6

Physiology sheet

Doctor 2022 -أثر- I medicine I MU

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DOCTOR

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Before we get into the lecture, pay attention to the following notes as they were missed from the last sheet:

- **It is important to make the patient as comfortable as he can while taking his blood pressure to avoid having false elevations of it as in cases of white- coat or office hypertension when blood pressure readings at a health care provider's office are higher than they are in other settings, such as at home (due to being afraid of the physicians' white coat or just being at a clinic).**
- **To avoid having an auscultatory gap we always inflate the cuff 30- 50 mmHg above the suspected value of systole → to ensure hearing all the sounds → No underestimation systole or overestimation of diastole happen.**

Thanks for our colleague who noted them.

Microcirculation

Introduction and Capillary Unit:

- **Once blood is pumped from left (L) ventricle into systemic circulation, it'll go through the largest artery we have (aorta), then to arteries then to the core (or center) of perfusion pressure which is called capillary unit; which is the crux of our lecture.**
- **The pressure applied on blood vessels (BVs) for perfusion has to be proportional with the amount of oxygen (O2) taken by cells and consequently amount expelled of CO2.**
- **Every and each type of BVs has its structure which is adapted to its function.**
- **Arteries with the largest of them being the aorta, have the function of contraction then stretching (relaxation) → pumping that's why it has to be elastic.**
- **After aorta the blood goes to systemic arteries with pulsation function rather than pumping; so, I need high pressure→ I need more smooth muscles or those BVs have to be muscular; to perform its destined function such in radial artery and femoral artery.**
- **Arterioles are the next destination which are very, very small arteries.**
- **Metarterioles are a part of the capillary unit. Once the blood gets into arterioles it goes through metarterioles which are continued with the name of thoroughfare channel where you'll find precapillary sphincters on its path and all of those constitute the arteriolar end of the capillary unit (bed). After that the venular part of the capillary unit starts with venous capillaries which are directly connected to the bigger venules followed by the largest veins. So, metarterioles (or thoroughfare channel if you will) connect arterioles with the venular end of the capillary unit.**

- To sum up, blood path is: arterioles → metarterioles (arteriolar end of the capillary bed) → venous capillaries (venular end of the capillary bed) → venules.

- What is the function of capillary unit? Since it has precapillary sphincters on the arteriolar end; it regulated blood flow. When there is an ↑ in metabolic activities → more O2 is needed as it has ↓ed → ↑ blood flow to the cells. Below the capillary unit there is interstitial tissues where it takes O2 from arterilolar part. So, whenever I need to ↑ metabolic activities (i.e. ↑ O2 levels in blood) → vascodilation (relaxation) of precapillary sphincter must happen → ↑ blood that passes through the capillary bed → ↑ oxygenation process. (there is a direct relatioship between blood flow and partial pressure of O2 (PO2). This relationship will remain linear until it reaches a point where no further ↑ in blood flow happens why? According to Ohm's law:

  $F = \Delta P/R$ Ohm's Law F: force, ΔP: pressure gradient and R: resistance

  $CO = \Delta P/TPR$ CO: cardiac output and TPR: total peripheral resistance

  → as massive ↑ in blood flow will ↑ BP which itself will ↑ R. Moreover, according to La Place's Law:

  $$\text{Laplace's Law: Wall stress} = \frac{\text{Pressure x Radius}}{\text{2 x Wall Thickness}} = \frac{\text{Pressure x Volume}}{\text{LV Mass}}$$

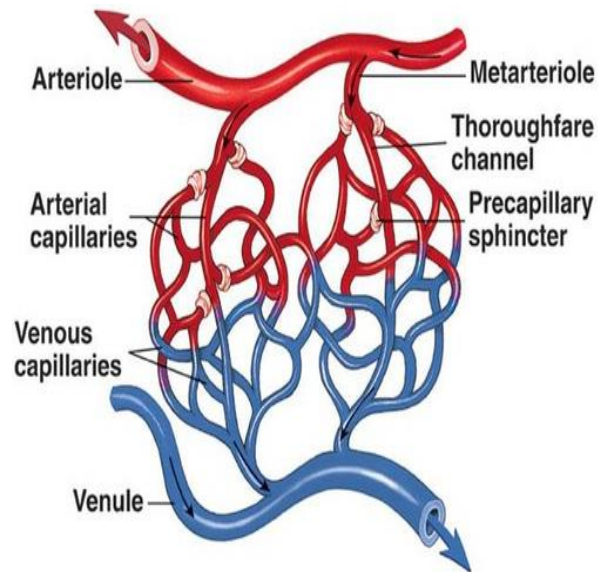
  Wall Stress

  → ↑BP → wall tension (stress)↑ → ↑ risk of rupture of BVs. Always use the laws and walk with them step by step to have a sequencial logic.

- Then blood completes its path; after leaving O2 to intersitium due to exchange with the arteriolar end; blood takes CO2 from the interstitium and goes with it to venous capillaries, then to venules (small veins) then medium veins (such as femoral vein and brachial vein) then to large veins (Superior/ inferior vena cava [SVC& IVC] where SVC receive from upper body parts and IVC receives from lower body parts) to systemic ciruclation.

- This is simply the concept of circulation; to maintain everything in a dynamic homeostasis: ↑ or ↓ according to person's need in day-to-day activity → our bodies will act accordingly. However, in both cases of ↑ing or ↓ing, we are always dealing with the lowest possible values and we won't exceed it → so, it does not yield a problem such as hypertension (HTN).

- **Here is the crux of all our information today so this is a capillary unit in a tissue, and this will be found anywhere in the body its ubiquitous and this is going to supply our tissues with all nutrient and oxygen and all that other nutrient needs to function**
- **What we are going to discuss these arteriole, precapillary sphincters and the metarteriole and you can see these banded with smooth muscle and these precapillary sphincters are smooth muscle**
- **and the function of these are a little bit different; the metarteriole is basically a vascular shunt for when these capillary sphincters are open or closed, serve either as thoroughfare channels to the venules, which bypass the capillary bed, or as conduits (channels) to supply the capillary bed. There are often cross-connections between the arterioles and venules as well as in the capillary network.**



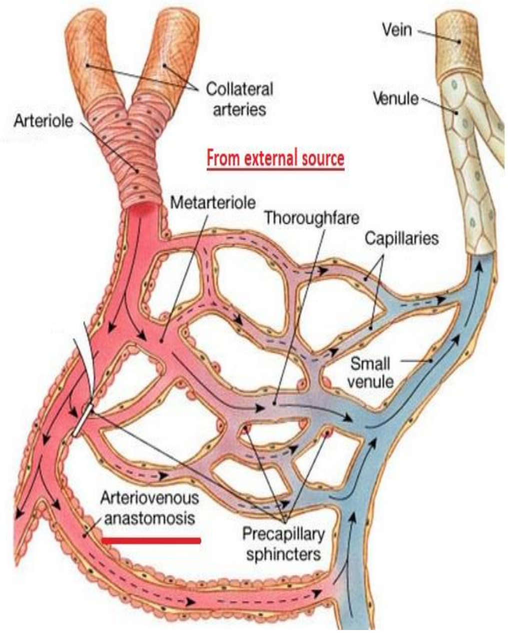
- **arterioles are terminal endpoint of systemic circulation with regard tissue perfusion**

Blood Flow:

- **During exercising → blood flow has to be to the highest possible value to give us ATP and O2, but in what organs exactly? This is a fight-or-flight situation not a rest-or-digest one. So, pumping of blood will be focused skeletal muscles → as I need more ATP. In this case, no need for gut, urinary tract or skin→ all their blood flow will be shifted (shunted) to skeletal muscles → this happens to a degree of almost 20 folds more than the normal blood flow to cover the high (increased) need of ATP. So, vasodilation of precapillary sphincter → ↑ blood flow to skeletal muscles → ↑ O2 and takes metabolic end products like lactic acid, hydrogen (H2), carbon dixoide (CO2) .. etc all back to veins.**

- **During rest-or-digest situations, do I need high blood flow to skeletal muscles? Nope, that's so wrong. Blood flow has to be focused now to gut to perform digestion first then absorption. That's why never eat and take path or go swim; as your blood is shifted towards digestion → once you swim it will be shunted directly to skeletal muscles → this may cause problems especially if this person has a heart- related problems → he will be susceptible to shock more.**

- This was the 1st function of metarterioles: vasodilation or vasoconstriction according to the situation. In some cases, I might be stressed and tense to a degree that I don't have time to go through the circle of exchange in capillary units (metarterioles and venules) → no time for exchange between capillaries and tissues. In such cases, metarterioles resort to its 2nd function: shunting or anastomosis. Which is simply finding another backup pathway for blood flow.
  So, instead of taking the usual path through capillary unit; the blood goes directly from metarterioles to veins.



- Think of anastomosis as a "short- cut" where blood goes directly to heart and back forth.
- To sum up, I resort to anastomosis when I'm in a stressful situation like being chased by a lion or exercising excessively → I have no time for exchange between capillary bed and interstitium → blood takes the shortcut from metarterioles to venules.

Anastomosis:

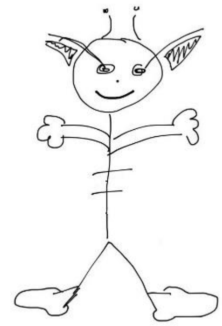
- **Alternative** pathway **for blood flow** (from metarterioles to venules directly). It is a backup pathway for shunting to blood flow to a specific area without affecting the general body situation→ cardiac output (CO), PO2 ..etc won't be affected → not considered as an occlusion or such things to affect them). It's found in each body tissue.

- Types of anastomosis:

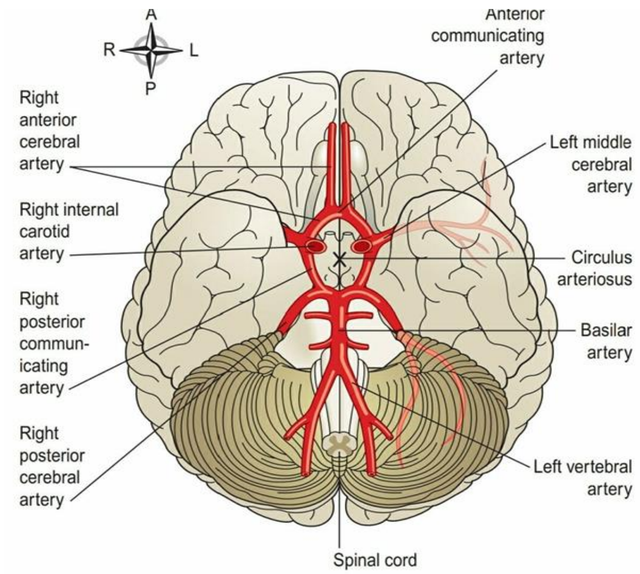
1. **Arteriovenous anastomosis:** via **metarteriole** (**thoroughfare channel**) that links arterioles and venules to redirect blood flow directly from arteries to veins.

2. **Arterial anastomosis:** a group of arteries connected all together in a network. If a problem (for example blockage) in a certain area, blood flow will find an alternative pathway to go through so it doesn't damage the tissue. An example is arterial anastomosis in brain which is also known as: **circle of Willis.**

- **In circle of Willis:**
  - **Imagine a person with 2 ears, 2 legs, 2 eyes and 2 hands or just look @ the figure below.**
  - **It is a group of arteries; coming from R or L ventricles called vertebral arteries then both R& L will go together in 1 common artery that is called basilar artery. Which will continue to work through communicating arteries located in: 1) anterior above, 2) posterior below and 3) middle for the edges. Do not know the names of the arteries; just have a good understanding of how it works.**



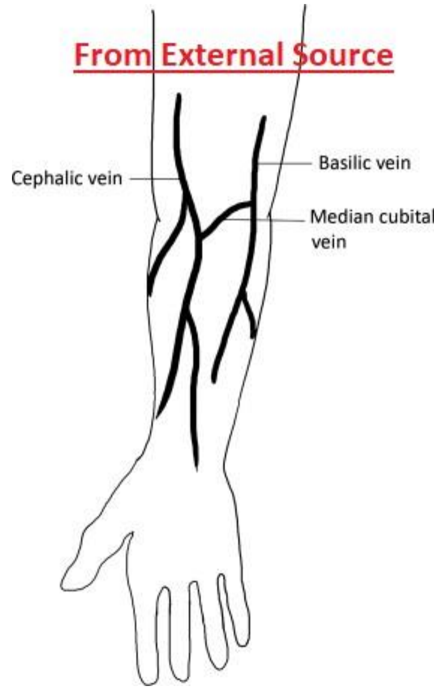
  - **For example, if blockage (occlusion or atherosclerotic plaque) happened to posterior communicating artery, its pathway will no longer be available. In this case, to maintain brain tissue oxygenation level (blood perfusion) in the parenchyma of the brain to an OK level to an extent, is to take another pathway. This is not called a stroke itself (the anastomosis) but it is usually caused by one (stroke is an occlusion or a burst of BVs supplying the brain or in the brain). This stroke might damage the affected tissue a little bit if we have anastomosis (so, we can't prevent full damage but we can minimize it a lot). The real problem happens in cases such as middle cerebral artery where there is no anastomosis (direct attachment with other arteries) → any occlusion can cause a massive da mage in such cases → permanent disabilities according to the area of brain affected if not death).**



Arteries forming the circulus arteriosus (circle of Willis) and its main branches to the brain. Viewed from below.

  - **To sum up, arterial anastomosis gives us pathways so in massively critical situations the blood will find it way and only a little damage (not a lot) happens. One of the most known example of arterial anastomosis is circle of Willis in the brain, others are found in different places such as heart.**

3. **Venous anastomosis:**
    - In this type a group of veins connect with each other. We have different examples the easiest are venous anastomosis in arm and venous anastomosis in leg.
    - Venous anastomosis in arm: **cephalic vein** located in the thumb side (lateral side) and **basilic vein** located in the little finger (pinky) side (medially). Those two veins are connected together with another vein called **median cubital vein.**
    - In case of blockage in either cephalic or basilic vein, the blood will go in a normal flow through medial cubital vein like nothing happened without any problems. This happens to maintain blood perfusion as possible and to ↓ the extent of any damage.



Regulation of Blood flow:

- During exact activity, I have to direct blood flow to specific organ because it is needed more → ↑ blood flow →↑ATP. This type of change in blood flow towards any specific organ is called active hyperemia:

1. In **Skeletal muscles active hyperemia:** a lot of metabolic end products accumulate such as CO2, H2 and lactic acid. All of those have to be taken by blood in a quick fashion to get rid of them. So, during **exercising, vasodilation** happens to precapillary sphincters to ↑blood flow towards skeletal musucles to meet their needs.
2. In **brain:** The area of in periphery of the brain (the edges, where it is supplied with blood) I have either of two scenarios:
    a. **High MAP** (which is also known as perfusion pressure). In this case, ↑ pressure is linked to ↑ wall tension (based on La Place law)→ ↑ rupture risk. That being said, ↑ blood flow beyond the limit may cause damage. For example, cerebral arteries are one of the easily affected ones in such cases. So, to avoid such problems → vasoconstriction happens to precapillary sphincters in a process called myogenic mechanism → to prevent blood flow to cerebral arteries → ↓ pressure that might affect brain tissue → prevent brain damage.
    b. **LOW MAP** → the exact opposite will happen. I have to ↑ blood flow to brain tissue or otherwise the person will pass out (called syncope). In this case **vasodilation** to the precapillary sphincters is done by ↑ing blood flow towards cerebral artery.

- **To sum up,**
  - ↑ MAP → vasoconstriction by ↓ blood flow.
  - ↓ MAP → vasodilation by ↑ blood flow.

- **The following part is a revision of topics from the previous lectures:**
  - **Is there a direct connection (not relationship) between pressure and radius? is there one law that puts them together? Can we say ↑ MAP → is due to ↑ radius?**
    - **Pressure is defined as force against ventricular wall (or any wall) on each stop (point) inside the wall.**
    - **So, to ↑ BP do I ↑ or ↓ radius? Neither! I control the force which is related to blood flow → ↑ force by ↑ blood floow → dilation. That being said, there is an indirect connection (NOT INVERSE in this context) between BP and radius.**
  - **What factors can be directly linked with radius?**
    - **Total peripheral resistance (TPR).**
    - **Imagine a hose linked with a faucet, I turned on the faucet to allow the flow → ↑ the flow along the hose. Now, to control this flow in the hose, I have to apply tension externally (to the outside of the hose) by doing constriction. Contstriction will ↓ flow due to ↑ in resistance → ↑ in BP.**
  - **Can we say that vasoconstriction has a direct effect in elevating BP?**
    - **Nope we can't. That is totally wrong.**
    - **Blood pressure will ↑ due to ↓ blood flow and ↑ in resistance.**
    - **Blood pressure has to be defined with tension.**
  - **In ventricular hypertrophy:**
    - **Radius is ↑ due to ↑ventricular walls thickness (hypertrophy of the whole muscle).**
    - **Does ↑ radius led to ↑ BP? No, it can't be justified like this. It's true that BP is very high, but the reason behind it is not ↓ in radius. It is due to ↑ in force against ventricular walls → all called tension (which is the rate of force against ventricular wall)→ that is why I put pressure in the numerator and ventricular wall in denominator in La Place Law.**

$$\text{Laplace's Law: Wall stress} = \frac{\text{Pressure x Radius}}{\text{2 x Wall Thickness}} = \frac{\text{Pressure x Volume}}{\text{LV Mass}}$$

Wall Stress

    - **↑ force against ventricular wall→ ↑ wall tension → ↑ pressure.**
    - **Remember, it is decreased compliance.**

- **<u>In dilated cardiomyopathy:</u>**
  - When I check the radius (at BV's lumen, from inside only not all of it as radius is not linked necessarily to thickness). Radius ↑ due to vasodilation → a lot of volume. However, the ↑ in volume will not yield the expected ↑ in P (it is a case of <u>increased compliance);</u> according to La Place Law:

$$\text{Laplace's Law: Wall stress} = \frac{\text{Pressure x Radius}}{\text{2 x Wall Thickness}} = \frac{\text{Pressure x Volume}}{\text{LV Mass}}$$

Wall Stress

  - ↓ thickness → ↑ in wall stress.
  - Moreover, as ↑↑↑ in volume will only ↑ pressure a little bit→ huge efforts are paid on ↑ pressure since volume can't easily ↑ it → this yields ↑ in tension to great levels.
  - Blood flow ↑ → BP ↑ → ↑ tension → ↑ risk of rupture.

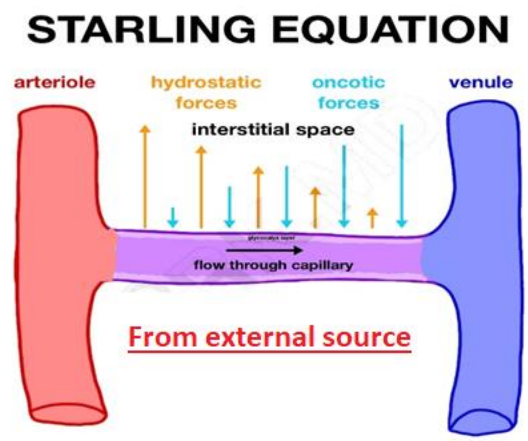
Regulation of Blood flow, continued:

3. **Lungs:** have a very significant unique feature that is different from any other organ.
   - <u>In any organ:</u> when partial pressure of O2 (PO2) ↓→ ↓ volume of O2 → ↑ blood flow to ↑ O2 by vasodilation of precapillary sphincter.
   - <u>In lungs:</u> if **PO2 decrease** → it has an alternative circulation that causes **blood shunt.** So, whenever this happens, this circulation will shunt blood from hypoxia affected deoxygenated areas (by vasoconstricting them) to oxygenated areas to save energy (as I have no time or energy to waste on this affected area) → I will save it completely by focusing on the oxygenated area to help me more with oxygenation. This is called <u>pulmonary shunting mechanism.</u>

4. In **GIT and skin:** Just like a fight-and-flight conditions; do we really need them? No. We cause **vasoconstriction** to precapillary sphincter to ↓ blood flow to those area and we shunt blood to other active organs.

- The <u>capillary unit</u> we talked about is directly connected with <u>interstitial tissues or cells.</u> Now, according to <u>Starling forces (hydrostatic pressure and osmotic [oncotic] pressure)</u>, blood will be 1st coming from <u>aorta,</u> towards <u>arteries</u> then ar<u>terioles</u> where blood volume is very large. This massive blood volume will yield a high-pressure difference (gradient) between the two compartments: BVs and interstitium, with high pressure in the first and almost zero in the latter. This gradient will cause a push of fluids towards interstitium by hydrostatic forces (check the figure).

- Now, as blood flows from arteriolar side of the capillary bed towards the venular side, hydrostatic forces gradually ↓ with the gradual ↑ in oncotic forces, until the oncotic forces are the dominant ones and causes blood to be pulled back towards the capillaries at the venular end (largest oncotic forces are found in veins). Remember, these oncotic forces are caused by plasma proteins and particularly albumin.



- If the amount of the fluids going to interstitium was very large → dynamic homeostasis must be maintained by pulling the extra fluid volume towards the venular end as we mentioned.
- The question is, does it all go back to BVs? Simply, nope. According to Starling forces:
    - The amount of volume filtered is 20 mL
    - The amount of volume pulled by the venular part is 17 mL
    - The net is around 2-3 mL. it might seem minute but if it accumulated → edema. So, it has to be drained to avoid such problems. This is the exact function of lymphatic system; it takes care of what's left (10% or 2-3 mL) from filtration process after veins take its volume.

Components of the Lymphatic System (Main Channels of Lymphatics):

- Lymphatic systems vessels look exactly like the vascular system ones. However, due to the difference in their functions → the structures somehow differ. Components are: (check the figure)

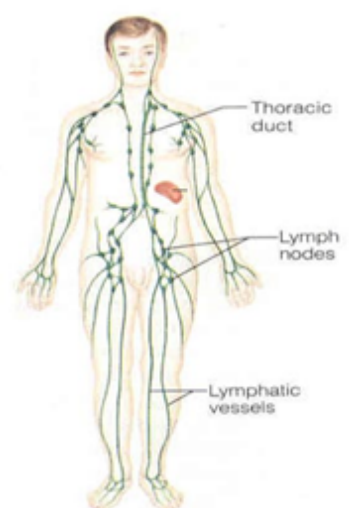
1. Lymphatic capillaries: takes the filtration drainage (now it is called lymph). Those are a bit larger than systemic blood capillaries to adapt to its function of draining lots of fluids. Simply, lymphatics originate as lymph capillaries. Capillaries unite to form larger vessels to which lymph will head next. Those are called:
2. Lymphatic vessels: resemble veins in structure. However, no subdivisions of arteries and veins here, just called vessels. Those connect to lymph nodes at various intervals. Followed by:
3. Lymphatic organs:
    a. Primary: bone marrow (BM) and thymus. Those (particularly BM) are responsible for producing B and T lymphocytes. However, T lymphocytes maturation occurs in the thymus afterwards.

b. Secondary: lymph nodes, spleen and tonsils. Responsible for cleansing (cleaning) the fluids drained by lymphatic system (called the lymph now). Lymphocytes originate from BM then they go to organs but in naïveté status (they are naïve; simply inexperienced). So, maturation happens in the secondary organs (except for T cells that happen in a primary organ [thymus]). Cleansing is the process of removing any pathogens (bacteria, viruses, tumors .. etc.) from the lymph. After the lymph is cleansed it will go to:

4. Lymphatic trunks: followed by their final destination in the lymphatics which is:
5. Lymphatic ducts: Lymphatics ultimately deliver lymph into 2 main channels:
   a. Right lymphatic duct:
      - Drains right side of head & right side of neck, right arm, right thorax
      - Empties into the right subclavian vein
   b. Left lymphatic duct or Thoracic duct:
      - Drains the rest of the body
      - Empties into the left subclavian vein
6. Then those two will direct lymph towards either SVC or IVC and the process continues. So, fluids will eventually end up delivered to the heart after it's cleansed.

Components of the Lymphatic System

- Lymph
- Lymphatic Vessels
  - Lymphatic Capillaries
  - Lymphatic Vessels
  - Lymphatic Trunks
  - Lymphatic Ducts
- Lymphatic Organs
  - Thymus
  - Lymph Nodes
  - Spleen
  - Tonsils
- Lymphatic cells



Lymphatic system

- We have lots of lymph nodes (LN) in our bodies examples include: cervical LN, thoracic LN, aortic LN, clavicular LN ..etc. all are groups located in a certain area that drains it. For example, in breast cancer we check axillary LN as they are the main ones responsible for draining the breast.
- In case of having a problem in the lymph nodes such in lymphadenitis (inflammation of lymph nodes due to infection of them by bacteria, viruses or fungi). Lymph nodes appear enlarged; however, I can't really know the cause (infection, cancer or else) until I take a biopsy. However, in cases of infection enlarged LN tend to be tender (painful upon touching) while in cancer→ painless.

Type of Cancer:	Carcinoma:	Sarcoma:
Originates From:	- Epithelial Tissues	- Connective Tissues
Spread Mostly by (Metastasize by):	- Lymphatic Vessels	- Blood Vessels

- Tumor: uncontrolled proliferation (division) of cells regardless its nature (benign or malignant).
- Metastasis: spreading of tumor cells to other sites than the original ones. In other words, tumor has spread to a different part of your body than where it started.
- Lymphatics are present in all organs except: CNS, Bone, Teeth, cartilage, epithelium, bone marrow.
- Lymphatic node swelling; bacterial or viral infection and carcinoma

- The following notes were not mentioned by the doctor but they were in the slides:
    - Open system; interstitial to open
    - Superficial with veins and Deeper arteries
    - Right angel right lymphatic duct, left angel thoracic duct Lymph node
    - Lymph node: Afferent metastasize carcinoma lymph node and grow lymphoma not tender.
    - 450 lymph nodes highest in the mesenteries
    - Immune system; cortex B cells, Paracortex T cells, medulla plasma cells, medullary sinus macrophages

آخر شيت لمادة علم وظائف الأعضاء ✓

فاللهم اجعل خير أعمالنا خواتمها، وخير أعمارنا أواخرها، وخير أيامنا يوم نلقاك..

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لا تنسونا ووالدينا من صالح دعائكم، ولكم بالمثل.