Host-Pathogen Interaction (Immunology)
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Lecture: 54
Adaptive Immunity-Antibody Types

So, in previous session we have learned about the antibody structure and function and those structures was basically elucidated~~icitated~~ with the help of simple biochemical methods. Biochemical methods includes the electrophoresis and the purification by chromatography and then generation of antibody against specific fragments. So, today in this session we will look at various kinds of antibodies and how what are the different types as well as how they are structurally different and when they are structurally different than their function is also different.

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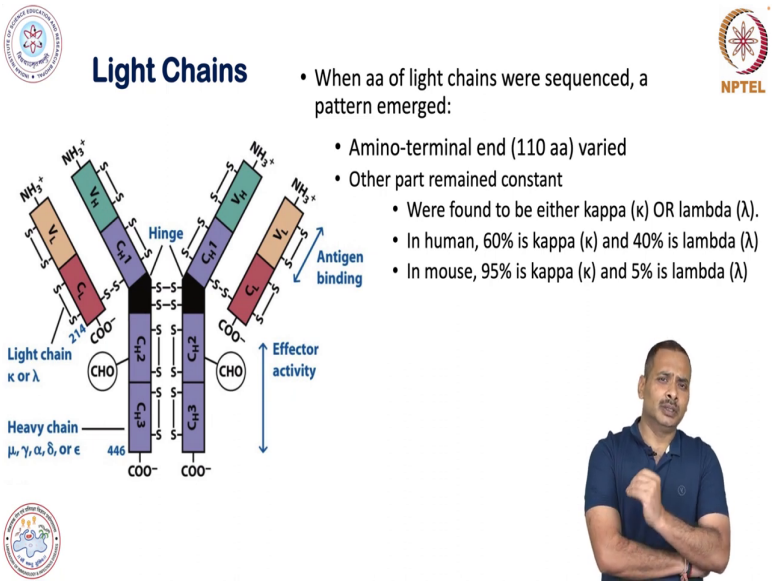

So, when this antibody structure was elucidated~~icitated~~ then there at that time the protein sequencing was also developed if you remember there is a if you studied the biochemistry you can understand there is a protein sequencing method was also there at that time. So, when amino acid of a light chain was sequenced. So, since the technology is there at that time. So, they found out some interesting thing.

First and foremost important thing is that the first Nn-terminal 110 amino acid they are having lot of variation and this variation is as now you know that this region is needed for the

binding of needed for the binding with the antigen and other part remains constant. So, this other part is remain constant means the sequence is not varying not ~~wear~~varing too much but they found out that there are two kinds of this the sequences there.

And these two kinds of sequences which is which is predominantly presented in almost all antibodies which are which were sequenced they are they are either kappa~~copper~~ type or Lambda type. So, they gave a name simple Kappa and Lambda is the name there are two kinds of sequence and these two kinds of sequence they call it as a Kappa or Lambda. So, whatever they have sequenced the constant region is either Kappa~~copper~~ type or Lambda type.

So, with this was a again emerged that this this light chain is having a highly variable region which is consists of approximately 110 amino acid and rest of about 100 amino acid they are constant approximately 100 amino acid if you see the structure the light chain is consists of 240~~9~~ amino acid. So, first 110 is variable and rest of 100 approximately 100 amino acid they are either copper type or Lambda type there are two categories of sequences.

And when these workers sequenced then they found out that in human the 60 percent of the constant region in light chain is a Kappa~~copper~~ type and 40 percent false in Lambda type and in Mouse it is about 95 percent is Kappa type and only five percent is Lambda type. So, this was a quite important information about the antibody.

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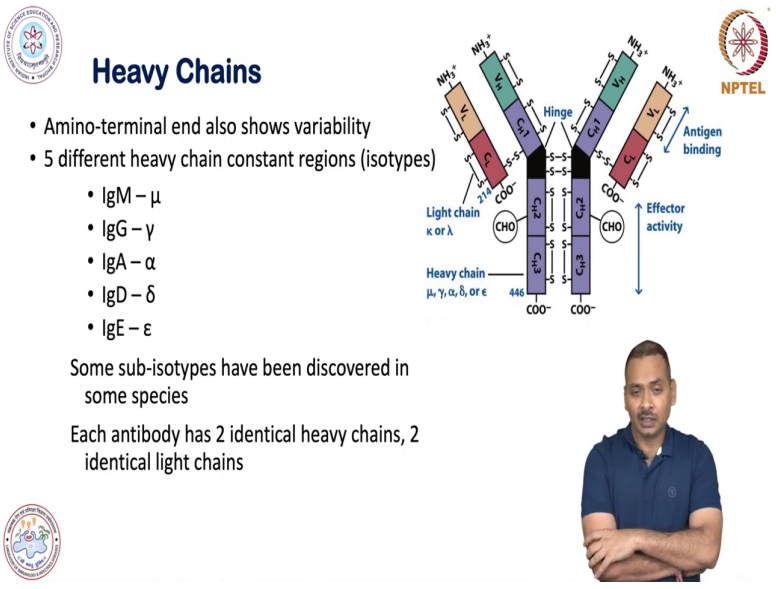

Because if you if you see that this antibody has a variable region and constant region. So, later on people wanted to address this thing based on the genetics. So, I will talk all those genetic component later on. So, the people also sequence the heavy chain which is consists of about 450 amino acid and they found out that again the N-terminal show a hyper variable variation in the amino acid which is approximately 110 amino acid.

And rest of the sequence they found out that these rest of constant region are five different types. And this five different types of heavy chain we call it as isotype or subtype of antibody and these are basically the chain which is present in these heavy chains they are mu, gamma, Alpha, Delta and Epsilon. So, they are they whatever they have sequenced they found out that most of this constant region fall either of any of these classes and that was the basis for the for the different kinds of antibody.

Some sub ISOso-type have also discovered for example you will see in this session that IgGG which is having a gamma heavy chain they have a little differences and these little differences is result to the formation of different subclasses for example IgG1 IgG2 something like that. So, we will discuss all those things in and this is not only in human this is also present in another species particularly Mouse.

Each antibodies body has a two identical heavy chain and two identical light chain that I have explained you in previous session that these antibodies are basically dimer of heterodimer. So, this dimer of heterodimer is a basically makes a complete antibody. So, now I will show you what kind of antibody could be there.

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TABLE 4-3 Chain composition of the five immunoglobulin classes in humans

Class*	Heavy chain	Subclasses	Light chain	Molecular formula
IgG	γ	γ1, γ2, γ3, γ4	κ or λ	$\gamma_2\kappa_2$ $\gamma_2\lambda_2$
IgM	μ	None	κ or λ	$(\mu_2\kappa_2)_n$ $(\mu_2\lambda_2)_n$ n = 1 or 5
IgA	α	α1, α2	κ or λ	$(\alpha_2\kappa_2)_n$ $(\alpha_2\lambda_2)_n$ n = 1, 2, 3, or 4
IgE	ε	None	κ or λ	$\epsilon_2\kappa_2$ $\epsilon_2\lambda_2$
IgD	δ	None	κ or λ	$\delta_2\kappa_2$ $\delta_2\lambda_2$

*See Figure 4-1 for general structures of five antibody classes.

There is a some kind of formula molecular formula for each antibody. Here you can see that in extreme left ~~corn~~ column there is a classes that is IgG IgM IgA IgE and IgD they have a different heavy chain like a gamma, mu, Alpha Epsilon and Delta. And there are in some cases there are some subclasses also. For example in case of IgG there are four subclasses like Gamma 1 gamma 2 gamma 3 gamma 4.

In case of IgA also there are alpha 1 Alpha two subclasses and this heavy chain can either interact with a Kappa chain or it can interact with Lambda chain. So, here you can see that in all classes of antibody it is either Kappa or Lambda. So, so then the ~~model~~ molecular formula could be here you can see that gamma 2 Kappa means there are two the heavy chain is two gamma heavy chain and two Kappa chain it is one possibility.

Another possibility is two gamma chain along with two Lambda chains. So, this is kind of a molecular formula and here you can you can also write in case of Ig~~G~~G it could be Gamma 1 2 Gamma 1 2 means there are the subtype will be Gamma 1 and it can combine with either Kappa or it can combine Lambda. So, then it will be a gamma 1 2 Kappa 2 or Gamma 1 2 Lambda 2. So, like that I am just trying to make you understand that this is not.

So, complicated if you if you see carefully and logically then you can understand quickly here you can see that IgM. They are basically present either in monomeric form or in pant~~a~~emeric form. Here you can see that in bracket there is a n and n could be one or five in case of IgA this can make a monomer or this can make a dimer timer or tetramer and rest other antibodies they don't make a multimeric form.

So, these are these are the information which is very important for for for understanding these antibody molecule. So, you with if you look at this formula you can understand that there are how many subtypes whether it is present in monomeric form or multi-meric form all those things.

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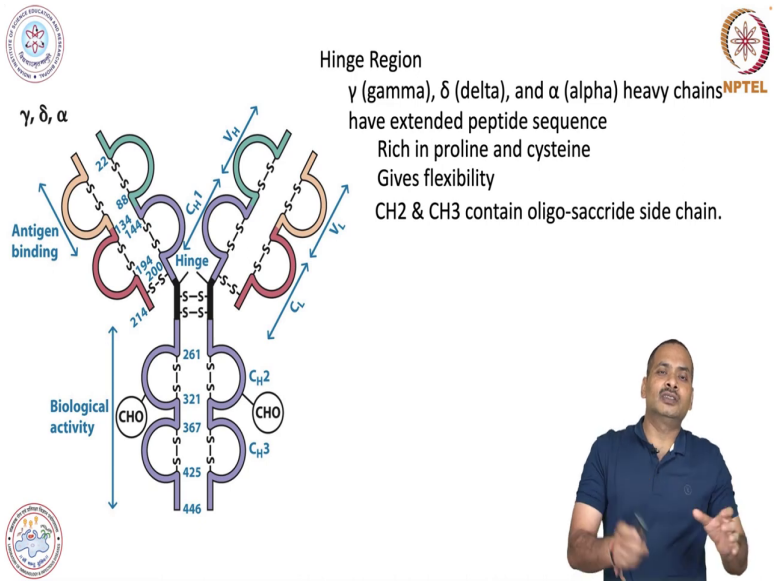

Now I will talk about individual immunoglobulin I will put it in one group here you can see that there is a IgGG and IgG Delta and IG and. So, IG G is basically encoded by gamma chain. So, IgG IgD and IgA which is encoded by Gamma, Delta and Alpha respectively. So, all these three classes of antibody they have some unique region in constant region in heavy chain they have a hinge region it is a hinge region.

And this hinge region is present in heavy chain and so, hinge region is nothing it is a basically having an extended amino acid there are more amino acid and they have some characteristic amino acid which I will show you. So, they this hinge region is basically rich in Proline and cysteine since it is rich in Proline and cysteine. So, this has a more flexibility and this can also make a more disulfide linkages.

So, you remember that in case of IgG IgG Delta and Ig Alpha this hinge region is present and this hinge region is nothing it is a more amino acid which is consists of predominantly consists of Proline and cysteinecystidine and this gives the flexibility to the molecule in in these classes of antibody or in these isotypes of antibody there is a CH2 and CH3 region and

this CH2 and CH3 region is quite heavily glycosylated there is a lot of oligosaccharide side chains.

And it is considered that this side chain basically play an important role in keeping these antibody in soluble form. So, this sugar basically these sugars are kind of hydrophilic and this keeps the molecule in soluble form.

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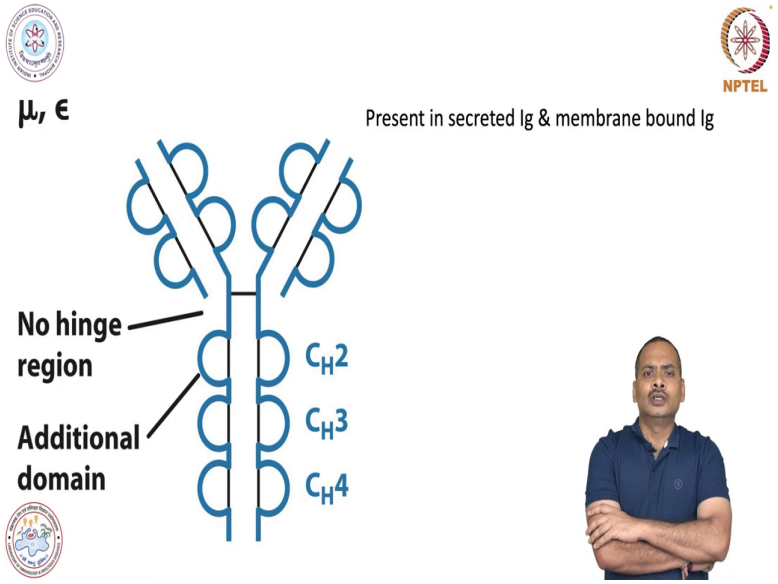

Another is Igm and IgE which is encoded by the heavy chain is encoded by mu and Epsilon chain they are present in a secreted immunoglobulin and it is generally present in a membrane-bound immunoglobulin. So, here you can see that there is a no hinge reason and but this has a additional immunoglobulin super family domain in in previous case you have seen that there is a only CH2 and CH3 is there. But in this case you can see that there is a CH2 CH3 and CH4 and there is no hinge region.

So, this is a basically present in secreted immunoglobulin and membrane-bound immunoglobulin this kind of structure.

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- Immunoglobulins can be secreted or membrane-bound
  - Membrane-bound differ in the carboxyl-terminal end:
    - Extracellular "spacer" of 26 aa
    - Hydrophobic transmembrane sequence
    - Cytoplasmic tail


So, immunoglobulin can be can be secreted you know that immunoglobulin is secreted by plasma cell or it may be membrane bound membrane bound immunoglobulin is present in B cells. So, if it is a membrane bound then the C terminal is part of the constant region of heavy chain will have some additional thing that that here you can see that this C terminal end will have a extra cellular spacer which is consists of 26 amino acid it is mainly hydrophobic in nature.

So, most of amino acid the 26 amino acid there will be hydrophobic and it is quite obvious because this is a transmembrane sequence. And there will be a cytoplasmic tail which will trigger the downstream signal. Although this tail is very small and this is not capable to activate the downstream signalling that is why this is bound with some another molecule which we which we call it as a immunoglobulin alpha beta chain which is not which is required for Downstream signalling the bottom line is that.

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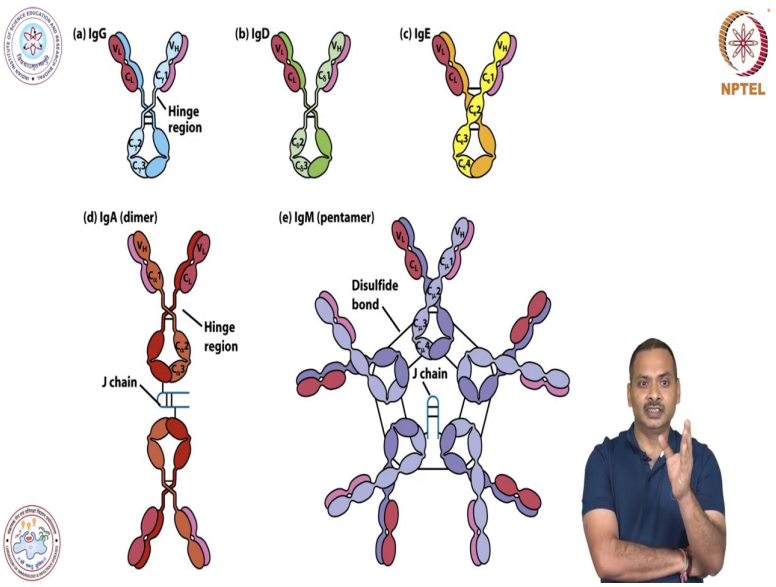

Here this is the structure of various immunoglobulin here you can see that there is a hinge region in case of IgG and IgD and IgA. So, this has a hinge region and here you can see the structure is quite different all immunoglobulins are quite different here you can see that in case of IgG there are C gamma 2 and C gamma 3 region is there and there is a predominant quite big hinge region in case of IgG and here you can see that IgGA they are present in dimeric form and there is a some region is there which we call it as aA J chain which basically combines these two subunits.

And here you can see that IgM it is present in pentameric form. And this each subunit each subunit in this pentameric antibody is joined by J chain.

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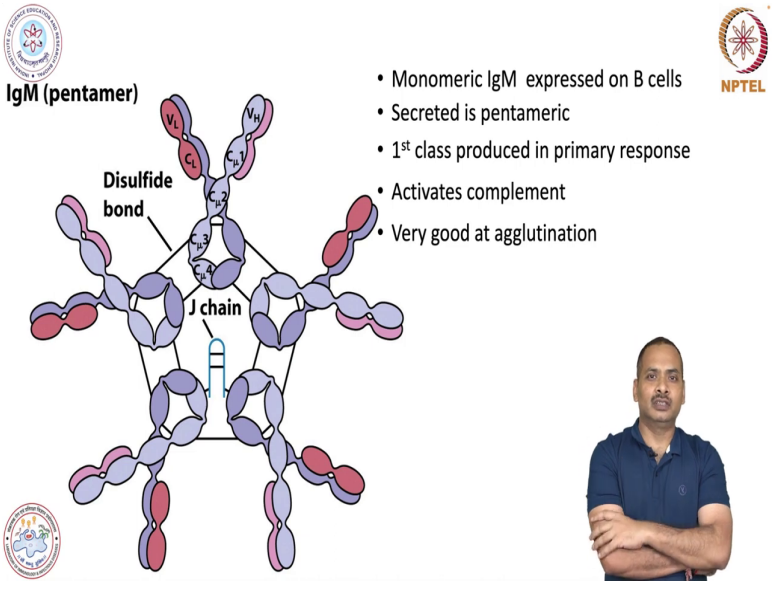

So, now I will talk little more about the particular subtype. So, IgM is basically present in pentaomeric form it is also present in monomeric form IgM is also present in monomeric form and expressed on the B cells. So, the first antibody which is generated in against the antigen is IgM and on mature b cells IgM is present in monomeric form. But when it is secreted then it is secreted in pentaomeric form this is a first class produced in primary immune response or primary response.

So, that I have already told you it can activate complements I have explained you this has a more potential to activate the complement compared to the other antibodies that is IgG this has a very good agglutinationanglutination property this IgGM agglutinationanglutination is just something like it will cross link several molecules and make a kind of Clump or agglutinin anglutinine and this constitute about five to ten percent of total serum immunoglobulin.

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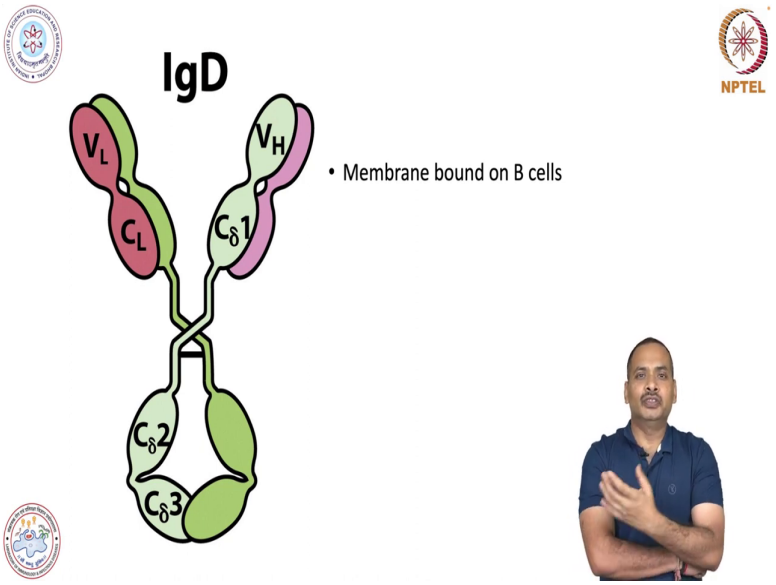

Another is IgD, IgD is basically present in bound form on B cells and this is the one antibody whose function is not very well understood. This is present during the development IgD is present during over the B cell during development or maturation of B cells we do not know what is the exact function of IgD.

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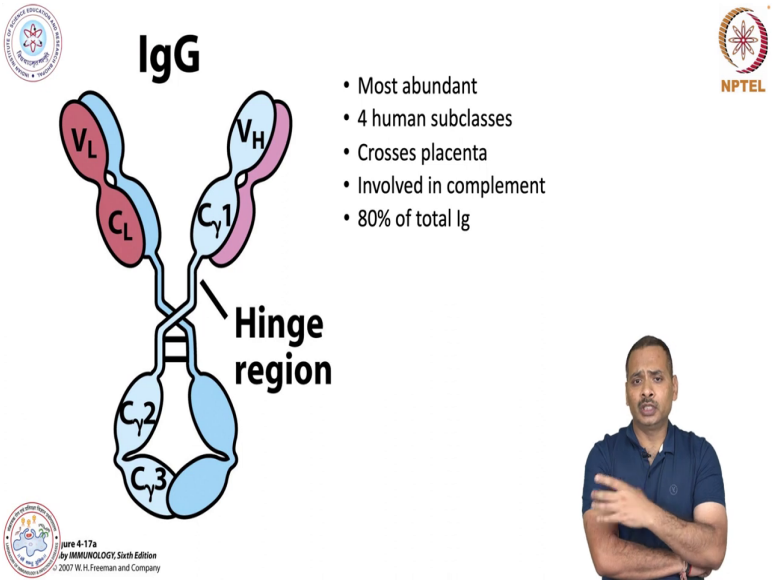

Another is IgG here you can see that there is a very big hinge region and it is a most abundant immunoglobulin and there are four subclasses of this IgG. If you remember the previous table where this molecular formula was given over there you have seen that there is a gamma 1 gamma 2 gamma 3 gamma 4 heavy chains are there. So, therefore IgG is of fouree subtype and you can call it as IgG one IgG 2 IgG 3 IgG 4.

These immunoglobulin can cross the placenta and give the protection to the fetus as well. They are involved in complement activation but not all I will show you in a short while which one is involved in activation of complement particularly IgG4 is not involved I will I will show you in a short while. And it constitutes about 80 percent of total immunoglobulin in serum.

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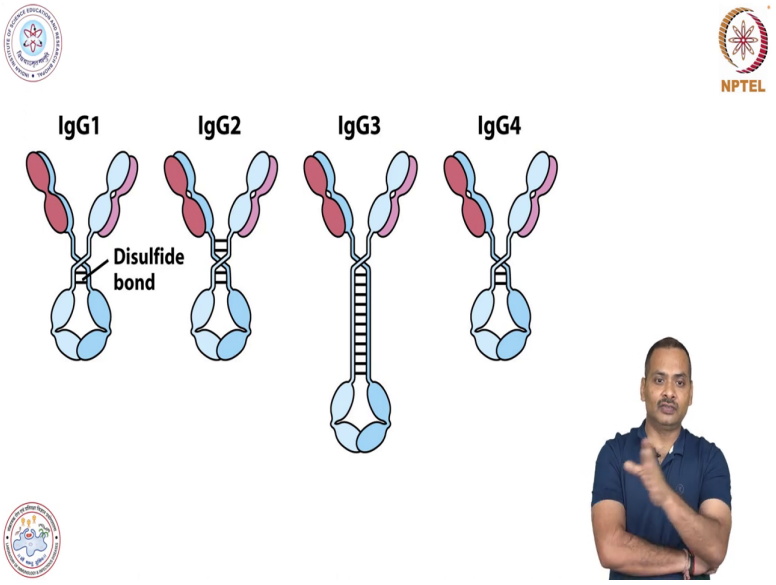

Here this is the structure here you can see that the hinge region is quite variable in different subclasses. So, IgG 3 has a quite huge hinge region and lot of disulfide linkages are there this you can understand.

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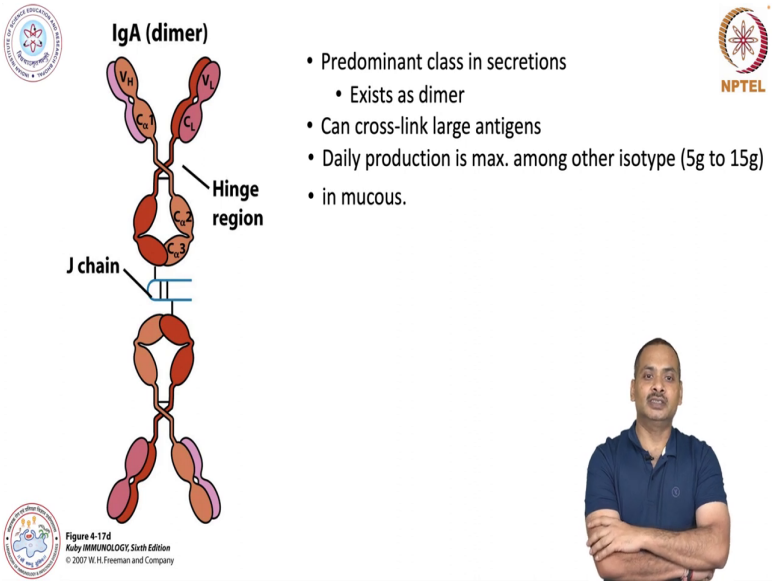

Another is a IgA which is in general present in dimeric form it is also present in a trimeric or tetrameric form. And this can this can cross link large antigen and this IgA is predominantly present in secretions various secretion in our body and they give a protection over there. And daily production is quite high among other IsoSO type every day about 5 gram to 15 gram is produced this IgA in mucous.

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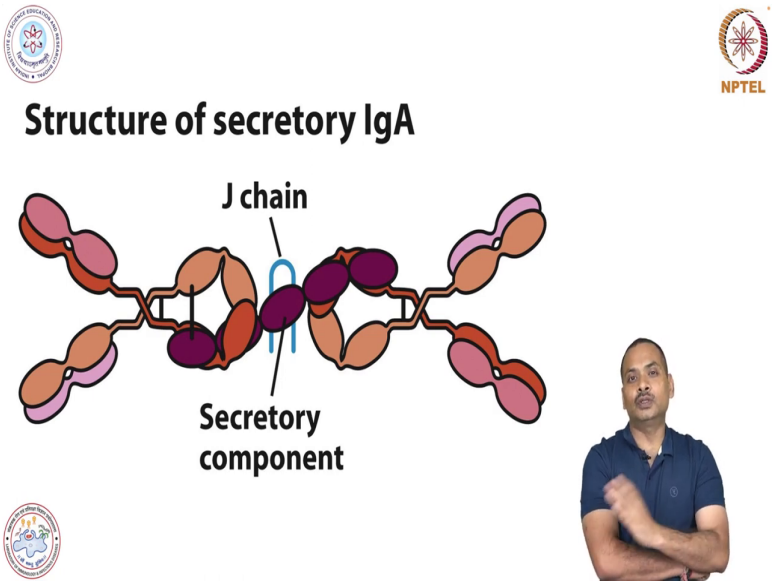

So, this is a structure of IgA this has a secretory component or J chain and this is very important for the transportation. So, IgA undergo transcytosis this is transported across the membrane.

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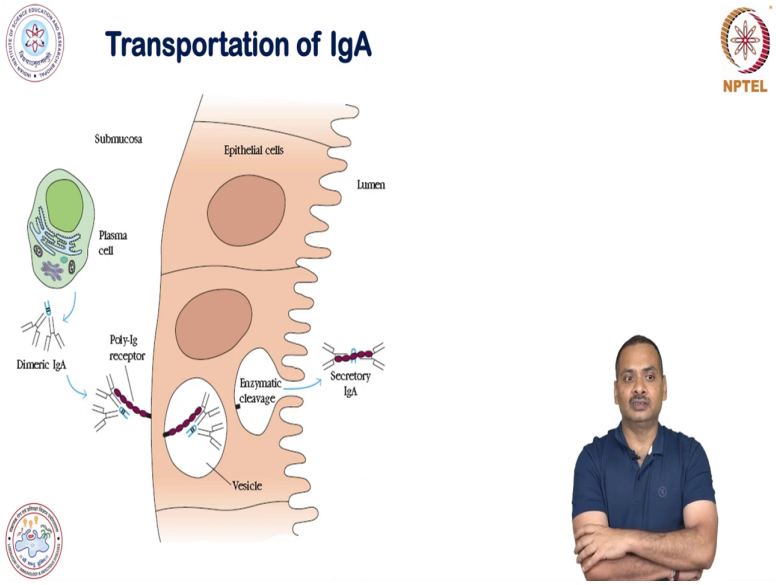

Here you can see this how the transportation of IgA is taking place. There is a poly immunoglobulin receptor which is binding with this dimeric form of IgA and then there will be a transcytosis and then it is transported across the cell layer.

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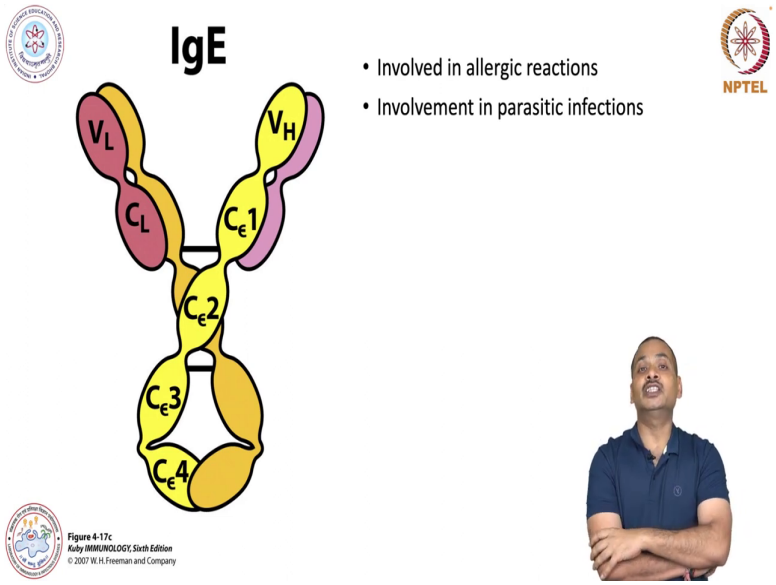

Last is IgE. So, IgE is basically involved in various kind of allergic reaction it is involved when a parasitic infection. Basically this is increased during the parasite infection and then at that times they there is a increase in eosinophils also and that condition we call it as an eosinophilia. This eosinophilia is a kind of marker for allergy or parasite infection.

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Property/Activity	IgG1	IgG2	IgG3	IgG4	IgA1	IgA2	IgM*	IgE	IgD
Molecular weight†	150,000	150,000	150,000	150,000	150,000–600,000	150,000–600,000	900,000	190,000	150,000
Heavy-chain component	γ1	γ2	γ3	γ4	α1	α2	μ	ε	δ
Normal serum level (mg/ml)	9	3	1	0.5	3.0	0.5	1.5	0.0003	0.03
In vivo serum half life (days)	23	23	8	23	6	6	5	2.5	3
Activates classical complement pathway	+	+/−	++	−	−	−	+++	−	−
Crosses placenta	+	+/−	+	+	−	−	−	−	−
Present on membrane of mature B cells	−	−	−	−	−	−	+	−	+
Binds to Fc receptors of phagocytes	++	+/−	++	+	−	−	?	−	−
Mucosal transport	−	−	−	−	++	++	+	−	
Induces mast-cell degranulation	−	−	−	−	−	−	−	+	

Now I will give you the kind of summary of all immunoglobulin here you can see that on top there is a molecular weight which you can see and I need not to tell. Here you can see that there is a different kinds of heavy chain in in different immunoglobulin there is a gamma 1 gamma 2 3 4 is there alpha 1 Alpha 2 is there mu is an Epsilon and Delta is there. And there is a normal serum level is also given and here you can see that IgG1 is present in quite high amount it is about nine milligram per ml.

And in Vivo serum half-Life so, all immunoglobulin they have some half-Life and if you see very carefully the class of IgG the subclasses of IgG they have a highest half-life in the serum that is IgG1 IgG2 and IgG4 they are present about 23 days the half-life is about 23 days. Which immunoglobulin can activate complement pathway. Here you can see that this IgG1 IgG2 and IgG3 they can activate complement but not IgG 4 and the very good complement activator is IgM.

IgG1 and IgG2 can also cross the placenta and they can give the protection to the fetus in addition IgG 3 and 4 also can also move across the placenta. So, which immunoglobulin is present on mature cell that is IgM. So, only IgM is present on mature cell. So, initially there will be IgM and which is present on mature B cell IgM plus IgD both are present and later on this there will be one phenomena which we call it as a class switching which I will discuss in subsequent session.

So, this class switching changes the type of antibody some of these are particularly IgG they can bind with a FC receptor of phagocytes and mucosal transportation is mainly taken take place for IgA. Here you can see that there are different the both subtype of IgA can be transported in mucosal area in addition IgM is also can be also transported to some extent and I gE is a only which can activate the masst cell degranulation.

You know that not only masst cell eosinophil can be also degranulated. So, this is the overall summary of all different types of antibody their structure as well as function. With this I am stopping here in next session we will look at the antibody diversity how the antibody diversity is generated. And another very important thing which we will learn is that how the one type of antibody is switches from one type to another type.

So, we will discuss all those things although I will just touch upon all these topics but I am not going to take you in a much more finer molecular detail it is a huge topic it will take a quite long time to finish. So, aim of this course is not that, thank you.