Hematology

HISTOLOGY

☑ Sheet ☐ Slide ☐ Handout

Number: 5

Subject: Lymph Nodes & The Thymus

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Price:

بسم الله الرحمن الرحيم

This sheet was written according to section 2 recording.

In the previous lecture we talked about Antigen Presenting cells (APC) which are:

1. Macrophages
2. Dendritic cells “Langerhans, Follicular, Interdigitating”
3. B- Cells

We said in order for an immune reaction to occur an APC should present the antigen to T- or B-lymphocyte, these cells **Process** the antigen and by processing we mean that the cell phagocytose and digest the antigen then attach what’s left of it to a protein called MHC which is of two types 1 & 2.

Now we begin with this lecture, we will continue talking about APC then we will talk about the **Lymph Nodes & The Thymus** and a little bit about the **Spleen**

- Normally these antigen presenting cells phagocytose the antigen first then present it on its surface, but anyhow Dr. Faraj said that some books say that the **Dendritic** cells can present antigens without “phagocytosing” them, so we should consider this difference between

*Also the doctor mentioned another valuable information that the **Follicular Dendritic Cell** and the **Macrophage** can present the antigen to B- lymphocyte without attaching it to an MHC protein (an exception to the rule)

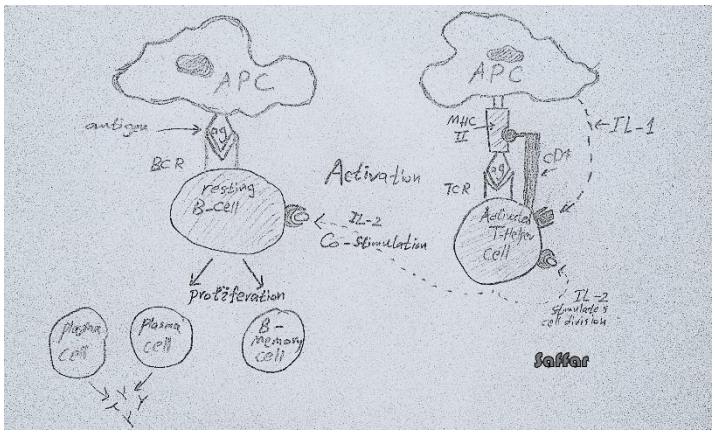
We said before that we have two types of Immune reactions in our body:

1- **Antibody** (Humoral) mediated by B-lymphocytes

2- **Cell mediated** by cytotoxic T-lymphocytes

Let's take an example of antibody mediated immune reaction:

- A bacteria entered the body, then a macrophage "phagocytosed" it and presented the antigen to a resting B-lymphocyte "without attaching it to a MHC protein", *it's called resting (or naïve, virgin) B-lymphocyte because it haven't been exposed to an antigen yet*.



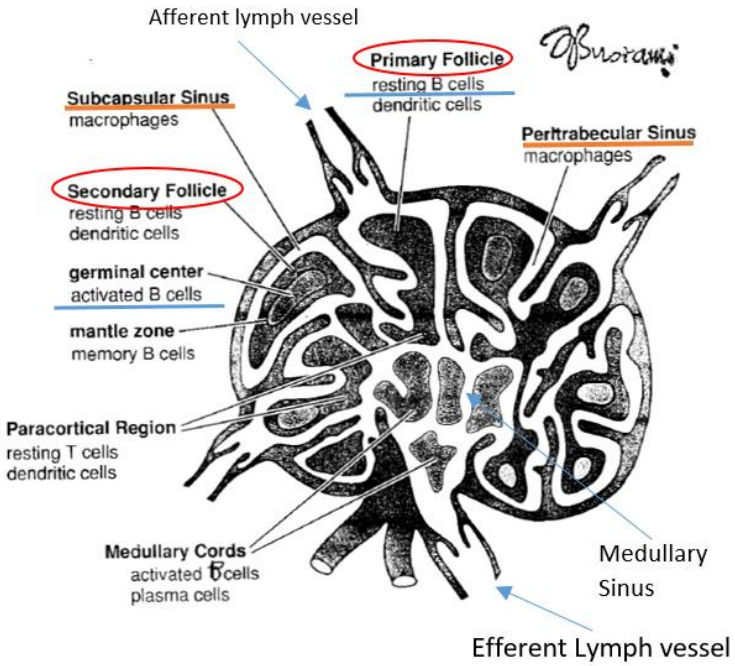
- But this isn't enough for the B-lymphocyte to proliferate to a plasma cell and start producing antibodies, it should receive another signal from a T-helper cell which recognizes the same antigen on an another APC but attached with an MHC II protein (cause only B-cells can recognize antigens without MHC as we said before), the T-helper cell gets activated after binding to the antigen then it produces cytokines and the most important one is IL2 which is released then goes and costimulate the earlier B-lymphocyte to get fully activated and will proliferate and give Activated B cell that will get further prolifretion into plasma cells that will produce antibodies and a memory B cell that will circulate in the blood so as to quickly recognize and react with the antigen of the bacteria if it entered the body another time in the future.
- (so , the proliferation and activation of B lymphocyte need to receive two signals the first is antigen recognition , and the second is co-stimulation by IL-2)

LYMPH ORGANS:

➢ Lymph Nodes:

Spherical or kidney shaped, on its concaved side there is a depression called the hilum, where arteries and nerves enter and veins exit, afferent lymph vessels enters the Node and efferent vessels comes out of it

They are covered by capsules of dense connective tissues, they send extensions called trabeculae to form partitions within the lymph nodes, followed by a network of reticular fibers ensheathed by reticular cells surrounding these trabeculae



Throughout this network 4 major types of cells present:

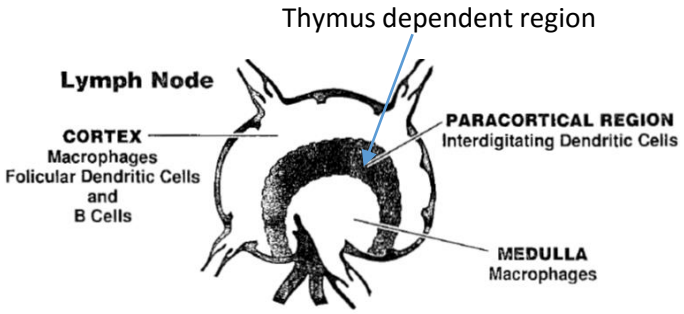
1. B-lymphocyte 2. T-lymphocyte 3.APC 4.Macrophage

These cells exists in any lymphatic organ: Lymph Nodes, Spleen, diffuse lymphatic tissue. (These three are called peripheral lymphatic organs)

Note: immune reaction occurs in these organs because they have the necessary components (B&T-lymphocytes, APC, and Macrophage)

- Major function of a lymph node is a filter to the lymph because it contains many macrophages in its sinuses that phagocytose 98% of antigens that enter the lymph node.

- *We can't recognize or feel the lymph nodes unless they are enlarged due to immune reaction*



- A Lymph node has an outer cortex and inner medulla and in between there is Paracortical region (deep cortex).

- the cortex we have lymph sinuses , the lymph arrived through the afferent lymphatics vessel , directly beneath the capsule there are subcapsular sinuses followed by peritrabecular sinuses between the trabeculae .the lymph contain a lot of foreign antigen. the sinuses house large number of macrophages which phagocyte 98% of these antigen.

- In the cortex we have to types of follicles, Primary & Secondary.
    - Primary Follicle: contains resting B-lymphocytes (naïve or virgin cells), not yet exposed to antigens formed in the bone marrow then migrated to the lymph node or the spleen, also accompanying the B-lymphocyte is it's servant the Follicular Dendritic Cell that presents the antigens to it.
    - Secondary Follicle: contains the activated B-lymphocytes (plasma cells) that produces the antibodies and B-memory cells, they go to the center of the secondary follicle and they look pale in color and called "Germinal Centers", which is a characteristic of the secondary follicle.
- Medulla: both of these cells (the Plasma and B-memory) migrate from the secondary follicle to the medulla forming "medullary cortex", 10% of these cells stay in the medulla while the other 90% leave the lymph node through the efferent lymphatic (or through veins) to the blood and circulate there.

- The B-memory cell transfer from a lymph node to another looking for its antigen which is usually presented by an APC, or it can find it in a tissue and react with it.
- The Plasma cells go to the bone marrow and start to produce antibodies there.(the main site of antigen production)

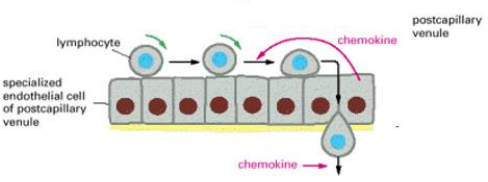
- *Remember: the immune reaction sites are the lymph nodes and spleen and other peripheral lymphatic organs, not the blood or lymph!!!*

- The Deep Cortex (Paracortex): settles between the cortex and medulla, contains mostly T-lymphocyte and its servant Interdigitating Dendritic Cell, it is a thymus dependent zone, Langerhans cell may migrate to this region to present their antigens-MHC II complex to T-Helper cells, which may cause increasing width of the cortex!

    - *Newly formed T-cells migrate to the medulla then leave the lymph node to an area of antigenic activity.*

    - The Paracortex have a special type of blood vessels called High Endothelial Venules or HEV (post-capillary venules) they are very important as they allow lymphocytes to return to lymph nodes through them “B-memory & T-memory mostly”. This process called lymphocyte recirculation or homing. if the lymphocyte was naïve , it have to return to lymph node or spleen . if it was memory cell, it goes to the tissue to react with the antigen .

    - On the surface of the lymphocyte (naïve or memory) there is certain proteins called Adhesion molecules or “Homing Receptors” (mainly L-selectin).
        - ❖ these molecules are useful for attraction to the post-capillary venules by Ligands present on the epithelium of these venules called **Addressins**

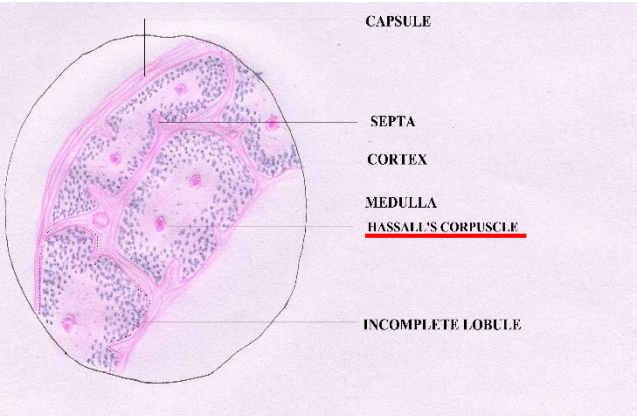


- ❖ In another word: these Addressins attracts the Adhesion molecules on the surface of the lymphocytes, this attraction causes the lymphocyte to enter to the node through the Post-Capillary Venules *(B- cells migrate to the outer cortex whereas most T-cells remain in the Paracortex)*
- ❖ The endothelium of the post-capillary venules is unique, the endothelium of normal capillary of venule is simple squamous, while in here it is simple cuboidal! *(to help in the diapedesis of lymphocytes to get inside the lymph node)*

➢ Thymus gland:

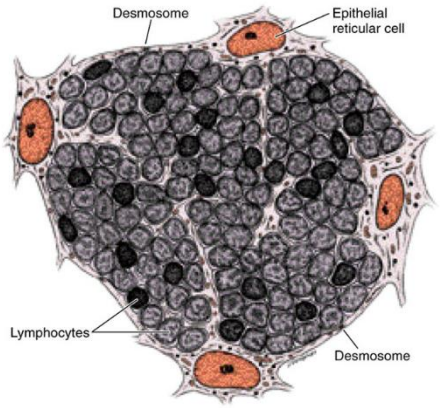
- Consists of two lobes behind the manubrium sterni and in front of the large vessels (Aorta and Pulmonary trunk), its weight at birth is about 15 gm; by puberty It weighs 30 gm, after puberty it atrophies and at old age it becomes 15 gm again.

- A capsule consisting of connective tissue envelopes the thymus and send extensions to the inside called septa.
- These septa form partial partitions that separate the tissues of the thymus into regions called lobules.
- Each lobule has an outer region called the cortex and an inner region called the medulla.



- In the cortex there is maturing T-lymphocyte (the Thymus is the site of T-cells maturation) to become immunocompetent in **isolation** from the antigens that could come from the blood, so it will not be exposed to any blood or antigens or else to will fail to mature and gets apoptosed, it may get exposed to self-antigens (MHC I & MHCII) but it should never recognize the proteins in the body "auto-immune disease"

- The T-lymphocytes are isolated from the blood and it's antigens by **Reticular Cells** which surrounds them, in the cortex there is type I,II,III and in the medulla there is type IV,V.



- Special type of capillaries are situated next to the Reticular cells, they are special because the endothelial cells have tight junctions between them (no space for the antigen to go through) ,and outside the endothelium there is thick basal lamina and outside it there is connective tissue and after that comes the reticular cells, these 4 layers "endothelium, basal lamina, connective tissue, reticular cells" are able to prevent any antigen coming from the blood to reach the T-lymphocytes

- The Reticular Cells have MHC I & MHC II on its surface and the T-lymphocyte can recognize them, and these cells contain hormonal like substances "thymosin, thymulin, thymopoietin, thymic humoral factor" that programs the T-lymphocytes to become immunocomptent, if the T-cell fails to recognize them then it will be useless "immuno-incompetent" and will undergo apoptosis.

- Other hormones outside the thymus also have a role in programming the T-cells "pituitary, thyroid, suprarenal and sex hormones", while glucocorticoids decrease the number of T-cells in the thymic cortex but in a physiological manner!

- *So in summation we can say that:*
    1) *If T-lymphocyte recognizes blood borne antigen or self-proteins it should undergo apoptosis in the thymus to avoid Autoimmune disease*

so as these cells won't be released and attack body tissues etc..

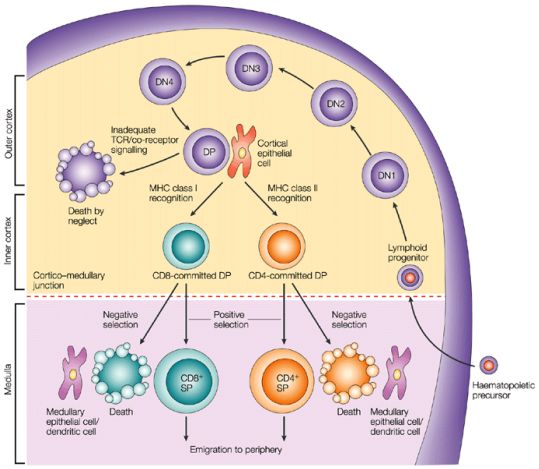
2) *If the T-lymphocyte didn't recognize MHC I & II of reticular cells it won't be useful "immuno-incompetent" so the thymus will get rid of it by making it induce apoptosis too.*

*so the summation of the apoptosed cells in 1 & 2 will be **98%** of the original number of the newly formed "unprogrammed" t-lymphocytes that entered the thymus,*
The resting 2% will be programmed properly and will be fully immunocompetent after they get:

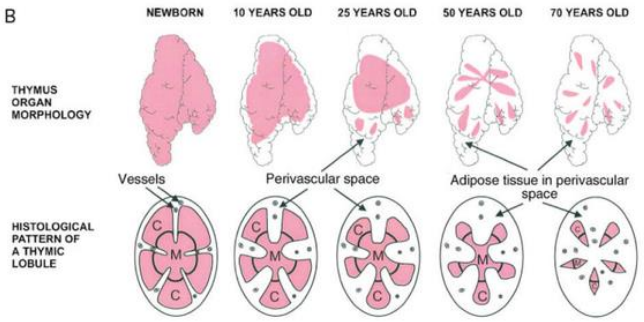
a) *The ability to recognize MHC proteins (a process called self-recognition)*
b) *They must lack reactivity to peptide fragments from self proteins, a process known as (self tolerance)*

Then they will be released from the thymus

❖ After the T-lymphocyte gets programmed in the cortex it migrates to the medulla as Virgin (naïve) T-cells then goes out of the medulla by efferent lymphatics or veins to the blood, then it settles in the <u>Thymus-dependent</u> zones of the lymph nodes and spleen “Paracortex in lymph nodes and Periarteriolar lymphoid sheaths in the spleen”

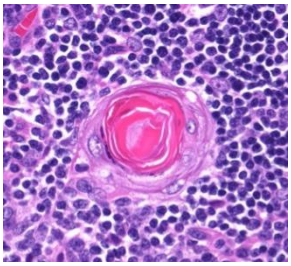


❖ If we took an experimental animal days after it's born and we dissected its thymus we can see clearly an atrophied deep cortex in the lymph nodes, but if we dissected the thymus of an old age animal nothing happens!, if we look at a section in thymus of that animal we can still see some lobules and its cortex and medulla but most of the gland has been replaced by adipose tissue



*Note: the bone marrow and the thymus are **PRIMARY** lymphatic organs while the spleen, lymph nodes and diffuse lymphatic tissues are **PERIPHERAL** lymphatic organs*

- If we look at the medulla of the thymus we can see a very prominent feature, a structures called Thymic corpuscles or (Hassall's bodies), it's a group of flattened epithelial reticular cells wrapped around each other in "concentric lamellation", their importance is unknown as they have no function, they are only useful as an indication to the tissue type as their presence means it's the thymus.



➢ The Spleen:

- It's the largest lymphatic organ, located in the left upper quadrant of the abdomen near the ribs, its long axis situated behind the 10th rib, and related to the diaphragm.
- It has a hilum in its inner surface where blood vessels and lymphatics enter and leave it.
- *The spleen doesn't have an afferent lymphatics! (only lymph nodes contain afferent and efferent lymphatics)*

- The basic structure of the spleen is similar to that of the lymph nodes, there is a capsule encloses it which sends septa to that inside and divides it to incomplete compartment.
- The spleen doesn't have cortex and medulla, instead there is a white pulp and a red pulp.
- The white pulp is lymphatic tissue, either as a follicle or a sheath, while the red pulp is a blood sinusoids.

The lecture ends here…

Le Fin.

Stars Can't Shine Without Darkness…