Immunology
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Lecture No -56
Active and Passive Immunity and Vaccination

Hello everybody, we are going to talk today about vaccine mostly and before that we are going to talk about active and passive immunity, what does it mean and also the vaccine. So it will be throughout this lecture and coming few lectures, we are going to go back and forth between different aspects of vaccine. Because, all our highly related I mean you cannot separate completely like we are going to go back and forth between vaccinations passive immunity, active immunity.

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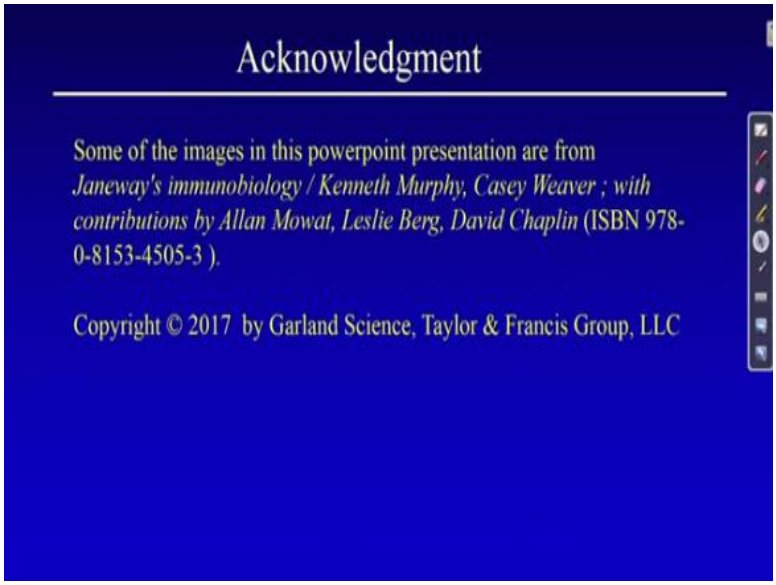

And as usual like this lecture also contains some of the images from Janeway's Immunobiology biology book which is copyrighted.

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And main topic that, now we are going to talk about the active immunity and passive immunity. What is active immunity? Active immunity means when our immune system gets some infection and in response to the infection when it elicits the immune response to fight against it then it is the active immunity. So this active immunity can be I mean happen in our immune system can response either the natural or real infection.

Or if we deliberately inject something which is pathogenic or and antigenic, rather immuno genic then it will also response to it and elicit the immune response and this both are active immunity, and these two immunity what is the difference one you will have the disease and another when we deliberately incorporating something that most of the time it is not going to activate the disease and that is vaccination or immunization.

And what is passive immunity? Passive immunity is when the immune response happen in some other places either I mean we can say some other organism or animal or human is already infected with some disease. And we isolate the blood or antibody from those individuals and give it to someone to cure for some other symptoms or the disease, so the immunity was active in some other organism or even human being and we are taking the help of that active immune system.

We are purifying the antibody molecule and injecting or the serum of that infected person and giving to another individual to protect from that particular disease is called passive immunity. It may be natural, it may be artificial, so we will discuss later on what is passive immunity. So first let us discuss active immunity and what is the vaccine and vaccination. Active immunity actually we discussed till last lecture, what happened, what are the components, how immune system reacts that was active immunity.

But major purpose of this, today's lecture on active immunity means we are going to talk about vaccine.

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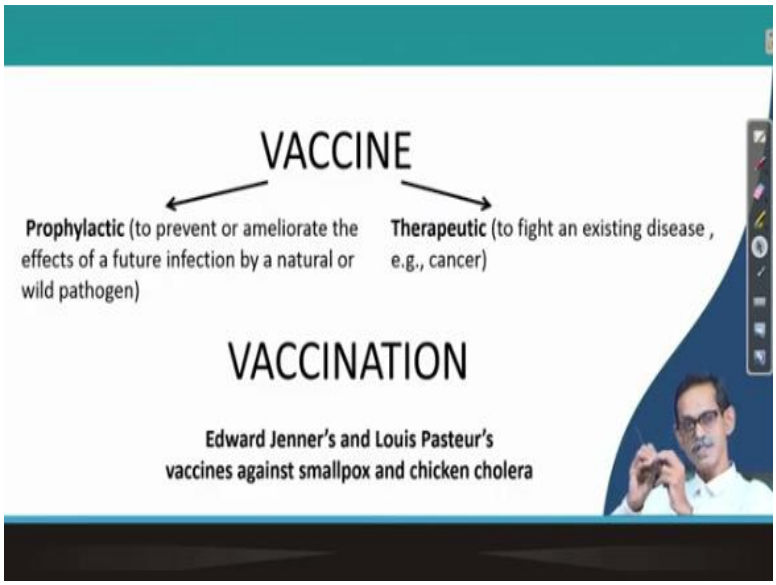

Vaccine is inducing the active immunity, what is vaccine? It is much easier to say what is vaccination than vaccine? Vaccine is nothing but antigen or immunogen, which we are going to forcefully or deliberately introduce or administered to an individual to raise the immune system. I am repeating again, so vaccine or vaccine candidate is basically the antigen or immunogen we deliberately administered into an organism or an individual to raise the immune response.

So that it can fight in future against that disease if it happens really or in reality. So it is the immunization material like by which we immunize, so vaccine can be of two types one is called prophylactic another is therapeutic. Prophylactic means to prevent or ameliorate the effects of the

future infection by natural or with pathogen. That means, we are priming the individual with vaccine. So that our immune system can see what is that.

Remember it the memory b-cell and t-cell they will stay inside the body. So next time if infection happen or the secondary infection it will act faster or much quicker way than the primary infection. So that is the part or the purpose of the vaccination and this is prophylactic and what is therapeutic, which is already to fight against an existing disease that means the cancer is already there.

So it is not that it will happen and we can vaccinate that someone will have cancer it is normally we do not do that. So if someone is having cancer then we induce the immune system with certain antigen or vaccine candidate. So that immune system specifically can help or treat or cure the cancer better way, it is in addition to the other treatment of cancer. So, this vaccine candidate we have to understand we have to purify and once it is done and then we have to use it.

And the use of vaccine is called vaccination, and we are going back to the first lecture. I started that immunology or modern immunology started with I mean if you go back to the history. We started with Edward Jenner today almost last part of the course we are coming back again to Edward Jenner and Louis Pasteur because they discover vaccine against smallpox and chicken cholera.

So almost 100 years gap and the vaccination term was proposed by Edward Jenner because vacuum means cow, so he used the cowpox buyers to do the immunization for smallpox. So he named vaccination, but in 1881 Louie Pasteur just to honor Edward Jenner he just said like or convince the people that these terms should be continued and still today, we are using the term vaccination. Vaccination means injecting or administration of vaccine candidate to an individual which can protect us from future infection.

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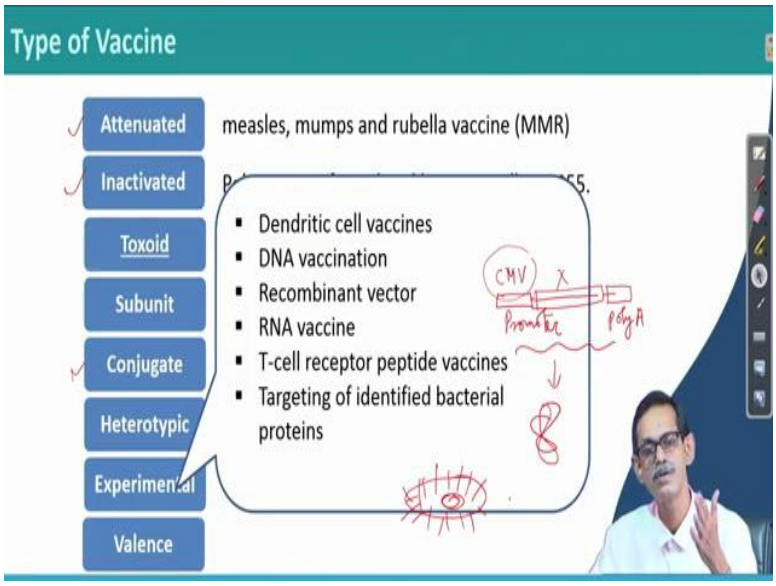

There are varieties or various type of vaccine, we will go slowly there if you see that Attenuated, Inactivated, Toxoid, Subunit vaccine, Conjugate vaccine, Heterotopic vaccine and there are a series of Experimental, Experimental means it is not a type of vaccine actually it is the different types of vaccine which is now under experiment is going on. So it is not yet finalized, so people are trying to develop a new kind of vaccine.

And there is another type of called vaccine called Valance, so what is Attenuated vaccine? Attenuated vaccine is some whole organism life organism life, but attenuated means they lost it infectivity or the virulence. They cannot cause disease anymore, what are the examples like measles, mumps, rubella vaccine and this is in short called MMR, measles, mumps and rubella. Inactivated means, when inactivated again can be the whole organism we killed it by some means.

We can use some chemicals to kill the whole organism or we can heat inactivated right you just if you heat any organism up to certain temperature they will die. So dead organism either chemically or by heat if you make them, so it is not going to lose its immunogenic activity because the surface protein. If you see any organism if you heat them they will die, but the surface protein of that organism may be denatured but it will remain there.

Denaturation is not a problem because denaturation is not going to lose it is a epitopes character, conformational epitopes will go away, but the linear epitopes, you have to go back and remember what is linear and what is conformational epitopes. So linear epitopes will remain intact and that is going to serve as the antigen and elicit the immune response. So whole organism initially was life but lost its pathogenicity or the virulence.

Second one is a whole organism but inactivated means they are dead they cannot do anything, but it is not degraded or something. Toxoid what is toxoid? Because there are many bacteria you know like Tetanus, Clostridium, cholera, Diphtheria so they produce exotoxin, exotoxin means you have to little bit go back to our microbiology course, hope you studied that bacteria secrete some protein molecules as a toxin and these toxin go and binds in one, if I remember correctly in one lecture I told something about that.

So, that this toxin goes and binds to our cell the target cell and then make damage. Different toxin has different activity. I already told it in a toxins in cholera toxin. So these toxin if you inject directly what will happen the toxin whether bacteria secrets inside the body or if it is a purified toxin little more dangerous right. So it will act on our cell and immediately severe situation will come. So what we do or the scientist started, they take the toxin molecule or the protein.

They heat denature it so what will happen that protein will be denatured, so it will not going to act as toxin molecule anymore but their epitopes will remain intact so that is called toxoid so heat inactivated toxoid mostly you see that tetanus and Diphtheria. So Tetanus and diphtheria we use toxoid, because the toxin directly we cannot use it because it will kill. Forth is subunit vaccine.

Subunit vaccine is not very old discovery normally the hepatitis virus vaccine is the subunit vaccine, what happened in like in a virus you know that there are so if this is the virus molecule there are some certain surface molecular here right. So what is going to happen either you inject that attenuated hepatitis B, hepatitis virus or you use the inactivated hepatitis virus. So either attenuated or inactivated both virus is possible.

But there are always chances for the attenuated virus to come back and gain the virulence. So what happened it was found that immunity against the hepatitis virus was mostly against the surface protein by antibody mostly, so what happened the scientists purify this surface protein separately and injected the surface protein alone. And it was found that itself; I mean the surface protein alone can be used as vaccination.

That means, if you inject the surface protein into an individual and after that hepatitis B infection happen in real life that individual can protect, so gradually it is improved so initially to as a whole protein, a whole protein cannot be epitope or whole person cannot we do not need because antibody will not bind the whole protein antibody may bind here certain region this epitope, may have this epitope.

So what can be done so if this is the protein and if suppose this is the gene you can instead of the whole protein you can make a construct a truncated version of the protein also you can express in heterologous system like you can express in yeast, you can express in bacteria, animal system. So this part you express and the truncated protein which is actually having both the epitopes, epitopes 1 and epitopes 2 you can use for vaccination.

This is the subunit many proteins you know there are multiple subunit Alpha, Beta, Gamma suppose on the Alpha is enough, so you do not have to make all the proteins only alpha subunit express purify then you inject, that is called subunit vaccine. So hepatitis virus is the first virus which is a subunit vaccine was used and discovered. Then conjugate vaccine is coming. What is conjugate vaccine?

It is Haemophilus influenza B, meningitis, pneumococcal these are the bacteria which has a Lippo polysaccharide on their surface. So if you want to kill them or if you want to neutralize them or stop their activity what we have to do. We have to have antibody against this polysaccharide molecule, but it is not I mean we know the T cell cannot process the polysaccharide.

So we have to think something else so that B cell will produce antibody against a polysaccharide but T cell is something, we will see something. So that is a mixture of protein and polysaccharide will show come later that is called conjugate vaccine. Then heterotypic vaccine, heterotypic vaccine means when you are giving when you are giving pathogens from other animals, that was how the vaccine or immunization first discovered.

If you remember the Jenner he used the cowpox virus to treat a human pathogen smallpox virus. This was a heterotypic, so pathogens of other animals that either do not cause disease in human or that particular organism or cause mild disease like pox, I just tell you and the BCG. This is the vaccine for Mycobacterium tuberculosis, it was very effective in certain country it is not at all effective in certain country for some reason.

So new discovery or new experimentation and going on, because BCG was very good one once it was very good protector for the child particularly child TB, experimental I will come later. But before that experimental has a separate or variety of things, dendritic cell vaccines, so what people are doing we were injecting dendritic cells along with the vaccine candidate, so that the presentation of antigen will be better.

People are trying that DNA vaccine so instead of giving the protein injecting the DNA directly so that the body will produce the protein and our immune system will see that this protein is foreign. So you do not have to have in this much easier, because preparation of DNA is much cheaper with respect to protein and less problematic, because protein has lot of problem if you want to isolate protein or purify protein or express a protein it is not that simple or straightforward.

In books or in board, I mean if I have a black board now in front of me in five minutes I can clone a gene, I can express a protein, I can purify it, 5 to 10 minutes. But it may take years just to clone and express a protein and get a pure protein in its form, so in with respect to that working with the DNA is much more simpler so isolation and purification of DNAs. So people thought or the scientists rather scientists thought that if you inject the DNA directly to the individual that particular individual can make protein from their DNA because sale has the capability.

So what we have to do, we have to inject the DNA in such a way that DNA goes to nucleus of our own cell, so if this our cell if you inject the DNA with enters into the cell nucleus cell will try to express it and what you need to express you need a promoter and your gene of interest that gene means, whatever you want to clone and the three prime poly A signal. This is poly A signal. And normally these promoters should be animal promoter or animal virus promoter normally.

We do Cytomegalovirus promoter CMV promoter so we make a plasmid and the gene of interest X whatever disease or the surface receptor or the target protein you would like to do clone it make a construct isolate the DNA, injected and cytomegalovirus promoter our transcription system or human transcription system can and I mean nicely utilize it and can transcribe. So what will happen?

There will be first mRNA and from that mRNA after transcript the protein will form, and that protein even if it is a cell protein into the internal protein it will be presented by MHC 1**.** An immune system will find it new because it was not our own protein, so that is how DNA vaccine works. T cell receptor peptide vaccines; it is also a new one so new chimeric receptor is making an T cell receptor for a particular vaccines injected with the vaccine.

So that; the presentation or the recognition or t-cell activation will be much easier. Targeting of identified bacterial protein: So if you know that this, say first one thing we have to understand the vaccine like once we would like to neutralize what killed, say in case of virus we have to neutralize the virus, so that it cannot bind to the target cell and do the damage or we have to activate the immune system the cytotoxic t-cells in such a way so that it can easily kill the virus infected cell at the primary level.

So that the spreading of virus will be much less or cannot harm the disease because for every disease or the manifestation of the disease you need certain number like one Vibrio cholerae bacteria which cause cholera cannot do cholera you need the Vibrio cholerae to grow in certain number then it will start create problem or we can see the manifestation of the disease. Similarly virus also few numbers cannot make much harm.

So in that level when the number is very little if the immune system can block them or stop them or kill them what will happen? So they will they cannot progress, so for that what you have to do actually you have to know exactly how virus is working how they are replicating, so their biology. And which part of that virus will be highly immunogenic, which part of that virus or bacteria not only immunogenic.

If you block it then your clearance or effective immunity will be better so that research is parallel. So you have to understand that biology and the immunology first and after you identify then what you can do is that particular protein you can over expressed, we can over expressed. Actually I thought I will tell it later, but now over expressed is like what I said in BCG, it is not working.

Now the protein which is actually helping to improve immunity if you overexpressed that particular protein in that bacteria and now inject what will happen initially suppose the bacteria has 10 molecule here and there 10 or 8 or 9 whatever it is, now whatever you recombinantly express this protein here inside and increase this number in much more, so what will happen that will make the immune system much more active, much more efficient.

That way also you can improve and that is going on in particularly BCG actually, people are trying to do that, that I will come again and then valence. So what is this valence? Valence is if you want to use the vaccine or make vaccine say there are 2 or 3 variety of one organism all cause disease. Some are mild, so you mix them together it may be same human virus or human pathogen or from hetero typique like 2,3 different strain so you mix them together and inject as a vaccine, so many times what happened it gives better protection, it better protection.

So instead of only one hole or attenuated or inactivated we are injecting 2, 3 different stains. And that is very, I mean in case of influenza you might have heard like H1N1, H1N2 and H1N6 what is that, that means their surface markers are different, different variety. So, instead of giving one if you are making a vaccine which can handle three different type of influenza virus that will be better or more effective.

Because they are changing I don't know which one is going to infect. So the both way you can do this, one is vaccination another is a natural infection, infection also will do the same thing if someone have is having influenza of a particular strain our body immune system will reactivated and if same influenza virus infect again what will happen that will give the protection. This is one way.

Other is the vaccine so you know I do not have influenza but I took the influenza vaccine. Immunize or priming the immune system so that in future if influenza virus at our body can take care of that, both will do almost similar take slight definitely the slight differences are there that I will come if while saying that what is the difference between attenuated and inactivated virus I mean no vaccine.

So but what I will prepare I think all of you will prefer I will not prefer the disease. If without having disease but the result I am getting the same, then I will definitely prefer the vaccination and it is happening like that so that is why whole world, World Health Organization everybody is trying to develop or generate vaccine so that instead of having the disease and gaining the immunity we should have it before that.

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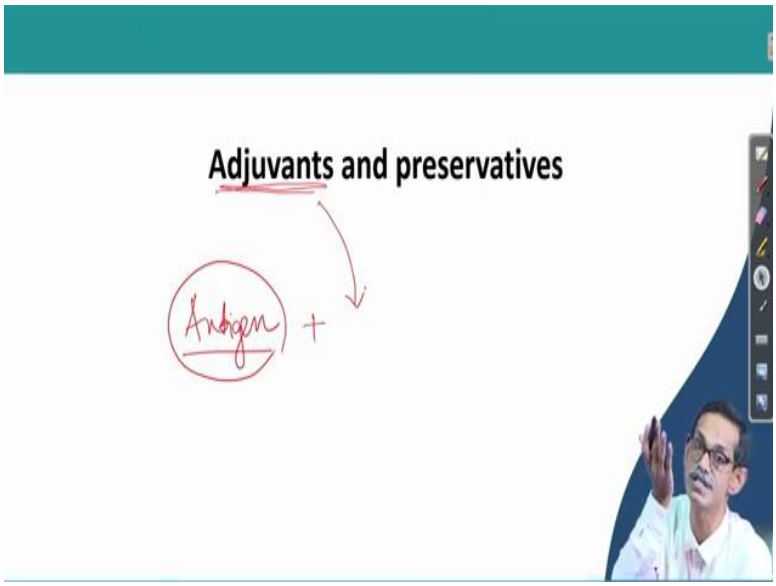

And to do this vaccination along with the vaccine candidate we need something else also, so only protein if you inject into an animal or say an individual human. Many times itself particularly it happened when we are going the toxoid, subunit vaccine that means pure protein we are giving not the whole cell. That is not normally this is not the problem for this attenuated and some cases the inactivated vaccine also need that.

So these toxoid, subunit vaccine and some cases in this inactivated vaccine they cannot work by themselves, they cannot activate the immune system by themselves all alone so then what we use, we use adjuvant and definitely you know what is the purpose of preservative, preservative we use in many many different places like in food for long storage food in pickles whatever we are buying from the market we add preservative.

Because preservative can protect the material or the thing from bacterial and fungal infection. So vaccine what will happen it is not possible like I will make vaccine in this hand and in the other hand I am going to inject to the patient or the individuals. So some companies producing vaccines they are storing it has just like a biomolecules. It cells attenuated live or deactivated or inactivate ourselves or a protein everybody as a self life, we have to keep it.

So it is not from production immediately we are producer. So company or of industry is making it if even if you are making in the lab it has certain life so if you want to keep them for a long time which is one of the major challenge for vaccine production. And use of vaccine or immunization procedure like the storage of vaccine so for storage you need to add some preservative so that it lasts long, it self life will be more so that we can use it for a long time.

Automatically the cost will if you can store them for a long time ultimately cost will be less. So what is adjuvant? Adjuvant is the material or chemicals you are adding with the so you have say antigen here. We have antigen which alone may not elicit the immune response that much and this and you need something which will add some immunity more or if you remember the super antigen that time I told so along with that region we mix it so that it boosts the immune system in general. So adjuvant like that there are varieties of adjuvant are there.

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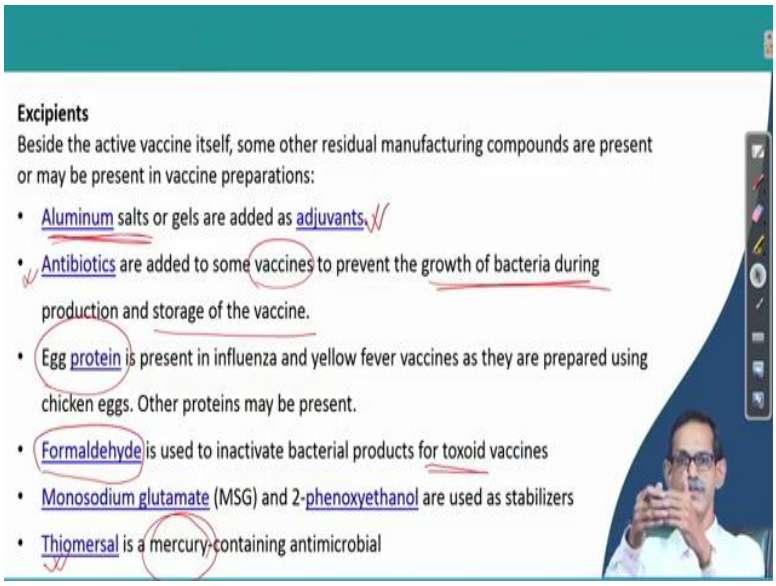

But in human we normally use this aluminum salts, aluminum salts call Elam, I will repeat it again. So what happened so I will come in adjuvant later, so before that just while discussing what is vaccine. When we are producing vaccine there are many other material, because I said varieties of different type of vaccine when we see the vaccine in a vial before injection or oral administration whatever it may contain many things.

Adjuvant we have purposefully we had in many times we have to have some cases we had to add antibiotics purpose, you know just vaccine to protect from growth of bacteria and storage of the vaccine. Egg protein is present in case of influenza in all of virus because while making the virus attenuated, so they are grown in egg cells, so in within the egg they used to grow.

So when you purify the vaccine candidate there is a possibility some make proteins maybe there, so it may contain so why I am telling formaldehyde is used, that is the chemical to make the top soil. So when you make a protein denature inactivated or add some chemicals normally we use formaldehyde to inactivate the bacterial products or the toxins. Monosodium glutamate is MSG you know that is the preserver or the stabilizer.

And there is another thing thymus and which is not very much used anymore because of the mercury containing antimicrobial. Ultimate goal of all this thing while production of the vaccine is I protect from virus and bacterial growth in because protein you are making a protein solution

which is very nice culture bacteria can grow happily so you have to stop them. So we give them adjuvant to activate the immune system or elicit the immune response little higher or much more efficient way.

So that only antigen or the vaccine may not do that job properly are completely. So these are the few things what you may have within a vaccine, so what will happen I will stop here now but this thing I will continue as if it is a it is not possible to continue I mean complete this in one, half an hour lecture, so I will continue this with the next lecture, see you.