Immunology
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Lecture No -58
Active and Passive Immunity and Vaccination (Contd.,)

So let us continue the active and passive immunity and vaccinations in different aspects, so in my last lecture you remember like we were talking about the same topic. Today also I mean in this lecture also we are going to continue, hope we will complete the up to passive immunization and the summary part in this lecture let us see.

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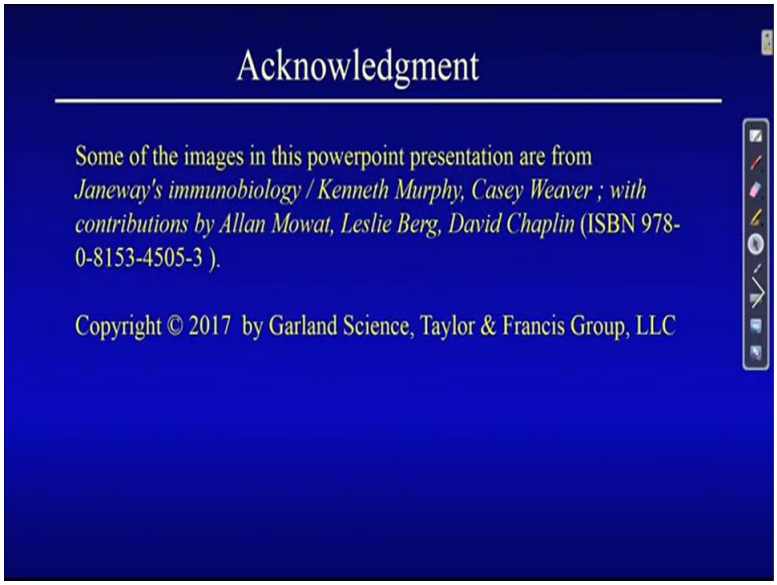

So this is the acknowledgement for use of PowerPoint presentation from Janeway's book.

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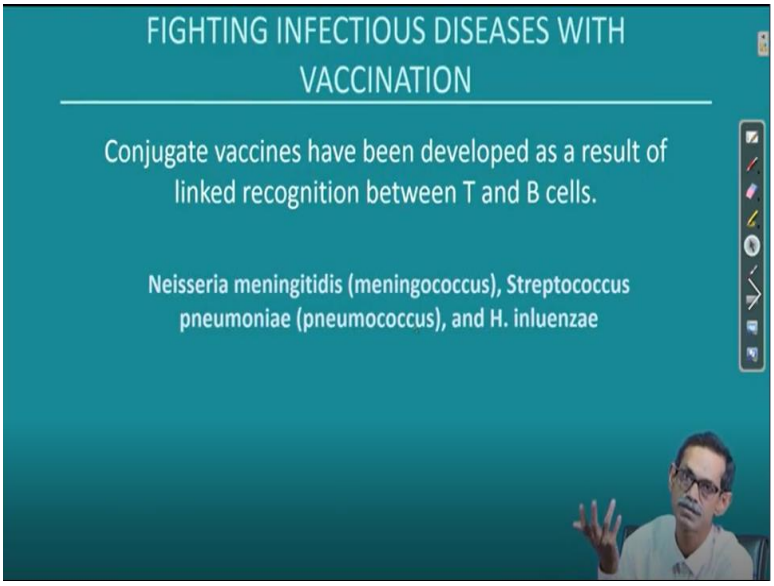

So now we are I mean after this attenuated vaccine, now I am going to talk about the conjugate vaccine. Conjugate vaccine have been developed as a result of linked recognition between T and B cells I just mentioned a little bit in the first lecture on this topic passive and active a vaccination process. Like if we would like to activate the immune system against the polysaccharide what is going to happen?

Because polysaccharide T-cell is not going to be activated by polysaccharide so what to do? And so new conjugate vaccine idea came and it was a very nice and clever idea I mean that was proposed and used and what are the bacterium this Neisseria meningitidis, Streptococcus pneumoniae and Haemophilus influenzae. So these organism of these bacteria actually produce some polysaccharide against which we need the vaccination, so how it happened I mean how it is done?

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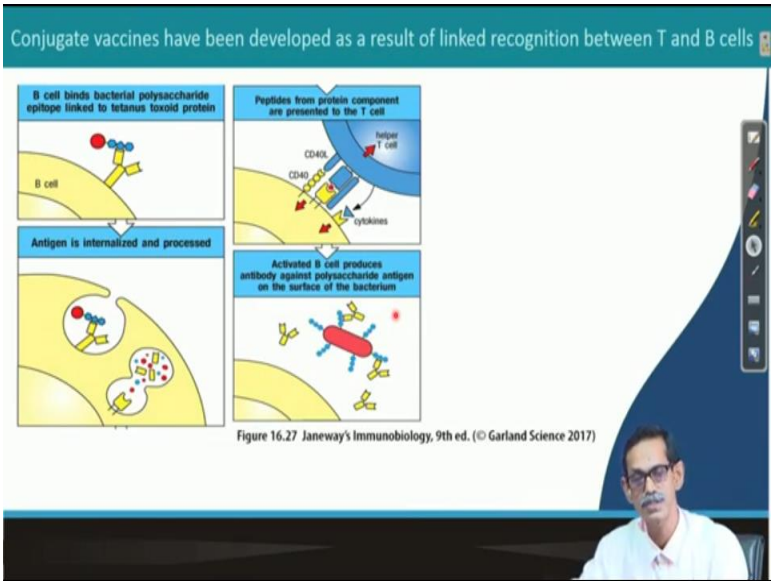

So you see we are coming back to immunology how immune system react. So this is B cell and say for example any particular B-cell receptor which can recognize this polysaccharide, which is outside the bacteria. So this B-cell receptor can recognize, but if it can bind but these binding what will happen after this binding it will internalize that part you know and then it will be degraded.

But in this degradation carbohydrate is not going to fit here which part will fit here, this red part red part is the conjugated part so what is that? This is tetanus toxoid. So tetanus toxoid has nothing to do with this in this particular case, but we can have double protection. So tetanus toxoid fused with that particular carbohydrate are taken up by the B-cell processed and presented by MHC 2, you see the MHC 2 is presenting the red part actually.

This red protein part is presented by MHC 2. So these MHC 2 presentation will attract helper T-cell it will bind activate and I am not going to be detailed on the how the T-cell you will activate B-cell you already know that, it will give signal. So this particular B-cell which has a receptor against carbohydrate will be activated by presenting a protein and that is why it is called conjugated protein.

That means carbohydrate and protein is conjugated so T-cell is seeing the protein part and activating the B-cell. B-cell is producing antibody where these antibodies binding antibody is

binding to the bacterial polysaccharide. So that is how this particular conjugated vaccine developed against these 3 bacteria what I just showed meningitidis, streptococcus and Haemophilus influenzae.

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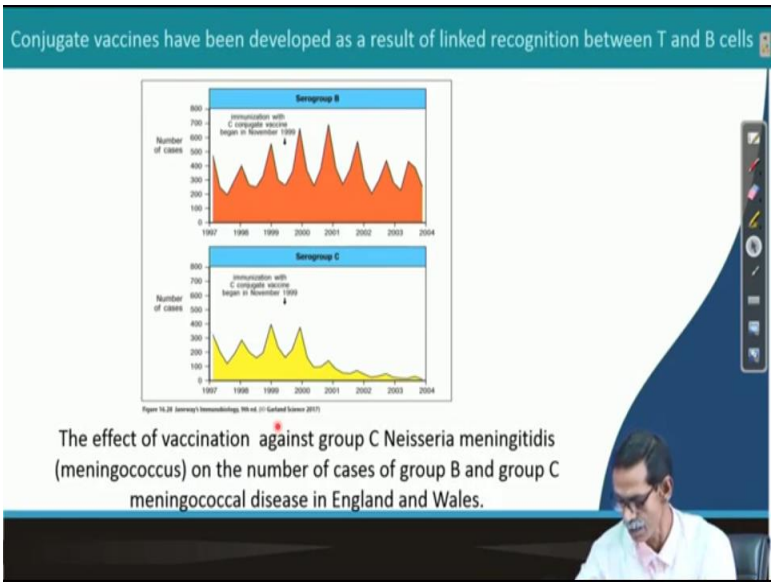

This is another conjugate vaccine development, this is particularly this immunization against meningococcus. The meningitidis so what happened there are two set of group this is a story of England and Wales. So to serogroup of B and C is there, so both used to create problem I mean cause disease. So when the conjugate this is and just to see I will show the effect how this how good is this conjugate vaccine is.

So this is the number of cases in different years from 97 to 2004, it is going up and down because it is a natural infection going up and down and in 99, 1999 I mean immunization against C conjugate vaccine introduced. You see, if you can consider these two groups sort of type good B and C, B remain intact so after 99 there is no change in cell type B. It is as usual like somewhere it is going down, somewhere is going up.

But what happened to Serogroup C after introduction of the conjugate vaccine if the number is gradually grow down in 2004 it is very minimum, I am sure now also it is good permanently I do not have the data but it is very minimum or no infection is there even if it is there the number is

pretty low. So that means the Sero conjugate vaccine against this meningitidis is working, it is the real case I mean it is not just the laboratory or the animal model

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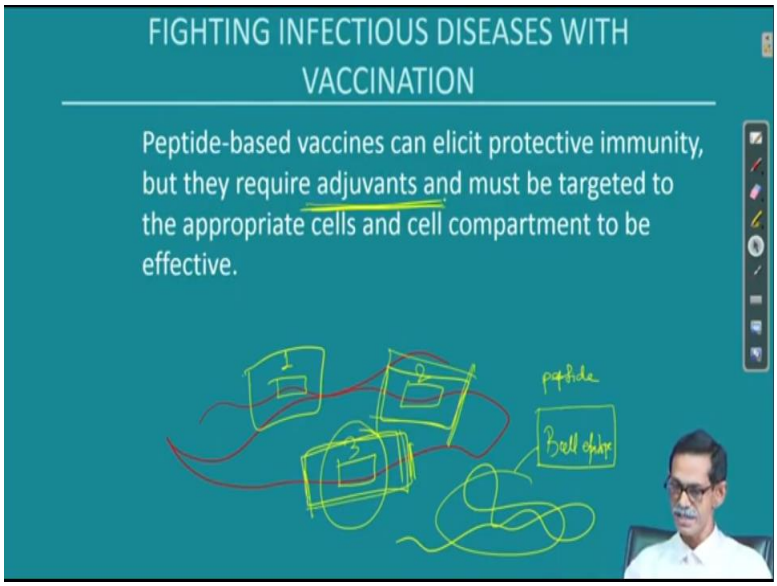

So, so far we said, what we said whole cell vaccine attenuated or heat kill then sub unit vaccine so much and so on but besides that there is one more type of vaccine is also possible it is called peptide based vaccine. Peptide based vaccine means say let me draw that so suppose this is the protein and in that protein we have different epitope so three epitopes are there.

So if I inject the whole protein what will happen antibody will be produced against epitope 1, epitope 2, epitope 3. So now instead of that instead of because many times what happened purification or the production of the complete protein is you I mean really expensive and cumbersome pure protein isolation of pure protein in many cases, it may not be possible for a variety of reasons.

This is not time or I do not have the time to explain all this thing variety of reason complete or pure protein isolation purification in large quantity is almost impossible for variety of reasons. So that time what I can do what I can think is instead of the whole protein I can just cut this region, so it is a small peptide okay which has one epitope you can have another how do you know which part is the epitope many white lab research.

You can determine which exactly the repeat of sequences besides that there are many algorithm based softwares are available where if you put the protein sequence or the primary sequence of the protein it can predict you how many B-cell epitopes are there how many T-cell epitopes are there. Definitely there are certain points how they determine it but so few points are very simple and straightforward.

Say one point, I can tell easily all of you can understand epitope for B-cell epitopes it must be hydrophilic right because it should be on the surface of the protein. So this is one. The length number of amino acids, there are many others I mean I am not going detail here anyway. So what happened, so this epitope prediction you can do by informatique analysis or immuno informatics you can test it in the lab and figure out that this epitope, I mean this peptide if I take out this big peptide, if I take that can be a good antigen.

But this peptide cannot elicit immune response by themselves. So you need to add one for any immune response, you need one you need one B cell epitope along with that what you need a T-cell epitopes. Because until unless you have a T-cell epitope it cannot act as immunogen. So many times what we do is we add a another big protein called carrier protein. This is a peptide we had a carrier protein along with that and with and given which is very important in that case, so carrier protein peptide combination and adjuvant together we have to make so peptide alone cannot elicit the immune response so this is slightly disadvantage here.

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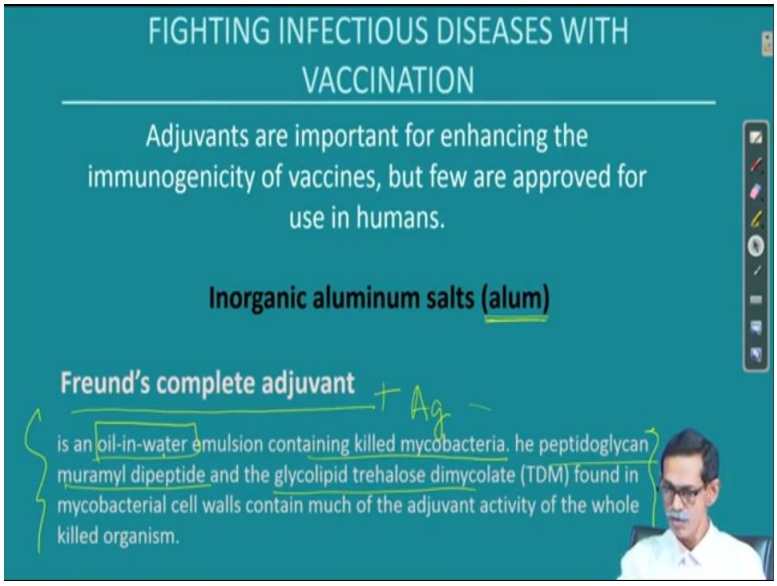

And adjuvant I already told in case of human only approved adjuvant is alum, but in case of animal because we need to raise antibody for many reasons in animal for regular day-to-day research activity for passive immune treatment that will come later. So there are another very important and very common adjuvant is there, it is called Freund's complete adjuvant which contains oil in water emulsion to make the muscle and another thing is use the heat killed Mycobactera.

Actually whole micro actin is not necessary peptidoglycan, minimal dipeptide is important and the glycolipid trehalose dimycolate is important but instead of that instead of purifying them the heat kill micro bacteria is mixed with oil in water emulsion and that is called Freund's completing adjuvant what we do actually for animal treatment when we inject or administer the antigen first time we do complete the whole thing here the whole thing here we inject.

So we mix this mixture along with the antigen, antigen plus Freund's completing adjuvant we inject but for booster dose we just use oil in water. So first injection complete and second injection or the booster on word we use in complete enjoyment what is incomplete we do not give this microwave to impart only while in water, so this is only in case of animal not in human only adjuvant is along.

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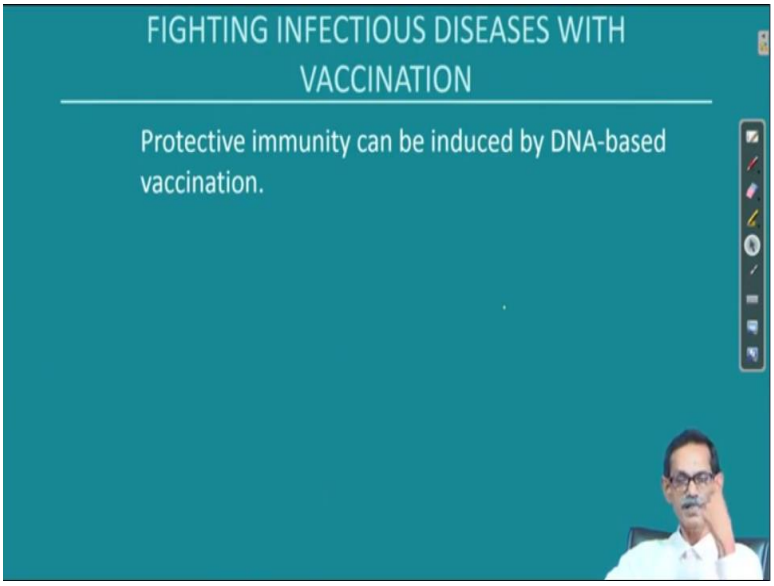

That I already discussed protective immunity can be induced by DNA based vaccination like the you can inject directly the DNA.

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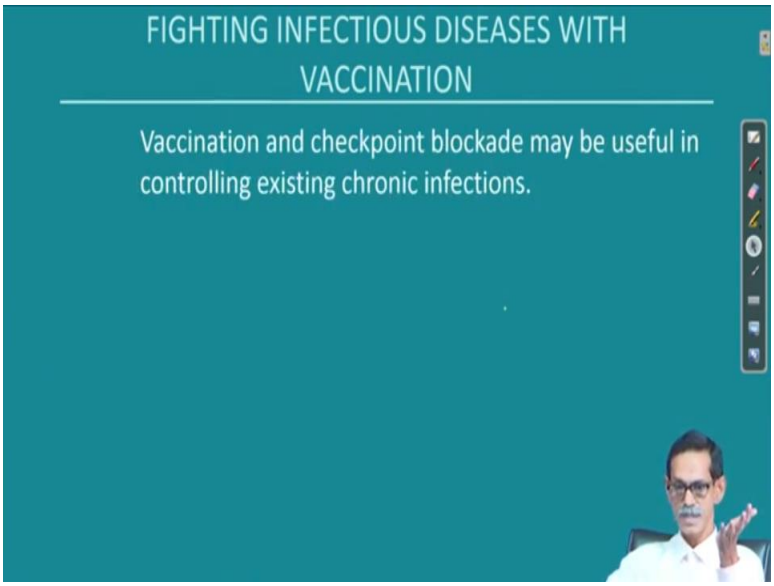

Vaccinations and checkpoint blockade may be useful in controlling existing chronic infection, that is important.

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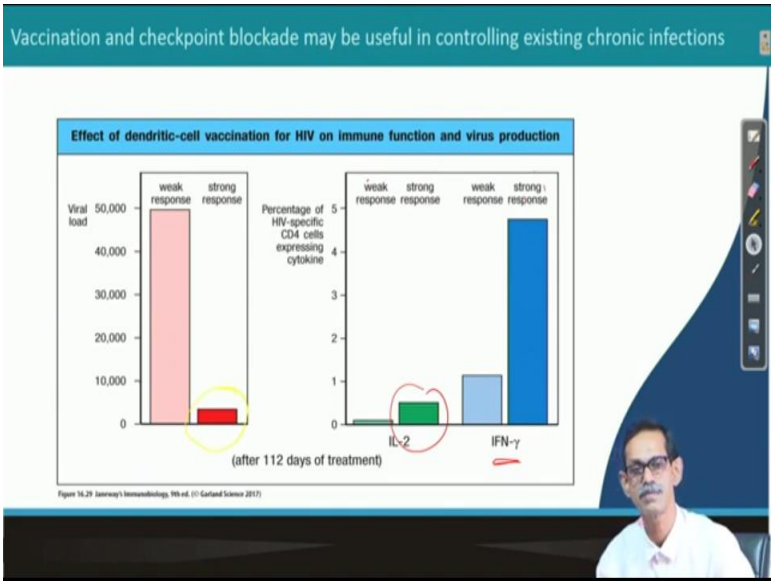

What people are now doing it now people are doing dendritic cell vaccination. So dendritic cell loaded with the antigen doing it outside and injecting it which actually what they are doing it they are inducing the different cytokine expression, so activated dendritic cell cytokine in activation which normally the immuno compromised or infected person this is the particular case of human HIV infected individual. So what happened many cases it happened if there is a weak response then this but if the response is good you see the viral load is much less.

So that means the dendritic cell mediated in vaccination is also studied and when it is shown that the vaccine mate what is happening in that case that dendritic cell mediated vaccination in fact this is the week response, if the Il-2 production is much less well where the response is good Il-2 is more in different gamma is more in strong response. So that means these particular dendritic cells vaccines this is all very new development of the vaccination it is the latest trend of vaccination.

It is just not because classical immunization process purification of the protein and injection is not enough for most of the disease, that is why a people are trying several other strategy. So that is this is the reason and a recent trend is a RNA vaccination arena vaccination is a lot of lab all over the world at this moment are trying to protect Covid Infection or Covid-19 infection at least next few years I know this is the Covid-19 infection here or the pandemic year everybody we know.

But even for next several years we will remember what is Covid, so what is RNA so not even the DNA two are in a step, so just directly for already a virus taking the positive strand RNA and making a nanoparticle as a carrier injecting the RNA directly. So that next a protein and the immune system can be active, so people are trying RNA vaccination also, so these are few things what about vaccination and vaccine production

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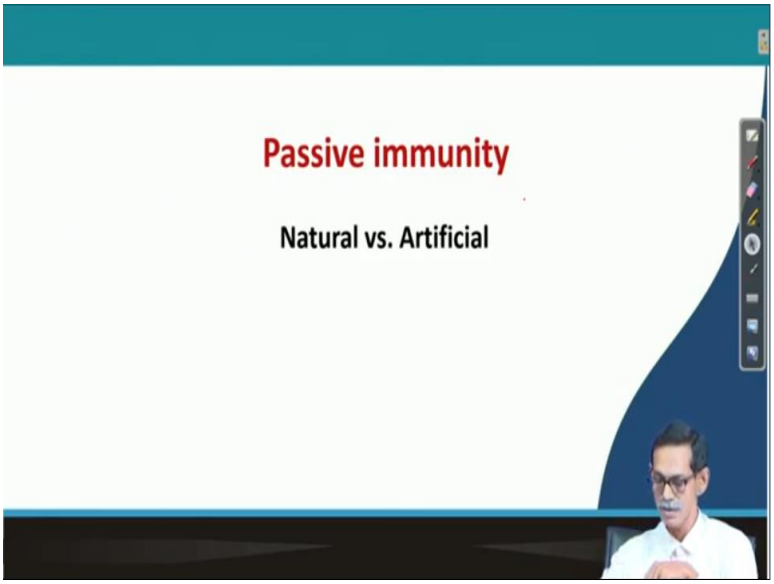

So before going to the passive immunity, I am let me talk about vaccine production. Vaccine production is what? Vaccine production is production of antigen, so if it is whole cell you have to grow the cell if it is whole attenuated what I told you so you have to do all this thing, if it is heat kill you have to grow the cell and then either heat killed or inactivated by the chemicals, if it is a recombinant protein you have to produce a recombinant protein.

But the problem here though, I told little bit in between the discussion the problem it is amount then total number of vials we need to scatter the whole world. In case of Covid 19, but in some disease what happened it is not happen every part of the country some part it is very much acute problem in some country you do not see all these disease and not all the population are affected by that.

But say polio I mean to eradicate polio from the whole world we have to vaccinate all the children and you need lot of vaccine for that. So that production you need a big industry you need a big fermenter for that to grow the cells and you need a huge system to purify the protein from that grown suppose you are producing a recombinant protein in bacteria. So you have to grow thousands of liters of bacteria.

And it is not like lab we do just centrifuge 5 ml, 10 ml bacteria in a central small change, just imagine 10000 liter you are growing not much 10,000 litre is a small scale 10000 litre medium you have grown bacteria you are sent refusing it. So everything is huge it is just not scale up is very easily. So upstream and downstream is two different. Purification is very tough precipitation of the cell is very tough when you say 200 ml, 2 liter culture is fine.

But 2000 litre, 20000 litre, 200000 litres is not that problem is there maintenance is a problem supply is a problem and administration is a problem, so we have to need a lot of trained manpower to do that. So it is just not the discovery of the vaccine we have to improve the whole system so that the vaccination is more effective and will be successful to remove or eradicate the disease in near future.

For almost all infectious disease I am definitely hoping some of you at least will study this in future do research and do something for vaccines and it is the doing something for the whole community whole world. So next what I am going to talk about this is whatever I told is the active immunity now the passive immunity. Passive immunity is what I already told passive immunity can be natural versus artificial.

Passive immunity means when antibodies raised somewhere and you are getting a ready-made antibody or T-cell to protect the disease directly natural means it is very common all of us know the passive immunity what happened when happened when the baby is in the mother’s womb what happened immune system is developing. So mother’s antibody are protecting the baby inside the mother’s womb.

Not only that I mean even the immediately after birth the immune system is completely. But they are not immunized and can protect immediately, so immediately after birth before the breast milk started there is another very thick material mothers body producing called call strap and this one contains lot of antibody at least for few days it can protect the baby. So here what is happening this antibody produced in mothers body protecting the baby.

This is also a passive immunity and the breast milk also contains some and gradually going down and slowly the amount of antibody reducing in the breast milk also, so maybe most value for six month a little amount of passive immune protection is coming from the mother that is natural immunity. And, what is artificial passive immunity? Artificial passive immunity means, say snakebite what we do we use anti-venom antibody which is already raised in other animal.

Other animals means mostly the horse why you use horse, because horse is a big animal we can isolate more blood more antibody. So normally what happened I think I told in one of the class if I remember that suppose tetanus or rabies what happened? So somebody got bite by a dog immediately we go to doctor for vaccination, but if the that dog is severely infected with the rabies virus, so that bite transmit a lot of virus.

So if you give immediately the vaccination what will happen vaccination will not work immediately it will take time but by that time the disease may progress, so what we need is vaccination, so that if anything happen the vaccination will protect but if something happen immediately vaccinations conduct protocol that is the difference between active and passive immunity.

So we need some antibody which is already made somewhere to inject into that person who got the bite to protect if there is any virus immediately transmitted to the body, so that case both vaccination like the active and passive immune protection is required. So vaccination of the rabies which is discovered long back is very effective will be injected as well as some antibody against the Rabies virus which will not cause the disease will also be injected.

In case of snake venom, there is no question of active immunity we need immediately neutralization of the venom or toxin. So we need some antibody to be injected and that antibody should be are ready, that is raised in horse and this is artificial one so this is the artificial one neutral one we discussed and artificial one also we discussed.

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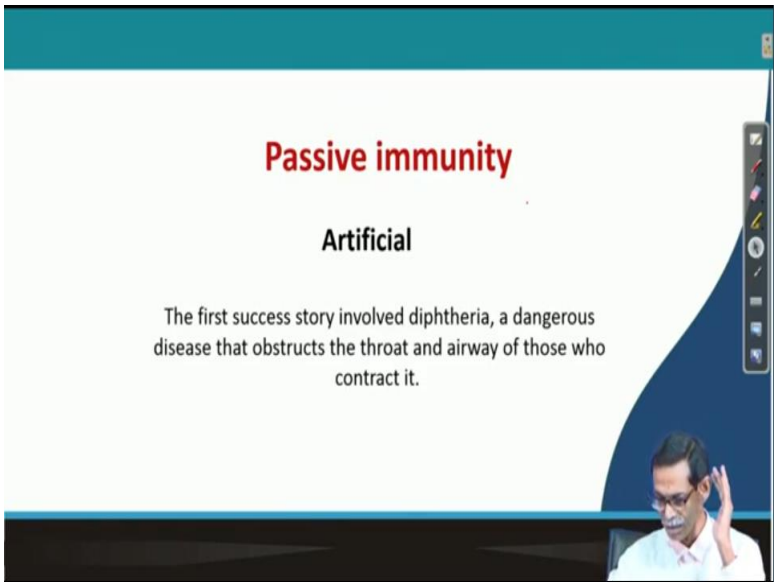

The first success story of the artificial passive immunity is the Diphtheria toxin. Diphtheria toxin dangerous disease for the kid particularly even for the elderly but normally it happened to kid that obstructs the throat and the airway, so the breathing problem and ultimately death. So what happened I mean people tried I mean the first experiment.

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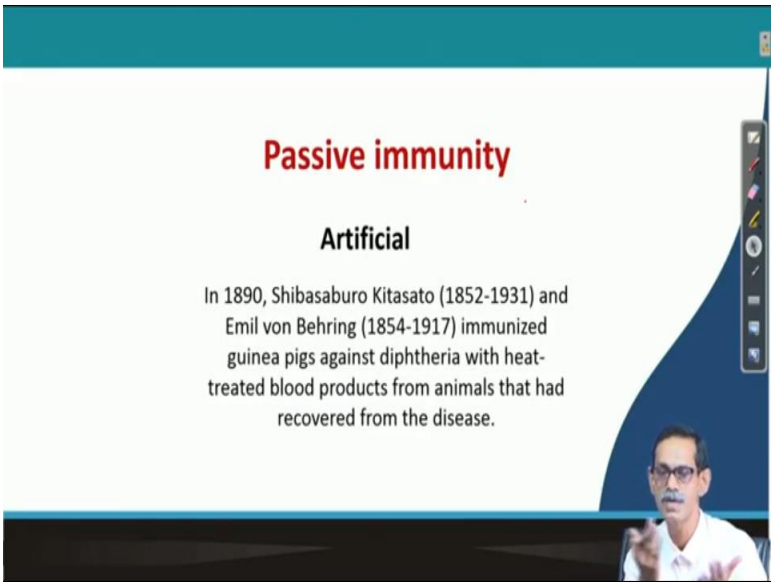

Is in the 1890 long back Shibasaburo Kitasato and Emily von Behring what they did they immunized the guinea pigs against diphtheria with heat treated blood product from animals that had recovered from the disease. So one animal which got diphtheria that blood and it was heat inactivated and injected into another animal and what they saw the protection and in fact that was the discovery of antibody.

So let me go back that was the discovery of antibody, so what happened they figured out that the blood produced something which can neutralize or which can bind with diphtheria they named as antitoxin. So that time antibody was not discovered they named us both of them received Nobel I think 1903 or some year like that and if you find the Nobel laureate history you will find many Physiology and medicine Nobel are from a immunology background.

With respect to all other branches of biology if you see the number of Nobel laureates in immunology is I never counted that way but it may be the most of them are immunologist, some will be biochemists, some will be protein chemists that way immunologist are really in good number that discoveries most of the discovery. So what happened not only they restricted this into animal that time you know the rules regulation and the act was not that strong.

So this antitoxin they figure it out they can protect the diphtheria infected individual also, so that first discovered that secondary or passive immune protection is possible and this is how it is this passive immunity discover and after that all snake venom all passive immunity and then rabbits whatever I just told this one is discovered.

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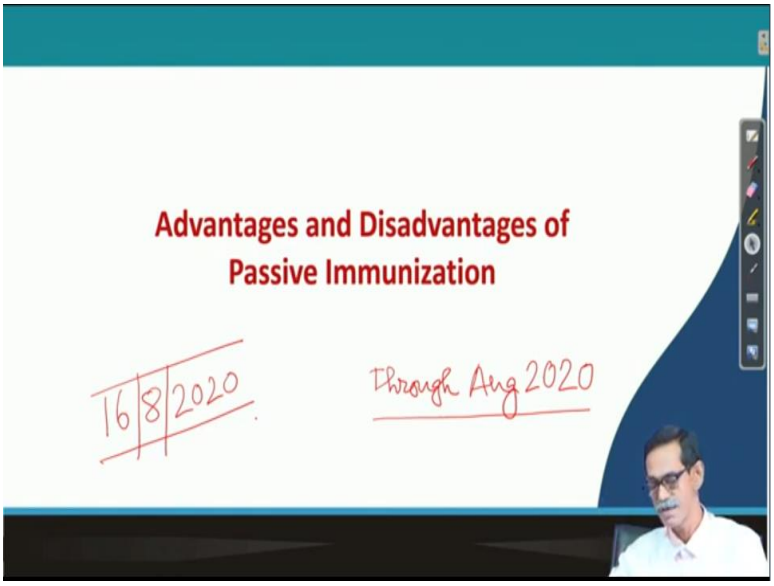

But what is the advantage of and disadvantage of passive immunization advantage definitely is there just if you consider the rabies virus infection or the dog bite, it gives immediate protection somebody got a cut go to hospital get tetanus vaccine that means if something happened, but if some patient come with tetanus infection and with the symptom that means toxin is spreaded all over the body you do not have the time for vaccination.

So you need creating the administration of the anti-tetanus serum or the antibody so that all tetanus toxin neutralized that only can save you. So that way active passive immunization is much faster and giving more quick result. So that immunization cannot do that but that there is a disadvantage what is the disadvantage normally we develop the antibody against all these toxin and other providers in other animal.

And this animal antibody may act immediately and neutralize and do its job the person may be survived but our immune system will find that horse antibody as a foreign protein. So, that I discussed one before also during idio type anti idio type. So that antibody will be treated as foreign our body will produce antibody against the horse antibody, so gradually it will be neutralized.

By that time purpose is over but what will happen that will not last for long time. So passive immunization that way is faster but we cannot avoid that there are many cases many cases and

here is also the similar problem like you have to have a lot of antigen to serve like just. For example, there are so many dog bite in country like India there is so many snake bite during the rainy season.

So just to cut those and they are not they are not going to do their job or that they are not working well throughout their life. So every passive immunization antibody also has a half life or the life or rather expiry date so after the expiry date, so normally what happened so if it is written what we do see in the medicine the expiry date, it if it is written in any vaccine or this kind thing like true this is also just for through August 2020.

So if it is written on this vial that means September 1 we are not supposed to use whether it is good or bad we should not care but if it is saying it is like fixed date 16 August 2020 if the expired it is written like this ok fixed date that means on 17th August we are not supposed to use. So this is how specific it is so main. I mean so when you are producing this any company of those who are producing this first they have to produce a lot.

Second if there is not used in time we have to throw it. So there are lot of loss in case of this kind of passive immunization material vaccine there is a demand and passive immunity the antibody produced in different company definitely there is a demand not only snakebite, scorpion bite is also not easily handleable so we have a antibody there are a lot of scorpion which is very toxic, mostly are toxic but some are very toxic that I mean that is the end result.

So in that case we need this kind of thing so what happened the passive immunization is not stopped here now people are trying how to avoid this animal to make the antibody in the laboratory, so that it will be more humanized means human will not figure it out as a foreign undeveloped antibody so that it can last long and that is actually the future trend.

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So this is the future trend and this future trend we are going to discuss in the next class and what will come many of you may know, the monoclonal antibody engineering there are many things are there. So in next lectures we are going to discuss how we can generate antibody in the lab purify it. So we do not have to have use the animal or harm the animal and that is not a really the single point that we are not the harm animal as well as that antibody will be humanized.

So that human will not figure it out or human immune system will not figure it out them as foreign. Bye, so see you in the next class.