ANATOMY

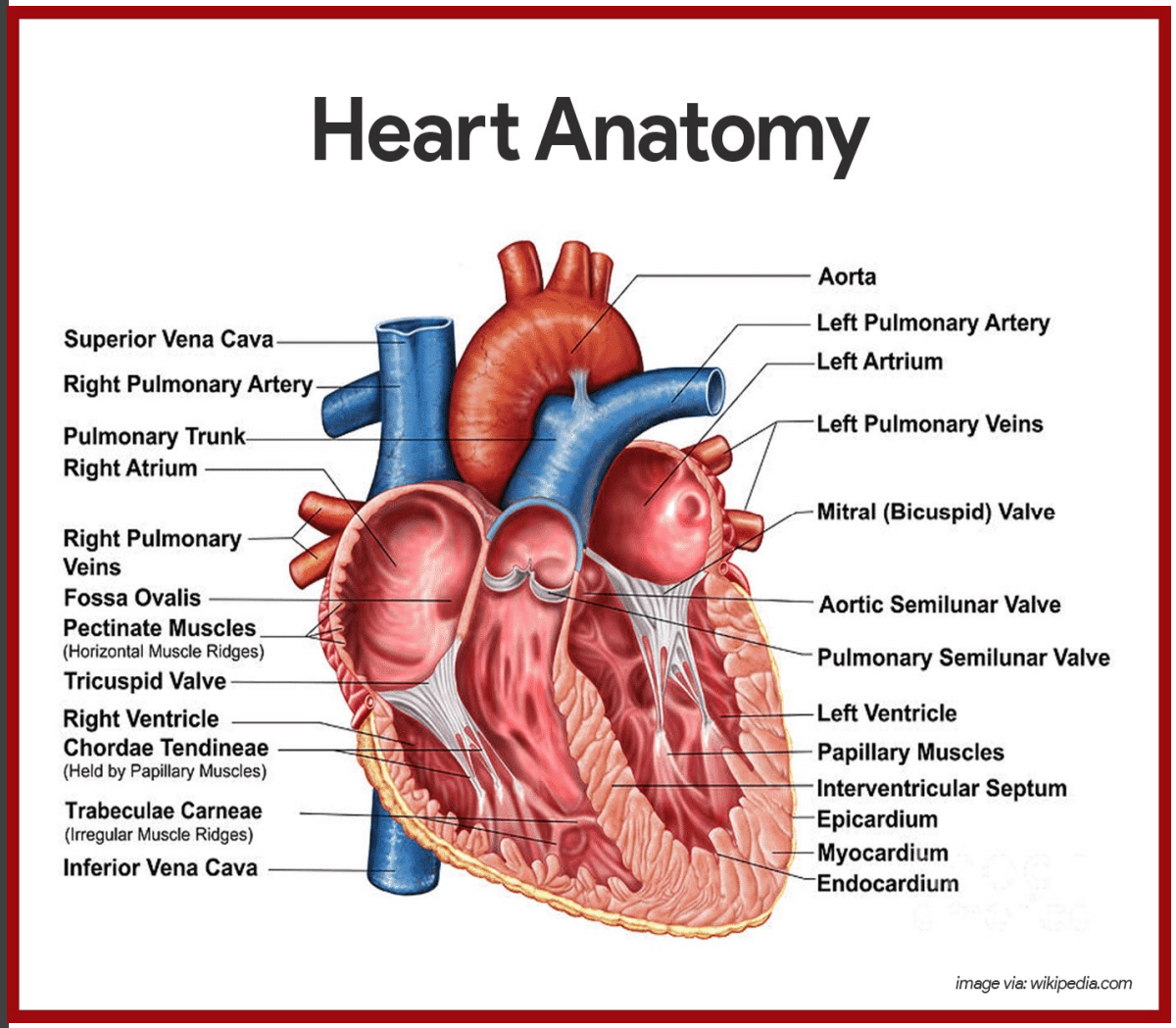
EMBRYOLOGY

EMBRYOLOGY

DEVLOPMENT OF THE HEART

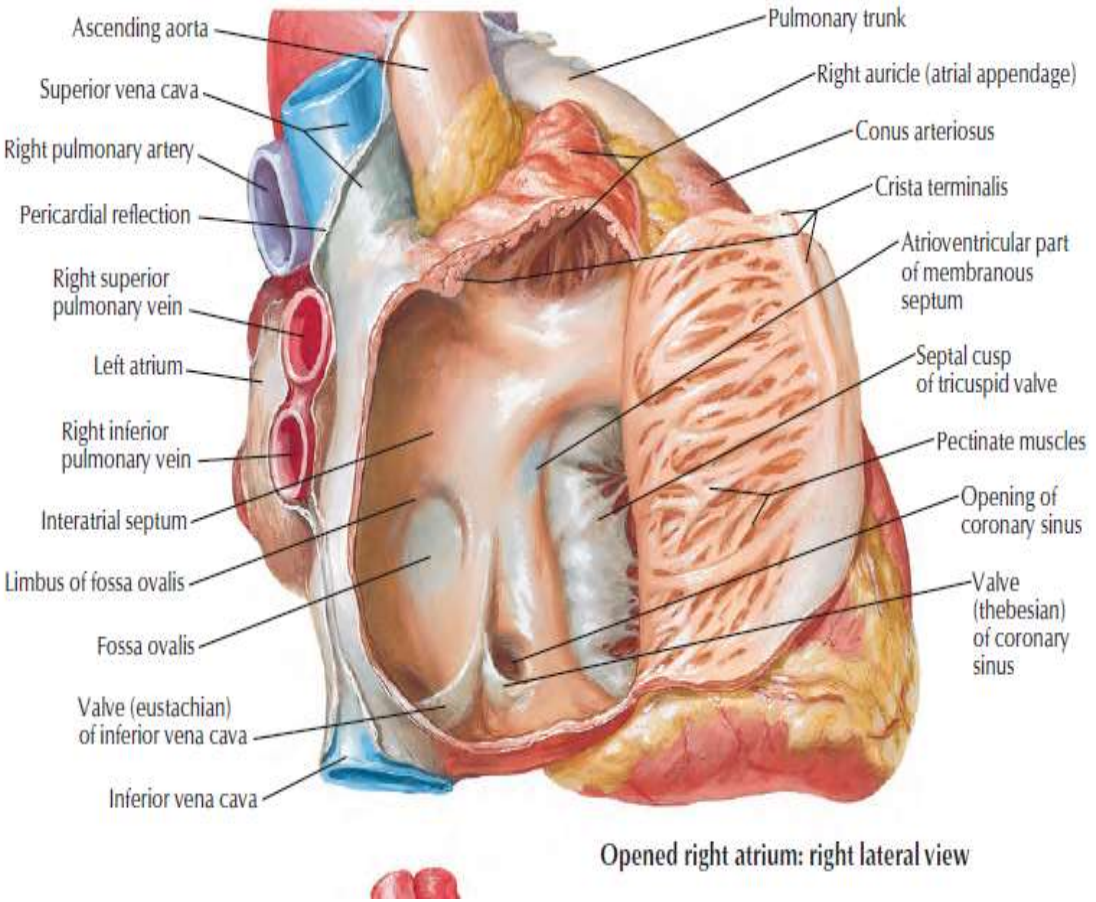
Normal Heart Structure

Heart Anatomy



HEART

Normal Anatomy



Opened right atrium: right lateral view

Development of The Heart

Contents

Development of Heart

The cardiovascular system is the first system to function in the Embryo.

Starts developing in the middle of the **third week**, and heart becomes functional at the beginning of **fourth week**

The cells of the **splanchnic mesoderm** in the **cardiogenic area** proliferate to form the **angiogenetic clusters**.

The canalization of angiogenetic clusters in the splanchnic mesoderm of cardiogenic area results in the formation of the paired **heart tubes**.

Development of the Heart

Day 16 **heart progenitor cells** migrate to area cranial to neural folds, horseshoe-shaped region of splanchnic lateral plate mesoderm. This is **primary**

heart field (PHF). PHF gives rise to atria,

left ventricle and part of right ventricle

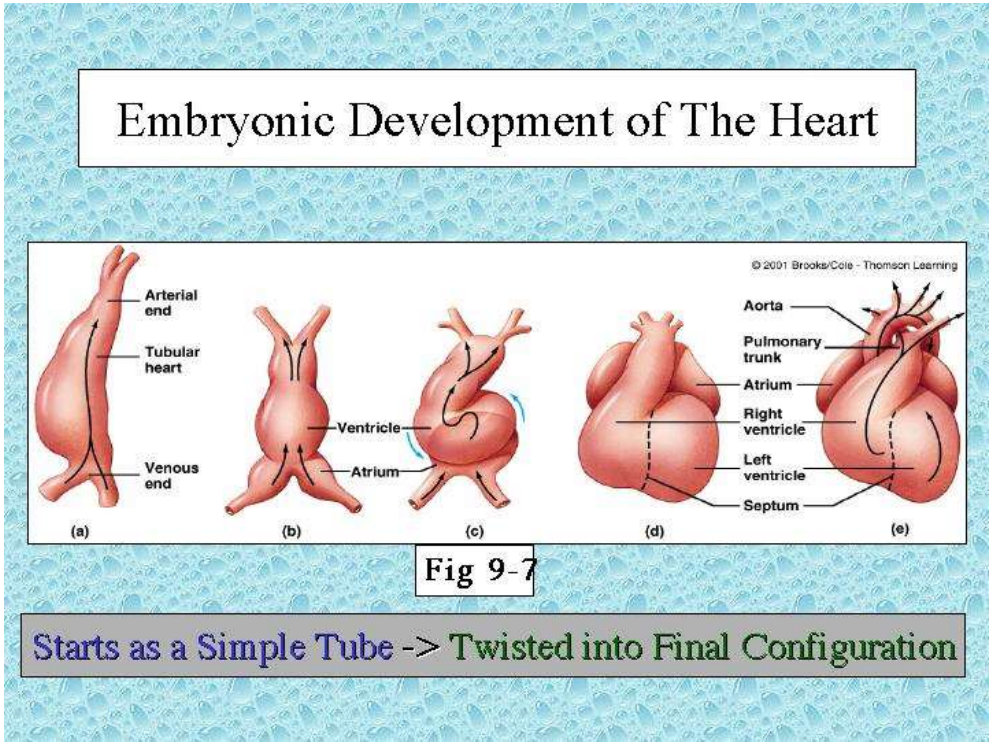
Secondary heart field (SHF) forms the

remainder of R. Ventricle, Conus Cordis

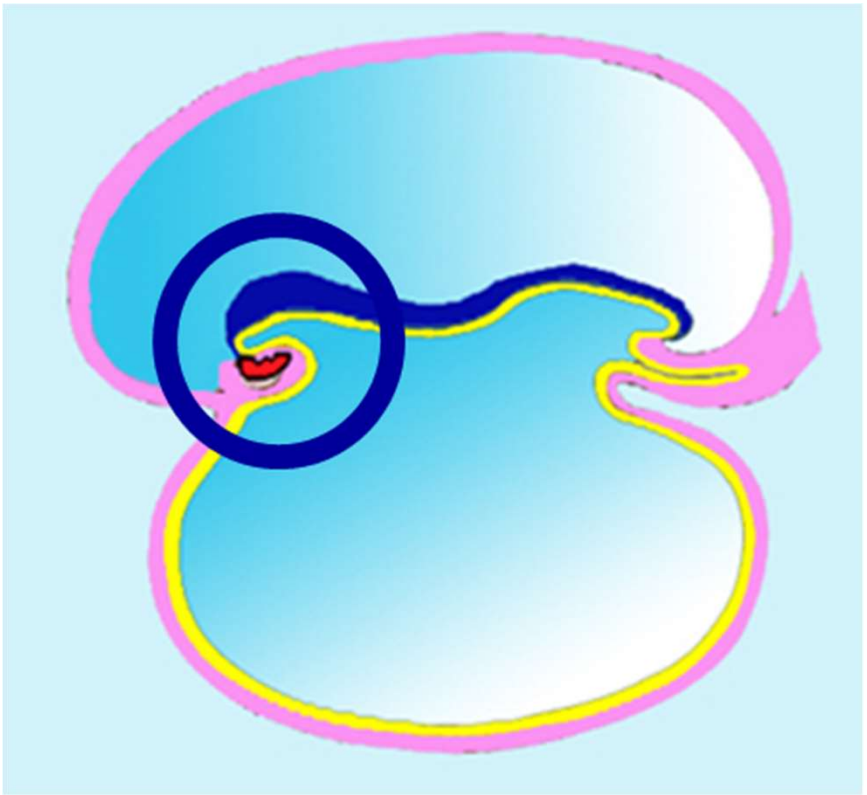
Truncus Arteriosus

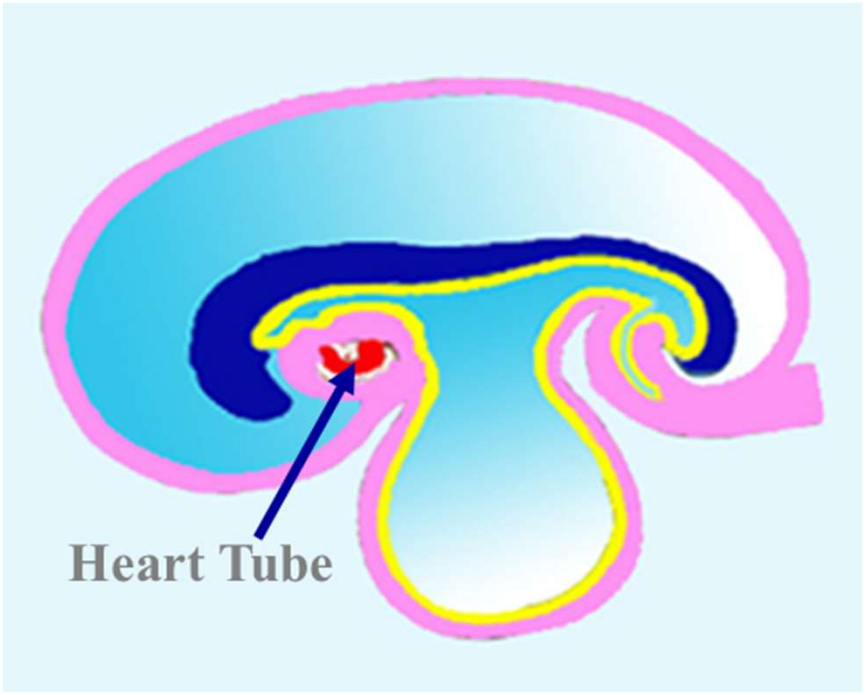
Development of the Heart

Diagrammatic



Development of the Heart



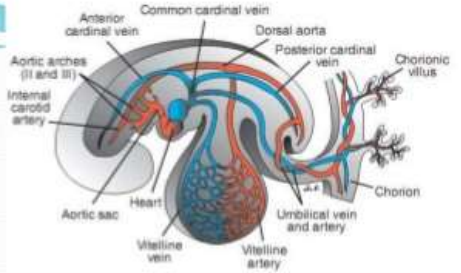


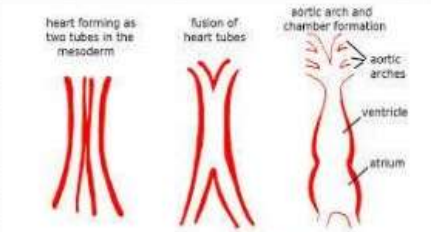
Development of the Heart

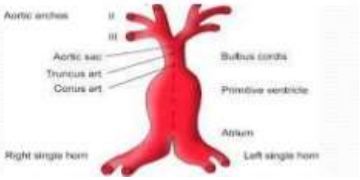
Development of the Heart Tube

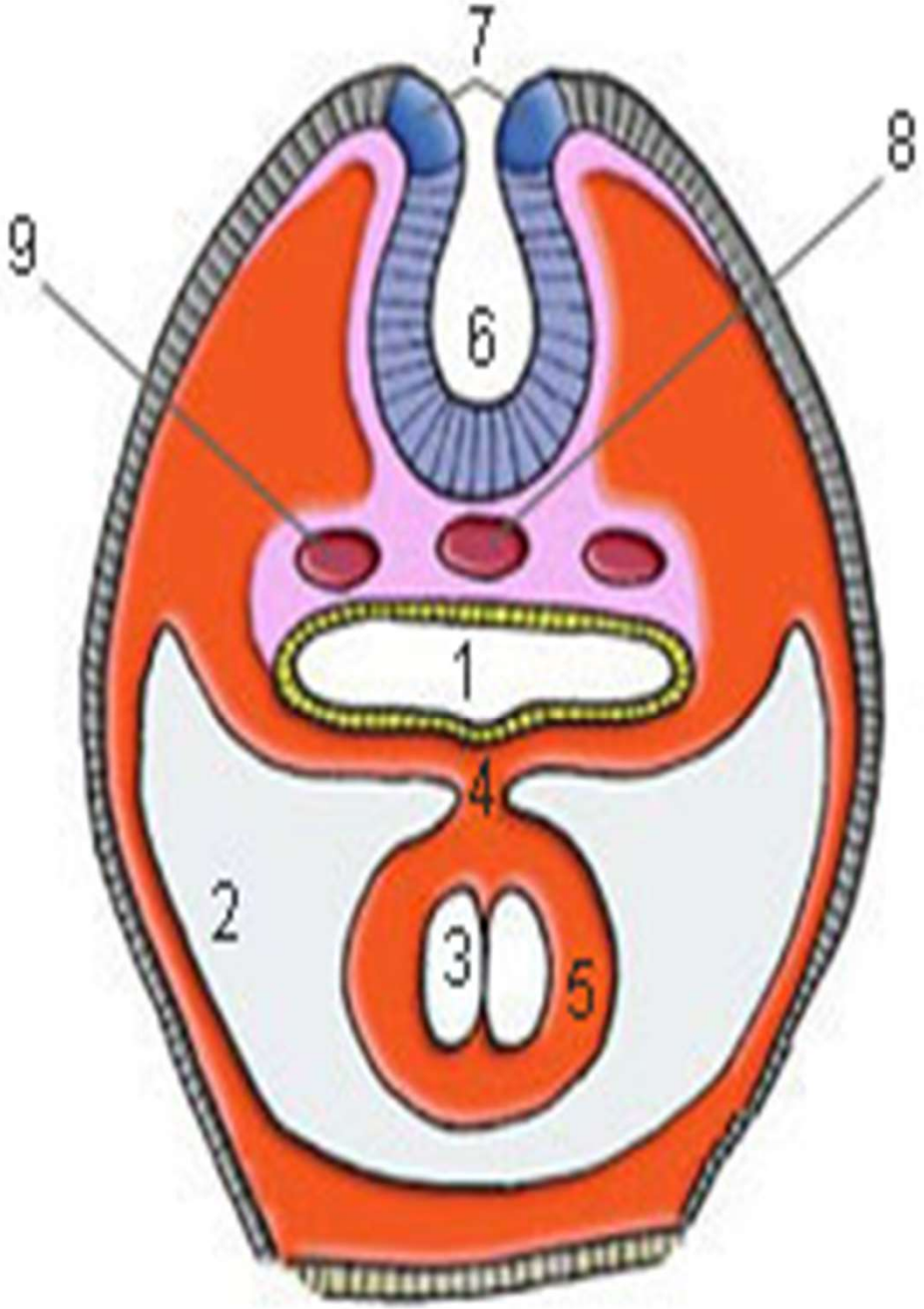
EMBRYOLOGY

- Develops during 3rd -8th week of the fetal life
- Ventral aorta partly fuse → Aortic sac
- Unfused parts remain as Rt & Lt horns of the sac
- The first arteries to appear in the embryo → Right & left primitive aorta
- Continuous with endocardial tube
- Each one – dorsal & ventral portion









1. Foregut
2. Intraembryonic coelom
3. Heart tubes
4. Dorsal mesocardium
5. Epimyocardium
6. Neural groove
7. Neural crest
8. Notochord
9. Dorsal aorta

Development of The Heart

SHF lies posterior to Pharynx in splanchnic mesoderm, is regulated by neural crest cells that migrate through pharyngeal arches in this region

Defects in SHF lead to defects of outflow tract, including transposition of great arteries, pulmonary stenosis, and others

NFX2.5 is the master gene for heart development, and is dependent in BMP's from endoderm underlying heart progenitor cells, and inhibition of WNT expression

Development of the Heart

HEART TUBE

Lateral folding of the embryo brings the primordial heart endothelial tubes towards the midline, where they **fuse in the caudal region**(future atria) to form a single heart tube surrounded by a myocardial mantle, which forms the future myocardium and epicardium

Heart tube is initially connected to pericardial cavity by a mesentery called **dorsal mesocardium**

Development of THE HEART

The heart tube dilatations

Truncus arteriosus

Bulbus cordis

Primitive ventricle

Primitive atrium and

Sinus venosus

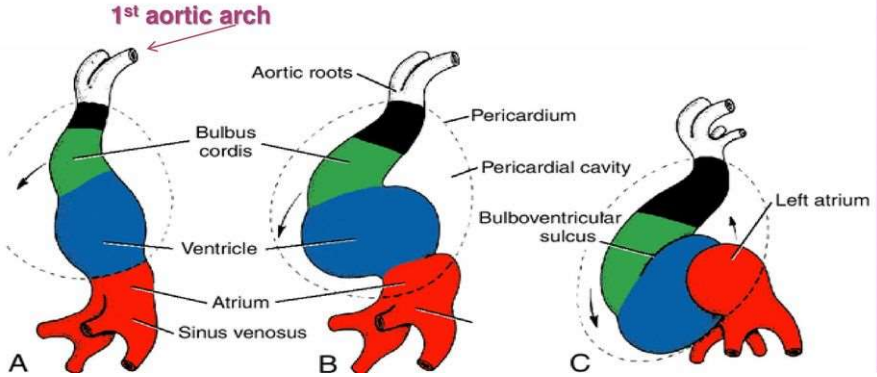
Development of Heart

Heart Tubes

PARTS OF THE HEART TUBE

Chambers of the heart tube:

- Three grooves are formed in the tube will form four chambers:
- Sinus venosus, Primitive atrium, Primitive ventricle and Bulbus cordis.



Derivatives of primitive Heart tube

Heart tube dilatation	Adult structure
Truncus Arteriosus	Aorta and Pulmonary trunk
Bulbus cordis	Smooth part of right ventricle [conus arteriosus] Smooth part of left ventricle [aortic vestibule]
Primitive ventricle	Trabeculated part of right ventricle Trabeculated part of left ventricle
Primitive atrium	Trabeculated part of right atrium Trabeculated part of left atrium
Sinus venosus	Smooth part of right atrium [sinus venarum] Coronary sinus Oblique vein of left atrium

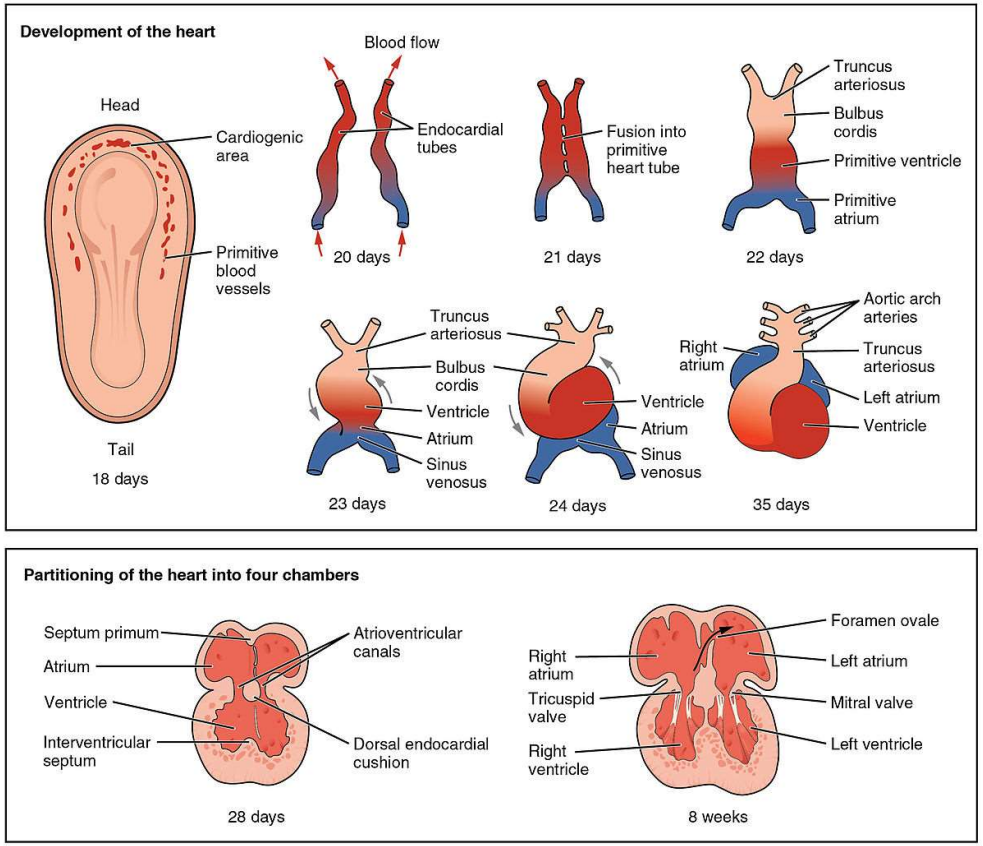
Cardiac looping

- During the 4th week, heart tube folds on itself and assumes its place in the left part of thorax with the atria posteriorly, and the ventricles anteriorly; the process is completed by day 28
- Failure of the heart to loop properly results in **dextrocardia** and the heart lies on the right side; dextrocardia with **situs inversus** can also occur earlier during gastrulation when laterality is disrupted

Partitioning of The Heart

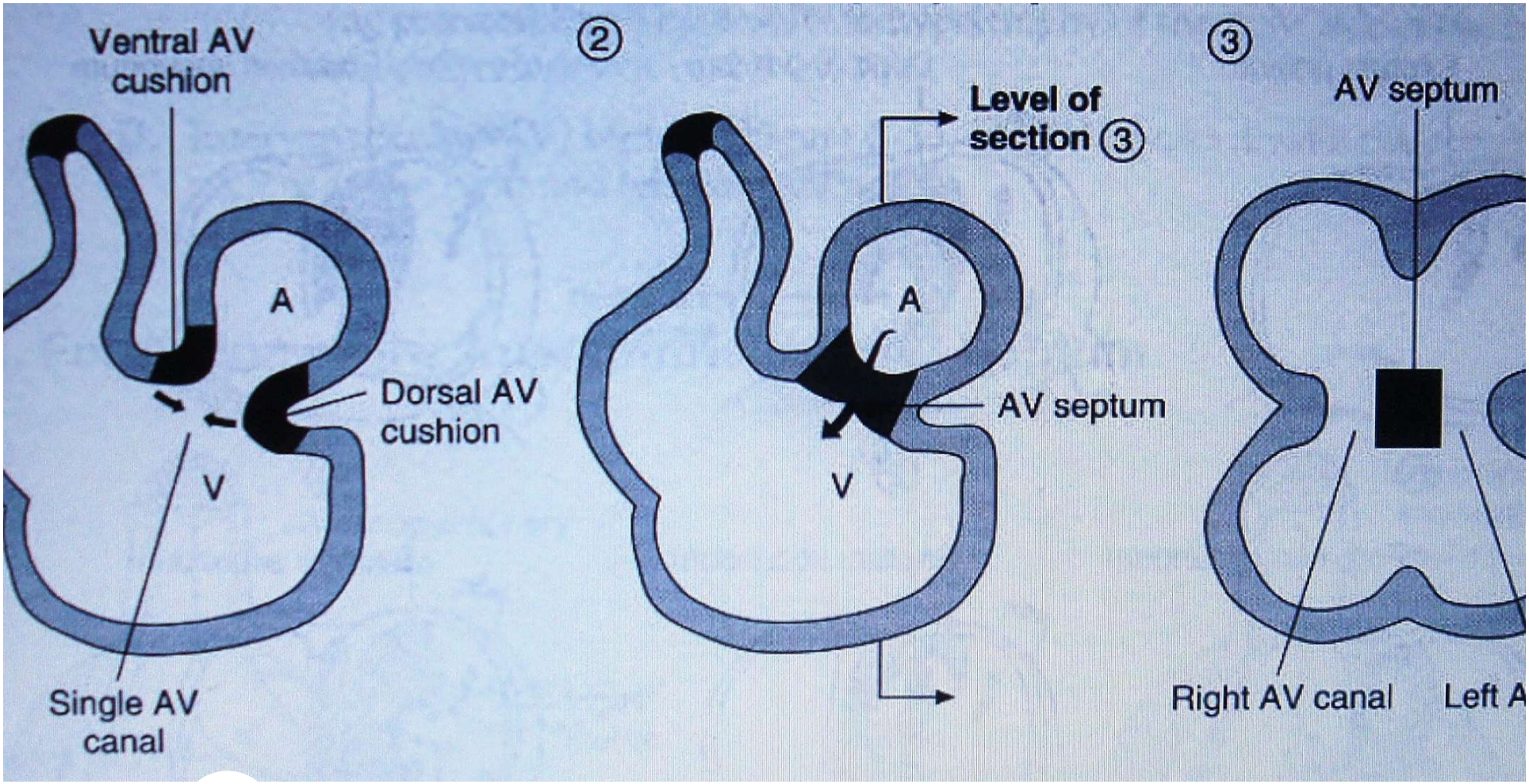
- Major heart septa are formed between days 27-35 of development. These tissue masses depend on extracellular matrices and cell proliferation and are called **endocardial cushions**.
- They develop in the **atrioventricular** and **conotruncal** regions, and form the **atrial and ventricular(membranous) septa**, the **atrioventricular canals** and **valves**, and **aortic and pulmonary channels**
- Septa also arise from atrial or ventricular walls that expand to meet the opposite wall

Endocardial Cushion



Left-Right Partitioning

- Interatrial septum
- Interventricular septum
- Spiral(aortico-pulmonary) septum
- Endocardial cushions (A-V cushions)



Formation of Atrioventricular [AV] septum

Septum formation in Atrioventricular canal

- Atrioventricular canal develops **anterior** and **posterior**, and **two lateral endocardial cushions**, which fuse and completely divide the **common atrioventricular canal** into right and left atrioventricular orifices by end of 5^{th} week
- **Valves** develop in these orifices and connected to the **Papillary muscle** of ventricular wall by **Chordae Tendinae**
- **Bicuspid(or mitral) valve** develops in left atrioventricular canal and **tricuspid valve** develops on right side

DEVELOPMENT OF THE HEART

Abnormalities of AV septum formation

1. Persistent atrioventricular canal
2. Tricuspid atresia: associated with patency of foramen ovale, ventricular septal defect (VSD), underdevelopment of right ventricle and hypertrophy of left ventricle

Cardiac Valves

Atrioventicular valves

1. **Tricuspid valve**
2. **Mitral valve**

Semilunar valves

1. Aortic valve
2. Pulmonary valve

DEVELOPMENT OF THE HEART

Abnormalities of AV septum formationBy the end of the 4th week, the **muscular interventricular septum** forms and grows towards the atrioventricular septum.

The **interventricular foramen** is found above the muscular interventricular septum

The interventricular foramen subsequently closes by the outgrowth of endocardial cushions downwards. This forms the **membranous interventricular septum**.

Ventricular Septal Defect [VSD]

- Most common congenital cardiac malformation, most are muscular septal defects and resolve as the child grows
- Serious defects involve the **membranous portion of septum** and causes left to right shunt into pulmonary arteries
- Most commonly involves **membranous** portion of interventricluar ventricular septum
- Eisenmenger syndrome develops later
- Right to left shunt = cyanosis

Formation of Atrial Septum

At the end of the fourth week, **septum primum** grows from the dorsocranial wall of the primitive atrium towards the endocardial cushions.

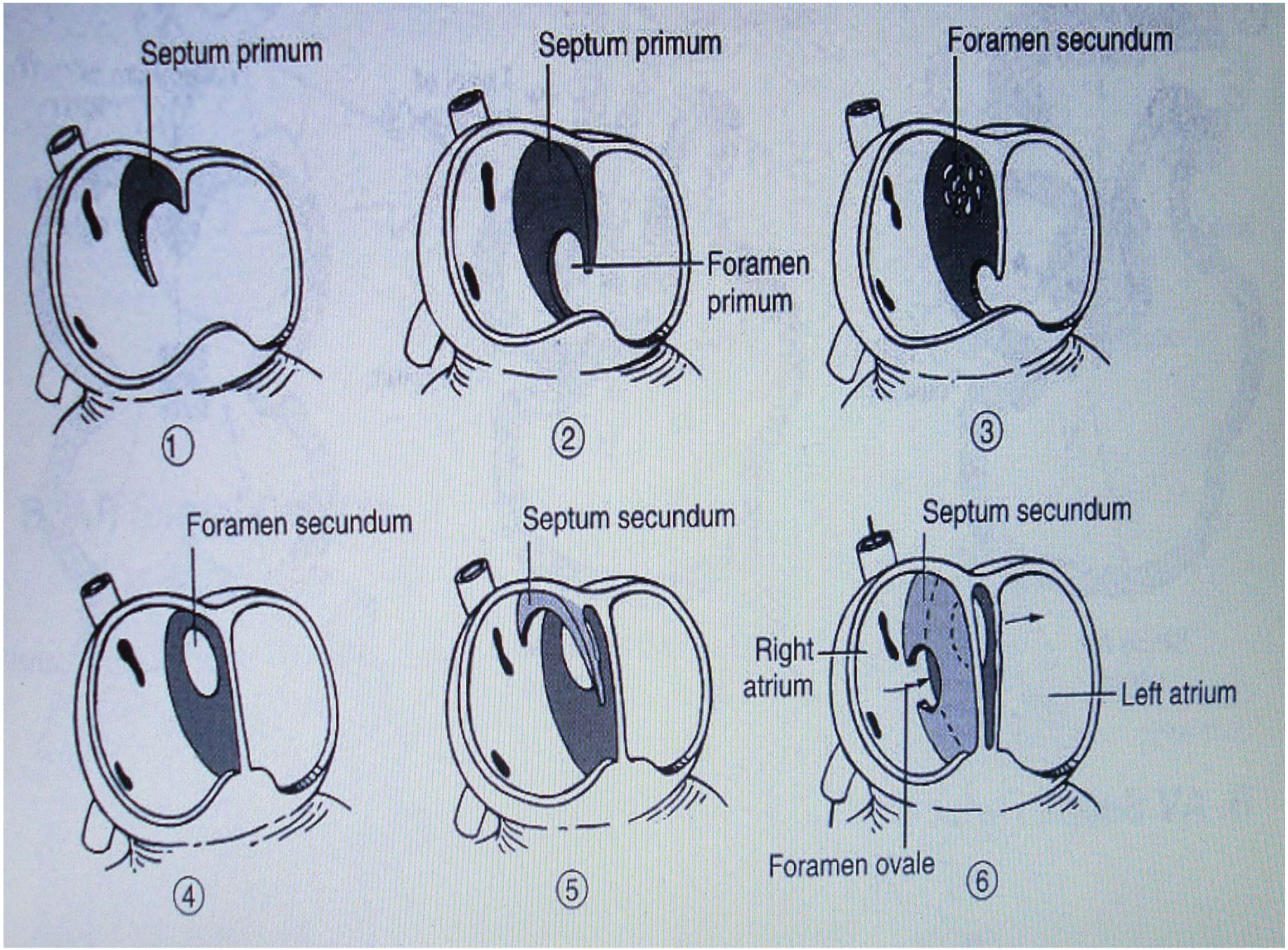
The temporary opening (**ostium primum**) between the lower rim of the septum primum and the endocardial cushions gradually closes.

Perforations in the upper part of the **septum primum** form the **ostium secundum**.

Subsequently, **septum secundum** grows from the right side of the septum primum and gradually covers the **ostium secundum**

The oval opening left by the septum secundum is called **foramen ovale**.

Remnant of septum primum forms the **valve of foramen ovale**


Septum primum
①
Septum primum
Foramen primum
②
Foramen secundum
③
Foramen secundum
④
Septum secundum
⑤
Septum secundum
Right atrium
Left atrium
Foramen ovale
⑥

Circulation at birth

- Lung circulation begins upon cutting umbilical cord, **left atrial pressure increases**, valve of foramen ovale is pressed against septum secundum, **obliterating the foramen ovale**, and separating the right and left atria. 20% births, this fusion is incomplete and there is probe patency of foramen ovale, however no interatriaal mixing of blood occurs

Atrial Septal Defect [ASD]

Most serious is complete absence of atrial septum called common atrium, or **cor triloculare biventriculare**

Ostium primum defect

Ostium secundum defect: most significant intracardiac shunting occurs from left to right

Occasionally, **premature closure of foramen ovale** occurs during prenatal life, leads to massive hypertrophy of right atrium and ventricle, and underdevelopment of the left side of heart, death shortly after birth

Aorticopulmonary Septum

During the 5th week, a **pair of opposing ridges** appear in the walls of the bulbus cordis and truncus arteriosus. **Neural crest cells** migrate into these ridges

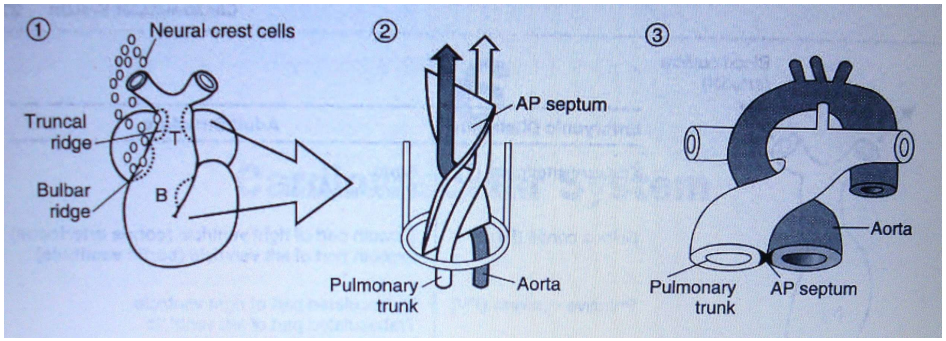
These ridges grow towards each other and join to form aorticopulmonary septum

Aorticopulmonary septum twists and forms a **spiral septum.**

This septum divides the

1. **bulbus cordis** into **smooth portions** of right and left ventricles
2. **truncus arteriosus** into two channels, the **aorta** and the **pulmonary artery**.

It also participates in the closure of the interventricular foramen


①
Neural crest cells
Truncal ridge
T
Bulbar ridge
B
②
AP septum
Pulmonary trunk
Aorta
③
Aorta
Pulmonary trunk
AP septum

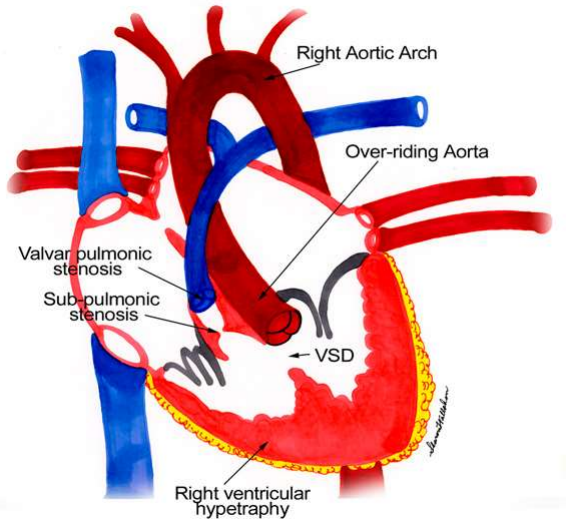
Abnormal development of Aorticopulmonary septum

Result from abnormal migration of neural crest cells

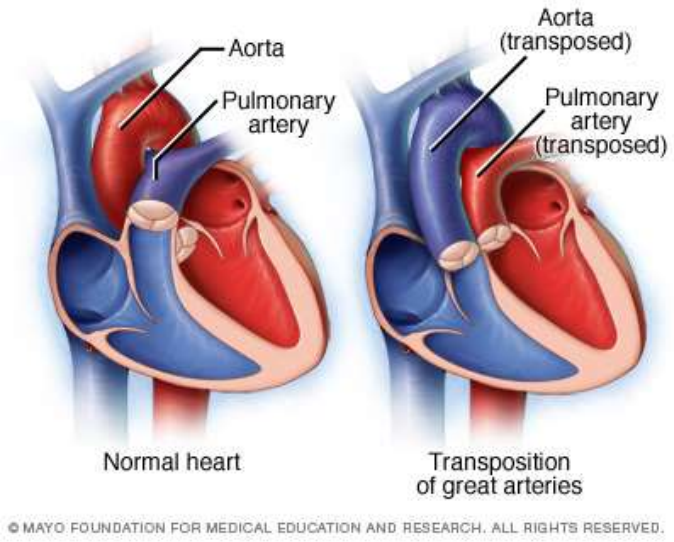
1. Persistent truncus arteriosus: AP septum **fails to develop**
2. Transposition of great vessels: AP septum **fails to twist**
3. Tetralogy of Fallot : AP septum **twists abnormally**
    1. Pulmonary stenosis
    2. Right ventricular hypertrophy
    3. Overriding of aorta
    4. Ventricular septal defects

In all these defects there is right to left shunt and hence will have cyanosis

Tetralogy of Fallot



Transposition of the great vessels



DiGeorge's syndrome

- 22q11 deletion characterized by a constellation of defects involving abnormal **neural crest** migration
- Facial defects, cardiac abnormalities like **persistent truncus arteriosus** and **Tetralogy of Fallot**, thymic hypoplasia, parathyroid dysfunction

Sinus venosus

- The sinus venosus (initially right and left sinus horns) receives blood from the umbilical, vitelline and common cardinal veins.
- Initially it is a separate chamber which opens into the caudal wall of the right atrium.
- As the primitive **right atrium** enlarges part of sinus venosus gets incorporated into its wall
- Smooth wall of right atrium (**sinus venarum**) forms from **right sinus horn**, **crista terminalis** divides the original rough part right atrial wall from smooth sinus venarum

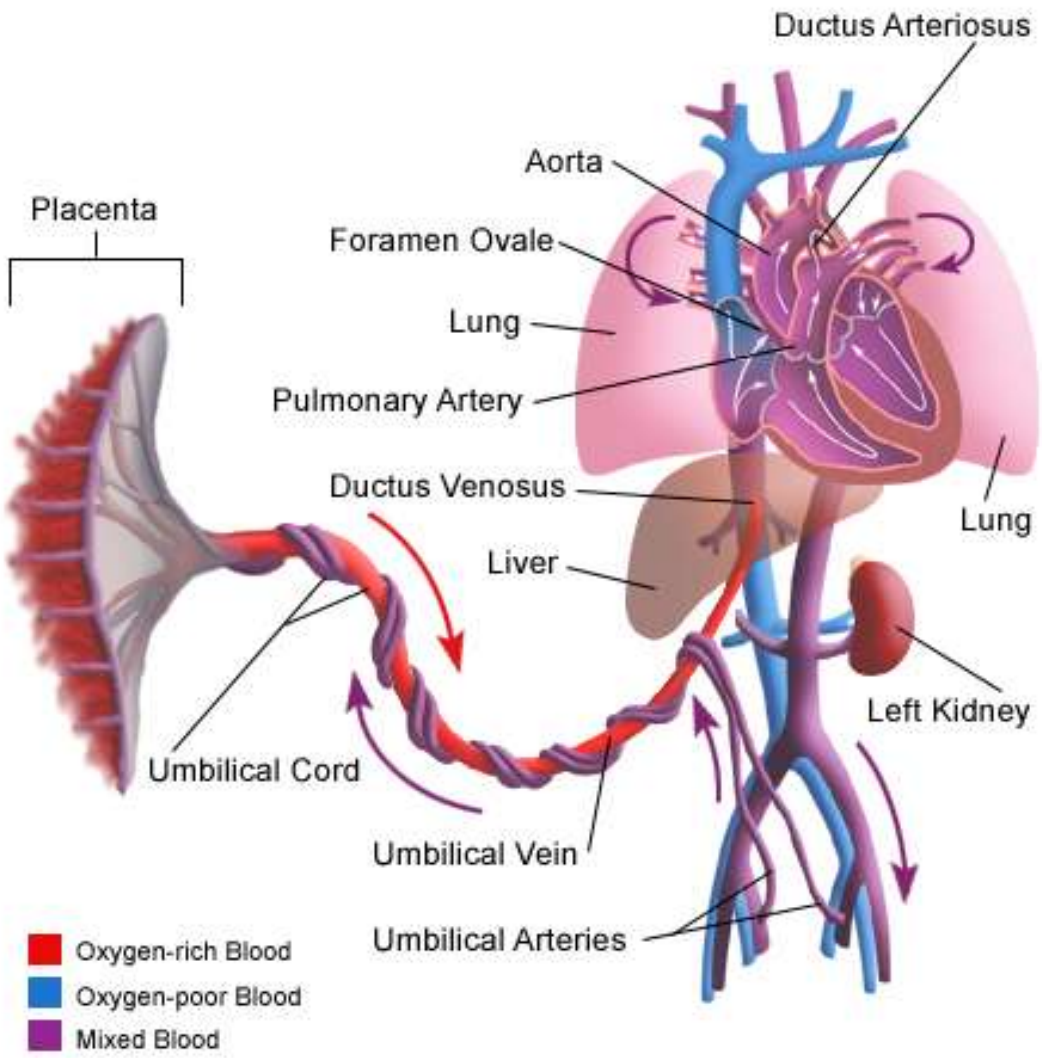
Fetal circulation

- The **fetal circulation** is designed to serve prenatal needs. Very little blood goes to the lungs before birth because they are nonfunctional.
- The **well-oxygenated** blood returns from the placenta into the **umbilical vein**, goes through the ductus venosus and vena cava inferior (which also receives deoxygenated blood from the portal vein) to the right atrium.
- Most of the blood goes through the foramen ovale into the left atrium and mixes with the blood from the pulmonary veins. The blood passes into the left ventricle and leaves via the ascending aorta.

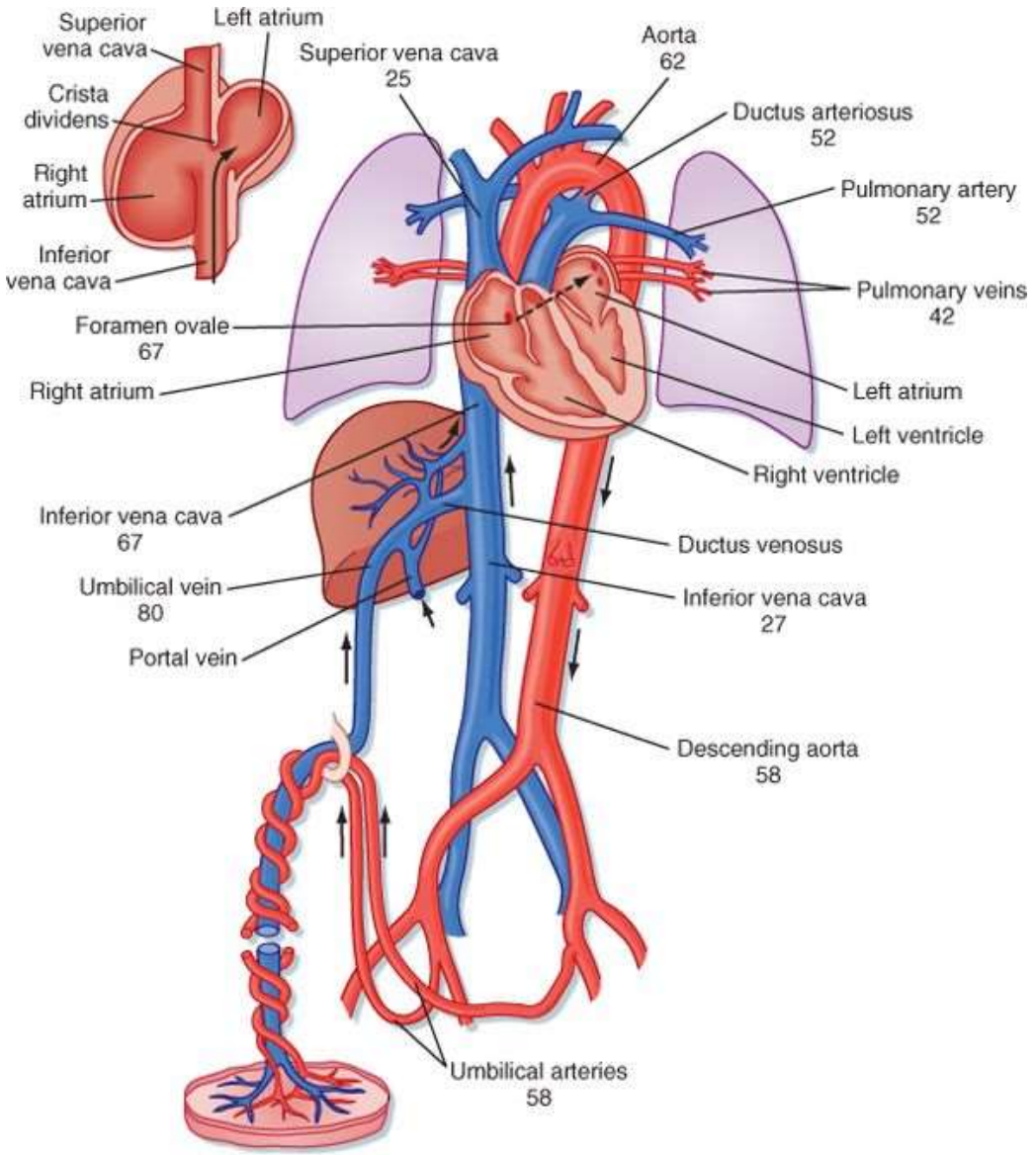
Fetal Circulation

- A small amount of blood goes from the right atrium into the right ventricle, leaves by the pulmonary trunk and through the **ductus arteriosus** into the aorta.
- The mixed blood from the descending aorta **returns** to the placenta through **umbilical arteries.**

Fetal Circulation



Fetal Circulation



Shunts in Fetal Circulation

- Shunt 1: **Ductus venosus** links umbilical vein to caudal vena cava
- Shunt 2: **Foramen Ovale** opening between two atria bypassing lungs R- L flow
- Shunt 3: **Ductus arteriosus** connects pulmonary artery to caudal aorta; hence blood flow from aorta to umbilical arteries

Fetal Circulation

- At birth, the circulation of the fetal blood through the placenta ceases and the lungs begin to function.
- The **foramen ovale**, **ductus arteriosus**, **ductus venosus** and **umbilical vessels** subsequently close or transform into corresponding ligaments.

Teratogens

- Classic examples are rubella virus, retinoic acid, alcohol, maternal diabetes, trisomy 18 (almost 100% heart defects), trisomy 21 (Down syndrome have VSD)
- Multifactorial, complex interplay of genetic and environmental factors

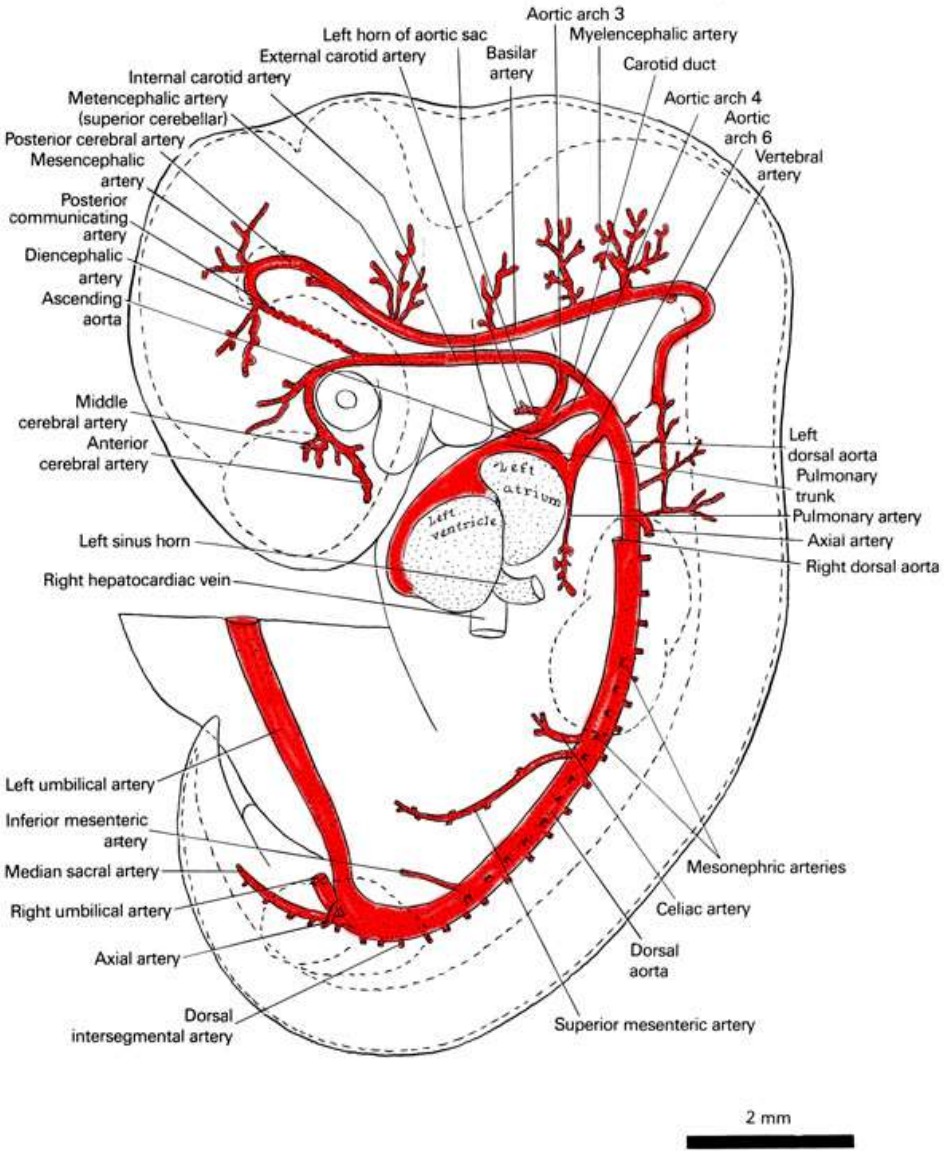
Formation of blood vessels

- Begins during **3rd week**
- Some mesodermal cells differentiate into **angioblasts** which aggregate to form **angiogenic clusters**
- Angioblasts flatten to form endothelial cells and small cavities appear in the angiogenic cluster [**blood islands**]
- Endothelium lined cavities fuse to form networks of endothelial channels [**vasculogenesis**]
- Endothelial budding leads to formation of new blood vessels [**angiogenesis**]

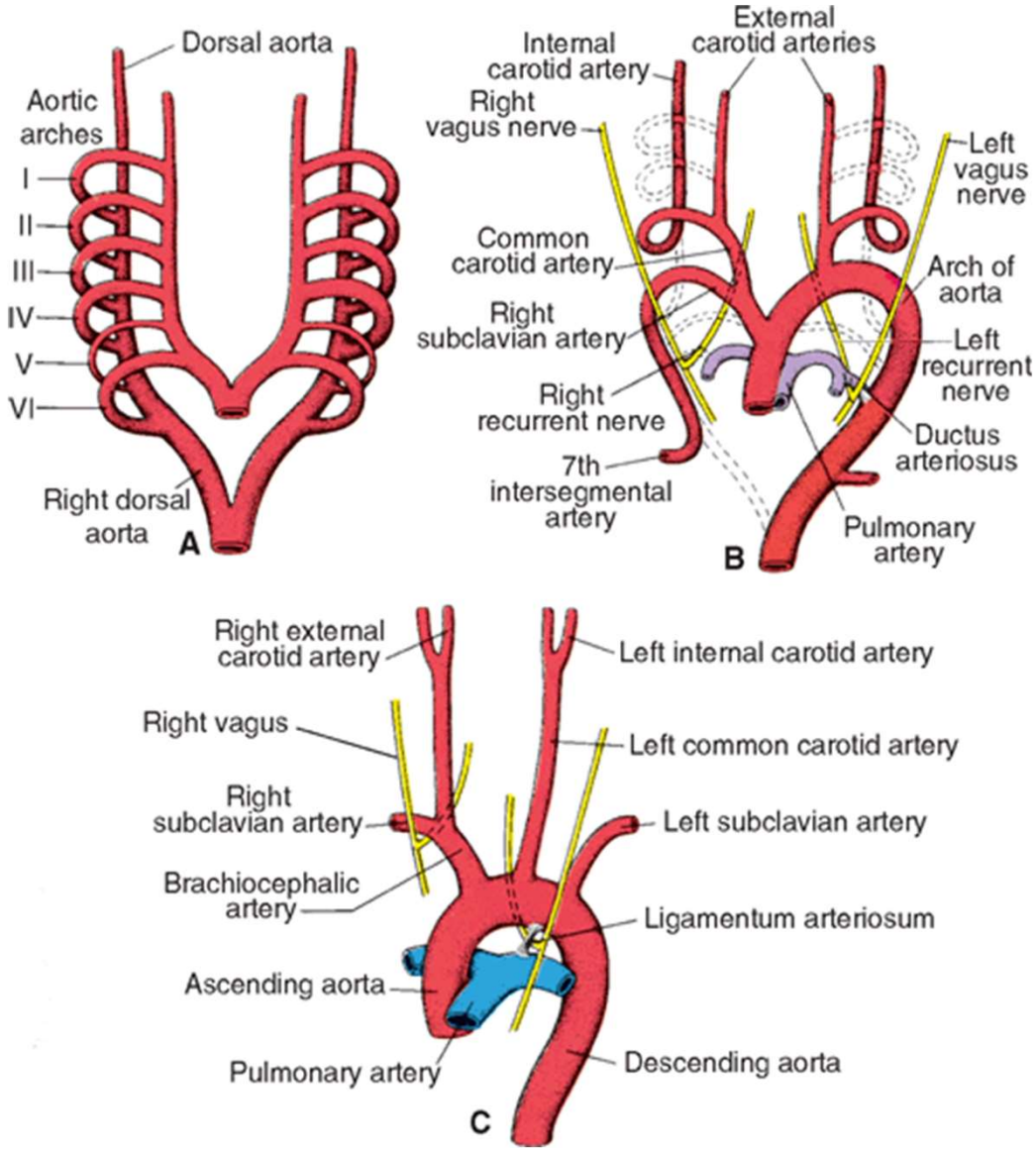
Aortic arch system

- **Aortic arches (arteries)** arise from the **aortic sac** which is part of truncus arteriosus and terminate in the paired dorsal aortae.
- During the 6th to 8th week, the primitive aortic arch pattern is transformed into the basic adult arterial arrangement.
- Aortic arches lie in each of the 5 pharyngeal arches, aortic arches I, II, III, IV, VI
- I aortic arch- maxillary artery
- II aortic arch- hyoid and stapedial arteries
- III aortic arch- common carotid, internal carotid, external carotid
- IV aortic arch- on left forms part of arch of aorta, on right forms proximal part of R. subclavian artery
- Distal part of subclavian is formed by R. dorsal aorta and 7^{th} intersegmental artery
- VI aortic arch- on right forms proximal part of R pulmonary artery, on left forms L. pulmonary artery, distal part forms ductus arteriosus

Aortic Arch System

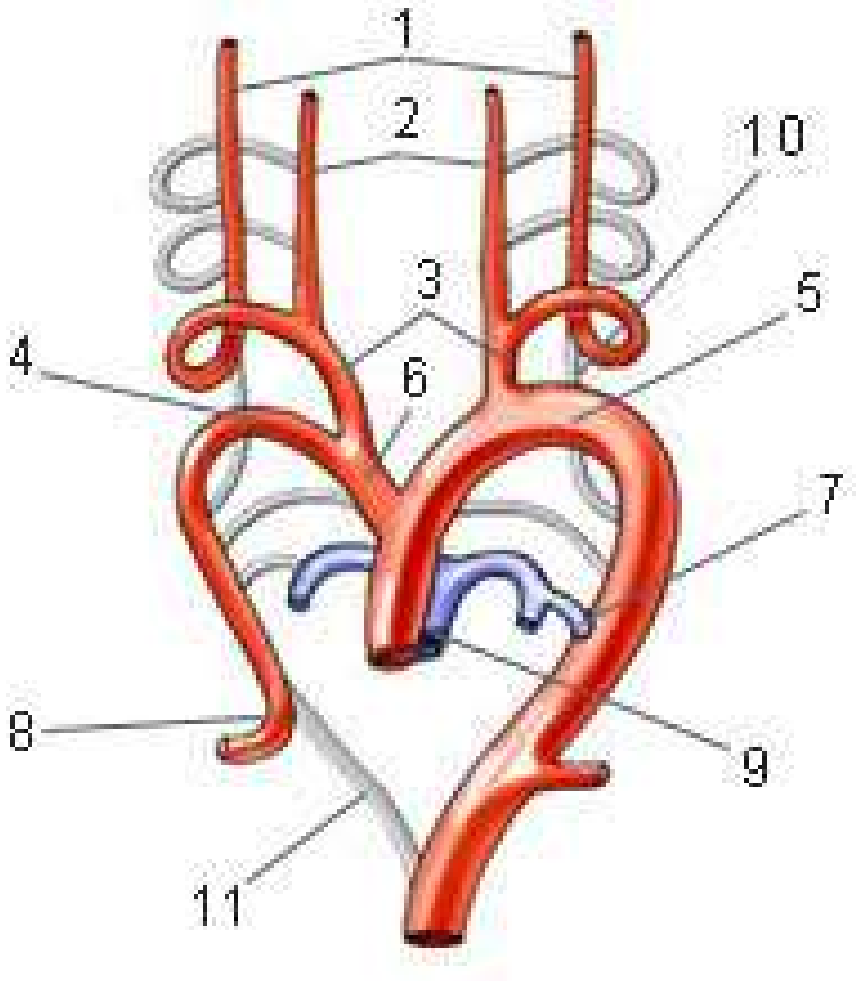


Aortic Arch System



Aortic Arch System

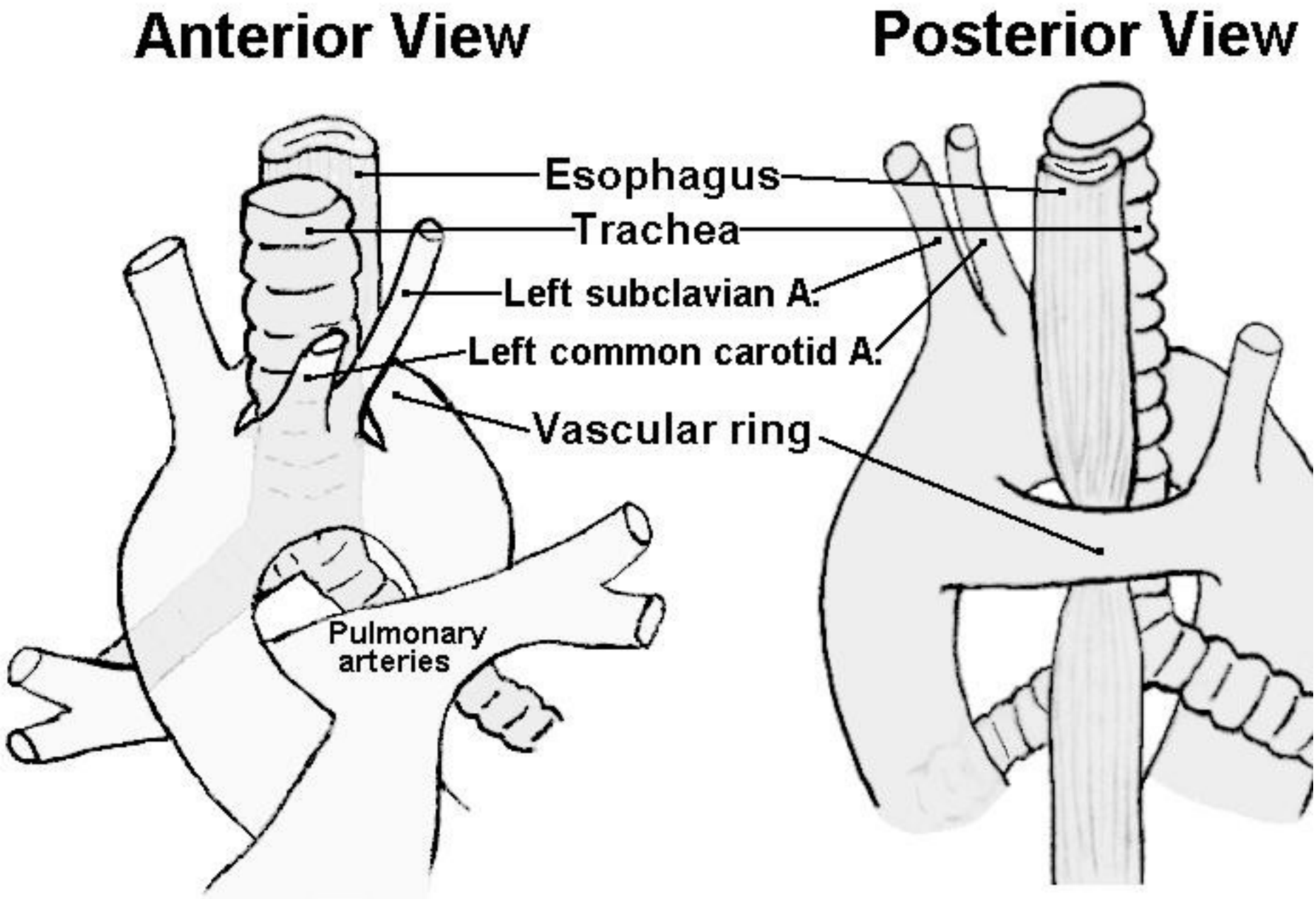
1. Internal carotid artery
2. External carotid artery
3. Common carotid artery
4. Right subclavian artery
5. Arch of aorta
6. Brachiocephalic artery
7. Ductus arteriosus
8. 7th intersegmental artery
9. Pulmonary artery
10. Carotid duct
11. Obliterated right dorsal aorta



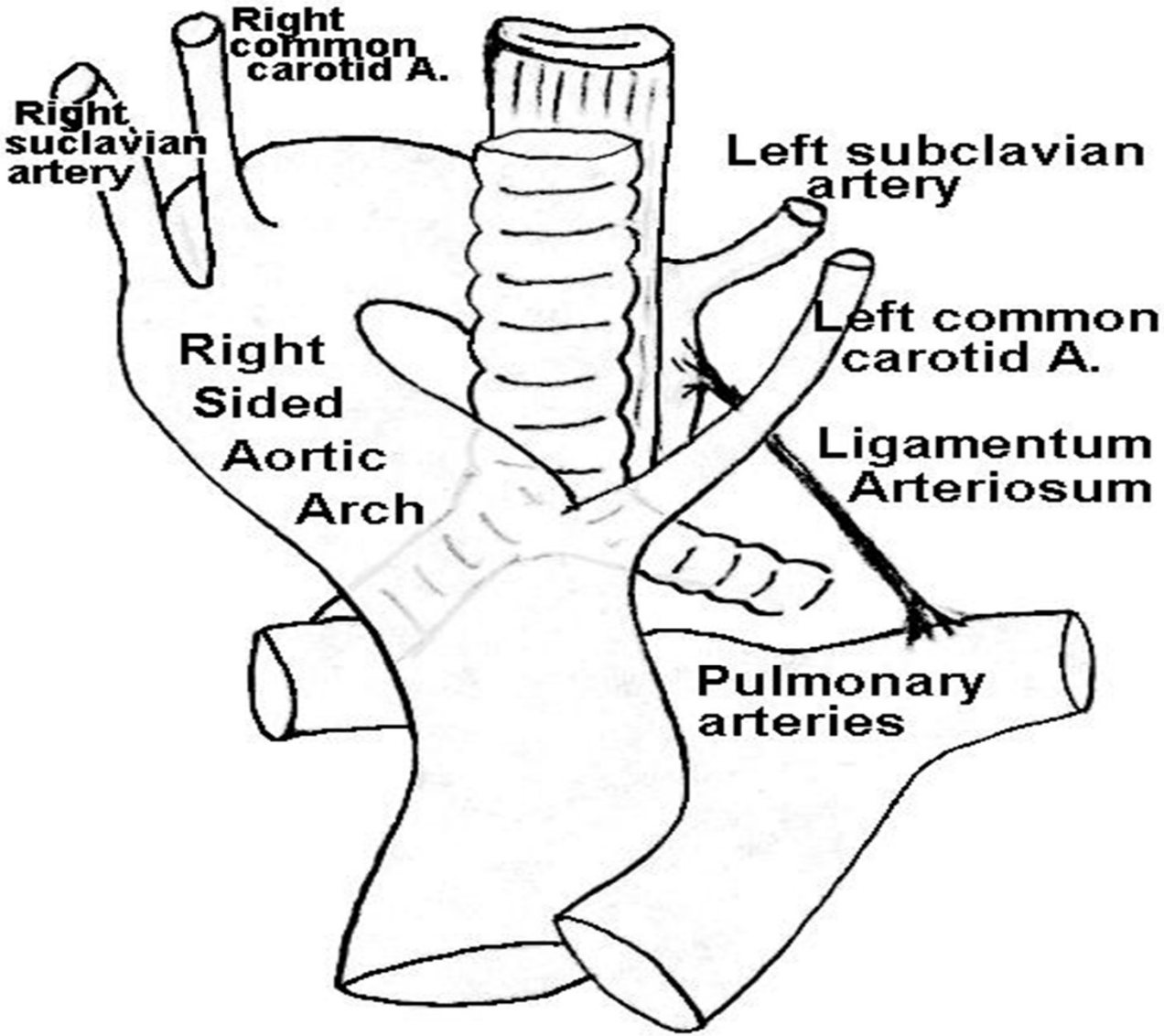
Recurrent Laryngeal Nerve

- Due to caudal shift of the heart the vagus nerve, the nerve of the 6th aortic arch, hooks around the sixth arch and then ascends to the larynx, hence ***recurrent*** course of the vagus
- On the right when the distal 6th arch diasppear the recurrent laryngeal n hooks around the **right subclavian artery**
- On the left, the distal 6th arch persists as the **ductus arteriosus,** hence the L. recurrent laryngeal n hooks under it

Double Aortic Arch

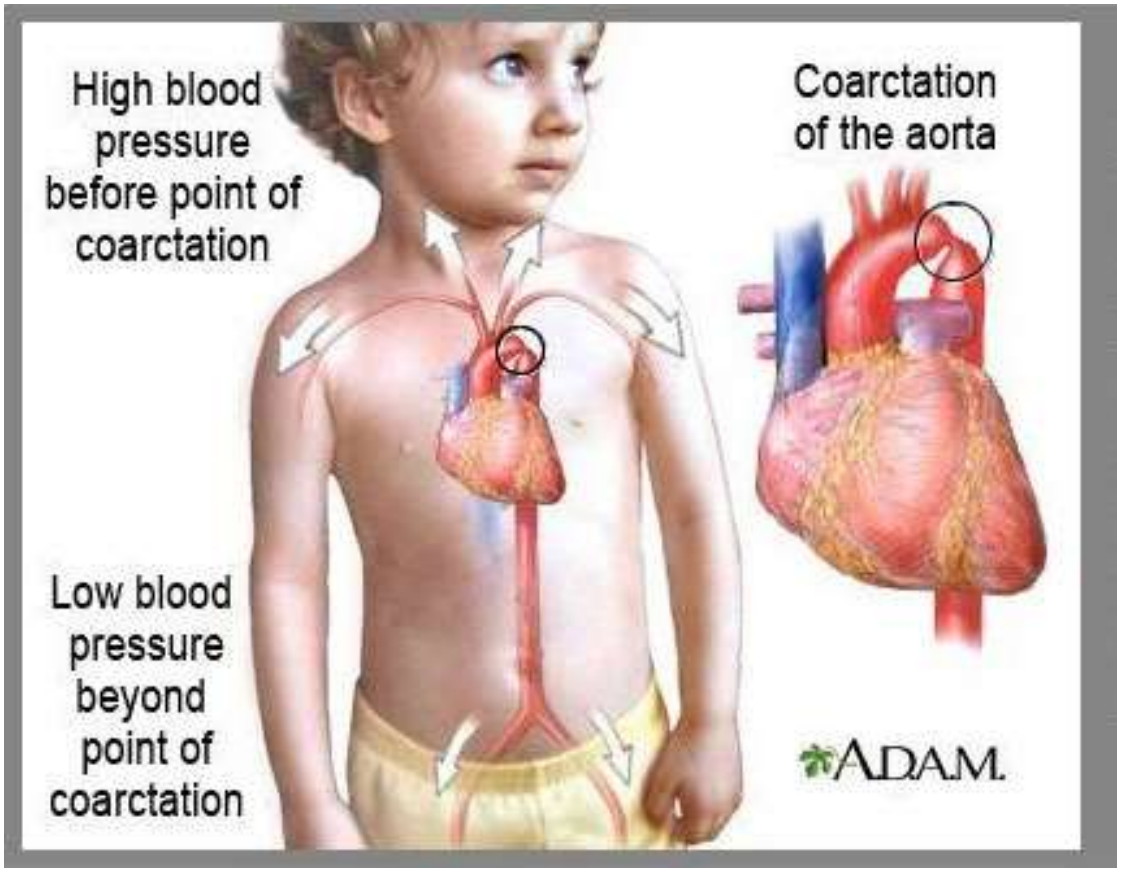


Right Sided Aortic Arch with Anomalous Left Subclavian A.



Patent Ductus Arteriosus

- Common in premature children
- Rubella infection is a risk factor
- Left to right shunt initially
- Eisenmenger syndrome results from
- reversal of shunt [right to left= cyanosis]



Coarctation of aorta

Vitelline and Umbilical Arteries

- **Vitelline** arteries initially supply the yolk sac and later form the arteries of dorsal mesentery of the gut
- In the adult they form the **celiac** and **superior mesenteric arteries**
- **Umbilical** arteries form the **inferior mesenteric arteries**
- Proximal part of umbilical artery form **internal iliac** and **vesicular arteries**; and distal portions are obliterated to form **Medial Umbilical Ligaments**

Embryonic structure	Adult derivative
Rt & Lt umblical arteries	Medial umblical ligaments
Left umblical vein	Ligamentum teres hepatis
Ductus venosus	Ligamentum venosum
Foramen ovale	Fossa ovale
Ductus arteriosus	Ligamentum arteriosum

Embryonic Remenants

- The umbilical vein forms the **ligamentum teres hepatis** and passes from the umbilicus to the porta hepatis where it attaches to the left branch of the portal vein

- The ductus venosus becomes the **ligamentum venosum** which passes through the liver from the left branch of the portal vein to the inferior vena cava

- The umbilical arteries (intra-abdominal portion) form the **medial umbilical ligaments**; the proximal portions persist as the **superior vesical arteries**

- The foramen ovale becomes the **fossa ovalis** with adhesion of the septum primum to the left margin of the septum secundum. The lower edge of the latter forms the limbus of the fossa ovalis (anulus ovalis)

- The ductus arteriosus becomes the **ligamentum arteriosum** passing from the left pulmonary artery to the aortic arch. This closes anatomically by the end of the third postnatal month