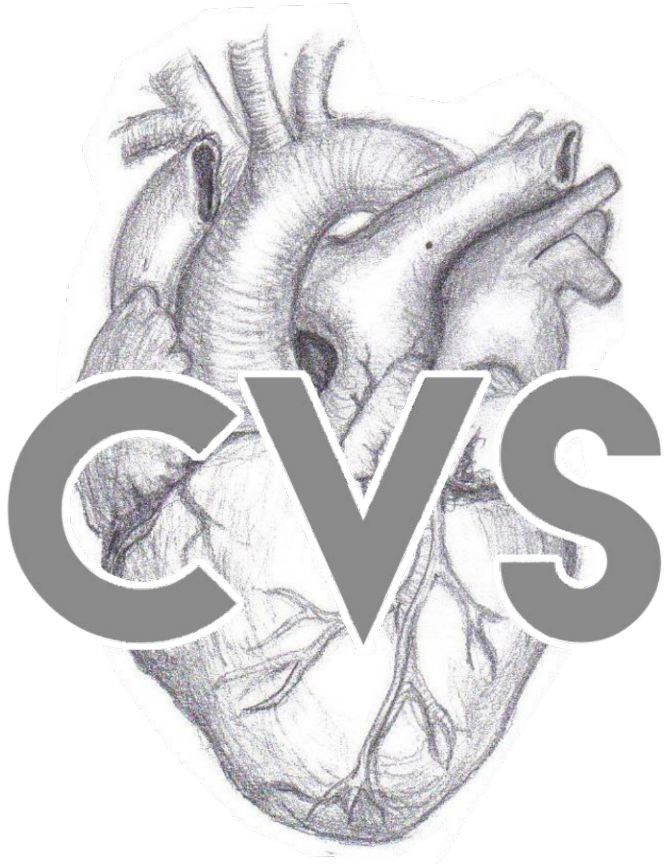

CVS

ANATOMY / HISTOLOGY

☑ Sheet ○ Slide ○ Handout

Number

1

Subject

Histology of blood vessels (1)

Done By

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Doctor

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Date: **00/00/2016**

Price:

(Record sec-2 , for the sake of comprehension I've made a lot of changes among the topics arrangement)

Content :

Introduction to CVS

These Information were not mentioned by the doctor , these are the "common sense" of CVS.

- ✓ The CVS 'Cardiovascular System' is composed of the heart and the vessels, obviously.
- ✓ The whole system is said to be CLOSED, this implies that any change upon one area will affect the whole system.
- ✓ The Heart, is separated functionally (pump-ly: P) into right heart and left heart:
    - the right heart is composed of right atrium and right ventricle , the right atrium receive venous blood from superior vena cava and inferior vena cava (SVC, IVC respectively) then the blood is pumped into the right ventricle through right atrioventricular valve then it is pumped through the pulmonary artery passing through the pulmonary valve to the lung.
    - the left heart is composed of Left atrium and left ventricle , the left atrium receive venous blood from pulmonary veins , the blood is pumped into L. ventricle passing through the left AV valve (mitral valve). Then the blood is pumped from L ventricle into the whole body through the aortic valve.
- ✓ the blood flow from right heart into lung then into left heart is called the pulmonary circulation
- ✓ the blood flow from left heart into the whole body then back to the right heart is called the systemic circulation
  -generally speaking

- ✓ The blood -as any liquid- tend to move with the pressure gradient –ie, from high pressure to low pressure.
- ✓ The function of the **valves** is to maintain the unidirectional blood flow, think of it, if we leave a liquid to move throughout 2 containers that are different in pressure what will happen eventually>> the liquid will tend to make each container reach equilibrium with respect to the other >> it will continue to flow in all possible direction to reach this equilibrium.
  Do we want this in CVS? No, we want to keep differences in pressure and volume between different areas of this system>> in order to maintain continuous blood flow to the whole body.

I hope this Introduction is fair enough, now we will discuss the histology of blood vessels (arteries, veins, capillaries)
Note : sheet 3 of the lab correspond to this sheet, studying it after this sheet will make it much easier. (Study the lab sheet on a laptop or sth electronic to see the colors of different stains)

Histology of Blood vessels:

Topics covered are:

1. General principles
2. Arteries
3. Capillaries
4. Veins
5. Special topics

1. General principles:

a. Blood vessels are mainlyarteries, veins and capillaries
   [arteries -> arterioles -> capillaries -> venules -> veins]
b. Basic structure of any vessel (Generally): -from the lumen to outside -Figure1
   I. Tunica Intima corresponds to the endocardium of the heart, composed of:
   - Endothelium (simple squamous epithelium) resting on

- Basal lamina, supported by
- Subendothelial (loose connective tissue + few longitudinal smooth muscle cells)
- Internal Elastic Lamina (IEL) –might be present or not

II. Tunica Media correspond to myocardium of the heart and it is the most variable layer in size and structure, it contains:

- Smooth muscle cells (SMCs)
- Collagen type III (sometimes called reticular fibers)
- Elastic tissue
- External Elastic lamina (EEL) –might be present or not

Note| | Tunica Media is composed from variable amounts of smooth muscle cells (SMCs), collagen and Elastic T throughout different blood vessels types. We will talk about this in details but put in mind that the ratio of these component will be different. In Elastic (large) vessels mainly Elastic T, In Muscular (medium sized arteries) >> mostly SMCs.
also notice that >> the internal elastic lamina and external elastic lamina look like they surround the Tunica media.

III. Tunica Adventitia (or tunica externa) correspond to the epicardium of the heart, composed of

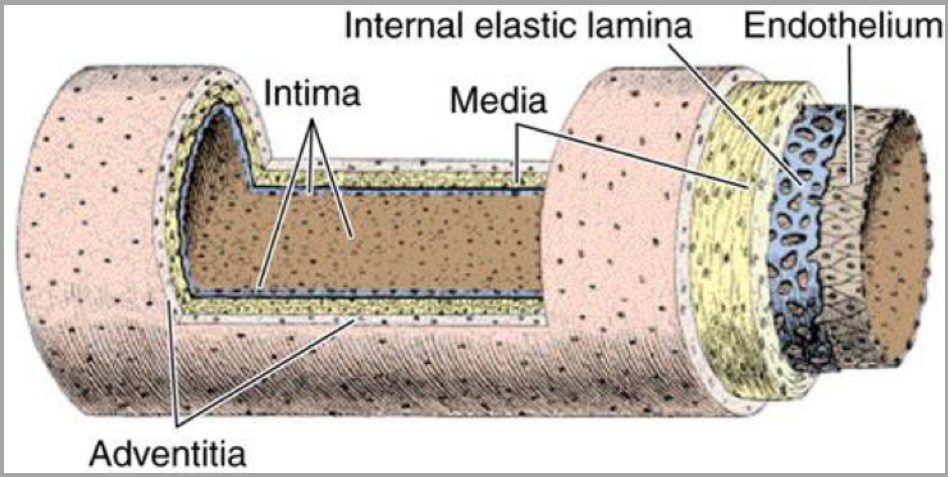
- Connective Tissue (Elastin + Collagen type I**)**
  also contains
- Unmyelinated autonomic (sympathetic) nerve fibers which when activated induce vasoconstriction of smooth muscle cell in tunica media
- Vasa vasorum (vessels of the vessels): -figure3
  these are arteries of the (arteries or veins), they are present to supply the outermost layers of the vessels (tunica adventitia + outer half of tunica media in elastic arteries), because:
  - Either, the wall is too thick to be nourished solely by diffusion from the blood in the lumen. E.g. the wall of elastic arteries such as the aorta
  - Or, the luminal blood carries deoxygenated blood. E.g. veins although they have thinner walls

    Note: veins usually have a much more extensive supply of vasa vasorums than arteries

Note||

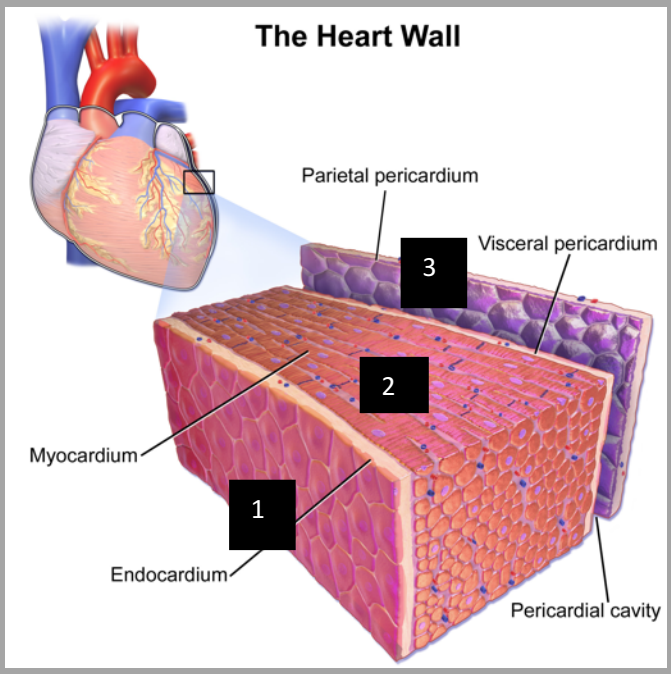
- Parasympathetic system which causes vasodilation do not have direct effect on blood vessels (no parasympathetic supply). So vasodilation is caused by local metabolites, like NO release from endothelium >>which will affect the smooth muscle cell >>vasodilation.
- Put in mind that the SMCs can contract by itself, not under the sympathetic contraction. This is called myogenic contraction
  -not mentioned here but in the lab-
  Myogenic contraction refers to a contraction initiated by the myocyte cell itself instead of an outside occurrence or stimulus such as nerve innervation or hormonal stimulation.

Figure1: Basic structure of blood vessels



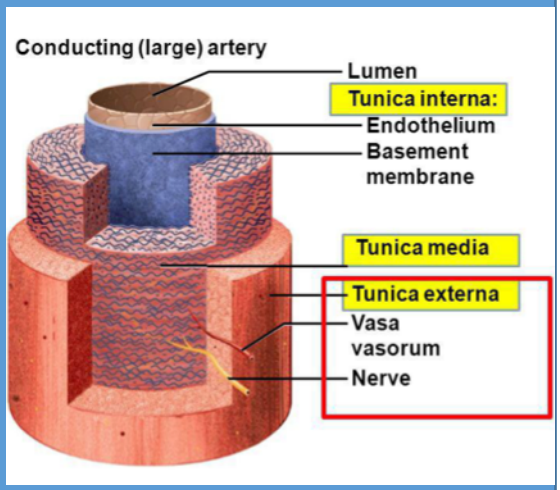
The blood vessel is composed from :
Tunica Intima , Tunica Media , Tunica adventitia

Figure 2: the heart wall correspond with vessels histology



1:The Endocardium correspond with the intima
2:the myocardium correspond with media
3:the epicardium correspond with adventitia.

Figure 3: Vasa vasorum



c. Blood flow:

Blood flow (flow rate) is the quantity of blood that passes a given point in the circulation in a given period of time.

In order for blood to flow through a vessel (or even across a heart valve) there:

1. must be a force propelling the blood. This force is the difference in blood pressure (i.e. pressure gradient ΔP) across the vessel length or across the valve. So blood flows from high pressure in the aorta to low pressure in the vena cavas.
   Note that It is the difference in pressure between the 2 ends of the circulation not the absolute pressure in the vessel that causes blood flow. For example: if the pressure in the aorta was 100 mm/HG and in the vena cavas also 100mm/Hg then ΔP=0 and thus flow=0

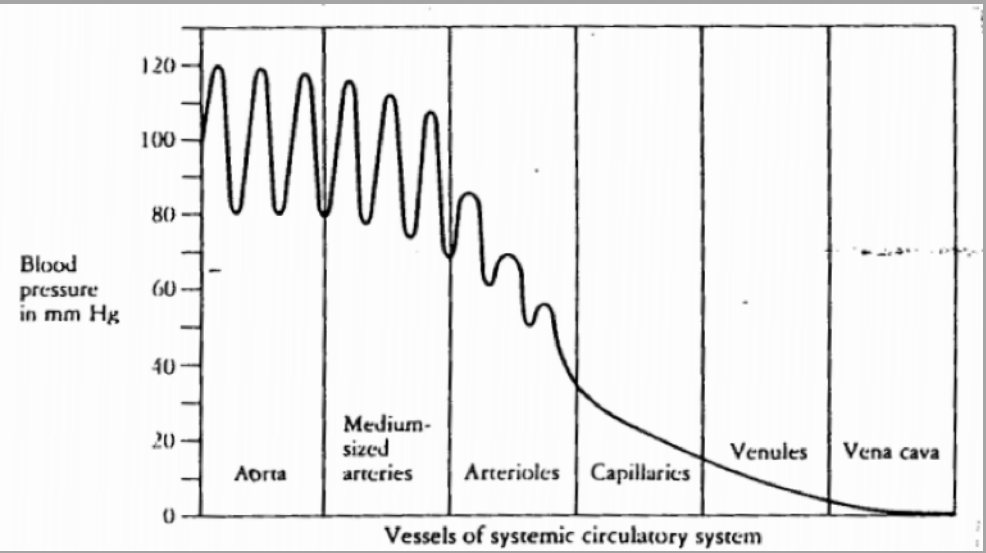
2. Resistance –R- (the impediment (hindrance) to blood movement in a vessel) to that flow.

So flow = ΔP / R OR ΔP= flow × R

In the cardio vascular system ventricular contraction is not the main reason of blood flow to organs. But!! It is resistance that will cause blood movement.

To understand how…please look at figure 3.

Figure 3: Blood pressure falls



Follow :the distribution of blood vessels VS the corresponding blood pressure.
overall the pressure decrease

From the figure you could notice:

1. When blood is pumped from the left ventricle to the aorta the mean (pressure value not the pressure difference) arterial pressure is 93 mm Hg due to the ventricular contraction.
2. When the blood reaches medium sized arteries the mean arterial pressure is approximately 65 mm/Hg so ΔP= 93-65=28 and thus if the vessels conducting blood from the ventricles to the organs were only composed of large arteries (the aorta) and medium sized arteries blood will not reach the organs.
3. When the blood reaches the small size arteries known as arterioles (say of the kidney) the mean arterial pressure becomes 37 mm Hg due to high **resistance.**

   ΔP= 93-37=56 mm/Hg and thus blood is able to reach organs.

   So resistance is the factor that will insure blood will flow and reach organs because ventricular contraction by its own is not sufficient to deliver blood to organs.

   How does the arteriole create such resistance (or why does the pressure fall in arterioles)??

   ✓ The arteriole has much smaller lumen than big arteries near the heart

   ✓ SMCs at the wall of the arterioles will also contract >> further minimizing the lumen>> higher resistance.

2. *Arteries :*

Arteries are classified according to their size into:

- Large arteries
- Medium sized arteries
- Small size arteries =arterioles

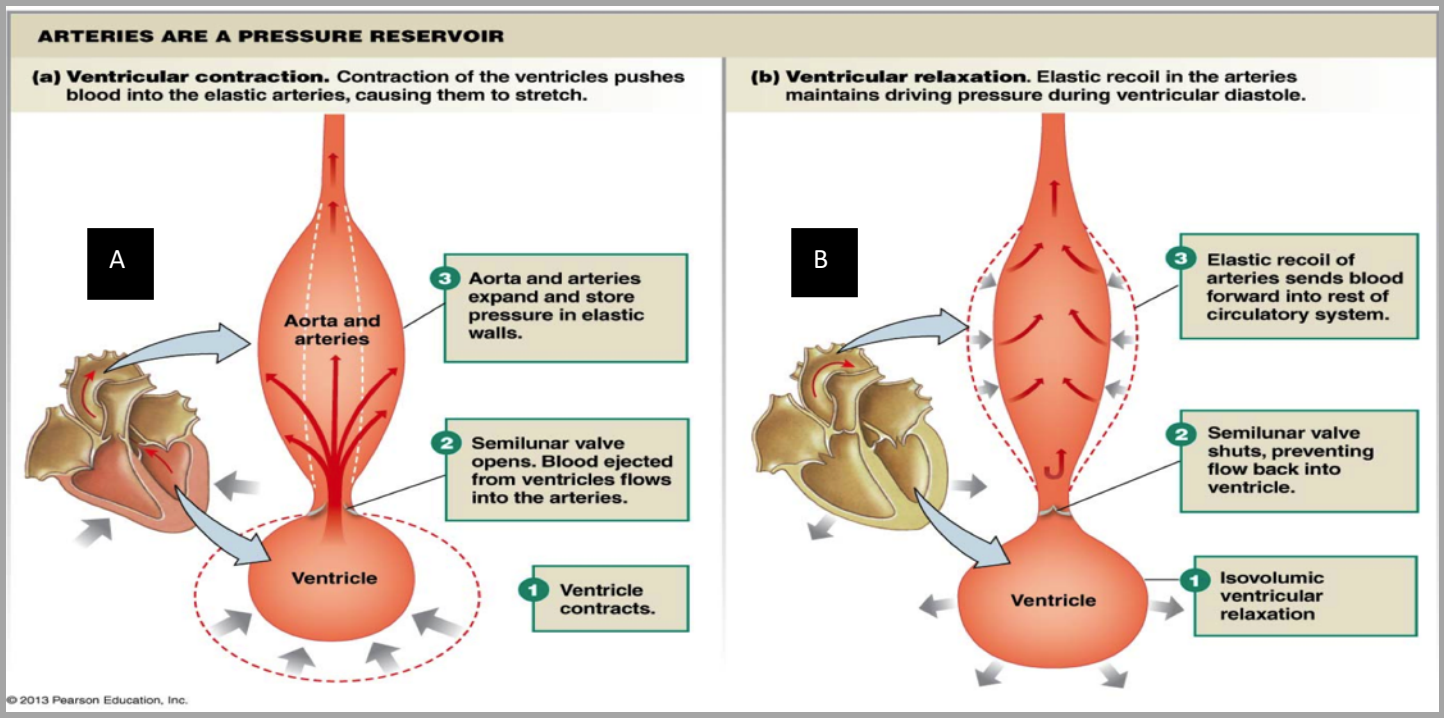
Large arteries

Large arteries OR elastic arteries OR conducting arteries, like the ascending aorta, arch of the aorta and its branches.

The most prominent feature of elastic arteries is the thick tunica media in which present around 40-70 fenestrated elastic lamina (sheaths of porous Elastic tissue).
Why do elastic arteries contain this high amount of elastic lamina??
Because Elastic Arteries recoil and expand …and thus ensure a continuous blood flow. So because elastic arteries contain a lot of elastin fibers in their media, they have the ability to expand when filled with blood during systole of the heart and recoil back during diastole of the heart.

This flexibility (ability to recoil) is what provides continuous blood flow; otherwise blood flow will be intermittent occurring only during systole.
Figure 4 (it is important to read the Key).

Figure 4: recoil after expansion (elastic arteries)



[A] During systole: in (isovolumetric contraction of the heart) the semilunar valves are closed .in ejection phase the semilunar valve open > the aorta filled with massive amount of blood here the aorta expand.
[B] During diastole > the valve close and the aorta recoil. >>recoiling pushes the blood and compensates the absence of the blood flow from the ventricle during this phase.

Medium sized Arteries

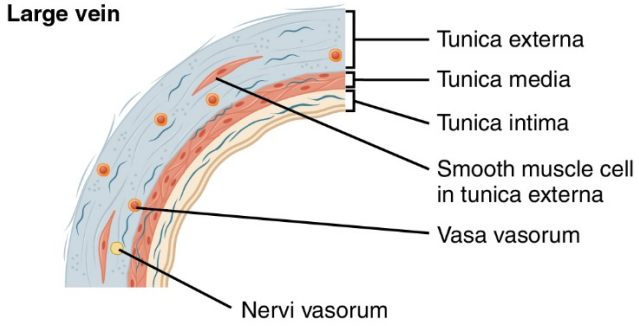
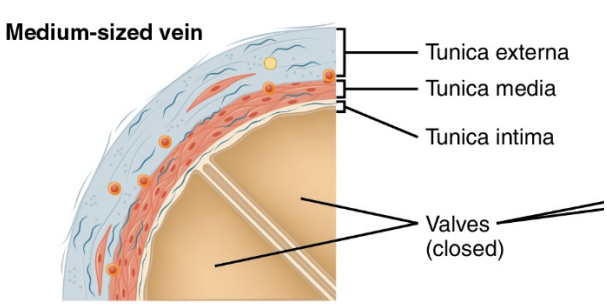
Medium sized arteries OR Muscular arteries OR distributing arteries. Example: ulnar, radial, femoral arteries.

Here the media is mainly composed of SMCs. 40 circular/ spiral layers of SMC. between SMC there are also collagen and elastic fibers.

Why they have called it distributing arteries?

Because with regard to blood supply to muscular Tissue, these arteries are 'the BOSS'; they control (by their SMCs) how much blood is distributed to muscles. if they contract >> they limit the blood flow to muscles

If they relax >> they enhance more blood flow to muscles

Elastic artery	Muscular artery
	
The Intima is thicker	The Intima is much thinner
The IEL is not clear here	IEL clear (2 layers)
Media : made of fenestrated elastic lamina (40-70) , in between there are SMC and collagen	Media: muscular mainly (40 layers)
EEL : not very clear	EEL : clear (3 layers)
Thinner adventitia	Thicker adventitia

Note| |

- Note the endothelium contain Weibel–Palade bodies , these contain special substances important for many endothelial function , like vWF for coagulation.
- (the doctor mentioned this in the lab) these fibers (collagen+ elastin) in vessel are synthesized by the endothelial cells , NOT fibroblasts.

Arterioles :

Arterioles OR small sized arteries. The smallest arterial blood vessel (less than .1 mm in diameter)
because arterioles provide high resistance to blood flow it is called 'major resistant vessel' ; because they create a high resistance that aid in creating pressure difference and eventually Blood movement.
The Arterioles are of two types : small and large (figure5)

Figure 5: small Vs large arterioles

Small arterioles	Large arterioles
Media : only SMCs (single layer)	Media : only SMCs (2-4 layers)
Intima : endothelium resting on BL	same
No separation between intima and media	Separation between intima and media

Note: We can identify the number of layers from the nuclei of SMCs

Metarterioles:

Arterioles supplying a capillary bed typically form smaller branches called metarterioles in which some smooth muscle cells are present between metarterioles junction with capillaries forming what is called precapillary sphincter. Between the arterioles and post capillary venules is a central channel formed from it arterial end by metarterioles and from its venous end by thoroughfare channels.

Note that central channels contain precapillary sphincter as part of the metarterioles at their arterial side ,but central channels don't contain precapillary sphincters at their venous side.

So from metarterioles blood can either: perfuse into the capillary bed or bypass it.

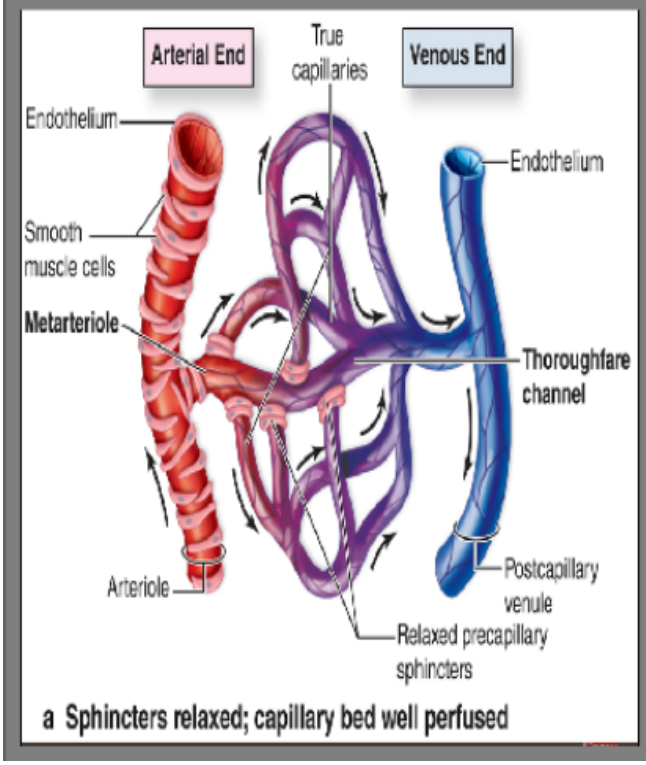
How??

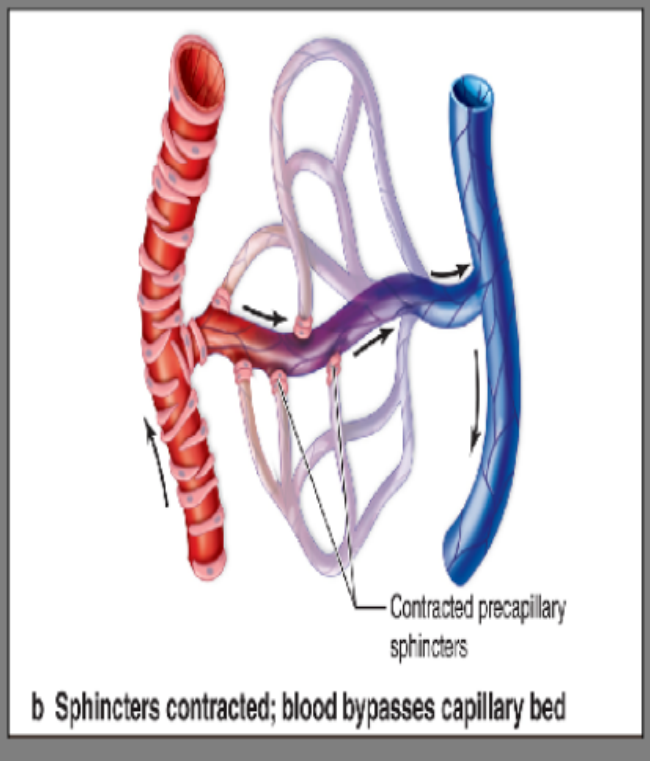
1. Blood perfuse into the capillary bed when the precapillary sphincter is relaxed

2. Blood bypasses capillary bed through the central channel when the precapillary sphincters are closed

For better understanding please study figure 6

Figure 6





Why do we need this system?
For the sake of regulation.
For example during exercise we need the blood to pass to the capillaries to wash out the accumulated lactic acid >> so the sphincter get relaxed.
During resting state>> blood flow to the capillaries is reduced >> so the sphincter closes.

What really happen is that the sphincter can only dilate as a response to local metabolites (like lactic acid and NO). These metabolites increase in amount when the organ is more active. At resting state the organ do not secret adequate amount of these metabolites as a result the sphincter stay contracted.

These changes in metabolites level cause dilation in Meta+pre:

- ✓ Raised in CO_2 (specially in CNS)

- ✓ Lowering the PH (by lactic acid)
- ✓ Increasing K^+ , Lactic acid (specially in muscles), Adenosine (specially in heart)

Note||

Local Metabolites Vs Sympathetic control

the arterioles are highly rich with sympathetically controlled SMCs

But!!!

Metarterioles (precapillary sphincters) are mainly controlled by local metabolites.

Arteriovenous shunt and temperature regulation:

Blood can pass to venules through either :capillaries (which was through metarterioles)or Arteriovenous shunt (also called Arteriovenous anastomosis) so what is Arteriovenous shunt?? a direct connection between arterioles and venules (without passing through the capillaries and the metarterioles). These shunts are rich with SMCs.

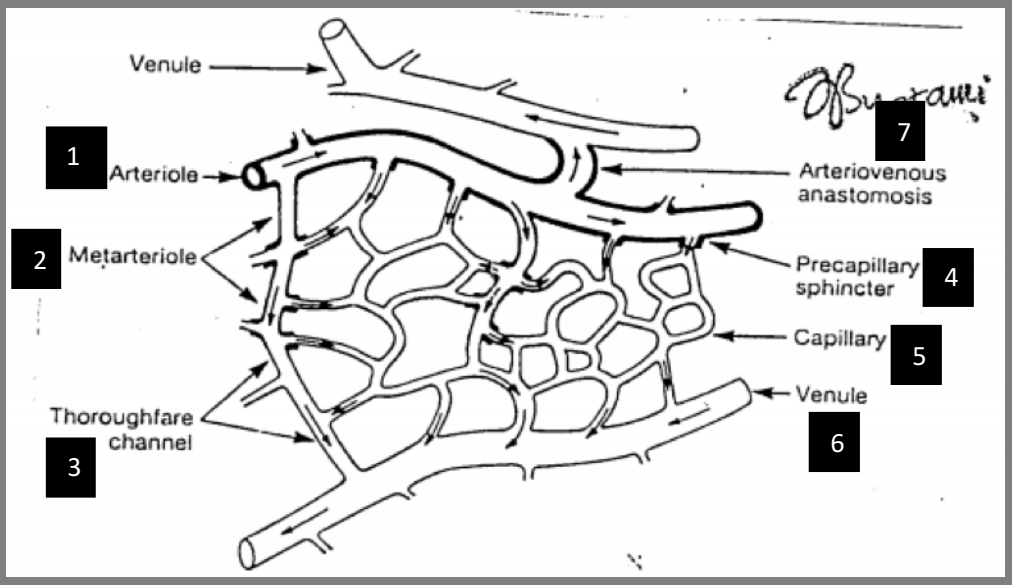
Structure of Arteriovenous shunt figure 7:

The arterial end and venous are similar to those of any artery or vein ,where as the intermediate segment has a thick tunica media and adventitia and richly innervated by autonomic nerve fibers.

It is believed that these shunts play a regulatory role with regard to temperature. The idea is based on that: if the blood could bypass the capillaries then this limits heat loss.
the hypothalamus is 'the master' of this process , if it sense excess heat in the body it work through a sympathetic reflex and notify the SMCs of these shunts to contract >> then blood pass by regular capillaries>> and heat is lost.
If someone felt cold >> we don't want him to lose heat >> AV shunt is relaxed >> heat is preserved.
To understand Arteriovenous shunts ,metarterioles, thoroughfare cannels pleas

study figure 7

Figure 7: metarterioles, thoroughfare channel and AV shunt



1: arteriole 2:Metarteriole 3:thoroughfare channel 4 : precapillary sphincter 5: capillary 6:venules 7:AV shunt

3. capillaries :

simple structure
Intima =endothelium resting on BL
media is absent
adventitia is minimal
[the capillary is really just an Intima=endothelium resting on BL]

Types of capillaries

classified according to the shape of the endothelium and BL (figure8)

- ✓ **Continuous capillary**
  - Both the endothelium cells and the basal lamina are continuous
  - NO GAPS between endothelial cells
  - Example : Blood Brain Barrier (BBB) of the brain, Muscles , Connective tissue

- ✓ **Fenestrated capillary**
  - Both endothelium and basal lamina are continuous
  - No GAPs between cells, however there are pores on the membrane of endothelial cells. (transcellular transport)
  - Present at Kidney, intestines villi, endocrine glands.

- ✓ **Discontinuous capillary (sinusoids)**
  - Both the endothelium cells and the BL are not continuous
  - There are gaps between cells
  - Present at the liver , BM & spleen
    (recall this aid in the filtration function of these organs
    like the red pulp of the spleen << the gaps between the endothelium cells only allow healthy RBCs to pass , also recall that these gaps contain macrophages that phagocytosis any old RBCs)

Note| |

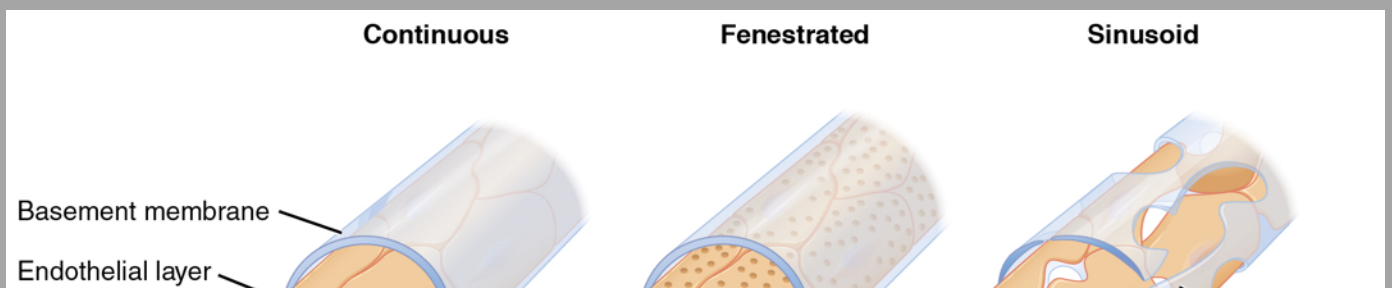
Blood Brain barrier

recall in pharmacology, we've said that a lot of drugs cannot cross BBB, while others can>>those cause CNS effects. So what is the blood brain barrier?

Modified continuous capillaries which have extremely low permeability

these capillaries have no Gap junctions, their basal lamina is thick and they are surrounded by special neuroglial cells (astrocytes)

Figure 8: Capillaries types



4. veins :

Venous system is classified according to the size into:

1. **Post capillary venules**
2. **small veins**
3. **Medium size veins**
4. **Large veins :not discussed in this lecture.**

1. Post capillary

- ✓ Composed from the union of many capillaries
- ✓ 10-50 micrometer in diameter
- ✓ Composed of :
  1. Tunica Intima: endothelium + basal lamina + Outside the BL there are some cells known as pericytes (have unknown function)
  2. Tunica media is absent in small venules
     As the vessel increases in size to reach a diameter of 50 micrometer scattered smooth muscles form incomplete tunica media
  3. Tunica adventitia: thin with collagen fibers
- ✓ function:

The thin wall of venules allow diapedesis of WBCs from blood stream to tissues

2. small size veins:

Circular smooth muscles form a complete tunica media (interspersed between smooth muscles: elastic + collagen fibers)

3. Medium size vein

- ✓ Most numerous in our body
- ✓ Their adventitia is very well developed (with a lot of vasa vasorum, we've explained why earlier in this sheet.
- ✓ 2-3 layers of SMCs (continuous layers) *thin
- ✓ Contains a lot of valves >> to make sure that the blood is flowing in one direction.
- ✓ These veins can be superficial or deep.
- ✓ The deep are supported by the muscles in which they are impeded in , while the superficial have longitudenal layers of SMCs to support their wall. example on that is the great saphenous vein of the lower limb (remember this vein is superficial (!)) which need a lot of support during standing.

Clinical correlation : Varicose Veins

usually there are bridging veins (perforating) between superficial and deep veins these bridging veins contain valves if these valves became dysfunctional>>then blood will pass from deep veins (where the pressure is high) into superficial (where the pressure is low) , when blood is present in high amounts in the superficial veins >> they will dilate and become varicose (tortuous) hence the name varicose veins.

5. Special topics:

First: Functional end arteries Vs Anatomical end arteries

End artery is an artery without anastomosis from adjacent arteries, this implies that whenever the end artery is occluded (say by thrombus) then no other artery can compensate >> and the area in which this artery supply will undergo ischemia and infraction. End arteries can be of two types:

- ✓ **Functional end artery**
  - Here there is some anastomosis (however it is not adequate >> as if it is not there)
  - Example coronary arteries of the heart
- ✓ **Anatomical end artery**
  - no anastomosis is present –truly –
  - Example: interlober arteries of Kidney. (the kidney is made from 5 lobes each lobe is supplied by interlober artery , there is no anastomosis between different interlober arteries , so if one artery get occluded then part of the kidney will actually die)

Note: also the spleen and the retina contain end arteries. Occlusion of one arteries of the retina cause sudden blindness >> as no compensation can occur.

second: Vascular tone

Note: some aspects where covered in the introduction pages 6 + 7

vascular tone is defined as the minimal contraction or basal contraction at the walls of arterioles without stimulation (only myogenic activity)>> which narrow down the lumen.

So normally the arteriole is narrower than its maximum size. It is stretched

what is the benefit from this?

By vascular tone we are setting a middle point from which we can both vasodilate and vasoconstrict the arteriole.

Without it (if the arteriole is relaxed) the only thing an arteriole can do is vasoconstriction.

In other words, If the arteriole is already stretched to its maximum Size we cannot dilate it further >> no vasodilation.

To sum up:
When the lumen is narrower than its maximum capacity (vascular tone)we can stretch it to its maximum size (vasodilation) or we can make it even narrower by vasoconstriction.

What is the importance of this is to maintain a constant blood flow when pressure changes. E.g. in hypertensive patients (high pressure) vaso constriction occurs in order to maintain constant blood flow.

Please study figure 9 in the last page (page 19)

Third: Differential stains for vessels :

We cannot depend on H&E stain to differentiate between different components of vascular tissue because most of the vessels components are red or pink stained so it would be hard to differentiate different layers and structures.

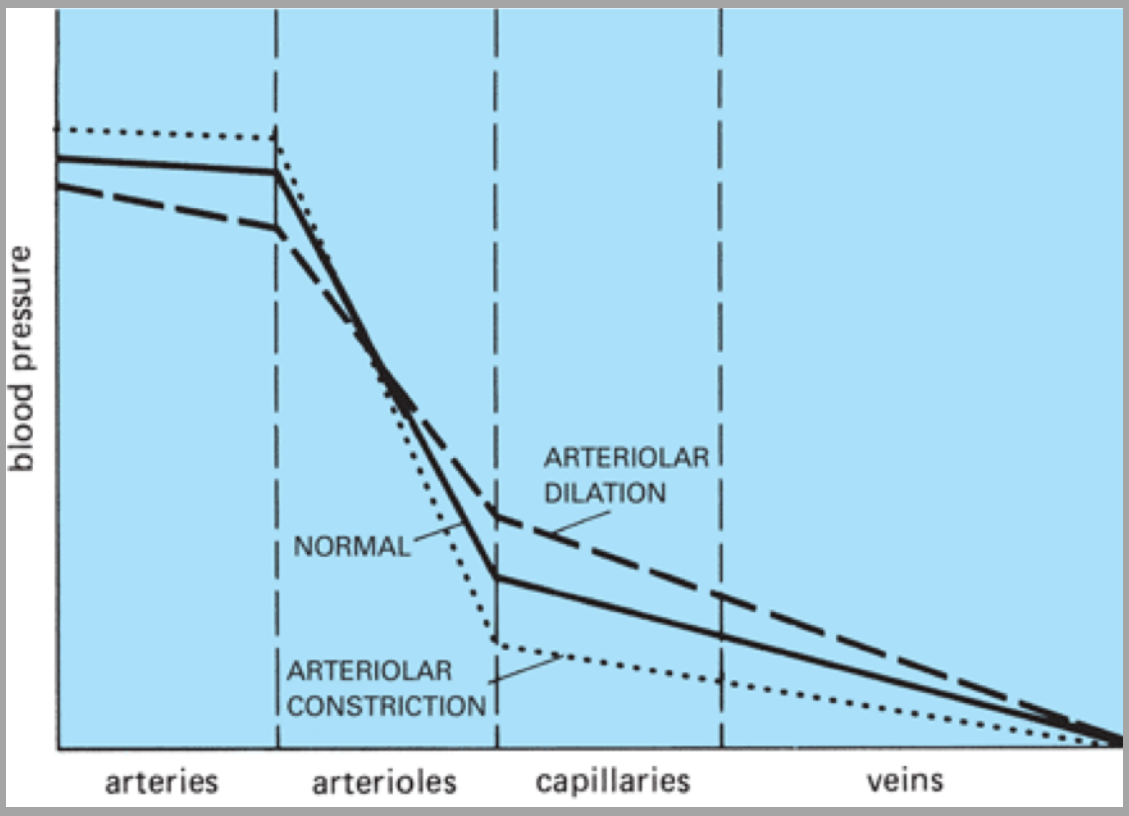
Recall that we differentiate between different types of vessels depending on different ratios of collagen, elastic and SMCs in media mainly>> so we cannot depend on H&E as they all appear similar.

	H&E	Elastin, Van Gieson	Masson's trichrome
Cytoplasm	Red or pink	Yellow to brown	Bright red
SMC	Red or pink	Yellow to brown	Bright red
collagen	Red or pink	Red	green
Elastin	Poorly stained pink	Blue/black	Blue /black

We really depend on Masson's trichrome as it stains each component differently.
-in the lab slides u will see a lot of Masson's trichome stained sections.

one thing left , I keep it to finish the sheet with –as it enhance the idea of considering the CVS as closed system (one tube)

Figure 9: CVS is a closed system (one tube)



First orient your-self with x and y axis.
We want to observe changes in pressure of different vessels if we change the diameter of the arterioles, so follow the lines starting from the arterioles then up to arteries, then down to capillaries and veins:

- **In Arteriolar constriction (by sympathetic) the blood will accumulate in arteries raising their pressure, while downstream (in capillaries and veins) the pressure will decrease. Due to decrease the pressure in the capillary absorption increases there.**
- **In arteriolar dilation (by local metabolites) the arteries will "empty" faster which decrease their blood pressure, while downstream (in capillaries and veins) the pressure will increase as more blood into there. So here filtration increase in the capillaries.**

-END OF TEXT :3