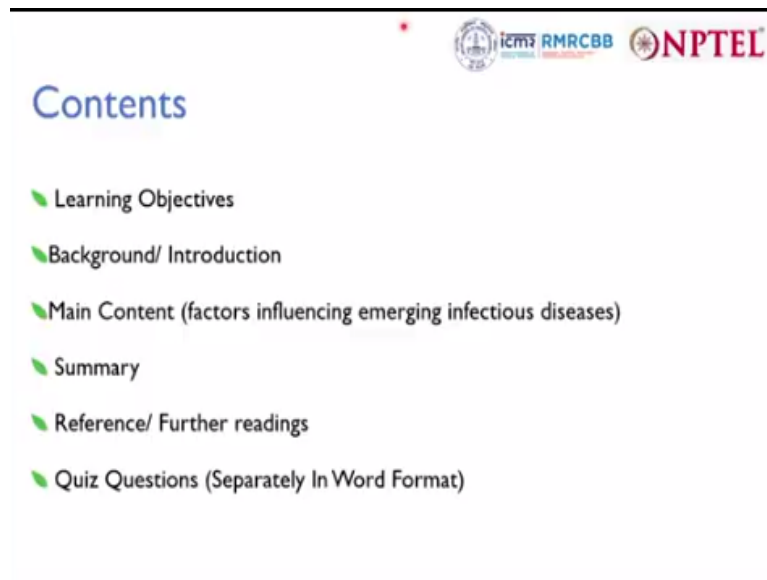


One Health
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Lecture - 10
The Factors Influencing an Emerging Disease

Hello, everyone. I am Dr. Sidhartha Giri. I am a medical microbiologist, and I am currently working as Scientist E at the ICMR Regional Medical Research Center, Bhubaneswar. Today I will cover the topic on factors influencing emerging infectious diseases. Basically, I will talk about emerging as well as reemerging infectious diseases and the causes for it.

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So the content of this presentation includes the learning objectives, the background, the main content, summary, reference, and further readings and finally, the quiz questions which are available in a separate format.

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Learning objectives

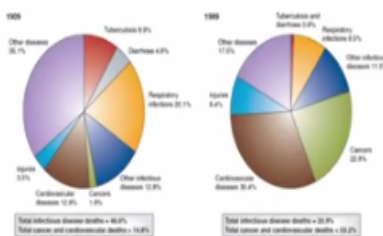
- Emerging infectious diseases and re-emerging infectious diseases
- Factors associated with emerging infectious diseases
- Diseases emerging due to the associated factors

So first coming to the learning objectives, I will cover what are emerging infectious diseases and reemerging infectious diseases, the factors associated with emerging infectious diseases and the diseases which have emerged and are associated with certain factors.

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Background

- Establishment of the germ theory and the discovery of specific microorganisms as the cause of a wide variety of infectious diseases led to substantial progress, such as the development of vaccines and antimicrobials
- In fact, at the end of the nineteenth century, scientists predicted the eradication of infectious diseases
- By 1950, with the discovery and wide spread use of penicillin, development of oral poliovirus vaccines, discovery of anti-tuberculous drugs, it was assumed by optimists that the war against infectious diseases had been won



Fauci AS, Clin Infect Dis, 2001
Weiss RA, et al Nature Medicine 2004

So establishment of the germ theory and the discovery of specific microorganisms for a wide variety of diseases actually led to a dramatic improvement and advancement in the field of microbiology and medicine. And it included the introduction of vaccines and antimicrobial agents because of which a lot of infectious diseases showed a decline.

In fact, at the end of the 19th century, scientists predicted the eradication of infectious diseases. By 1950 people have with the discovery of widespread use of penicillin, discovery of anti-tuberculous drugs and the development of oral polio vaccines as well as injectable polio vaccines, it was assumed by many scientists that the war against infectious diseases had been won.

And if you look at this graph, which shows the burden of disease in 1909 and 1999, you can see that infectious diseases had decreased dramatically from 47.7% of deaths to contributing to only 21% in 1999.

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Background

- ✔ In 1972, Burnet and White commented, "The most likely forecast about the future of infectious disease is that it will be very dull. There may be some wholly unexpected emergence of a new and dangerous infectious disease, but nothing of the sort has marked the past fifty years"
- ✔ However, many scientists remained sceptical due to failures such as controlling the infections in the developing world, rise of antimicrobial resistance, and emergence of new diseases



Fourni AS, Clin Infect Dis, 2001
Weiss RA, et al Nature Medicine, 2004

In fact in 1972, Burnet and White commented that, you know the future of infectious diseases will be dull, it will be boring, because nothing spectacular had happened in the last 50 years after swine, the Spanish Influenza. So however, many scientists remained skeptical due to the failures such as controlling infectious diseases in the developing world, the rise of antimicrobial resistance and of course, the emergence and reemergence of certain diseases.

As you can see from the map on the right, there have been several diseases which have emerged or reemerged during the last few decades.

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Definition



ICMR RMRCBB



NPTEL

Emerging infectious diseases are infections:

- That have recently appeared in humans
- Whose incidence is increasing fast
- There is a sudden increase in geographic range

Emerging infectious diseases can be caused by:

- New infectious agents which were previously unknown (HIV/AIDS, SARS, COVID-19)
- Previously known infectious agents which have spread to new geographical areas or new population groups (Dengue, Chikungunya)
- Previously known infectious agents whose role in specific diseases were unknown (Hepatitis C, *Helicobacter pylori*)
- Re-emergence of infectious agents causing disease in humans whose incidence had significantly decreased (re-emerging infectious diseases) (Tuberculosis in certain western countries)

Now coming to definition, emerging infectious diseases are infections that have recently appeared in humans, or whose incidence is increasing fast, or there has been a sudden increase in geographic range. And emerging infectious diseases can be caused by new infectious agents which were previously unknown like the human immunodeficiency virus causing the Acquired Immunodeficiency Syndrome, AIDS.

The Severe Acute Respiratory Syndrome, SARS and of course the recent one that is COVID-19 caused by the SARS Coronavirus-2 virus. Second is previously known infectious agents which have spread to new geographical areas or new population groups, for example, dengue and chikungunya, which are mosquito-borne diseases and have spread to new populations.

Now it is previously known infectious diseases whose role in specific diseases were unknown previously, like Hepatitis C, causing hepatocellular carcinoma and *Helicobacter pylori* causing gastric ulcers and gastric cancers. And finally, the reemergence of infectious diseases causing disease in humans, incidents have dramatically declined, but have shown resurgence. For example, tuberculosis in certain Western and Eastern European countries.

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The factors leading to infectious diseases include various drivers, which includes the first of all the biological drivers leading to emergence of infectious diseases, which basically includes the microbial adaptation and change which happens because of which the microorganisms change over time. They adapt well to spread in the human population and with that susceptibility of the human population to new infections.

The social drivers which include population growth, increasing density of human population. Example, overcrowding especially in urban areas, aging population, social inequality and poverty, globalization of food, manufacturing and marketing and social disruption due to war and conflict. Environmental drivers include environmental contamination, climate change and deforestation leading to changing or expanding vector habitats and more contact with wild animals.

Other drivers include international travel, spread in healthcare facilities, drug resistance breakdown in healthcare systems, public health systems and intentional biological attacks.

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- ✓ Factors which favour an emerging infectious disease to become established:
 - ✓ The pathogen has to be introduced into a vulnerable population
 - ✓ The pathogen must be able to spread readily from person to person
 - ✓ The infection is sustained in the population due to more people getting infected continuously

When a disease emerges, when an infectious disease emerges, to become established in a human population, the pathogen has to be introduced into a vulnerable population or susceptible population. If the population is immune, the pathogen will not be able to spread.

The pathogen must be able to spread readily from person to person, that is, it should be easily transmissible and the infection should be sustained in the population and as more and more people continue to get infected.

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ICMR RMRCBB NPTEL

Biological drivers: Adaptation in microorganisms and susceptibility to infection

- ✓ Influenza virus has ability to change genetic information
- ✓ Human immune system is not able to recognize and protect against the new variant
- ✓ Pandemics can result depending on ability to spread
 - ✓ In 1997, avian flu (H5N1) resulted in limited infection in humans as the variant was not able to spread rapidly (high mortality rate)
 - ✓ 2009 H1N1 influenza which crossed over from swine (pigs) to humans, was able to spread quickly resulting in a pandemic

Gene Segments, Hosts, and Years of Introduction

Triple Reassortment

Classical Swine

Current Swine

2009 A/H1N1

Garten RJ, et al, Science, 2009

Now coming to the biological drivers, as I said, adaptation in microorganisms and increasing susceptibility of the population to infection. The classic example for this is the influenza virus, which has the ability to change genetic information. So this virus is actually a RNA virus where the RNA genome is segmented, there are eight segments and recombination can happen between the RNA segments from different species like avian and swine.

So with this new variants emerge periodically and the human immune system is not able to recognize and protect against the new variant. And these new variants will be able to cause pandemics that is global spread of infection. There are two examples here. One is the 1997 avian flu H5N1 which started from Hong Kong, but was not able to spread quickly.

One of the reasons was that this virus had a high mortality rate, and the variant was not able to spread rapidly. In contrast, the 2009 H1N1 swine flu crossed over from pigs to humans, the mortality rate was low. The virus easily was highly transmissible and was able to spread quickly resulting in a pandemic.

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The slide is titled "Transmissibility and globalization" and features logos for ICMZ, RMRCBB, and NPTEL at the top. It contains several bullet points with green checkmarks, a world map with red and green dots, and a citation at the bottom right.

- Changing human behaviour and environment leads to two events in emergence of infectious diseases:
 - Increased opportunity for animal-human transmission of infection
 - Onward transmission after a person has become infected
 - 1918-1919 influenza pandemic, HIV/AIDS, SARS
- Fatal infections not necessarily coupled with transmissibility/ infectiousness (H5N1 avian flu)
- Fatal infections may not spread at all from index case (Rabies) or may spread just to close contacts (Lassa fever, Ebola virus)
- Air travel has led to rapid spread of infectious diseases (SARS, 2009 H1N1 pandemic, COVID-19)

Boiler RE, Nature Reviews, 2022

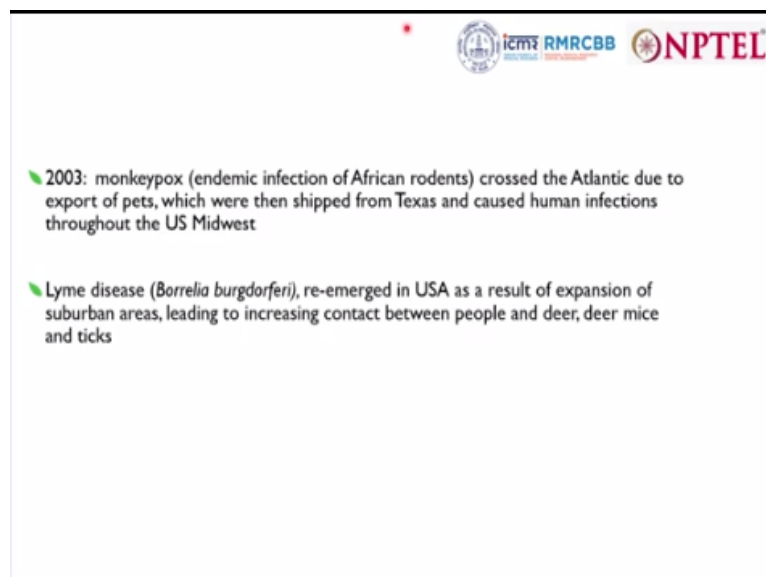
The next factor is transmissibility and globalization. So changing human behavior and environment leads to two events in the emergence of infectious diseases. One is increased opportunity for animal to human transmission of infection. And the second, once the

transmission happens, the onward transmission should happen after a person gets infected, so that there is a continuous population of newly infected people.

So examples include the 1918-19 influenza pandemic HIV causing AIDS, SARS, COVID-19, we all know that. So one thing is fatal infections are not necessarily coupled with infectious disease. As I mentioned earlier, the H5N1 avian flu was not able to spread quickly. It had a higher mortality rate. In fact, fatal infections may not spread at all from the index case, as we see in rabies, or may spread to some close contacts like we have seen Lassa fever and Ebola virus infections.

However, during the last few decades, air travel has led to rapid spread of several emerging infectious diseases, especially causing respiratory infections, which includes the SARS, 2009 H1N1 pandemic and COVID-19.

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There are some other examples such as the 2003 incident where monkeypox which is an endemic infection of African rodents crossed the Atlantic due to export of pets. And these pets were then shipped from Texas to other areas and caused human infections throughout the US Midwest. The Lyme disease reemerged in USA as a result of expansion of suburban areas leading to increasing contact between people and deer, deer mice and ticks.

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Environment and emerging infectious diseases

- ✔ As humans continue to encroach into previously uncultivated forest areas, new contacts between wild animals and humans and their livestock increases the risk of cross-species infection
- ✔ 1998: northern Malaysia, nipah virus crossed over from fruit bats to pigs and then to pig handlers/ farmers. Subsequently, nipah virus outbreaks have been reported from other parts of Asia, primarily from Bangladesh and India
- ✔ 1997: Australia, Hendra virus crossed over from Australian fruit bats and fatally infected a veterinarian treating a sick horse
- ✔ Increase in range and prevalence of dengue fever because its mosquito vector breeds rapidly in the urban environment. The 2001–2002 epidemic in Hawaii is reminder that dengue has also re-emerged in areas once considered to be dengue-free



The next important factor in emerging infectious diseases is the environment. As we are all aware of, humans continue to encroach into previously uncultivated forest areas, due to which new contacts happen between humans, wild animals and livestock, which leads to the risk of cross-species infection. Other than the corona viruses, which I have talked about earlier, in 1998 in northern Malaysia nipah virus crossed over from fruit bats to pigs and then to pig handlers or farmers.

Subsequently nipah virus outbreaks have been reported from other parts of Asia, including India and Bangladesh. In 1997, near Sydney, Australia, Hendra virus crossed over from Australian fruit bats, and fatally infected a veterinarian treating a sick horse. These are all spillover events where an infectious pathogen crosses species. As you can see, the Hendra virus has been transmitted from Australian fruit bats to horses and then to humans.

Another reason for spreading of infectious diseases is that the vectors are spreading due to rapid changes in the urban environment. For example, the mosquito vector for dengue fever has spread to many areas. And the 2001-2002 epidemic in Hawaii is a constant reminder that dengue can emerge in areas which were previously dengue free.

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Globalization of food manufacturing and marketing

- ✓ Undernutrition remains a major cause of ill health globally and global food demand is projected to increase substantially by 2100 AD
- ✓ Increase in agricultural production can improve human health globally, but can lead to emergence and re-emergence of infectious diseases
- ✓ Establishment of fresh water habitats required for agriculture, can lead to increase in diseases such as malaria, dengue, schistosomiasis



Rohr JR, Nature Sustainability, 2019

The next factor is globalization of food manufacturing and marketing. Undernutrition remains a major cause of ill health globally and global food demand is going to increase substantially by 2100 AD. Increase in agricultural production is necessary and can improve human health globally, but it can also lead to the emergence and reemergence of infectious diseases.

For example, due to increased demand of agricultural production, there will be deforestation, there will be more humans and contact between wild animals and humans. And there will be spread of other diseases which require freshwater habitats. For example, diseases such as malaria, dengue, schistosomiasis will increase. And unfortunately, the rural population where these agricultural production is going to take place will be the one who will be the most vulnerable to such increases in infectious diseases.

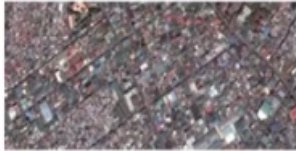
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Social and economic conditions, geopolitical instability, behavioural changes

- ✔ Vulnerable population, socially disordered, living in unhygienic conditions and close contact- susceptible to microbial colonization
- ✔ HIV/AIDS in Africa due to widespread poverty, political instability
- ✔ Cholera, diphtheria outbreaks in Yemen due to conflict and warfare
- ✔ Other factors:
 - ✔ Increase in urbanization, population size and density, poverty (especially in urban slums),
 - ✔ Increase in political, economic, and environmental refugees, conflict and warfare
- ✔ Rapid urbanization leads to increase in childhood diarrhea, pneumonia, tuberculosis and dengue, and facilitates emergence and spread of various 'emerging' diseases such as SARS, MERS, 2009 H1N1 pandemic, COVID-19

The next important factor is social and economic conditions, geopolitical instability and behavioral changes. Vulnerable population, socially disordered, living in unhygienic conditions and overcrowding leads to susceptibility to microbial colonization with new and emerging pathogens. Other factors include increase in urbanization, population size and density, poverty, especially seen in urban slums.

There has been also increasing political, economic and environmental refugees. People are migrating from one continent to another continent, due to various factors such as conflict and warfare. For example, HIV AIDS in Africa has increased due to widespread poverty, political instability. And cholera, diphtheria outbreaks have been seen in Yemen, due to conflict and warfare.

And in general, rapid urbanization leads to increase in diseases such as childhood diarrhea, pneumonia, tuberculosis, dengue, and facilitates the emergence and spread of various emerging diseases such as SARS, the Middle Eastern Respiratory Syndrome, MERS 2009, H1N1 pandemic and COVID-19.

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Food borne infections

- Common pathogens leading to food borne illness: norovirus, *Salmonella*, *Campylobacter*, *E. coli*
- E. coli* O157:H7, which is harmless to cattle but toxic to humans who get infected through food, milk, water, or direct contact with animals
- Salmonella enteritidis* in chickens
- Variant Creutzfeldt-Jakob disease (vCJD) in UK arising due to consumption of contaminated food products of cattle affected by mad cow disease (BSE)



<https://www.who.int/india/health-topics/food-safety>

Now infections which are food borne, again comprise another important group of emerging and reemerging infections. Common pathogens leading to food borne illness are Norovirus, *Salmonella*, *Campylobacter*, *E. coli*. In fact, in many countries with the introduction of rotavirus vaccination in the under-five age group, norovirus is emerging as one of the leading causes of viral gastroenteritis in the under-five age group.

Escherichia coli O157:H7, again it is harmless to cattle, which is a reservoir, but it is toxic to humans who get infected through milk, water, food, or direct contact with animals. This bacteria can cause severe bloody diarrhea and hemolytic uremic syndrome. Gastroenteritis due to bacteria such as *Salmonella enteritidis* in chickens is also emerging as an important food borne infection.

And variant Creutzfeldt-Jakob disease vCJD appeared in the UK in 1996 due to consumption of contaminated food products of cattle affected by mad cow disease or bovine spongiform encephalopathy. So these are important examples of food borne infections. And as the food production increases, the demand for food increases, unhygienic conditions increase as people continue to move towards urban areas.

Food borne infections will continue to be an important cause of emerging and reemerging infectious diseases.

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Bioterrorism and biowarfare

- History:
 - ▶ Catapulting of plague-ridden corpses over enemy walls in the 1346 siege of Caffa (Ukraine)
 - ▶ Dispatch of smallpox-impregnated blankets to Indians by British officers in the Seven Years War (1754–1763)
- ▶ In 1984, a religious cult in Oregon, USA, spiked restaurant salad bars with *Salmonellae* in an attempt to influence a local election
- ▶ An anthrax attack in 2001, anthrax-spore-filled letters were mailed by a terrorist to prominent figures in the US, including two senators, resulted in illness in at least 18 people and the death of 5 people



The next important and interesting factor is Bioterrorism and Biowarfare. Now there have been examples in history where biological weapons have been used in warfare. For example in 1346 in a war in Ukraine, plague infected bodies were thrown over the enemy walls so that people will die of the infection.

During the Seven Years War between the French and British forces in the Americas, the smallpox impregnated blankets were dispatched to the Native Americans who got infected. And in the last few decades also there have been examples of bioterrorism using biological weapons. In 1984, a religious cult in Oregon, USA spiked restaurants salad bars with *Salmonellae* in an attempt to influence a local election.

And in 2001, anthrax-spore-filled letters were mailed by a terrorist to prominent figures in the US, including two senators, because of which 18 people became ill and 5 of them died. So in future also biowarfare and agents of bioterrorism will continue to emerge as a very important area.

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Health care associated emerging infections

- ✔ Technological advances in medicine and public health has also led to emergence of pathogens with drug resistance
 - ✔ Methicillin resistant *Staphylococcus aureus* (MRSA)
 - ✔ Extended spectrum beta lactamases (ESBL) producing gram negative bacteria
 - ✔ Multi-drug resistant tuberculosis
 - ✔ *Candida auris*
- ✔ Most effective vector of infectious diseases in health care setups: syringe and needle (massive increase in injecting equipment over the last few decades, which led to spread in HBV, HCV, HIV)
- ✔ Transmission of west nile virus by blood transfusion, and organ transplantation reported

MDR-TB



Mycobacterium tuberculosis

The next is healthcare associated emerging infections. There has been a tremendous development and advancement in medicine and public health during the last 100 years, and this has unfortunately led to emergence of pathogens with drug resistance.

Examples include methicillin resistant *Staphylococcus aureus* MRSA, the extended spectrum beta lactamases producing gram negative bacteria such as *Escherichia coli* and *Klebsiella*, which are very important causes of hospital acquired infections, especially bloodstream infections and infections of other organs as well.

Other examples include multidrug resistant tuberculosis and *Candida auris*. *Candida auris* is an invasive fungal pathogen, and it is quite resistant to drugs and causes serious infections in the hospital setups. The most effective vector of infectious diseases in healthcare are the syringes and needles. There has been a massive increase in injecting equipment over the last few decades, which has led to spread of infections such as Hepatitis B virus, Hepatitis C virus and HIV.

There have been also reports of viral infections such as West Nile virus, which has happened due to blood transfusion and organ transplantation, which are again, important areas. These are areas which will develop rapidly in future and we need to take a note of these hospital associated causes of emerging infections.

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Microbial agents and chronic diseases

- ✔ Infections caused by pathogens that are associated with chronic diseases: one of the most challenging categories of newly emerging (or at least newly recognized) infections
- ✔ HBV, HCV: chronic liver damage, hepatocellular carcinoma
- ✔ Human papilloma virus (HPV): cancer of uterine cervix
- ✔ Epstein-Barr virus (EBV): Burkitt's lymphoma (Africa), nasopharyngeal carcinoma (China)
- ✔ Human herpesvirus 8 (HHV-8): Kaposi's sarcoma
- ✔ Helicobacter pylori: gastric ulcers, gastric cancer

For certain chronic diseases we knew the disease well. There have been several cancers, ulcers. But we didn't know that microbial agents can cause such chronic diseases. So infections caused by pathogens that are associated with chronic diseases are one of the most challenging category of newly emerging infections.

Examples include, the Hepatitis B virus and hepatitis C virus which cause chronic liver damage and hepatocellular carcinoma. The human papilloma virus, which causes cancer of uterine cervix, the Epstein-Barr Virus causing Burkitt's lymphoma and nasopharyngeal carcinoma, the human herpesvirus 8, which causes Kaposi's sarcoma, especially in AIDS patients, Helicobacter pylori which causes gastric ulcers and gastric cancers.

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Summary

- ✔ While life expectancy continues to increase globally, and there has been a decline in morbidity and mortality due to infectious diseases, the threat of emerging and re-emerging infectious diseases will continue
- ✔ Rapid urbanization, pollution, climate change, increased demand for food production, will lead to emergence and spread of infectious diseases such as HIV, SARS, COVID-19
- ✔ Climate change may lead to spreading of vector borne diseases to new locations
- ✔ Global travel, international conflict, and human migration, may help in rapid transport of pathogens

So to summarize, while life expectancy continues to increase globally and there has been substantial decline in morbidity and mortality due to infectious diseases, the threat of emerging and reemerging infectious diseases will continue. Rapid urbanization, pollution, climate change, increased demand for food production will lead to emergence and spread of infectious diseases such as HIV, SARS, COVID-19.

Climate change may lead to spreading of vector borne diseases to new locations, such as dengue, chikungunya, malaria. And global travel, international conflict and human migration may help in rapid transport of emerging and reemerging pathogens.

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Reference/ further readings

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So these are some of the important references which can be used for further readings. All these articles contain very useful information regarding factors associated with emerging and reemerging diseases. Thank you for your attention.