Starting bat surveys in a specific location is vital, but it is equally important to monitor other animals living in the same natural environment either at the same time or shortly after, including possible hosts for cross-species disease transmission events (Ruiz-Aravena et al., 2022). Integrating the sampling of diverse animal categories and assessing anthropological and human behavioral hazards must be an essential component of the planning and execution stage (Saylors et al., 2021). It is essential to prioritize communities and consider societal and cultural issues in studies to ensure comprehensive surveillance (Bedson et al., 2021). Initially, monitoring at predetermined locations can provide a rough approximation of animal host species (including both bats and non-bats), host movement behaviors, and viral release. This data can guide strategic choices for establishing prolonged monitoring at suitable locations.

Using concise genetic material sequences from an updated test aids in identifying variety and tracing changes in virus excretion patterns within populations over time, whether seasonally or based on a predetermined timetable (e.g., monthly). This method allows for the observation of both the presence and variety of coronaviruses among bats and other animals or pets sampled, while also collecting ecological information to explore factors impacting viral survival. Additionally, this data can offer a fundamental assessment of the risk linked to potential transmission opportunities (Geldenhuys et al., 2021).

Spatial and temporal dynamics of animal's pathogen

• Spatial distribution patterns of pathogens

Communal resting, a phenomenon where organisms gather during their dormant hours, is observed across a multitude of species, encompassing primates, bats, birds, and even invertebrates. This behavior, also known as colonial roosting or aggregation during rest, is prevalent among an array of fauna, showcasing the diversity of this natural occurrence (Stuart et al., 2023). These social gatherings can vary in size, ranging from small groups like tent-making bats and some loosely colonial seabirds to large assemblies of hundreds or even thousands of individuals, observed in colonial seabirds, pre-murmuration roosts of European starlings, cave-roosting bats, and social bees.

The patterns of communal roosting play a significant role in infectious diseases, as the frequency of interactions can impact the likelihood of infection and the spread of pathogens. The clustering behavior within communal species has been shown to facilitate the transmission of various pathogens, such as the fungal agent responsible for white-nose syndrome in bats (Pseudogymnoascus destructans), phocine distemper virus in harbor seals, and West Nile virus in American crows and robins (Lunn et al., 2021). Examining the extent of spatial correlation can provide insights into how parasites disperse across landscapes and explain their modes of transmission (Turner et al., 2021). For instance, spatial correlation observed over significant distances may indicate the impact of key climatic factors, whereas proximity-based spatial correlation suggests a localized infection process. Similar investigations into wildlife diseases can help identify transmission pathways and inform disease management strategies. If scientists find that a zoonotic illness shows significant spatial connection within its animal host population, this could lead to the deployment of widely spread sampling locations to reveal environmental factors. Furthermore, the size and range of spatial connections carry consequences for the wider theoretical understanding of disease spread dynamics. The intensity and range of spatial connection are probably shaped by the traits of the hosts and pathogens in question. Pathogens that can survive in the environment for extended periods are likely to be more affected by environmental variations compared to those transmitted directly. Moreover, highly mobile creatures such as large predators or migrating bats may effectively spread pathogens throughout the environment, reducing spatial correlation (Albery et al., 2022). The movement of animals is a significant factor in the spread of the porcine reproductive and respiratory syndrome virus (PRRSV) between farms (Sanchez et al., 2023). In the United States, the swine industry is characterized by a highly interconnected network of pig movements between farms due to the vertical integration of the sector. Piglets are transported from breeding facilities to growing operations (such as nurseries, finishing units, and wean-to-finish farms) and then to slaughter, with ownership maintained throughout the production process. These movements frequently cover long distances, ranging from several hundred to thousands of kilometers, rendering the US pork industry vulnerable to outbreaks of infectious diseases. The relocation of animals is a critical risk factor for the occurrence of PRRSV (Porcine Reproductive and Respiratory Syndrome Virus), and a farm's position within the broader movement network is associated with its susceptibility to the disease. The industry's structure, which involves the transportation of pigs across vast geographical areas, facilitates the rapid spread of pathogens, posing a significant challenge to disease control and prevention efforts (VanderWaal et al., 2020).

Although climatic and meteorological factors are implicated in the appearance of certain vector-borne zoonotic illnesses (VBZDs), they are not the most frequently cited reasons. Instead, changes in land utilization are the most frequently cited factor contributing to the emergence of vector-borne and zoonotic diseases (VBZD), accounting for 26% of all VBZD illnesses. The second-largest category is unspecified or unknown drivers of emergence (14%), followed by international trade and commerce (11%), emphasizing the impact of globalization in bringing people, vectors, and pathogens into closer contact. Environmental factors, including climate and weather patterns, are the fourth leading contributor to the emergence of vector-borne and zoonotic diseases (VBZDs), accounting for 10% of the identified VBZDs examined in this research (Swei et al., 2020).

• Temporal dynamics of disease outbreaks (seasonality, epidemical cycle)

There are several ways in which infectious illnesses in cattle can spread. Livestock trading is one of the primary routes of transmission. The movement of livestock is especially significant because contagious animals can spread disease over great distances between locations. Therefore, when a highly contagious disease like classical swine fever breaks out, substantial trade restrictions are put in place (Cochran et al., 2023). However, the disease can spread freely through trade before the first case is discovered. This unlimited trading phase, which can last for weeks or months, is known as the "high-risk period". Among the largest pig sectors in the world is found in Germany. Germany was the third-largest pork producer in the world in 2011–2013, behind China and the

United States. Germany produces about 4.5 million tons of pork meat annually. An estimated 7 billion euros are gained in manufacturing value annually. It has been demonstrated that trading in sick pigs was the most common source of infection in subsequent outbreaks for the classical swine fever epidemics that occurred in Germany in the 1990s. Many diverse parties can be involved in the trade-related transmission of an infectious disease, such as farmers, slaughterhouses, or traders. Diverse interactions between hosts are a major element in the unequal transmission of pathogens, as infectious people can contribute to new infections in diverse ways (Arthur et al., 2017). Individual differences in behavior and other characteristics, as well as shifts in the general patterns of interaction throughout time and space, all contribute to variations in contact rates. Epidemiology is one of the fastest-growing applications of network theory. In order to understand and model contact patterns, network theory has been applied frequently. Characterizing contact networks in community contexts, like homes, schools, or hospitals, has been important recently in order to discover therapies for diseases requiring intimate touch and to forecast transmission patterns with high accuracy. There may be geographical "hotspots" for the spread of illness in confined spaces, and establishing the contact network is essential to the success of control initiatives. Rainfall, humidity, and temperature are examples of environmental factors that can either directly or indirectly affect how animal infections spread (Bett et al., 2017). For instance, warm and humid conditions may favor the survival and reproduction of certain pathogens or their vectors, leading to increased transmission rates. Similar to this, modifications to land use or habitat layout can have an impact on disease dynamics by changing the abundance and distribution of host species. Contact networks have been utilized in farm animal farming contexts to characterize vast spatial scales within or between nations in the transfer of diseases from farm to farm. Animal movement databases are utilized to create connections between farms.

Since the seminal work of Kermack and McKendrick (1927) (Guckenheimer and Holmes 1983; Strogatz 2018), much epidemiological modeling has been grounded in evaluations of deterministic, nonlinear dynamical systems. These studies have mostly focused on determining the stability of attractors, or the singular solutions to which all trajectories eventually converge, such as chaotic attractors, equilibria, or limit cycles (Schwartz and Smith 1983; Diekmann and Heesterbeek 2000; Brauer et al. 2019). The management outcomes have generally significantly improved as a result of these temporally nuanced techniques. Every node's infection risk must be evaluated in order to put effective disease control and surveillance mechanisms into place. So-called centrality measures have been defined for this aim. Among these centrality measures is the range mentioned above. The degree of a node is the most basic centrality metric, and it is simply computed by counting the number of neighbors (Krnc & Škrekovski, 2020). A member of the Flavivirus genus of the Flaviviridae family of viruses, the virus that causes West Nile virus (WNV). People have been found to contract WNV from mosquito bites. Before the mid-1990s, it was a rare illness that was originally discovered in Uganda, East Africa, in 1937. Romania saw the first significant WNV outbreak in 1996. Since then, WNV has spread around the world, becoming endemic in Asia, Africa, the Middle East, West Asia, Europe, and North America. WNV spread over all 48 of the US's continental states between 1999 and 2005, starting in New York State. WNV initially occurred in the United States in 1999 (Nash et al. 2001). By 2003, WNV had proliferated to seven Canadian provinces after being discovered for the first time in Ontario and Quebec in 2001. In humans, WNV can result in neurological illness and even death. 5674 WNV human cases were recorded in the US in 2012 alone (CDC 2013a), with 92% of cases resulting in sickness at the site and 5% (286) deaths. The primary vector of WNV, female mosquitoes, is responsible for most human transmissions. In nature, WNV is spread through a cycle that involves mosquito-bird transmission. The main WNV reservoir is birds. More than 17 native bird species in North America are known to be WNV carriers. The mosquito species that transmit WNV differ depending on the region. The most common species in the Midwest and West are Culex quinquefaesciatus and Culex tarsalis, but the most common species on the east coast of North America is Culex pipiens (Hayes et al. 2005). It can infect horses, humans, and other mammals. The virus enters a mosquito's circulation when

it bites an infected bird. An infected mosquito, which permits the virus to infect the bloodstream and seriously sickens the victim bites a human or animal. Twenty percent or so of those infected with WNV go on to get West Nile fever. For birds and mammals, influenza (often referred to as the flu) is a common respiratory illness brought on by RNA (ribonucleic acid) viruses. Numerous influenza A viruses have their natural hosts in wild aquatic birds. Airborne influenza is spread by breathing. When someone with the virus coughs or sneezes, virus-laden droplets enter the air and can be breathed in by another person, exposing them to the infection. Hands infected with the virus can also transmit the virus. Additionally, direct touch with virus-containing bird droppings or nasal secretions as well as contact with infected surfaces can spread influenza.

Table 4. Temporal dynamics of diseases

Disease	**Cause/symptoms**	**Animals**	**Distribution**	**Transmission**	**Seasonality**	**frequency**	**Reference**
Japanese Encephalitis serocomplex	Encephalitis, meningitis, or meningo-encephalitis	Humans, horses, and several species of birds	Worldwide, highest in Uganda in East Africa, Africa, North America, Romania, Europe, West Asia, and the United States	Vector borne, mosquito-bird transmission Culex pipiens, Culex tarsalis. Culex quinquefaesciatus	Starts in summer & continues to fall (Mid-April to November)	2,205 cases reported each year	Mencattelli, G., et.al. (2023).
Avian and Human Influenza	Depression, appetite loss, stop-laying eggs, anxious symptoms, swelling and blue staining of wattles and combs from blood circulation disruption, coughing, sneezing, and diarrhea	Wild birds, poultry, and occasionally people	Africa, North America, the Middle East, and Asia	Exposure to saliva, mucous, or feces from infected birds	Between December and February	3–5 million cases severe illness and about 250,000–500,000 deaths each year.	Huang, M. L., Wu, H. D. I., & Chao, D. Y. (2023).

Disease	**Cause/symptoms**	**Animals**	**Distribution**	**Transmission**	**Seasonality**	**frequency**	**Reference**
Schistosomiasis	Liver enlargement, kidney damage and bladder and ureteric fibrosis	Cattle, sheep, goats ,primates, rodents & humans	Africa, the Middle East, the Caribbean, China, Indonesia, the Philippines, Brazil, Venezuela, and Suriname, as well as Corsica, France	Through snails	Rainfall		Léger, E., et.al. (2020).
Brucellosis	Oozing skin sores in horses ("fistulous withers"), mastitis and lameness in goats, and arthritis in cows and pigs.	Goat, pigs, horses, sheep cattle & buffaloes	West Asia, India, the Middle East, Southern Europe, and Latin America have the highest prevalence of brucellosis, followed by the Mediterranean basin, the Middle East, Central Asia, China, the Indian subcontinent, sub-Saharan Africa, and portions of Mexico, Central America, and South America.	Through contact with infected birthing tissues and fluids (e.g., placenta, aborted fetuses, fetal fluids, vaginal discharges),direct contact with infected animals.	Spring and summer seasons, which are the livestock's offspring seasons	500,000 cases annually	Khoshnood S, et.al. (2022)

Disease	Cause/symptoms	Animals	Distribution	Transmission	Seasonality	frequency	Reference
Anthrax	high fever, muscle tremors difficult breathing, depression and sometimes swelling	domestic and wild herbivores as well as most mammals and several bird species	all over the world except Antarctica	Inges-	rainfall leading to prolonged droughts and diminished hydrological regimes	20,000 to 100,000 cases annually	Stears, K., et.al. (2021).
Foot-and-mouth disease (FMD)	A decrease in milk production, a fever, depression, hypersalivation, appetite loss, weight loss, growth retardation, and blisters (or vesicles) on the nose, tongue, or lips, inside the oral cavity, between the toes, above the hooves, on the teats, and at pressure points on the skin	Pigs, sheep, goats, cattle, and other ruminants with cloven hooves	A few regions of South America, much of Africa, the Middle East, and several regions of Asia	Direct contact with infected animals or indirect contact with secretions or excretions (including semen and milk) from infected animals or by mechanical vectors (people, horses, dogs, cats, birds, vehicles) or air movement over land or water	Rainy season and the cold and dry season (and not in January in the middle of the rainy season)		Guerrini, L., et.al. (2019)

Conclusion:

The movement of pathogens by human activity to new areas or species, known as "pathogen pollution," poses a significant threat to both human and animal health in our interconnected world. Invasive alien species (IAS) refer to organisms like animals, plants, fungi, or microorganisms that humans have introduced to environments beyond their natural habitats. Once established, these species can disrupt local ecosystems through rapid reproduction, extensive dispersal, and adaptability to new environments. This often results in the displacement of native species and contributes to global biodiversity loss. In addition to their impact on biodiversity and economies, these translocated species can also facilitate the spread of diseases in the areas they invade (Chinchio et al., 2020). These dangerous biohazardous pathogens, like extremely virulent avian flu, hoof and mouth ailment, and brucellosis, possess the potential to greatly influence both affluent and impoverished nations, impacting animal well-being, financial stability, food protection, and public welfare

(Roth & Sandbulte, 2021). The capacity of foodborne pathogens to transfer between animals and humans, along with their capability to generate toxins leading to illnesses or fatalities, is significant enough to acknowledge the gravity of the issue (Abebe et al., 2020). Microscopic pathogens have the potential to induce illness by ingesting animal products tainted with microorganisms or their toxins (Gallo et al., 2020).

Pathogen adaptation during immunization initiatives has been noted in instances where vaccines fail to suppress pathogen populations below communicable thresholds or do not elicit protection against various antigens (Day et al., 2022). For example, oral poliovirus immunization has demonstrated a return to natural virulence as a result of adaptation, underscoring the complexities of vaccine development (Layman et al., 2021).

The possible advantageous impacts of immunization on antigenically changeable pathogens include decelerating antigenic evolution by augmenting immunity and diminishing the overall frequency or population size of the pathogen (Wen et al., 2022). The historical evolutionary progression of canine distemper virus (CDV) has resulted in occurrences of CD in immunized animals, raising doubts about the efficacy of existing vaccines. The development of CDV has been influenced by selective forces and the co-evolution of codon sites within H gene sequences, where specific residues in the H protein play a vital role in host cell penetration. These findings are instrumental in shaping investigations into vaccines and potential treatment targets (Wang et al., 2023).

Temporal dynamics of disease outbreaks can be influenced by factors such as seasonality, climate, host behavior, and pathogen characteristics (Semakula et al., 2023). Geospatial and chronological analysis tools, such as geographic information systems (GIS), spatial statistics, time-series analysis, and mathematical modeling, have been employed to investigate the dynamics of COVID-19 disease infection and dissemination. Integrating spatial and temporal analysis can offer a more holistic comprehension of the dynamics of pathogens and disease outbreaks (Cuadros et al., 2020; Owusu et al., 2022).

Reference:

Abebe, E., Gugsa, G., & Ahmed, M. (2020). Review on major food-borne zoonotic bacterial pathogens. Journal of tropical medicine, 2020.

Aida, V., Pliasas, V. C., Neasham, P. J., North, J. F., McWhorter, K. L., Glover, S. R., & Kyriakis, C. S. (2021). Novel vaccine technologies in veterinary medicine: a herald to human medicine vaccines. Frontiers in Veterinary Science, 8, 654289.

Albery, G. F., Sweeny, A. R., Becker, D. J., & Bansal, S. (2022). Fine-scale spatial patterns of wildlife disease are common and understudied. Functional Ecology, 36(1), 214-225.

Andersson, D. I., Balaban, N. Q., Baquero, F., Courvalin, P., Glaser, P., Gophna, U., Kishony, R., Molin, S., & Tønjum, T. (2020). Antibiotic resistance: turning evolutionary principles into clinical reality. FEMS microbiology Reviews, 44(2), 171-188.

Arthur, R. F., Gurley, E. S., Salje, H., Bloomfield, L. S., & Jones, J. H. (2017). Contact structure, mobility, environmental impact and behaviour: the importance of social forces to infectious disease dynamics and disease ecology. Philosophical Transactions of the Royal Society B: Biological Sciences, 372(1719), 20160454.

Asante, J., Noreddin, A., & El Zowalaty, M. E. (2019). Systematic review of important bacterial zoonoses in Africa in the last decade in light of the 'One Health'concept. Pathogens, 8(2), 50.

Bedson, J., Skrip, L. A., Pedi, D., Abramowitz, S., Carter, S., Jalloh, M. F., Funk, S., Gobat, N., Giles-Vernick, T., & Chowell, G. (2021). A review and agenda for integrated disease models

including social and behavioural factors. Nature human behaviour, 5(7), 834-846.

Bett, B., Kiunga, P., Gachohi, J., Sindato, C., Mbotha, D., Robinson, T., Lindahl, J., & Grace, D. (2017). Effects of climate change on the occurrence and distribution of livestock diseases. Preventive veterinary medicine, 137, 119-129.

Brake, D. A., Kuhn, J. H., Marsh, G. A., Beer, M., & Fine, J. B. (2020). Challenges and opportunities in the use of high and maximum biocontainment facilities in developing and licensing risk group 3 and risk group 4 agent veterinary vaccines. ILAR journal, 61(1), 46-61.

Brüssow, H. (2021). On the role of viruses in nature and what this means for the COVID-19 pandemic. Microbial Biotechnology, 14(1), 79.

Cahana, I., & Iraqi, F. A. (2020). Impact of host genetics on gut microbiome: Take-home lessons from human and mouse studies. Animal models and experimental medicine, 3(3), 229-236.

Cai, R., Cheng, C., Chen, J., Xu, X., Ding, C., & Gu, B. (2020). Interactions of commensal and pathogenic microorganisms with the mucus layer in the colon. Gut microbes, 11(4), 680-690.

Chinchio, E., Crotta, M., Romeo, C., Drewe, J. A., Guitian, J., & Ferrari, N. (2020). Invasive alien species and disease risk: An open challenge in public and animal health. PLoS pathogens, 16(10), e1008922.

Cochran, H. J., Bosco-Lauth, A. M., Garry, F. B., Roman-Muniz, I. N., & Martin, J. N. (2023). African Swine Fever: A Review of Current Disease Management Strategies and Risks Associated with Exhibition Swine in the United States. Animals, 13(23), 3713.

Collett, S. R., Smith, J. A., Boulianne, M., Owen, R. L., Gingerich, E., Singer, R. S., Johnson, T. J., Hofacre, C. L., Berghaus, R. D., & Stewart-Brown, B. (2020). Principles of disease prevention, diagnosis, and control. Diseases of poultry, 1-78.

Correa, A. M., Howard-Varona, C., Coy, S. R., Buchan, A., Sullivan, M. B., & Weitz, J. S. (2021). Revisiting the rules of life for viruses of microorganisms. Nature Reviews Microbiology, 19(8), 501-513.

Costa, L., Duarte, E. L., Knific, T., Hodnik, J. J., van Roon, A., Fourichon, C., Koleci, X., van Schaik, G., Gunn, G., & Madouasse, A. (2020). Standardizing output-based surveillance to control non-regulated cattle diseases: aspiring for a single general regulatory framework in the European Union. Preventive veterinary medicine, 183, 105130.

Cuadros, D. F., Xiao, Y., Mukandavire, Z., Correa-Agudelo, E., Hernández, A., Kim, H., & MacKinnon, N. J. (2020). Spatiotemporal transmission dynamics of the COVID-19 pandemic and its impact on critical healthcare capacity. Health & place, 64, 102404.

Day, T., Kennedy, D. A., Read, A. F., & Gandon, S. (2022). Pathogen evolution during vaccination campaigns. PLoS biology, 20(9), e3001804.

De Kort, H., Prunier, J. G., Ducatez, S., Honnay, O., Baguette, M., Stevens, V. M., & Blanchet, S. (2021). Life history, climate and biogeography interactively affect worldwide genetic diversity of plant and animal populations. Nature Communications, 12(1), 516.

de las Heras, F. G. (2011). Overview of neglected tropical diseases. Third World Diseases, 1-46.

El-Saadony, M. T., Zabermawi, N. M., Zabermawi, N. M., Burollus, M. A., Shafi, M. E., Alagawany, M., Yehia, N., Askar, A. M., Alsafy, S. A., & Noreldin, A. E. (2023). Nutritional aspects and health benefits of bioactive plant compounds against infectious diseases: a review. Food Reviews International, 39(4), 2138-2160.

Fan, P., Bian, B., Teng, L., Nelson, C. D., Driver, J., Elzo, M. A., & Jeong, K. C. (2020). Host genetic effects upon the early gut microbiota in a bovine model with graduated spectrum of genetic variation. The ISME Journal, 14(1), 302-317.

França-Silva, J. C., Giunchetti, R. C., Mariano, R. M. d. S., Machado-Coelho, G. L. L., Teixeira, L. d. A. S., Barata, R. A., Michalsky, É. M., Rocha, M. F., Fortes-Dias, C. L., & Dias, E. S. (2023). The Program for the Control of Visceral Leishmaniasis in Brazil: The Effect of the Systematic Euthanasia of Seropositive Dogs as a Single Control Action in Porteirinha, a Brazilian City with an Intense Transmission of Visceral Leishmaniasis. Pathogens, 12(8), 1060.

Gallo, M., Ferrara, L., Calogero, A., Montesano, D., & Naviglio, D. (2020). Relationships between food and diseases: What to know to ensure food safety. Food Research International, 137, 109414.

Ganter, M. (2015). Zoonotic risks from small ruminants. Veterinary microbiology, 181(1-2), 53-65.

Geldenhuys, M., Mortlock, M., Epstein, J. H., Pawęska, J. T., Weyer, J., & Markotter, W. (2021). Overview of bat and wildlife coronavirus surveillance in Africa: A framework for global investigations. Viruses, 13(5), 936.

Glud, H. A., George, S., Skovgaard, K., & Larsen, L. E. (2021). Zoonotic and reverse zoonotic transmission of viruses between humans and pigs. Apmis, 129(12), 675-693.

Godwin, E. J. O., Chandrasekaran, V., Smah, A. C., & Faith, E. O. (2022). Emerging Infectious Food System Related Zoonotic Foodborne Disease–A Threat to Global Food Safety and Nutrition Security. In Foodborne Pathogens-Recent Advances in Control and Detection. IntechOpen.

Gong, Y., Chen, T., Feng, N., Meng, X., Sun, W., Wang, T., Zhao, Y., Yang, S., Song, X., & Li, W. (2020). A highly efficient recombinant canarypox virus-based vaccine against canine distemper virus constructed using the CRISPR/Cas9 gene editing method. Veterinary Microbiology, 251, 108920.

Gongal, G., Rahman, H., Thakuri, K. C., & Vijayalakshmy, K. (2022). An overview of transboundary animal diseases of viral origin in South Asia: What needs to be done? Veterinary Sciences, 9(11), 586.

Harvey, E., & Holmes, E. C. (2022). Diversity and evolution of the animal virome. Nature Reviews Microbiology, 20(6), 321-334.

Hernandez, R. E., Gallegos-Monterrosa, R., & Coulthurst, S. J. (2020). Type VI secretion system effector proteins: effective weapons for bacterial competitiveness. Cellular microbiology, 22(9), e13241.

Hill, E. M., Prosser, N. S., Ferguson, E., Kaler, J., Green, M. J., Keeling, M. J., & Tildesley, M. J. (2022). Modelling livestock infectious disease control policy under differing social perspectives on vaccination behaviour. PLoS Computational Biology, 18(7), e1010235.

Hodnik, J. J., Acinger-Rogić, Ž., Alishani, M., Autio, T., Balseiro, A., Berezowski, J., Carmo, L. P., Chaligiannis, I., Conrady, B., & Costa, L. (2021). Overview of cattle diseases listed under category C, D or E in the Animal Health Law for which control programmes are in place within Europe. Frontiers in Veterinary Science, 8, 688078.

Hoffman, M., Chigbu, D. I., Crumley, B. L., Sharma, R., Pustylnikov, S., Crilley, T., Ginwala, R., Loonawat, R., Joseph, J., & Sales, D. (2020). Human acute and chronic viruses: Host-pathogen interactions and therapeutics. Advanced concepts in human immunology: Prospects for disease control, 1-120.

Huang, S.-W., & Wang, S.-F. (2020). The effects of genetic variation on H7N9 avian influenza virus pathogenicity. Viruses, 12(11), 1220.

Hugo Dunlop, B. (2021). Serologic monitoring of herds with and without bacterin vaccination for Actinobacillus pleuropneumoniae. Journal of Swine Health and Production, 29(1).

Huitzil, S., Huepe, C., Aldana, M., & Frank, A. (2023). The missing link: how the holobiont concept provides a genetic framework for rapid evolution and the inheritance of acquired characteristics. Frontiers in Ecology and Evolution, 11, 1279938.

Islam, R., Pandey, A., & Saha, T. (2022). Alternatives to Antibiotics in Animal Farming. In Alternatives to Antibiotics: Recent Trends and Future Prospects (pp. 147-175). Springer.

Izac, J. R., O'bier, N. S., Oliver Jr, L. D., Camire, A. C., Earnhart, C. G., Rhodes, D. V. L., Young, B. F., Parnham, S. R., Davies, C., & Marconi, R. T. (2020). Development and optimization of OspC chimeritope vaccinogens for Lyme disease. Vaccine, 38(8), 1915-1924.

Jia, N., Wang, J., Shi, W., Du, L., Sun, Y., Zhan, W., Jiang, J.-F., Wang, Q., Zhang, B., & Ji, P. (2020). Large-scale comparative analyses of tick genomes elucidate their genetic diversity and vector capacities. Cell, 182(5), 1328-1340. e1313.

Jia, W., Chen, S., Chi, S., He, Y., Ren, L., & Wang, X. (2022). Recent progress on tick-borne animal diseases of veterinary and public health significance in China. Viruses, 14(2), 355.

Kern, L., Abdeen, S. K., Kolodziejczyk, A. A., & Elinav, E. (2021). Commensal inter-bacterial interactions shaping the microbiota. Current opinion in microbiology, 63, 158-171.

Kogut, M. H., Lee, A., & Santin, E. (2020). Microbiome and pathogen interaction with the immune system. Poultry science, 99(4), 1906-1913.

Krnc, M., & Škrekovski, R. (2020). Group degree centrality and centralization in networks. Mathematics, 8(10), 1810.

Layan, M., Dellicour, S., Baele, G., Cauchemez, S., & Bourhy, H. (2021). Mathematical modelling and phylodynamics for the study of dog rabies dynamics and control: A scoping review. PLoS neglected tropical diseases, 15(5), e0009449.

Layman, N. C., Tuschhoff, B. M., & Nuismer, S. L. (2021). Designing transmissible viral vaccines for evolutionary robustness and maximum efficiency. Virus Evolution, 7(1), veab002.

Li, F., Li, B., Niu, X., Chen, W., Li, Y., Wu, K., Li, X., Ding, H., Zhao, M., & Chen, J. (2022). The development of classical swine fever marker vaccines in recent years. Vaccines, 10(4), 603.

Lunn, T. J., Peel, A. J., McCallum, H., Eby, P., Kessler, M. K., Plowright, R. K., & Restif, O. (2021). Spatial dynamics of pathogen transmission in communally roosting species: Impacts of changing habitats on bat-virus dynamics. Journal of Animal Ecology, 90(11), 2609-2622.

Ma, J., Wang, S., Zhu, X., Sun, G., Chang, G., Li, L., Hu, X., Zhang, S., Zhou, Y., & Song, C.-P. (2022). Major episodes of horizontal gene transfer drove the evolution of land plants. Molecular Plant, 15(5), 857-871.

Mack, A. (2016). Global health impacts of vector-borne diseases: workshop summary (2016). Global health impacts of vector-borne diseases: workshop summary (2016).

Madapong, A., Saeng-Chuto, K., Tantituvanont, A., & Nilubol, D. (2022). Using a concurrent challenge with porcine circovirus 2 and porcine reproductive and respiratory syndrome virus to compare swine vaccination programs. Sci Rep, 12(1), 15524.

Marchesini, R., & De Sanctis, S. (2021). The virus paradigm: A planetary ecology of the

mind. Cambridge University Press.

Marmion, M., Macori, G., Ferone, M., Whyte, P., & Scannell, A. (2022). Survive and thrive: Control mechanisms that facilitate bacterial adaptation to survive manufacturing-related stress. International Journal of Food Microbiology, 368, 109612.

Marrana, M. (2022). Epidemiology of disease through the interactions between humans, domestic animals, and wildlife. In One Health (pp. 73-111). Elsevier.

Marsella, A., Pascoli, F., Pretto, T., Buratin, A., Biasini, L., Abbadi, M., Cortinovis, L., Berto, P., Manfrin, A., & Vanelli, M. (2022). Efficacy of DNA Vaccines in Protecting Rainbow Trout against VHS and IHN under Intensive Farming Conditions. Vaccines, 10(12), 2062.

McLaren, M. R., & Callahan, B. J. (2020). Pathogen resistance may be the principal evolutionary advantage provided by the microbiome. Philosophical Transactions of the Royal Society B, 375(1808), 20190592.

Mears, M. (2022). Vaccine Development Strategies for Crimean-Congo Hemorrhagic Fever Virus and its Tick Vector

Méthot, P.-O., & Alizon, S. (2015). Emerging disease and the evolution of virulence: The case of the 1918–1919 influenza pandemic. Classification, Disease and Evidence: New Essays in the Philosophy of Medicine, 93-130.

Mikelez-Alonso, I., Magadan, S., Gonzalez-Fernandez, A., & Borrego, F. (2021). Natural killer (NK) cell-based immunotherapies and the many faces of NK cell memory: A look into how nanoparticles enhance NK cell activity. Advanced Drug Delivery Reviews, 176, 113860.

Montibeller, G. (2022). Decision Making for Enhanced Health Security. International Series in Operations Research and Management Science.

Muteeb, G., Rehman, M. T., Shahwan, M., & Aatif, M. (2023). Origin of antibiotics and antibiotic resistance, and their impacts on drug development: A narrative review. Pharmaceuticals, 16(11), 1615.

Osorio, J. S. (2020). Gut health, stress, and immunity in neonatal dairy calves: the host side of host-pathogen interactions. Journal of animal science and biotechnology, 11(1), 105.

Owusu, G., Yu, H., & Huang, H. (2022). Temporal dynamics for areal unit-based co-occurrence COVID-19 trajectories. AIMS Public Health, 9(4), 703.

Pandey, P., Vidyarthi, S. K., Vaddella, V., Venkitasamy, C., Pitesky, M., Weimer, B., & Pires, A. F. (2020). Improving biosecurity procedures to minimize the risk of spreading pathogenic infections agents after carcass recycling. Frontiers in Microbiology, 11, 623.

Pastor-Fernández, I., Collantes-Fernández, E., Jiménez-Pelayo, L., Ortega-Mora, L. M., & Horcajo, P. (2021). Modeling the ruminant placenta-pathogen interactions in apicomplexan parasites: current and future perspectives. Frontiers in Veterinary Science, 7, 634458.

Peng, S., Chen, Q., & Liu, E. (2020). The role of computational fluid dynamics tools on investigation of pathogen transmission: Prevention and control. Science of the Total Environment, 746, 142090.

Perreau, J., & Moran, N. A. (2022). Genetic innovations in animal–microbe symbioses. Nature Reviews Genetics, 23(1), 23-39.

Petrini, S., Martucciello, A., Grandoni, F., De Matteis, G., Cappelli, G., Giammarioli, M., Scoccia, E., Grassi, C., Righi, C., & Fusco, G. (2021). Evaluation of safety and efficacy of an

inactivated marker vaccine against Bovine alphaherpesvirus 1 (BoHV-1) in water buffalo (Bubalus bubalis). Vaccines, 9(4), 355.

Pontier, D., Guiserix, M., Fouchet, D., Sauvage, F., & Gonzalez, J.-P. (2009). Emergence of infectious diseases: when hidden pathogens break out. Comptes rendus. Biologies, 332(6), 539-547.

Rafique Khan, S. M., Akhter, T., & Hussain, M. (2021). Ethno-veterinary practice for the treatment of animal diseases in Neelum Valley, Kashmir Himalaya, Pakistan. PLoS one, 16(4), e0250114.

Rahman, M. T., Sobur, M. A., Islam, M. S., Ievy, S., Hossain, M. J., El Zowalaty, M. E., Rahman, A. T., & Ashour, H. M. (2020). Zoonotic diseases: etiology, impact, and control. Microorganisms, 8(9), 1405.

Rajput, M., & Thakur, N. (2023). Advances in host-pathogen interactions for diseases in animals and birds. Frontiers in Veterinary Science, 10.

Rao, A. M., & Sharma, S. (2023). Emerging Zoonotic Diseases and Strategies for Their Management. Journal of Communicable Diseases (E-ISSN: 2581-351X & P-ISSN: 0019-5138), 30-34.

Rehman, M. S.-u., Rehman, S. U., Yousaf, W., Hassan, F.-u., Ahmad, W., Liu, Q., & Pan, H. (2021). The potential of toll-like receptors to modulate avian immune system: exploring the effects of genetic variants and phytonutrients. Frontiers in Genetics, 12, 671235.

Rosenberg, E. (2022). Rapid acquisition of microorganisms and microbial genes can help explain punctuated evolution. Frontiers in Ecology and Evolution, 10, 957708.

Roth, J. A., & Sandbulte, M. R. (2021). The role of veterinary vaccines in livestock production, animal health, and public health. Veterinary vaccines: Principles and applications, 1-10.

Ruiz-Aravena, M., McKee, C., Gamble, A., Lunn, T., Morris, A., Snedden, C. E., Yinda, C. K., Port, J. R., Buchholz, D. W., & Yeo, Y. Y. (2022). Ecology, evolution and spillover of coronaviruses from bats. Nature Reviews Microbiology, 20(5), 299-314.

Sanchez, F., Galvis, J. A., Cardenas, N., Corzo, C. A., Jones, C., & Machado, G. (2023). Spatiotemporal relative risk distribution of porcine reproductive and respiratory syndrome virus in the southeastern United States. arXiv preprint arXiv:2301.05774.

Sanna, S., Kurilshikov, A., van der Graaf, A., Fu, J., & Zhernakova, A. (2022). Challenges and future directions for studying effects of host genetics on the gut microbiome. Nature genetics, 54(2), 100-106.

Saylors, K., Wolking, D. J., Hagan, E., Martinez, S., Francisco, L., Euren, J., Olson, S. H., Miller, M., Fine, A. E., & Thanh, N. N. T. (2021). Socializing One Health: an innovative strategy to investigate social and behavioral risks of emerging viral threats. One Health Outlook, 3(1), 11.

Semakula, M., Niragire, F., Nsanzimana, S., Remera, E., & Faes, C. (2023). Spatio-temporal dynamic of the COVID-19 epidemic and the impact of imported cases in Rwanda. BMC Public Health, 23(1), 930.

Shapiro, H. G., Pienaar, E. F., & Kohl, M. T. (2022). Barriers to management of a foreign animal disease at the wildlife-domestic animal interface: the case of rabbit hemorrhagic disease in the United States. Frontiers in Conservation Science, 3, 857678.

Sharrock, J., & Sun, J. C. (2020). Innate immunological memory: from plants to animals. Current opinion in immunology, 62, 69-78.

Shillcock, G. N. (2022). A Theoretical Perspective on Parasite-Host Coevolution with Alternative Modes of Infection The University of Western Ontario (Canada)].

Singh, A. (2021). Pandemic and the emerging threshold of disaster law in South Asia. Dhaka Univ. LJ, 32, 152.

Singh, A. P., Shrivastava, K., Hagos, T. H., & Pandey, H. O. (2024). Bioengineering prospects in livestock production. In Engineering Applications in Livestock Production (pp. 129-158). Elsevier.

Smith, D., Price, D. R., Burrells, A., Faber, M. N., Hildersley, K. A., Chintoan-Uta, C., Chapuis, A. F., Stevens, M., Stevenson, K., & Burgess, S. T. (2021). The development of ovine gastric and intestinal organoids for studying ruminant host-pathogen interactions. Frontiers in cellular and infection microbiology, 11, 733811.

Stuart, S. N., Magige, F. J., Hamerlynck, O., Newmark, W. D., Stephano, F., Spawls, S., Nahonyo, C., Mgaya, Y. D., Moyer, D. C., & Msuya, C. (2023). Tribute to Kim Monroe Howell (1945–2022). In: Taylor & Francis.

Swei, A., Couper, L. I., Coffey, L. L., Kapan, D., & Bennett, S. (2020). Patterns, drivers, and challenges of vector-borne disease emergence. Vector-Borne and Zoonotic Diseases, 20(3), 159-170.

Tanga, C., Remigio, M., & Viciano, J. (2022). Transmission of zoonotic diseases in the daily life of ancient Pompeii and Herculaneum (79 CE, Italy): a review of animal–human–environment interactions through biological, historical and archaeological sources. Animals, 12(2), 213.

Tenthorey, J. L., Emerman, M., & Malik, H. S. (2022). Evolutionary landscapes of host-virus arms races. Annual Review of Immunology, 40, 271-294.

Tizard, I. R. (2021). Feline vaccines. Vaccines for Veterinarians, 167.

Tomassone, L., Berriatua, E., De Sousa, R., Duscher, G. G., Mihalca, A. D., Silaghi, C., Sprong, H., & Zintl, A. (2018). Neglected vector-borne zoonoses in Europe: Into the wild. Veterinary parasitology, 251, 17-26.

Tsikalas, S. G., Whitesides, C. J., Butler, D. R., & Cavin, R. M. (2023). Animal hazards—their nature and distribution. In Biological and Environmental Hazards, Risks, and Disasters (pp. 155-181). Elsevier.

Turner, W. C., Kamath, P. L., Van Heerden, H., Huang, Y.-H., Barandongo, Z. R., Bruce, S. A., & Kausrud, K. (2021). The roles of environmental variation and parasite survival in virulence–transmission relationships. Royal Society open science, 8(6), 210088.

van den Brom, R., de Jong, A., van Engelen, E., Heuvelink, A., & Vellema, P. (2020). Zoonotic risks of pathogens from sheep and their milk borne transmission. Small ruminant research, 189, 106123.

VanderWaal, K., Paploski, I. A., Makau, D. N., & Corzo, C. A. (2020). Contrasting animal movement and spatial connectivity networks in shaping transmission pathways of a genetically diverse virus. Preventive veterinary medicine, 178, 104977.

Varghese, P. M., Kishore, U., & Rajkumari, R. (2022). Innate and adaptive immune responses against influenza A virus: immune evasion and vaccination strategies. Immunobiology, 227(6), 152279.

Vrba, S. M., Kirk, N. M., Brisse, M. E., Liang, Y., & Ly, H. (2020). Development and applications of viral vectored vaccines to combat zoonotic and emerging public health threats. Vaccines, 8(4), 680.

Walker, P. J., Siddell, S. G., Lefkowitz, E. J., Mushegian, A. R., Adriaenssens, E. M., Alfenas-Zerbini, P., Davison, A. J., Dempsey, D. M., Dutilh, B. E., & García, M. L. (2021). Changes to virus taxonomy and to the International Code of Virus Classification and Nomenclature ratified by the International Committee on Taxonomy of Viruses (2021). Archives of virology, 166(9), 2633-2648.

Wang, H., Guo, H., Hein, V. G., Xu, Y., Yu, S., & Wang, X. (2023). The evolutionary dynamics history of canine distemper virus through analysis of the hemagglutinin gene during 1930–2020. European Journal of Wildlife Research, 69(3), 56.

Wen, F. T., Malani, A., & Cobey, S. (2022). The potential beneficial effects of vaccination on antigenically evolving pathogens. The American Naturalist, 199(2), 223-237.

Wiesmann, C. L., Wang, N. R., Zhang, Y., Liu, Z., & Haney, C. H. (2023). Origins of symbiosis: shared mechanisms underlying microbial pathogenesis, commensalism and mutualism of plants and animals. FEMS Microbiology Reviews, 47(6), fuac048.

Yadav, M. P., Singh, R. K., & Malik, Y. S. (2020). Emerging and transboundary animal viral diseases: Perspectives and preparedness. Emerging and transboundary animal viruses, 1-25.

Yashavarddhan, M., Bohra, D., Rana, R., Tuli, H. S., Ranjan, V., Rana, D. S., & Ganguly, N. K. (2023). Comprehensive Overview of 2022 Human Monkeypox Outbreak and Its Pathology, Prevention, and Treatment: A Strategy for Disease Control. Microbiological Research, 127504.

Yasmin, H., Adhikary, A., Al-Ahdal, M. N., Roy, S., & Kishore, U. (2022). Host–pathogen interaction in leishmaniasis: immune response and vaccination strategies. Immuno, 2(1), 218-254.

Zilber-Rosenberg, I., & Rosenberg, E. (2021). Microbial-driven genetic variation in holobionts. FEMS Microbiology Reviews, 45(6), fuab022.

About The Authors

Ghanwa Maryam received her Bechalor degree in 2023 from Cholistan University of Veterinary and Animal Sciences, Bahawalpur, Pakistan. Her research interests include Molecular biology, Fisheries and conservation and biodiversity of animals (Vertebrates and Invertebrates).

Email: ghanwamaryam@gmail.com ORCID: 0009-0000-5968-3246

Nazish Fatima earned Bachelor's in applied microbiology from Cholistan university of veterinary and animal sciences (CUVAS) Bahawalpur Pakistan. Currently she is doing M.phil in Microbiology from Cholistan university of veterinary and animals sciences (CUVAS) Bahawalpur Pakistan. Her research interest in Microbial genetics, Molecular biology, soil microbiology, plant Microbiology and food quality and its application. She has a single publication in international journals.

E. Mail: nazishfatima511@gmail.com ORCID: 0009-0005-7730-7961

Hamna Shahid earned a Bachelor's degree in biotechnology from the Virtual University of Pakistan, Lahore, Pakistan. Currently, she is pursuing an M.Phil in Microbiology at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. Her research

interests include Genomics, antimicrobial resistance, industrial biotechnology, pharmaceutical microbiology, and food microbiology. She has one publication in international journals.

E-mail: hamnashahid250@gmail.com ORCID: 0009-0001-6525-324X

Muhammad Ejaz earned Bachelor's in applied microbiology from Cholistan university of veterinary and animal sciences (CUVAS) Bahawalpur Pakistan. His research interest in Microbial genetics, Molecular biology, and food quality and its application.

Email: ijazrasheed334@gmail.com ORCID: 0009-0006-1709-6653

Minahal Fatima and She is doing M.Phil in Zoology, Wildlife and Fisheries from University of Agriculture, Fasilabad, Pakistan. Her research interest includes fish survival via changing the environmental factor. Not only the fish survive it also counts the progeny's survival. She has only one paper in International Journal and 12 Chapters in national and international Journals.

Email: fatimaabdulhameed08@gmail.com ORCID: 0009-0003-4387-6854

Aansa Tahreem earned a Bachelor's in applied microbiology from the Cholistan University of Veterinary and Animal Sciences (CUVAS) in Bahawalpur Pakistan. Currently, she is doing an M. Phil in Microbiology from the University of Veterinary and Animal Sciences (UVAS) in Lahore Pakistan. Her research interests are in Microbial genetics, Molecular biology, soil microbiology, plant Microbiology, and food quality and its application. She has a single publication in international journals.

E-mail: aansa45tehreem@gmail.com ORCID: 0009-0001-6208-8090

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as "Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone". His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

To Cite This Chapter

MARYAM G et al., (2024). Dynamics of animal pathogens. In Current Studies in Health and Life Sciences 2024 (pp.465-492). ISRES Publishing.

Innovations and Principles of Vaccine Development for Livestock

Arooj FATIMA

Shafeeq ur REHMAN

Faizan ALI

Minahal FATIMA

Khizar ABBAS

Mehmet OZASLAN

Muhammad SAFDAR

1.Introduction

Numerous animal illnesses can be effectively prevented by vaccinations. Numerous successful vaccines developed in the field of vaccination have greatly lessened the impact of a number of serious illnesses in livestock and companion animals. Nowadays, cell membrane chemicals, toxoids, or live attenuated, dead, or inactivated microorganisms make up the great majority of veterinary vaccinations that are approved for use in medicine (McVey and Shi, 2010, Unnikrishnan et al., 2012). Because live attenuated vaccines elicit both humoral and cellular immune responses, they have the potential to be very successful. Yet, a significant worry surrounding these kinds of vaccinations is the possibility that the microbe may revert to a virulent phenotype. Attenuated vaccinations may have more efficacy than killed or inactivated vaccines, despite the fact that the former are usually safer. Due of their requirement for complicated components in the culture medium, commercial vaccines based on toxoids (inactivated toxins) have some disadvantages. It is necessary to develop better and safer vaccinations that can prevent, control, or eradicate animal illnesses since the three currently available vaccine types have limits and certain diseases have not yet been effectively treated with an effective vaccine (Dunham, 2002, Redding and Weiner, 2009).

A number of logically created and subunit vaccines have already made it to the veterinary market. Recombinant vaccines provide an appealing method of overcoming the constraints of traditional immunizations. Around the world, work is being done to use recombinant DNA technology to create vaccinations that are more effective against a wide range of illnesses. Recombinant vaccines are created utilizing structure-based design, epitope-focused design, or genomic-based screening, which are based on carefully crafted recombinant highly purified antigens. (Correia et al., 2014, Dellagostin et al., 2011). These molecular approaches have not only improved our understanding of the genes causing virulence and made it easier to identify the factors that determine protective immune responses, but they have also given rise to new techniques for creating innovative vaccines against illnesses that are infectious, parasitic, or metabolic. To guarantee the success of recombinant vaccines, strong and secure adjuvants are required, as the intrinsic immunogenicity of recombinant antigens is frequently lower than that of more conventional vaccinations. Lack of exogenous immune stimulating components is the cause of the poor immunogenicity often seen in recombinant antigens. Adjuvants for recombinant antigens vary, and the immunomodulatory effects of a certain adjuvant when combined with a particular antigen are known.

1.1. Overview of vaccine development and principles

Veterinary vaccines are developed to increase production of livestock including cattle and poultry, improve the health of companion animals, and prevent animal-to-human transmission from domestic and wild animals. Aggressive vaccination strategies globally have eliminated rinderpest, a devastating cattle disease in 2011. This was the first livestock disease, to have ever been eradicated through vaccination efforts, and the global benefits of rinderpest eradication are estimated to be in the billions of dollars (Thomas et al., 2022). Vaccination strategies are required to eliminate

diseases of livestock so as to increase the food security in a rapidly changing world due to climate changes. Increase in temperature will lead to proliferation of pathogens where some species may become more susceptible to a novel pathogen during heat stress (Rojas-Downing et al., 2017). A vaccine is a biological product that can be used to safely induce an immune response that confers protection against infection and/or disease on subsequent exposure to a pathogen. To achieve this, the vaccine must contain antigens that are either derived from the pathogen or produced synthetically to represent components of the pathogen (Pollard & Bijker, 2021).

Early vaccines formulated with whole microbial pathogens supply an extensive repertoire of different epitopes that, in general assure sufficient immune stimulatory activity within an immunogenic heterogeneous population. In contrast, highly purified antigens, probably consisting only of a limited number of epitopes, may pose the risk of insufficient interaction with individuals missing the adequate immune-receptor repertoire (Zepp, 2010). Moreover, genetic heterogeneity of the pathogen may counteract the expected benefit of highly purified vaccine antigens. In other words, while being highly specific towards the pathogen against which it should provide protection, the initiation of the vaccine-related immune response has to be adequate to fulfill this task for every individual of a given population. From its emergence out of immunology, vaccine-logy has focused on understanding the natural, course of an infectious disease especially with regard to the specific steps leading to a protective immune response. In order to learn from nature, as a first step, vaccinology dissects the natural immune response to identify the components most relevant for the protection from infection and/or disease. Because protective immune response mechanisms vary significantly depending on the pathogenesis, of the infectious disease (Table 1) (Zeepo 2010), this task requires profound understanding of the cellular and molecular elements of the human immune system involved.

Over several decades, the approach to vaccine design moved from a time where there was little understanding of how vaccines activate the immune system (even though many of these vaccines are still available today) to the situation now where the understanding of the immune system has underpinned the development of vaccines with higher specificity due also to advances in the manufacture of highly purified antigens. With these advances, a major challenge emerged that needed to be tackled; highly purified and defined antigens can have the unwanted consequence of impaired immunogenicity in comparison with less purified vaccines. From quite early in the history of vaccinology, additional components, adjuvants (from the Latin word adjuvare, meaning 'to help or aid'), were introduced in to vaccine formulations to improve the immunogenicity of vaccines. The most commonly used adjuvant today is based on aluminium salts (Brewer, 2006). It is now known that aluminium salts (and other adjuvants) are able to provide pro inflammatory or immune-stimulatory effects as well as prolong the persistence of vaccine antigens by slowing down antigen degradation (Brewer, 2006). However, it is also demonstrated that aluminium salts primarily promote antibody responses, with little or no effect on Th1 and cytotoxic cell immune responses (Zepp, 2010). That is probably the reason why aluminium salts have been used more successfully in vaccines against pathogens where antibodies represent the primary mechanism of protection. For vaccines designed against pathogens where it is important to induce a cytotoxic T cell-mediated immune response, aluminium salts have been found to be inadequate to induce the required protection (Collier, 2017). Recently accumulating knowledge has clarified that this is essentially due to a lack of' intrinsic immune defense triggers' usually present in the pathogen, such as pathogen-associated molecular patterns (PAMPs) (Zepp, 2010). Naturally available PAMPS may be reduced or even become lost during the selection process for relevant vaccine antigens or in course of the purification processes. PAMPs represent conserved' danger signals 'that are recognized by pattern-recognition receptors (PRRs),mainly of the innate immune system but to some degree also found on Band T cells, including so- called Toll-like receptors (TLRs) (Mogensen, 2009). The triggering of PRRs by PAMPs provides an important early activation signal that is affected by what type of pathogenesis involved, and can alert multiple aspects of the adaptive immune responses, i.e. type, magnitude and quality of specific B and T cell activation, immune memory induction, etc.

Hence, it is by the recognition of particular PAMPs, the innate immune system cancer ate different immunological environments that can shape the type of protective adaptive immune responses. It was logical step to target the 'danger-sensing' PRRs in order to improve the quality and persistence of vaccine-related immune responses in all population groups. In the context of vaccine development, this has led to area appraisal of the role of adjuvants as substitutes of natural immune-defence triggers to activate the appropriate DC response (Leroux-Roels, 2010). The deficits of aluminum salts as adjuvants, especially with regard to their capacity to induce cytotoxic T cell-mediated immune responses, have triggered extensive research and effort to develop new adjuvants that can improve immunogenicity as well as the type of adaptive immune response. The most successful examples of these developments are emulsions, virosomes and adjuvant systems, as described in a companion paper. Most recently the improved understanding of the important role of TLR signaling has led to the recognition of a role for immune-stimulatory DNA, such as CpG (Higgins et al., 2007), and other TLR agonists, such as deacylated monophosphoryl lipid A (MPL), as vaccine adjuvants. Moreover, adjuvant systems based on the combination of a classical adjuvant plus immune enhancing molecules, have been developed to modulate aspects of the immune system to help achieve the desired protective response (Garçon et al., 2007).

2. Principles of Vaccine Development

Modern vaccine design builds on the principal concept of inducing protective immunity against a disease by mimicking the naturally occurring immuo-response, against the disease-causing pathogen, but without inducing the disease. To achieve this, the factors that define the interaction between the human organism and an infectious agent have to be considered at the level of the population, individual, cells and, most recently, genes (Fig. 1) (Hammer et al., 2014). In most instances, vaccines are developed to protect human beings from infectious diseases on a population-based level. This implies that vaccines provide protection for basically every individual within an immune genetically heterogeneous population.

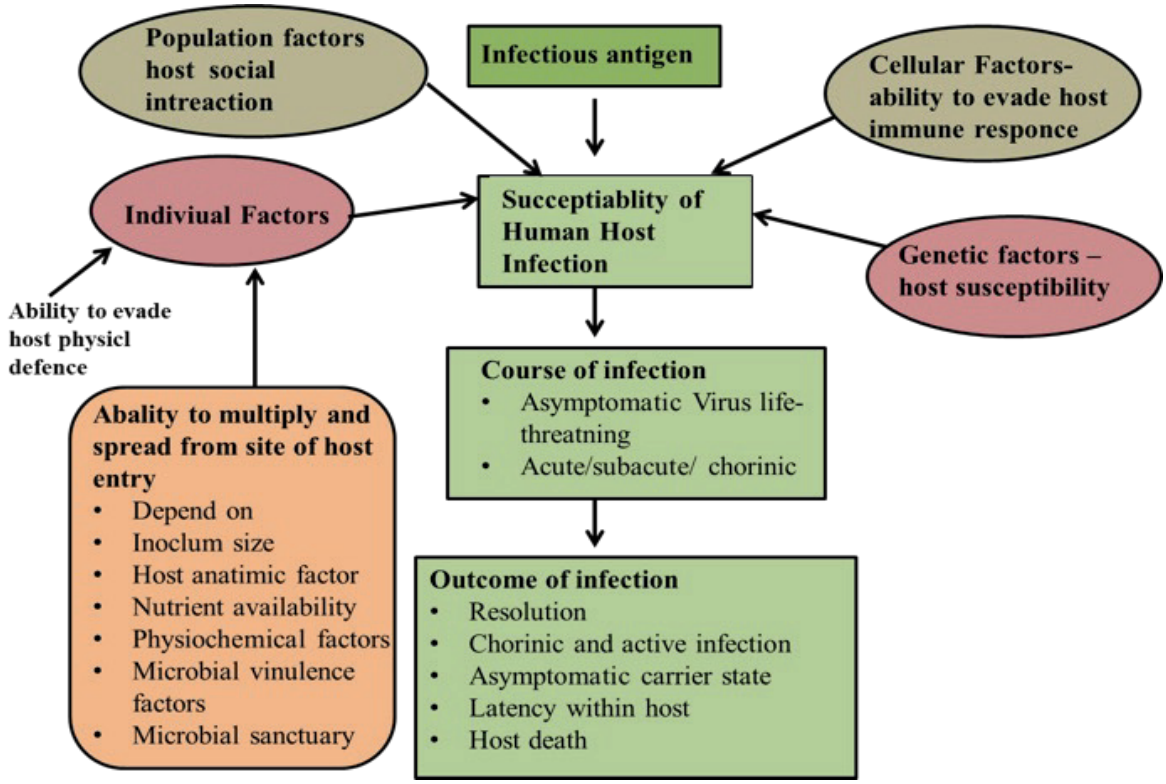


Figure 1 principle of vaccine development

2.1. Immunological basis of vaccination

The immune system is composed of two major populations: B-cells, producing antibodies, and T-cells, mediating cellular immunity. T-cells are divided into CD4 and CD8 subsets and the CD4 T-cells are divided, based on the pattern of cytokine secretion, into ThI, Th2 and Th3 cells. The differences between B- and T-cells are not only functional but are also seen in the mechanism of recognition of antigens. The B-cells, via the Ig receptor, recognize both conformational and linear epitopes directly on the surface of native macromolecules. In certain cases the recognition of epitopes leads to activation and differentiation of B-cells directly, i.e. T-independent antigens. In other cases they need the help of CD4 T-cells, i.e., T-dependent antigens (Broere & van Eden, 2019). The isotope of antibodies is dependent on collaboration with T-cells. Whereas Thl cells polarize the response to IgG2, the collaboration with Th2 leads to IgG 1 and IgE. The polarization of isotopes is caused by cytokines secreted by these subsets that represent second signals: interleukin-2 (IL-2), and interferon) in the case of Thl and IL-4, IL-5, and IL-l in the case of Th2 cells (Ding, 2000). Antibodies exert their protective capacity by blocking the microbial receptor through which they bind to the cellular receptor of permissive cells, promoting phagocytosis via opsonins and complement dependent lysis. In contrast to B-cells, T-cells are unable to recognize the antigens on the surface of native macromolecules. They recognize only fragments of degraded antigens in association with MHC molecules. CD4 T-cells recognize peptides or glycopeptides in association with class II MHC molecules. The peptides are produced from the processing of exogenous proteins in the endosomes of professional antigen-presenting cells (APCs; B-cells, macrophages, and dendritic cells), where they bind to nascent and empty class II molecules (Bona, 2002). The peptide-class II complex is trans located to the membrane, where interaction with the T-cell receptor (TCR) of T cells occurs. Figure 1 illustrates cellular events leading to generation of a class II-peptide complex within professional APCs. CD8 T-cells recognize the peptides in association with class I MHC molecules. The peptides are derived from endogenous proteins, including proteins of intracellular microbes. The proteins are fragmented by proteasomes, and the peptides are bound to transporter proteins (TAPs), and taken to the endoplasmic reticulum (ER), where they are released and bind to nascent class I MHC molecules (Perreault, 2010). The peptide-class I complex is transferred via the Golgi apparatus to membranes and is recognized by CD8 T-cells. The generation of a class I-peptide complex. T-cells or natural killer (NK) cells can recognize lipopeptides or glycopeptides in association with CDI molecules, which are less polymorphic than MHC molecules. The major functions of cells involved in host response to vaccines. Interdisciplinary contributions of accumulated knowledge and new methodologies have led to the development of new vaccines stimulating production of antibodies, cytokines, and cytotoxic responses, contributing to the recovery process from infectious diseases (Bona, 2002).

This also contributed to the development of immunotherapeutic ideally, a vaccine should display the following properties:

1. The antigen should be pure and chemically well defined.

2. It should induce a protective immune response.

3. It should exhibit a constant antigen specificity without being the subject of genetic variation

4. The protection should be lifelong or induced promptly after a booster dose.

5. It should be devoid of side effects.

6. The manufacturing should be inexpensive.

Table 1 Protective immune responses to infection differ according to type of disease.

Sr .No	Disease	Pathogenesis	Immune response
1.	Cholera	Local infection, enterotoxin	IgA (mucosa) IgG (neutralization)
2.	Diphtheria	Local infection, exotoxins	IgG(neutralization)
3.	Hepatitis B	Systemic infection	IgG (elimination of the virus) IFN γ, T cells (infected cells)
4.	Influenza	Local infection Systemic infection	IFN γ, IgA,IgG T cells(infected cells)
5.	Tuberculosis	Systemic infection	T cells, IFN γ Macrophages

2.2. Types of vaccines (live attenuated, inactivated, subunit, etc.)

The essential component of most vaccines is one or more protein antigens that induce immune responses that provide protection. However, polysaccharide antigens can also induce protective immune responses and are the basis of vaccines that have been developed to prevent several bacterial infections, such as pneumonia and meningitis caused by Streptococcus pneumoniae, since the late 1980s (Pollard & Bijker, 2021). Vaccines are generally classified as live or non-live (sometimes loosely referred to as 'inactivated') to distinguish those vaccines that contain attenuated replicating strains of the relevant pathogenic organism from those that contain only components of a pathogen or killed whole organisms (Fig. 2). In addition to the 'traditional' live and non-live vaccines, several other platforms have been developed over the past few decades, including viral vectors, nucleic acid-based RNA and DNA vaccines, and virus-like particles. The distinction between live and non-live vaccines is important. The former may have the potential to replicate in an uncontrolled manner in immune-compromised individuals (for example, children with some primary immune-deficiencies, or individuals with HIV infection or those receiving immunosuppressive drugs), leading to some restrictions to their use (Rubin et al., 2014). By contrast, non-live vaccines pose no risk to immune-compromised individuals live vaccines are developed so that, in an immune-competent host, they replicate sufficiently to produce a Finding an immune response that correlates with protection can accelerate the development of and access to new vaccines (Plotkin, 2020) The antigenic component of non-live vaccines can be killed whole organisms (for example, whole-cell pertussis vaccine and inactivated polio vaccine), purified proteins from the organism (for example, acellular pertussis vaccine), recombinant proteins (for example, hepatitis B virus (HBV) vaccine) or polysaccharides (for example, the pneumococcal vaccine against S. pneumoniae) (Table.2). Toxoid vaccines (for example, for tetanus and diphtheria) are formaldehyde-inactivated protein toxins that have been purified from the pathogen. Non-live vaccines are often combined with an adjuvant to improve their ability to induce an immune response (immunogenicity). There are only a few adjuvants that are used routinely in licensed vaccines. Vaccines contain other components that function as preservatives, emulsifiers (such as polysorbate 80) or stabilizers (for example, gelatine or sorbitol) (Mitkus et al., 2013). Various products used in the manufacture of vaccines could theoretically also be carried over to the final product and are included as potential trace components of a vaccine, including antibiotics, egg or yeast proteins, latex, formaldehyde and/or gluteraldehyde and acidity regulators (such as potassium or sodium salts) (Eldred et al., 2006).

Table 2 Types of vaccine first introduces (Plotkin 2020).

Sr.No	Type of vaccine	Licensed vaccines Used	First introduced
1.	Live attenuated (weakened or inactivated)	Measles, mumps, rubella, yellow fever, influenza, oral polio, typhoid, Japanese encephalitis, rotavirus, BCG, varicella zoster	1798 (smallpox)
2.	Killed whole organism	Whole-cell pertussis, polio, influenza, Japanese encephalitis, hepatitis A, rabies	1896 (typhoid)
3.	Toxoid	Diphtheria, tetanus	1923 (diphtheria)
4.	Subunit (purified protein, recombinant protein, polysaccharide, peptide)	Pertussis, influenza, hepatitis B, meningococcal, pneumococcal, typhoid, hepatitis A	1970 (anthrax)

3. Adjuvants and delivery systems for enhancing vaccine efficacy

One effective method of avoiding infectious illnesses is vaccination. They function by exposing the body to a weakened or dormant version of a microbe or virus, which aids in the immune system's development of disease resistance. But on their own, some vaccinations fail to elicit a potent enough immune response. Adjuvants and delivery methods are useful in this situation.

Ingredients called adjuvants are added to vaccinations in order to enhance the immunological response.

They function in many ways, including:

• **Drawing immune cells, including antigen-presenting cells (APCs), to the injection site:** This produces a small-scale inflammatory response that draws immune cells to the location. Antigen-presenting cells, or APCs, are white blood cells that absorb and digest the components of viruses or bacteria that the immune system recognizes (Fachada, 2008).

• **Assisting APCs in more efficiently presenting antigens:** After absorbing antigens, APCs fragment them into smaller pieces and display them to other immune cells, such T cells and B cells, on their surface. Adjuvants can aid in the development of APCs and increase their capacity to present antigens (Grødeland et al., 2015).

• **Activating immune cells:** Adjuvants can also directly stimulate the production of more antibodies or other immunological components by immune cells.

Another strategy to increase vaccination effectiveness is through delivery methods. They serve as transporters, shielding the antigen and assisting in its delivery to the appropriate immune system cells. Typical delivery methods include the following:

• Liposomes are microscopic spheres composed of lipid molecules that have the ability to encase antigens. Antigens can be directed towards APCs and shielded from destruction by liposomes.

• Polymer nanoparticles are artificial polymer-based particles with the ability to encase antigens. It is possible to engineer polymer nanoparticles so that they release antigens gradually over time, perhaps promoting a longer-lasting immune response (Zhou et al., 2023).

• Viral-like particles, also known as VLPs, are essentially viral shells that have been modified to contain antigens. Because VLPs may imitate a virus's structure, they may aid in eliciting a potent immune response (Shirbaghaee & Bolhassani, 2016).

• By using adjuvants and delivery systems, scientists can develop more effective vaccines that provide longer-lasting protection against infectious diseases.

Here are some of the benefits of using adjuvants and delivery systems in vaccines:

Enhanced immunogenicity: Vaccines can be rendered more immunogenic, or more likely to elicit a potent immune response, by the addition of adjuvants and delivery mechanisms.

Broader immune reaction: Certain adjuvants have the ability to boost the cellular immune response, which destroys infected cells, as well as the humoral immunological response, which creates antibodies (Schijns et al., 2020).

Lower vaccine dosage: Adjuvants and delivery methods may occasionally permit the use of a lower dose of antigen in a vaccination, hence lowering the possibility of adverse reactions.

Better thermostability: Certain delivery methods can shield antigens from deterioration at high temperatures, which can facilitate the storage and transportation of vaccinations. In general, adjuvants and delivery methods play a significant role in the creation of contemporary vaccines. They may improve the safety, efficacy, and convenience of vaccination administration.

4.Innovations in Vaccine Design

Microbial pathogens have developed complex and efficient ways of counteracting and evading innate and adaptive immune mechanisms. The strategies used by pathogens determine strongly the type of immune response a vaccine should elicit and how the vaccine should be formulated. Improved knowledge of immune response mechanisms has brought successes in the development of vaccines that protect against challenging pathogens as well as vaccines that can be used in immune-compromised and elderly populations. This includes the production of highly purified antigens that provide a better reactogenicity and safety profile than some of the early whole-pathogen vaccines. Successful attempts to improve anti- gen purity, however, can result in weakened immunogenicity. Modern human vaccine development builds on understanding of the etiology, epidemiology and pathogenesis of the target infection or disease, as well as the target population (Meyer & Zepp, 2022).

4.1. Genetic engineering approaches in vaccine development

The development of vaccines has been transformed by genetic engineering, which provides precise techniques for the creation of efficient and tailored vaccinations. The following is how the creation of vaccines uses genetic engineering:

4.1.1 Subunit Vaccines:

This is a popular method in which genetic engineering techniques are used to introduce a gene expressing a particular antigen (protein that elicits immunity) from a virus or bacteria into a harmless host cell (bacteria, yeast). This approach makes it safer by removing the need to handle the pathogen in its whole. The host cell machinery then creates the antigen, which is purified and utilized in the vaccine. One effective example of a subunit vaccination created by genetic engineering is the Hepatitis B vaccine (Jorge & Dellagostin, 2017).

5.1.2. Viral Vector Vaccines:

In this instance, the gene encoding a desired antigen from another disease is transferred into a weaker virus. By acting as a vector, this altered virus enters the host cells and delivers the antigen. Once within, the antigen is produced by the host cells, which prompts the immune system to identify and mount an attack against the pathogen of interest. Vaccines using viral vectors have the potential to stimulate both cellular and humoral (antibody) immune responses with great efficacy. Two examples of vaccinations using viral vectors are the COVID-19 and the human papillomavirus (HPV) vaccines (Lundstrom, 2020).

4.1.3. DNA Vaccines:

The strategy here makes use of plasmids, which are tiny circular DNA molecules that carry the target antigen's gene. The body is immediately injected with the plasmid DNA. The plasmid is taken up by host cells, which then use its genetic material to create the antigen and start an immunological reaction (Shedlock & Weiner, 2000). While still in the early stages of research, DNA vaccines have the potential to be advantageous due to their simple manufacturing and capacity to stimulate both humoral and cellular immunity.

4.1.4. Reverse Vaccinology:

To find possible targets for vaccines, this method makes use of genetic data from pathogens. To identify genes encoding proteins necessary for the pathogen's survival or infection process, scientists examine the genome of the pathogen. Then, depending on their capacity to elicit immunity these proteins are assessed as possible candidates for vaccination. Reverse vaccinology can be helpful in discovering antigens from novel or complicated diseases and enables a more focused approach to vaccine development (Sette & Rappuoli, 2010). With the use of genetic engineering, vaccinations can be more precisely, safely, and effectively designed. We may anticipate even more developments in this area as research goes on, which will result in the creation of vaccinations against a larger variety of illnesses.

5. Recombinant vaccines and vectored vaccines

When it comes to combating infectious illnesses, recombinant and vectored vaccines are the fruits of genetic engineering's potent tree. Though they employ distinct strategies, they both aim to boost immunity:

5.1. Recombinant Vaccines: The Targeted Approach

Concept is that the antigen, a protein molecule that the immune system recognizes and mounts defenses against, is the precise target that recombinant vaccines aim to deliver.

Method used was by inserting the gene encoding a desired antigen from a virus or bacteria into a harmless host cell, such as yeast or bacteria, scientists can achieve their goals through genetic engineering. This cell produces a lot of the antigen, almost like a factory. After purification, the antigen is added to the vaccine.

Importance:

They pose little danger of infection because they don't contain the entire virus or bacterium.

Precision: They concentrate the immunological response by targeting the particular antigen that confers immunity.

Proven Efficacy: Several effective vaccinations, such as the Shingles (Herpes Zoster) vaccine and the Hepatitis B vaccine has been proved greater efficacy.

5.2. Vectored Vaccines: The Trojan Horse Strategy

The Idea was that Vectored vaccines transfer the genetic information needed to produce the target antigen by using a modified, weakened virus as a carrier. The technique used was genetic engineering, researchers may transfer the gene encoding for an antigen from one disease to a weaker virus (vector). The antigen is subsequently injected into the body's cells by means of this altered virus. The immune system is triggered to identify and combat the target pathogen by the antigen that the cells create after interpreting the instructions.

Importance:

1. Strong immunological Reaction: Viral vectors may trigger a strong immunological response that includes both cellular immunity and antibody production. They are also highly effective in delivering the antigen. This is comparable to an illness that occurs naturally, providing robust defence.

2. Flexible Platform: Vaccine development can be more effectively accomplished by using the same weakened virus as a vector to transmit antigens from several infections. Examples include the COVID-19 vaccine (AstraZeneca) and the HPV vaccination.

5.3. Key Differences

• **Delivery method:** Recombinant vaccines deliver the purified antigen directly, while vectored vaccines use a modified virus as a carrier.

• **Immune response:** Vectored vaccines often induce a stronger immune response due to the stimulating effect of the viral vector.

• **Development time:** Recombinant vaccines can be faster to develop compared to vectored vaccines, which require engineering a safe and effective vector.

In essence, recombinant vaccines are like giving the immune system a clear picture (the antigen) of the enemy. Vectored vaccines, on the other hand, are like sending an undercover agent (modified virus) carrying the enemy's blueprint (antigen gene) to trigger a more vigorous response. Both approaches have revolutionized vaccine development, offering safe and effective ways to prevent infectious diseases.

6. Nanotechnology and novel delivery platforms

Nanotechnology has emerged as a game-changer in vaccine development, offering innovative ways to deliver vaccines and enhance their efficacy.

What is Nanotechnology?

Nanotechnology deals with manipulating materials at the atomic and molecular level, creating structures in the range of 1-100 nanometers (nm). For comparison, a human hair is about 80,000 nm wide! At this nanoscale, materials exhibit unique properties that can be harnessed for various applications, including medicine.

Nanotechnology offers advantages in delivering therapeutic cargoes for modulating immune cell activity, including selective targeting, controlled release, greater bio distribution, and prolonged effects. It can enhance anti-tumor immunity of immune cells like T cells or NK cells, and "re-educating" tumor-associated immune cells like tumor-associated macrophages (TAMs) is a promising strategy for immunotherapy and immune-engineering. TAMs, classified as M2d, are critical therapeutic targets as they constitute the major immune cell populations in tumors and mediate immunosuppression through IL-10 and TGF-β. Strategies to deplete or re-polarize TAMs have been extensively investigated, and tumor micro environment (TME) reprogramming approach is a promising therapeutic strategy for cancer immunotherapy by enhancing anti-tumor immunity. Combining nanotechnology with immune-modulatory agents, particularly checkpoint blockade and microenvironment reprogramming, is a promising approach for cancer immunotherapy.

6.1. Delivery of protein-based immune-modulators

In recent years, the development of checkpoint inhibitors, particularly monoclonal antibodies (mAbs), has significantly advanced. PD-1, a major immune checkpoint, is expressed by activated T cells, B cells, and monocytes. Cancers often hijack this pathway to evade immune surveillance, enhancing anti-tumor immunity. Despite the clinical success of mAb-based checkpoint blockade therapy, systemic administration can still suffer from premature degradation and off-target toxicities. Several groups have worked on direct delivery of PD-1 antibodies using biodegradable

Nano carriers like PLGA or UCNP. PD-1 antibodies can be co-delivered with other adjuvants or small molecule inhibitors to improve efficacy. Recent advances have focused on triggered-release systems based on tumor microenvironment cues, such as pH, reactive oxygen species (ROS), or matrix metalloproteinase (MMP) expression. A MMP-mediated, biodegradable DNA nano-cocoon has been developed, allowing both CpG-oligodeoxynucleotides (CpG-ODN) and PD-1 antibodies to be co-loaded into the same nanocomplex for preventing postsurgical tumor relapse. The release of the cargoes is mediated by the cleavage of the triglycerol monostearate capsules encasing the restriction enzyme Hhal by MMPs. A separate study utilizing MMP2-mediated degradation co-encapsulated IMD-0354-containing lipid nanoparticles with PD-1 antibodies in a Nano gel to achieve PD-1 blockade and TAM repolarization. This combination approach targeted both T cells and M2 TAMs, leading to significant tumor growth inhibition and extended survival of mice bearing B16 tumors. Other checkpoint inhibitors have been directly delivered or combined with other Nano materials to achieve greater therapeutic efficacy.

6.2. Delivery of nucleic acid-based immune-modulators

Nucleic acids, such as plasmid DNA (pDNA), messenger RNA (mRNA), short interfering RNA (siRNA), and microRNA, have been found to modulate the immune system. The negative charge of nucleic acids allows them to be encapsulated using cationic materials with high efficiency. SiRNA-mediated knockdown has been formulated into various types of nanoparticles composed of lipids, polymers, and inorganic matrices for modulating the target immune cell. RNA therapeutics have a significant advantage over DNA therapeutics for immunotherapy because RNA can function readily in the cytosol, whereas DNA must localize to the nucleus for proper expression. This creates a major barrier for non-viral plasmid DNA delivery into immune cells, including primary T cells, NK cells, DCs, and macrophages.

Recent efforts have focused on developing biodegradable platforms for clinical translation, like protein therapeutics. These biodegradable platforms could consist of either polymeric, lipid, or inorganic materials. A hybrid lipid calcium phosphate nanoparticle (LCP NPs) was developed that encapsulated PD-1 siRNA, resulting in greater killing efficacy and cytokine production. Hanafy et al. developed lipid nanoparticles containing acid-labile PEG linkers for the down regulation of PD-1 on tumor-infiltrating lymphocytes (TAMs). They observed increased uptake of the acid-sensitive PEG lipid nanoparticles in macrophages, leading to reduced tumor size and PD-1 expression. To enhance the efficacy and targeting of TAMs, researchers have focused on key receptors, such as CD163 and CD206. Zhang et al. synthesized a poly (β-amino ester) (PBAE) Nano-carrier coated with poly (glutamic acid)-mannose for the targeted co-delivery of in vitro-transcribed (IVT) IRF5 and IKK mRNA (3:1) in an ovarian cancer mouse model. However, the authors did not observe complete eradication of tumors in the various mouse models tested, suggesting that this approach is best used in combination with other therapies for efficacy.

7. Vaccination Strategies for Livestock

Effective livestock vaccination methods priorities biosecurity measures, follow a well-defined schedule taking age and illness into account, target herd immunity, and customize immunizations to unique farm hazards (core vs. non-core). These strategies help assure healthy herds. By keeping track of vaccines, an all-encompassing strategy for food safety and animal protection may be developed, including tracking and revaccination.

7.1. Herd immunity and vaccination coverage

Although direct protection of individuals through vaccination has been the focus of most vaccine development and is crucial to demonstrate for the licensure of new vaccines, it has become apparent that a key additional component of vaccine-induced protection is herd immunity, or more correctly ‘herd protection’(Fine, 1993). Vaccines cannot protect every individual in a population directly, as some individuals are not vaccinated for various reasons and others do not mount an

immune response despite vaccination. Fortunately, however, if enough individuals in a population are vaccinated, and if vaccination prevents not only the development of disease but also infection itself (discussed in more detail below), transmission of the pathogen can be interrupted and the incidence of disease can fall further than would be expected, as a result of the indirect protection of individuals who would otherwise be susceptible. For highly transmissible pathogens, such as those causing measles or pertussis, around 95% of the population must be vaccinated to prevent disease outbreaks (Ruderfer & Krilov, 2015), but for less transmissible organisms a lower percentage of vaccine coverage may be sufficient to have a substantial impact on disease (for example, for polio, rubella, mumps or diphtheria, vaccine coverage can be ≤86%). variable from season to season and is also confounded by the variability in vaccine effectiveness each year (Wright, 2022). Modest vaccine coverage, of 30–40%, is likely to have an impact on seasonal influenza epidemics, but ≥80% coverage is likely to be optimal (Pollard & Bijker, 2021). Interestingly, there might be a downside to very high rates of vaccination, as the absence of pathogen transmission in that case will prevent natural boosting of vaccinated individuals and could lead to waning immunity if booster doses of vaccine are not used. Apart from tetanus vaccine, all other vaccines in the routine immunization schedule induce some degree of herd immunity which substantially enhances population protection beyond that which could be achieved by vaccination of the individual only. Tetanus is a toxin-mediated disease acquired through infection of breaks in the skin contaminated with the toxin-producing bacteria Clostridium tetani from the environment so, vaccination of the community with the tetanus toxoid will not prevent an unvaccinated individual acquiring the infection if they are exposed. As an example of the success of herd immunity, vaccination of children and young adults (up to 19 years of age) with capsular group C meningococcal vaccine in a mass campaign in 1999 resulted in almost complete elimination of disease from the UK in adults as well as children (Borrow et al., 2017). Currently, the strategy for control of capsular groups A, C, W and Y meningococci in the UK is vaccination of adolescents, as they are mainly responsible for transmission and vaccine-mediated protection of this age group leads to community protection through herd immunity (Pollard & Bijker, 2021). The HPV vaccine was originally introduced to control HPV-induced cervical cancer, with vaccination programs directed exclusively at girls, but it was subsequently found to also provide protection against HPV infection in heterosexual boys through herd immunity, which led to a marked reduction in the total HPV burden in the population (Brisson et al., 2016).

7.2. Vaccination schedules and timing

For most vaccines that are used in the first year of life, 3–4 doses are administered by 12 months of age. Conventionally, in human vaccinology, 'priming' doses are all those administered at less than 6 months of age and the 'booster' dose is given at 9–12 months of age. So, for example, the standard WHO schedule for diphtheria–tetanus–pertussis-containing vaccines (which was introduced in 1974 as part of the Expanded Program on Immunization) consists of 3 priming doses at 6, 10 and 14 weeks of age with no booster (Liang, 2018). This schedule was selected to provide early protection before levels of maternal antibody had waned (maternal antibody has a half-life of around 30–40 days, so very little protection is afforded to infants from the mother beyond 8–12 weeks of age) and because it was known that vaccine compliance is better when doses are given close together (Healy et al., 2020). However, infant immunization schedules around the world are highly variable few high-income or middle-income countries use the Expanded Programed on Immunization schedule and were largely introduced with little consideration of how best to optimize immune responses. Indeed, schedules that start later at 8–12 weeks of age (when there is less interference from maternal antibody) and have longer gaps between doses (8 weeks rather than 4 weeks) are more immunogenic. A large number of new vaccines have been introduced since 1974 as a these have generally been fitted into existing schedules without taking into account the optimal scheduling for these new products. It should also be noted that surveys show vaccines are rarely delivered on schedule in many countries and, thus, the published schedule may not be how vaccines are actually delivered on the ground. This is particularly the case in remote areas (for

example, where health professionals only visit occasionally) and regions with limited or chaotic health systems, leaving children vulnerable to infection (Healy et al., 2020).

8. Challenges and Solutions in Vaccine Development for Livestock

Livestock vaccines face unique challenges due to their diverse immune responses, cost-effectiveness for farmers, and specific diseases. The complex immune systems of livestock require multiple vaccinations or adjuvants, and developing vaccines for diseases in developing countries may not be commercially attractive for pharmaceutical companies. Additionally, thermo stability issues can hinder vaccines in regions with limited cold chain infrastructure. To overcome these challenges, research is focusing on novel platforms like recombinant technology and nanoparticles to create more immunogenic and thermo stable vaccines. Collaborations between public and private sectors are crucial to prioritize vaccines for neglected diseases and ensure affordability in resource-limited settings. Innovation in delivery methods, such as single-dose or mucosal vaccines, can further improve livestock vaccination programs.

8.1. Antigenic variation and pathogen diversity

Infectious diseases are primarily caused by Antiviral Viruses (AVPs), which escape immunity through changes in molecular structures recognized by antibodies or T cells. The development of vaccines against AVPs presents an unprecedented challenge, as researchers must consider the mechanism of action of immune cells and the complex interaction between these cells and rapidly changing epitopes in APVs and cancer cells. CD8C T cells are key components of the immune response against many intracellular pathogens and tumors, and effective vaccines against AVPs will likely need to induce broad and potent cellular immune responses (Servín-Blanco et al., 2016).

The observation that whole protein antigens (Ags) are not necessarily essential for inducing protective immunity has led to the emergence of "structural vaccinology." Structure-based vaccines are designed on the rationale that suitable epitopes should be sufficient to induce protective immune responses against pathogens, including AVPs. Epitope recognition in MHC-restricted T-cell responses involves two different binding events: small peptides bind to MHC molecules after Ag processing, and the resulting peptide-MHC (pMHC) complex is bound by T-cell receptor (TCR) leading to cell activation (Wu et al., 2019).

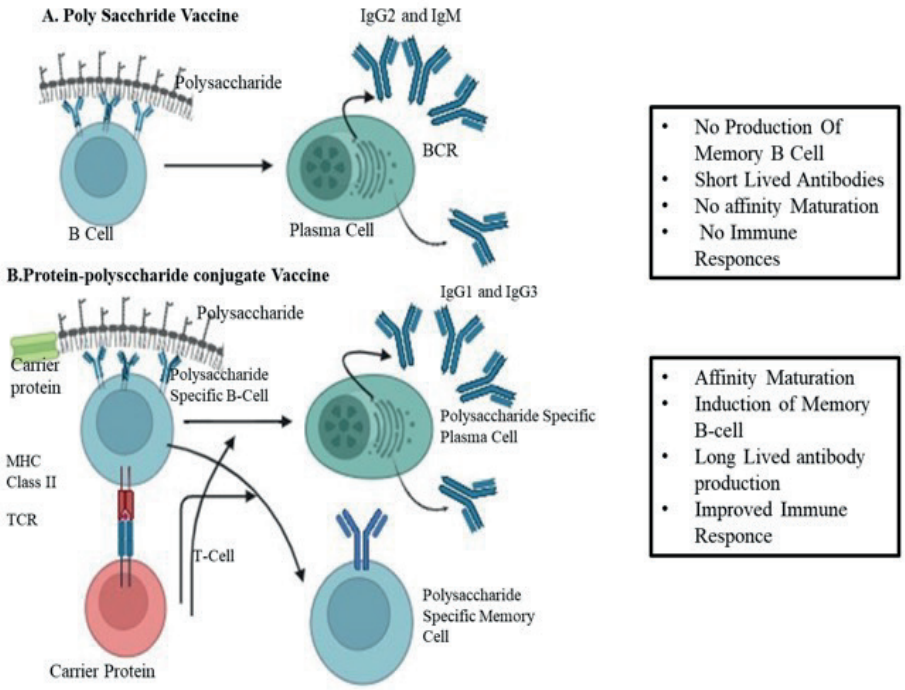


Figure 3: Immune Response of Vaccine

Unprecedented TCR promiscuity explains how a relatively small number of T cells provide effective immune recognition of all possible peptides or why TCRs are cross-reactive. Combinatorial synthetic peptide libraries were used to elucidate the nature of TCR promiscuity, explaining why TCR/MHC interactions are of low affinity and degenerate (Trenh, 2018).

Another important emerging challenge faced by scientists is the presence of a large number of potential epitopes in viral, tumor, and model systems, encoded by short non-primary open reading frames (sORF) and referred to as defective ribosomal products (DRiPs). These "unexpected" epitopes may be targets of a significant portion of yet unappreciated cellular immune responses. AVPs (Antiviral Virulence Factors) have been identified as key factors in the development of universal safe anti-influenza vaccines. Current influenza vaccines rely on inducing antibodies specific for hemagglutinin (HA) and neuraminidase (NA), but due to antigenic variability and immune evasion, yearly vaccinations are necessary. A universal influenza vaccine has been an important objective for decades, but many failed attempts have been made. Recent studies have shown that memory cytotoxic T lymphocytes (CTLs) specific for conserved epitopes of the novel H7N9 influenza A virus can elicit strong CTL responses against any human influenza A virus. However, specific HLA alleles expressed by certain ethnic groups, such as indigenous Australian and Alaskan populations, were associated with poor CTL responses, indicating additional challenges for vaccine development (Hensen et al., 2021).

Recent results highlight the need to design novel high-impact CTL inducing vaccines with greater capacity to suppress antigenic drift, as prior population immunity may reduce the expected impact of vaccines for pandemic influenza control. Successful preclinical studies have shown that vaccination of mice with a mixture of virus-like particles (VLPs) individually displaying four different HAs offered significant protection against a variety of influenza A viruses. Stable HA stem Ags, bearing smaller versions of full-length HA called "mini-HAs" or HA stem mimics, were engineered and shown to protect mice in lethal heterologous and hetero-subtypes challenge models and reduce fever after sub-lethal challenge in cynomolgus monkeys.

DENV, the etiologic agent of dengue fever, has also faced challenges due to high genetic/antigenic variability and the existence of four viral serotypes. The outcome of DENV infection depends on the balance between favorable and unfavorable immune responses, and specific Abs and T cells induced by vaccination may have both protective and detrimental effects. A live-attenuated tetravalent vaccine (DENGVAXIA) containing antigens from all four DENV serotypes has been licensed recently, addressing OAS to some extent. Further research is warranted to develop a universal vaccine against HCV, which causes most acute and chronic liver diseases worldwide (Silva, 2023).

9. Vaccine efficacy in diverse livestock populations

Vaccination has long been considered the most effective defense against infectious diseases, with the primary goal of improving animal health and preventing or reducing pathogen transmission to mitigate the impact of infectious diseases on livestock production. However, the effectiveness of available vaccines is contentious, as they often only confer limited sterilizing immunity, may not prevent infection, and may only partially reduce pathogen transmission. An effective vaccine should reduce within-host pathogen burden, prevent or alleviate disease-induced clinical signs, and improve the general health conditions of exposed animals (Yadav et al., 2020).

Different desirable properties of an effective vaccine include high safety, high sterilizing immunity against a wide range of variant pathogen strains, fast onset of protection, high immunogenicity, and vaccine responsiveness in a broad range of hosts. However, few vaccines on the market satisfy all of these properties. These properties play a crucial role in pathogen transmission and vaccine effectiveness on a population level. Sterilizing immunity affects a host's susceptibility to infection with a heterologous strain, while the impact of a vaccine on pathogen shedding affects an individual's infectivity. Vaccines that accelerate host recovery reduce pathogen transmission by reducing the

infectious period of a host. However, delay in onset of protection or host heterogeneity in vaccine response limit the time or extent of effective vaccine coverage in a population, enabling continued pathogen transmission (Yadav et al., 2020). The effectiveness of a given vaccine in the field depends on the properties of the vaccine itself, how the vaccine is applied, and other biosecurity measures in place. For example, herd closure during a disease outbreak is promoted as a highly effective disease control strategy, while continuous influx of new susceptible, possibly non-vaccinated individuals contributes to long-term disease persistence in a herd (Opriessnig & Doeschl-Wilson, 2019).

Common vaccination strategies for livestock diseases include prophylactic and reactive mass vaccination. Prophylactic vaccination is applied before introducing a pathogen into a herd to prevent recurrence of disease outbreaks or to minimize the risk of a major epidemic. Reactive vaccination, although less effective than prophylactic vaccination, is typically used to control ongoing epidemics. However, the application of either strategy is often hindered by insufficient vaccine availability, economic reasons, safety restrictions, and logistic delays. These factors affect the frequency and timing of vaccination and the effective vaccine coverage in a population (Opriessnig & Doeschl-Wilson, 2019). There is currently no theoretical framework to systematically assess how different vaccine properties and vaccination strategies influence infection invasion and transmission in herds with different demographics. This makes predictions of vaccine effectiveness in the field extremely difficult. For example, the Porcine Reproductive and Respiratory Syndrome (PRRS), caused by the PRRS virus (PRRSv), is an infectious disease that requires a comprehensive framework that combines diverse factors compromising vaccine effectiveness (Johnson, 2009). PRRS is one of the most significant and costly swine diseases globally, with estimated costs per year over $650 million in the United States and almost 1.5 billion € in Europe. Failed vaccination programs have raised an urgent demand for more effective vaccines, and concerns have been raised about the epidemiological consequences of vaccination and the evaluation of vaccination effectiveness.

PRRS vaccines, categorized into modified-live virus (MLV) and inactivated or killed virus (KV), have not been fully effective in preventing the spread of the virus within a herd. MLV vaccines, which are attenuated live vaccines, have shown delayed but effective protection against homologous and some heterologous PRRSv strains. However, their limited sterilizing immunity and immunogenicity to many circulating PRRSv strains have raised concerns about vaccine effectiveness (Zhou et al., 2021). KV vaccines, containing adjuvants, are known for their high safety but have limited sterilizing immunity against homologous or heterologous PRRSv strains. They often fail to significantly reduce clinical signs, viremia, and duration of shedding in naïve animals. In PRRSv-negative pigs, KV vaccines have failed to elicit detectable antibodies and barely elicit cell-mediated immune response. In PRRSv-positive pigs, reactive vaccination has been reported to strengthen both types of immune responses to the infecting virus, speeding up recovery and potentially reducing infectivity (Bitsouni et al., 2019). Efforts over the last three decades to understand PRRS pathogenesis and vaccinology have been tremendous, but effective PRRS vaccines with safety, broad sterilizing immunity, and high immunogenicity are still lacking. Little is known about how existing vaccines affect virus transmission in a herd or how they could be most effectively applied to prevent or reduce PRRS outbreaks. Mathematical models have proven powerful tools for assessing the combined effects of several interacting factors on virus transmission and predicting the outcome of different types of vaccines or vaccination strategies (Lunney et al., 2016).

10. Future Directions in Livestock Vaccine Development

Looking further into the future, we can expect many more advances in vaccinology and new licensed vaccines, not only against infectious diseases but also against other diseases or chronic disorders not necessarily associated with an infectious pathogen. With therapeutic cancer vaccines, there have been promising results with a number of spontaneous tumor animal models, including models of breast, prostate, pancreatic and colon cancer (Ostrand-Rosenberg, 2004), involving antigen-specific vaccines and DC vaccines formulated with patients' Ds loaded with

tumor- associated antigens (Tagliamonte et al., 2014). Also, several cytokines are beinge valuated as cancer vaccine adjuvants, most notably GM-CSF. DC vaccines and ASCI (antigen-specific cancer immuno therapeutics) represent the most advanced approaches in cancer immuno therapy. DC vaccines work by isolating and culturing the cancer patient's DC s in the laboratory. When in culture, the DCs are exposed to compounds that include tumors associated antigens, so that upon the ire introduction to the patient, these DCs promote a cytotoxic T cell response against the tumors. The DC vaccine targeted against prostate cancer, Provenge® (sipuleucel-T; Dendreon Corp, Seattle, USA),has recently been licensed by the FDA (Cheever & Higano, 2011). ASCI includes a potential novel class of compounds that target antigens that are selectively expressed by tumor cells, this approach his aimed at teaching the patient's immune system of fight cancer. One of the lead tumor antigens used in the ASCI approach his MAGE-A3 that is expressed in a variety of tumors such as melanoma, NSCLC, bladder and hepato carcinoma. MAGE-3 has been formulated with an Adjuvant System selected for its stability to induce high antibody and robust T cell responses. This formulation has shown encouraging results: proof of concept has been established in phase II studies on Non-Small- Cell-Lung-Cancer (NSCLC) and melanoma, and the Phase III studies are under way on both cancers (Brichard & Lejeune, 2008). A different approach is tried with an epidermal growth factor vaccine against NSCLC. It targets the epidermal growth factor receptor which is over expressed in up to 80% of NSCLC patients and associated with resistance to cytotoxic agents (Vinageras et al., 2008). Allergic diseases affect upto 25% of the population in western countries and may result in life-threatening allergic reactions. Novel immunotherapies are currently under development. Among them a vaccine including aTLR-9 agonist (Broide, 2009).

A phase 2 study with a ragweed allergen conjugated to immune stimulatory DNA (CpG) showed reduction in symptoms of allergic rhinitis during the ragweed season (Creticos et al., 2006), but further studies are needed to confirm these observations. Advances are also expected to treat autoimmune diseases like, type 1 diabetes, arthritis, Alzheimer's disease, or multiple sclerosis. Encouraging results with DNA vaccines have been found in Phase 1 and 2 studies for multiple sclerosis and type 1 diabetes, with intravenous immune globulin Sina Phase1 study for Alzheimer's disease (Relkin et al., 2009). The continuing progress in vaccine technologies and in the understanding of the mechanisms underlying in the immune response is producing a more and more refined approach to vaccine design tailored to the desired effect of combating disease.

11. Conclusion

Vaccine development for livestock aims to prevent animal illnesses and improve companion animal health. Traditional immunizations are based on cell membrane chemicals, toxoids, or live microorganisms. Recombinant vaccines use structure-based design, epitope-focused design, or genomic-based screening to overcome limitations. Vaccines are developed to increase livestock production, improve companion animal health, and prevent animal-to-human transmission. Modern vaccine design mimics the naturally occurring immune response without inducing the disease. Adjuvants like aluminum salts have been introduced to improve immunogenicity. Vaccines are classified as live or non-live, and contain adjuvants and delivery systems to enhance their immunological response. These factors improve the safety, efficacy, and convenience of vaccination administration, leading to more effective vaccines. Vaccine design has evolved due to microbial pathogens' complex immune mechanisms, leading to the development of vaccines for challenging pathogens, immune-compromised, and elderly populations. Genetic engineering approaches, such as subunit, viral vector, DNA, and reverse vaccinology, have revolutionized vaccine development. Nanotechnology has also played a significant role in vaccine development, offering innovative ways to deliver vaccines and enhance efficacy. Livestock vaccination strategies prioritize biosecurity measures, follow a well-defined schedule, target herd immunity, and customize immunizations to unique farm hazards. Livestock vaccines face unique challenges due to their diverse immune responses, cost-effectiveness, and specific diseases. Research focuses on novel platforms and collaborations between public and private sectors to improve livestock vaccination programs.

References

Bitsouni, V., Lycett, S., Opriessnig, T., & Doeschl-Wilson, A. (2019). Predicting vaccine effectiveness in livestock populations: A theoretical framework applied to PRRS virus infections in pigs. PLoS One, 14(8), e0220738.

Bona, C. A. (2002). Principles of Vaccine Development. Immunotherapy for Infectious Diseases, 129-147.

Borrow, R., Alarcón, P., Carlos, J., Caugant, D. A., Christensen, H., Debbag, R., De Wals, P., Echániz-Aviles, G., Findlow, J., & Head, C. (2017). The Global Meningococcal Initiative: global epidemiology, the impact of vaccines on meningococcal disease and the importance of herd protection. Expert review of vaccines, 16(4), 313-328.

Brewer, J. M. (2006). (How) do aluminium adjuvants work? Immunology letters, 102(1), 10-15.

Brichard, V. G., & Lejeune, D. (2008). Cancer immunotherapy targeting tumour-specific antigens: towards a new therapy for minimal residual disease. Expert opinion on biological therapy, 8(7), 951-968.

Brisson, M., Bénard, É., Drolet, M., Bogaards, J. A., Baussano, I., Vänskä, S., Jit, M., Boily, M.-C., Smith, M. A., & Berkhof, J. (2016). Population-level impact, herd immunity, and elimination after human papillomavirus vaccination: a systematic review and meta-analysis of predictions from transmission-dynamic models. The Lancet Public Health, 1(1), e8-e17.

Broere, F., & van Eden, W. (2019). T cell subsets and T cell-mediated immunity. Nijkamp and Parnham's principles of immunopharmacology, 23-35.

Broide, D. H. (2009). Immunomodulation of allergic disease. Annual review of medicine, 60, 279-291.

Cheever, M. A., & Higano, C. S. (2011). PROVENGE (Sipuleucel-T) in prostate cancer: the first FDA-approved therapeutic cancer vaccine. Clinical Cancer Research, 17(11), 3520-3526.

Collier, M. A. (2017). Formulation and Characterization of Carrier Vehicles for Infectious Disease Treatment and Modulation of the Innate Immune System The University of North Carolina at Chapel Hill].

Creticos, P. S., Schroeder, J. T., Hamilton, R. G., Balcer-Whaley, S. L., Khattignavong, A. P., Lindblad, R., Li, H., Coffman, R., Seyfert, V., & Eiden, J. J. (2006). Immunotherapy with a ragweed–Toll-like receptor 9 agonist vaccine for allergic rhinitis. New England Journal of Medicine, 355(14), 1445-1455.

Ding, Y. (2000). Molecular mechanisms of interleukin-10-mediated immune regulation. University of Michigan.

Eldred, B. E., Dean, A. J., McGuire, T. M., & Nash, A. L. (2006). Vaccine components and constituents: responding to consumer concerns. Medical journal of Australia, 184(4), 170-175.

Fachada, N. (2008). Agent-based simulation of the immune system. Master's thesis, Instituto Superior Técnico, Lisboa (July 2008).

Fine, P. E. (1993). Herd immunity: history, theory, practice. Epidemiologic reviews, 15(2), 265-302.

Garçon, N., Chomez, P., & Van Mechelen, M. (2007). GlaxoSmithKline Adjuvant Systems in vaccines: concepts, achievements and perspectives. Expert review of vaccines, 6(5), 723-739.

Grødeland, G., Fossum, E., & Bogen, B. (2015). Polarizing T and B cell responses by APC-

targeted subunit vaccines. Frontiers in Immunology, 6, 145930.

Hammer, G. D., McPhee, S. J., & Education, M.-H. (2014). Pathophysiology of disease: an introduction to clinical medicine. McGraw-Hill Education Medical New York.

Healy, C. M., Rench, M. A., Swaim, L. S., Timmins, A., Vyas, A., Sangi-Haghpeykar, H., Ng, N., Rajam, G., Havers, F., & Schiffer, J. (2020). Kinetics of maternal pertussis-specific antibodies in infants of mothers vaccinated with tetanus, diphtheria and acellular pertussis (Tdap) during pregnancy. Vaccine, 38(37), 5955-5961.

Hensen, L., Illing, P. T., Bridie Clemens, E., Nguyen, T. H., Koutsakos, M., van de Sandt, C. E., Mifsud, N. A., Nguyen, A. T., Szeto, C., & Chua, B. Y. (2021). CD8+ T cell landscape in Indigenous and non-Indigenous people restricted by influenza mortality-associated HLA-A* 24: 02 allomorph. Nature communications, 12(1), 2931.

Higgins, D., Marshall, J. D., Traquina, P., Van Nest, G., & Livingston, B. D. (2007). Immunostimulatory DNA as a vaccine adjuvant. Expert review of vaccines, 6(5), 747-759.

Johnson, W. S. (2009). Porcine reproductive and respiratory syndrome virus (PRRSV): Immunization strategies, virulence of various isolates, and efficacy of DNA vaccination. Iowa State University.

Jorge, S., & Dellagostin, O. A. (2017). The development of veterinary vaccines: a review of traditional methods and modern biotechnology approaches. Biotechnology Research and Innovation, 1(1), 6-13.

Leroux-Roels, G. (2010). Unmet needs in modern vaccinology: adjuvants to improve the immune response. Vaccine, 28, C25-C36.

Liang, J. L. (2018). Prevention of pertussis, tetanus, and diphtheria with vaccines in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. Recommendations and reports, 67.

Lundstrom, K. (2020). Application of viral vectors for vaccine development with a special emphasis on COVID-19. Viruses, 12(11), 1324.

Lunney, J. K., Fang, Y., Ladinig, A., Chen, N., Li, Y., Rowland, B., & Renukaradhya, G. J. (2016). Porcine reproductive and respiratory syndrome virus (PRRSV): pathogenesis and interaction with the immune system. Annual review of animal biosciences, 4, 129-154.

Meyer, C. U., & Zepp, F. (2022). Principles in Immunology for the Design and Development of Vaccines. Vaccine Design: Methods and Protocols, Volume 1. Vaccines for Human Diseases, 27-56.

Mitkus, R. J., Hess, M. A., & Schwartz, S. L. (2013). Pharmacokinetic modeling as an approach to assessing the safety of residual formaldehyde in infant vaccines. Vaccine, 31(25), 2738-2743.

Mogensen, T. H. (2009). Pathogen recognition and inflammatory signaling in innate immune defenses. Clinical microbiology reviews, 22(2), 240-273.

Opriessnig, T., & Doeschl-Wilson, A. (2019). Predicting vaccine effectiveness in livestock populations: A theoretical framework applied to PRRS virus infections in pigs.

Ostrand-Rosenberg, S. (2004). Animal models of tumor immunity, immunotherapy and cancer vaccines. Current opinion in immunology, 16(2), 143-150.

Perreault, C. (2010). The origin and role of MHC class I-associated self-peptides. Progress in molecular biology and translational science, 92, 41-60.

Plotkin, S. A. (2020). Updates on immunologic correlates of vaccine-induced protection.

Vaccine, 38(9), 2250-2257.

Pollard, A. J., & Bijker, E. M. (2021). A guide to vaccinology: from basic principles to new developments. Nature Reviews Immunology, 21(2), 83-100.

Relkin, N. R., Szabo, P., Adamiak, B., Burgut, T., Monthe, C., Lent, R. W., Younkin, S., Younkin, L., Schiff, R., & Weksler, M. E. (2009). 18-Month study of intravenous immunoglobulin for treatment of mild Alzheimer disease. Neurobiology of aging, 30(11), 1728-1736.

Rojas-Downing, M. M., Nejadhashemi, A. P., Harrigan, T., & Woznicki, S. A. (2017). Climate change and livestock: Impacts, adaptation, and mitigation. Climate risk management, 16, 145-163.

Rubin, L. G., Levin, M. J., Ljungman, P., Davies, E. G., Avery, R., Tomblyn, M., Bousvaros, A., Dhanireddy, S., Sung, L., & Keyserling, H. (2014). 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clinical infectious diseases, 58(3), e44-e100.

Ruderfer, D., & Krilov, L. R. (2015). Vaccine-preventable outbreaks: still with us after all these years. Pediatric Annals, 44(4), e76-e81.

Schijns, V., Fernández-Tejada, A., Barjaktarović, Ž., Bouzalas, I., Brimnes, J., Chernysh, S., Gizurarson, S., Gursel, I., Jakopin, Ž., & Lawrenz, M. (2020). Modulation of immune responses using adjuvants to facilitate therapeutic vaccination. Immunological reviews, 296(1), 169-190.

Servín-Blanco, R., Zamora-Alvarado, R., Gevorkian, G., & Manoutcharian, K. (2016). Antigenic variability: obstacles on the road to vaccines against traditionally difficult targets. Human vaccines & immunotherapeutics, 12(10), 2640-2648.

Sette, A., & Rappuoli, R. (2010). Reverse vaccinology: developing vaccines in the era of genomics. Immunity, 33(4), 530-541.

Shedlock, D. J., & Weiner, D. B. (2000). DNA vaccination: antigen presentation and the induction of immunity. Journal of leukocyte biology, 68(6), 793-806.

Shirbaghaee, Z., & Bolhassani, A. (2016). Different applications of virus-like particles in biology and medicine: vaccination and delivery systems. Biopolymers, 105(3), 113-132.

Silva, J. P. (2023). Immunogenicity of the NIAID's Live Attenuated Tetravalent Dengue Vaccine in Primary Human Systems Icahn School of Medicine at Mount Sinai].

Tagliamonte, M., Petrizzo, A., Tornesello, M. L., Buonaguro, F. M., & Buonaguro, L. (2014). Antigen-specific vaccines for cancer treatment. Human vaccines & immunotherapeutics, 10(11), 3332-3346.

Thomas, S., Abraham, A., Rodríguez-Mallon, A., Unajak, S., & Bannantine, J. P. (2022). Challenges in veterinary vaccine development. Vaccine Design: Methods and Protocols, Volume 2. Vaccines for Veterinary Diseases, 3-34.

Trenh, P. (2018). An Examination of MHC, Peptide, and TCR Interactions

Vinageras, E. N., de la Torre, A., Rodríguez, M. O., Ferrer, M. C., Bravo, I., del Pino, M. M., Abreu, D. A., Brooks, S. A., Rives, R., & del Castillo Carrillo, C. (2008). Phase II randomized controlled trial of an epidermal growth factor vaccine in advanced non-small-cell lung cancer. Journal of clinical oncology, 26(9), 1452-1458.

Wright, T. J. (2022). Subnational Data to Inform Measles Vaccination Campaigns in Children Under 5 Years in Tanzania Walden University].

Wu, P., Zhang, T., Liu, B., Fei, P., Cui, L., Qin, R., Zhu, H., Yao, D., Martinez, R. J., & Hu, W. (2019). Mechano-regulation of peptide-MHC class I conformations determines TCR antigen

recognition. Molecular cell, 73(5), 1015-1027. e1017.

Yadav, D. K., Yadav, N., & Khurana, S. M. P. (2020). Vaccines: present status and applications. In Animal biotechnology (pp. 523-542). Elsevier.

Zepp, F. (2010). Principles of vaccine design—lessons from nature. Vaccine, 28, C14-C24.

Zhou, D.-W., Wang, K., Zhang, Y.-A., Ma, K., Yang, X.-C., Li, Z.-Y., Yu, S.-S., Chen, K.-Z., & Qiao, S.-L. (2023). mRNA therapeutics for disease therapy: principles, delivery, and clinical translation. Journal of Materials Chemistry B, 11(16), 3484-3510.

Zhou, L., Ge, X., & Yang, H. (2021). Porcine reproductive and respiratory syndrome modified live virus vaccine: a "leaky" vaccine with debatable efficacy and safety. Vaccines, 9(4), 362.

About The Authors

Arooj Fatima earned Bachelor in microbiology from Cholistan university of veterinary and animal sciences (CUVAS) Bahawalpur Pakistan. currently she is doing M.phil in Microbiology from Cholistan university of veterinary and animals sciences (CUVAS) Bahawalpur Pakistan. Her research interest in Microbial genetics, Molecular biology, soil microbiology, plant Microbiology and food quality and its application. She has published more than 3 articles and 6 in national and international journals.

Email: aroojfatima31202@gmail.com ORCID:0000-0002-4709-4177

Shafeeq Ur Rehman earned his Bachelor in Applied microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. Currently he is pursuing M. phil in Microbiology from Cholistan University of Veterinary and Animal Sciences (CUVAS) Bahawalpur Pakistan. He is also working as research assistant in a project titled as "Robust Molecular Detection of Silent Circulation of FMD and PPR Viruses in Cholistan as a Model for Disease-Free Zone". His research interest is in FMD and PPR Viruses, Mucosal Immunity, Virology, Molecular cell biology, Cell culture, Microbial genetics and CRISPR case tools for combating viral diseases. He has published 7 articles and many book chapters in national and international journals.

Email: shafeequrrehmanbhutta@gmail.com ORCID: 0000-0003-3571-8226

Faizan Ali is doing BS Applied Microbiology from Cholistan university of veterinary and animal sciences (CUVAS) Bahawalpur Pakistan. His research interests are cell culture techniques, virology, genetics and molecular cell biology.

Email: faizansarwarali@gmail.com ORCID: 0009-0008-1066-7446

Minahal Fatima and She is doing M.Phil in Zoology, Wildlife and Fisheries from University of Agriculture, Fasilabad, Pakistan. Her research interest includes fish survival via changing the environmental factor. Not only the fish survive it also counts the progeny's survival. She has only one paper in International Journal and 12 Chapters in national and international Journals.

Email: fatimaabdulhameed08@gmail.com ORCID: 0009-0003-4387-6854

Khizar Abbas earned Bachelor in Applied microbiology from Cholistan university of veterinary and animal sciences(CUVAS) Bahawalpur Pakistan. Currently he is doing M.phil in Microbiology from Cholistan university of veterinary and animals sciences (CUVAS) Bahawalpur Pakistan. His research interest in Microbial genetics, Virology, Molecular biology and Biotechnology.

Email: khizarabbas2395@gmail.com ORCID:0009-0005-9044-1161

Dr. Muhammad SAFDAR earned his PhD in Molecular Biology and Genetics from Gaziantep

University, Turkey. He is Lecturer in the Breeding and Genetics department at Cholistan University of Veterinary and Animal Sciences (CUVAS), Bahawalpur, Pakistan. His research interests are molecular genetics and genomics, nutrigenomics, nano-genomics, bioinformatics, biotechnology, and their applications. He has published more than 70 research articles in national and international journals. He has also written many book chapters as well as an edited book. He is an associate editor for international journals.

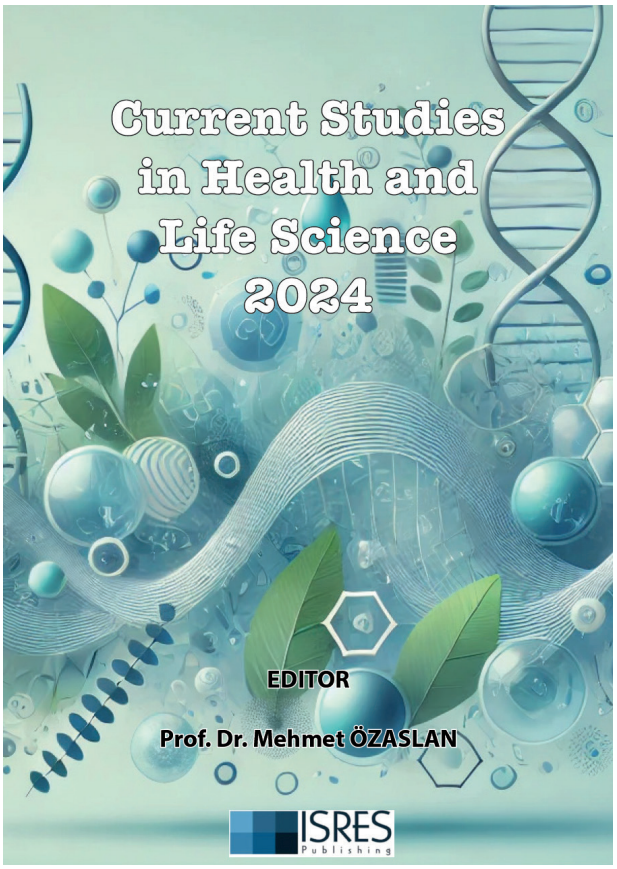
E-mail: msafdar@cuvas.edu.pk ORCID: 0000 0002 3720 2090

Prof. Dr. Mehmet ÖZASLAN received his PhD in 1995 Institute of Natural Sciences at Cukurova University, Turkiye. He is a Professor in Molecular Biology and Genetics. His research interests are included Cancer Genetics, Molecular Virology, Molecular Genetics, Microbiology, and Genetic mutations etc. He has published more than 200 research articles in national and international well reputed journals. He also has written many book chapters as well as edited books. He is an editor and editor-in-chief of many well-reputed national and international journals.

E-mail: ozaslanmd@gantep.edu.tr, ORCID: 0000 0001 9380 4902

To Cite This Chapter

FATIMA A et al., (2024). Innovations and principles of vaccine development for livestock. In Current Studies in Health and Life Sciences 2024 (pp.494-512). ISRES Publishing.



Current Studies in Health and Life Sciences-2024 is published annually from the selected papers invited by the editors.

This edition includes 3 sections and 24 papers from the field of Current Studies in Health and Life Sciences.

All submissions are reviewed by at least two international reviewers.

The purpose of the book is to provide the readers with the opportunity of a scholarly refereed publication in the field of Current Studies in Health and Life Sciences-2024.

Current Studies in Health and Life Sciences-2024 is published by ISRES Publishing

ISRES Publishing