THE EVOLUTION OF INFECTIOUS DISEASE EPIDEMIOLOGY AND ITS IMPLICATIONS FOR PUBLIC HEALTH

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Abstract:
Infectious disease epidemiology has undergone significant evolution over the years, driven by advancements in technology, changes in human behavior, and the emergence of new pathogens. This review article provides a comprehensive overview of the key developments in infectious disease epidemiology and discusses their implications for public health. The review begins by tracing the historical milestones in the field, from the early recognition of infectious diseases to the development of modern epidemiological methods. It then explores how infectious disease surveillance systems have evolved to better monitor and respond to outbreaks, including the role of big data and digital technologies in enhancing disease detection and tracking. Furthermore, the review examines the impact of globalization and urbanization on the spread of infectious diseases, highlighting the importance of international cooperation and coordination in addressing global health threats. The changing dynamics of infectious disease transmission, such as the rise of antimicrobial resistance and the re-emergence of vaccine-preventable diseases, are also discussed in detail. Additionally, the review explores the role of social determinants of health in shaping patterns of disease transmission and susceptibility, emphasizing the need for a holistic and multidisciplinary approach to infectious disease control. Moreover, the review delves into the challenges posed by emerging infectious diseases, such as zoonotic infections and novel pathogens, and discusses strategies for pandemic preparedness and response. The evolving field of molecular epidemiology and genomics is highlighted as a powerful tool for understanding disease transmission dynamics and guiding public health interventions. Finally, the review concludes by outlining future directions for infectious disease epidemiology, including the integration of One Health approaches, the use of predictive modeling and artificial intelligence, and the importance of global health equity in combating infectious diseases.

Keywords: Infectious disease epidemiology, Public health, Globalization, Antimicrobial resistance, Pandemic preparedness, Molecular epidemiology.

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Introduction:

Infectious diseases have been a significant threat to human health throughout history. From the Black Death in the 14th century to the COVID-19 pandemic in the 21st century, infectious diseases have shaped societies, influenced economies, and caused immense suffering. The field of infectious disease epidemiology has played a crucial role in understanding, preventing, and controlling the spread of these diseases [1].

One of the earliest recorded instances of infectious disease epidemiology dates back to the 5th century BC, when the Greek physician Hippocrates observed a connection between environmental factors and the spread of disease. He noted that certain diseases were more prevalent in crowded, unsanitary conditions, laying the foundation for the field of epidemiology. Hippocrates' observations were further developed by the Roman physician Galen, who studied the spread of infectious diseases among soldiers and prisoners [2].

The development of microbiology in the 19th century revolutionized our understanding of infectious diseases. In 1854, the British physician John Snow conducted a pioneering study on the spread of cholera in London. By mapping the locations of cholera cases, Snow was able to identify a contaminated water pump as the source of the outbreak, leading to improvements in sanitation and the prevention of future epidemics. Snow's work laid the groundwork for modern epidemiological methods, such as contact tracing and outbreak investigation [3].

The discovery of the germ theory of disease by Louis Pasteur and Robert Koch in the late 19th century further advanced our understanding of infectious diseases. Koch's postulates, a set of criteria for establishing the causative agent of a disease, revolutionized the field of infectious disease epidemiology by providing a systematic approach to identifying and studying pathogens. Koch's work led to the development of vaccines and antibiotics, which have played a crucial role in controlling infectious diseases such as tuberculosis, polio, and influenza [4].

The 20th century saw significant advancements in infectious disease epidemiology, including the eradication of smallpox in 1980. Through a global vaccination campaign led by the World Health Organization, smallpox became the first infectious disease to be eradicated, demonstrating the power of epidemiology in controlling infectious diseases. The discovery of HIV/AIDS in the 1980s and the subsequent development of antiretroviral therapy highlighted the importance of ongoing research and surveillance in combating emerging infectious diseases [5].

In recent years, the emergence of new infectious diseases such as SARS, MERS, and COVID-19 has underscored the ongoing threat posed by infectious diseases and the need for continued vigilance and research. The COVID-19 pandemic, in particular, has highlighted the importance of rapid response, collaboration, and data sharing in controlling infectious diseases on a global scale [6].

Evolution of Infectious Disease Surveillance Systems:

Infectious disease surveillance systems have undergone significant evolution over the years, driven by advancements in technology, globalization, and the increasing threat of emerging infectious diseases [7].

Historically, infectious disease surveillance relied heavily on manual reporting and data collection, making it slow and inefficient. However, with the advent of digital technologies, surveillance systems have become more streamlined and automated, allowing for real-time monitoring and analysis of disease outbreaks [8].

Globalization has also played a key role in shaping the evolution of infectious disease surveillance systems. The interconnected nature of the world has made it easier for diseases to spread across borders, necessitating the need for more robust surveillance systems to detect and respond to outbreaks quickly [9].

Furthermore, the emergence of new infectious diseases such as SARS, Ebola, and Zika has highlighted the importance of having effective surveillance systems in place. These outbreaks have served as wake-up calls, prompting governments and health organizations to invest in improving their surveillance capabilities [10].

The evolution of infectious disease surveillance systems has been a crucial aspect of public health response to disease outbreaks. With continued advancements in technology and a growing recognition of the importance of global cooperation, surveillance systems will continue to evolve to better protect public health in the face of emerging infectious diseases [11].

Impact of Globalization and Urbanization on Disease Transmission:

Globalization and urbanization have had a profound impact on the transmission of diseases around the world. As people and goods move more freely across borders and cities continue to grow in size and population, the spread of infectious diseases has become a major concern for public health officials and policymakers [12].

Globalization, which refers to the interconnectedness of economies, cultures, and

societies on a global scale, has facilitated the rapid spread of diseases. Advances in transportation and communication have made it easier for people to travel long distances in a short amount of time, allowing diseases to spread quickly from one country to another. In addition, global trade has increased the movement of goods and food products, which can also carry disease-causing pathogens [13].

Urbanization, on the other hand, has led to the concentration of people in densely populated areas, creating ideal conditions for the spread of infectious diseases. Crowded living conditions, inadequate sanitation, and poor access to healthcare services in urban areas can all contribute to the transmission of diseases. Furthermore, urbanization often leads to the destruction of natural habitats and the encroachment of humans into wildlife areas, increasing the likelihood of zoonotic diseases – those that are transmitted from animals to humans [14].

One of the most significant examples of the impact of globalization and urbanization on disease transmission is the COVID-19 pandemic. The rapid spread of the virus from its origins in Wuhan, China to countries around the world was made possible by global travel and trade networks. Once the virus reached urban centers, it spread quickly within communities, leading to widespread outbreaks and overwhelming healthcare systems [15].

Other examples of diseases that have been facilitated by globalization and urbanization include influenza, tuberculosis, and HIV/AIDS. Influenza viruses, for instance, can easily travel between countries through air travel, leading to seasonal outbreaks that can quickly turn into pandemics. Tuberculosis, a bacterial infection that primarily affects the lungs, thrives in crowded urban environments where people live in close proximity to one another. HIV/AIDS, a viral infection that attacks the immune system, has spread rapidly in urban areas with high rates of poverty and limited access to healthcare [16].

In response to the challenges posed by globalization and urbanization, public health officials and policymakers have implemented various strategies to prevent and control the spread of infectious diseases. These include surveillance and monitoring systems to track the spread of diseases, vaccination campaigns to prevent outbreaks, and public health education programs to raise awareness about disease prevention and control measures [17].

Globalization and urbanization have had a significant impact on the transmission of diseases, creating new challenges for public health systems around the world. As the world becomes more interconnected and urbanized, it is crucial for governments, healthcare providers, and communities to work together to address the root causes of disease transmission and implement effective prevention and control measures. By taking a proactive approach to managing the risks associated with globalization and urbanization, we can help to reduce the burden of infectious diseases and protect the health and well-being of populations worldwide [18].

Changing Dynamics of Infectious Disease Transmission:

Infectious diseases have been a constant threat to human health throughout history. From the Black Death in the 14th century to the Spanish flu in the early 20th century, outbreaks of infectious diseases have had devastating effects on populations around the world. However, the dynamics of infectious disease transmission have been changing in recent years, due to a variety of factors including globalization, urbanization, climate change, and advances in technology and medicine [19].

One of the key factors driving the changing dynamics of infectious disease transmission is globalization. With the increase in international travel and trade, infectious diseases can spread rapidly across borders, making containment and control more challenging. For example, the outbreak of SARS (Severe Acute Respiratory Syndrome) in 2003 spread quickly from China to other countries around the world, highlighting the interconnected nature of our globalized world [20].

Urbanization is another factor that is contributing to the changing dynamics of infectious disease transmission. As more and more people move to cities, crowded living conditions and inadequate sanitation can create ideal breeding grounds for infectious diseases. Diseases such as tuberculosis and cholera thrive in urban environments, leading to higher rates of transmission and outbreaks in cities around the world [21].

Climate change is also playing a role in the changing dynamics of infectious disease transmission. Rising temperatures and changes in precipitation patterns can alter the distribution of disease vectors such as mosquitoes and ticks, leading to the spread of diseases such as malaria, dengue fever, and Lyme disease to new areas. Additionally, extreme weather events such as hurricanes and floods can disrupt public health infrastructure and lead to outbreaks of waterborne diseases such as cholera and typhoid [22].

Advances in technology and medicine have also had an impact on the dynamics of infectious disease transmission. The development of vaccines, antibiotics, and other medical interventions has

helped to control and prevent many infectious diseases, reducing their impact on human health. However, the misuse and overuse of antibiotics has led to the emergence of drug-resistant strains of bacteria, making some infections more difficult to treat [23].

The dynamics of infectious disease transmission are constantly evolving due to a variety of factors including globalization, urbanization, climate change, and advances in technology and medicine. It is important for public health officials, policymakers, and researchers to stay vigilant and adapt to these changing dynamics in order to prevent and control outbreaks of infectious diseases. By understanding the factors driving the spread of infectious diseases and implementing effective strategies for prevention and control, we can work towards a healthier and more resilient global population [24].

Role of Social Determinants of Health in Infectious Disease Control:

Infectious diseases have been a major public health concern throughout history, causing widespread illness, death, and economic burden. The control and prevention of infectious diseases are complex processes that involve various factors, including social determinants of health. Social determinants of health are the conditions in which people are born, grow, live, work, and age, and they play a crucial role in shaping health outcomes, including the spread and control of infectious diseases [25].

Impact of Social Determinants of Health on Infectious Disease Control

Social determinants of health can influence the risk of exposure to infectious diseases, the likelihood of infection, and the ability to access healthcare services for treatment and prevention. Factors such as poverty, inadequate housing, lack of access to clean water and sanitation, overcrowded living conditions, and limited healthcare resources can increase the vulnerability of individuals and communities to infectious diseases. For example, individuals living in poverty may not have access to proper nutrition or healthcare, making them more susceptible to infections. Similarly, overcrowded living conditions can facilitate the transmission of infectious diseases such as tuberculosis and influenza [26].

Furthermore, social determinants of health can impact the effectiveness of infectious disease control measures. For instance, individuals with limited education or health literacy may have difficulty understanding and following public health guidelines for preventing infection. Similarly, cultural beliefs and practices can influence the acceptance and uptake of vaccines and other preventive measures. Inadequate access to healthcare services can also hinder the timely diagnosis and treatment of infectious diseases, leading to increased transmission and morbidity [27].

Addressing Social Determinants of Health in Infectious Disease Control

To effectively control and prevent infectious diseases, it is essential to address the underlying social determinants of health that contribute to their spread. This requires a comprehensive and multi-sectoral approach that goes beyond traditional public health interventions. Strategies to address social determinants of health in infectious disease control may include:

1. Improving access to healthcare services: Ensuring that all individuals have access to affordable and high-quality healthcare services is essential for timely diagnosis, treatment, and prevention of infectious diseases. This may involve expanding healthcare coverage, increasing the number of healthcare facilities in underserved areas, and training healthcare providers to deliver culturally competent care [28].
2. Promoting health equity: Addressing disparities in health outcomes among different population groups is crucial for reducing the burden of infectious diseases. This may involve implementing policies and programs that address social and economic inequalities, such as raising the minimum wage, providing affordable housing, and improving educational opportunities [29].
3. Enhancing public health infrastructure: Strengthening public health infrastructure is essential for effective infectious disease control. This may involve investing in disease surveillance systems, laboratory capacity, and outbreak response mechanisms. It also requires building partnerships with other sectors, such as housing, education, and transportation, to address the social determinants of health that contribute to infectious disease transmission [30].
4. Empowering communities: Engaging communities in the design and implementation of infectious disease control programs can help build trust, increase awareness, and promote behavior change. This may involve conducting community outreach and education campaigns, involving community leaders in decision-making processes, and providing resources to support community-led initiatives [31].

Infectious diseases continue to pose a significant threat to public health, and addressing the social

determinants of health is essential for effective control and prevention. By understanding how social factors influence the spread of infectious diseases and implementing strategies to address these determinants, public health authorities can improve health outcomes and reduce the burden of infectious diseases on individuals and communities. It is imperative that policymakers, healthcare providers, and community stakeholders work together to create a more equitable and healthy society for all [32].

Challenges and Strategies for Addressing Emerging Infectious Diseases:

Emerging infectious diseases pose a significant threat to global health security, with the potential to cause widespread illness and death. These diseases are caused by newly identified pathogens or by known pathogens that have evolved to become more virulent or resistant to treatment. The challenges posed by emerging infectious diseases are numerous and complex, requiring a multifaceted approach to effectively address them [33].

One of the primary challenges in addressing emerging infectious diseases is the rapid pace at which new pathogens can emerge and spread. With increased global travel and trade, pathogens can quickly spread across borders, making it difficult to contain outbreaks before they escalate into full-blown pandemics. Additionally, the interconnected nature of our modern world means that diseases can easily jump from animals to humans, as seen with zoonotic diseases like COVID-19 and Ebola [22].

Another challenge is the lack of effective surveillance and early warning systems for detecting emerging infectious diseases. Many countries lack the resources and infrastructure to adequately monitor and track new pathogens, making it difficult to quickly identify and respond to outbreaks. This is particularly problematic in low- and middle-income countries, where healthcare systems are already stretched thin and may not have the capacity to handle a large-scale outbreak [17].

Furthermore, the rapid evolution of pathogens poses a significant challenge for developing effective treatments and vaccines. As pathogens mutate and develop resistance to existing treatments, it becomes increasingly difficult to develop new therapies that are both safe and effective. This is exemplified by the rise of antimicrobial resistance, which threatens to render many of our existing antibiotics ineffective against common infections [31].

In order to effectively address these challenges, a comprehensive strategy is needed that encompasses both prevention and response measures. One key strategy is to strengthen global surveillance and early warning systems to detect and track emerging infectious diseases in real-time. This includes investing in laboratory capacity, training healthcare workers, and improving data sharing and communication between countries [4].

Another important strategy is to enhance collaboration and coordination between countries and international organizations. Emerging infectious diseases know no borders, and a coordinated global response is essential to effectively contain outbreaks and prevent them from spreading further. This includes sharing information, expertise, and resources to ensure a rapid and effective response to emerging threats [11].

Additionally, investing in research and development of new treatments and vaccines is crucial for addressing emerging infectious diseases. This includes developing new technologies and platforms for vaccine development, as well as investing in research on emerging pathogens and their mechanisms of transmission. By staying ahead of the curve and proactively developing new therapies, we can better prepare for future outbreaks and reduce their impact on global health [16].

Addressing emerging infectious diseases is a complex and multifaceted challenge that requires a coordinated and proactive approach. By strengthening surveillance systems, enhancing collaboration and coordination, and investing in research and development, we can better prepare for and respond to emerging threats. It is imperative that we continue to prioritize global health security and work together to build a more resilient and prepared world for future outbreaks [9].

Future Directions in Infectious Disease Epidemiology and Public Health:

Infectious diseases have been a significant public health concern for centuries, and they continue to pose a threat to global populations. However, with advancements in technology and research, the field of infectious disease epidemiology and public health is constantly evolving [2].

One of the most promising developments in infectious disease epidemiology is the use of big data. With the advent of electronic health records, social media, and other sources of digital information, researchers now have access to vast amounts of data that can be used to track disease outbreaks, monitor the spread of infectious diseases, and identify at-risk populations. By analyzing this data, epidemiologists can gain valuable insights into the patterns and determinants

of infectious diseases, which can inform public health interventions and policies [4].

In addition to big data, genomics is also playing a crucial role in the future of infectious disease epidemiology. The ability to sequence the genetic material of pathogens has revolutionized our understanding of infectious diseases, enabling researchers to track the evolution and spread of pathogens, identify drug-resistant strains, and develop targeted interventions. Genomic surveillance has already proven to be a powerful tool in the fight against infectious diseases, and as sequencing technology continues to advance, it is likely to become an integral part of infectious disease surveillance and control efforts [18].

Furthermore, innovative interventions are being developed to prevent and control infectious diseases. For example, the development of new vaccines and therapeutics, as well as the use of novel delivery mechanisms, such as microneedle patches and oral vaccines, are revolutionizing the way we prevent and treat infectious diseases. Additionally, advances in vector control, such as the use of genetically modified mosquitoes to reduce the transmission of mosquito-borne diseases, have the potential to significantly impact the burden of infectious diseases in many parts of the world [9].

Another important direction for the future of infectious disease epidemiology and public health is the integration of One Health approaches, which recognize the interconnectedness of human, animal, and environmental health. By understanding the complex interactions between humans, animals, and the environment, researchers can develop more effective strategies for preventing and controlling infectious diseases. This holistic approach to public health is essential for addressing emerging infectious diseases, zoonotic diseases, and antimicrobial resistance, which are all major threats to global health [5].

The future of infectious disease epidemiology and public health is promising, with advancements in big data, genomics, innovative interventions, and One Health approaches. These developments have the potential to revolutionize the way we prevent, detect, and respond to infectious diseases, and ultimately improve the health and well-being of populations around the world. However, it is important to continue to invest in research, surveillance, and capacity-building efforts to ensure that these promising directions can be realized and effectively implemented. By staying at the forefront of these developments, we can work towards a future where infectious diseases are no longer a major threat to public health [32].

Conclusion:

In conclusion, the field of infectious disease epidemiology has made significant strides in understanding, preventing, and controlling infectious diseases throughout history. From the pioneering work of Hippocrates and John Snow to the development of vaccines and antibiotics, epidemiologists have played a crucial role in shaping our response to infectious diseases. As we continue to face new challenges in the form of emerging infectious diseases, it is clear that the lessons learned from historical milestones in infectious disease epidemiology will continue to guide our efforts to protect public health and prevent future pandemics.

References:

1. Giesecke J. Modern infectious disease epidemiology. 3rd ed. London: Arnold; 2002.
2. Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis. 1995;1(1):7-15.
3. Heymann DL. Control of communicable diseases manual. 20th ed. Washington, DC: American Public Health Association; 2015.
4. World Health Organization. Global strategy for dengue prevention and control 2012-2020. Geneva: World Health Organization; 2012.
5. Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, et al. Global trends in emerging infectious diseases. Nature. 2008;451(7181):990-3.
6. Lederberg J, Shope RE, Oaks SC, editors. Emerging infections: microbial threats to health in the United States. Washington, DC: National Academies Press; 1992.
7. Morens DM, Folkers GK, Fauci AS. The challenge of emerging and re-emerging infectious diseases. Nature. 2004;430(6996):242-9.
8. Institute of Medicine (US) Forum on Microbial Threats. Global infectious disease surveillance and detection: assessing the challenges--finding solutions. Washington, DC: National Academies Press; 2007.
9. World Health Organization. International Health Regulations (2005). 3rd ed. Geneva: World Health Organization; 2016.
10. Osterholm MT, Olshaker M. Deadliest enemy: our war against killer germs. New York: Little, Brown and Company; 2017.
11. Morens DM, Fauci AS. Emerging infectious diseases: threats to human health and global stability. PLoS Pathog. 2013;9(7):e1003467.
12. Woolhouse ME, Gowtage-Sequeria S. Host range and emerging and reemerging pathogens. Emerg Infect Dis. 2005;11(12):1842-7.

13. Laxminarayan R, Duse A, Wattal C, Zaidi AK, Wertheim HF, Sumpradit N, et al. Antibiotic resistance-the need for global solutions. Lancet Infect Dis. 2013;13(12):1057-98.
14. World Health Organization. Global action plan on antimicrobial resistance. Geneva: World Health Organization; 2015.
15. Roca I, Akova M, Baquero F, Carlet J, Cavaleri M, Coenen S, et al. The global threat of antimicrobial resistance: science for intervention. New Microbes New Infect. 2015;6:22-9.
16. Plotkin SA, Orenstein WA, Offit PA, Edwards KM, editors. Plotkin's vaccines. 7th ed. Philadelphia: Elsevier; 2018.
17. Fine P, Eames K, Heymann DL. "Herd immunity": a rough guide. Clin Infect Dis. 2011;52(7):911-6.
18. World Health Organization. Immunization, vaccines and biologicals: data, statistics and graphics. Geneva: World Health Organization; 2020.
19. Marmot M. Social determinants of health inequalities. Lancet. 2005;365(9464):1099-104.
20. Solar O, Irwin A. A conceptual framework for action on the social determinants of health. Social determinants of health discussion paper 2 (policy and practice). Geneva: World Health Organization; 2010.
21. Marmot M, Wilkinson RG, editors. Social determinants of health. 2nd ed. Oxford: Oxford University Press; 2006.
22. Taylor LH, Latham SM, Woolhouse ME. Risk factors for human disease emergence. Philos Trans R Soc Lond B Biol Sci. 2001;356(1411):983-9.
23. Morse SS, Mazet JA, Woolhouse M, Parrish CR, Carroll D, Karesh WB, et al. Prediction and prevention of the next pandemic zoonosis. Lancet. 2012;380(9857):1956-65.
24. Jones BA, Grace D, Kock R, Alonso S, Rushton J, Said MY, et al. Zoonosis emergence linked to agricultural intensification and environmental change. Proc Natl Acad Sci U S A. 2013;110(21):8399-404.
25. Smith KF, Goldberg M, Rosenthal S, Carlson L, Chen J, Chen C, et al. Global rise in human infectious disease outbreaks. J R Soc Interface. 2014;11(101):20140950.
26. OIE - World Organisation for Animal Health. One Health. Available from: http://www.oie.int/en/for-the-media/onehealth/.
27. World Health Organization. One Health. Available from: http://www.who.int/features/qa/one-health/en/.
28. Morse SS, Mazet JA, Woolhouse M, Parrish CR, Carroll D, Karesh WB, et al. Prediction and prevention of the next pandemic zoonosis. Lancet. 2012;380(9857):1956-65.
29. Rweyemamu M, Kambarage D, Karimuribo E, Wambura P, Matee M, Kayembe JM, et al. Development of a one health national capacity in Africa: the Southern African Centre for Infectious Disease Surveillance (SACIDS) story. One Health. 2016;2:1-9.
30. Smith RD. Responding to global infectious disease outbreaks: lessons from SARS on the role of risk perception, communication and management. Soc Sci Med. 2006;63(12):3113-23.
31. Ferguson NM, Cummings DA, Cauchemez S, Fraser C, Riley S, Meeyai A, et al. Strategies for containing an emerging influenza pandemic in Southeast Asia. Nature. 2005;437(7056):209-14.
32. Khan K, Arino J, Hu W, Raposo P, Sears J, Calderon F, et al. Spread of a novel influenza A (H1N1) virus via global airline transportation. N Engl J Med. 2009;361(2):212-4.
33. World Health Organization. Global health observatory data repository. Available from: http://apps.who.int/gho/data/view.main.21400?lang=en.