Host-Pathogen Interaction (Immunology)
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Lecture-66
Influenza Virus and Disease-4

Hi. So, in previous session, we have discussed so many things about the influenza virus and in this session we will continue. So, you have seen the structure of HA protein, which is the functional unit is trimeric in order to induce the fruitful infection**.** And you have seen the monomer structure; I gave you a little detailed structure of HA protein. So, I will continue after that.

So, how HA is basically inducing, so you if you remember my previous session, you must be remembering that there this HA protein has a two key functions. One is that attachment with the target cell, where the predominant sugar is sialic acid. So, this sialic acid, there is one motif of sialic acid and other sugar molecule and this is sensed by the HA protein**.** So, this is the first key function.

Another is they are playing very important role in membrane fusion**.** So, this membrane fusion is very much needed, if somehow if we inhibit this membrane fusion, then that will basically inhibit the viral replication**.** So, for binding of this HA with a target molecule over the host cell, we also need a low pH**.** And yesterday you have learned that we need some enzymes, which will cleave this HA molecule**.**

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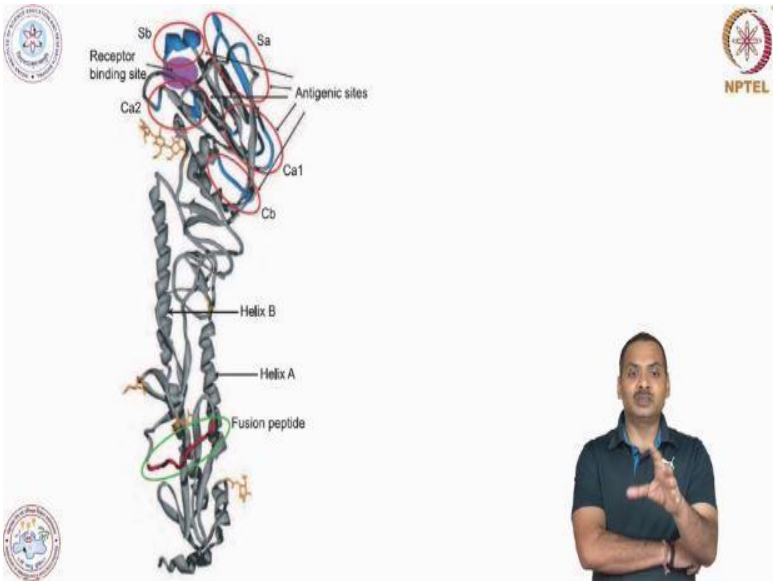

So, let us look at this molecular detail. So, this is again I am showing the structure of this monomer of HA hemagglutinin and here you can see that there are some red circles. So, these circles are basically antigenic side; what do you mean? It means if these surfaces are masked by some antibody, then this will not interact with the molecule on target cells and therefore there will be no fruitful infection.

The infection will be somehow inhibited if these surfaces are masked**.** So, that is why these surfaces we call it as antigenic side**.** There is a some receptor binding site, which is basically so when this molecule come in contact with or when there will be a low pH, at that time this molecule open ups.

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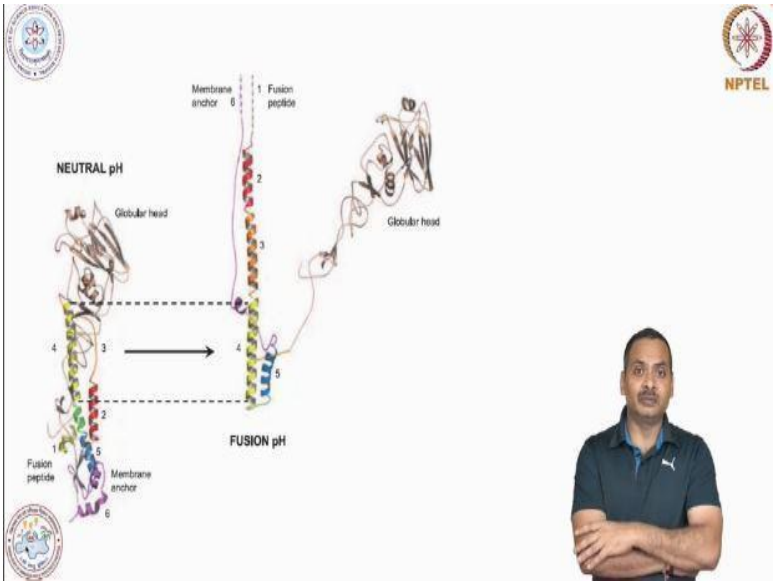

Here you can see this how there will be a changes in this molecule when there will be a change in pH**.** So, here you can see that there the one region the fusion peptide is basically exposed and there is a the sixth region is also present next to the fusion region, which the main role of sixth region is to anchor in the membrane**.** So, and here you can see that the globular head are kind of separated and overall, this physically facilitates the binding as well as membrane fusion.

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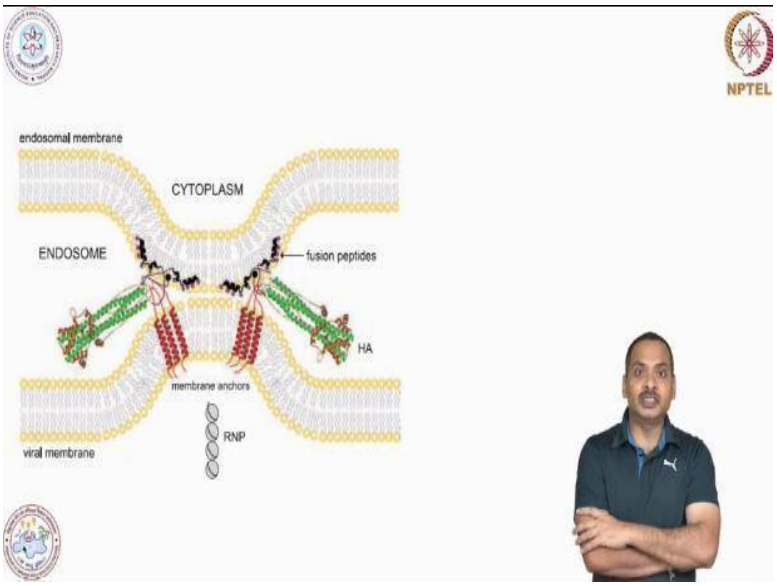

As you can see in this image, here you can see there is a fusion peptide**.** And here you can see the HA protein. So, this is basically facilitating the fusion of two membranes; here you can see there is the endosomal membrane and there is also viral membrane and this fusion is taking place with the help of HA protein**.** And here you can see the open conformation of this HA protein.

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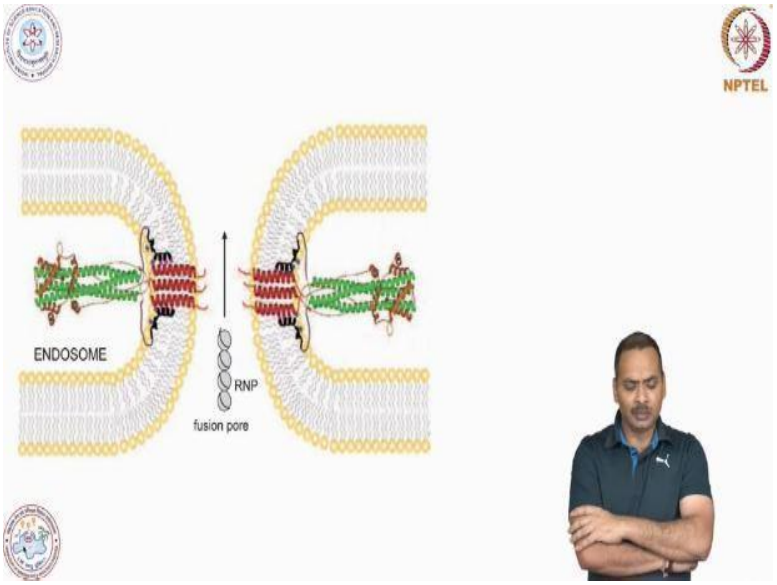

And there this fusion is fruitful, then there will be a translocation of RNP ribonucleoproteins from viruses and then subsequent step will take place**.** And I will show you in this session or maybe next session after fusion what is happening**.** So, this fusion basically the virus is translocated into the cell by various mechanisms; there are various entry mechanisms are there**.**

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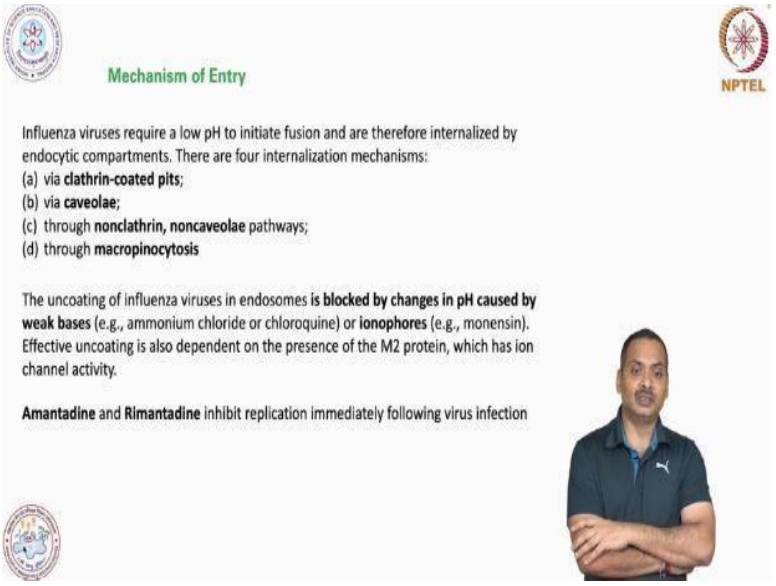

And these entry mechanisms are basically playing very important role. If you inhibit, if you do something at this stage, then virus cannot replicate and then there will be a no infection. Therefore, there are some drugs which is basically interfering this entry step**.** Let us look at how the entry is going on. So, in order to infect the host cell influenza virus needs low pH; you can understand this needs a little acidic pH to initiate fusion and therefore internalization by endocytic compartment**.**

So, there are four internalization mechanisms, which you are quite, I hope you are aware if you have studied the cell biology. So, one the first most important is clathrin-coated pits mediated entry. Another is caveolae-mediated entry; there is also non-clathrin and ~~non-caveolae~~non-caveolae pathway and this virus also uses those pathways in order to make fruitful entry in the cell. This can also be translocated in the cell through macropinocytosis. So, these are some of the mechanism.

And basically, the uncoating of influenza, so once they enter in the cell, there is a need of uncoating of this virus in order to release the RNP~~'~~s. So, that this RNP~~'~~s will move to right place and then there will be a transcription in order to make the protein, as well as there will be need of making more copies of this genome. And all those things will be initiated when the virus will be un~~qu~~coa~~o~~ted.

So, basically, if you remember the structure of influenza virus, this has a one very important protein, which we call it as a M2 and I have explained you this is the ion channel. So, they through M2, the protons are entering inside the cell and once it will enter then that will basically trigger the uncoating of this virus. Uncoating means, there will be a removal of this envelope.

And then this RNP is ribonucleoprotein is exposed and then it will be translocated in the particular organelle in order to make the copies. I have one very beautiful video and that will really help you in understanding and that video I will show you towards end of this influenza sessions. So, here I just want to say that if we change the pH of somehow if we block the acidification, then we can prevent the influenza virus infection.

And this can be very easily done, at least in vitro situation. You just put the ammonium chloride in the culture and then you put the influenza virus or you can infect the cells with influenza virus and also add the ammonium chloride. Then, this low pH will be some it will be stopped. You can also treat the cells with chloroquine that will also make it alkaline. The inner endosomal content will be alkaline.

So, in that way, you can block the infection, chloroquine can also effectively block this release of RNP. There are some ionophores probably you are aware that you if you have a studied

biochemistry. Monensin, this monensin can be also used. So, this will be just disrupt the ion transportation**.** So, in that way, one can control the entry of or release of RNP from the viruses**.**

There are some drugs; here, you can see that the there are drug known as Amantadine and Rimantadine. So, these drugs are basically work; their mode of action is similar as this molecules like a chloroquine and ammonium chloride. So, this drug is used in treatment of influenza virus**.**

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So, now we will look at the pathogenesis in human. So, basically this virus infects the superficial cells of respiratory tract**.** So, more appropriately this infects the epithelial lining initially and later on they can infect the alveolar macrophages or dendritic cells**.** And the site of optimal growth in the respiratory tract for influenza virus is in part, determined by prevalence of here you can see that, this is a sialic acid alpha 2, 3 Galactose**.**

So, this is a just a motive. So, wherever this sugar is there they will infect or there is this sialic alpha 2, 6 Gal receptors where this influenza virus can very readily attach in order to gain the accesses inside the cell**.**

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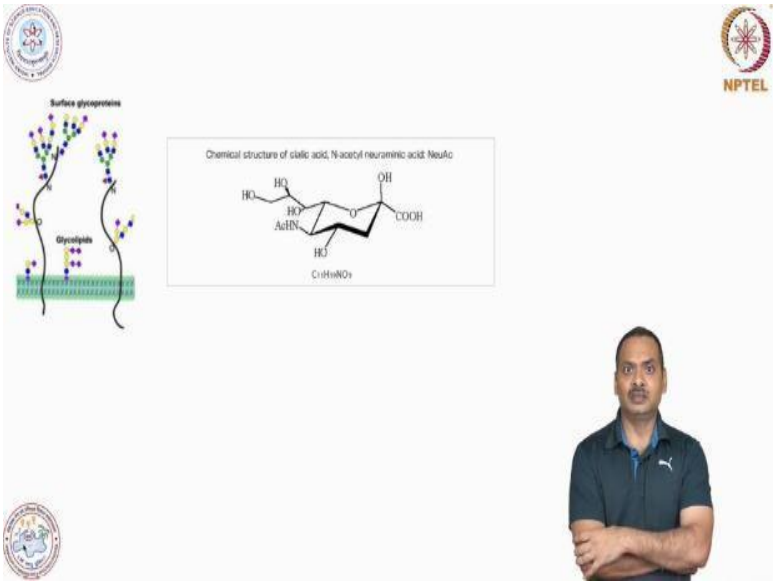

So, these sugar molecules are basically here; you can see they are present on the cell surfaces and this is the structure of neuraminic acid or sialic acid**.** This is also called as N-acetylneuraminic acid. So, this is needed in order to make fruitful infection**.** So, in this session, I will stop here and in next session, I will take it further how this virus after infection what it is doing, what kind of symptom it is inducing, what is the physiological effect of this virus infection? Thank you very much.