Host-Pathogen Interaction (Immunology)
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Lecture-68
Influenza Virus and Disease-6

Hi. So, in previous session you have seen there are some broad symptoms of influenza virus**.** And now, we will talk about more clinical features of this infection and which result to the disease**.**

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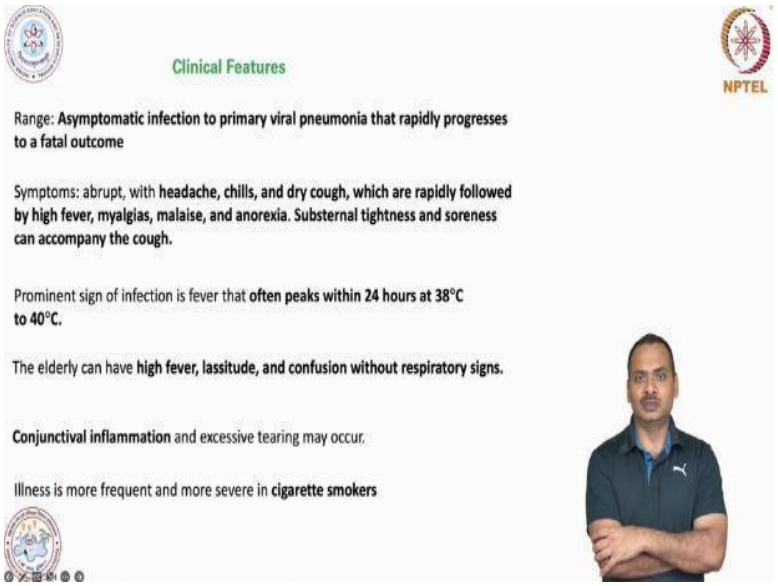

So, there are quite a lot of clinical features. First, I would like to say that many people are asymptomatic also. There is an asymptomatic infection to the primary viral pneumonia that rapidly progresses to the fatal outcome. So, there is a very wide range; many people are asymptomatic and in many individuals this will severely affect the lungs, which may be result to the fatality**.**

Symptoms, I have told you, I will repeat it again. There are some more symptoms like there will be a headache, chills, dry cough which is rapidly followed by high fever**.** This is a kind of signature of influenza. Muscle pain, there will be a malaise and there is anorexia; anorexia is also associated with influenza. There is a sub sternexternal tightness in a simple word something like a jacqueline in Hindi, in chest region and soreness can accompany the cough**.**

The prominent sign of infection is fever and often peak within 24 hours and it could go to the 38 degree centigrade to 40 degree centigrade, which is very high fever. Elderly can have a high fever and here there is a word lassitude. Lassitude means it is that you feel very much exhausted; there is no energy kind of thing, no strength, no energy. So, that we call it as a lassitude**.** So, elderly can have a high fever, lassitude and confusion without respiratory signs**.**

This can affect the eyes; conjunctival inflammation and excessive tear may occur**.** Illness is more frequent and more severe in people, who smoke cigarette smokers**.** So, this is a kind of supportive to the influenza the people, who smoke. Not only influence all this viral infection, which is taking place through this respiratory tract**.** It is a true for influenza and it is also true for SasARS-Covid2 and other rhinovirus and all those things.

The individual, who smokes they develop more severe symptoms and for them it is very hard to overcome or that may take a longer time**.** So, smoking is not good for these infections.

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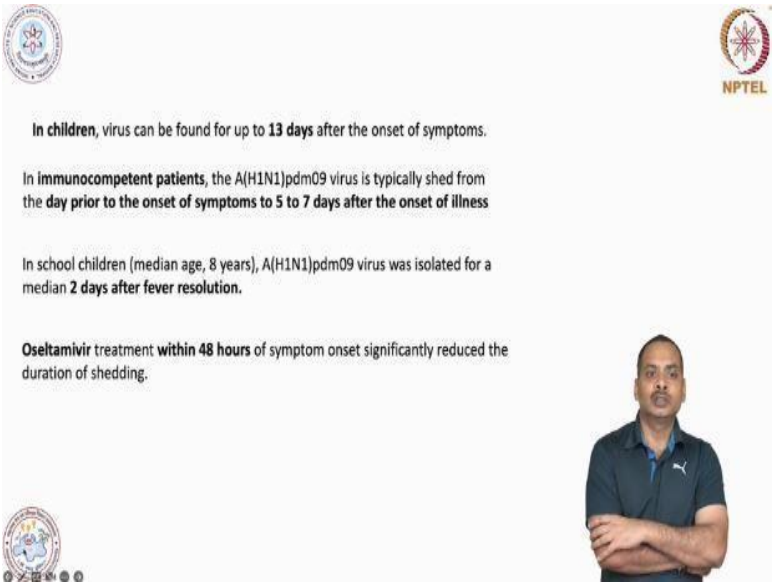

So, in children, virus can be found for up to 13 days after the onset of symptom**.** In immunocompetent patients, this is a little case study in immunocompetent patients, this virus H1N1 which caused the pandemic in 2009 it is about that**.** So, the influenza virus, which is caused pandemic in 2009, is typically shadered from the day prior to the onset of symptoms. So, this is much more dangerous situation.

So, individual will not know and they can infect other healthy individual, because symptom is coming late, so onset of symptom to 5 to 7 days after the onset of illness**.** In school children,

the median age about 8 years, the same virus was isolated for median 2 days after fever resolution. So, they can infect. So, once they will be healthy, after becoming healthy they can spread the virus for few more days. So, this is little interesting and one has to take the precaution. And as I told you, Oseltamivir treatment within a 48 hour of symptom onset significantly reduce the duration of shedding of virus. So, these are the sum of key symptom.

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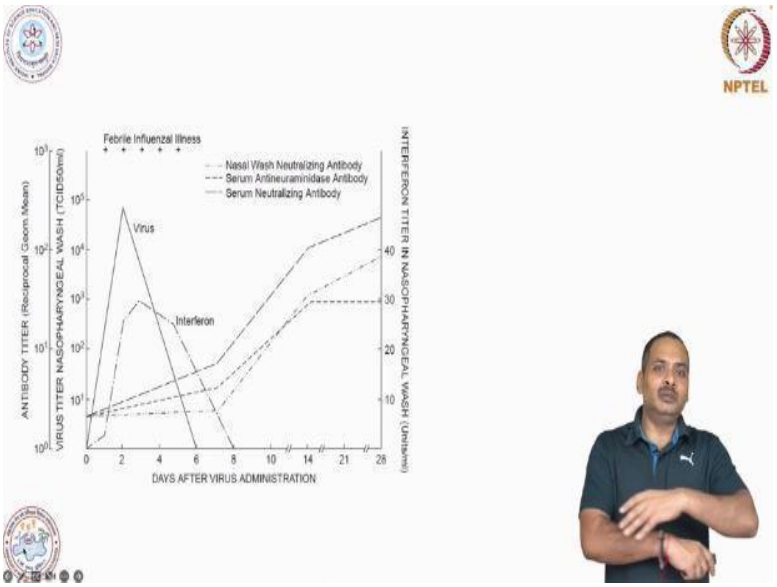

Here, I will show you a very nice information. Here, you can see that, there is a antibody titer. There is a virus titer in nasopharyngeal wash, which is this wash they have measured the amount of virus. So, here you can see that around day 2, the viruses in peak. Please note this virus you will not find in the blood. This is very important information. You do not find this virus in blood; it will be present in the swabs nasal swap or oral swabs.

So, it is present only this respiratory tract; oral tract. So, here you can see on day 2, there is a very high viral load. And you know that type 1 interferon is an antiviral in nature. And this type 1 interferon is initially quite low. And this around day 1 it is very low; around day 2 it is increasing. And this increased there is a kind of plateau from day 2 to day 6. And during that time, the virus is drastically reducing in the respiratory tract and all this virus is reduced in day 6.

So, at that time interferon is reasonably high and the interferon is reducing around day 8. So, here you can see that the initially there is low interferon and when there is a high interferon, this virus is started declining. Here, you can see that presence of this is a very good graph,

which explains the innate as well as adaptive immune responses against the influenza virus and the physiological state.

So, here you can see there is a measurement of nasal wash neutralizing antibody, which can control and serum antineuraminidase antibody and serum neutralizing antibody. So, here you can see all these guys, all these antibodies because you know that antibody generation takes about 7 to 10 days. So, initially there is a low, but after day 7 here you can see there is an increase in this antibody production and that controls the virus infection.

So, this is very good data or result. So, now I would like to talk what is happening. You have seen in a previous session that this influenza virus can infect variety of animal. So, what is happening in those animals? So, those individuals or animals are divided into 3 major categories.

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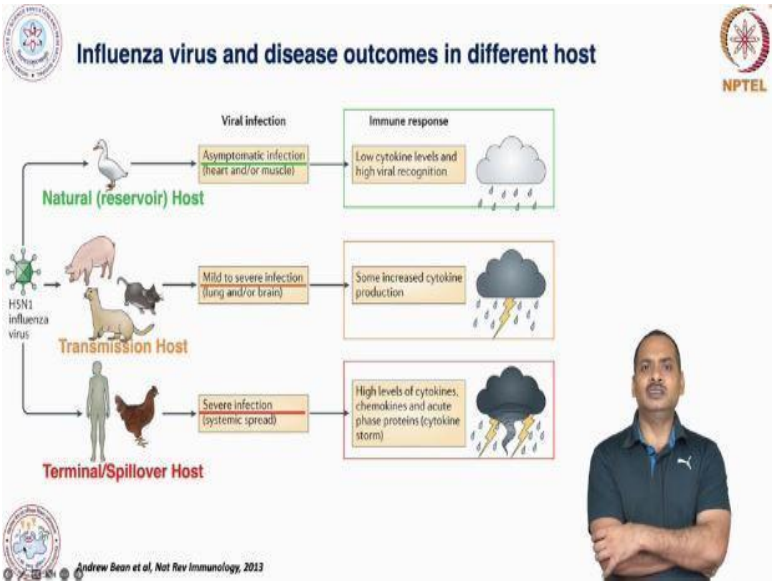

Here, you can see there is an aquatic bird; there is a pig, ferret, rat and human and chicken. So, these are the three major kind of host. The duck, the aquatic birds we call it as a natural reservoir host. And this natural reservoir host is in general asymptomatic. They have some mechanism in order to control this virus. They are asymptomatic to the infection, maybe it is present in heart and muscle, but they are in general asymptomatic.

They produce very low level of cytokine and here you can see it is depicted as an immune response low cytokine level and high viral recognition. So, somehow this is controlled by their immunity. So, that's ~~is~~ why since they can have it and they can control also. So, that is why

they are natural reserves, they are not affected. Another is a transmission host. Here, you can see there is a pig, ferret, rat, they just show little mild or severe very mild symptoms.

Generally, this is present in lungs and brain and shows some increased cytokine production. And another is terminal or spillover host. So, terminal and spillover host is chicken and human. They show very much severity. There is a severe infection this can be spread systemic. And there will be a very high level of cytokine, chemokine and acute phase protein productions and that result to the cytokine storm.

So, you can understand the different host responds differently to the influenza infection. That is why since this is not affecting severely to other animal or other species. So, that is why they can easily jump to the human and then that they cause the severity.

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So, what is the pathology of this disease? So, infection induces changes throughout the respiratory tract, but the most clinically important pathology develops in lower respiratory tract. So, acute diffuse inflammation in larynx, trachea and bronchi are observed with mucosal inflammation and edema. And there is a one phenomena taking place that is desquamation. Desquamation is nothing.

So, this is a destruction of epithelial lining of the lung and that opens the gate for the bacterial infection. So, it is a shading of an epithelial line; that we call it as a desquamation. Infiltration of neutrophil and mononuclear cell, that is quite obvious. Since, it is an inflammation a quite

inflammatory location. So, there will be a rush of neutrophils and monocyte cells. So, influenza virus-specific antigen is a present in alveolar epithelial cells.

There will be a necrotized change may occur with rupture of alveoli and bronchiole walls. So, this is much more severe pathology. And complete healing of this epithelial damage takes up to 1 month time. So, after recovery individual will still face some or other problem especially, related with this respiratory tract. So, at that time individual is quite susceptible to the other respiratory infection and complete healing will take about a month time.

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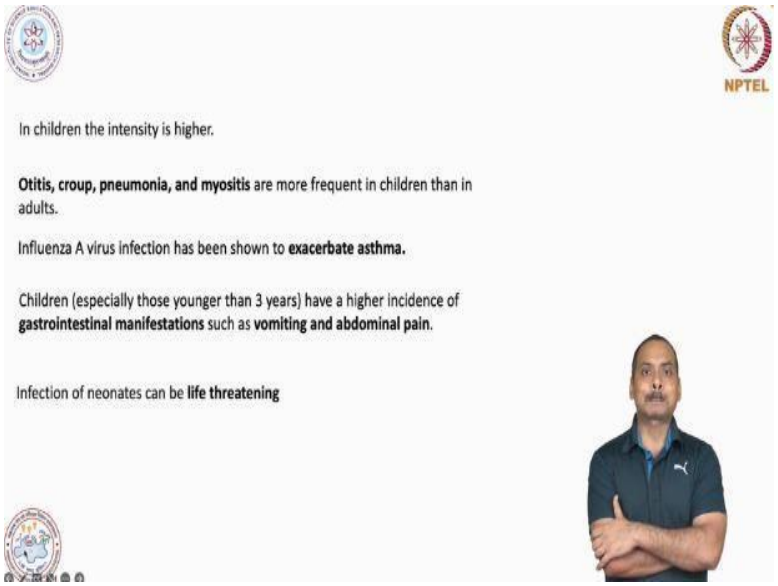

In children, the intensity is higher as you can understand their immunity is not very well developed. There could be some more symptoms like otitis, there will be inflammation in ears. Croup, pneumonia, myositis are more frequent in children than adults. Influenza A virus infection has been shown to exacerbate asthma. So, this kind of increase or enhance the asthma, in those individuals who are already having ~~a stomacha~~ asthma.

Children especially those younger than 3 years have a higher incidence of gastrointestinal manifestations such as vomiting and abdominal pain. So, this is also common in another kind of viral infection. The small kids; they generally have this nausea feeling, they vomit. Infection of neonates can be a life-threatening. So, newborn baby if there is an influenza infection that could be a life-threatening.

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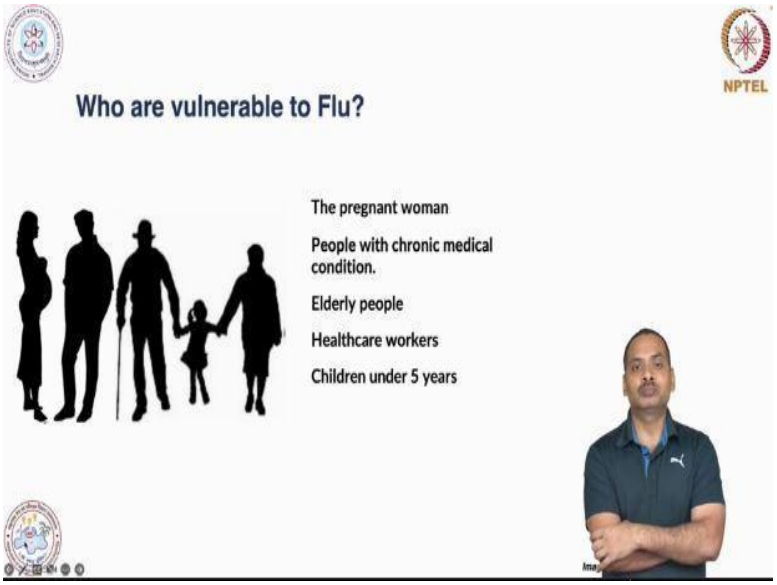

So, here I am just depicting in a pictorial mode who are vulnerable to the flu? So, here you can see that, the pregnant woman is highly vulnerable to the flu, then people with chronic medical condition. Chronic medical condition means the individual might have some metabolic disease like hypertension, diabetes or they might have a cardiovascular disease and they are taking drugs for these diseases. So, I mean to say that the chronic medical condition**.**

Elderly people are reasonably more susceptible. And of course, health care workers, because they are taking care of all kinds of patients. So, these are highly susceptible. In addition, the children under 5 year ages they are highly susceptible**. (Video Starts: 16:51)** Here, just I am depicting our scientific effort against influenza virus by this cartoon. Here you can see that this dragon kind of animal, they are keeps on varying**.**

And this is keeps on varying~~wearing~~ and our sustained effort is not so sufficient in order to control the influenza virus**.** So, this is just I have depicted in using this cartoon; it may be interesting to you. Now, I will show you a very nice video and this will show how the infection is taking place and how the virus is moving to the cell and that all these things**.** Influenza infection it might start with a sneeze, but the underlying infection can cause far worse.

Hundreds of thousands of people every year die from severe influenza virus infection**.** Everything begins when the virus enters our airways. Here, influenza viruses specifically attached to the surface of the epithelial cells. The viral membrane envelope contains the

neuraminidase protein NA important for the efficient release of newly produced viruses. The M2 ion channel promotes viral structural changes during cellular entry.

And the influenza ~~hemoglobin~~ hemagglutinin in protein HA the key player for viral internalization, which facilitates viral binding to sialic acid-decorated receptors and subsequently viral fusion proteolytic cleavage by host enzymes, is critical for the activation of the HH primers. Soluble or cell-bound host proteases cleave the precursor HA molecules into two parts HA1 and HA2**.** Influenza virus particles are internalized into early endosomes by clathrin-mediated endocytosis.

In late endosomes, the pH drops triggering the conformational change of the cleaved HA molecules. HA1 opens up and allows HA2 to form a triple alpha helix bundle, which extends towards the endosomal membrane. Once the fusion peptides are anchored in the endosomal membrane, the whole molecule can fold back allowing the fusion of the viral and endosomal membranes.

After fusion, the viral genome can be released into the cytosol. The eight viral RNA segments make their way into the cell nucleus and the production of the new virus begins. Just hours after the initial infection, thousands of new viruses bought off the cell surface and infect neighbouring cells. To stop the Influenza virus ~~influence~~ infection, through cell researchers have discovered fully human monoclonal antibodies capable of neutralizing the virus.

These antibodies specifically bind to the HA and are internalized together with the virus. When the pH drops in late endosomes, the antibodies remain bound to a highly conserved epitope located in the stem of the HA. The antibodies now block the conformational change of HA, thereby preventing viral fusion and infection. Trapped virus degrades, leaving the cell unharmed. Some of crucial new antibodies can also prevent the initial cleavage of HA.

They bind to a highly conserved epitope close to the HA cleavage site, thereby preventing host proteases from activating the virus. The unclean virus is not infectious. So, the cell and patient are safe. Crucells neutralizing antibodies prevent the spread of influenza infection and may save your life. **(Video Ends: 21:41)** With this I will stop here. And I will complete the influenza virus infection and in next session.

We will discuss about one more family of viruses. I will give you a generalized overview about those family of viruses; we call it as a arboreal virus**.** So, arboreal virus is basically, all those viruses which is transmitted through the arthropods, that includes dengue, there are so many dengue, chikungunya**.** There is a West Nile virus so and so. I am not going to take all this virus; I will just talk in general about the arboreal viral infection**.** And with this we will finish this week term**.** Thank you very much.