The Cardio-VASCULAR System

- ○ Anatomy
- ○ Histology
- ○ Pathology
- ○ Pharmacology
- ○ Physiology
- ○ Microbiology
- ● **EMPRYOLOGY**

Lec #: **2**

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- ○ Handout
- ● Sheet
- ○ Slide

Fetal circulation and congenital anomalies of heart development

- Flashbacks from the first lecture

- Oxygenated blood will come from the placenta along the left umbilical vein, this blood will bypass the liver and open into the inferior vena cava which will open in the right atrium then this highly oxygenated blood passes to the left atrium. What are the factors that facilitate movement of this oxygenated blood from right to left atrium?

1. During fetal life the blood pressure in the Right atrium is higher than the left atrium, this helps in the movement of blood by down-pressure gradient.
2. The valve of inferior vena cava will guide most of the oxygenated blood to run from the right atrium to the left atrium
3. Lower edge of septum secundum which is called **crista dividens** creates a boundary between oxygenated blood coming from the I.V.C and venous blood from S.V.C and coronary sinus, thus the greater volume of oxygenated blood will pass to the left atrium and the remainder join with the venous blood and pass the right ventricle.

-always remember the origins of each part of the atrial champers of the heart:

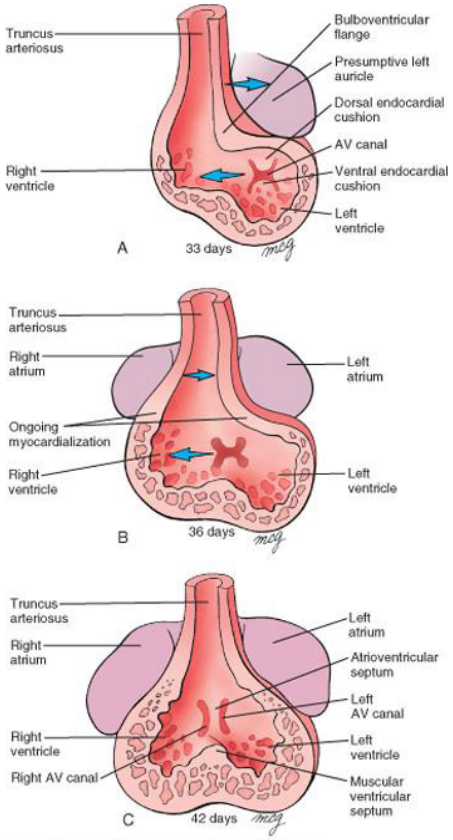
Right atrium: the anterior rough part is derived from right half of primitive atrium while the posterior smooth part (sinus venerum) is derived from the right horn of sinus venosus.

Left atrium: only the auricle is rough and it is derived from the left half of the primitive atrium, the remainder of the left atrium is smooth and it's derived from the pulmonary vein.

Ventricular septation

- Septation of the primitive ventricle into right and left ventricles occurs **simultaneously** along with the septation of the primitive atrium to right and left atria.
- Sequence of ventricular septation are:

1- Initially there was a septum between bulbus cordis and primitive ventricle, seen as a sulcus from outside called deep bulbo-venticular sulcus, this septum gradually disappears then bulbus cordis and primitive ventricle form one chamber called **bulboventicular chamber.**



2- The first indication of the division of bulboventicular chamber to right and left ventricle is the formation of the muscular part of the septum (called ventricular septum), this muscular part will grow from the floor upwards toward **septum intermedium**

3- Before the muscular part reaches and fuses with septum intermedium, a gap is found between the 2 parts called **interventricular foramen**

4- More distal from the floor of the bulboventicular chamber 2 septa will be formed: **proximal bulbar septum** (was initially two bulbar ridges then fused) which divides the middle part of bulbus cordis to infundibulum on the right and aortic vestibule on the left and **distal bulbar septum** dividing the upper part of the bulbus cordis and forming a pulmonary valve above the infundibulum and an aortic valve above the vestibule.

How will the interventricular septum close? By proliferation of:

A- Fused endocardial cushions (septum intermedium)
B- Proximal bulbar septum

The proliferation of these two parts will form the **membranous part of interventricular septum which has an anterior interventricular part and a posterior atrioventricular part. Keep in your mind that the closure of the interventricular foramen happens a long time before birth.**

Why the interventricular septum has interventricular and atrioventricular parts?

This is related to the attachment of septal cusp of tricuspid valve to the membranous part of interventricular septum. Normally during development septum premium grow in the upper part and reach septum intermedium and muscular part of interventricular septum grows upward and fuse with septum intermedium, due to differential growth the interatrial septum move the septum intermedium upwards while the ventricular septum move the septum intermedium downwards, initially the interatrial septum and interventricular septum are not at the same level, but due to this movement they reach the final form and become at the same level. And when the septal cusp attaches to the membranous interventricular septum its posterior part above septal cusp becomes atrioventricular.

Which parts of the bulboventicular chamber form the right and left ventricle? Both rough and smooth parts of right ventricle are formed by bulbus cordis, while rough part of left ventricle ->Primitive ventricle. While smooth part and aortic vestibule from bulbous cordis.

Distal bulbar septum

In the distal portion of bulbus cordis four endocardial cushions will be formed: anterior, posterior and 2 lateral, 2 ridges will form in the middle of each of the two

lateral cushions until they fuse forming the distal bulbar septum. As a result from that the distal portion of the bulbus cordis is now divided to pulmonary orifice anteriorly and aortic orifice posteriorly.

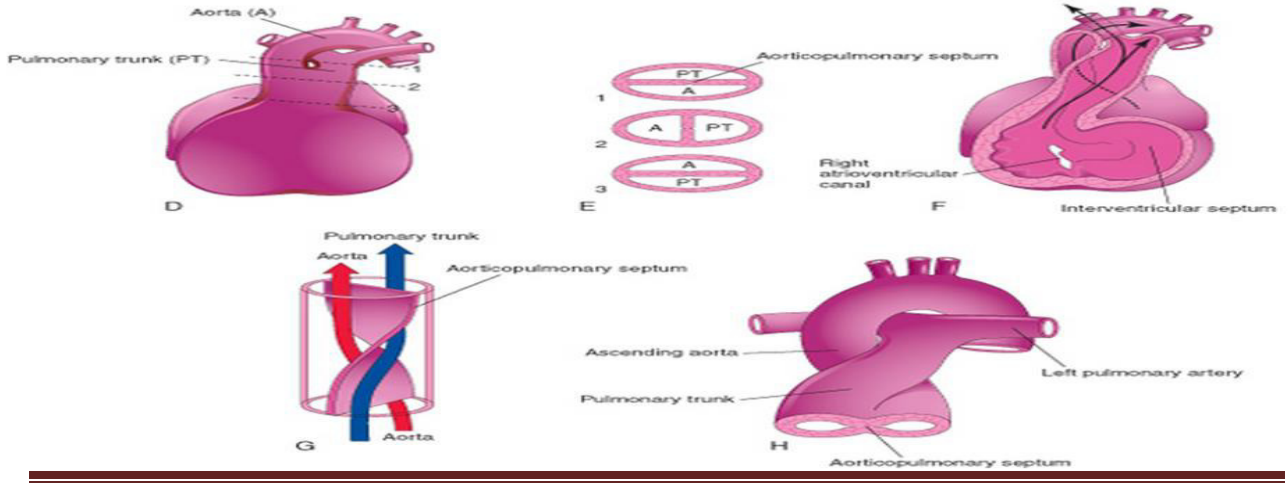
The formation of distal bulbar septum divides each lateral cushion into two cushion consequently both the pulmonary and aortic orifice will have 3 cushions which form pulmonary and aortic semilunar valves.

initially the cusps of pulmonary valve were 2 posterior and one anterior while the aortic valve 2 cusps anterior and 1 cusp posterior then because of rotation of pulmonary vessel around aorta the position of these cusps will become reversed (aortic valve: 2 P + 1 A, pulmonary: 2 A and 1 P)

Septation of truncus arteriosus

Truncus arteriosus represents the arterial end of primitive heart tube (the most cranial end), 2 ridges will be formed inside truncus arteriosus (right and left ridge) the position of these ridges vary according to the part of truncus arteriosus, in the lower part of truncus arteriosus they were right and left ridges -> in the middle part the right ridge became anterior and left ridge became posterior -> in the upper part the anterior ridge became right while the posterior ridge became left.

When these two ridges fuse with one another a **spiral septum** called aorticopulmonary septum dividing truncus arteriosus to aorta and pulmonary trunk



*because the aorticopulmonary septum is spiral and not straight a triple relation will be formed between aortic arch and pulmonary trunk (VIP) these relations are:

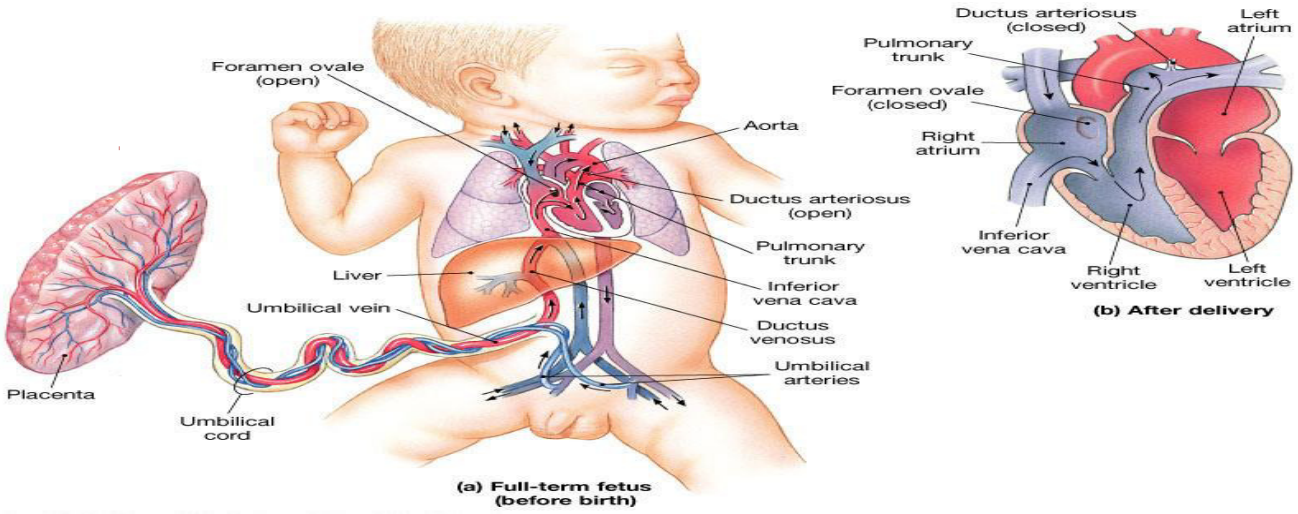
1- At the beginning the pulmonary trunk is **anterior** to the ascending aorta
2- Then the pulmonary trunk becomes to **the left** of the ascending aorta
3- Then the pulmonary trunk under the arch terminates **posterior** to the aortic arch

Transposition of great arteries

- It is a congenital anomaly characterized by the presence of a straight aorticopulmonary septum instead of a spiral one, this will cause deoxygenated blood to pass through the aorta and highly oxygenated blood to pass through the pulmonary trunk.
- Normally the presence of a spiral aorticopulmonary septum ensures that the pulmonary trunk carry deoxygenated blood from the right ventricle and the aorta carry oxygenated blood from the left ventricle
- This condition is **incompatible with life** because the brain will receive deoxygenated blood **UNLESS there was an interatrial or interventricular septal defect leading to mixing of blood so that the blood carried by the aorta is mixed (oxygenated and deoxygenated) other than that the fetus die early** in life

Fetal circulation

- This is one of the most important subjects in the cardiovascular system since it is related to many congenital anomalies that can form.



- Highly oxygenated blood from the placenta will be carried through left umbilical vein (right umbilical vein disappears very early). If we follow the left umbilical vein it will open into the **left branch of portal vein**, logically when blood pass through the portal vein it must reach the liver for metabolism however in the fetus the contents of the blood are already metabolized in the placenta so there is no need for this blood to go into the liver, how would the blood from left umbilical vein bypass the liver? **Through ductus venosus which arise from left branch of portal vein and shunt the oxygenated blood to the I.V.C and little blood pass into the liver.**
- Blood in the I.V.C will eventually reach to the right atrium. So the right atrium receives two types of blood: Oxygenated through umbilical vein -> IVC and deoxygenated blood from the upper half of the body through Superior vena cava. Even though these 2 types of blood enter through the same chamber, <u>little mixing of blood actually occurs</u>, how? By the action of **valve of inferior vena cava which directs the movement of blood from IVC directly toward foramen ovale, this limits mixing between the two blood types.**

- Most oxygenated blood pass from the right atrium to the left atrium through foramen ovale by **pressure difference** (before birth pressure of the R.atrium is higher than L.atrium), then from the left atrium to left ventricle through mitral opening -> Ascending aorta –> Arch of the Aorta -> Upper half of the body

- Deoxygenated blood pass to the right atrium and little mixing with oxygenated blood happens so oxygen saturation of that blood remains less than the oxygen saturation of the blood coming from the placenta. From the right atrium blood pass to the right ventricle then to the pulmonary trunk which divides into right and left pulmonary arteries, **from the left pulmonary artery ductus arteriosus will arise and attach this artery to the distal part of arch of the aorta, this will make the lower half of the body receive poorly oxygenated blood shunted from the pulmonary artery through ductus arteriosus. This blood will return through the umbilical artery back to the placenta.**

Oxygen saturation changes in the blood coming from the placenta:

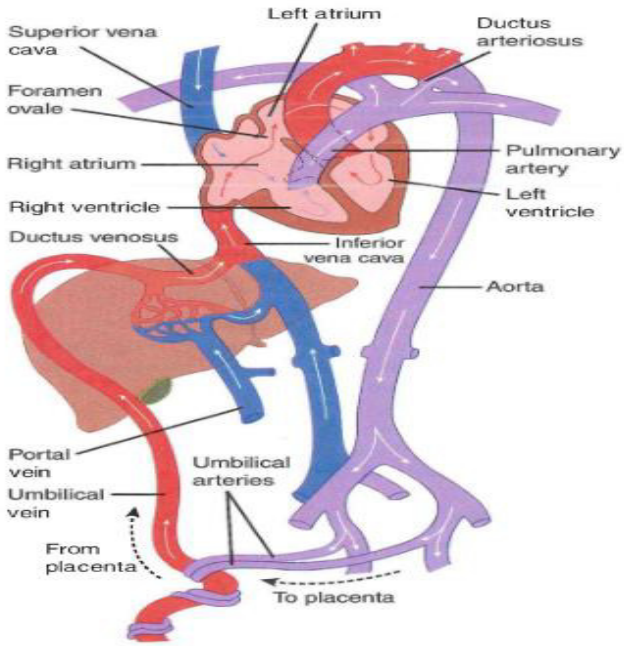
Blood coming from the placenta through left umbilical vein have an oxygen saturation of 80%, then mixing of blood appears at many stages including:

1- At the level of ductus venosus: deoxygenated blood from the gut through portal vein mix with the oxygenated blood
2- In the inferior vena cava : deoxygenated blood from the lower half of the body mix with the oxygenated blood coming from the placenta
3- In the right atrium there is a little mixing with the deoxygenated blood coming from superior vena cava
4- In the left atrium: there is a little mixing with deoxygenated blood coming from the lungs through pulmonary veins
5- In the distal part of Arch of the aorta: deoxygenated blood shunted from ductus venosus mix with the oxygenated blood in the aorta.

Eventually oxygen saturation will drop from 80% to 62% in the left atrium but still we consider it highly oxygenated (because of reasons will study in physiology later).

Recap on the entire fetal circulation

Oxygenated blood (from placenta) ⇨ Left umbilical vein ⇨ left branch of portal vein ⇨ ductus venosus ⇨ Inferior vena cava ⇨ Right atrium (little mixing) ⇨ left atrium (through foramen ovale ⇨ left ventricle ⇨ Arch of Aorta (supply highly oxygenated blood to the upper part of the body by its branches then it becomes partially Deoxygenated because of ductus arteriosus shunt ⇨ Internal iliac arteries ⇨ from internal iliac arteries right and left umbilical arteries will arise and carry this partially deoxygenated blood to the placenta to become oxygenated and get carried by left umbilical vein then the cycle continues .



Changes in the fetal circulation after birth (Important)

- Immediately after birth the fetus is separated from the placenta by ligation of the umbilical cord <u>2-3 fingers away</u> from the abdominal wall, why? in order to avoid cutting the fetus gut if there was a persistent umbilical hernia, we took before in the embryology of the GI tract that the mid-gut rotate and stay in the umbilical cord between week 6 and 9 of gestation, this may persist till birth in some cases so when we cut the umbilical cord we cut 2-3 fingers away from the abdominal wall.
- After that the newborn takes his first breath -> the lungs will expand -> the arterioles within the lung will also expand -> **decrease in pulmonary vascular resistance to blood flow ->** Blood will flow easily in the pulmonary trunk -> **this will consequently decrease the blood pressure in the pulmonary trunk, right ventricle and right atrium**, this what happens in the pulmonary circulation.

- **What happens in the systemic circulation? (focus here)**

  Recall that the systemic circulation is made of many resistance areas (renal circulation, hepatic circulation, placental circulation …… etc.), these resistances are connected على التوازي not على التوالي which means that their total resistance equals:

  1/ total resistance = 1/R1 +1/R2 + 1/R3

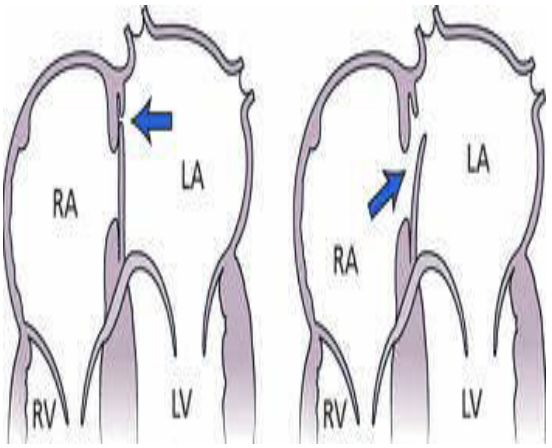
  If they were connected على التوالي the total resistance equals to the sum of all of peripheral resistances

  -Now when we ligate the umbilical cord we removed one of these peripheral resistances which is the placental resistance what will happen to the total resistance?

  According to the law the total resistance will **INCREASE** (if you don't understand this you will later in physiology)

- Since the total systemic circulation has increased, the blood pressure in the Aorta will increase which will increase the blood pressure in left ventricle eventually increasing the blood pressure in the left atrium.

Note: remember that we said when the lung expands the blood pressure inside the right atrium decrease and now we said that the blood pressure in left atrium increase because of higher systemic resistance -> **this high blood pressure in the left atrium will push septum premium on septum secundum closing foramen ovale**.



- Recall that we have 4 major shunts in the fetal circulation which are :(important)

1- Interventricular foramen: closed many weeks before birth
2- Foramen ovale: closed immediately after birth

3- Ductus venosus: which shunts the blood from the left umbilical vein to the IVC bypassing the liver, how is this shunt closed? By ligating the left umbilical vein, no blood will pass through ductus venosus so it will collapse and turn into a ligament.

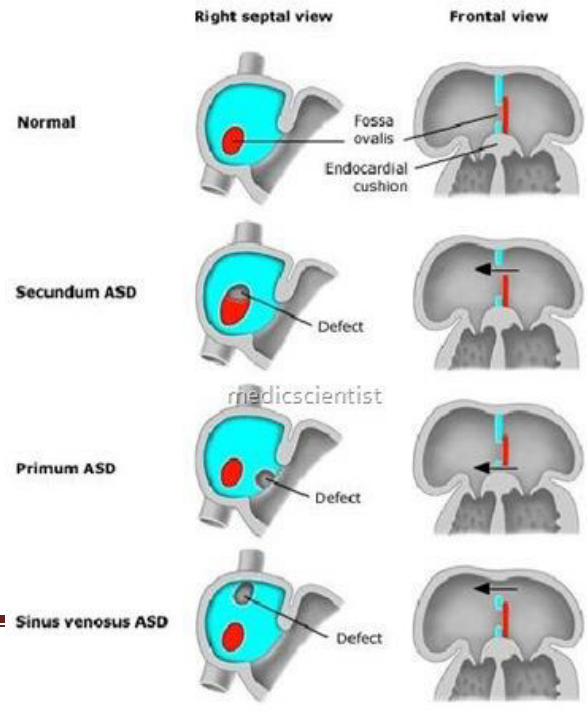
4- **Ductus arteriosus**: this shunt will remain open for 1-2 days after birth and then it will close, how it closes? Recall that ductus arteriosus is subjected to low oxygen tension (poorly oxygenated blood) coming from the pulmonary artery into the aortic arch. After birth the pressure inside the Aortic arch increases due to increase systemic resistance, so highly oxygenated will blood can pass from the aorta to the pulmonary through ductus arteriosus by pressure gradient consequently the smooth muscles in the wall of ductus arteriosus will become subjected to high pressure tension -> these smooth muscles will contract constricting the vessel (ductus venosus is a vessel) and after 1-2 days ductus arteriosus will become converted into ligamentum arteriosum. (always remember that this shunt doesn't close immediately after birth like 2+3 it takes 1-2 days)

Congenital anomalies of heart development

Atrial septal defect

-It is an opening between the right and left atria in the interatrial septum .this defect has many types:

1- **Low atrial septal defect**: caused from persistence of ostium primum. We said that normally before septum primum fuses with septum intermedium (fused endocardial cushions) there was an opening called **ostium primum** this opening may persist and form a type of atrial septal defect called **low atrial septal defect. This**



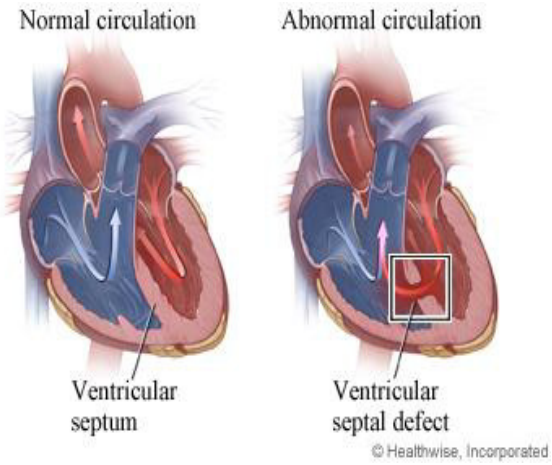
defect is usually caused from a defect in the endocardial cushions.

2- **High atrial septal defect:** caused from failure of septum secundum to develop so that foramen secundum remains wide open.
3- **Patent foramen ovale** : septum primum and secundum form normally but oblique passage between them (foramen ovale) remains open

Clinical consequences: if the defect was large enough blood will be **shunted** from left atrium (higher pressure after birth) to right atrium -> right ventricle -> pulmonary trunk -> lungs -> back to left atrium -> part of the blood will be shunted to right atrium and the remaining goes to left ventricle.

From this we conclude that the patient will have decreased cardiac output from the left ventricle so he will have symptoms similar to heart failure (fatigue, weakness …)

Ventricular septal defect



If it was small no shunting of blood will happen this is called Roger septal defect and the patient is asymptomatic, but if the defect was large blood will be shunted from the left ventricle to the right ventricle during **systole** only, why?

Because during systole wall of the ventricle contract exerting pressure of about 120-130 mmHg in left ventricle while the pressure is 25 mmHg in the right ventricle so blood will be shunted according to pressure gradient, while in diastole the pressure is 0 mmHg in both champers.

Remember that this defect is most common in the membranous part of interventricular septum

Clinical presentation: same as atrial septal defect there will be decreased cardiac output from left ventricle because some of the blood is passing to right ventricle.

On long outcome:

1- The right and left ventricles undergo **hypertrophy**, because the right ventricle is pumping more blood than it supposed to (venous blood +shunted blood from left ventricle). Left ventricle undergoes hypertrophy because it is pumping blood to both Aorta and right ventricle. (IMPORTANT)

2- The arterioles of the lungs undergo vasoconstriction since they are receiving more blood than normal, this vasoconstriction will increase the blood pressure in the pulmonary circulation (pulmonary hypertension) which will elevate the blood pressure in the right ventricle. **If the blood pressure in the right ventricle became more than the left ventricle the shunt will be reversed from right to left, this condition is called Eisenmenger's syndrome.**