

DEVELOPMENT OF CARDIOVASCULAR SYSTEM

Objectives

- 1-Appreciate the sources and steps of development of the heart tube and the three layers of the heart.
- 2-Understand the embryogenesis of septation and formation of valves of the heart.
- 3-Follow developmental stages of blood vessels and their varieties.
- 4-Appreciate fetal circulation and its postnatal changes.
- 5-Overview development, derivatives and anomalies of aortic arches and great veins.
- 6-State the prevalence, mechanisms, and hemodynamic changes of the common congenital abnormalities of the cardiovascular system.
- 7-Overview pattern of branches and distribution of great vessels of the body.

Introduction

The cardiovascular system is the first major system to function in the embryo. Primordial heart and vascular system appear in the middle of the 3rd week. The heart starts to function early in the 4th week. The heart begins to beat on day 22. The rapidly growing embryo can no longer satisfy its nutritional and oxygen requirements by diffusion alone.

Development, laterality (right and left sidedness), lengthening of the heart and blood vessels is controlled by regulatory genes and signaling molecules.

Embryonic sources of development of the cardiovascular system

- 1-**Epiblast cells** provide progenitor heart cells. These cells migrate during days 16-18 into splanchnic mesoderm where they form horse-shoe cluster of cells cranial to the neural tube. Epiblast cells form the **endocardium**.
- 2-**Splanchnic mesoderm** provide myoblasts of the **myocardium**.
- 3-**Intraembryonic coelom**. Coelom in the lateral mesoderm form the **pericardial** cavity.
- 4-**Neural crest cells** are involved in formation of cardiac cushions and **valves** of heart.

Primitive blood vessels and blood cells

Angiogenesis (blood vessel formation)

- Early in week 3, blood vessels form in extraembryonic mesoderm of the yolk sac, connecting stalk and chorion. Mesenchymal cells differentiate into **angioblasts** (vessel forming cells) that aggregate to form **blood islands**. Peripheral cells flatten to form endothelial lining of blood vessels. These cavities fuse to form networks of channels. Vessels sprout by buddings and fuse with other vessels to form **capillary plexuses**. **Vitelline vessels** form in the yolk sac, and **umbilical vessels** in the chorion (fig.1&2).
- Embryonic blood vessels develop from intraembryonic mesoderm in a similar way 2 days later. Extraembryonic vessels join intraembryonic vessels. The surrounding mesenchyme differentiates into muscles and connective tissue of blood vessels.

Hematogenesis (blood cell formation)

-Some centrally located cells in the blood islands detach and differentiate into blood cells. Blood formation first occurs in the **liver, spleen, lymph nodes, thymus, and bone marrow**. By the 4th month of pregnancy, the red bone marrow takes over the function of blood cell formation and becomes the main source of blood cells.

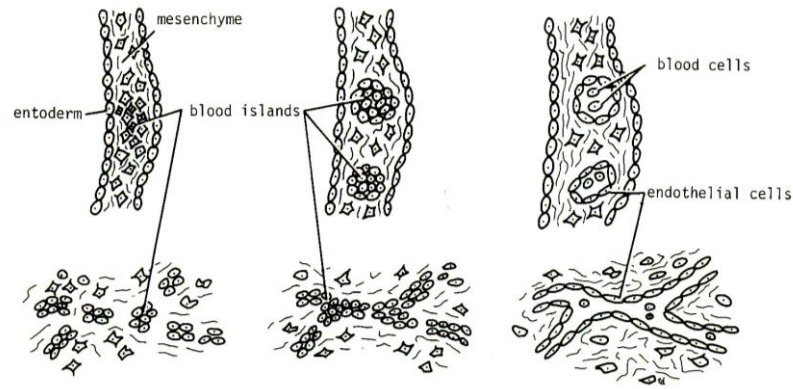


Fig.1. Mesenchymal cells form endothelium-lined blood vessels and blood cells.

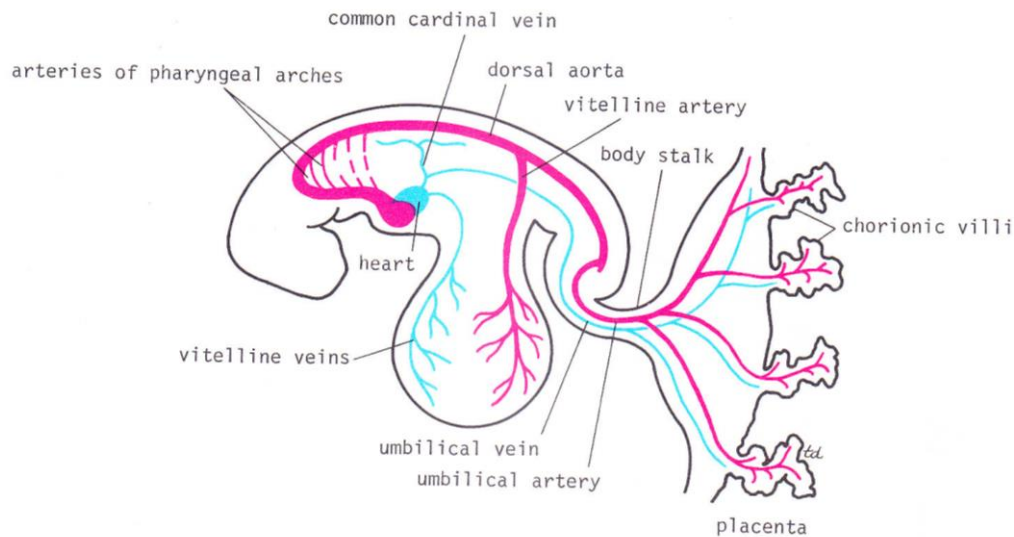


Fig.2. CVS in 21 days embryo shows extra- and intra-embryonic blood vessels.

DEVELOPMENT OF THE HEART

CARDIOGENIC AREA

-In the middle of the 3rd week, **progenitor heart cells** in the epiblast migrate into and through splanchnic layer of lateral mesoderm where they form horseshoe cluster of cells called **cardiogenic area** (fig.3). The cardiogenic area is in front of the neural tube.

-Other clusters of angiogenic cells appear bilaterally and acquire lumen to form a pair of longitudinal vessels, the **dorsal aortae**. Dorsal aortae gain connections with the caudal ends of the heart tubes.

-Cells of cardiogenic area canalize to form two thin-walled **endocardial heart tubes**.

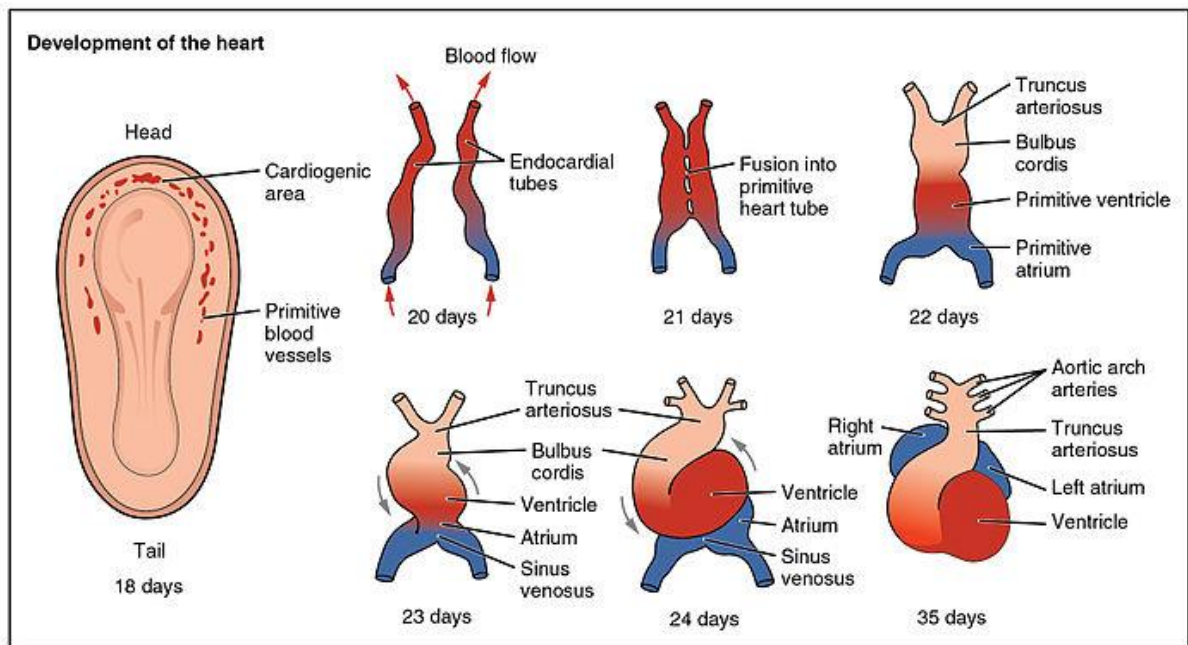


Fig.3. Cardiogenic area and formation of heart tube and primitive vessels.

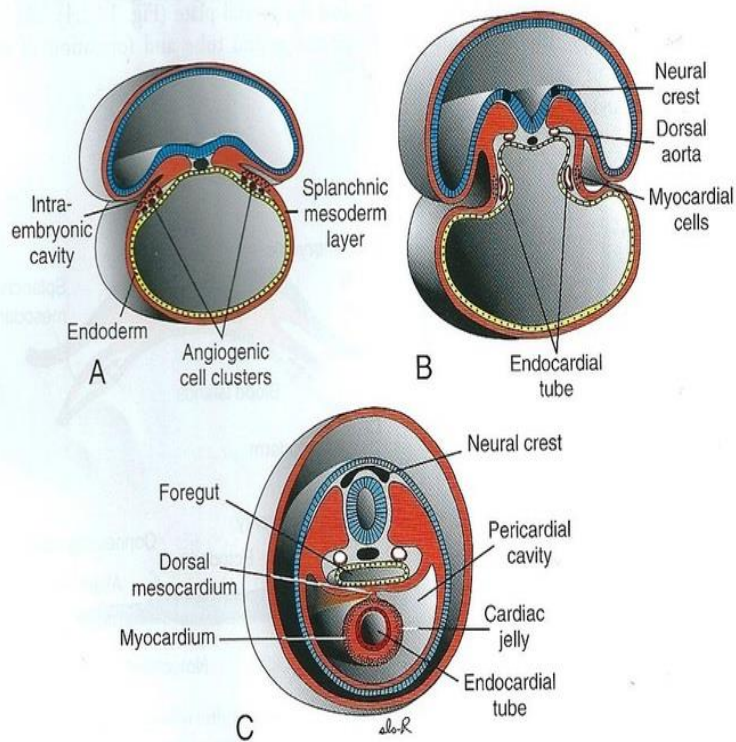


Fig.4. Cross section of 18 days embryo showing fusion of lateral body folds and how the two endocardial heart tubes fuse into one.

HEART TUBE

Effects of folding of the embryo on the heart tube and pericardium

1-As the embryo folds laterally, the two endocardial heart tubes approach each other and fuse to form a single heart tube.

2-When head fold forms, the heart tube is reversed (180 degrees rotation) so that the the dorsal aortae are curved cranially instead of caudally forming the first aortic arches (Fig.5). Venous end of the heart becomes caudal instead of cranial.

3-The heart and pericardial cavity come to lie ventral to the foregut.

4-The pericardial cavity becomes ventral to the heart. The heart and pericardium move to a cervical and finally a thoracic position.

5-The *septum transversum* is reversed and becomes caudal to the heart, and eventually will form the diaphragm.

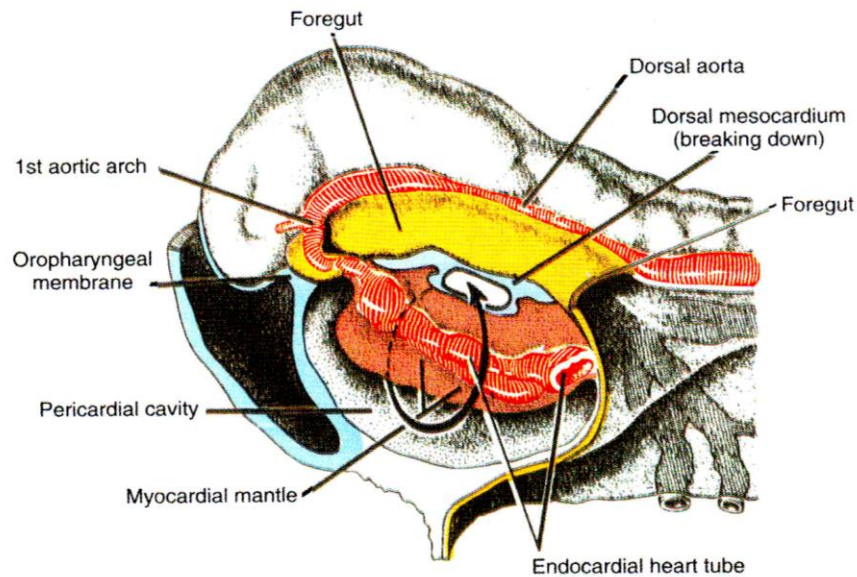


Fig.5. Layers of the heart. Effects of rotation and embryonic folding on heart tube.

Development of the three layers of the heart

a)Endocardium forms endothelial lining of the heart, is derived from *epiblast cells*.

b)Myocardium forms muscular wall of the heart is derived from *splanchnic mesoderm*.

c)Epicardium or visceral pericardium covers the surface of the heart, is derived from the wall of sinus venosus and septum transversum. This outer layer shares in formation of coronary arteries.

d)Parietal pericardium and pericardial cavity are derived from cranial part of the *celomic cavity*. **Fibrous pericardium** is derived from *septum transversum*.

Formation of the cardiac loop and its dilatations

The heart tube continues to grow and elongate. This lengthening is essential for formation of the outflow tract and looping process. As the outflow tract lengthens, the cardiac tube begins to bend (fold) on day 23. The cephalic portion of the tube which is the truncus arteriosus and primitive ventricle bends ventrally and to the right (dextral looping). The atrial (caudal) portion of the tube shifts cranially and to the left. The bending creates the cardiac loop which is complete by day 28. The cardiac loop is U-shaped (seen from the side) and S-shaped (seen from above). Looping (folding) places chambers of the heart in their postnatal anatomical position. While the cardiac loop is forming, local expansions become visible and develop alternate dilatations and constrictions (Fig 6).

These dilatations are oriented in a cephalo-caudal order as follows:

- 1-*Truncus arteriosus (TA).***
- 2-*Bulbus cordis (BC).***
- 3-*Primitive ventricle (V).***
- 4-*Primitive atrium (A).***
- 5-*Sinus venosus (SV).***

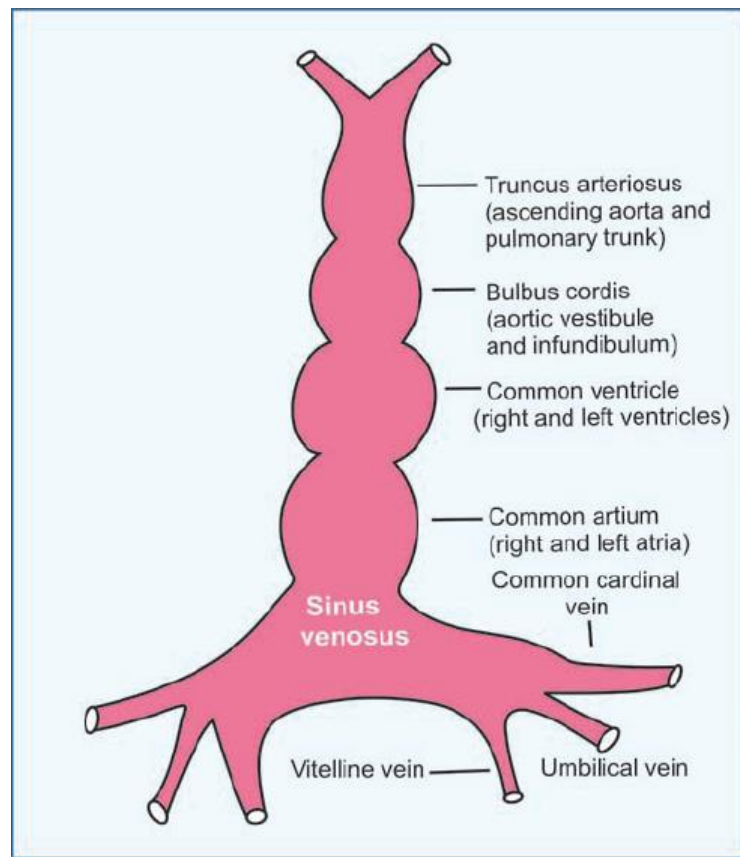


Fig.6.Dilatations of the heart tube.

Development and fate of sinus venosus (4th to 10th week)

-In the middle of the 4th week the sinus venosus receives blood from right and left horns. Each horn receives blood from three veins:

- 1-**Umbilical vein** carries oxygenated blood from the placenta.
- 2-**Vitelline (omphalomesenteric) vein** carries deoxygenated blood from the yolk sac.
- 3-**Common cardinal vein** carries deoxygenated blood from embryo.

Soon the entrance of the SV into the atrium shifts to the right. This results in:

- a) The left horn of the sinus venosus decreases in size. All what remains are the **coronary sinus** and **oblique vein of the left atrium**.
- b) The right horn enlarges and receives all blood through the superior and inferior vena cava. The right horn becomes incorporated to form the smooth part of the right atrium. The **sinoatrial orifice** is flanked on each side by a valvular fold, the **right and left venous valves**. The left valve fuses with the developing **inter-atrial septum**. The cranial part of the right sinoatrial valve is indicated by the **crista terminalis** while the lower part develops into **valve of inferior vena cava** and **valve of the coronary sinus** (fig.7).

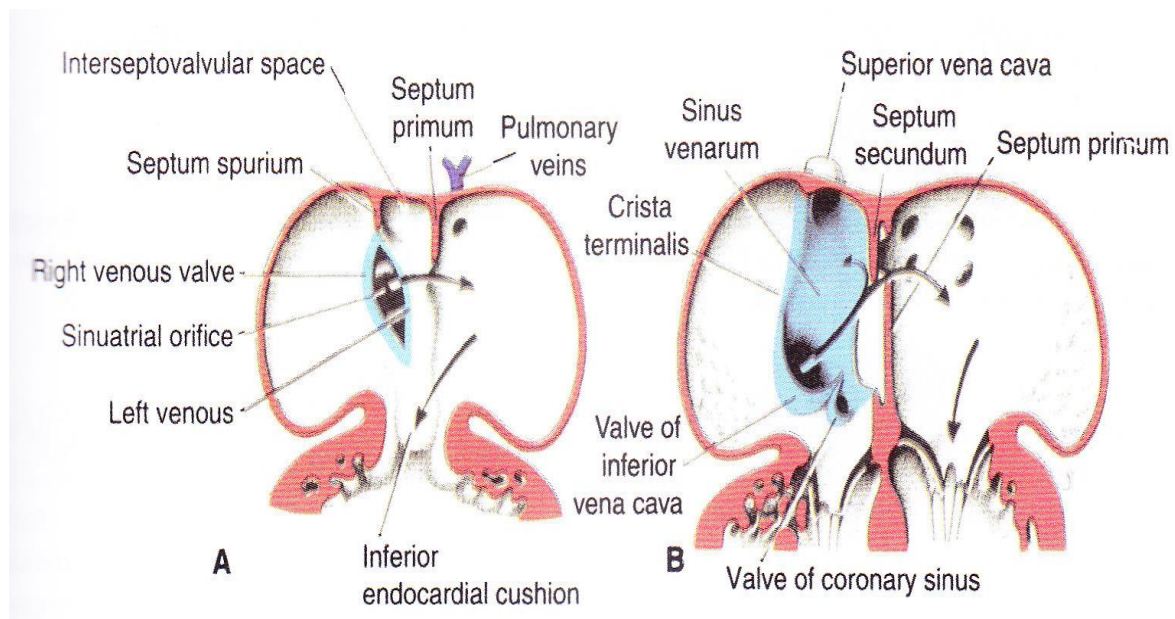


Fig.7. Fate of sinus venosus, heart is open and seen from the front.

PARTITIONING (SEPTATION) OF THE HEART (4th to 8th week)

Endocardial cushions

By the end of the 4th week, *endocardial cushions* form in the atrioventricular. Cushions appear in the dorsal and ventral walls of the atrioventricular canal. AV cushions approach each other and fuse dividing the AV canal into right and left AV canals. The cushions develop from the cardiac jelly where neural crest cells are involved. The cushions contribute to the formation of **valves** and **septa** of the heart.

Septation of the primordial atrium

During the 4th week, a crescent-shaped membrane known as *septum primum* grows from the roof of the atrium toward the endocardial cushions and partially divides the atrium into right and left atria. A large opening, *foramen (ostium) primum* forms between the free edge of the septum primum and the AV cushions. Foramen primum serves as a shunt enabling oxygenated blood to pass from the right to the left atrium. Foramen primum becomes smaller and disappears as the septum primum fuses with the AV cushion. Before foramen primum disappears, perforations (produced by programmed cell death) appear in the central part of the septum primum. Perforations coalesce to form another opening, *-foramen (ostium) secundum* near the roof of the atrium (Fig. 8). Foramen secundum ensures flow of oxygenated blood from the right to the left atrium.

A new crescent-shaped fold, - *septum secundum* descends on right side of septum primum. Septum secundum forms an incomplete partition between the atria leaving a foramen below it, - *foramen ovale (oval foramen)*. The remaining part of septum primum forms *valve of oval foramen (valvula foraminis ovale)*. Foramen ovale and its valve allow most of oxygenated blood entering right atrium from inferior vena cava to pass into left atrium, and prevent passage of blood in an opposite direction.

Primordial pulmonary vein and formation of the left atrium

Most of the wall of left atrium is formed by incorporation of the *primordial pulmonary vein*. This vein develops as an outgrowth of the posterior atrial wall that gains connection with veins coming of the developing lungs. As atrium expands, the primordial pulmonary vein and its main branches are gradually involved into the wall of left atrium. As a result 4 pulmonary veins form and open in the left atrium.

Septation of atria and ventricles

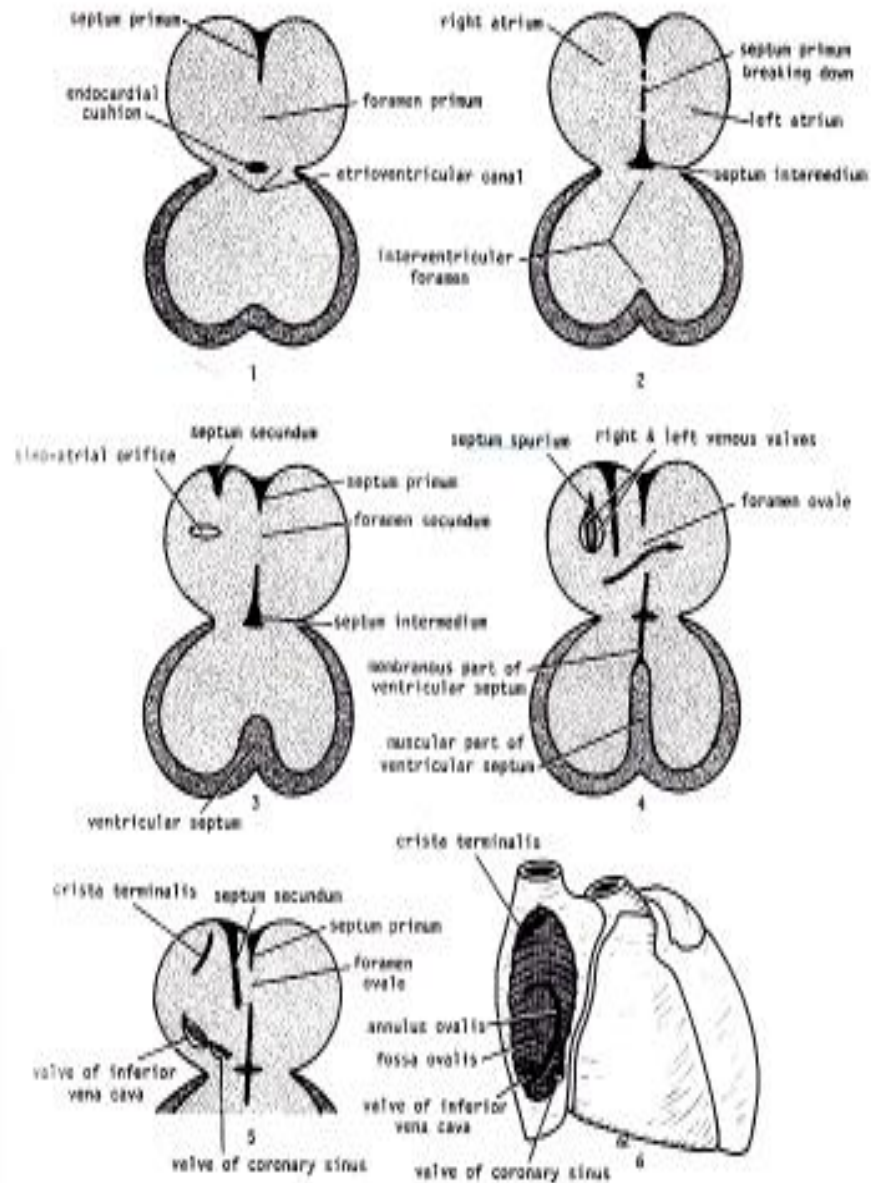


Fig. 8. Steps of septation of the heart.

Septation of the ventricles

By the end of the 4th week, the two primitive ventricles expand. Medial walls of the expanding ventricles become apposed and fuse forming the **muscular interventricular septum**. The **interventricular foramen** is reduced. A down growth from the AV cushion forms the **membranous part of the interventricular septum** which fuses with the muscular part of the IV septum closing the interventricular foramen. IVS closes completely by the end of the 7th week. Cavitation of the inside of the ventricular walls forms as a sponge of muscular bundles called **trabeculae carnae**. Some of these muscular bundles become the **papillary muscles** and **chordae tendineae**.

Partitioning of bulbus cordis and truncus arteriosus (5th to 8th week)

During the 5th week, proliferations of mesenchymal cells (derived mainly from neural crest cells) form ridges in the common tube of BC and TA. These ridges (cushions) are right superior and left inferior. Cushions grow to fuse in a spiral way. Spiraling is caused by the pattern of stream of blood coming from the ventricles. Fusion of these cushions results in formation of the **spiral aortopulmonary septum** (Fig. 9). This septum divides the BC and TA into two channels, - **ascending aorta** and **pulmonary trunk**. Because of the spiraling of the aortopulmonary septum the pulmonary trunk twists around the ascending aorta.

Proximal third of BC is incorporated into the walls of the definitive ventricles to form:

- a) **Infundibulum** of the right ventricle which gives origin of the pulmonary trunk.
- b) **Aortic vestibule** of the left ventricle just below the aortic valve.

Semilunar valves

Two minor cushions, one dorsal and one ventral, grow inwards from the wall of the common tube (BC&TA). As the spiral aortopulmonary septum separates the ascending aorta from the pulmonary trunk and as a result of development of the dorsal and ventral cushions, each of the two arteries will have three cusps for their valves (fig.10). Also, as a result of 45-degree rotation of the common trunk, the pulmonary trunk will have two anterior and one posterior cusps for its valve, whereas the ascending aorta will have one anterior and two posterior cusps for its valve.

Atrioventricular valves

Atrio-ventricular valves develop from localized proliferations of mesenchymal tissues around the A-V canals. Two valve leaflets form the **mitral (bicuspid) valve** and three leaflets form the **tricuspid valve**. This region has the appearance of a cross with the atrial and ventricular septa forming the vertical bar, and the atrioventricular cushions the crossbar. Integrity of this cross is an important sign in ultrasound of the heart.

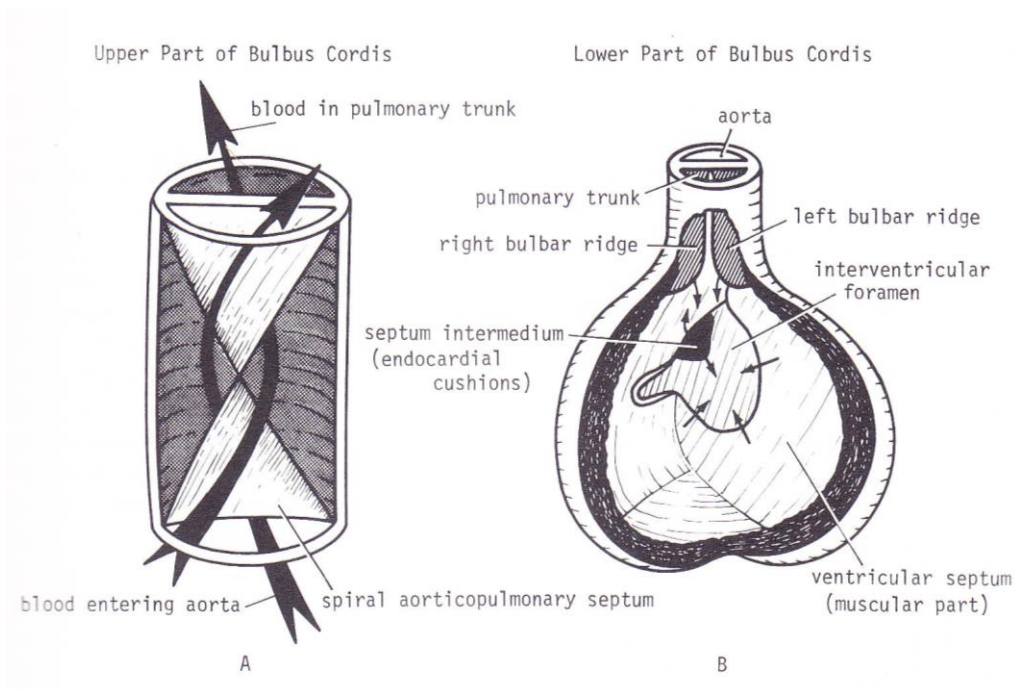


Fig. 9. Partitioning of BC and TA and formation of valves of the heart.

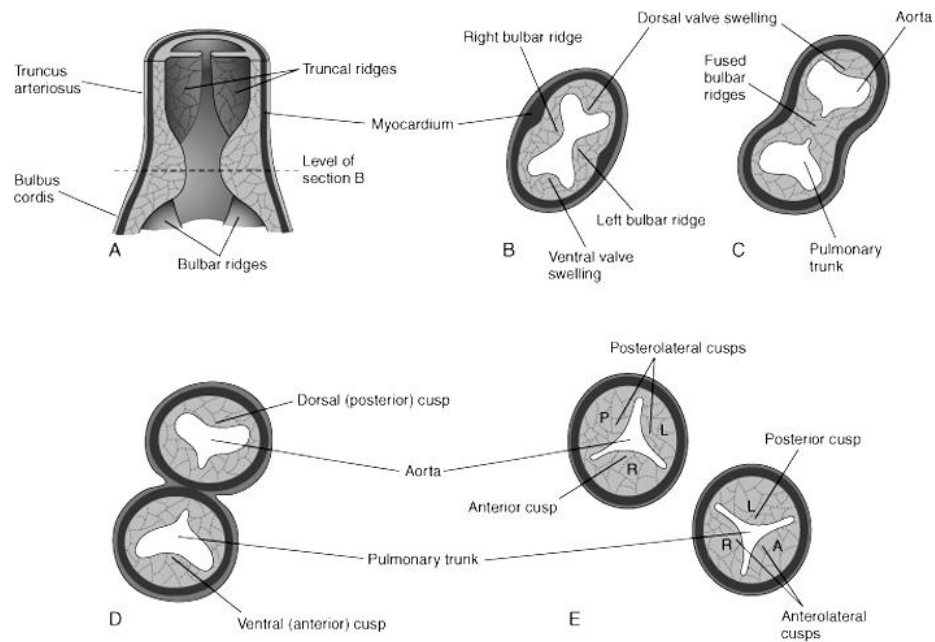


Fig. 10. Formation of the semilunar valves.

Congenital anomalies of the heart (fig. 11)

-Congenital heart defects (CHDs) are common (8/1000 births).

-Causes of CHDs

a) Single gene or chromosomal abnormality (8% of CHDs).

Single gene or chromosomal abnormality (12% of CHDs and 33% of chromosomal abnormalities are associated with CHDs). Genes regulating cardiac development are now identified and mapped. Mutation in heart-specifying gene on chromosome 5 produce ASDs. Fallot tetralogy and A-V conduction delay is an autosomal dominant fashion. Holt-Oram syndrome (VSD and forelimb defects) is an example of heart-hand syndromes. The same gene regulating forelimb development plays a role in septation of the heart. Mutation in genes regulating sarcomere proteins (myosin) causes hypertrophic cardiomyopathy.

b) Exposure to teratogen such as viruses, alcohol, thalidomide and hypervitaminosis A.

c) Maternal diseases as diabetes and hypertension predisposes to CHDs.

d) Multifactorial inheritance combines genetic and environmental factors together.

-Most of CHDs are well tolerated during the fetal life; however at birth when the infant loses contact with the maternal circulation, the impact of CHDs becomes apparent.

-Some types of CHDs are incompatible with life; some others cause very little disability.

-Disturbance of migration of neural crest cells is usually associated with CHDs.

-A cardiac defect causes blood to flow in an abnormal path that produces murmur.

-Diagnostic tests include cardiac catheterization, electrocardiography, echocardiography and chest X-ray.

-Some of the CHDs can be treated surgically.

-Some CHDs are associated with early cyanosis, e.g. transposition of great arteries, persistent truncus arteriosus and tetralogy of Fallot (all start with T). These anomalies are characterized by right to left shunts. Other anomalies that may cause left to right shunts e.g. atrial septal defect, ventricular septal defect and patent ductus arteriosus (all have D) cause late cyanosis because of the prolonged overload of the right ventricle.

1-Acardia

Agensis of the heart is compatible with life in conjoined twins.

2-Dextrocardia

The heart and its vessels are reversed left to right as in a mirror image.

3-Ectopia cordia

Ectopia cordia is abnormal location of the heart; it is a rare abnormality.

Forms

a)Thoracic ectopia cordia; the heart is exposed on the surface of the thorax.

b)Abdominal ectopia cordia; the heart protrudes through the diaphragm into abdomen.

4-Atrial septal defects (ASDs)

ASDs are common anomalies (6:10,000 births) more frequently in females than males. Depending on the size of the defect, manifestations vary from clinically not significant to considerable left to right shunt with overload on the right ventricle. The mechanism of ASD is failure of closure of foramen oval.

Forms:

-Probe patent oval foramen (in 25% of people)

It is a small defect in the superior part of the foramen oval.

-Foramen (ostium) secundum ASD

It is the most common type of ASDs. Large foramen secundum is caused by defective formation of septum secundum. Ostium secundum ASD is well tolerated during childhood. Symptoms such as pulmonary hypertension appear after the age of 30 years.

-Foramen (ostium) primum ASD

Failure of fusion of septum primum with the endocardial cushions results in patent foramen primum..

-Common atrium (cor triloculare biventriculare)

Complete absence of interatrial septum.

5-Ventricular septal defects (VSDs)

Ventricular septal defects are the most common types of CHDs (25% of CHD). VSDs are more frequent in males. They may occur in any part of the IV septum. Many small VSDs close spontaneously (30-50%) during the first year. Large VSD results in pulmonary hypertension, right ventricular overload and heart failure.

Forms:

-Membranous VSD is due to failure of the membranous part of the IV septum to develop.

-Muscular VSD is less common and is due to excessive cavitation of myocardium during formation of the ventricular wall. Sometimes small multiple defects in the muscular septum are present giving the “*swiss cheese VSD*”.

-Absent IV septum (single ventricle).

Eisenmenger syndrome is any congenital heart defect such as VSD and ASD which leads to pulmonary hypertension and cyanosis.

6-Persistent truncus arteriosus (TA) is due to failure of normal development of the aorticopulmonary septum. TA overrides an accompanied VSD. Single arterial trunk arises from the ventricles and supplies systemic and pulmonary circulations. Early cyanosis is present.

7-Transposition of great arteries (TGA)

TGA is the most common cause of cyanotic heart disease in newborn infants. It is often associated with other cardiac anomalies (ASD and VSD). Aorta arises from the right ventricle and the pulmonary trunk arises from the left ventricle. ASD and VSD permit change between pulmonary and systemic circulations. Without surgical correction, infants usually die within few months. TGA is due to defective migration of neural crest cells that are involved in formation of truncal cushions. This results in failure of the spiral course or reversed pattern of the aorticopulmonary septum.

8-Fallot tetralogy

It is a common abnormality (1:1000 births). It is due to unequal division of TA and anterior displacement of the aorticopulmonary septum. This manifests in four defects:

- a)Pulmonary stenosis.
- b)VSD.
- c)Right ventricular hypertrophy.
- d)Overriding of the aorta above VSD.

Cyanosis is an obvious sign of Fallot tetralogy, but is not often present at birth.

9-Valve anomalies

a)Pulmonary stenosis

Pulmonary stenosis is narrowing of the pulmonary valve. It ranges in severity from so mild that requires no treatment to severe that is life threatening. In most of the moderate stenosis the right ventricle contracts at a higher pressure and less blood is pumped to the lungs to be oxygenated.

b)Aortic stenosis

The aortic valve usually has only two leaflets resulting in narrow opening. Consequently, the left ventricle pumps with higher pressure and blood flow to the body is inadequate. The case is surgically treated by balloon valvoplasty.

Other anomalies

-Premature closure of foramen oval in prenatal life leads to massive hypertrophy of RA and RV, and underdevelopment of the left side of the heart. Death usually occurs shortly after birth.

-Ebstein anomaly, tricuspid valve is displaced toward the apex of the right ventricle, with hypertrophy of the RA and small RV.

-DiGeorge syndrome (microdeletion of chromosome 22q), abnormal neural crest cell development with facial defects, thymic and parathyroid hypoplasia and cardiac defects (outflow tract anomalies) .

-Eisenmenger syndrome is any anomaly associated with pulmonary hypertension and cyanosis.

Development of conducting system

A-V node is the first to appear as an outgrowth from *cells* of the *dorsal atrioventricular canal*. **A-V bundle** is a subsequent extension from the **A-V node** which gives rise first to **left** then to **right bundle branches**. Bundle branches are distributed throughout the ventricular myocardium.

S-A node is the last of the conducting system to appear (week 5) from the *right wall of the sinus venosus* at entrance of the superior vena cava.

Anomalies of conducting system

Abnormalities of the conducting system or its neuro-regulation causes **sudden infant death syndrome (SIDS)** which accounts for 50% of infant deaths during the first year.

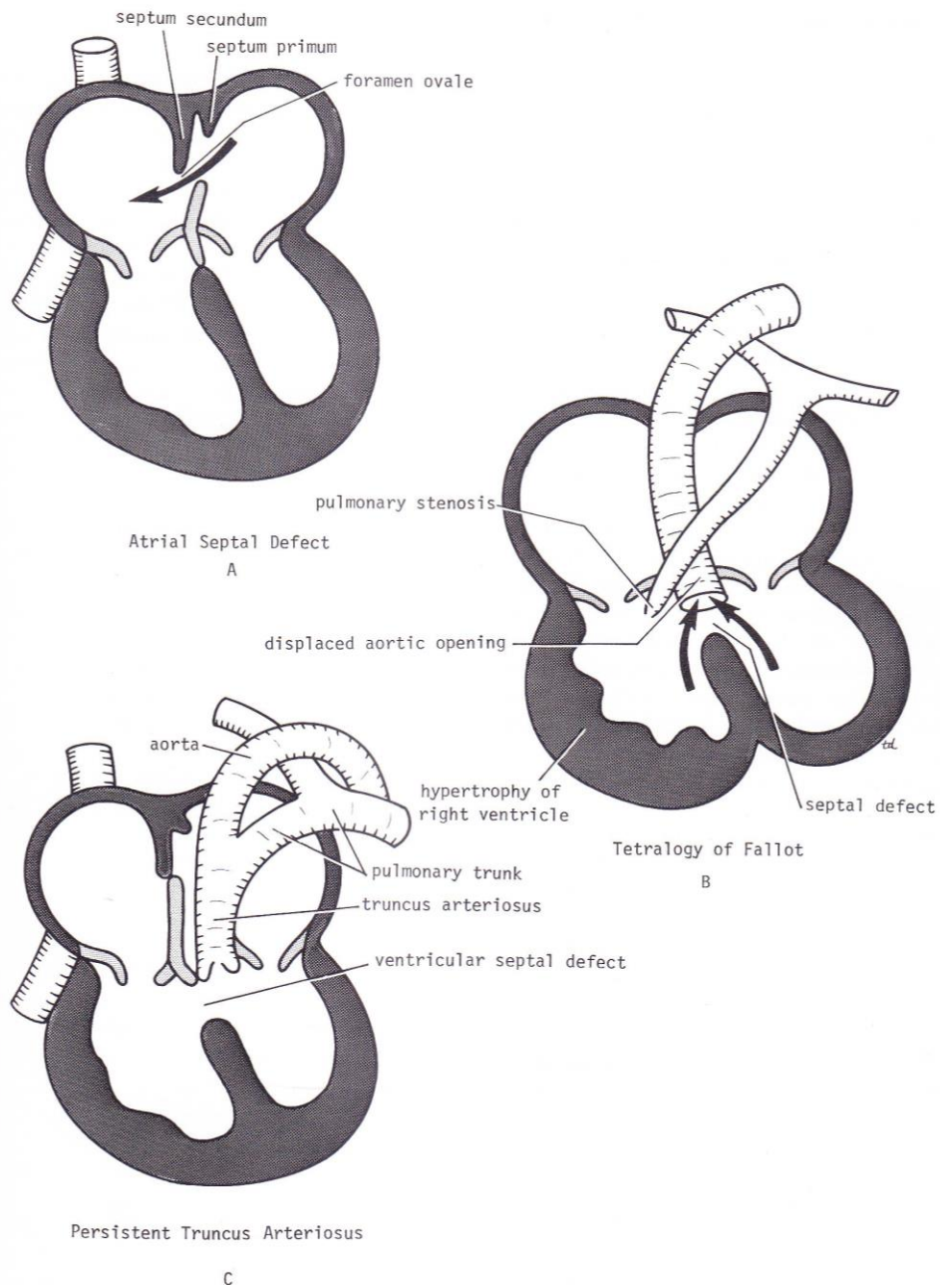


Fig.11: Diagrams illustrating anomalies of the heart.

Aortic arch derivatives

Pharyngeal arches and their aortic arches appear in a craniocaudal sequence. Aortic arches arise from the aortic sac and terminate in right and left dorsal aortae. Caudal to the pharyngeal arches the dorsal aortae fuse to form single descending aorta. When the branchial arches disappear, aortic arches disappear or leave certain arteries (Fig. 13).

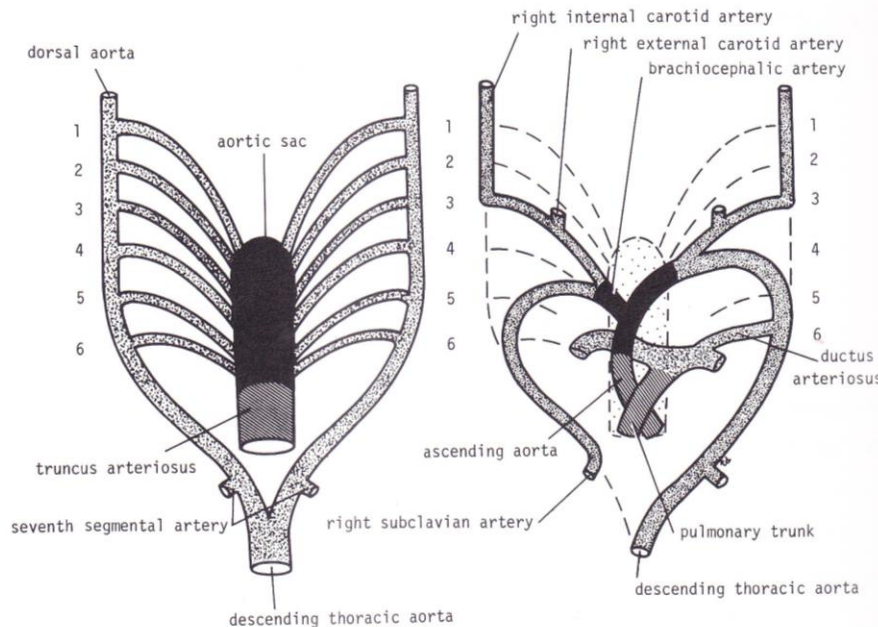


Fig.13: Fate of aortic arches.

Fate of aortic arches

Aortic sac

-Proximal part of aortic arch.

Dorsal aortae

-Left dorsal aorta

-Distal part of aortic arch.

-Right dorsal aorta

-Distal part of right subclavian artery.

First aortic arches

-Disappear leaving maxillary artery.

Second aortic arches

-Disappear leaving stapedial and hyoid arteries.

Third aortic arches

-Form carotid arteries.

Fourth aortic arches

-Left 4th aortic arch

-Form middle part of aortic arch.

-Right 4th aortic arch

-Form proximal part of right subclavian artery.

Fifth aortic arches

??????????

Sixth aortic arches

-Left 6th aortic arch

-Gives left pulmonary artery and ductus arteriosus.

-Right 6th aortic arch

-Gives right pulmonary artery.

Anomalies of aortic arches

1-Coarctation (constriction) of the aorta

Coarctation is narrowing of the aorta. It is an abnormality of the aortic media followed by intimal proliferation. It is due to genetic or environmental factors. It occurs in 10% of CHD, more in males than in females.

Symptoms and signs of coarctation of the aorta

Patients suffer from hypertension in upper body and hypotension in lower body. Legs and feet are pale and cold with weak pulse. There is headache and signs of congestive heart failure. Costal notches are prominent in the ribs as appearing in X-ray. Diagnosis is made by radiography, ultrasonography, CAT scan and MRI.

Types:

i-Preductal (infant type): the constriction is proximal to DA. DA usually remains open. Blood flows through DA to descending aorta. Closure of DA at birth results in rapid deterioration of the infant. Prostaglandin infusion is given in an attempt to reopen DA.

ii-Postductal (adult type): is more common type. DA is usually closed. The constriction is distal to DA. This permits development of collateral circulation between intercostal arteries, internal thoracic arteries and descending thoracic aorta to assist passage of blood into the lower parts of the body.

2-Double aortic arch

Mechanism is failure of distal part of right dorsal aorta to disappear.

3-Right aortic arch

When the entire right dorsal aorta persists and the distal left dorsal aorta involutes.

Coronary arteries develop from blood islands deep to epicardium. During the 6th week capillary plexuses form and join the coronary arteries (that grow from ascending aorta) and cardiac veins that open in the coronary sinus.

Anomalies of coronary arteries

1-Common trunk for coronary arteries.

2-Third coronary artery.

3-Abnormal origin: from pulmonary, carotid, subclavian or internal thoracic arteries.

Development of veins

Fate of vitelline veins

Vitelline veins share in formation of:

- a) **Liver sinusoids.**
- b) **Hepatic veins.**
- c) **Portal vein.**
- d) **Inferior vena cava.**

Fate of umbilical veins

As the liver develops, umbilical veins lose connection with the heart and share in forming **liver sinusoids**. Right umbilical vein disappears.

Fate of cardinal veins

- 1-The **anterior cardinal veins** connect by anastomosis which shunts blood from the left to the right. This shunt becomes the **left brachiocephalic vein**. The cranial portions of the anterior cardinal veins form the **internal jugular veins**. The **Superior vena cava** forms from the right anterior cardinal vein and the right common cardinal vein.
 - 2-The **posterior cardinal veins** disappear.
- Other cardinal veins form part of IVC.

Development of superior vena cava (SVC)

SVC develops from the right anterior cardinal vein and the right common cardinal vein.

Development of inferior vena cava (IVC)

- Hepatic segment** from cranial part of right vitelline vein.
- Renal segment** from the right subcardinal vein.
- Sacrocaval segment** from the right sacrocaval vein.

Anomalies of venae cavae

- 1-**Double superior vena cava.**
- 2-**Left superior vena cava.**
- 3-**Double inferior vena cava.**
- 4-**Absence of hepatic segment of IVC.**

Fetal Circulation (Fig .14)

-Oxygenated blood (80% oxygen saturation) returns from the placenta in the umbilical vein. On reaching the liver about half of this blood passes to inferior vena cava via **ductus venosus**. The other half flows into sinusoids of the liver and mixes with portal blood and enters IVC through hepatic veins. Oxygen saturation in IVC is 67%, lowered because it contains poorly oxygenated blood from lower limbs.

-Most of blood in IVC guided by valve of IVC is directed to foramen oval to left atrium.

-In the left atrium blood is mixed with small amount of poorly oxygenated blood returning from the lungs. From left atrium blood passes to left ventricle and leaves it through ascending aorta (62% oxygen saturation). Arteries of the heart, head, neck, brain and upper limbs receive well oxygenated blood.

-Small amount of well oxygenated blood from IVC remains in right atrium and mixes with poorly oxygenated blood from superior vena cava and coronary sinus and passes to right ventricle. This blood leaves through pulmonary trunk. Resistance in fetal pulmonary vasculature is high, so only 10% of pulmonary blood goes to the lungs. Most of pulmonary blood passes through **ductus arteriosus** to descending aorta. Ductus arteriosus protects the lungs from circulatory overloading and allows the right ventricle to strengthen in preparation for functioning full capacity at birth. The right ventricular wall is thicker than the left ventricular wall in the fetus and newborn infants. By the end of the first month, the right ventricular wall becomes thinner because of atrophy associated with lighter workload.

-Only 10% of blood from ascending aorta enters descending aorta to supply the viscera and lower part of the body. Remaining blood passes into umbilical arteries (oxygen saturation is 58%) and is returned to the placenta for reoxygenation.

Changes at birth in the fetal circulation

Postnatal changes of the fetal circulation are caused by cessation of placental blood flow and beginning of respiration. Changes seem to occur in the following order:

1-Immediately after birth, bradykinin released from the lungs with initial inflation causes closure of ductus arteriosus by contraction of its walls. Complete anatomical closure takes from 1-3 months and the DA becomes the **ligamentum arteriosum**.

2- Closure of foramen oval is caused by increased pressure in LA combined with decreased pressure in RA. The first breath pushes the septum primum against the septum secundum. During the first days of life this closure is reversible. Crying by the baby creates a shunt from right to left which accounts for cyanotic periods in the newborn. Constant apposing leads to fusion of the two septa in about one year to form **fossa oval**.

3-Closure of the umbilical arteries by contractions of its muscular walls is caused by thermal or mechanical stimulation. Arteries close few minutes after birth while actual obliteration takes from 2-3 months. The distal parts of the umbilical arteries form the **medial umbilical ligaments**.

4-Closure of the left umbilical vein occurs shortly after closure of the umbilical arteries. Closure of the umbilical vein forms **ligamentum teres** of the liver.

5-Closure of the ductus venosus forms **ligamentum venosum** of the liver.

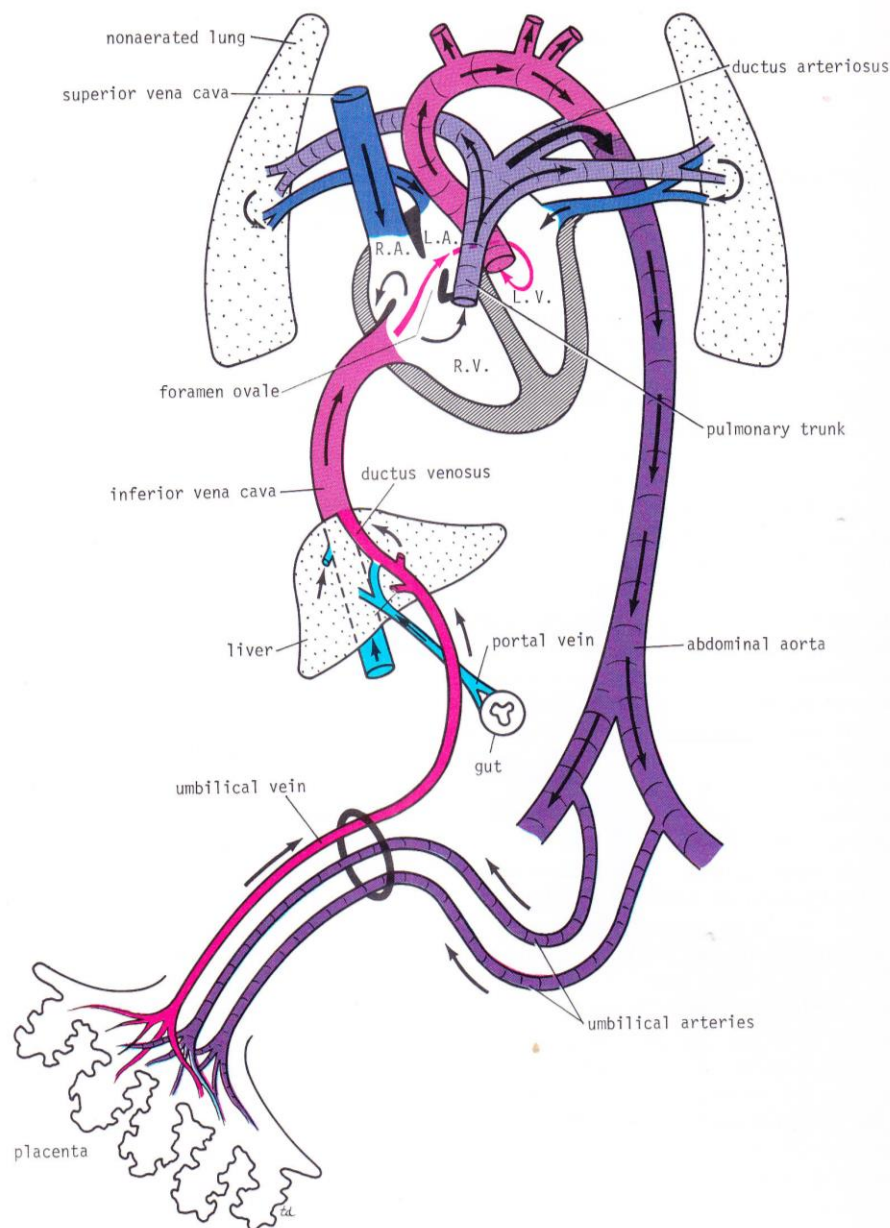


Fig. 14. Diagram illustrating the fetal circulation.

Patent ductus arteriosus is a common anomaly (1:1000 births) is due to failure of the muscular wall of DA to close. Aortic blood is shunted into pulmonary trunk. It may be due to (a) maternal rubella, (b) premature infants, (c) hypoxia, (d) respiratory distress syndrome, (e) large difference between aortic and pulmonary pressure (as in pulmonary stenosis, coarctation of aorta and transposition of great arteries).

Branches of dorsal aortae and their fate

Dorsal aorta develops *ventral, lateral and posterolateral branches.*

1-Ventral branches of dorsal aorta

a)Vitelline arteries are paired arteries fuse and form single arteries in dorsal mesentery of the gut:

i-Celiac trunk to the foregut.

ii-Superior mesenteric artery to the midgut.

iii-Inferior mesenteric artery to the hindgut.

b)Umbilical arteries, the proximal part gives superior vesical and internal iliac arteries, the distal part obliterates to form medial umbilical ligament.

2-Lateral splanchnic arteries supply intermediate mesoderm. They give renal, suprarenal, phrenic and gonadal arteries.

3-Posterolateral branches are somatic branches. They are *30 pairs of dorsal inter-segmental arteries* that pass in between and carry blood to somites and their derivatives. Most of original connections of intersegmental arteries to dorsal aorta disappear:

-In the neck they join to form the **vertebral, ascending cervical, deep cervical, superior intercostals, and subclavian arteries.**

-In the thorax they persist as **posterior intercostals arteries.**

-In the abdomen they remain as **lumbar arteries.** The 5th pair of lumbar inter-segmental arteries forms the common iliac arteries.

-In the pelvis they form the **lateral sacral arteries.**

The caudal end of the dorsal aortae becomes the **median sacral artery.**

Arterial system

Ascending Aorta

The ascending aorta arises from the LV and conducts blood going to the body systems. It is 5 cm long and 3 cm in diameter. It contains 3 dilatations, aortic sinuses at its beginning. These sinuses are above its semilunar valve. It ascends to end opposite the sternal end of the right second costal cartilage by continuing as aortic arch.

Branches

1-**Right coronary artery** arises from the anterior aortic sinus. It supplies most of the right side of the heart and the conducting system.

2-**Left coronary artery** arises from the left posterior aortic sinus. It supplies most of the left side of the heart and the inter-ventricular septum.

Aortic arch

The aortic arch is a continuation of the ascending aorta. It is curved upward and backward to end opposite the 4th thoracic vertebra by becoming the descending thoracic aorta. It is about 4.5 cm long and 3 cm in diameter.

Branches

1-Brachiocephalic artery

This is the first and largest branch of the aortic arch. It arises behind the manubrium and ascends until the right sternoclavicular joint where it divides into right common carotid artery and right subclavian artery.

2-**Left common carotid artery**. It enters the neck behind the left sternoclavicular joint.

Common carotid arteries enter the carotid sheath in the neck and divide into two main branches; internal and external carotid arteries at the level of the upper border of the thyroid cartilage. The **internal carotid artery** enters the skull to supply the brain and the eye. The **external carotid artery** gives branches that supply pharynx, thyroid gland, tongue, face, salivary glands, scalp, teeth, jaws and paranasal sinuses.

3-Left subclavian artery

Subclavian arteries arch superior to apex of lung cross the first rib and then enter the axillae to supply the upper limbs. In the neck subclavian arteries give branches that supply thyroid gland, vertebrae, spinal cord, brain stem and deep structures of the neck.

Descending thoracic aorta

The thoracic aorta is the continuation of the aortic arch at level of T4. It descends in front of the vertebral column to enter the aortic opening of the diaphragm at level of T12 where it continues as the abdominal aorta.

Branches

1-**Posterior intercostal arteries** from 3-12 supplying intercostal spaces in both sides.

2-**Left bronchial artery** supplying lung tissue of the left lung.

3-**Oesophageal branches**, 4-5 branches supplying thoracic portion of the oesophagus.

4-**Twigs to pericardium**.

5-**Twigs to the diaphragm**.

Venous system

The right atrium receives venous blood returning from the different parts of the body through superior vena cava and inferior vena cava.

Inferior vena cava

The IVC is 20 cm long and 2 cm wide. It is formed by union of two common iliac veins at level of L5. It ascends on the right side of the abdominal aorta and grooves the inferior surface of the liver until it pierces the central tendon of the diaphragm at level of T8 to open in the lower part of the right atrium. Its opening is guarded by a faint valve.

Superior vena cava

The SVC is 7.5 cm long and carries venous blood returning from the head, neck, brain upper limbs and thoracic walls. It is formed by union of two brachiocephalic veins behind the right first costal cartilage. Each brachiocephalic vein is formed by union of two veins; the internal jugular vein (drain blood from the head, neck and brain) and subclavian vein (draining blood from the upper limb). It descends on the right side of the ascending aorta to open in the upper part of the right atrium.

Tributaries

- 1-Several small **pericardial** and **mediastinal** veins.
- 2-**Azygos vein**.

Azygos system of veins

There are three azygos veins; azygos vein on the right side, superior hemiazygos and inferior hemiazygos on the left side.

Azygos vein begins in the abdomen from the back of the IVC and ascends in the aortic opening of the diaphragm. In the thorax it ascends behind the oesophagus, arches above the root of the right lung to end in the SVC. Its tributaries are the right posterior intercostal veins, hemiazygos veins, bronchial veins, oesophageal veins and pericardial veins.

Hemiazygos veins drain left posterior intercostal veins and cross the vertebral column to end in the azygos vein.

Questions of development of the heart and blood vessels

I-Multiple choice questions

Choose ONE correct answer

1-The cranial part of the right sinoatrial valve leaves

- a) AV node.
- b) Interatrial septum.
- c) Crista terminalis.
- d) Valve of coronary sinus.
- e) Oblique vein of left atrium.

2-Early neonatal cyanosis is mainly due to which cardiovascular anomaly

- a) Fallot tetralogy.
- b) Aortic stenosis.
- c) Patent ductus arteriosus.
- d) Transposition of great arteries.
- e) Dextrocardia.

3-The endocardial heart tube is mainly derived from

- a) Progenitor cells in the epiplast.
- b) Endoderm of the foregut.
- c) Somatic lateral mesoderm.
- d) Neural crest cells.
- e) Thoracic dermatomyotomes.

4-Formation of foramen secundum in the developing atrium is due to

- a) Disappearance of septum primum.
- b) Disappearance of foramen primum.
- c) Programmed cell death in the upper part of septum primum.
- d) Fusion of cushions in the atrioventricular canal.
- e) Development of the venae cavae.

5-Spiraling of the aorticopulmonary septum is mainly caused by

- a) Twisting of pulmonary trunk on ascending aorta.
- b) Streams of blood coming from ventricles.
- c) Rotation of bulbotruncal canal.
- d) Presence of 4 cushions inside the truncus arteriosus.
- e) Delayed formation of interventricular septum.

6-The commonest congenital heart anomaly is

- a) Coarctation of aorta.
- b) Patent ductus arteriosus.
- c) Atrial septal defect.
- d) Ventricular septal defect.
- e) Aortic valve stenosis.

7-The first of the conducting system of the heart to develop is

- a)SAN.
- b)AVN.
- c)AVB.
- d)Purkinje fibers.
- e)Moderator band.

8-Sudden infant death syndrome during the first year of life is mainly due to

- a)Abnormalities of the conducting system and its neuro-regulation.
- b)Aortic valve defects.
- c)Coarctation of the aorta.
- d)Pulmonary hypertension.
- e)ASD.

9-Carotid arteries remain from

- a)Aortic sac.
- b)Cranial part of dorsal aorta.
- c)Third aortic arches.
- d)Fourth aortic arches.
- e)Truncus arteriosus.

10-Coronary arteries develop from

- a)First aortic arches.
- b)Blood islands deep to epicardium.
- c)Aortic sac.
- d)Internal carotid arteries.
- e)Descending thoracic aorta.

11-15- Match event in column I with appropriate embryonic day in column II

Column I	Column II
11-Complete looping of heart tube.	a)Day 49.
12-Development of SAN.	b)Day 28.
13-Complete fusion of interventricular septum.	c)Day 70.
14-Disappearance of sinus venosus.	d)Day 22.
15-Start beating of the heart.	e)Day 35.

16-20- Match cardiovascular anomaly in column I with manifestation in column II

Column I	Column II
16-Double aortic arches.	a)Late cyanosis.
17-Coarctation of aorta.	b)Thoracic exposure of the heart.
18-Defective development of conducting system.	c)Dysphagia.
19-Fallot tetralogy.	d)Weak pulse of lower limbs.
20-Ectopia cordia.	e)Sudden infant death.

II-Complete

1-Anomalies associated with Fallot tetralogy are:.....,.....,.....,.....

2-Branches of the permanent aortic arch are:.....,.....,.....

3-Superior vena cava is formed by fusion of.....

4-Tributaries of azygos vein are

- a)
- b)
- c)
- d)

5-Eisenmenger syndrome is characterized by

- a)
- b)

6-Cardiac anomalies with left to right shunts with potential late cyanosis are

- a)
- b)
- c)

7-Cardiac anomalies with early cyanosis are

- a)
- b)
- c)

8-State main signs of coarctation of the aorta

- a)
- b)
- c)

III-Explain why

a)Foramen oval is patent during prenatal life.

b)Ascending aorta and pulmonary trunk are twisted around each other.

c)Left horn of sinus venosus is less important than the right horn.

d)Two endocardial heart tubes become one.

e)Only posterior part of right atrium is smooth while most of left atrium is smooth.

IV-Cases

1-A pediatrician detected a cardiac defect in an infant, and he explained to the baby's mother that this is a common birth defect.

- a)What is the most common congenital cardiac defect and what is its percentage?
- b)What problems would the infant likely have if this cardiac defect was large?

2-After pregnancy complicated by rubella virus, a female infant was born with congenital cataract and congenital heart defect. A radiograph of the infant chest showed increased pulmonary vasculature and cardiac enlargement.

- a)What CHD is commonly associated with maternal rubella?
- b)What probably caused the cardiac enlargement?

3-A child is born with severe craniofacial defects and transposition of the great arteries.

- a)What cell population might play a role in both anomalies? And what type of insult might have produced this?
- b)Suggest a possible mechanism for TGA.
- c)What is the main signs of TGA in the newborn?

4-A patient complains about having difficulty swallowing.

- a)What vascular abnormality might produce this complaint?
- b)What is the embryological basis of this abnormality?

5-During prenatal monitoring, a doctor discovered prenatal closure of the foramen oval. Which chamber of the heart is expected to be overloaded? Would any procedure be indicated to help this fetus?