Host-Pathogen Interaction (Immunology)
Prof. Himanshu Kumar
Laboratory of Immunology and Infectious Disease Biology
Department of Biological Sciences
Indian Institute of Science Education and Research-Bhopal

Lecture-67
Influenza Virus and Disease-5

Hi, so in previous session you have learned how this virus is gaining access inside the cell. Now let us look at when this virus increasing the number then what kind of things are happening, what kind of signatures or what kind of there will be a perturbation of vital signatures in physiological state what is going on? So, in a simple word what are the symptoms after the infection, after entry of this virus in the host?

Here I will talk some symptom and later on I will also talk there could be variability in these symptoms depends on the individual genetics or there are various conditions.

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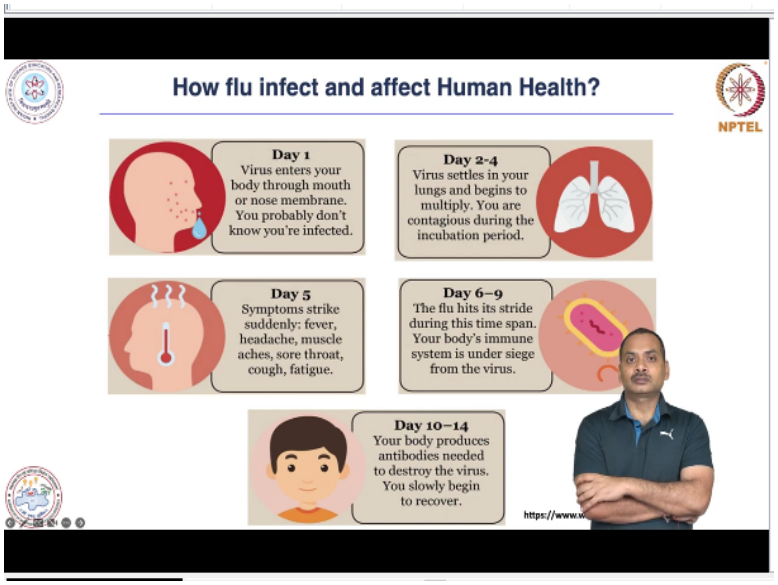

So, how this flu infect and affect the human health? So, here you can see that so when this virus enters in your body through respiratory tract or maybe through mouth you probably do not know whether you are infected. So, first when you are infecting then you will not aware that you are infecting with the virus, its initial stage but after some time after day 2 or 4 or during that time the virus settle in your lungs and begin to multiply.

Now they are coming in a stage to perturb or to disturb the homeostasis of lungs. At that time you are quite contagious. Contagious means you can infect another individual, you can also transfer the virus and another healthy individual can be also infected. So, during this incubation period, so all these things are happening, maybe around day 4 or 5 the symptom basically strike means you will experience a massive symptom.

That will be a very high fever, there will be a headache, there will be a muscle pain. This muscle pain is also there, technically we call it as a myalgia, there will be a sore throat, there will be a cough and you feel fatigue means you will feel very low energy. So, these are the key symptoms and later on around day 6 and day 9 the epithelial lining of this respiratory tract were quite severely damaged and since it is damaged and it is kind of open gate for bacteria.

So, since this epithelial barrier is quite severely damaged your immunity is also quite down, at that time there is a possibility of secondary infection that is bacterial infection. So, that makes situation more worst and that is the point of concern. So, probably you know that in virus infection doctor also prescribe antibiotic. Antibiotic is to avoid this secondary bacterial infection more precisely.

So, at that time your immunity is also quite well kicked off, it will initiate because this is already 7 to 9 days. So, your adaptive immune system is start working and around day 10 or second week you will start feeling a little bit well because this antibody production, cytotoxic T-cells, all are started working against this virus. So, this is a normal scenario, but there is another scenario maybe this situation will get worse.

They can trigger the cytokinesis storm and then the patient will be maybe in that shape and if it is too much then that may result to the fatality. That is why in 1918 there was huge fatality. **(Video Starts: 05:37)** So, here I have a one very nice video which you can which you can observe here the individual is infected then lung epithelial was infected and then the cells of lung epithelial was infected.

And then this is basically lot of viruses there and then there will be a release of virus and then again they can infect another individual. So, this is a very simple video. **(Video Ends: 06:13)**
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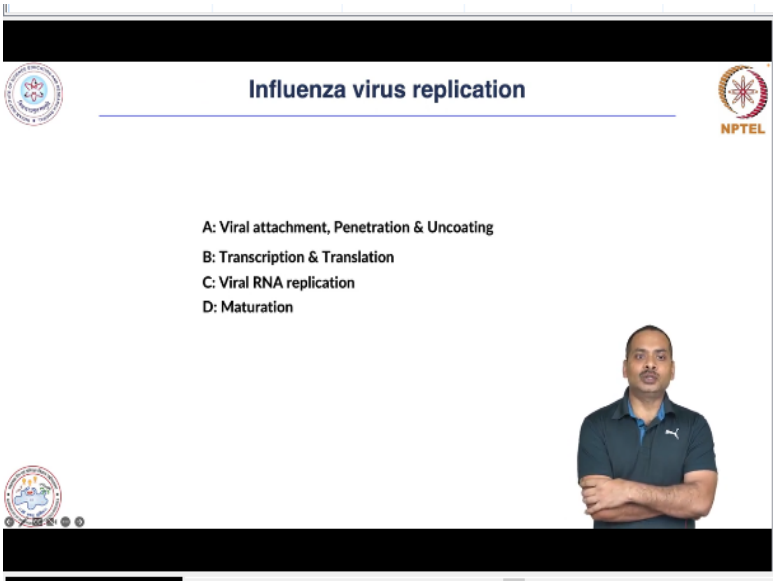

So, now let us move on how this influenza virus replicate we need to understand they entered, they caurse the symptom but let us look at how this virus is making more copy. So, there are several steps. One is that viral attachment, penetration and uncoating. Another is transcription and translation. Transcription and translation is for making their more copies of genome and protein.

For example there are various proteins, like a polymerase protein M 1, M 2, all those proteins are needed in order to make a mature viral particle so that needs a transcription and translation. Viral RNA replication and finally maturation and release of this virus. So, all these things are needed in order to generate the mature viral particle.

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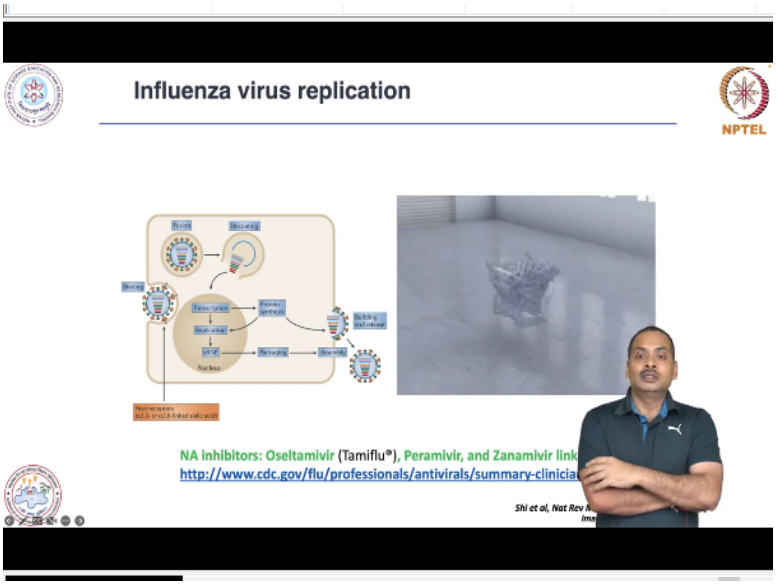

So, let us look at how it is basically taking place, it is a very simple. Here you can see that the virus is binding to the cell and here you can see there is a host receptor which is linked with sialic acid and here you can see this virus will reach into the endosomes and then this virus will fuse the membrane of endosome and the membrane of virus and then there will be a release of RNPs.

Here you can see that RNPs are released, you can see these lines are the genomic segments, it is a segmented virus. So, the genome is not continuous, there are 8 segments of RNA molecule and this RNA molecule are, all these molecules are released and then there will be a transcription, replication and there will be a synthesis of viral RNP's. Viral RNPs is synthesized and then there will be a packaging and assembly and then this virus will be released.

So, at the release stage there is a need of action of neuraminidase in order to release this virus. If neuraminidase is inhibited then this virus cannot be released. **(Video Starts: 09:14)** So, this virus production is something like the assembly of car on assembly line in factories, here you can see I just made some analog in order to understand this viral replication. Here you can see that the car is assembled, the engine and all body parts are coming and they are assembled on the assembly line and then eventually the mature or fully functional car is moved out.

So, as I told you there is a some molecule which inhibit the neuraminidase and the one of very effective molecule is a Oseltamivir, this is a drug and this is also known as Tamiflu. There are some similar drugs. Peramivir, Zanamivir. So, these are all anti-influenza drug and they basically they are inhibitor of neuraminidase enzyme and these drugs can very effective if it is given within 48 hour of appearance of symptom, these drugs can significantly reduce the viral load and reducelease the symptom.

However, there is a generation of this drug resistant influenza virus also. So, this is a point of concern. So, we need to deal this thing more smartly, we need to find out some another way to interfere this viral replication. In my previous session if you remember when I have discussed the interferon independent way to control the viruses at that time I have discussed about two micro RNA that was our work, the micro RNA 485 and micro RNA 324. So, those micro RNA could be a very effective therapeutic agent in future.

Because they can target the polymerase and polymerase is in general same I have shown you during that session, this polymerase sequence where this micro RNA is targeting they are highly conserved in very old influenza virus as well as in current influenza virus, it is a highly conserved. So, this kind of target will be very effective in order to control the influenza virus irrespective of any kind.

There are so many kinds, so if we have this molecule we can control this influenza virus replication. However, this needs some more study reason is that these micro RNA which is generated by the host cell they have also other targets, these micro RNA also control other transcripts. So, we need to find out the way by which we can smartly use this micro RNA and control the influenza virus. **(Video Ends: 12:57)**

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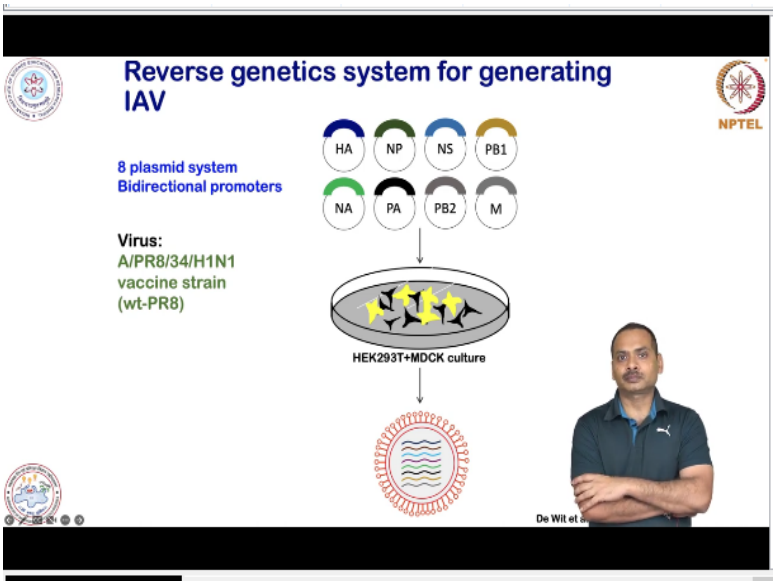

So, in laboratory we generally study the influenza virus and we use this reverse genetic system. So, reverse genetic system it is a system in which we have a plasmid which can encode protein as well as RNA molecule and we introduce this plasmid inside the cell and then we can generate the virus in the lab and we can study, we can investigate all those properties, we can also test the drugs. So, we use this reverse genetic system in order to understand the influenza pathogenicity. In our study we also use this system.

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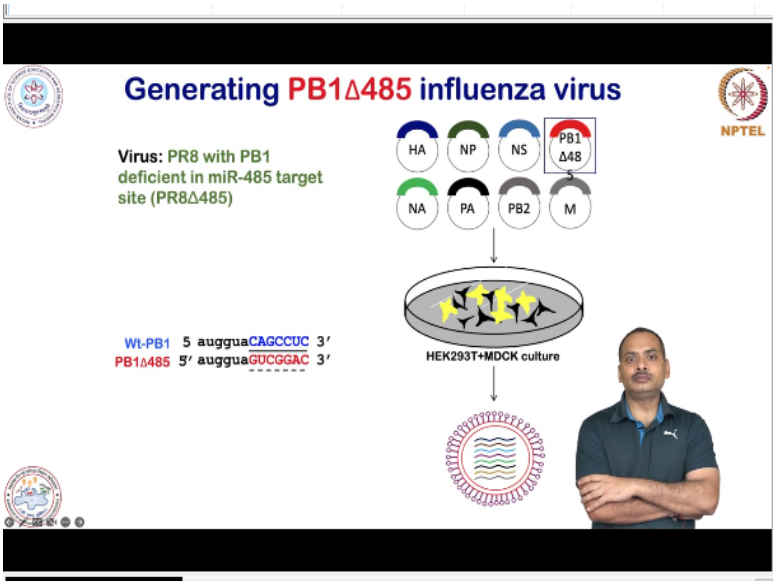

So, this is just you can mutate. So, whatever gene you want to mute it you can easily mute it and then you can investigate the phenomena. Here I am just showing this the micro RNA 485 binds to the one region, in PB1. So, we have made a mutation and then we have investigated further or we basically validated our observation.

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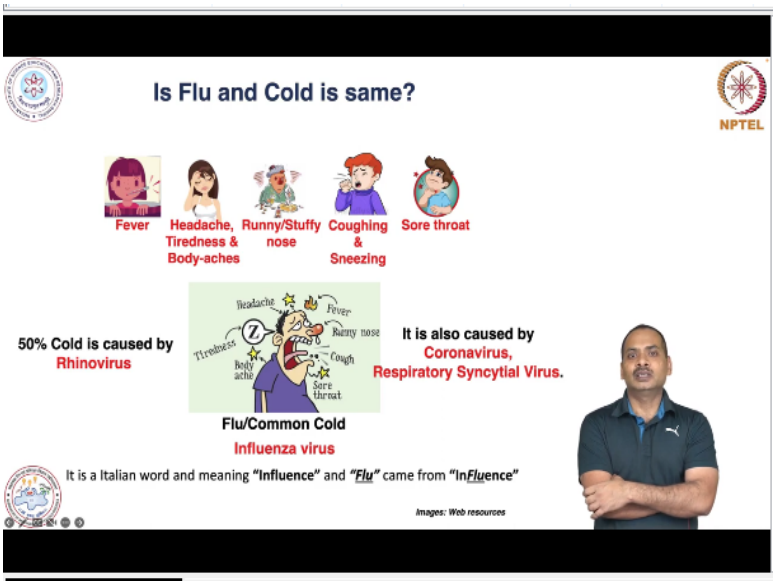

So, there is often there is a one question that is flu cold is same or it is a different? So, basically when we talk in a simple conversation we consider both flu and cold are kind of set of symptoms which is consists of fever, headache, tiredness, body pain, runny stuffy nose, cough and sneezing and there is a sore throat. And all these symptoms are basically induced by various kind of viruses.

Like a rhinoviruses most of in general we have a rhinovirus infection and this will be easily managed after some time, it is also caused by corona virus, respiratory syncytial virus. Now you know very well about the corona virus, it is a probably you might have experienced. So, all these symptoms are induced by this family of viruses in addition it is also induced by influenza virus.

So, influenza virus is basically it is Italian word meaning influence and this flu word came from influence, this is just a piece of information, so that you will be more clear. This session I will stop here and in next session we will discuss more about this disease, clinical part of this disease, thank you very much.