One Health
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Lecture – 07
Mechanisms of Pathogen Cross Over across Species Boundaries

Hi as part of unit 2 emerging infectious diseases and antimicrobial resistance module.

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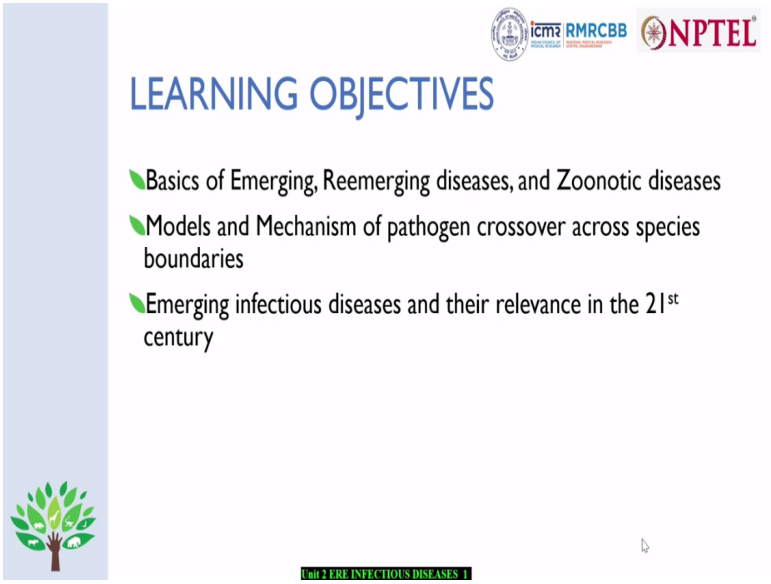

Today, I will be discussing the basics of emerging and reemerging diseases and zoonotic diseases, models and mechanisms of pathogen crossover across species boundaries, emerging infectious diseases and their relevance in the 21st century.

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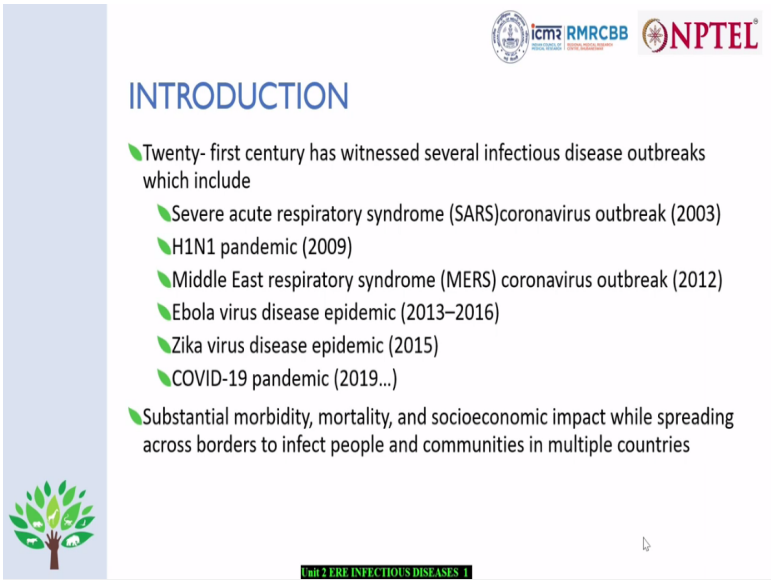

To start with 21st century has witnessed several infectious disease outbreaks which include severe acute respiratory syndrome of 2003, HINI pandemic of 2009, Middle East respiratory syndrome of 2012, Ebola virus disease epidemic which occurred between 2013 to 2016 in West Africa, Zika virus disease epidemic of 2015 and the most recent COVID-19 pandemic which still continues to haunt us.

The understanding what we have gained from these experiences is that these diseases have the ability to cause substantial morbidity, mortality and socioeconomic impact and they also have the ability to spread across borders to infect people and communities in multiple countries within a short span of time.

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Here, I will be discussing the definitions of emerging and remerging diseases and zoonotic diseases. When it comes to the definition of emerging infectious disease, it is defined as an outbreak of previously unknown disease, for example, COVID-19. A Known disease that are rapidly increasing in incidence and geographic range in the last two decades or 20 years Zika or Lyme diseases or persistence of infectious diseases that cannot be controlled.

Dengue is the best example where we do not have a vaccine and this disease is causing public health threat as well as it has the ability to cause very high morbidity and mortality in the community. Moving on to reemerging infectious diseases, these are the diseases that re-appear after they have been significant decline. So, the best example is malaria which kind of showed decline in 1970s due to public health interventions.

And then showed ways and still continues to be a public health threat and the other diseases include influenza, tuberculosis, cholera and pertussis. Zoonotic diseases, these are the diseases which transmit from an infected animal to an human through direct contact or through food, water or the environment. Nearly 70% of the zoonotic diseases are emerging infectious diseases. So, both emerging and reemerging infectious diseases could be of zoonotic origin.

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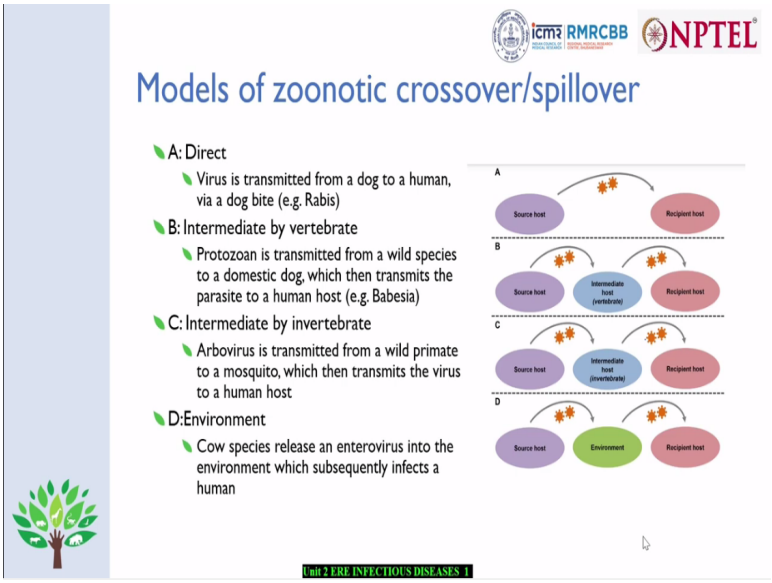

Here I would be discussing the four models of zootonic crossover or spillover. These are the accepted modes of disease transmission. One is direct, where a virus is transmitted from a domestic dog to the human; the best example is rabies. This is through the bite of infected rabid dog. Next is the intermediate so the intermediate host could be vertebrate or invertebrate.

So, when it comes to vertebrate say protozoan is transmitted from a white species to a domestic dog which then can transmit the parasite to humans, the best example is Babesiosis. Intermediate by invertebrate so here the arbovirus can be transmitted from a wild primate to a mosquito and then the mosquito can subsequently pass on the virus to human host. Next is the environment, where say cow is infected with particular enterovirus.

This can be transmitted to humans by contaminated water where the cow sheds the bacteria with the virus in the dung and this could cause infection. Next is the environment, for example, cow species could release the enterovirus such as e-coli into the environment which would contaminate the water source and which can subsequently infect humans on consumption of the contaminated water.

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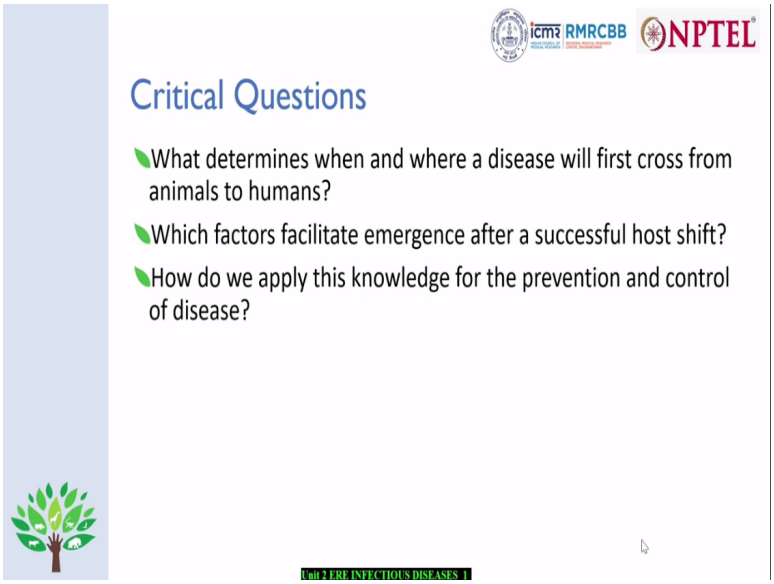

There are three critical questions which we have to keep in mind when we are discussing about the mechanism of crossover. One is what determines when and where a disease will first cross from animals to humans, which factors facilitate emergence after a successful host shift, how do we apply this knowledge for the prevention and control of diseases.

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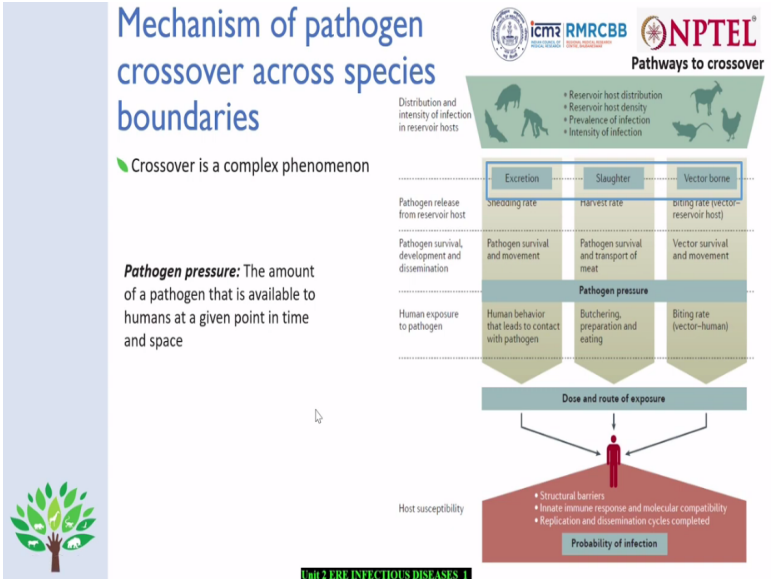

Here I would spend few minutes in discussing the mechanism of pathogen crossover across the species. As you all see on the figure on the right side, pathway of crossover is very complex phenomena. So, here the first stage is distribution and the intensity of infection in the reservoir

host. So, this depends upon the reservoir host distribution, reservoir host density, prevalence of infection in the reservoir host and intensity of infection.

So, the simple part to understand is the reservoir host the distribution basically how these population or the reservoir host populations are distributed in a particular geographic area or reservoir host density which basically means the population size are these animals thickly populated or spacely populated is one of those factors and prevalence of infection. So, if the infection is highly prevalent in a particular reservoir host the chances of spillover is also high.

And then intensity of a infection again the prevalence is dependent on intensity of infection and intensity of infection is the ability of the pathogen to infect multiple animals, in a quick session or within a short duration of time. So, this kind of helps in building the prevalence as well as incidence of disease in particular reservoir host. So, the next stage is the pathogen release from the reservoir host.

So, this could occur through excretion, slaughter or a vector. Following this stage it again becomes a very crucial stage where pathogen survival, development and dissemination. So, this is a stage where we discussed about the pathogen pressure. So, pathogen pressure basically means the amount of pathogen that is available to humans at a given point in time and space.

So, basically the amount of pathogen at a particular time in a particular geographic area. So, following this again humans have to come in contact with the pathogen. So, human exposure to pathogen has to occur. So, this is again dependent on the human behaviour mostly. One is humans coming in contact with contaminated source of water. Second thing is butchering, preparing and eating the carcass meat.

Again this is also a behaviour. Next the biting rates of the vectors. So, humans have to come in contact with the vectors to pick up the disease. So, say we have good dose of bacteria and the pathogen has found a route of entry. There is still some structural barriers and our own immunity and molecular capabilities and then replication and dissemination cycles have to be completed before the pathogen actually establishes in the human body.

So, the take home message from this slide is that the mechanism of pathogen crossover is complex phenomena and it leads at least pathogen to pass through multiple stages before it actually reaches the humans and even within the human body there are mechanisms which can prevent the disease from occurring.

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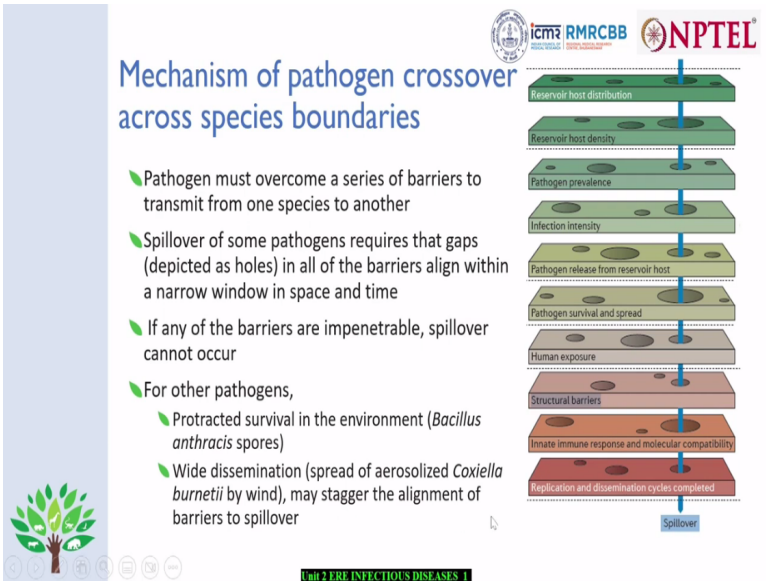

Moving on with the discussion on mechanism of pathogen crossover. The pathogen as I was discussing earlier must overcome a series of barriers to transmit from one species to the another. So, spillover of some pathogens require all the gaps so these are depicted as host in the various stages in this figure on the right side. So, all of the barriers aligned within the narrow window in space and time.

So, basically pathogen to have a successful spillover, it has to pass through all the barriers and then if any of these barriers are impenetrable, the spillover cannot occur. So, this also gives us an hint that breaking one or two of these part of the transmission chain could help in preventing the disease. For other pathogens protected survival in the environment will play a major role, for example, the bacillus anthracis spores.

So, they can survive up to 6 to 7 decades and cause the infection. So, again here the environment plays a role and the way the pathogen can adopt to that and then the other one is the widespread

dissemination of coxiella burnetti. So, this basically depends on the spread of aerosols. So, again here the regular infection transmission might not apply for these spillover.

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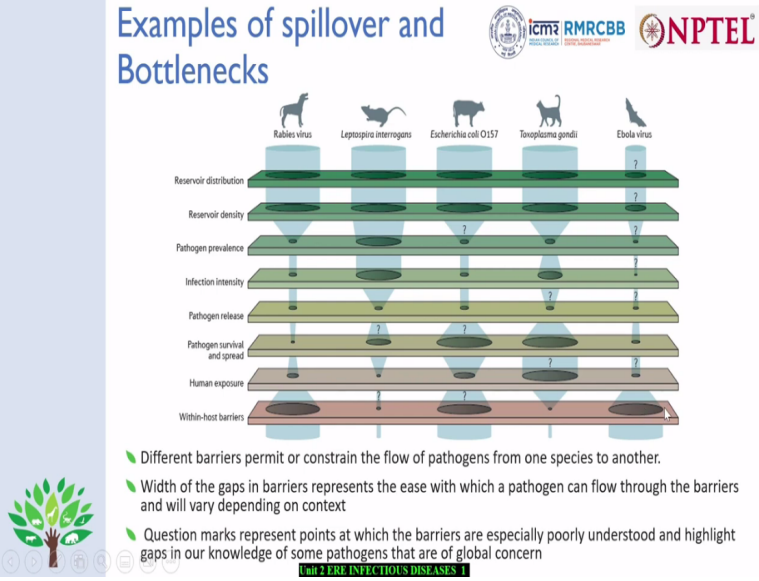

So, here I will be giving some examples of spillovers and the bottlenecks and how much understanding we have in terms of these zoonotic diseases spillovers from animals to humans. So, different barriers permit or constraint the flow of pathogens from one species to another. So, that is kind of shown in the form of the funnels and then how these barriers are penetrated. So, the width of the gaps in the barriers represent the ease with which pathogen can flow through the barriers and will vary depending on the context.

And the question mark represent the points at which the barriers especially poorly understood there are high gaps in the knowledge. So, for example, if we take rabies so the reservoir distribution and the reservoir density of the animal population. So, basically the dogs are quite abundant in the urban areas of India so whereas the prevalence of the disease or infection intensity or pathogen release.

So, when we look at these other factors so they are very constraint by the time they actually come and reach the humans there are lot of constraints the pathogen has to pass through and then once it reaches the human, the infection kind of establishes and there is no way the person

recovers. So, it's most of the time it results in death. So, in case of Leptospirosis we see a larger funnel so the gaps in the reservoir distribution.

Reservoir density, prevalence and even the intensity of infection. So, when we look at these gaps they are quite broad which basically means that the pathogen can pass through these barriers very easily. After that the pathogen release and then the pathogen survival and spread. So, here the constraint starts and by the time it's actually percolates to the humans it is very restricted.

So, that is one of the reasons why Leptospirosis is not highly prevalent in all the populations other than the incidences where humans come in contact with the contaminated environment with leptospira. Again the E. Coli I think this example we have already seen. So, the constraints are in terms of prevalence, intensity of infection, pathogen release and once the pathogen kind of crosses this, the barriers are quite wide.

We can actually see that the pathogen can easily pass through though the understanding is still lacking. So, similarly for toxoplasma gondii we can see a different levels we see constraints and ease with which the pathogens passes. Ebola is one of the diseases we know that the virus is prevalent in bats. So, here the first few barriers such as reservoir distribution, reservoir density to some extent are broader.

So, after that the knowledge about how this is actually gains an entry into the human population is very restricted and once it reaches the human population, again the human body as such does not have much of a role in protecting itself. So, that is one of the reasons why it is one of those dreaded disease which humans are facing. So, this kind of helps us understand the role of various stages through which the pathogen has to pass through before it can actually establish as a human pathogen.

So, once say for example, Ebola virus reaches the humans so it can transmit to other humans quite easily. In case of barrier where we have the host barrier for rabies the disease kind of is restricted to the person who is infected, so it does not pass on from there on, but it causes mortality in the humans.

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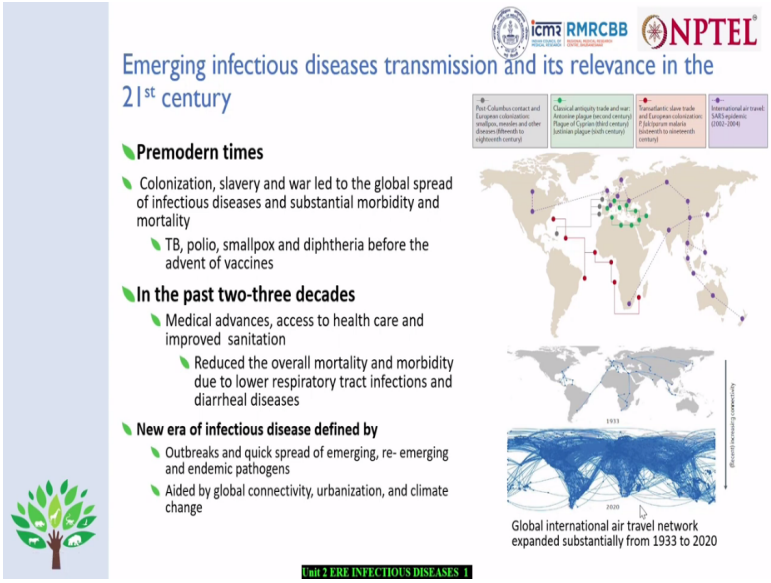

So, moving on with the discussion on emerging infectious, disease transmission and its relevance in the 21st century. So, to give some background during the premodern times it was the colonization, slavery and war which led to global spread of infectious diseases and these diseases used to cause substantial morbidity and mortality. So, the diseases include TB, Polio, smallpox, diphtheria before the advent of vaccines.

In the past two to three decades there have been lot of medical advances and improved access to healthcare and improved sanitation. So, this has reduced the overall mortality and morbidity due to lower respiratory track infections and diarrheal disease. The new era of infectious diseases, these are defined by outbreaks and quick spread of emerging and remerging diseases.

So, this is mainly aided by global connectivity, urbanization and climate change. We look at the way the connectivity has been in the last century or so. What is very striking is that during the post Columbus era the connectivity was mainly between parts of Europe and Caribbean. So, this was very simple root and then the other one is the classic and the trade routes.

So, this was the war which was mainly confined to Europe, parts of Middle East and North Africa. So, then came the slave trades routes which is depicted in red. So, we can see that parts of North America, South America connected with the South Africa and other African regions.

So, if we look at the 2004 SARS epidemic. So, the connectivity is very high we can see that most of the parts of the world are connected well.

So, when compared to 1933 where we had hardly any connection so what we see here in 2020 is that global international air travel network has expanded substantially between 1933 to 2020.

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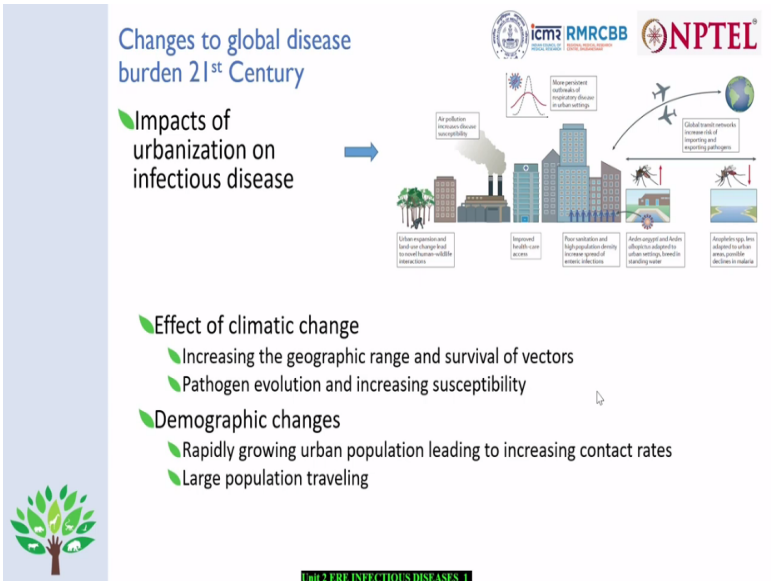

Moving on with the discussion on changes to the global disease burden in 21st century. So, this is mainly impacted by urbanization, climate change and demographic changes. So, the impacts of urbanization on the infectious diseases is nicely depicted in this figure. So, I will be just focusing on those aspects which facilitate emergence of infectious diseases. One is encroachment of the forest by human population.

So, with rapid expansion of urban areas this is leading to more interaction with the wild life and the spillover risk. The second thing is increasing population leading to poor quality of life. One is with the rise in population growth more persistent outbreaks occur and especially the respiratory diseases in urban areas. Second thing is poor sanitary conditions due to high population density.

This increases the spread of enteric infections, the aspect which is more scary is that the vectors are nicely adopting to the urban setting especially the vectors such as Aedes aegypti and Aedes

albopictus which transmit dengue. So, these are well adopted to the urban areas and cause huge outbreaks in humans. The fourth aspect which is also of concern is the global transit network.

So, this is increasing the risk of importing and exporting the diseases very quickly from various parts of the world. So, moving on to the effect of climate change. So, here I am just briefly touching upon the effect of climate change and demographic changes. One is with the climate change there is increase in geographic range and survival of vectors. So, some of the vectors which were not found in parts of Himalaya for example, the Aedes species.

Now because of rapid change in climate we do find outbreaks of dengue in parts of Himalayas also. The pathogen evolution and increase susceptibility is another issue. So, with more interactions with the wild life coming up and then the changing climate so there is increase susceptibility also in the human population to these diseases which are evolving new life.

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So, now the question is how are we going to tackle these challenge? One is forward looking so basically we do have institutional structures built to address old enemies. These can be adopted for emerging infectious disease threats. The second thing is increased attention needs to be paid to pathogens currently circulating both in wild life as well as domestic animals. So, this is also most important act.

So, basically we need to strengthen the surveillance in the wild life as well as domestic animals. The second thing is reinterpretation of information available from classic tools such as PCR and leveraging the multiplex serological approaches to detect pathogen emergence. New technology including advances in data collection and surveillance needs to be harnessed, increased interest in integrating multiple serological platforms from genomics to case data to a better understanding of pathogen spread.

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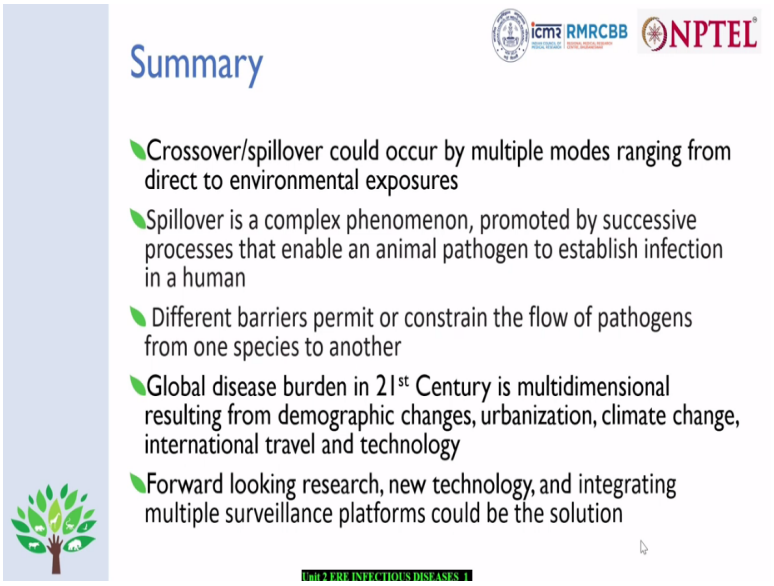

In summary, crossover or spillover could occur by multiple modes ranging from direct to environmental exposure. Spillover is a complex phenomena which is promoted by successive processes that enable animal pathogen to establish infection in humans. Different barriers permit or constraint the flow of a pathogens from one species to another and better understanding of these barriers could help in developing public health interventions to prevent and control the disease.

Global disease burden in 21st century is multidimensional. This is result of demographic changes, urbanization, climate change and international travel and development of technology. Forward looking research and new technology and interpreting multiple surveillance platforms could be a solution. Thank you.