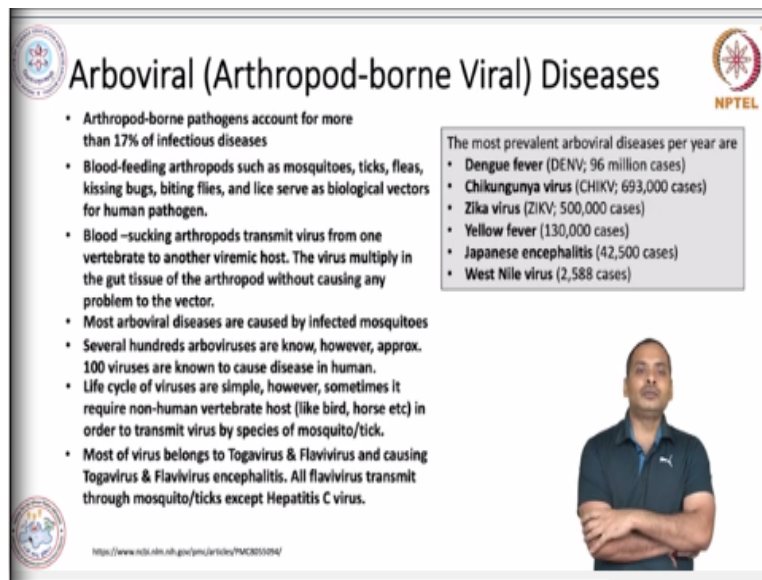


Host-Pathogen Interaction (Immunology)
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Lecture-69
Introduction to Arbovirus Infection

Hi, so in previous session we have discussed extensively about the influenza virus and now let us move on and in this session we will discuss about the arbovirus and we will discuss arbovirus infection and the disease caused by the arboviruses. So, in this session I will give you a brief introduction about all arboviruses. And in next session I will discuss about the dengue virus, I will not take you in too much detail but I would like to give you the overview about the dengue virus. And in subsequent session I will discuss about Zika virus. So, let us begin with arbovirus.

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Arboviral (Arthropod-borne Viral) Diseases

- Arthropod-borne pathogens account for more than 17% of infectious diseases
- Blood-feeding arthropods such as mosquitoes, ticks, fleas, kissing bugs, biting flies, and lice serve as biological vectors for human pathogen.
- Blood-sucking arthropods transmit virus from one vertebrate to another viremic host. The virus multiply in the gut tissue of the arthropod without causing any problem to the vector.
- Most arboviral diseases are caused by infected mosquitoes
- Several hundreds arboviruses are known, however, approx. 100 viruses are known to cause disease in human.
- Life cycle of viruses are simple, however, sometimes it require non-human vertebrate host (like bird, horse etc) in order to transmit virus by species of mosquito/tick.
- Most of virus belongs to Togavirus & Flavivirus and causing Togavirus & Flavivirus encephalitis. All flavivirus transmit through mosquito/ticks except Hepatitis C virus.

The most prevalent arboviral diseases per year are

- Dengue fever (DENV; 96 million cases)
- Chikungunya virus (CHIKV; 693,000 cases)
- Zika virus (ZIKV; 500,000 cases)
- Yellow fever (130,000 cases)
- Japanese encephalitis (42,500 cases)
- West Nile virus (2,588 cases)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3051094/>

So, arbovirus what do you understand by arbovirus? Probably this is a little new term to you. So, arboviruses is nothing it is all those viruses which is transmitted through the arthropods, arthropods for example the mosquito, there are so many arthropods, one of the unique and most prominent arthropod which transmit the viruses is mosquito. So, let us look at these arboviruses. So, arthropod borne pathogen account for more than 17% of infectious disease, it is a quite reasonably big number.

So, most of infectious diseases are basically is through this arthropod-borne pathogen. So, here I am talking about the arthropod-borne pathogen, it is not only the viruses, please note it. So, for example you know there is malaria, so malaria is a one of a serious disease which is caused by the protozoans. So, overall if you see then this is a quite big number, so these arthropods can transmit not only viruses they can transmit another infectious agent.

So, basically they are blood sucking arthropod, so this is quite obvious that these are supports will be take the blood meal. And most of these arthropods are prominent arthropods which transmit this pathogen are mosquito; mosquito is number 1, ticks. There are ticks I will show you what is tick, probably you might be aware about the ticks but I do not know maybe you are not able to visualize.

The ticks are basically present in animals, in probably if you have a pet. So, sometimes you will see a very hard shell kind of thing sticking to these animals, especially near the ear region or head region. Because over there they cannot remove these animals, if it is in lower trunk then they can scratch it and remove it. So, the tick is also one of the key arthropod which can transmit the disease, fleas, kissing bugs, biting flies and lice serve as a biological vector for human pathogen.

So, please note it is not only for the viruses, this is for all kind of pathogen. So, this blood sucking arthropod transmit virus, now we are talking about the viruses; viruses from one vertebrate to another viremic host. So, they take the blood meal from viremic individual and then they transmit to another individual. In general the virus basically multiplies in the gut tissues of the arthropod without causing any problem to the vector.

So, I never heard that this mosquito looks is not well, you never heard this statement or mosquito may have a fever. So, what I want to say that they harbor, the virus they multiply the virus but they do not fall sick that is what I want to say. Most arboviral diseases are caused by infected mosquito. So, mosquito is a main ~~carrier~~ **carrier** for this virus. Several 100 arboviruses are known, however approximately 100 viruses are known to cause disease in human.

This is a one very important fact. And life cycle of viruses are quite simple, however sometime they require non-human vertebrate in order to sustain or to multiply like birds, sometimes there is a bird cycle also. They infect the bird and then in bird they will make more number, it could be bird; it could be horse in order to transmit virus by species of a mosquito or tick. Most of virus belong to there is a family of virus which we call it as a Togavirus and Flavivirus.

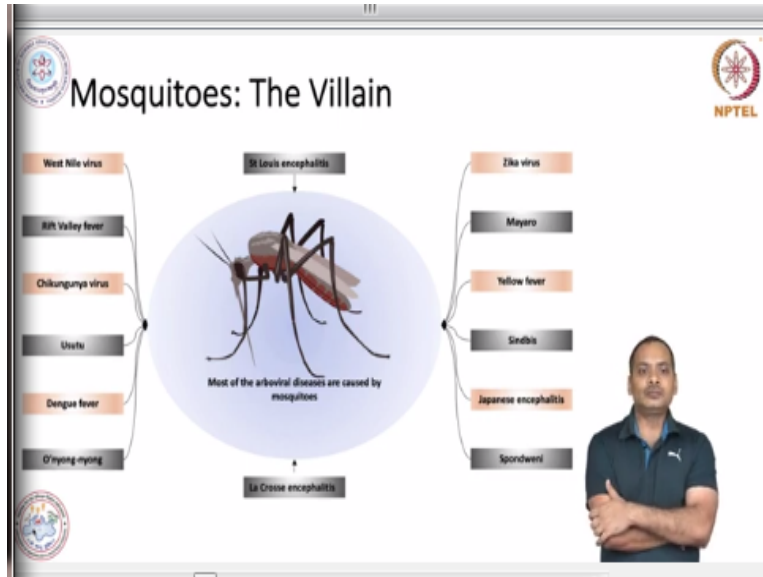
So, most of these arboviruses are belong to this Togavirus family or Flavivirus family. And basically they cause the Togavirus and Flavivirus in general they cause the encephalitis. What is encephalitis? Encephalitis is basically inflammation of central nervous system that includes brain and spinal cord. So, these virus infections can cause the encephalitis that is inflammation of brain and spinal cord.

So, all Flavivirus basically transmitted through this mosquito or tick except one virus which is a hepatitis C virus, so this is a characteristic of Flavivirus. So, hepatitis C virus basically transmitted through this contaminated food or water. So, except hepatitis C virus all Flavivirus is transmitted through this vector that is mosquito or tick. So, this arbovirus cause a lot of there is a quite huge burden of various kind of diseases by the arboviral diseases here you can see.

One is the dengue virus, about 96 million cases are there per year chikungunya, this is also another important virus which causes this fatal disease chikungunya and caused by chikungunya virus. And if you see the number of cases is also reasonably high it is a 6,93,000 it is a quite big number. Zika virus, about 5 lakh people get infected, yellow fever that is 130,000, Japanese encephalitis which is about 42500 cases, West Nile virus.

So, this is also 2588 and now it is increasing from sometime back it is increasing. And this virus is also jumped from another species to the human and now it is causing reasonably good amount of disease or fatality.

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So, for all this thing who is the villain? Villain is the mosquito. Here you can see that most of the arbovirus disease is caused by the mosquito. Here you can see West Nile virus, chikungunya virus, dengue virus, Zika virus, yellow fever and Japanese encephalitis, so these are quite well known viruses and quite well known the disease. In addition there are some more like Rift valley fever, it also caused by the virus, this arbovirus.

Usutu, this is also a viral disease, O'-nyong-nyong, this is also Arboviral diseases, St Louis encephalitis, La crosse encephalitis, **M**mayaro, **S**sindbis and **S**spondweni. So, these are another not so common but they are the Arboviral diseases.

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Ticks can also spread the virus
 Tick bites can cause diseases like Tick-borne encephalitis (TBE) and Powassan virus infection

Unengorged Ixodes ricinus ticks in different developmental stages. From the top, anticlockwise, one adult female, two larvae, and one nymph.

Uniquist L, Yapahli O. Tick-borne encephalitis. The Lancet. 2008 May 31;371(9627):1841-71.

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So, tick can also spread the virus, so here how the tick looks like. Here you can see that tick bite can cause the disease like tick-borne encephalitis and Powassan virus infection. Here this is the image of tick, this animal stick to the animals. And then they will suck the blood and they throw the anticoagulant in order to take the blood meal. If they will not throw this an anticoagulant then the blood will clot and they cannot feed, so these are the ticks.

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What makes you attracted to Mosquitoes

Body odor
 NH₃ CO₂
 Certain compounds present in our breath, skin, and sweat attract mosquitoes

Skin bacteria
 High diversity of microbes on skin may be less attractive to mosquitoes

Pregnancy
 37 °C
 Pregnant women may be more attractive to mosquitoes due to body temperature increase

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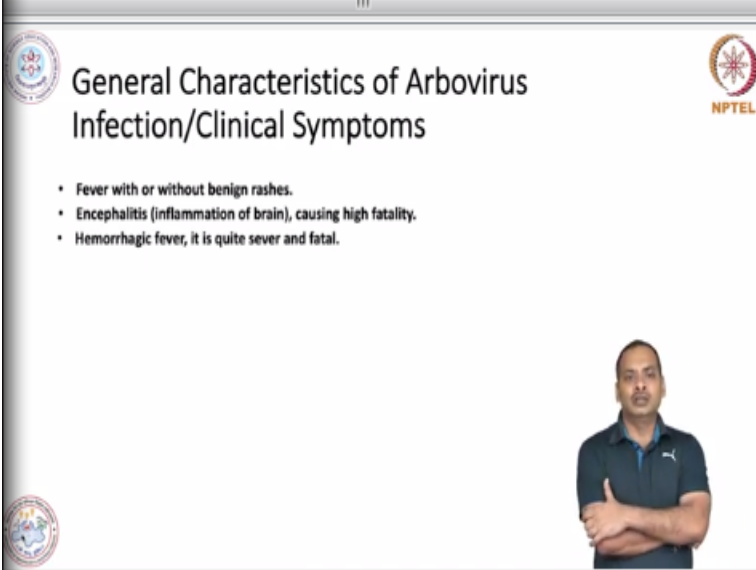
So, what makes you why this mosquito is a main thing? So, basically you know that mosquito bite is quite common in our country. But why this mosquito moves to the individual? So, you probably very well aware that these mosquitoes are female; they need a blood meal in order to

nourish the egg. So, there are several reasons why a mosquito bites or why mosquito comes? They need to take a blood meal that is why they come, and why they come?

Because of there are several things, there is a body odour. So, certain compound present in our breath like here you can see there is an ammonia, carbon dioxide and there is a sweat, this attracts the mosquito. Skin bacteria also are there high diversity of micro-borne skin may be less attractive, it is not a good for mosquito, so they will be not attracted if there is a high number of bacteria.

But body temperature is another important thing, so they sense this body temperature and then they are attracted and then they are biting in order to take the blood meal. And this is quite prominent in case of a pregnant woman, so in general their body temperature is little elevated. And these pregnant women may be more attractive to mosquito due to this little elevated temperature that is why the mosquito come and they are attracted towards the human host.

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The slide is titled "General Characteristics of Arbovirus Infection/Clinical Symptoms". It features a list of three bullet points: "Fever with or without benign rashes.", "Encephalitis (inflammation of brain), causing high fatality.", and "Hemorrhagic fever, it is quite sever and fatal." The slide also includes logos for the Indian Institute of Technology (IIT) Bombay and NPTEL (National Programme on Technology Enhanced Learning). A presenter is visible in the bottom right corner of the slide frame.

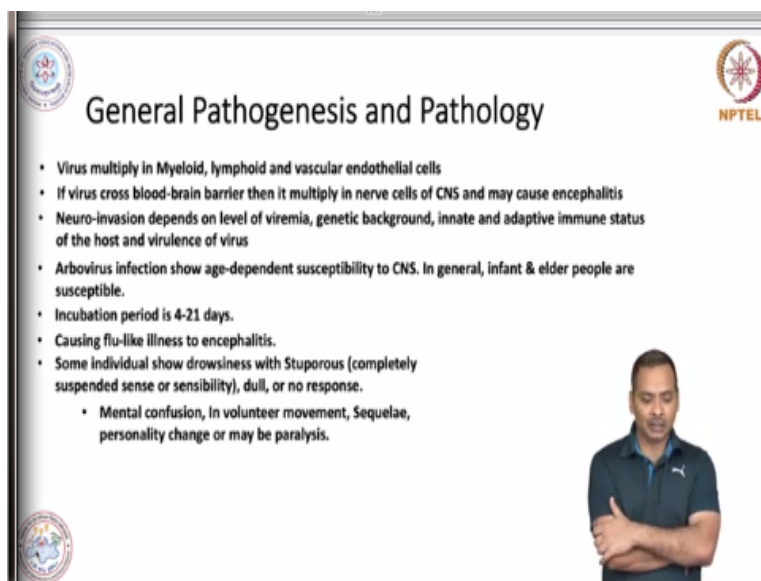
So, here I will talk about the general characteristic of arbovirus infection or clinical symptoms. So, these ~~are~~ arbovirus infection are mainly associated with fever, so they cause the fever. And this fever is also associated with, in most of cases it is associated with some rashes, some benign rashes which is not very dangerous, so some rushes will be there in several cases when there will be a Arboviral infection.

Another is encephalitis; most of these arboviruses cause the inflammation of central nervous system which is consist of brain and spinal cord. And due to this can cause very high fatality, there will be a more risk. Another very characteristic point is that most of arboviruses they cause hemorrhagic fever. What is hemorrhagic fever? It is a internal bleeding, there will be internal bleeding and that internal bleeding will cause the hemorrhagic fever.

So, you try to understand there will be a bleeding and this bleeding will be sensed by the immune cells. And these are the blood is a ~~DAMP~~^{damp} kind of thing and that will cause a inflammation. So, we also call it as a hemorrhagic fever and this hemorrhagic fever can result to the more inflammation and this more inflammation can result to the some shock like condition, so this is quite a complex.

And in most of arboviral infection any one of these signatures will be there, sometime 1 will be there, some time 2 will be there, sometime all 3 signatures this clinical symptoms will be there. In general, when there is a first infection then there will be you may not notice, you may have a little mild symptom. But there is a possibility or some proportion of the population they are highly susceptible and they show these signatures. So, in that scenario it is very important to take care of that patient and then the patient should receive some treatment.

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The slide is titled "General Pathogenesis and Pathology" and features the NPTEL logo in the top right corner. It contains a list of bullet points describing the pathogenesis and pathology of arboviral infection. A small image of a man in a dark blue polo shirt is positioned in the bottom right corner of the slide.

- Virus multiply in Myeloid, lymphoid and vascular endothelial cells
- If virus cross blood-brain barrier then it multiply in nerve cells of CNS and may cause encephalitis
- Neuro-invasion depends on level of viremia, genetic background, innate and adaptive immune status of the host and virulence of virus
- Arbovirus infection show age-dependent susceptibility to CNS. In general, infant & elder people are susceptible.
- Incubation period is 4-21 days.
- Causing flu-like illness to encephalitis.
- Some individual show drowsiness with Stuporous (completely suspended sense or sensibility), dull, or no response.
 - Mental confusion, In volunteer movement, Sequelae, personality change or may be paralysis.

So, now I will talk about the general pathogenesis and pathology. So, basically these viruses multiply in myeloid cell, lymphoid cell and there is an endothelial endothelium in there in blood vessel or we call it as a vascular endothelial cell, they rapidly divide over there. And if this viremia is too much then they will cross the blood brain barrier and then they start infecting the nerve cells of central nervous system and that results to the development of encephalitis, inflammation of brain that is a very complicated situation.

Neuro-invasion basically depends on level of viremia, I have told you in addition of course and obvious it depends on the genetic background of the host, the innate and adaptive immune status of the host and the virulence of the virus. So, all are very closely related or all these factors are dependent on each other. Genetic, if you see there is just some genetic factor is there, some genetic factor is very important.

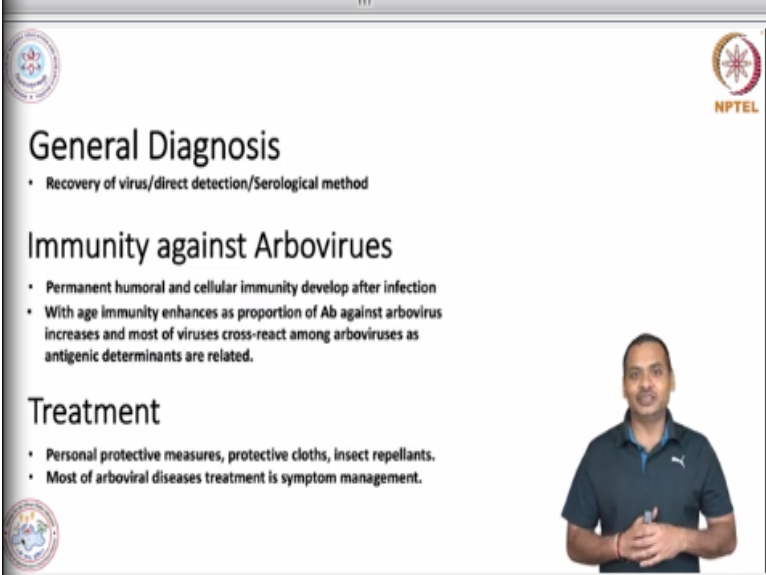
But if you look at the innate and adaptive immune response may be if individual is in at that particular time the immunity is low due to some other infection then those guys are or those individuals are more susceptible, so this is a very important. So, arbovirus infection shows age dependent susceptibility to the central nervous system. So, generally younger people and older people they are more susceptible to the arboviruses.

And in between the full adult individual they are kind of they can tolerate this infection. In general for all arboviral infection the incubation time will be about 4 to 21 days, so during this time the virus will replicate in a huge number and then you will experience the infection. It is basically initiated with flu like illness and then that flu like illness will become a more complicated and it may result to the encephalitis, inflammation of brain.

Some individuals show drowsiness, so this is a one of another signature of arbovirus infection. Individual may show the drowsiness; drowsiness is also associated with stuporous. Stuporous is a kind of a little technical term, meaning a completely suspended sense or sensibility. So, they are not able to sense if you say maybe they will listen but they will not respond, their sense are kind of a down.

You can understand this is infecting the neuronal cells, individual will be dull or they will not show any response. There is a possibility that if the infection is very high there will be a mental confusion. And it is also possible that the individual the patient will show some involuntary movement, so sometime some hand or some part of body will keep on shaking on that they do not have a control. There will basically personality change or there may be a paralysis if it is not managed well.

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General Diagnosis

- Recovery of virus/direct detection/Serological method

Immunity against Arboviruses

- Permanent humoral and cellular immunity develop after infection
- With age immunity enhances as proportion of Ab against arbovirus increases and most of viruses cross-react among arboviruses as antigenic determinants are related.

Treatment

- Personal protective measures, protective cloths, insect repellants.
- Most of arboviral diseases treatment is symptom management.

So, the general diagnosis is a very simple and straightforward, one can recover the virus and there could be a direct detection is possible or there is some serological method. There will be anti-sera and if it is reacting with that sample then you can say that the individual may have ~~this is~~ infection. This is one way of diagnosis, another way is that you look at the signatures of immunity, there will be virus specific antibodies.

For example IGM, IGG if you detect then you can also diagnose the infection. So, immunity against the arbovirus is basically it is a permanent humoral and cellular immunity develop after infection. So, of course there will be a memory against these viruses which if there will be a re-infection then memory will expand and provide the antibody or cytotoxic T-cells. However in some cases there is a problem, so these viruses keep on mutating and there is a very little antigenic difference.

And sometime that is a beneficial to the virus and there will be 1 phenomena which we call it as antibody dependent enhancement, that could take place and that result to more fatality, more severity. But in general there is a very good immunity after some time after say 7 days or 14 days the individual develop a good immunity. And to be very honest the individual recovers based on their immunity, so there is a no treatment for these virus infections.

We do not have any drugs which can treat this virus infection; I will come to that point. So, with age, immunity enhances as a proportion of antibody against, so you can understand there will be a multiple bite of mosquito and there will be a production or there will be a synthesis of antibody and this antibody memory will be remain there. So, with age there will be a good repertoire of antibody the host must be having and that gives a protection.

Because these arbovirus are kind of having a similar antigenic determinants in several cases. However as I told you sometime the virus uses this strategy in order to increase their number, I will discuss this phenomena in case of dengue virus in subsequent session. So, **so** most of the viruses cross react among arboviruses as antigenic determinants are related, so this is protective as well, this can give a protection.

Treatment is we do not have any precise treatment just it is better to take a personal protective measures, protective cloths, use the insect repellent. And most of arbovirus disease treatment is a symptom management. Here I would like to say that we do not have a drug for this dengue and all those things, we basically do the symptom management. So, for example there is a virus infection and that is causing the hypotension.

So, this hypotension we have a drug which can enhance the blood pressure since the blood pressure is going down they will give the drug which can increase or bring it to the norm, you need to adjust the dose in such a way that it will just reach to the normal value. So, this is a standard kind of treatment. During this infection there is a severe loss of blood, severe loss of thrombocytes or platelets.

So, we basically we can infuse and our overall aim is to keep the individual or to keep the patient in almost normal condition and wait until the host innate and adaptive immunity triggered sufficient in order to control this virus infection. So, we do not give any drug which can treat the virus or which can remove the virus or something, no, we do not have any drug, we basically manage the symptom.

There is a very high fever; the patient will simply receive the paracetamol, so that will bring down the fever. But there is some limit for giving paracetamol, if you give too much then that will damage the liver. So, in that scenario if the paracetamol is also not reducing the fever. Then in that case a particularly in case of dengue infection they will put you on the ice to bring down the temperature.

Because if the temperature will reach too high then that will damage another component of body, that may damage the neurons, that may damage the liver. So, these are basically all this arboviral diseases over there, there is a symptom management. So, whatever symptom is deviated, whatever vital signatures are deviated we bring it down and try to maintain the condition of the host.

And wait for the production of antibody and cytotoxic T-cells which will eventually take over this virus. So, with this I will stop this session, in next session I will talk about the dengue virus, thank you very much.