



Host-Pathogen Interaction (Immunology)
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Lecture: 9
Immune organs - 1


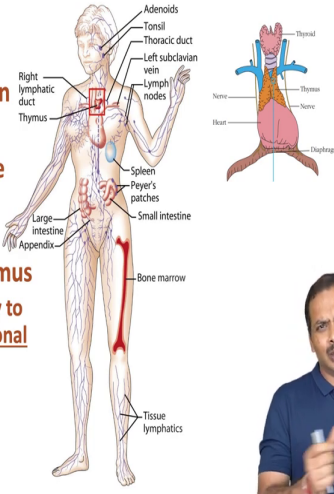
In previous session I have introduced about immune organ and I have explained there are two major classes of immune organ that is primary and secondary lymphoid organ. The primary lymphoid organ basically the site for generation of immunocompetent lymphocytes it could be B cells it could be T cells. And another set of organ we call it as a secondary lymphoid organ.

And these secondary lymphoid organs are basically playing a very important role in interaction between immunocompetent lymphocyte and antigen and over there is a appropriate environment. So, these secondary lymphoid organs are very important. So, now I will take you to various immune organ and first we will take it take the thymus.

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 **Thymus (Primary)** 

- **Anterior, superior, mediastinum, Bilobed Organ on Top of Heart**
- **Pinkish-gray color soft tissue**
- **30g infants, 3g in adults**
- **95-99% of T Cells Die in Thymus**
 - **Self reactivity or no reactivity to Antigen (Ag) by process of clonal selection or clonal deletion.**



So, as you know this is a primary lymphoid organ and this is a key sight for the development of T cells and we call it as a thymocyte. So, basically this thymus is you can see in this slide that the thymus is basically present over the heart and it is basically having a it is present over the heart and there are several organs as you can see in this in this Slide the over the diaphragm there is a heart and over the herd there will be a thymus.

And this the precise anatomical location is that it is anterior Superior. Superior means above mid sternum by lobe the organ on the top of heart. Basically this thymus is a pinkish gray colour soft tissue. And if you want to visualize this this organ in mice then you need to open the very young mice I will tell you in a short while that this thymus is an unique organ which is bigger in size in early ages.

And this starts degenerated as the animal or human age. So, this is a kind of unique property it is not growing it is a other way around it is a it is basically reducing in the size. So, this is basically in human it in infant it is about 30 gram weight of this organ is 30 gram and at the age of 35 its weight reduces to about 24 grams and at the age of 65 its weight only 2 gram of this thymus tissue remains.

Of course there will be a lot of fatty tissues present in that organ but the active organ will be only 2 grams. So, you can you can understand this thymus is having an unique property. So, with age it is reducing the size. And this is a place where T cells are generated and it is a very interesting to know that most of T cells which is generated in or educated in the thymus most of these cells are basically undergo apoptosis programmed cell death or they die.

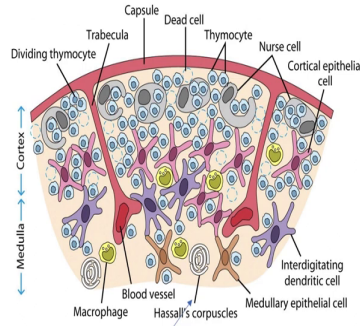
And why they die because there is a very strict selection process in the thymus in order to become immunocompetent T cells immunocompetent naive T cells and basically this phenomena we call it as a clonal selection or clonal deletion. So, this is a process by which the T cells finally selective for the generation of immunocompetent naive T cells. And I will take these phenomena this clonal selection and clonal deletion later on when we will probably study the T cells.

So, at the moment just you can understand that this clonal selection and clonal deletion is a there is a lot of cellular and molecular changes taking place in the cell and all those cells which is reacting with our own antigen they are basically eliminated they are deleted or they undergo the apoptosis and all those cells which is not reacting with our own cells they are selected. So, this is in a brief this is a this is the meaning about the clonal selection and clonal deletion.

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Cross-section of Thymus



Eosinophilic type VI reticular cells produce cytokine TSLP (Thymic Stromal lymphopoietin)

**Thymectomy- dramatic decrease of T cells
In human DiGeorge's Syndrome**



- Consists of Cortex (immature T cells & densely packed) and Medulla (not densely packed).
- DCs, Macrophages & epithelial cells (important for growth & development of developing thymocytes)



Now let us look at the cross section of this thymus how the thymus looks like basically it has a two major region one is a cortex region generally this cortex region is the outer region of the organ. And there is a medulla region which is inner side of the organ and here you can see that there are dividing thymocytes. And this cortex region is basically quite densely packed with immature T cells.

And here you can see that there is a lot of dividing thymocytes and there is a structure known as trabecula this is a kind of partition. So, there will be a subsection in the organ. So, this trabecula is basically a separating the various section in thymus and there is a capsule it is a kind of covering over the over the thymus and there are here you can see that there are dead cells. So, all those cells which is auto reactive they are they are programmed to die they are basically dead cell.

And there are some cells which is alive and they are probably become a immunocompetent naive T cells. And in addition to this there is a nurse cell which basically provides the factors which is needed for the growth of these cells. And there is a cortical epithelial cell which is again providing some or other factor in order to grow these thymocytes and there are interdigitating this dendritic cells.

So, all basically all these cells plays a very important role in development of these immunocompetent naive T cells and there is one structure which we call it as a Hassall's corpuscle. So, basically this provides basically eosinophilic type IV a reticular cell. This basically provide a cytokine molecule which we call it as a TSLP it is a thymic stromal

lymphopoietin and it is needed for the development of these cells this thymocytes developing thymocytes.

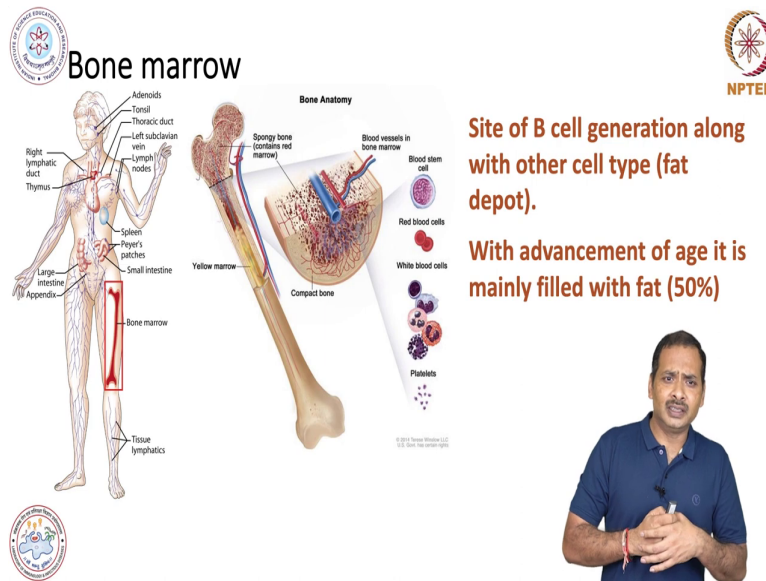
And here you can see that there are macrophages dendritic cells as I explained you previously. So, all these cells basically support the development of T cells or thymocyte or developing thymocytes and it is a very interesting. If, There are several cases in which this thymus is not present in the baby and those individuals or if we do the experiment if we remove the thymus in early stage in the mice then there will be a severe reduction of T cells in that particular animal.

And those animals are kind of quite immunocompromised they are susceptible to many infection and generally they cannot make a long life. So, you can understand this thymus is very important in early stage of life and there are some in human there are some cases in which the thymus is absent this is due to some congenital issues or some developmental issue or it may be associated with genetic.

So, those individual they cannot they cannot or they cannot survive very long and at early stage they will have a recurrent fever and a lot of recurrent infection and those patients we call it as a DiGeorge's syndrome. So, this you can understand the importance of thymus. And here I just I want to mention that at early stage you may have this question that this thymus is reducing with the age.

So, our immune system; how our immune system work at a later stage? So, here I would like to say that these these these these functions are taken over by the lot of mucosal Associated lymphoid tissue and we will discuss later maybe in this session or next session about the mucosal mucosal Associated lymphoid tissue.

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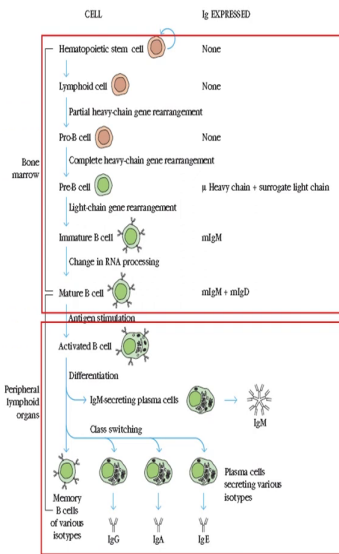
So, now another primary lymphoid organ is bone marrow. So, bone marrow is a very important place for the generation of almost all cells which is present in the blood. Here you can see there is a bone marrow and this bone marrow is basically the cavity which is present in long bones. So, over there this there is a one specialized cell which we call it as a hematopoietic stem cell.

So, this hematopoietic stem cell differentiates into variety of blood cells as well as they are differentiated into the immune cells. In bone marrow the most important cells which are generated are the B cells. Of course, besides other blood cells like platelets and another white blood cell we will discuss all those immune cell such as neutrophil, basophil, eosinophil all these cells are generated from this common progenitor which we call it as a hematopoietic stem cell.

So, then they differentiate into various lineages and then they make various kind of immune cells. Bone marrow is a key site for the development of or generation of the B cells this is a site for generation of B cells besides other cells and this bone marrow also kind of age with aging means the most of this the bone marrow cavity is filled with a fat cell as the individual age and probably due to that there is a there is a decline of immunity in those individual.

So, with the with the advancement of age most of this bone marrow cavity is filled with the fat cells which is about 50 percent.

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And and this is a site for B cell and how B cells here you can see that there are different stages of development of B cell here I am just showing a snapshot I am not going to take this thing in more detail I will discuss when I will take up the B cell development. But just for your information I want to show that in bone marrow this B cells are started developing from hematopoietic stem cell and when the B cell exit from bone marrow they are mature immunocompetent B cells.

And then they will move to the peripheral lymphoid organ and mainly explain or some lymph node and over there they will interact with antigen and then they will become a means and they will generate the antigenous specific antibodies after differentiation to the plasma cell. So, it will take up all those things in great detail when we will take the antibodies or B cell development.

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Bone marrow



- It is not a site of B cell maturation in all species
- e.g.
 - In birds-Bursa of Fabricius (an outpouching of the intestine, the bursa, which is located close to the cloaca)
 - In cattle and sheep –Fetal spleen, Peyer's patch
 - Rabbit-appendix



So, bone marrow is a site for the development or key site for the development of B cells but it is not true for other animals. For example, in Birds this is a there is a specialized organ which we call it as a bursa of fabricious this is an out an outpost pouching of this in intestine over there this B cells are developing. So, basically this is common in the birds I will show you. In cattle's and sheep the spleen is the key site for the development of B cells and Peyer's spire patches are also the site for the development of B cells.

In human also later on in later stage when this bone marrow is not so, functional or not. So, active at that time this mucosal associated lymphoid organ are basically making the B cells. And in mucosa associated lymphoid tissues the Peyer's spire patch comes. In rabbit the this is a the appendix, appendix is a site for the B cell development or generation of a B cells.

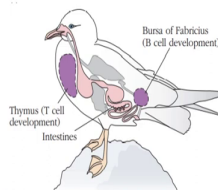
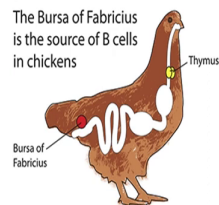
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Bursa of Fabricius

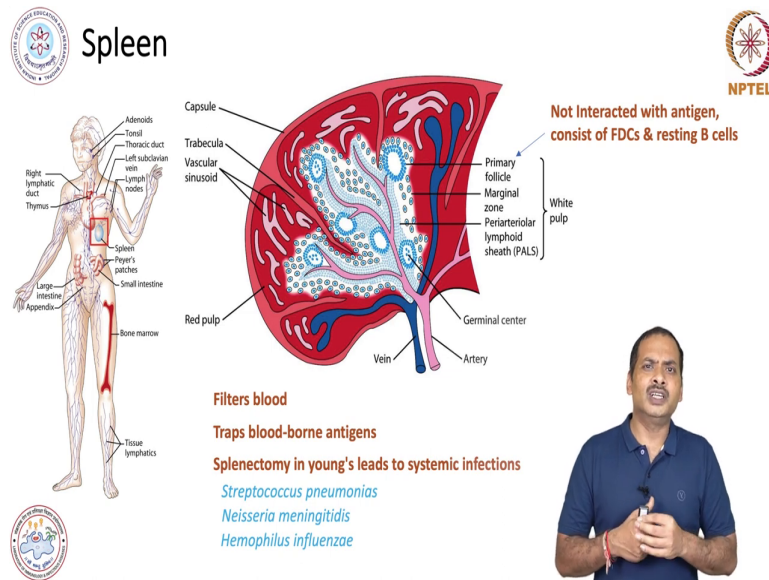


The Bursa of Fabricius is the source of B cells in chickens



Here this is a organ which is I was talking in Birds here you can see that this is a basically towards end and this is a this is this is taken out from the from the bird basically the hen. And here you can see in this bird also this organ this bursa of fabricious is there and this is the site for B cell development in avian mainly avian Birds.

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Next organ is the spleen which is a secondary lymphoid organ if you remember the primary lymphoid organ is thymus and bone marrow and secondary lymphoid organ or peripheral lymphoid organ is spleen and lymph node and mucosal associated lymphoid tissue. So, now we will discuss about the spleen. So, this is a location of a spleen here you can see the spleen is located in our body.

And this spleen has a this is a cross section of a spleen and here you can see there are two major regions one we call it as a red pulp you can see in this slide that red area is we call it as a red pulp and there is a white area and we call it as a white pulp. So, red area is not. So, important in point of immunity the white area is most important for the immunity. Here you can see various structure and there is a capsule which covers this this organ it is a kind of membranous kind of thing and consists of epithelial cell.

And there is a trabecula which is just again making a partition in the in this spleen and there is a vascular sinusoid. So, vascular sinusoid it is a kind of open structure there is an over there blood is there but it is a there is no blood vessel. So, blood is flowing in a space. We call it as a vascular sinusoid and all this area we call it as a red pulp. And when you look at the white region there is a primary follicle I will explain you what is primary follicle.

And there is a marginal zone and there is a structure which we call it as a peri-arteriolar lymphoid sheath. So, this is this constitute the white pulp and what is this primary follicle. So, here I will just give you the concept of primary follicle, secondary follicle or germinal center. So, primary follicle is the region in which this antigen is present which is not yet reacted with the immunocompetent lymphocytes.

So, over there a basically, immunocompetent naive lymphocytes are there. Another is there is a FDC, FDC stands for follicular dendritic cells and there is a resting B cells. Resting B cells or you can also understand is as a immuno competent naive B cells or resting cells they are same thing. So, this primary follicle is ~~consist~~consisting of ~~these component~~these components and there is a another term which we call it as a secondary follicle.

Secondary follicle is over there will be a lot of interaction between FDC's antigen presenting cells dendritic cells all are very active. They will be actively secreting the plasma making or differentiating B cells are differentiating to the plasma cell. So, all those very active area we call it as a secondary follicle or germinal center. So, when the antigen will be will come initially it will interact and there will be a no activity and then we call it as a primary follicle.

And later on when there is a lot of immune reaction is taking place and then there will be a differentiation of this naive B cell into the this naive B cell will differentiate into the plasma cells and that will actively secrete the antibody molecule. So, those centers we call it as a germinal center. In experiment we basically when we challenge the animal with some antigen then we will we look for this germinal center which is very active by immuno histology.

So, this is the structure of the primary follicle and probably you may understood about this germinal center or secondary follicle. So, this is a structure of a spleen and there is a here you can see there is a vein, artery and germinal center. So, germinal center here you can see it is a much more compact and very active. So, what is the function of a spleen. So, the most important function of a spleen which you have studied probably in earlier classes.

This is a place where the quality control of blood cells are taking place particularly RBC's and we also call it as a graveyard of RBC's. So, whatever RBC's which is old, aged, damaged everything will be will be removed by ~~spleen~~this ~~plane~~ basically all blood will filter or pass

through this organ and whatever the damage RBC's are there they will be removed. So, this is a one of very important function.

So, due to this function the spleen is a place where all blood borne antigens are coming and there will be a development of immune response. Blood borne means so, antigen can go by various ways. One way is that the antigen is transported in our blood in blood vessel then this antigen will go into this spleen and over there this antigen will be trapped and then there will be a development of appropriate immune response.

Appropriate immune response means there will be a development of B cell mediated immune response T cell mediated immune response. So, the immunity point of view this is a one of important function and if non-immune function is the removal of damage RBC's and it will be removed and then the blood will be again returned to the system. So, I already explained this trap the blood borne antigen just now.

And if we remove the spleen from Young individual then that can cause a severe problem it will cause a systemic infection and the among systemic infection these in some bacterial infection is very common such as a Streptococcus pneumonias. So, this basically a very invasive bacteria and that can cause various wide range of symptoms it can affect the central nervous system.

Another is a Neisseria meningitis this infection basically infection of this bacteria result to the some neurological problem it basically affects the central nervous system and meninges. So, meninges probably you may remember that this is a covering over the brain and spinal cord. So, this can these bacteria can infect those key organ and that that is quite fatal if it is not treated then the individual may die very quickly.

And another is Hemophilus influenzae. So, Hemophilus influenzae it is not an influenza it is a different from influenza. So, they do share some symptom of influenza that is why this name is there but influenza is basically caused by virus, influenza virus. It is a Orthomyxoviridae orthomixic-family virus and we will discuss when we will take up the viruses. So, all these infection we can easily treat by a simple antibiotic but it is very important to note this infection and immediately a treat or we can treat with a wide range of antibiotics.

So, with that with this I will stop here and in next session I will talk about other lymphoid organ such as mucosal associated lymphoid organ or lymphoid tissue I will talk about the lymph node. And then finally I will talk about the lymphatic system which is basically integrating all this system thank you thank you very much.