Review Article

Tackling Infectious diseases with special reference to India: Need for multidimensional approach

Abstract

Infectious diseases have long been a major cause for concern since they frequently result in pandemics. Undoubtedly, we have some degree of infection control, but the recent COVID-19 outbreak has reduced us to powerless bystanders watching people perish. The majority of infection-related deaths are caused by respiratory viral diseases, including tuberculosis. The oncovirus as a cause of cancer is a severe health issue that demands attention. The emergence of new harmful forms worsens the problem of infectious diseases. The antigenic profile of pathogens is constantly shifting, which reduces the effectiveness of vaccines or encourages the emergence of medication resistance. The necessity for an all-inclusive strategy is apparent after undertaking a thorough analysis of the scientific knowledge now in existence regarding genesis, transmission, pathophysiology, and availability, as well as the efficacy of medications against infections. There are many grey regions that require attention. For instance, we need to comprehend the biology of the diseases that new infections cause as well as the origin of those infections, the processes and factors that make some hosts vulnerable while others are resistant, the comorbid factors in a population that favours certain infections, and the potential oncogenic viruses of common cancers. We only have a few antimicrobial medicines or vaccines, and many of them are losing their efficacy daily due to bacteria' development of clever neutralizing defences. To find novel therapeutic targets, we must launch a comprehensive research effort. As an alternative, we must go the other way by utilizing passive immunity strategies or researching antiviral medicinal plant products, created chemical analogues, probiotics, and their derived bacteriocins that will demonstrate effective effects against pathogenic bacteria. The action's mechanism can then be understood. As a result, it is imperative that everyone work together to complement one another's skills in order to launch a multifaceted strategy to fill in all the knowledge gaps related to infectious diseases.

Keywords: Infectious viruses, pathogenesis, therapeutic intervention, drug-resistant strains,

Introduction

Despite efforts to prevent communicable diseases, 2.7 million people died from infectious diseases in 2019; since then, the SARS-CoV2 pandemic alone has been responsible for about 5 million additional deaths (1). These death statistics are shameful and upsetting to everyone. According to science, there are three major reasons for such a great loss of human life: 1) the lack of current scientific understanding of communicable diseases or their treatment, 2) the emergence of new pathogenic variants, and 3) the failure to take seriously the ongoing threat of re-emerging and recently evolving infectious diseases capable of causing outbreaks and pandemics. Drugs for all harmful bacteria are still lacking, and treatments for infections are either ineffective or only partially successful against resistant strains (2). The bacteria are constantly at work. They have amazing genetic plasticity that they continue to produce, enabling them to arise with new pathogenic capabilities in favorable conditions, to circumvent population immunity by generating new antigens, and to acquire antibiotic resistance that evades human attempts to treat them (3).

The upper respiratory infections (influenza, SARS virus, etc.), tuberculosis, and oncovirus-related malignancies (which account for 15-20% of cancer-related mortality) pose the greatest health risks of all the infectious diseases (4). All of these contagious diseases appear to be continuously appearing and resurfacing and are becoming more common. In order to provide a constant line of defense against illnesses that are continually changing, we must stay up. For instance, the development of novel varieties like omicron pushes us to the breaking point even after the development of numerous vaccinations for SARS-2 (5). The development of antivirals and antibacterial still faces many difficulties and unanswered questions (6). To target viral proteins or cellular components that are essential for viral replication, certain powerful medicines have been produced (7). However, they have mostly not yet found clinical utility. Additionally, medication resistance and broad-spectrum side effects are making the currently available antimicrobial treatments less effective. Novel treatments are therefore absolutely necessary (8). There is a need to conduct a thorough search to find fresh treatment targets and prevention strategies. The new successes may open the door for enhanced antiviral and antibacterial medications. Natural compounds derived from plant and microbial sources are still a possibility for developing powerful antimicrobial drugs and for combating MDR infections (9) (10). Pathogen investigations must be conducted in specialised biosafety labs and in line with established guidance by government bodies in order to prevent the potential leakage and spread of harmful pathogens from the laboratory. A facility like this will strengthen our ability to tackle harmful microbes, advance our scientific knowledge, and get ready for any potential outbreaks in the future. Scientists from all around the world have gathered to tackle the challenge of understanding the biology of infection and transmission, finding new therapeutic targets from all accessible sources of plants, microbes, synthetic chemicals, and antibody development. This multifaceted strategy is more effective than occasional, one-off initiatives. Both in-vitro and in vivo approaches will be used with all advanced techniques and technology to make the studies conclusive.

Today's world is dealing with a plethora of new infectious diseases (11). Antimicrobial resistance has developed in a variety of microbial strains, including those that cause all of the life-threatening diseases (12). Relevantly, viruses that are capable of causing urogenital, gastrointestinal, and respiratory illnesses are now posing an ever-greater hazard. The coronavirus disease-19 (COVID-19) has had a tremendous influence on the world over the past two years in terms of causing economic disruption, depleting local and international public health resources, and, most significantly, negatively affecting human health. (13). As an adjuvant therapy for COVID-19 patients, there is currently no evidence to recommend the use of any supplements. Additionally, there is still inadequate global regulation of the SARS-CoV2, highly mutated pathogenic strains of influenza, dengue, ebola, and Zika viral diseases (1) (14). Finding alternative, risk-free methods to reduce the likelihood of these disorders is therefore essential. For the treatment and prevention of viral RTIs like the common cold, even a modestly effective medication could lower the morbidity and monetary expenses linked to this illness (15). The effectiveness of vaccinations against viral illnesses is constrained by the high rates of mutation of viruses, especially RNA viruses (16). Studies of these emerging diseases highlight the evolutionary characteristics of pathogenic microbes as well as the dynamic relationships between bacteria, their hosts, and the environment. The World Health Organization issued a warning that infectious diseases are evolving at a rate that has never been seen before in each report. Since the 1970s, around 40 infectious diseases have been identified, including SARS, Ebola, MERS, chikungunya, swine flu, avian flu, Zika, and, most recently, COVID-19, which is brought on by the SARS-CoV-2 coronavirus (14). People are travelling considerably more frequently and over much longer distances than in the past, living in densely inhabited areas, and coming into closer touch with wild creatures, thus the potential for new infectious illnesses to spread quickly and trigger worldwide epidemics is a serious concern. Furthermore, illnesses from bioterrorism agents might evolve as a consequence of purposeful introduction into animal, human, or plant populations for terrorist reasons. Anthrax, smallpox, and tularemia are among these illnesses. The aspects that subsidize to the appearance or recurrence of infectious diseases include pathogen evolution over time, zones, which occur when an infectious agent is transmitted from animals to humans; climate change, which allows mosquitoes to spread their range; antimicrobial resistance, and so on.

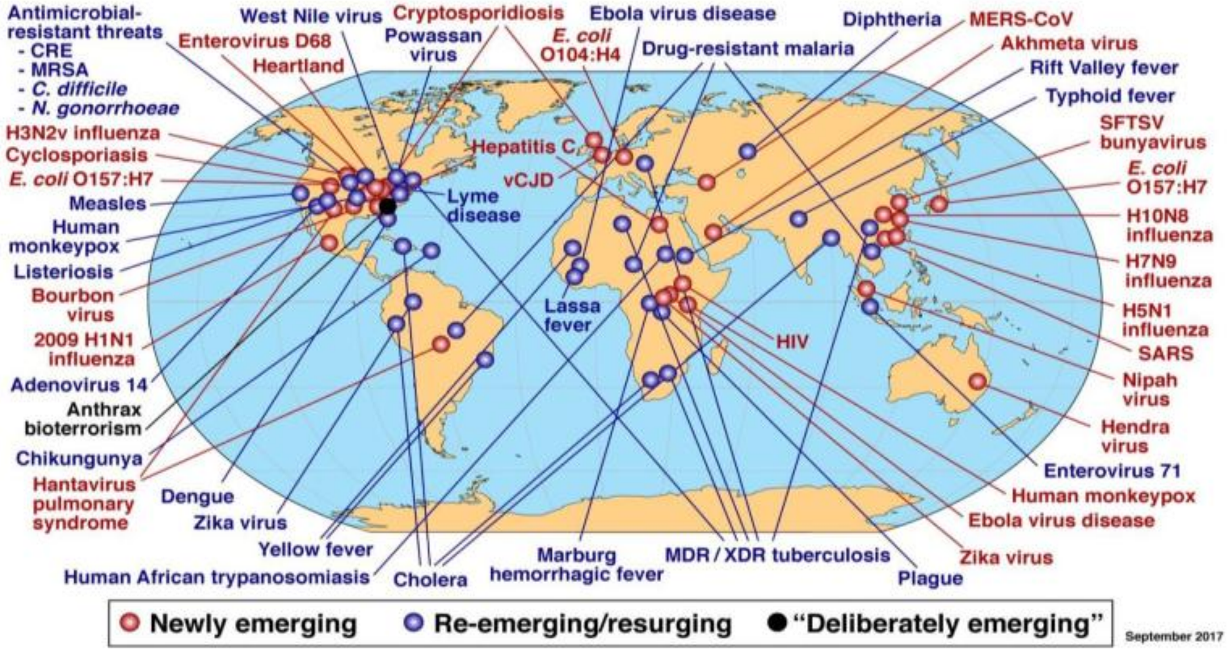

Figure 1: Different infectious disease around the World

Improved access to insurance, increased health awareness and infrastructure, and the availability of a huge pool of well-trained medical personnel are all major drivers to the Indian health sector's growth. Infectious illness burden in India is quite high, with rural populations being the primary sufferers (17). Climate change, poor sanitation, a lack of fresh water, deforestation, urbanization, and changes in lifestyle are all variables that impact the survival of microbes that cause illnesses (18). Because the instances occur in rural places, a large percentage of infectious outbreaks go undetected. The infection resurfaces as a result of drug resistance (19). Malaria, Cholera, Dengue

Fever, Jaundice, Hepatitis, Typhoid, Japanese Encephalitis, Plague, HIV, and Rabies are some of the most common infectious illnesses in India (20). In India, the Nipah and chandipura virus has just recently surfaced (21).

Covid-19

Corona viruses represent a group of enveloped viruses consists of single-stranded positive-sense RNA molecule and viral particles that resemble like a crown. These viruses belong to the order: *Nidovirales*, family: *Coronaviridae* and subfamily: *Orthocoronavirinae* (22). Such viruses can attack mammals, including humans causing mild infections and occasionally can lead to severe localized outbreaks like those caused in mainland China (2003) by the “Severe Acute Respiratory Syndrome”(SARS) virus, in the Kingdom of Saudi Arabia (2012) by the “Middle East Respiratory Syndrome”(MERS) virus and in South Korea (2015) (23). In response to SARS pandemics, the world faces plenty of challenges, as they were not prepared to deal with it. Although several research advances were made with respect to SARS pandemics seventeen years ago, but till date still issues remain undiscovered.

Recently, a coronavirus outbreak has originated from China and is rapidly expanding to other countries. On December 2019, in Wuhan city of China, a group of pneumonia with unknown origin was identified (24). In the next month (January 2020), Chinese authorities came up with the sequence of a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (25). Later on, the disease caused by SARS-CoV-2 was named as coronavirus disease 2019 (COVID-19). After two months of the first reported cases, the virus not only spread rapidly to the major portion of the China, but also affected 28 other countries (26) (27). Due to its rapid spread to the other countries, The World Health Organization (WHO) declared COVID-19 as a pandemic, with more than 118,000 cases in 114 countries and 4,291 deaths as on 12th march 2020. It should be noted here that there exist no anti-viral treatments or vaccines till date, which can be used to prevent or manage the pandemic. Although commonly used anti-retroviral drugs like Lopinavir and Ritonavir, which are used to treat HIV/AIDS patients are in use against coronaviruses and seems to exert beneficial effects. Some of the other drugs used against coronaviruses include GS-734 (Remdesivir): an anti-viral drug developed against the Marburg and the Ebola viruses, Umifenovir (Abidol): used against severe influenza cases, anti-inflammatory drugs, neuraminidase inhibitors, RNA synthesis inhibitors and EK1 peptide (28).

Influenza

For generations, influenza has afflicted mankind (29). Humans are endemic to influenza A and B viruses, which cause annual epidemics around the world. From 1918 to 2009, influenza A viruses of the virus's eight gene segments to be replaced, resulting in a unique variety. Novel influenza A viruses circulate among animals, according to the CDC's article "Viruses of Special Concern." Some new influenza A virus's strains are thought to offer a bigger pandemic hazard than others, and they are of particular concern due to the potential impact on public health if they obtain the ability to move readily from person to person, perhaps causing the next influenza pandemic. Infection with a new influenza A virus strains humans is a disorder that must be reported to the Centers for Disease Control and Prevention (CDC) (CDC 2021). According to Professor Michael Osterholm in a news report by telegraph, director of the Centre for Infectious Disease Research and Policy at the University of Minnesota, a global influenza out-break could be far worse than the COVID-19 pandemic, with models suggesting that it could kill up to 33 million (3.3 crore) people in the first six months, and "Prior to COVID-19, influenza pandemics were the number one biological risk to humans and this hasn't changed," " There were four influenza pandemics between 1918 and 2018, a century (30). This clearly demonstrates that there is a substantial and present danger of a pandemic of influenza. The World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC) accordingly developed scoring methods to assess influenza viruses that are pre-pandemic in three main categories: (1) Viral characteristics, (2) Human population characteristics, and (3) Viral ecology and epidemiology. Vaccination against the flu avoided around 7.5 million flu infections, 105,000 hospitalizations, and 6,300 deaths during the 2019-2020 flu season (Centre for Disease Control and Prevention, 2021).

Annual and pandemic influenza are major causes of illness and death throughout the world (31). In temperate locations, human influenza infection rates peak during the winter months; however, the influenza pattern in tropical and subtropical regions differs, with some places seeing year-round circulation and other regions experiencing biennial peaks (32). The timing of vaccination efforts in tropical areas is particularly challenging because of the variable seasonality of influenza in the tropics (33). From north to south, India has distinct seasons that vary greatly. Jammu and Kashmir, India's most northern state, experiences harsh winters from December to March, while Delhi, the nation's capital, experiences milder conditions. It has been shown by sentinel surveillance for influenza that India has distinct influenza peaks. Pervaiz K et al 2014 X conducted influenza surveillance in Srinagar and New Delhi, two cities in northern India that are separated by 2500 km, during the 2011–2012 influenza season providing implications for influenza vaccine strategy and timing (32). 22,186 cases of swine flu have been reported across India, according to health ministry data from the Government of India, and specialists believe this is because the virus's strain has changed.

Avian influenza

Avian influenza is a global threat to poultry, as well as human health (34). The highly pathogenic avian influenza A (H5N1) virus, which has repeatedly spread to humans since its first report in 1996, and the novel avian influenza A (H7N9) virus, which was first discovered in March 2013, both pose current pandemic threats and both have resulted in serious human infections across China (35) (36). Wild birds have contributed to the development of the influenza A(H7N9) virus. (37) and might have played a role in the spread of this virus to parts of Asia, Europe, and Africa after a 2005 outbreak in birds at Qinghai Lake in China (38). Recent studies have suggested that wild birds may have contributed to the influenza A (H5N8) virus's unanticipated debut and spread in Europe in November 2014 and in North America in December 2014; genetically related lineages have also been discovered in South Korea and Japan. Concern over extremely pathogenic avian influenza viruses has occasionally attracted attention and funding along with certain subtypes. For instance, the concern over the influenza A (H5N1) virus led to the immediate expenditure of hundreds of millions of dollars for research pertaining to wild birds worldwide. A variety of subtypes of the avian influenza virus are naturally present in wild birds, which also serve as dynamic reservoirs for the virus' development and transmission to domestic flocks and mammals (39). Wild birds have been found to have the majority of hemagglutinin (HA) and neuraminidase (NA) subtypes, though some only occasionally (40). Diverse wild bird species from many locations have been identified to carry highly dangerous avian influenza viruses, which may be spread through transcontinental flyways (40).

The HPAI H5N1 virus outbreaks in India were first noted in February 2006 in poultry at Navapur, Maharashtra, and 104 outbreaks of both poultry and wild and migratory birds have since been recorded in India from 2006 to 2016 (41). Retrospective seroprevalence of AI H5N1 and H9N2 viruses in India were conducted using the archived avian serum samples collected earlier (1954-1981) and indicated no serologic evidence of H5N1 and H9N2 . Two H6N2 viruses were reported to have been genetically and antigenically characterised from domestic ducks that appeared to be in good condition in Kerala and Assam, India, in 2014 and 2015, respectively. Highly pathogenic avian influenza (H5N8) viruses in waterfowl at 2 zoos in India in October 2016 were detected by Nagarajan et.al., (2017) (42). The two viruses were distinct H5N8 7:1 reassortants that were recovered from wild birds in the Russian Federation and China in May 2016 suggesting that the viruses propagated during the southward winter migration of birds. Cases of Avian Influenza were being reported from as many as eight Indian states; Kerala, Himachal Pradesh, Madhya Pradesh, Uttar Pradesh, Odisha, Punjab, Haryana and Rajasthan. A central team visited Alappuzha in Kerala, which is the worst affected region. On January 4, 2021, the Department of Animal Husbandry alerted the public that samples of deceased ducks from the Keralan districts of Alappuzha and Kottayam had been found to contain the avian influenza virus (H5N8). Panchkula District of Haryana chicken tests have also shown a similar report of avian influenza."

Oncogenic Virus Cancer is considered to be one of the leading causes of death globally (43). The cancer has a significant negative impact in lower-middle-income nations like India because of low knowledge, limited access to inexpensive care, and poor prognosis (44). Geographical variations in genetic factors, environmental exposures, and patterns of malignancies vary between regions as a result of variability in ancestries, socioeconomic and cultural characteristics, dietary habits, and lifestyles. So far, we know of seven cancer-causing viruses, and one of them is the Merkel Cell Polyomavirus (MCV), a new virus discovered in 2008. It causes Merkel Cell Carcinoma (MCC)—a rare type of cancer that affects skin cells known as Merkel cells. Cervical cancer is one of the most prevalent cancers in Indian women and the second most common cancer in women worldwide. It is caused primarily by the Human Papillomavirus (HPV). Despite the fact that there are various approaches for preventing cervical cancer, vaccination is emerging as the most effective strategy, with two vac-cines now available (45).

Oncogenic Viruses

Viruses are known to play significant causative roles in a variety of human and animal malignancies, accounting for over one-fifth of all cancer cases (46) (47). Cancer biology and virology have a unique application to viral-associated malignancies (48). There are currently seven human viruses with clear epidemiological connections to cancer in humans. Hepatitis B and C (HBV and HCV), human gamma herpes viruses (HHV4/Epstein-Barr Virus (EBV) and HHV8/Sarcoma-Associated Kaposi's Herpes virus (KSHV), Merkel cell polyomavirus (MCPyV), and human T-cell leukemia virus I are some of these (HTLV-1) (49) (50) (51) (52). These oncoviruses include members of the DNA, RNA, and retroviridae families of viruses, which are all very different from one another. Despite the species diversity, these oncoviruses are believed to have characteristics in common that allow them to cause cancer. Key cellular pathways necessary for the regulation of cell growth and metabolism are taken over by oncoviruses. However, numerous viruses that do not cause cancer disrupt these pathways and interact similarly with hosts. Therefore, it is unclear what characteristics endow viruses with carcinogenic potential in human populations. The hallmarks of cancer are multiple biological pathways that oncogenic viruses disrupt (53). As anticipated, these cancer hallmarks can easily be layered with viral-associated cancer pathways (54).

Hepatitis

Hepatitis is a condition in which the liver cells become inflamed (55). This condition is brought on by bacterial infection, chronic alcohol and drug use, as well as exposure to hazardous substances like paint thinners and aerosol sprays and there are five distinct viruses that can cause this condition: viruses A, B, C, D, and E (56) (57). Hepatitis can be short-term (acute) or long-term (chronic). Acute hepatitis can heal on its own or develop into chronic hepatitis. Chronic hepatitis can lead to liver damage, liver failure, or liver cancer over time. Hepatitis A, which is prevalent all throughout the world, is a self-limiting illness that is spread by infected water and, in some cases, parenteral (58). Hepatitis B is spread by close contact and from mother to child, as well as orally (through contaminated water) (59). Hepatitis C is transferred by blood transfusions or the use of parenteral drugs (60). Hepatitis D, often known as delta hepatitis, is an infection caused by the hepatitis D virus (61). It generally comes along with hepatitis B and makes it worse. Hepatitis E is spread by drinking contaminated water. Hepatitis E cannot cause chronic illness, although it can be lethal to pregnant women (62).

The "big three" infectious diseases, HIV/AIDS, malaria, and tuberculosis, are now considered to be just as serious as viral hepatitis in terms of their impact on public health and health care expenditures (63). Acute viral hepatitis outbreaks and sporadic infections are both caused by the enterically transmitted hepatitis A and E viruses. Hepatitis B and C viruses are known to cause chronic hepatitis, which can develop into significant complications such liver cirrhosis and hepatocellular carcinoma. They are typically spread by the parenteral route. HEV is the primary cause of sporadic and pandemic AVH cases in India (Hepatitis E virus) (64). The National Viral Hepatitis Control Program (NVHCP), which aims to eradicate viral hepatitis, was introduced in India recently. More people are infected and killed by the illness than by HIV, malaria, and tuberculosis combined, according to experts. According to Times of India, a national newspaper, senior medical expert KK Aggarwal is a former national president of the Indian Medical Association (IMA) "It is crucial to recognise the severity of the hepatitis threat. Viral hepatitis is the cause of liver cancer in more than 80% of cases."

Multidrug resistance (MDR)

The magnitude of the antimicrobial resistance crisis is unknown because of the absence of systemic monitoring in developing countries (65). Era of antibiotics that led to optimism regarding infectious disease control and prevention has vanished (66) (67). Emergence of resistance among microbes smashed the effectiveness of antibiotics that altogether changed the lifesaving paradigm of antibiotics (68). Many of the germs that the Centers for Disease Control and Prevention (CDC) has identified as posing urgent, serious, and worrying risks already place a significant clinical and financial burden on the American health care system, patients, and their families (CDC 2013). It is imperative to work together to enact new regulations, redouble research efforts, and explore crisis management strategies.

Antimicrobial resistance (AMR) is still a significant public health concern due to the deaths it causes and the financial harm it causes. The health authorities of several nations, including India's, have created containment programmes. In the fight against AMR, it is crucial to acknowledge the contributions of all four domains: people, animals, food, and the environment (69). This evaluation of One Health from an Indian viewpoint covers every facet of the concept. India has one of the highest rates of antibiotic resistance in both people and food animals. Environmental samples, particularly those taken from water bodies, have shown the presence of resistant organisms or their genes. Due to certain social and cultural factors, it is more difficult to contain resistance in India. AMR is mostly caused in India by the indiscriminate use of antimicrobials and inadequate waste water treatment. National Action Plan on Antimicrobial

Resistance (NAP-AMR), Government of India, 2017–2021. Sludge in agriculture, inefficient livestock disposal, and the aquaculture sector are all thought to contribute to AMR in other nations, but there is little information on these in India. The Indian health authorities have started fighting AMR, but they are just getting started (69). Future investigations should be organized to address this threat while taking into account the difficulties specific to India.

Conclusion

The multidimensional approach has a very high impact in the current scenario of the world which is crippled by the Covid-19 pandemic. Economies are down, movement of the public is ceased, education is severely hit, mental health is at its lowest state, and above all, we just are watching dying our dears and nears. This huge immeasurable devastation is from just a single highly contagious virus SARS-2. Many more pathogens are there that have the potential to seek similar attention of the world at any time. On top of all, the emergence of the new variant of pathogens makes the available interventions against them ineffective, has frustrated the entire scientific community. Considering such a huge loss and threat, there cannot be any better priority area of research than multidimensional approach. On a holistic scanning of the information available on infectious diseases from origin to evolution and transmission to pathogenicity, and more importantly, in prevention and treatment, everyone can readily agree that less is known and much more needs to be done on every front.

References

1. Sharma A, Tiwari S, Deb MK, Marty JL. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2): a global pandemic and treatment strategies. International journal of antimicrobial agents. 2020 Aug;56(2):106054.
2. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. P & T : a peer-reviewed journal for formulary management. 2015 Apr;40(4):277-83.
3. Nikaido H. Multidrug resistance in bacteria. Annual review of biochemistry. [Research Support, N.I.H., Extramural

Review]. 2009;78:119-46.

4. Petersen E, Koopmans M, Go U, Hamer DH, Petrosillo N, Castelli F, et al. Comparing SARS-CoV-2 with SARS-CoV and influenza pandemics. The Lancet Infectious diseases. [Research Support, Non-U.S. Gov't

Research Support, U.S. Gov't, P.H.S.

Review]. 2020 Sep;20(9):e238-e44.

5. Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R. Features, Evaluation, and Treatment of Coronavirus (COVID-19). StatPearls. Treasure Island (FL)2022.

6. Fair RJ, Tor Y. Antibiotics and bacterial resistance in the 21st century. Perspectives in medicinal chemistry. [Review]. 2014;6:25-64.

7. Lino CA, Harper JC, Carney JP, Timlin JA. Delivering CRISPR: a review of the challenges and approaches. Drug delivery. [Review]. 2018 Nov;25(1):1234-57.

8. Singh L, Kruger HG, Maguire GEM, Govender T, Parboosing R. The role of nanotechnology in the treatment of viral infections. Therapeutic advances in infectious disease. [Review]. 2017 Jul;4(4):105-31.

9. Anand U, Jacobo-Herrera N, Altemimi A, Lakhssassi N. A Comprehensive Review on Medicinal Plants as Antimicrobial Therapeutics: Potential Avenues of Biocompatible Drug Discovery. Metabolites. [Review]. 2019 Nov 1;9(11).

10. Cowan MM. Plant products as antimicrobial agents. Clinical microbiology reviews. [Review]. 1999 Oct;12(4):564-82.

11. Olsen B. Inaugural editorial. Infection ecology & epidemiology. 2011;1.

12. Davies J, Davies D. Origins and evolution of antibiotic resistance. Microbiology and molecular biology reviews : MMBR. [Review]. 2010 Sep;74(3):417-33.

13. Nicola M, Alsafi Z, Sohrabi C, Kerwan A, Al-Jabir A, Iosifidis C, et al. The socio-economic implications of the coronavirus pandemic (COVID-19): A review. International journal of surgery. [Review]. 2020 Jun;78:185-93.

14. Reperant LA, Osterhaus A. AIDS, Avian flu, SARS, MERS, Ebola, Zika... what next? Vaccine. [Review]. 2017 Aug 16;35(35 Pt A):4470-4.

15. Dalton K, Byrne S. Role of the pharmacist in reducing healthcare costs: current insights. Integrated pharmacy research & practice. [Review]. 2017;6:37-46.

16. Beaty SM, Lee B. Constraints on the Genetic and Antigenic Variability of Measles Virus. Viruses. [Research Support, N.I.H., Extramural

Review]. 2016 Apr 21;8(4):109.

17. Neiderud CJ. How urbanization affects the epidemiology of emerging infectious diseases. Infection ecology & epidemiology. 2015;5:27060.

18. Wu X, Lu Y, Zhou S, Chen L, Xu B. Impact of climate change on human infectious diseases: Empirical evidence and human adaptation. Environment International. 2016 2016/01/01/;86:14-23.

19. Seung KJ, Keshavjee S, Rich ML. Multidrug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis. Cold Spring Harbor perspectives in medicine. [Review]. 2015 Apr 27;5(9):a017863.

20. Mani RS, Ravi V, Desai A, Madhusudana SN. Emerging Viral Infections in India. Proceedings of the National Academy of Sciences, India Section B. 2012;82(1):5-21.

21. Mourya DT, Yadav PD, Ullas PT, Bhardwaj SD, Sahay RR, Chadha MS, et al. Emerging/re-emerging viral diseases & new viruses on the Indian horizon. The Indian journal of medical research. [Review]. 2019 Apr;149(4):447-67.

22. Carlos WG, Dela Cruz, C. S., Cao, B., Pasnick, S., & Jamil, S. Novel Wuhan (2019-nCoV) coronavirus. American Journal of Respiratory and Critical Care Medicine. 2020;https://doi.org/10.1164/rccm.2014P7.

23. Gralinski LE, & Menachery, V. D. Return of the coronavirus: 2019-nCoV. Viruses. 2020;12(2).

24. Wuhan City Health Committee (WCHC). Wuhan Municipal Health and Health Commission's briefing on the current pneumonia epidemic situation in our city 2019. Available from: http://wjw.wuhan.gov.cn/front/web/showDetail/2019123108989. Accessed 14 Jan 2020.

25. European Centre for Disease Prevention and Control (ECDC). Rapid Risk Assessment: Outbreak of acute respiratory syndrome associated with a novel coronavirus, Wuhan, China. Stockholm: ECDC; 2020. Available from: https://www.ecdc.europa.eu/en/publicationsdata/risk-assessment-outbreak-acute-respiratory-syndrome-associated-novel-coronavirus. first update - 22 January 2020.

26. European Centre for Disease Prevention and Control (ECDC). Outbreak of acute respiratory syndrome associated with a novel coronavirus, China: first local transmission in the

EU/EEA – third update. Stockholm: ECDC; 2020. Available from: https://www.ecdc.europa.eu/en/publicationsdata/risk-assessment-outbreak-acute-respiratory-syndromeassociated-novel-1. 31 January 2020. .

27. European Centre for Disease Prevention and Control (ECDC). Geographical distribution of 2019-nCov cases globally 2020. Stockholm: ECDC. [Accessed 12 Feb 2020]. Available from: https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases. 02 February 2020.

28. Liu T, Hu, J., Kang, M., Lin, L., Zhong, H., Xiao, J., et al. Transmission dynamics of 2019 novel coronavirus (2019-nCoV). . bioRxiv https://doiorg/10 1101/20200125919787. 2020.

29. Piret J, Boivin G. Pandemics Throughout History. Frontiers in microbiology. [Review]. 2020;11:631736.

30. Martini M, Gazzaniga V, Bragazzi NL, Barberis I. The Spanish Influenza Pandemic: a lesson from history 100 years after 1918. Journal of preventive medicine and hygiene. [Historical Article]. 2019 Mar;60(1):E64-E7.

31. Madhav N, Oppenheim B, Gallivan M, Mulembakani P, Rubin E, Wolfe N. Pandemics: Risks, Impacts, and Mitigation. In: rd, Jamison DT, Gelband H, Horton S, Jha P, Laxminarayan R, et al., editors. Disease Control Priorities: Improving Health and Reducing Poverty. Washington (DC)2017.

32. Koul PA, Broor S, Saha S, Barnes J, Smith C, Shaw M, et al. Differences in influenza seasonality by latitude, northern India. Emerging infectious diseases. [Research Support, U.S. Gov't, P.H.S.]. 2014 Oct;20(10):1723-6.

33. Nakaya HI, Wrammert J, Lee EK, Racioppi L, Marie-Kunze S, Haining WN, et al. Systems biology of vaccination for seasonal influenza in humans. Nature immunology. [Research Support, N.I.H., Extramural

Research Support, Non-U.S. Gov't]. 2011 Jul 10;12(8):786-95.

34. Peiris JS, de Jong MD, Guan Y. Avian influenza virus (H5N1): a threat to human health. Clinical microbiology reviews. [Research Support, N.I.H., Extramural

Research Support, Non-U.S. Gov't

Review]. 2007 Apr;20(2):243-67.

35. Taubenberger JK, Morens DM. Influenza: the once and future pandemic. Public health reports. [Historical Article

Research Support, N.I.H., Intramural

Review]. 2010 Apr;125 Suppl 3:16-26.

36. Shibata A, Okamatsu M, Sumiyoshi R, Matsuno K, Wang Z-J, Kida H, et al. Repeated detection of H7N9 avian influenza viruses in raw poultry meat illegally brought to Japan by international flight passengers. Virology. 2018 2018/11/01/;524:10-7.

37. Li YT, Linster M, Mendenhall IH, Su YCF, Smith GJD. Avian influenza viruses in humans: lessons from past outbreaks. British medical bulletin. [Research Support, N.I.H., Extramural

Research Support, Non-U.S. Gov't

Review]. 2019 Dec 11;132(1):81-95.

38. Li Y, Liu L, Zhang Y, Duan Z, Tian G, Zeng X, et al. New avian influenza virus (H5N1) in wild birds, Qinghai, China. Emerging infectious diseases. [Research Support, Non-U.S. Gov't]. 2011 Feb;17(2):265-7.

39. Hassan MM, Hoque MA, Debnath NC, Yamage M, Klaassen M. Are Poultry or Wild Birds the Main Reservoirs for Avian Influenza in Bangladesh? EcoHealth. 2017 Sep;14(3):490-500.

40. Verhagen JH, Lexmond P, Vuong O, Schutten M, Guldemeester J, Osterhaus AD, et al. Discordant detection of avian influenza virus subtypes in time and space between poultry and wild birds; Towards improvement of surveillance programs. PloS one. 2017;12(3):e0173470.

41. Upadhyay RK, Kumari N, Rao VSH. Modeling the spread of bird flu and predicting outbreak diversity. Nonlinear analysis Real world applications. 2008 Sep;9(4):1638-48.

42. Nagarajan S, Kumar M, Murugkar HV, Tripathi S, Shukla S, Agarwal S, et al. Novel Reassortant Highly Pathogenic Avian Influenza (H5N8) Virus in Zoos, India. Emerging infectious diseases. 2017 Apr;23(4):717-9.

43. Krump NA, You J. Molecular mechanisms of viral oncogenesis in humans. Nature reviews Microbiology. [Research Support, N.I.H., Extramural

Review]. 2018 Nov;16(11):684-98.

44. Shah SC, Kayamba V, Peek RM, Jr., Heimburger D. Cancer Control in Low- and Middle-Income Countries: Is It Time to Consider Screening? Journal of global oncology. [Review]. 2019 Mar;5:1-8.

45. Kaarthigeyan K. Cervical cancer in India and HPV vaccination. Indian journal of medical and paediatric oncology : official journal of Indian Society of Medical & Paediatric Oncology. 2012 Jan;33(1):7-12.

46. McLaughlin-Drubin ME, Munger K. Viruses associated with human cancer. Biochimica et biophysica acta. [Research Support, N.I.H., Extramural

Research Support, Non-U.S. Gov't

Review]. 2008 Mar;1782(3):127-50.

47. Vilchez RA, Butel JS. Emergent human pathogen simian virus 40 and its role in cancer. Clinical microbiology reviews. [Research Support, Non-U.S. Gov't

Research Support, U.S. Gov't, P.H.S.

Review]. 2004 Jul;17(3):495-508, table of contents.

48. Javier RT, Butel JS. The history of tumor virology. Cancer research. [Historical Article

Review]. 2008 Oct 1;68(19):7693-706.

49. Glenn WK, Ngan CC, Amos TG, Edwards RJ, Swift J, Lutze-Mann L, et al. High risk human papilloma viruses (HPVs) are present in benign prostate tissues before development of HPV associated prostate cancer. Infectious agents and cancer. 2017;12:46.

50. Agorastos T, Chatzistamatiou K, Katsamagkas T, Koliopoulos G, Daponte A, Constantinidis T, et al. Primary screening for cervical cancer based on high-risk human papillomavirus (HPV) detection and HPV 16 and HPV 18 genotyping, in comparison to cytology. PloS one. 2015;10(3):e0119755.

51. Coppola N, De Pascalis S, Onorato L, Calo F, Sagnelli C, Sagnelli E. Hepatitis B virus and hepatitis C virus infection in healthcare workers. World journal of hepatology. [Review]. 2016 Feb 18;8(5):273-81.

52. Goncalves DU, Proietti FA, Ribas JG, Araujo MG, Pinheiro SR, Guedes AC, et al. Epidemiology, treatment, and prevention of human T-cell leukemia virus type 1-associated diseases. Clinical microbiology reviews. [Research Support, Non-U.S. Gov't

Review]. 2010 Jul;23(3):577-89.

53. Sever R, Brugge JS. Signal transduction in cancer. Cold Spring Harbor perspectives in medicine. [Review]. 2015 Apr 1;5(4).

54. Coussens LM, Werb Z. Inflammation and cancer. Nature. [Research Support, Non-U.S. Gov't

Research Support, U.S. Gov't, P.H.S.

Review]. 2002 Dec 19-26;420(6917):860-7.

55. Osna NA, Donohue TM, Jr., Kharbanda KK. Alcoholic Liver Disease: Pathogenesis and Current Management. Alcohol research : current reviews. [Review

Research Support, U.S. Gov't, Non-P.H.S.]. 2017;38(2):147-61.

56. Shtivelman E, Cohen FE, Bishop JM. A human gene (AHNAK) encoding an unusually large protein with a 1.2-microns polyionic rod structure. Proceedings of the National Academy of Sciences of the United States of America. [Research Support, Non-U.S. Gov't

Research Support, U.S. Gov't, P.H.S.]. 1992 Jun 15;89(12):5472-6.

57. He Y, Feng D, Hwang S, Mackowiak B, Wang X, Xiang X, et al. Interleukin-20 exacerbates acute hepatitis and bacterial infection by downregulating IkappaBzeta target genes in hepatocytes. Journal of hepatology. [Research Support, N.I.H., Extramural

Research Support, N.I.H., Intramural

Research Support, U.S. Gov't, Non-P.H.S.]. 2021 Jul;75(1):163-76.

58. Franco E, Meleleo C, Serino L, Sorbara D, Zaratti L. Hepatitis A: Epidemiology and prevention in developing countries. World journal of hepatology. 2012 Mar 27;4(3):68-73.

59. Franco E, Bagnato B, Marino MG, Meleleo C, Serino L, Zaratti L. Hepatitis B: Epidemiology and prevention in developing countries. World journal of hepatology. 2012 Mar 27;4(3):74-80.

60. Mohamed AA, Elbedewy TA, El-Serafy M, El-Toukhy N, Ahmed W, Ali El Din Z. Hepatitis C virus: A global view. World journal of hepatology. [Review]. 2015 Nov 18;7(26):2676-80.

61. Sellier PO, Maylin S, Brichler S, Bercot B, Lopes A, Chopin D, et al. Hepatitis B Virus-Hepatitis D Virus mother-to-child co-transmission: A retrospective study in a developed country. Liver international : official journal of the International Association for the Study of the Liver. [Observational Study]. 2018 Apr;38(4):611-8.

62. Khuroo MS, Khuroo NS. Transmission of Hepatitis E Virus in Developing Countries. Viruses. [Review]. 2016 Sep 20;8(9).

63. Makam P, Matsa R. "Big Three" Infectious Diseases: Tuberculosis, Malaria and HIV/AIDS. Current topics in medicinal chemistry. [Review]. 2021;21(31):2779-99.

64. Satsangi S, Chawla YK. Viral hepatitis: Indian scenario. Medical journal, Armed Forces India. 2016 Jul;72(3):204-10.

65. Aslam B, Wang W, Arshad MI, Khurshid M, Muzammil S, Rasool MH, et al. Antibiotic resistance: a rundown of a global crisis. Infection and drug resistance. [Review]. 2018;11:1645-58.

66. Golkar Z, Bagasra O, Pace DG. Bacteriophage therapy: a potential solution for the antibiotic resistance crisis. Journal of infection in developing countries. [Review]. 2014 Feb 13;8(2):129-36.

67. Wright GD. Something old, something new: revisiting natural products in antibiotic drug discovery. Canadian journal of microbiology. [Research Support, Non-U.S. Gov't]. 2014 Mar;60(3):147-54.

68. Spellberg B, Gilbert DN. The future of antibiotics and resistance: a tribute to a career of leadership by John Bartlett. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. [Research Support, N.I.H., Extramural]. 2014 Sep 15;59 Suppl 2:S71-5.

69. Taneja N, Sharma M. Antimicrobial resistance in the environment: The Indian scenario. The Indian journal of medical research. [Review]. 2019 Feb;149(2):119-28.