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-63
Influenza Virus and Disease-1

Hi, so in previous week we have learnt about adaptive immunity and now we have learnt about viruses what are the innate immune responses against viruses, what are the adaptive immune responses against viruses and of how virus evade the immunity and establish the disease. So, in this series let us continue with one model virus, so we are going to learn about the influenza virus and what kind of disease it cause.

Influenza virus is a highly variable virus, thiese viruses keep on changing. And due to this property of influenza virus we always have a some or other epidemic all over the world and probably you are very well aware about 100 years back this cause a massive pandemic and that killed many, many people. So, let us begin about the influenza virus it is a very interesting virus, it is little unconventional kind of virus that I will discuss in this session.

So, we will have several sessions about the influenza virus and towards the end we will learn what kind of disease, how they infect the host cell, what are the target cells, what are the hosts they are infecting. So, we will learn everything; let us begin with influenza virus.

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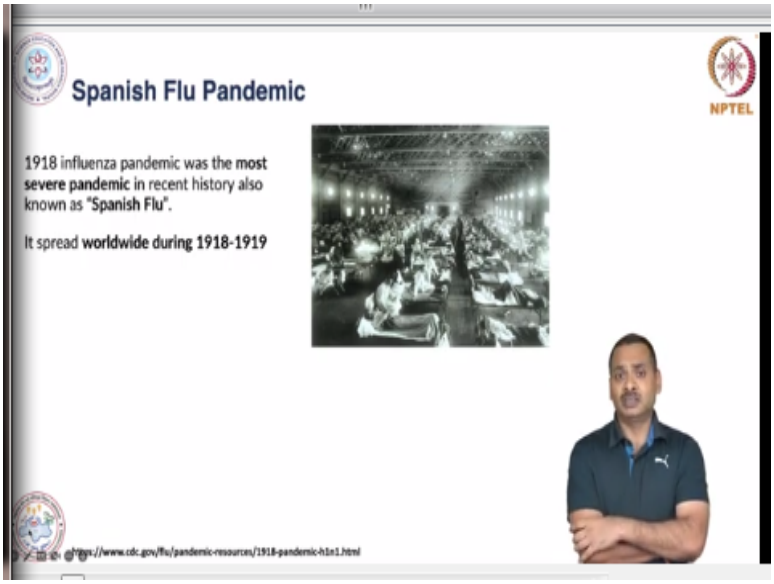

So, as you know that influenza virus caused a Spanish Flu in around 1918 and since 1918 it was there for several years. And this Spanish flu as you can see because the most severe pandemic. So, here I will just clarify few of the terms for example pandemic, so what do you understand by epidemic and pandemic, it is a close term and but they have a different meaning. So, epidemic is basically it is a outbreak which is localized to some small region.

And when this epidemic becomes a bigger size and far more bigger size? Far more bigger size means they cross the continents, you know that we have several continents. So, when the pathogens cross the continent and cause severe disease then we call it as a pandemic. And you know this now I think you are very well aware about this word pandemic due to this Corona virus or SARS-COVID 2 pandemic.

Currently we are in pandemic situation, so this pandemic is always very fatal, in general it is very fatal. And 100 years back it happened and still we are in the pandemic due to SARS-COVID 2. So, this is Spanish Flu because pandemic in 1918 and this is spreaded from 1918 to 19, several years, it is not only 1919 after 1918 there are several year it was spreading and causing disease as well as fatality.

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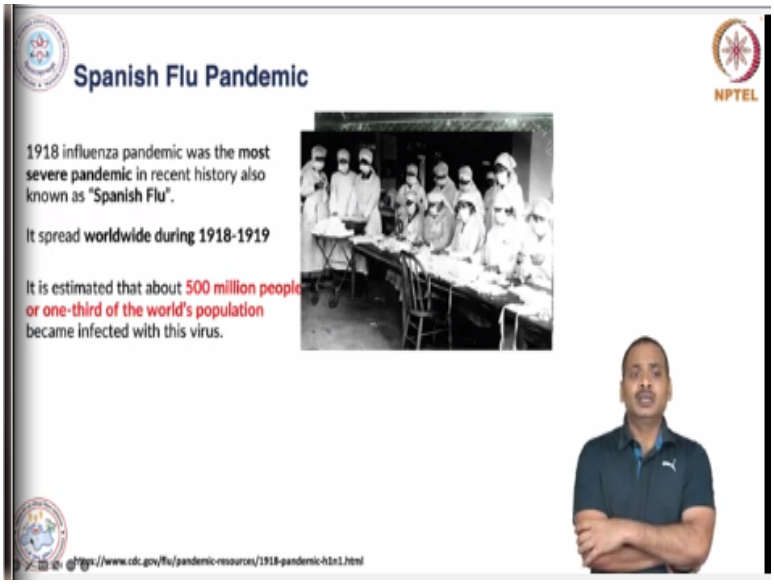

So, it is estimated that about one third of world population the whole world population at that time were infected with influenza virus. And about 500 million people they are basically infected or you can say 500 million people or one third world population they are infected and it caused a massive death.

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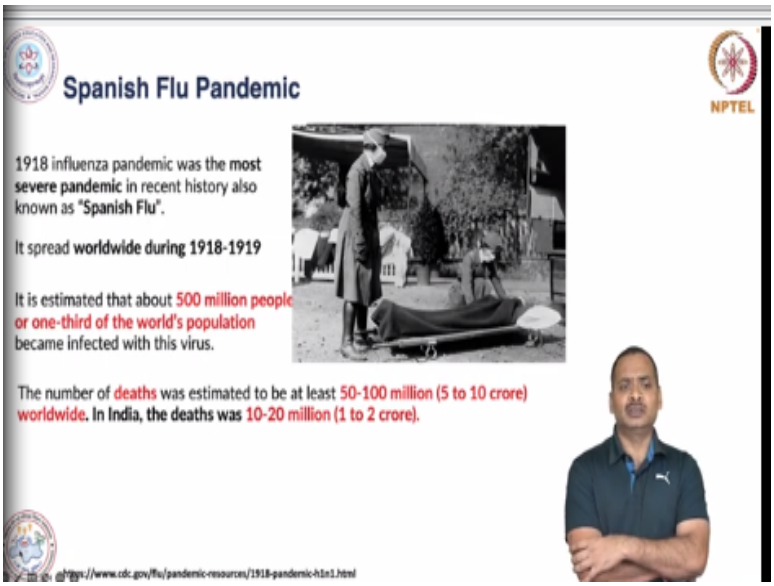

It was estimated that about 50 to 100 million people died by influenza virus, in our numbering system which is about 5 to 10 crore people died at that time. It is a worldwide, it also affected India and it is estimated that about 10 to 20 million about 1 to 2 crore people died in India. So,

you can understand the strength of this pandemic. And in current scenario the SARS-COVID-2 you have seen this was spreaded quite rapidly, why?

The reason is that this virus, now we have a very good means of transportation. So, this transportation basically also facilitates the spread of this virus, so this virus is very quickly spreaded all over the world. And that is the reason for rapid spread but on another hand if you see in this pandemic we had a far more well developed scientific things. That is why we are able to create the vaccine against SARS-COVID-2 in extremely short duration.

Try to understand creation of vaccine, if you look at the history creation of vaccine and administration to the human that takes a more than decade time. But here in this situation it was quite rapid, it is a rapid I will say, extremely rapid. So, this is a benefit of science or basic understanding.

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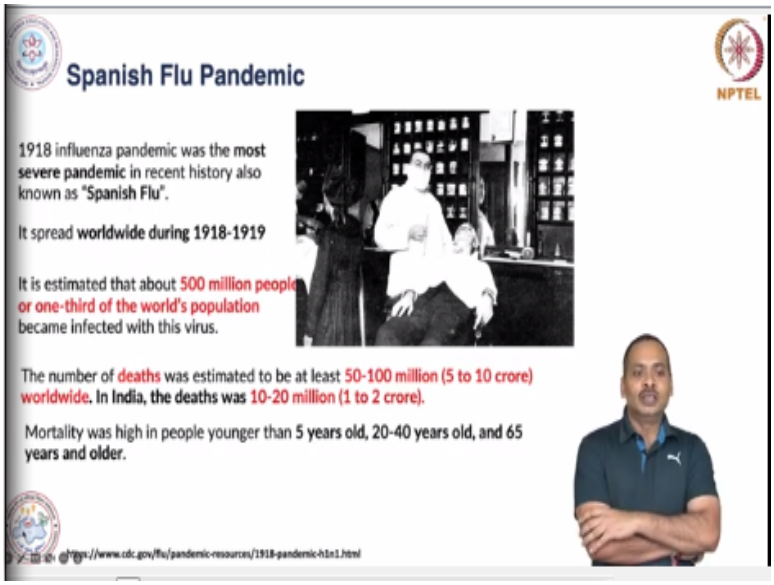

Now let us come back to the Spanish Flu or influenza virus. So, mortality was high in people younger people and about 5 year old kids are very much susceptible, 20 to 40 year old people are also very much susceptible or older people are also highly susceptible to this influenza virus. So, here you can see the images I am just showing you that in barber shop people are wearing mask and having a haircut. And this situation we saw in lifeve in current situation in a last year or few

year back, couple of years back when it was started. So, I think we are very well aware about the pandemic.

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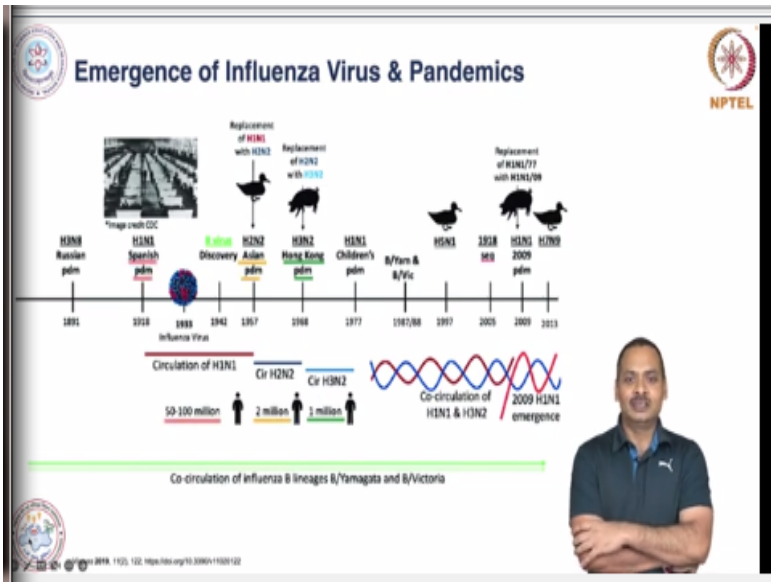

Now I would like to tell this emergence of influenza virus and pandemics, so here you can see that in 1918 this pandemic was happened. And the pandemic was basically started with H1N1, the influenza virus is a H1N1 and then this was in circulation in the world, it is not completely eradicated. I will tell you this influenza virus is a very smart virus, I think far more smart, they keep on changing and causing death and causing severity, this virus is extremely smart virus.

So, after that there was a Asian pandemic, here you can see that this Asian pandemic was happened in 1957. And then there was a Hong Kong pandemic which was happened in 1968 and in 1977 there was a children's pandemic and most recently in 2009 also this influenza pandemic was happened. So, try to understand these pandemics were restricted due to the knowledge and all those things and due to the scientific awareness.

But these viruses have a pandemic potential, means they can spread all over the world but they were very quickly controlled. And due to that this bigger pandemic means we avoided the bigger pandemic. Similarly in case of SARS-CoV, if you remember the SARS-COV which was this is a SARS-COVID-2 which caused the pandemic before that there was a SARS-COV which was spreaded through the wild cat.

And this is spreaded in 2002 if I remember correctly 2002 or 2003 from China. And at that time it was very rapidly spreading but due to this knowledge and information, scientific knowledge this was very quickly controlled. I remember I was traveling to the Japan at that time and my flight was landed in Hong Kong at that time in 2003. So, at that time everybody came with mask and this wearing PPE and they were checking each traveler.

I am just telling an example due to awareness and scientific knowledge we could able to avoid that pandemic. But due to that there was a severe loss of economy because export and import was a severely hampered all over the world and there are so many losses or there is a massive losses of human life as well. So, I am just giving the perspective of a pandemic. Now let us move to this virus in more detail.

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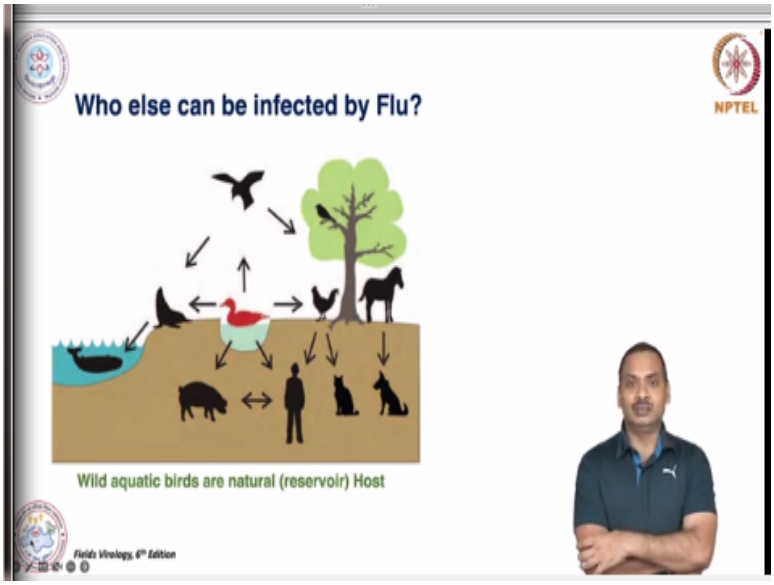

So, this virus basically influenza virus they are present in almost all living animals. Here you can see in this image this virus is present in sea animal like whale, seals, this is also present in birds, they can present in horse, hen, pig and one of the very important animal they are present in ferret, ferret is a one animal which is present in Europe generally if people use ferret for performing experiment using influenza virus.

And the main reservoir of this influence of virus is aquatic birds, aquatic birds means like duck they are the key reservoir of influenza virus. From there they hoop to another species and then they can come in contact with human. There is a one more very important animal where this not only this virus all dangerous viruses are present that is fruit bat.

So, this fruit bat is a reservoir for all very dangerous viruses that includes influenza, Ebola, Marburg and so on so, so this is a reservoir kind of thing. So, here I told you that this aquatic bird is a reservoir, so they are reservoir and they can hold various kind of influenza and they can create also more pathogenic strain. So, you know that there is a WHO World Health Organization.

And there is a one another organization which keep eye on all these animal and animal viruses and they are looking at whether this pathogen can this pathogen hoop to the human and all those things and influenza is also included in that.

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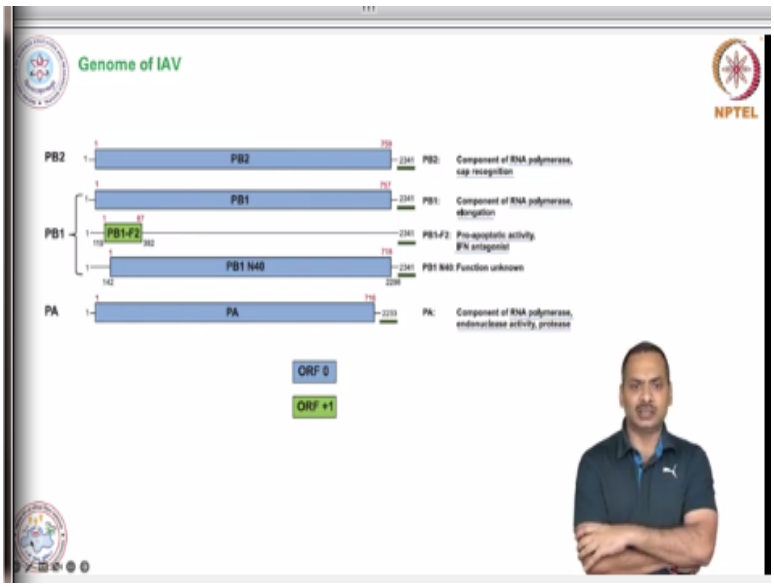

Now let us look at the genome of influenza A virus. So, here it is a genome, here you can see that there is a PB2, PB1 and PA, so PB2, PB1 and PA this makes a complex which is having the RNA polymerase activity. And this RNA polymerase activity is needed in order to make more copies of influenza virus. Let us look at the function of individual protein PB2, here you can see that the size of this RNA molecule, so it is 2341 basis.

So, try to understand this is a RNA virus it is not base pair, it is a 2341 basis. And this is a component of RNA polymerase and they play important role in CAP recognition. Another is a PB1 and there is a 2 and 3 variants of this PB1, so there are several mature protein, the original full length protein basically consists of here you can see that again it is consists of 2341 bases. And it is again component of RNA polymerase and playing mainly important role in elongation.

There is a PB1-F2; this is a small fragment, so it is not alternative splicing, so this full length of DNA can make a different protein, so here you can see there are 3 proteins. So, PB1-F2 this is having a pro apoptotic activity and it is basically a type 1 interferon antagonist. So, you know that type 1 interferon plays an important role in antiviral activity, so it is basically nullifying or it is suppressing the type 1 interferon effect.

Another is PB1-N40, so the function of this protein is not very well understood. The last is PA and this is a component of RNA polymerase and having an endonuclease activity and protease activity. So, this complex, here you can see that all these three proteins are involved in RNA polymerase. So, basically this is the RNA polymerase with different additional activity. So, now here there are several ORF which I have shown you in blue colour as well as in green colour.

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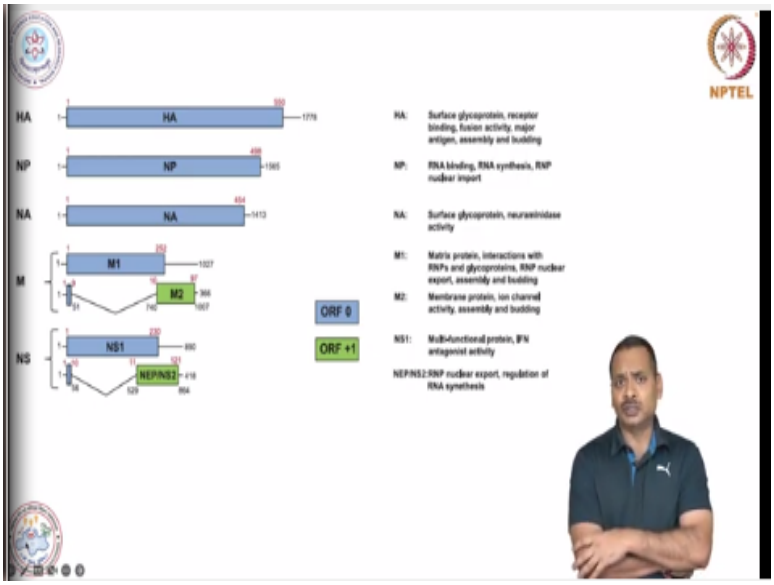

Now this is another segment of influenza virus genomic segment which is encoding HA protein. So, HA protein is about 1778 base and this HA protein plays a very important role in infection, this is a surface glycoprotein, receptor binding, it has a fusion activity, so they basically fuse the membrane. And this is one of major antigenic determinant and it plays an important role in assembly and budding off from after infection.

Another is a NP protein, this is consists of 1565 bases and it has a role in RNA binding, RNA synthesis RNP nuclear import. Another protein is NA, so this NA is neuraminidase, this is a surface glycoprotein and it has a neuraminidase activity. And this protein or these enzyme activities needed for the release of virus after infection. So, when the cell is infected and then this will make a lot of virus, so in order to release this virus, this neuraminidase activity is needed.

If neuraminidase activity is inhibited then we can control the virus infection. So, there are several drugs which is a inhibitor of neuraminidase. And you probably aware about that there is a drug known as Tamiflu, this Tamiflu is a inhibitor of neuraminidase which is used for the treatment of influenza infection. And now there are Tamiflu resistant influenza viruses, so now we have to find out some new strategy in order to control the influenza virus.

Now let us move to another protein that is M1 protein, it is basically consists of 1027 base. M1 protein is basically a matrix protein; I will show you the structure in subsequent slide. It is a matrix protein and it is basically interacting with the RN and TP's and glycoproteins. It is playing important role in RNP nuclear export assembly and budding. From same RNA there is another protein known as M2 protein, this is another ORF.

And this M2 protein plays a very important role, basically this is a membrane protein and this has ion channel activity this takes the proton and plays important role in assembly and budding. The last protein is NS1 protein non-structural 1 protein and it encodes to polypeptide, one is basically 890 bases. So, NS1 has a multifunctional protein, basically this protein is playing important role in immune invasion. They antagonize the activity of a type 1 interferon; another protein is NEP NS2 NEP NS2 play a important role in again RNP nuclear export regulation of RNA synthesis.

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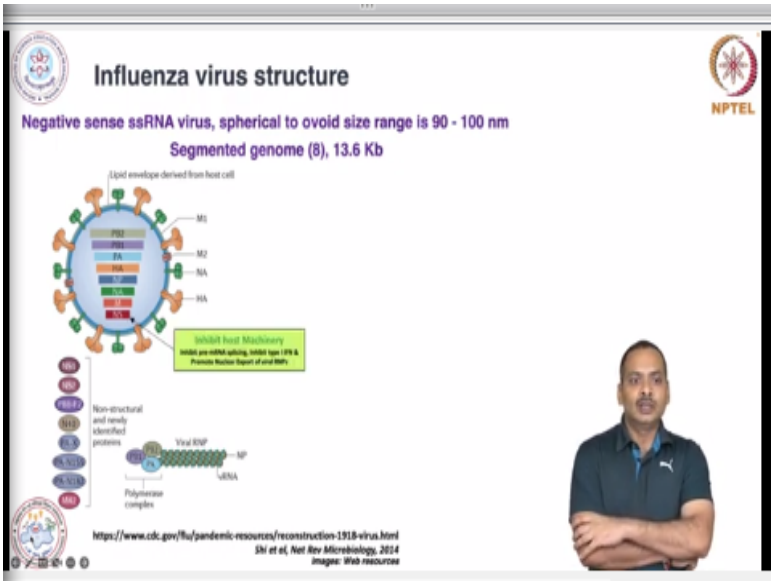

So, now let us look at how this influenza virus looks like, here you can see that. So, influenza virus is a basically negative sense single stranded RNA virus. It is a spherical to oavoid shape, it is not perfectly spherical but it is a kind of oval or ovoid and the size ranges from 90 to 100 nanometer. And it has a segmented genome, segmented genome means the genome is not continuous there are segments of genomes there.

And these segments are 8 in number and if you join all these segments the total size of the nucleic acid will be about 13.6 kilo base. Here you can see the structure and inside this virus you can see that the genome PB2, PB1, PA, HA, NP, NA, M and NS. And the size is basically depicted; here you can see there is relatively the size is reducing when you move from top to bottom.

This is just denoting the size of genome, the NS is the smallest and PB2 is a largest. I have already told you that the function of each component, so like NS protein plays an important role in inhibiting the pre mRNA splicing, inhibit type 1 interferon, promote nuclear export of viral RNP.

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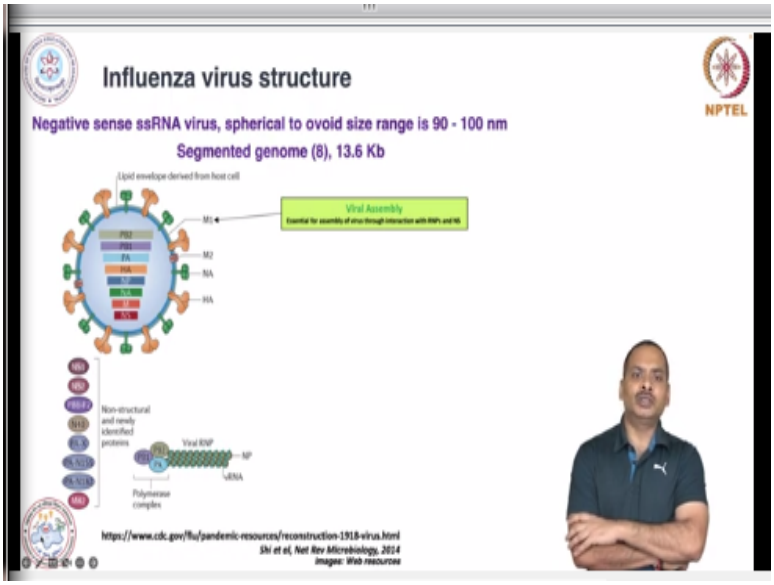

M1 protein plays a very important role in viral assembly.

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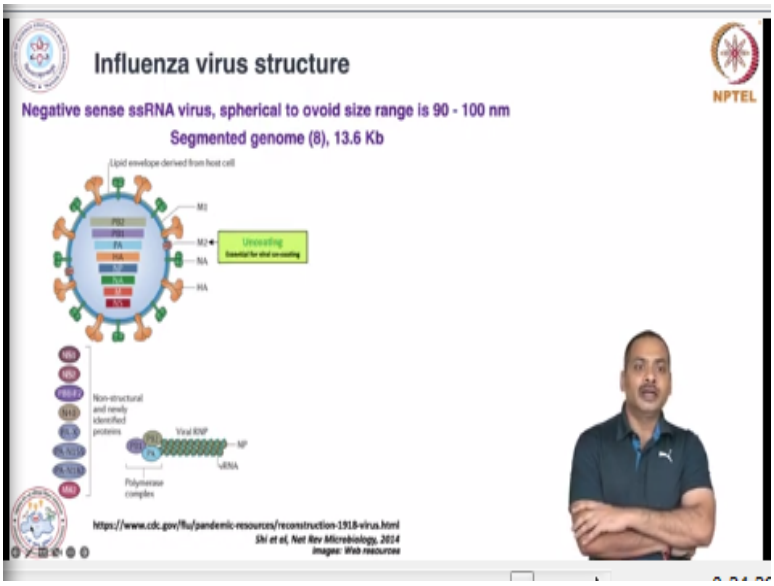

M2 protein plays a very important role in uncoating, they take the proton and then that the virus get dismantled inside the cell. And then the genomic RNA is transported and then this will be used for making another viral particle.

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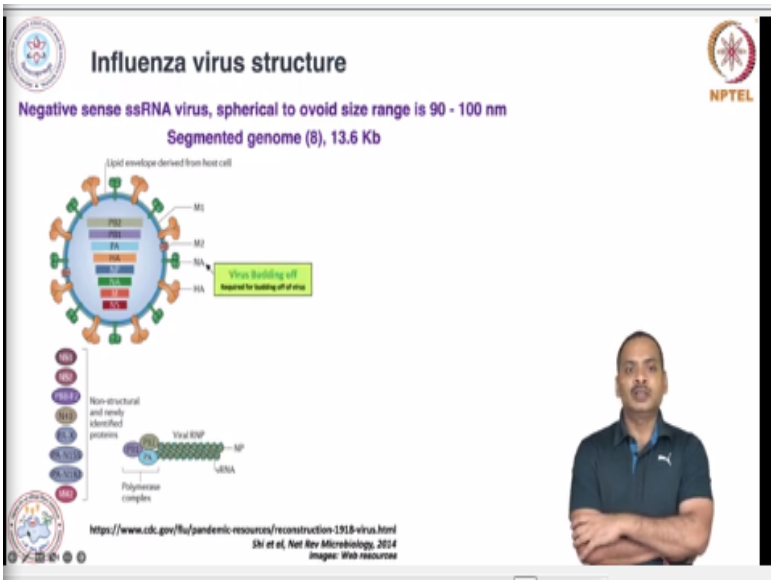

NA this is playing very important role in virus budding off, this is an enzyme and is a neuraminidase.

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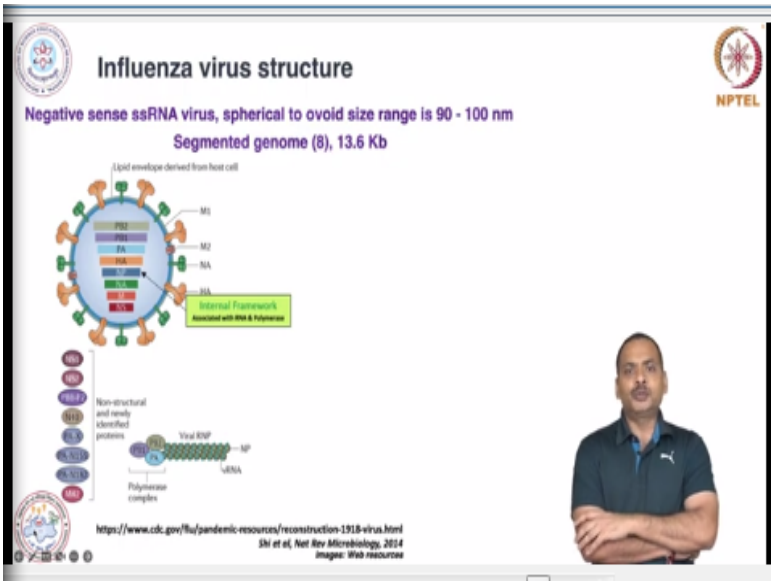

And NP protein is basically providing an internal framework in order to when all this genome is packing then this is providing a kind of framework.

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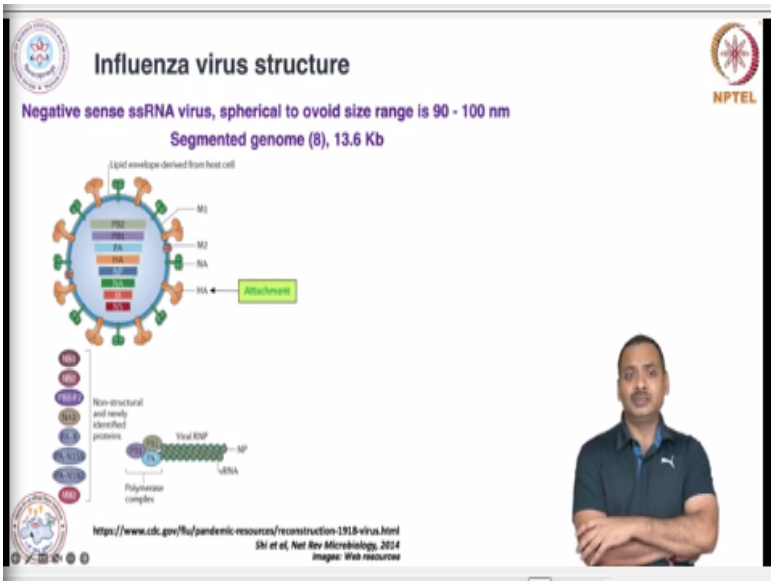

HA protein is very important in attachment with the target cell, basically I will explain you HA protein is binding with a sialic acid on target cells. And there is a polymerase this is a PB1, PB2 and PA this makes a polymerase complex and this is needed for the replication of a virus.

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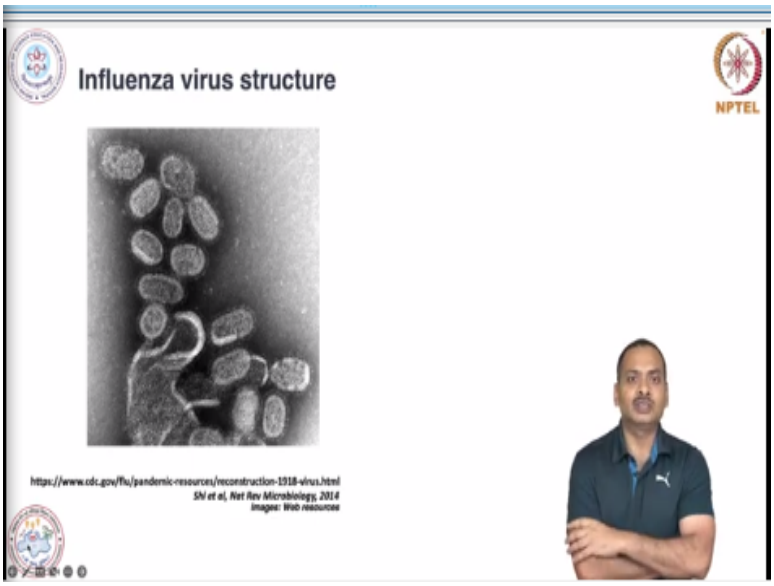

Here this is electron micrograph of influenza virus which is in black and white; this is the original electron micrograph.

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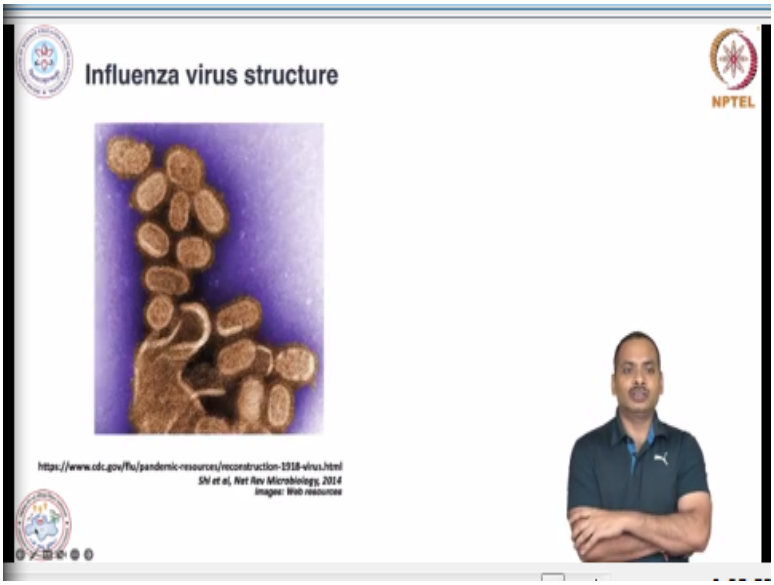

And this is a pseudo coloured electron micrograph.

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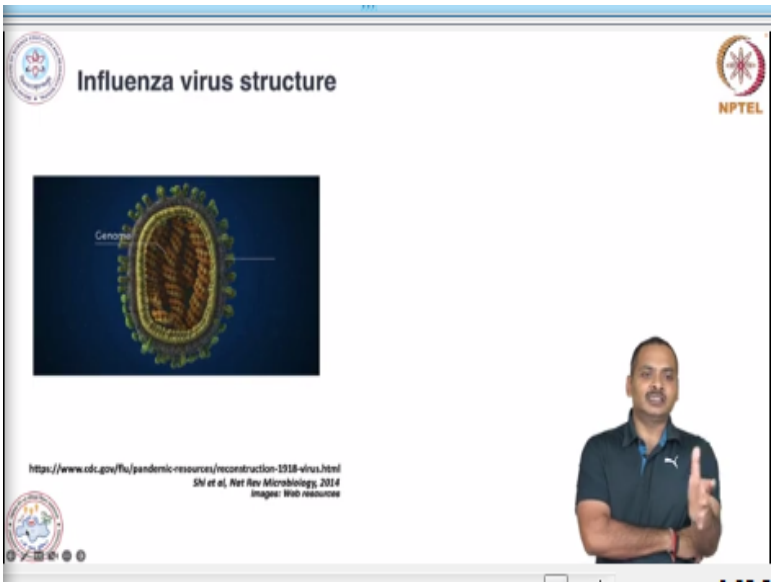

And here you can see this is a very nice schematic, this will give you how the virus is. Here you can see that there is a HA protein, neuraminidase and M2 channel and this is the genome is arranged in inside the viral particle. So, with this I am stopping this session, in next session I will further discuss about the influenza virus, thank you.