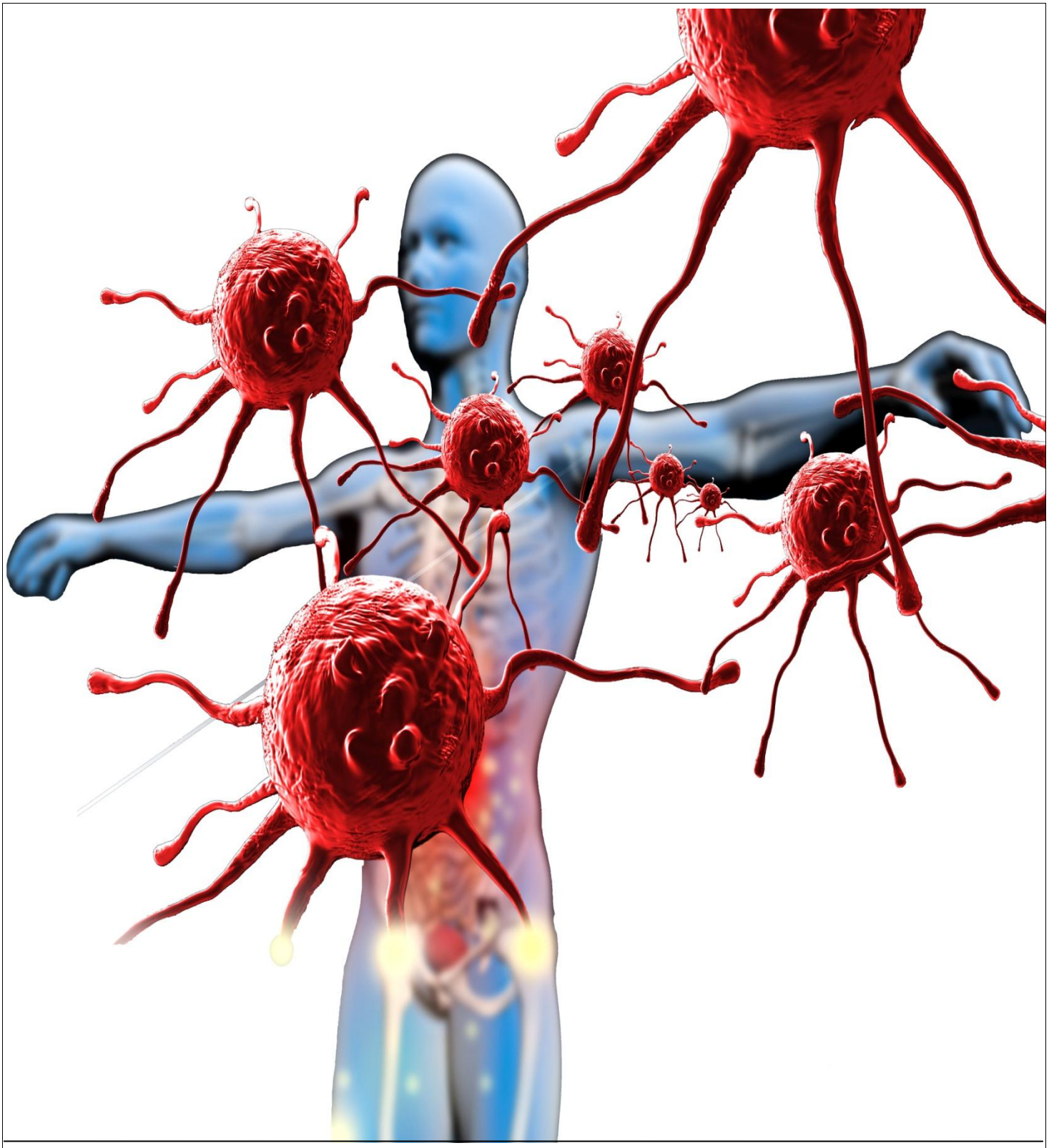

IMMUNOLOGY

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IMMUNOLOGY.

The environment around us is full of possible threats viruses, bacteria, parasites, toxins…. That can cause pathological effects on the body; here comes the role of our immune system.

The response of the immune system is quite powerful it can destroy cells, tissues even organs so our immune cells should be able to recognize self-cells from non self-cells to ensure that only pathogens are to be destroyed while our body remains safe, this will be further discussed later on.

So the immune system can recognize body cells from pathogens, immobilize them then get rid of the pathogens, or at least that's the situation normally, in some cases you could have a problem with your immune system it could be either deficient (can't protect body properly) or in other cases the immune system fails to recognize self from non self thus becoming the threat itself and harming the body, destroying its cells this is known as "Autoimmunity" leading to an autoimmune disease.

Furthermore, in some cases the immune system recognizes pathogens and attacks them which is normal however the immune response might proceed for a long time causing damage to the surrounding tissue this is known as hypersensitivity, this and other pathologies will be discussed later on.

The immune system has two elements:

1. Cellular element, the cells that carry out the immune response.
2. Immune tissues which can be divided into 2 varieties depending on maturation.
   - ❖ One where production and maturation of immune cells occurs , this of course starts in the yolk sac and the liver but later in life after birth the production site changes to the bone marrow.

   In the bone marrow all these cells are produced from the stem cells, some cells don't continue their maturation in the bone marrow but leave at an early stage to the thymus, mature there then move to the blood, these cells are known as T-cells (T from thymus) (T lymphocytes).

Written by Rajai Zurikat

So all the cells are produced within the bone marrow, most mature there while these T-cells move to the thymus to mature.

So the pluripotent stem cell is in the bone marrow, from here we have 2 development lines (related to immunology) the first is known as the myeloid line and the other as the lymphoid line.

Myeloid line:

It gives rise to the platelets but this doesn't concern us, it also gives rise to the granulocytes and the monocytes (mononuclear phagocytic cells).

So we are talking about the white blood cells. How many white blood cells do we have in our blood? It's usually between 4000-11000 cells per cubic millimeter. This is normal the value can be higher or lower under abnormal conditions.

Granulocytes: Neutrophils 60-65%, eosinophils 3%, basophils less than 1%, monocytes about 7%, while the lymphocytes are around 1/3 of the total cells around 35% you should know these values .

Neutrophils:

Also known as polymorphonuclear leukoctes (PMLs) because usually the nucleus appears to be segmented as the cell develops through its life.

The life span of these cells is 2-3 days then they will be broken down.

Neutrophils are the most abundant white blood cells; also they are the first to respond to an immune response.

They are known as neutrophils because their granules don't stain neither proper pink nor purple but in-between, the granules contain a lot of substances, most of them are hydrolytic enzymes as the main function of these cells is to destroy pathogens by phagocytosis (engulfment of the pathogens then the release of the enzymes to destroy it), the cell will die after this causing the release of some of these enzymes to the surrounding tissues this will form pus (the dead pathogens, dead neutrophils, and dead tissue) this is a pyogenic infection (forms pus containing dead neutrophils).

So, neutrophils are indeed scavengers or garbage men as they look for pathogens and get rid of them.

CD molecules or cells: these cells contain a lot of molecules on their surfaces used for many functions, some of these adhere to extracellular matrix, some adhere to other cells while others serve as receptors to cytokines to transmit messages to the inside of the cells some also recognize pathogenic compounds (antigens). So there are a lot of them and at first they were named after their function but then a numerical system was established.

So CD stands for cluster of differentiation; cluster indicating the antibodies that can recognize these cells (originally these cells were discovered in labs using antibodies) so what happened is that the people that created the system used all the antibodies to differentiate between the cells which lead to the formation of antibody clusters as each cell could bind with more than one antibody thus the word cluster, while the word differentiation comes from the fact that different cells bind to different antibody groups or different antibodies, i.e. differentiating the cells.

We have almost 300 of these molecules we won't memorize all of them however some very common types are important such as CD4 present on T-helper cells, CD8 on cytotoxic T cells and CD19 on B-cells but this will be discussed later.

So we have a system to name these cells but some are still known by their functional name.

So neutrophils have some CD receptors (pattern recognition receptors) that can recognize non-self cells, also they could have receptors for immunoglobulins; the function of these here is to identify pathogenic cells, how does this happen? This is done as immunoglobulins stick to pathogens now the neutrophils will recognize the immunoglobulin carrying the pathogen rather than the pathogen itself and engulf the whole complex.

Eosinophil:

In most white blood cells the immunoglobulin receptors present are for IgG class (remember we have different classes of immunoglobulins Ig e,m,a,g,d) so the main is for IgG. However IgE is the main receptor on eosinophils.

The eosinophil is larger than the neutrophil its 12-15 microns (RBCs are 7 microns). It has a lot of granules (stuffed) these look red or pink in colour that's why they are called eosinophil referring to the stain eosin which is an acid so the granules are basic (as acidic stains colour basic molecules).

So these granules have a lot of basic compounds in them mostly basic proteins which are great against parasites, eosinophils don't engulf especially that parasites are usually large (100 microns maybe more) and can't be engulfed so instead it pores these proteins on the parasites to kill it unlike neutrophils that engulf and digest bacteria.

The main receptor on eosinophils is IgE which is believed to be against parasites, so IgE settles on the parasite, the receptors on eosinophils recognize IgE bind to it and secrete their components on the parasites to kill it.

The percentage of eosinophils is usually 3% but under allergic reactions and parasitic infections the number of cells will increase significantly while the number of neutrophils usually increases in cases of pyogenic bacterial infections. These facts help in diagnosing a patient.

Mast cells and basophils:

So these cells are in fact related but they develop along different lines (they were thought to be of the same origin before).

These cells are to all intensive purposes identical when comparing their contents and functions, the main difference is that the basophils are found in the blood while the mast cells are found in the body tissues.

The granules are usually purple or deep blue purple because they bind with hematoxylin meaning they contain acids, the main acid is histamine others are present.

*Histamine is an important mediator of inflammation, has many functions including dilating blood vessels, increasing vascular permeability so white blood cells can escape and reach inflammation sites, does it have chemotactic function?? it is debatable.

*Histamine causes smooth muscle contraction and also irritates nerves causing pain and an itch all these functions are responsible for the signs of inflammation redness, hotness, swelling, pain & loss of function.

So basophils and mast cells (especially because they are present in tissues) are very important in mediating inflammation, they have receptors on them and also here its for IgE again (why is IgG more common then? because neutrophils are higher in number than both these types of cells).

Monocytes:

7%

They are produced in the bone marrow then enter the circulation (blood) then leave the circulation and settle in tissues this will lead them to change their functions as they settle in different tissues; in bones they give rise to osteoclasts which are really phagocytic cells, in the liver they give rise to kupffer cells, in the brain they form microglia all of these are really resident phagocytic cells.

Monocytes are usually referred to as macrophages especially in tissues while in the blood they are reffered to as monocytes.

Monocytes are large 16-18 microns in diameter they have a longer life span than neutrophils and perform phagocytosis making them scavengers as well (destroying dead cells, pathogens….).

The main immunoglobulin receptor here is IgG, so we have FC gamma receptors for IgG.

They also have receptors for complement breakdown products, complement systems will be discussed later.

In addition these, macrophages have a more refined function which is antigen presentation:

So we know we have t and b lymphocytes, B-lymphocytes can recognize foreign antigens as it is (native antigen), while T-lymphocytes (both cytotoxic and helper cells) can't recognize an antigen as it is, here comes the role of the macrophages, the macrophages engulf the antigen break it down and represent parts of it on its surface so the t-cells can recognize them.

*So macrophages digest antigens, these are broken down into peptides which will be displayed on the macrophages surface for the activation of the t-cells.

APC is an antigen presenting cell like a macrophage in this scenario.

So both neutrophils and macrophages are scavengers but **only macrophages** can represent antigens for T-cells.

Dendritic cells:

These cells have many long extensions or dendrites, some people think that it comes from a different path but it comes from the same origin as the other cells, which is the bone marrow.

They have a similar function to that of macrophages yet they aren't really scavengers, but rather they sample the environment so the dendritic cell uses pinocytosis to collect antigens from the environment, after they are done they travel to lymph nodes and other places to present these antigens to T-cells.

So these dendritic cells are professional antigen presenting cells, better than macrophages.

These cells are present extensively **under mucous membranes, under skin these cells are known also as Langerhans cells.**

There is another cell not present on the doctors slide's pictures it's called: **follicular dendritic cell** it is mesenchymal in origin has nothing to do with dendritic cells but they still have dendrites they are known as follicular because they are found in the follicles of lymph nodes. Their function will be discussed later on.

The lymphoid line:

1. **T-lymphocytes** these develop in the thymus into 2 types (we will not discuss details now) the types are: **helper T-cells** (these produce cytokines or chemicals that help all the other immune cells with their functions promote and activate other cells), the other type is the **cytotoxic T-cells** which kill cells; these cells can be either foreign cells or body cells infected with pathogens or even damaged (not working well) or could be cancer cells. Remember they need an APC (antigen presenting cell).
2. **B-lymphocytes** so called because they are produced in the bone marrow and develop there, (the doctor said bursa of fabricius which is the site of hematopoiesis in birds this was the first place to discover b-cells)
   These cells can recognize an antigen as it is without the need for APCs.
   Once they recognize an antigen they change into plasma cells which in turn produce antibodies against pathogens with that specific antigen.

Important: b-cells don't actually produce antibodies but evolve into plasma cells that do.

Another type of lymphocytes, with nothing to do with the other two types, which was referred to as **large lymphocytes** {(the other lymphocytes are

identical in a blood section) the only way to differentiate between lymphocytes is by detecting the molecules and receptors on their surfaces, example: CD19 only on B-cells, while for T-cells you look for CD3, if present on the lymphocyte it is then a t-cell but to figure out if its helper or cytotoxic further markers are studied … helper has CD4 and toxic cells have CD8 on them}.

So these large cells are larger than regular lymphocytes 15 microns while regular ones are 10 microns, they have a larger granular cytoplasm these are known as natural killer cells because killing is in their nature ☺ they are part of the innate immunity. Function is killing cells.

We have 2 types of immunity innate or natural immunity or acquired (adaptive).

The lymphocytes constitute for 35% of all white blood cells, the natural killer cells constitute for 10-15% of all lymphocytes , B-cells 20-25%, cytotoxic t-cells 20-25% , while t-helper cells constitute for 40% of lymphocytes.

So this was an over review of all the immune cells.

Immune tissues:

Primary immune tissue in these tissues the production and maturation of immune cells occur, these are the bone marrow and the thymus.

So these tissues are responsible for production, division and maturation of the immune cells.

After that the cells go to the blood and later they colonize in other tissues these are the:

Secondary immune tissues

These are the **lymph nodes, spleen, tissues associated with mucosa** (cells accumulate under them but are not organized as in lymph nodes) - {mucosa associated lymphoid tissues, such as: tonsils, adenoids, Peyer patches associated with the small intestines these are really collections of white blood cells under mucous membranes} again they aren't organized as in lymph nodes (which resemble pomegranates as they have septa with cells inside them).

The function of these tissues is to contain the white blood cells and here the immune cells are faced with pathogens and produce a reaction.

As you know lymph nodes are present all over the body, so they drain the whole body so if you have an infection in one place you can feel the swollen lymph nodes which that part of the body drains in, so a cold sore in your mouth will cause your submandibular nodes to become swollen.

The spleen cleans the blood so anything dead will be found there.

Why do we need MALT (mucus associated lymph tissues) because we know these tissues are more prone to infection than other tissues, such as skin, which is a barrier against pathogens unlike the soft mucosal tissues.

END OF THIS GOD-FORESAKEN SHEET!

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And of course the correction team

"I don't care what you think about me.

I don't think about you at all ".

Written by Rajai Zurikat