14 Development of Cardiovascular System

Competencies covered in this chapter

AN 25.2: Describe development of heart

AN 25.3: Describe fetal circulation and changes occurring at birth

AN 25.4: Describe embryological basis of atrial septal defect

AN 25.4: Describe embryological basis of ventricular septal defect

AN 25.4: Describe embryological basis of Fallot's tetralogy

AN 25.5: Describe developmental basis of congenital anomalies, transposition of great vessels and dextrocardia

AN 25.5: Describe developmental basis of coarctation of aorta

AN 25.5: Describe developmental basis of patent ductus arteriosus

AN 25.6: Mention development of coronary sinus

AN 25.6: Mention development of superior vena cava and inferior vena cava

AN 25.7: Mention the development of aortic arch arteries

Learning Objectives

At the end of this chapter, students would be able to define and understand the following:

- Development of the interatrial septum and the atria
- Development of the interventricular septum and the ventricles
- Development of the spiral septum and division of the truncus arteriosus
- Development of the pharyngeal arch arteries
- Development of the inferior vena cava (IVC)
- Fetal circulation

Keywords: Sinus venosus, atrial septal defect, ventricular septal defect, coarctation of aorta, dextrocardia, Fallot's tetralogy

Introduction

Cardiovascular system is the first system to commence its function. The blood begins to circulate through it toward the end of the third week. In *cardiogenic area, cranial to the prechordal plate, a pair of endothelial cords called cardiogenic cords* appear in the third week. They acquire lumen to form tubes. With the lateral folding of the embryo, the two heart tubes fuse in the craniocaudal sequence to form a single heart tube (**Fig. 14.1**).

Position of the Heart Tube

As the head folding occurs, the heart tube reverses its position in relation to the pericardial coelom and projects into the pericardial cavity from the dorsal side. Initially, the tube is ventral and the cavity is dorsal to it and both are cranial to the prechordal plate. Then both come to lie ventral to the prechordal plate, with the tube being behind the cavity. Finally, both lie caudal to the prechordal plate (buccopharyngeal membrane), and the tube is suspended into the cavity from the dorsal side by *dorsal mesocardium. As it disappears, the transverse pericardial sinus is formed* (**Fig. 14.2** and **Fig. 14.3**).

As the primitive heart tube grows, the mesenchyme around it forms myoepicardial mantle. The endothelial heart tube forms endocardium. It is separated from the myoepicardial mantle that forms the myocardium and the epicardium (visceral pericardium). Soon the heart tube undergoes differential growth and thus shows dilatations and constrictions. From the caudal (venous end) to cranial (arterial end) side, these are: (1) sinus venosus, (2) primitive atrium, (3) primitive (common) ventricle, (4) bulbus cordis, and (5) truncus arteriosus.

The venous and the arterial ends of the developing heart tube are fixed by the septum transversum and the branchial arch arteries, respectively. Therefore, as the tube elongates, it folds to form bulboventricular loop. Normally, it is the right looping that occurs; instead, if the heart tube undergoes left looping, it results in dextrocardia (**Fig. 14.4**). It may be associated with the situs inversus (transposition of the viscera).

Primitive Circulation

The primitive heart begins to contract on day 22; however, the circulation through it is ebb and flow type at *this stage*. The blood is received into the sinus venosus through three paired veins:

- Common cardinal veins—from the embryo.
- Umbilical veins—draining the placenta.
- Vitelline veins—draining the yolk sac.

Blood from the sinus venosus enters primitive atrium via sinoatrial opening guarded by the right and left sinoatrial/sinus valves. Then the blood passes through atrioventricular canal, common ventricle, bulbus cordis, and truncus arteriosus into the dorsal aortae to be distributed to the embryo, the placenta, and the yolk sac.

Sinus Venosus

It is the most caudal dilatation at the venous end of the heart tube. It has two horns: the right and the left. Each horn receives blood from (1) the embryo via common cardinal vein, (2) the placenta via umbilical vein, and (3) the yolk sac via vitelline vein.

Initially, the sinus venosus opens into the center of the posterior wall of the primitive atrium (**Fig. 14.5**). Its two horns, right and

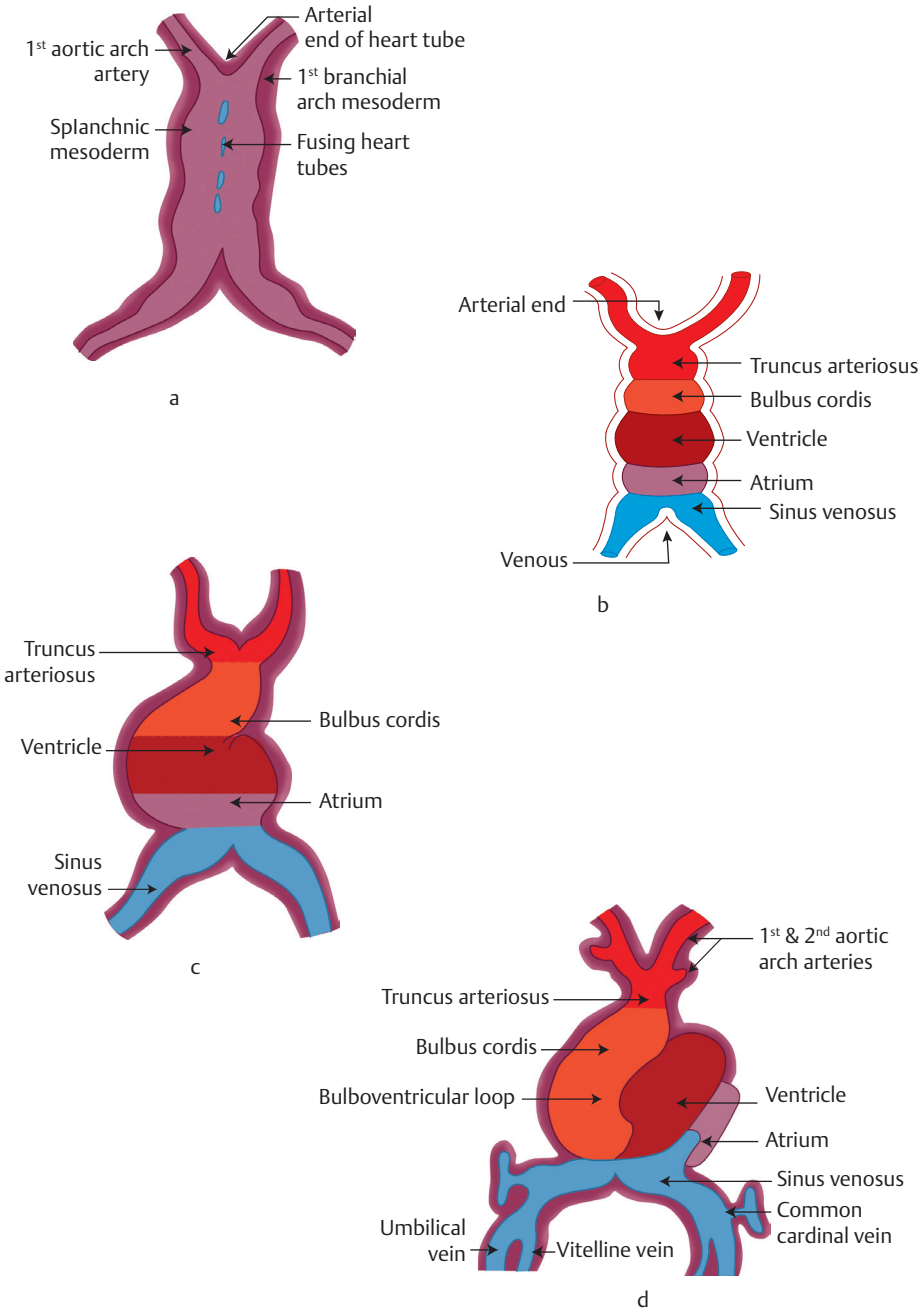


Fig. 14.1 (a–d) Illustrations showing formation of the heart tube followed by its differential growth and formation of the bulboventricular loop.

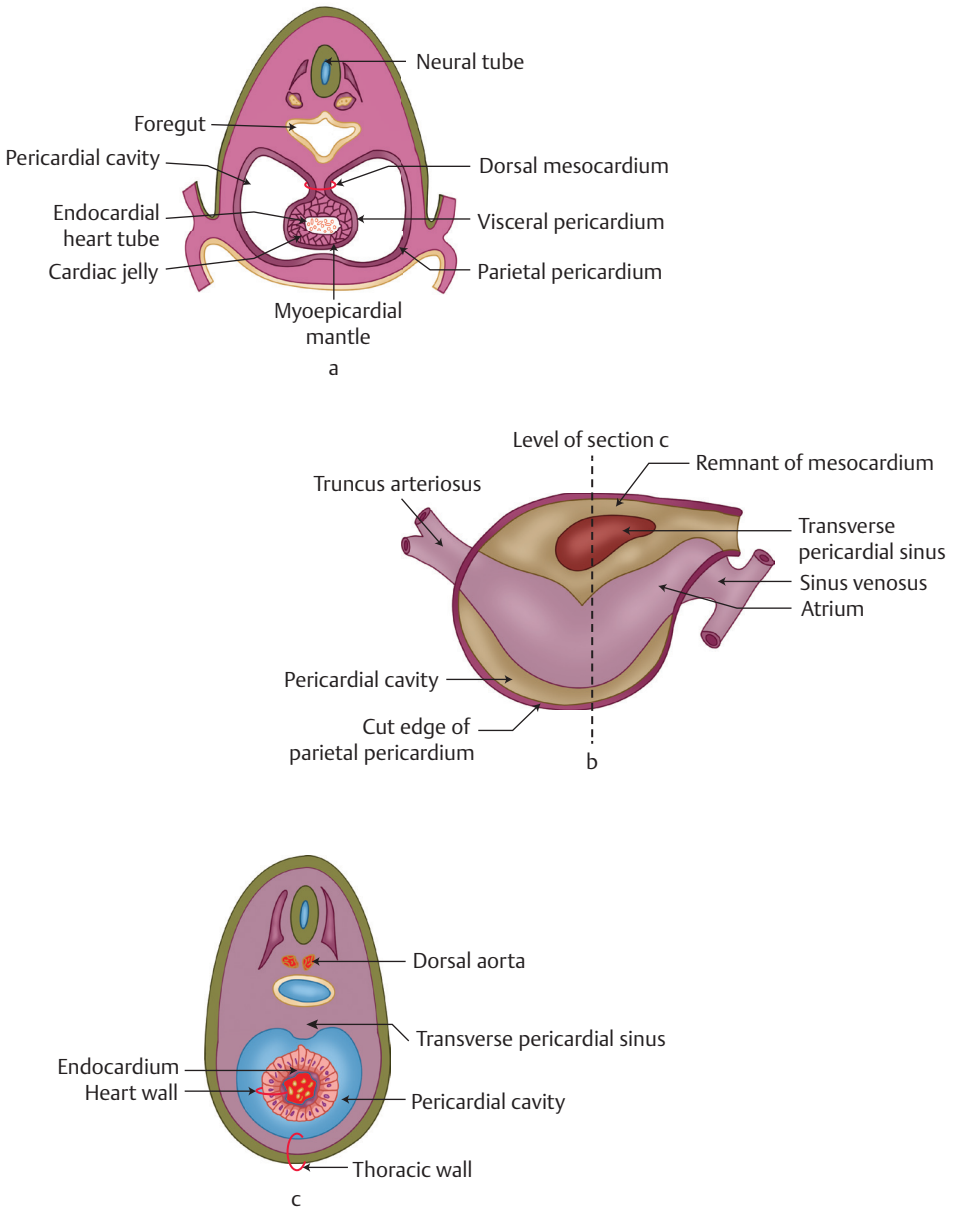


Fig. 14.2 (a–c) Illustrations showing formation of transverse pericardial sinus by degeneration of the dorsal mesocardium.

left, are almost equal in size. Subsequently, two left-to-right shunts develop.

- **Oblique anastomosis:** It is between two anterior cardinal veins and diverts blood from the left to the right side.
- **Ductus venosus:** It directs blood (with better PO_2) from the left umbilical vein via left branch of the portal vein to the left hepatic vein or to the inferior vena cava (IVC) without being relayed into

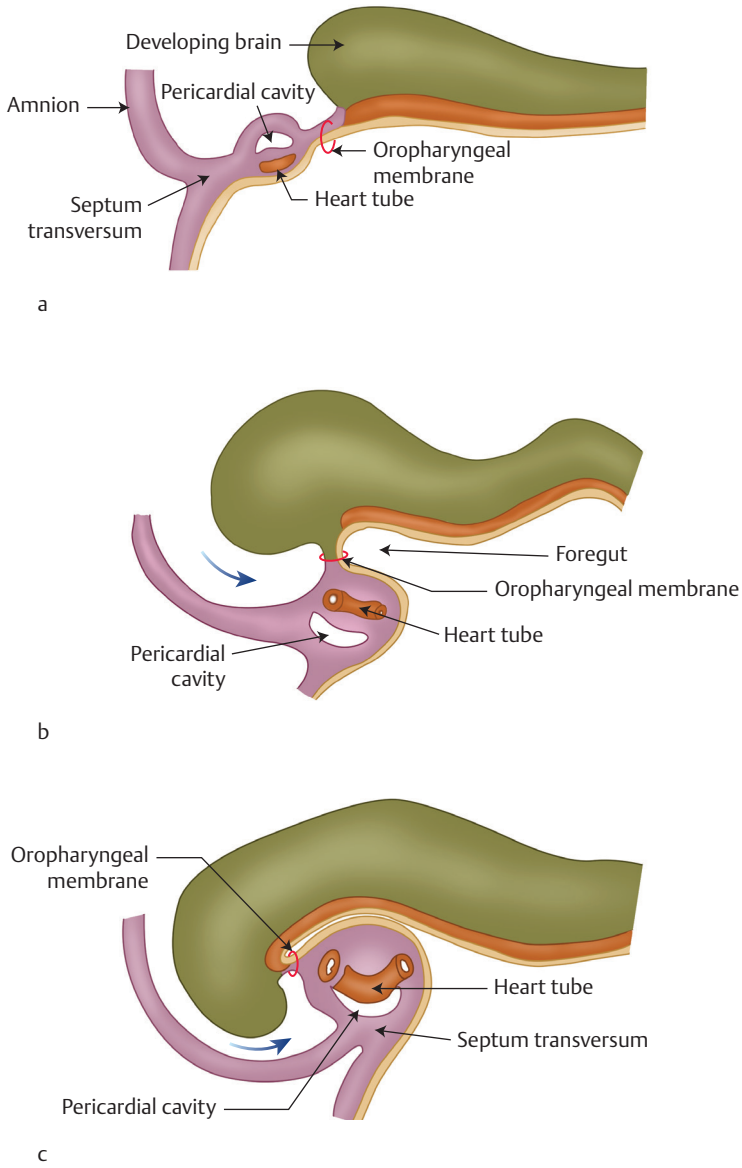


Fig. 14.3 (a–c) Illustrations showing longitudinal sections of the cranial part of the embryo. Note the change in the relationship of the heart tube and the pericardial coelom due to formation of the head fold.

the hepatic sinusoids. The purpose is to conserve the oxygen content of the blood coming from the placenta. After birth, it obliterates to form *ligamentum venosum.*

With these two shunts, the right horn enlarges as compared with the left. The left horn regresses in size. The result being the shift of the sinoatrial opening to the right side.

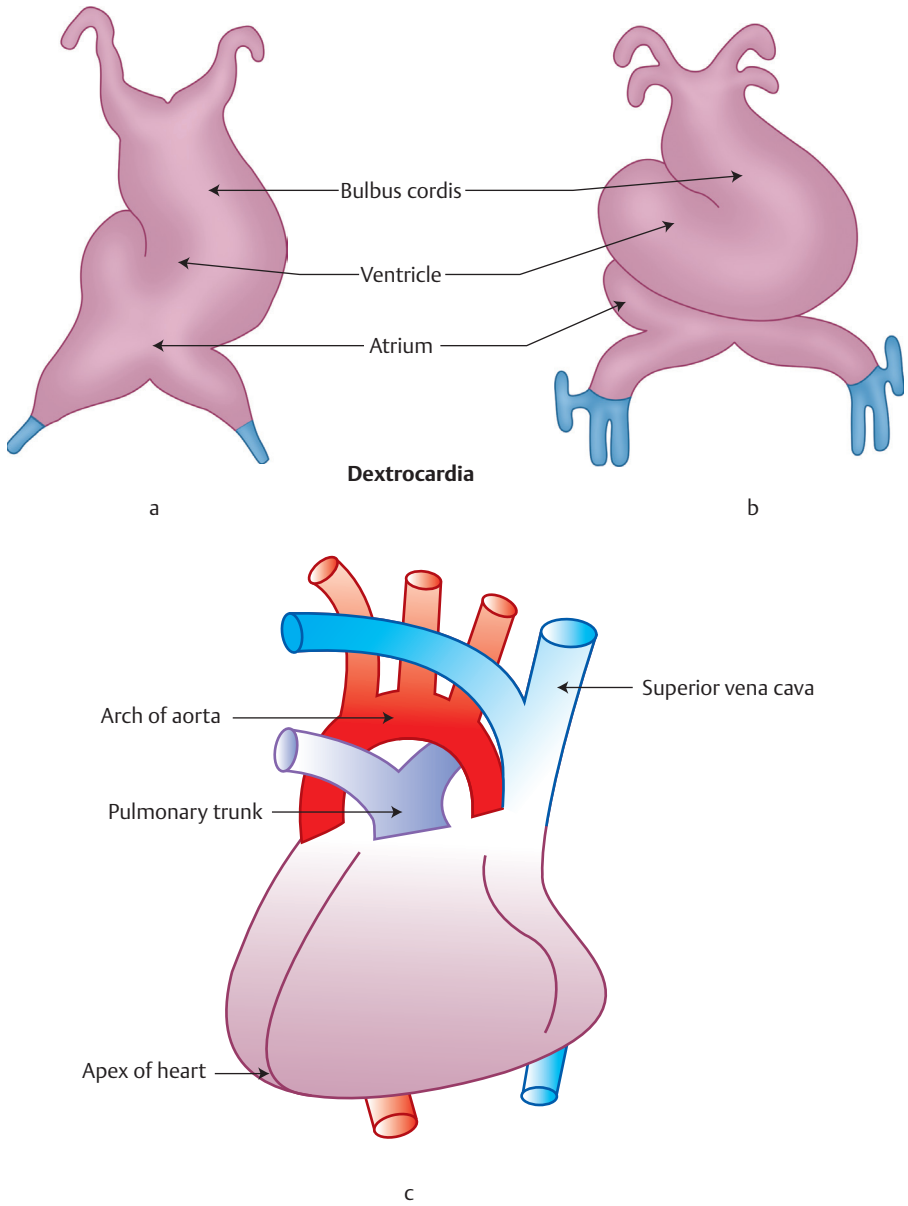


Fig. 14.4 **(a–c)** Illustrations showing genesis of dextrocardia.

Fate of Sinus Venosus

- **The right horn:** It is progressively incorporated into *the dorsal aspect of the primitive atrium and forms sinus venarum*, the smooth posterior part of the right atrium.
- **The left horn:** It *regresses and forms the coronary sinus* (**Fig. 14.6**).
- **Right sinoatrial valve:** It *forms crista terminalis, valve of IVC (eustachian valve), and the valve of coronary sinus.*
- **Left sinoatrial valve:** It fuses with the septum secundum and contributes

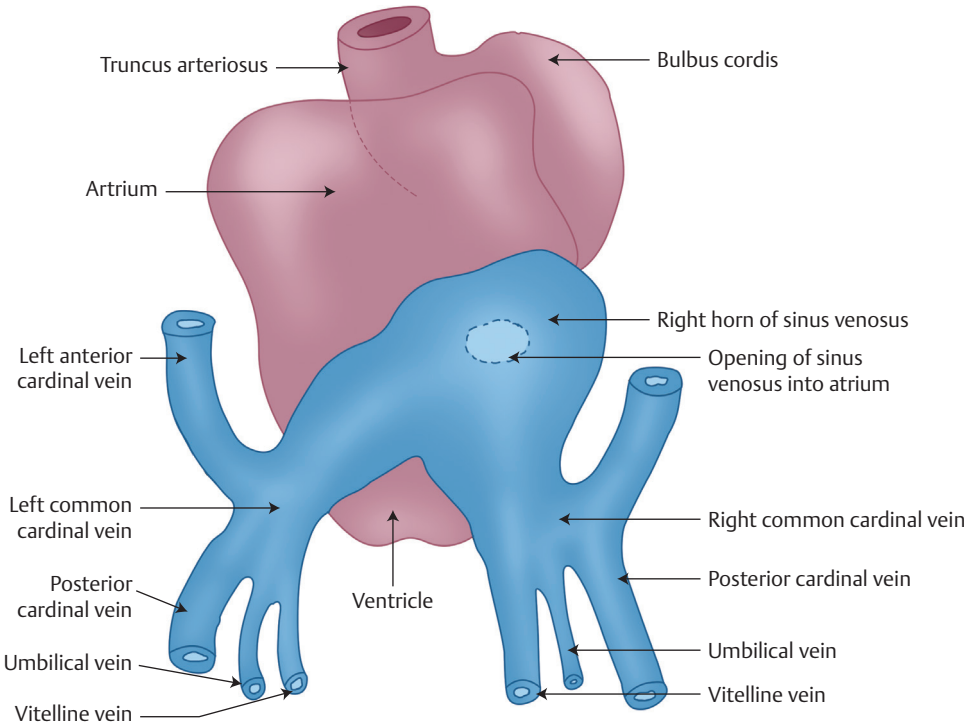


Fig. 14.5 Illustration showing the horns of the sinus venosus and the primitive atrium, a dorsal view.

to the formation of interatrial septal complex.

- **Septum spurium:** When the right and the left sinoatrial valves are traced cranially, they fuse to form septum spurium. It also contributes to the interatrial septum (**Fig. 14.7**).

Fate of Veins Around

- **Oblique anastomosis:** It forms left brachiocephalic vein.
- **Right anterior cardinal vein:** (a) With cranial to oblique anastomosis, it forms the right brachiocephalic vein, and (b) with caudal to oblique anastomosis, it forms the part of the superior vena cava (SVC).
- **Right common cardinal vein:** It forms the part of the SVC after receiving azygos vein.
- **Right posterior cardinal vein:** Its terminal part forms the root of the azygos vein.

Development of Atria and Interatrial Septum

The primitive atrium is divided into the right and left by development of the interatrial septum, that is, partitioning of the primitive (common) atrium occurs. Around the fourth week, the dorsal and ventral endocardial cushions develop from the respective walls of the atrioventricular canal. These fuse with each other forming septum intermedium (fused endocardial cushion). This divides the atrioventricular canal into the right and the left atrioventricular canals (**Fig. 14.7**).

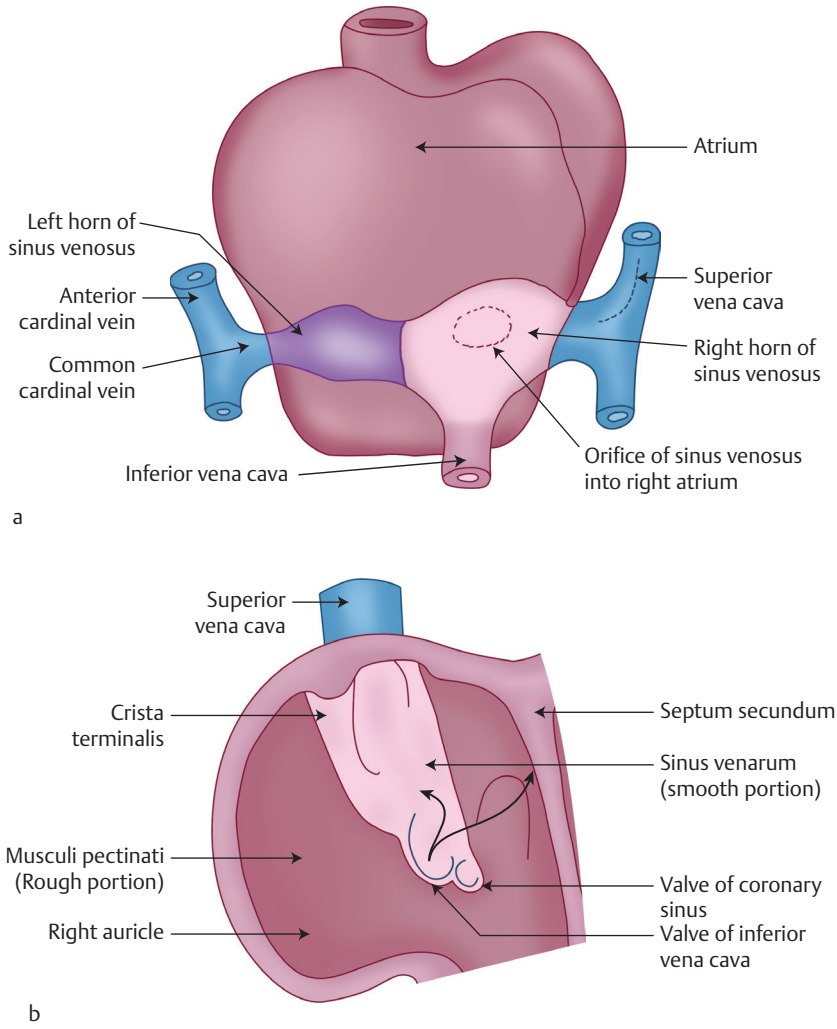
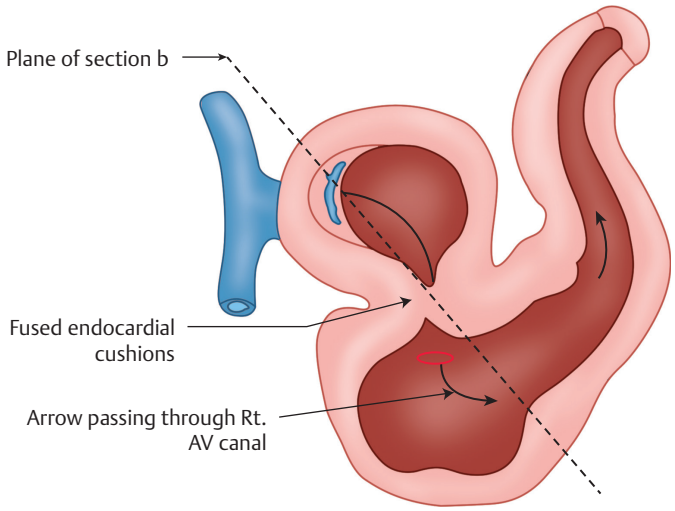


Fig. 14.6 Illustrations showing fate of sinus venosus: **(a)** Dorsal view and **(b)** interior of the right atrium.

Interatrial Septum

It develops from the following elements: (1) septum primum, (2) septum secundum, (3) septum spurium, and (4) left sinoatrial valve.

- **Septum primum:** It develops as a thin crescentic fold from the dorsocranial wall or roof of the primitive atrium. The large gap between its caudal edge and the endocardial cushion is called *foramen primum.* It obliterates when septum primum fuses with fused endocardial cushion/septum intermedium. Before this happens, small perforations appear in the upper part of the septum primum. These perforations coalesce to form *foramen secundum* (**Fig. 14.8**).
- **Septum secundum:** To bridge foramen secundum, another thick crescentic fold grows downward from the ventrocranial side of the primitive atrium immediately to the right of the



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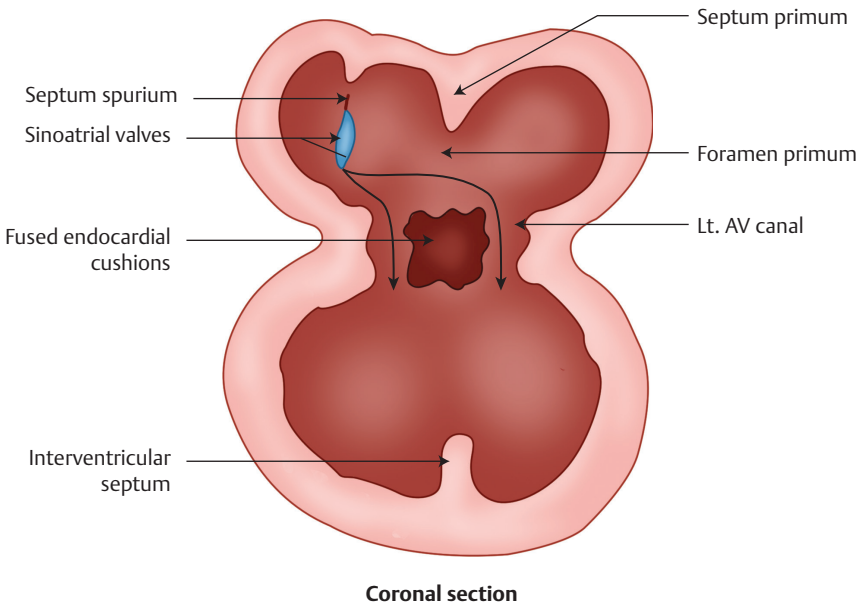

b

Fig. 14.7 Illustrations showing **(a)** sagittal section with fused endocardial cushions, dividing atrioventricular canal and **(b)** section showing initial development of the interatrial and interventricular septa. AV, atrioventricular; Lt, left; Rt, right.

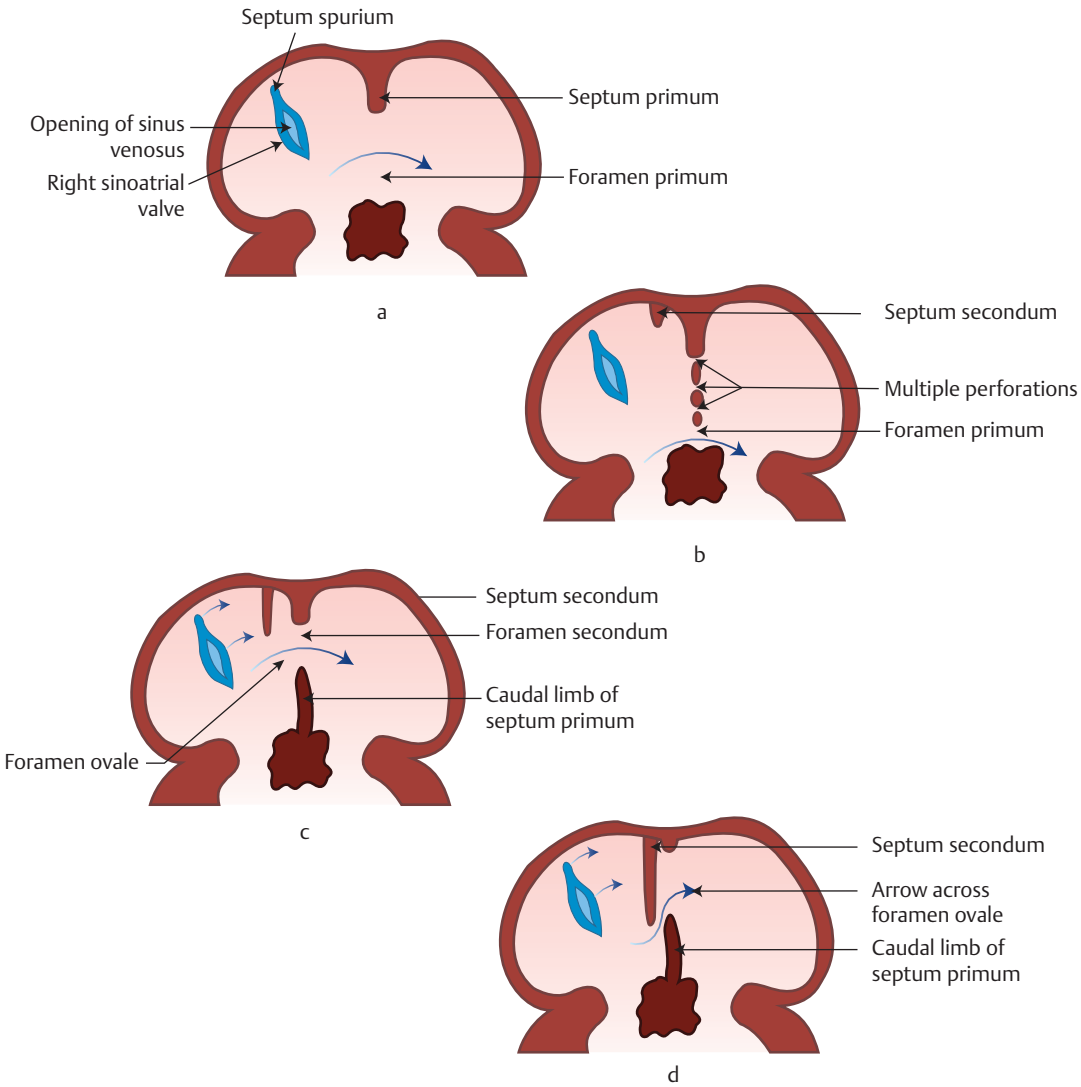

Fig. 14.8 (a–d) Illustrations showing development of interatrial septum.

septum primum. This is called septum secundum. Between its caudal edge and the caudal limb of the septum primum exists a valvular gap called foramen ovale. The cranial limb of the septum primum degenerates and its caudal limb forms the valve of foramen ovale.

- **Septum spurium:** The right and left sinoatrial valves, when traced cranially, fuse to form septum spurium, which eventually fuses with septum secundum.
- **Left sinoatrial valve:** Along with the right sinoatrial valve, it guards the opening of sinus venosus into the primitive atrium. Eventually, the left sinoatrial valve merges with the interatrial septum.

Why and When Does the Foramen Ovale Close?

The foramen ovale closes at birth. To understand why it closes, we need to know the following background.

Input to the right atrium is received from the entire body, while the left atrium receives blood only from the lungs, which are nonfunctional in prenatal life. Hence, the pressure within the right atrium is more than on the left side, and the blood flows from the right to the left atrium across foramen ovale. At birth, pulmones (lungs) start functioning; so, more blood is diverted to them. More of it is returned to the left atrium, and so the pressure within it rises. Once it equals pressure in the right atrium, the pressure gradient is lost and the valvular foramen ovale closes. Initially, it is the functional closure at birth, followed by anatomical closure, that is, fibrosis occurs between the two septa, the primum and the secundum.

Anomalies

Atrial septal defect (ASD) occurs at a frequency of 6 per 10,000 births. It is more prevalent in females. ASDs are often associated with chromosomal defects, that is, trisomy 21/Down's syndrome. The defect may be of a variable magnitude.

- **Probe patent foramen ovale:** It occurs in about 25% of people and results from incomplete fusion between the septum secundum and the valve of foramen ovale (caudal limb of septum primum). It is clinically silent.
- **Secundum type of ASD:** It results from an abnormal resorption of the septum primum or defective development of the septum secundum.
- **Primum type of ASD:** Failure of fusion of the septum primum with the fused endocardial cushion results in primum type of ASD. In this, the foramen primum remains patent.
- **Sinus venosus type of ASD:** The defect is located in the upper part of the interatrial septum. It is rare. It results from an incomplete absorption of sinus venosus into the right atrium with abnormal development of the septum secundum.
- **Triloculare biventriculare:** There is complete absence of interatrial septum. The heart is three-chambered with one (common) atrium and two ventricles.

Right Atrium

It presents with posterior, smooth part called sinus venarum, derived from absorption of the right horn of the sinus venosus. It is separated from the anterior rough part (musculi pectinati) by crista terminalis. The anterior part is derived from the right part of the primitive atrium. Crista terminalis is derived from the right sinoatrial valve. The septal wall, that is, interatrial septum, develops from septum primum, septum secundum, septum spurium, and the left sinoatrial valve (**Fig. 14.8**).

Left Atrium

Most of the wall of the left atrium is smooth and is derived from the progressive incorporation of primitive pulmonary vein and its branches. The primitive pulmonary vein develops as an outgrowth from the dorsal wall of the common atrium, just to the left of septum primum. As the left atrium develops and expands, the primitive pulmonary vein and its branches are incorporated into the wall of the left atrium; as a result four pulmonary veins seem to open into it (**Fig. 14.9**).

Left auricle is a small appendage presenting with rough interior derived from the primitive atrium. The septal wall, that is, interatrial septum as mentioned earlier, develops with contribution from three septae, septum primum, septum secundum, and septum spurium, and the left sinoatrial valve.

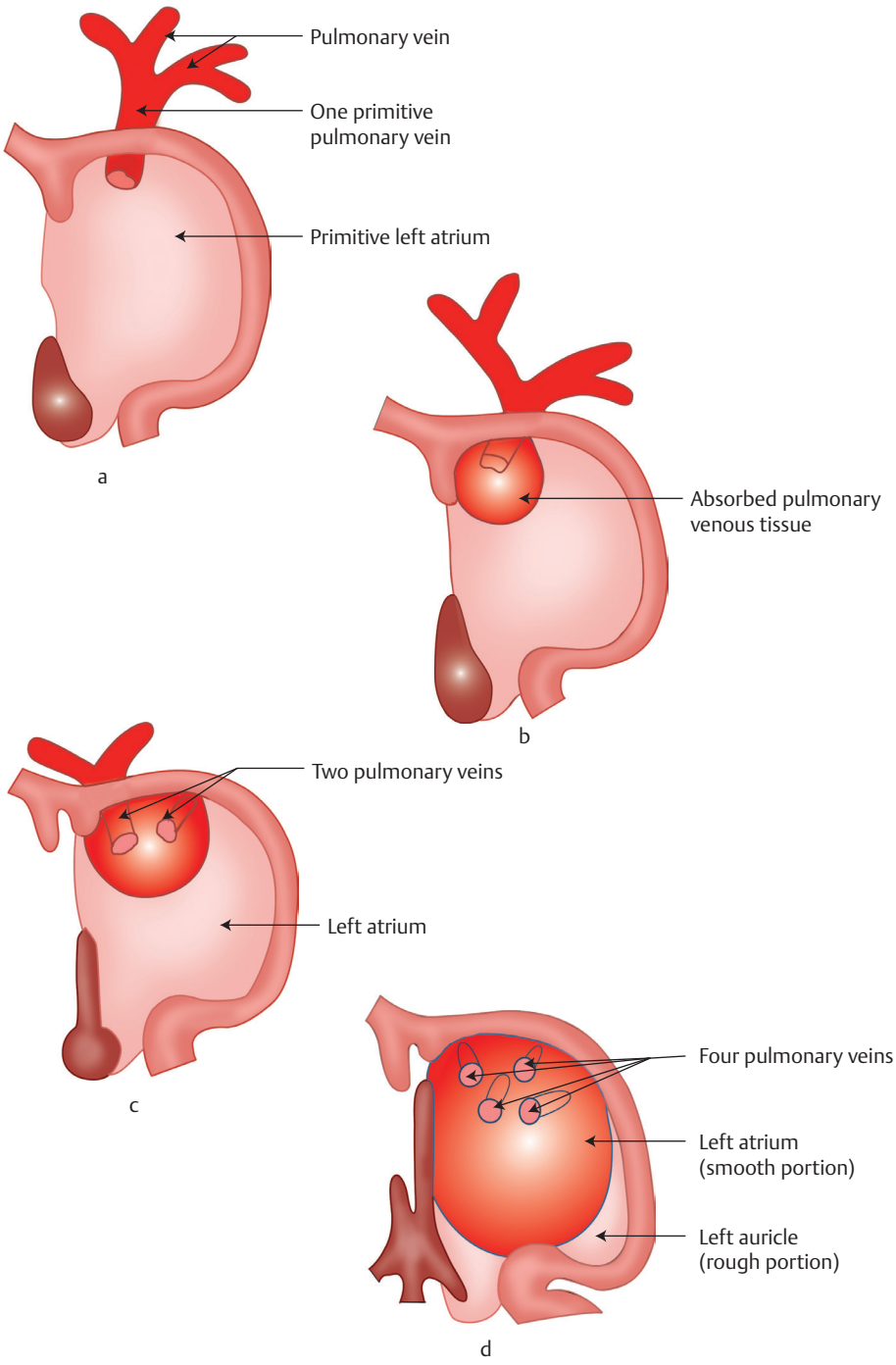

Fig. 14.9 (a–d) Illustrations showing progressive development of the left atrium, most of which has smooth interior formed by absorption of pulmonary venous tissue.

Separation of Primitive Ventricle and Development of Interventricular Septum

The first hallmark in the development of the interventricular septum is in the form of a muscular ridge along the floor of primitive ventricle near the apex.

It forms the thick crescentic fold with a concave upper margin. This gains height because of dilatation of the ventricles on either side of it. However, in the latter stages, there is an active proliferation of the myoblasts, giving rise to the muscular part of interventricular septum (**Fig. 14.10**).

Interventricular foramen: It is located between the upper free edge of the muscular part of the interventricular septum and the fused endocardial cushion. It permits communication between the right and left ventricles. By the end of the seventh week, the interventricular foramen closes by the fusion of tissues from (1) the right bulbar ridge, (2) the left bulbar ridge, and (3) the fused endocardial cushion. The thin membranous part of the interventricular septum is derived from an extension of the tissue from the right side of the fused endocardial cushion. This tissue blends with the aortico-pulmonary septum and the muscular part of interventricular septum. This sets the pulmonary trunk in communication with the right ventricle and the aorta communicates with the left ventricle.

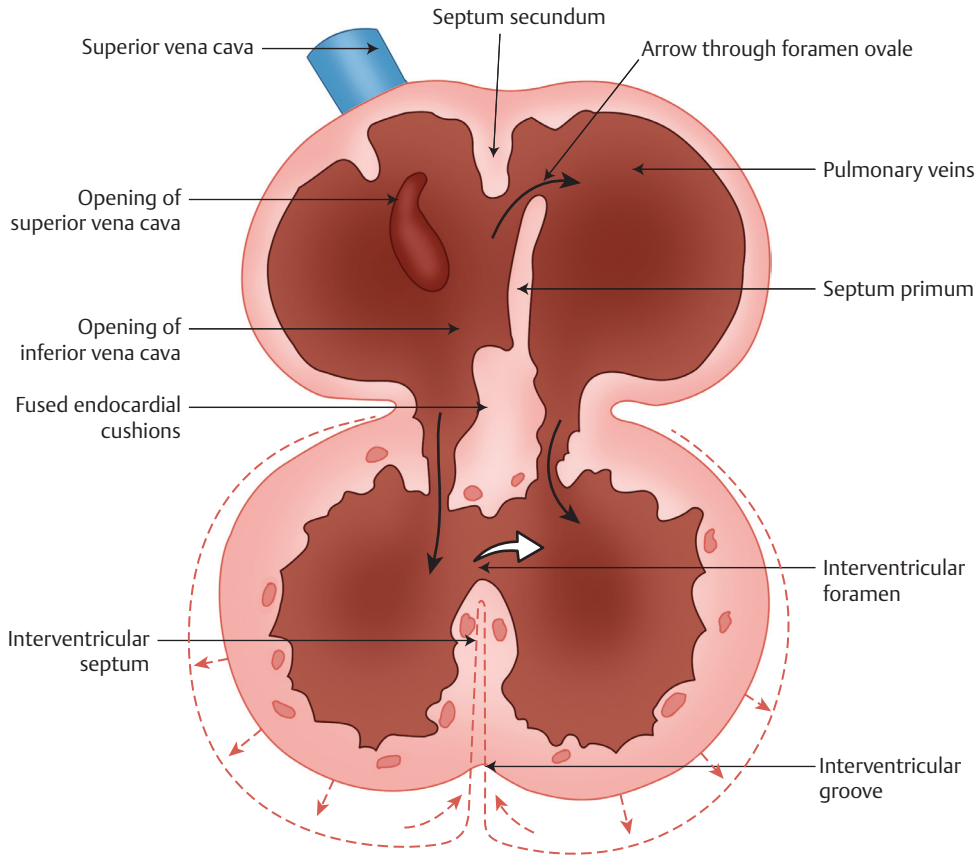

Fig. 14.10 Illustration showing coronal section through the developing heart showing its partitioning and expansion of the ventricles.

Anomalies

Ventricular septal defects (VSDs): It forms the most common type of cardiac malformations. VSDs form approximately 25% of the cardiac defects. An isolated VSD occurs with the frequency of approximately 10 to 12 per 10,000 births. Following are the types of VSDs:

- **Membranous VSD:** It results from the incomplete closure of interventricular foramen due to the failure of development of the membranous part. Usually, it is the failure of extension of the tissue from the right of the fused endocardial cushion. It fails to fuse with the aorticopulmonary septum and the muscular part of the interventricular septum.
- **Muscular VSD:** It results from abnormal resorption of the septal tissue.
- **Cor triloculare biatriatum:** In this condition, the interventricular septum is completely missing. The heart is three-chambered with one ventricle and two atria.

Separation of the Bulbus Cordis and the Truncus Arteriosus

In the fifth week, proliferation of the mesenchymal cells in the walls of bulbus cordis form right and left bulbar ridges. In the same fashion, truncal ridges are formed in the truncus arteriosus (**Fig. 14.11**). The truncal ridges are continuous with the bulbar ridges. The ridges get spiral orientation because of streaming of blood from the ventricles. This gives rise to spiral aorticopulmonary septum.

The bulbus cordis now divides into infundibulum (conus arteriosus) of the right ventricle and an aortic vestibule of the left

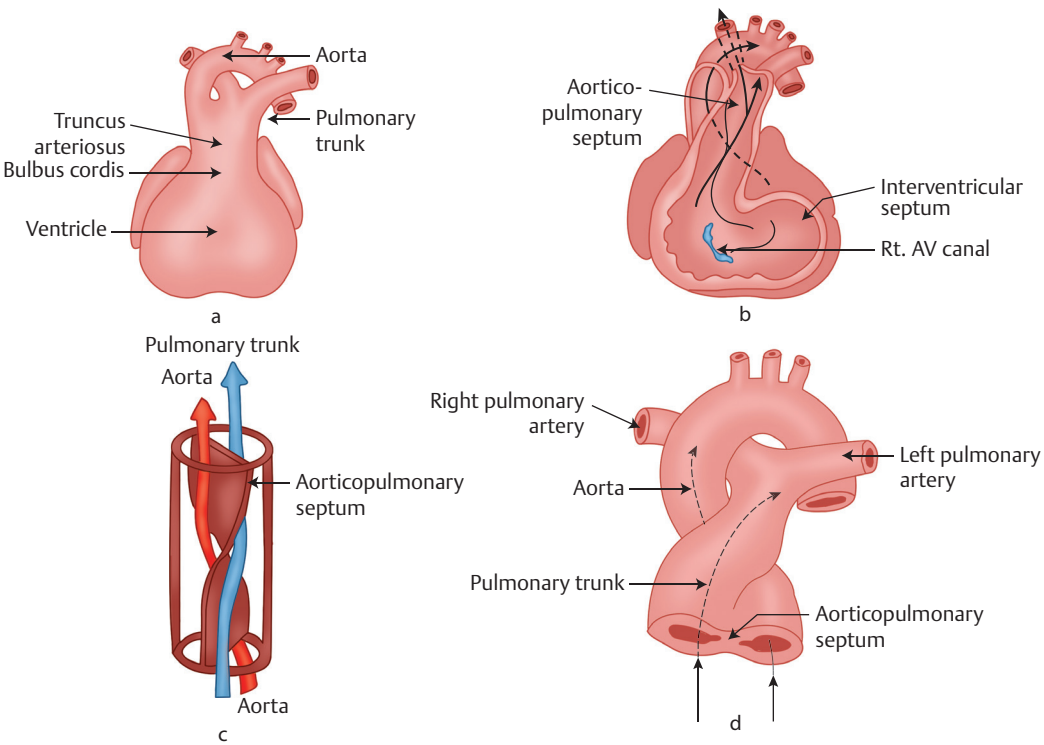

Fig. 14.11 (a–d) Illustrations showing division of bulbus cordis and the truncus arteriosus to form pulmonary trunk and aorta. AV, atrioventricular; Rt, right.

ventricle. The truncus also divides to form the pulmonary trunk and the aorta.

Anomalies

Deviation of spiral septum may give rise to pulmonary stenosis or aortic stenosis depending on the shift of the spiral septum.

Development of Ventricles

Right Ventricle

It has a rough part, the trabeculae carneae, that develops from the primitive ventricle, while its smooth (outflowing) part called infundibulum develops from bulbus cordis. The two portions are separated by crista supraventricularis (**Fig. 14.12**).

Anomalies include various types of VSDs, membranous or muscular, and Fallot's tetralogy.

Fallot's Tetralogy

It was described by Étienne-Louis Arthur Fallot in 1888. Following are the four classic malformations:

- Overriding of aorta: It receives blood from both the ventricles. This leads to narrowing of the pulmonary trunk.
- Pulmonary stenosis.
- Right ventricular hypertrophy due to pulmonary stenosis.
- High VSD.

Treatment: Surgical correction.

Left Ventricle

It presents an inflowing rough part, the trabeculae carneae, that develops from the primitive ventricle and a smooth (outflowing) part called *aortic vestibule* that develops from bulbus cordis. The interventricular septum develops in two parts: the muscular and the membranous parts (details vide supra) (**Fig. 14.13**).

Development of Arteries

In the fourth to fifth weeks, the pharyngeal arches are seen on the side of the neck. Each arch contains an artery, connecting aortic sac (ventrally) to the dorsal aorta of the respective side. The fate of these arch arteries is as follows (**Fig. 14.14**):

- **The first aortic arch arteries:** They mostly disappear; however, the remaining portion forms maxillary arteries. It is also believed to contribute to formation of external carotid arteries.
- **The second aortic arch arteries:** They form stapedial arteries.
- **The third aortic arch arteries:** The proximal part forms common carotid artery, while the distal part forms internal carotid artery on the respective side.
- **The fourth aortic arch arteries:** This pair of arteries has differential fate on two sides. The left fourth aortic arch artery forms part of the *arch of aorta* of which the proximal part is formed by the aortic sac, while the distal portion is formed by the left dorsal aorta.

The right fourth aortic arch artery contributes to the *formation of proximal part of the right subclavian artery*, while its distal part is formed by the right dorsal aorta followed by the right seventh intersegmental artery.

- **The fifth aortic arch arteries:** These are rudimentary and eventually degenerate.
- **The sixth aortic arch arteries:** The sixth aortic arch arteries also have differential fate on two sides. On both sides, the proximal part of sixth aortic arch arteries form pulmonary artery, but the distal part on the left side

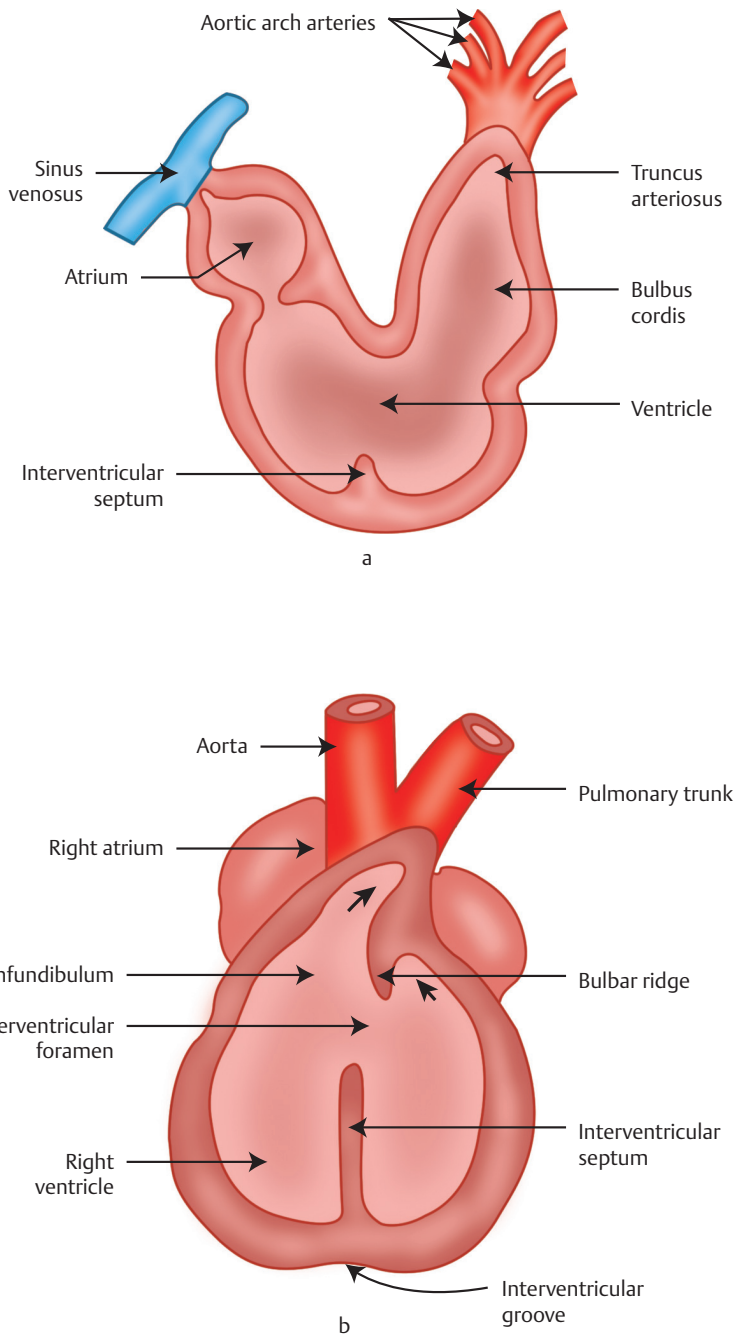

Fig. 14.12 **(a, b)** Illustrations showing development of outflowing part of the two ventricles: infundibulum of the right ventricle and aortic vestibule of the left ventricle from bulbus cordis.

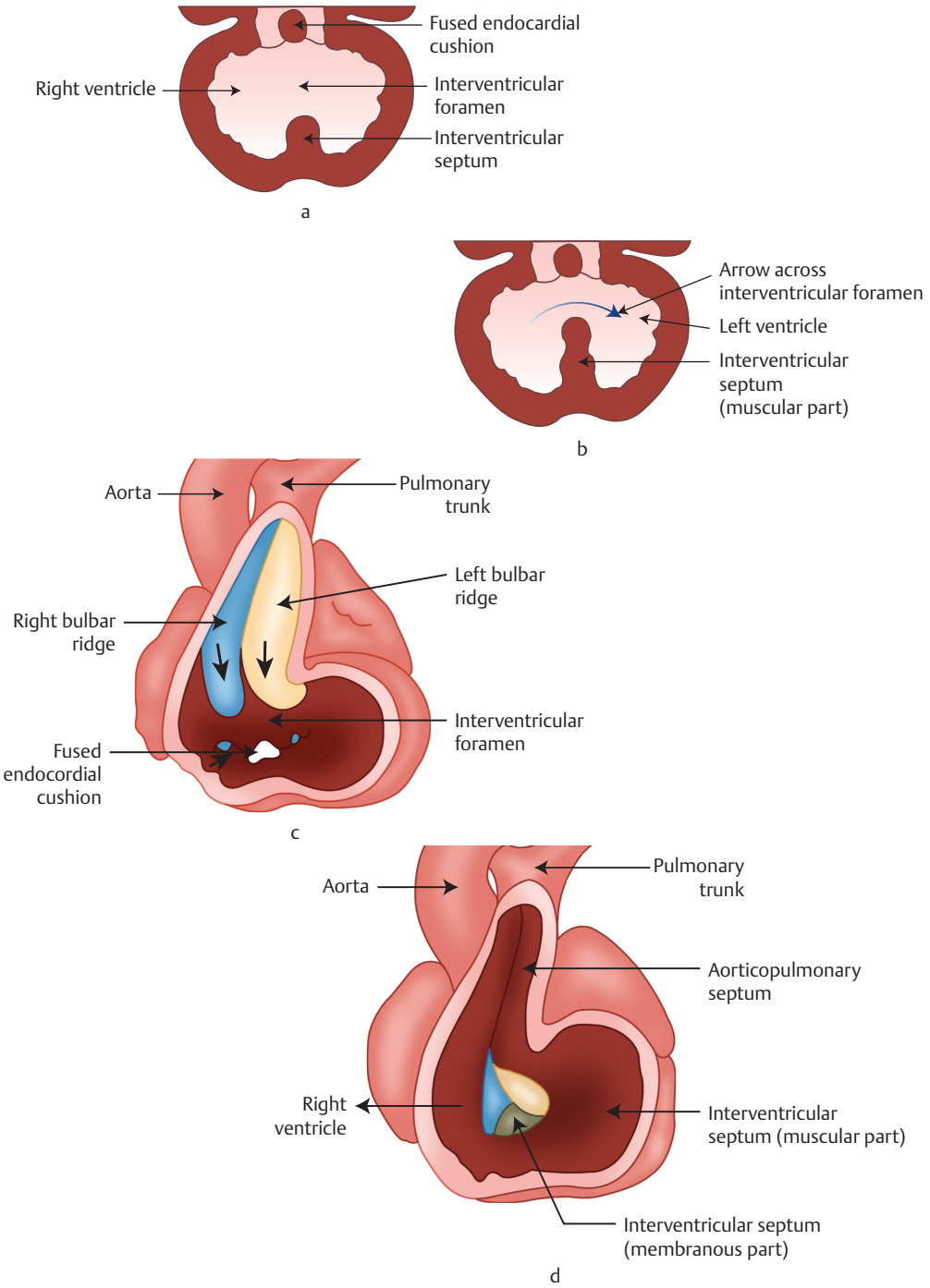

Fig. 14.13 Illustrations showing development of **(a, b)** muscular part and **(c, d)** the membranous part of the interventricular septum.

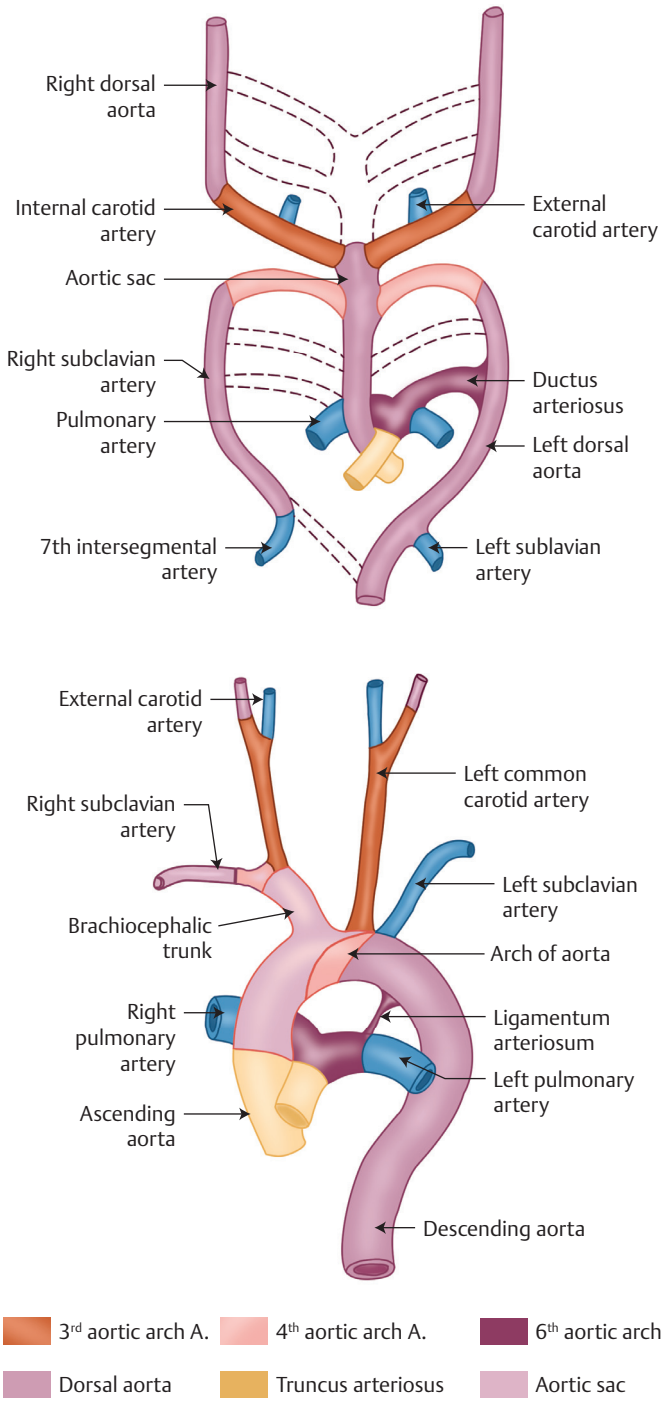

Fig. 14.14 Illustrations showing fate of the pharyngeal arch arteries and formation of the arch of aorta.

forms ductus arteriosus connecting left pulmonary artery to the arch of aorta.

However, on the right side, the distal part degenerates and disappears. This accounts for the differential course taken up by the right and left recurrent laryngeal nerves.

On the left side, the nerve is retained in the thorax by the ligamentum arteriosum (obliterated ductus arteriosus), while on the right side, the right recurrent laryngeal winds under the right subclavian artery in the neck.

Anomaly

Coarctation of aorta: It is characterized by narrowing of the part of aorta close to the ductus arteriosus. Depending on the site of narrowing, it is labeled as preductal, ductal, or postductal coarctation. The preductal coarctation is less frequent. The postductal coarctation is more commonly observed. In this, the constriction of the aorta is just distal to the ductus arteriosus. This allows better collateral circulation (**Fig. 14.15**).

Causes

- It is believed that the muscular element of ductus arteriosus may invade the wall of arch of aorta. So, when the ductus contracts, this muscular element also contracts leading to coarctation.
- An abnormal involution of a small part of the left dorsal aorta may cause coarctation.
- Persistent isthmus: The part of aorta between the left subclavian artery and the ductus arteriosus is narrow in fetal life and is called *isthmus*. After birth, this part normally dilates but if it persists as isthmus, it causes coarctation.
- Double aortic arch: In this, a vascular ring is formed around the trachea and the esophagus. The embryological reason being failure of the distal part of the right dorsal aorta to disappear.
- Abnormal right subclavian artery: At times, right subclavian artery arises from the descending thoracic aorta and takes retroesophageal course to reach the right upper limb.

Development of Major Veins

Vitelline Veins

The two vitelline veins drain the yolk sac into the sinus venosus. In the region of the developing liver (within septum transversum), the hepatic sinusoids of the developing liver get linked to the vitelline veins. Hepatic veins are formed from the right vitelline vein. Around developing duodenum, the vitelline veins form an anastomosis. A part of this anastomosis disappears, and the remaining part forms the *portal vein.*

Fate of umbilical veins: The right umbilical vein and the part of the left umbilical vein cranial to the developing liver disappear. Remaining left umbilical vein brings oxygenated blood from the placenta toward the embryo. In the region of the developing liver, the ductus venosus connects it to the IVC, bypassing the hepatic sinusoids. This is done to conserve the oxygen contents of the blood. This, however, causes reduction in the size of the left lobe of the liver. After birth, the left umbilical vein obliterates to form ligamentum teres hepatis, and the obliteration of ductus venosus forms ligamentum venosum.

Cardinal Veins

Initially, there are two pairs of cardinal veins: the anterior cardinal veins draining cranial part and the posterior cardinal veins draining the caudal part of the embryo. The anterior and the posterior cardinal veins of one side unite to form common cardinal vein, which drains into the sinus venosus. In the eighth week, an oblique anastomosis develops between the two anterior cardinal veins shunting blood from the left to right side;

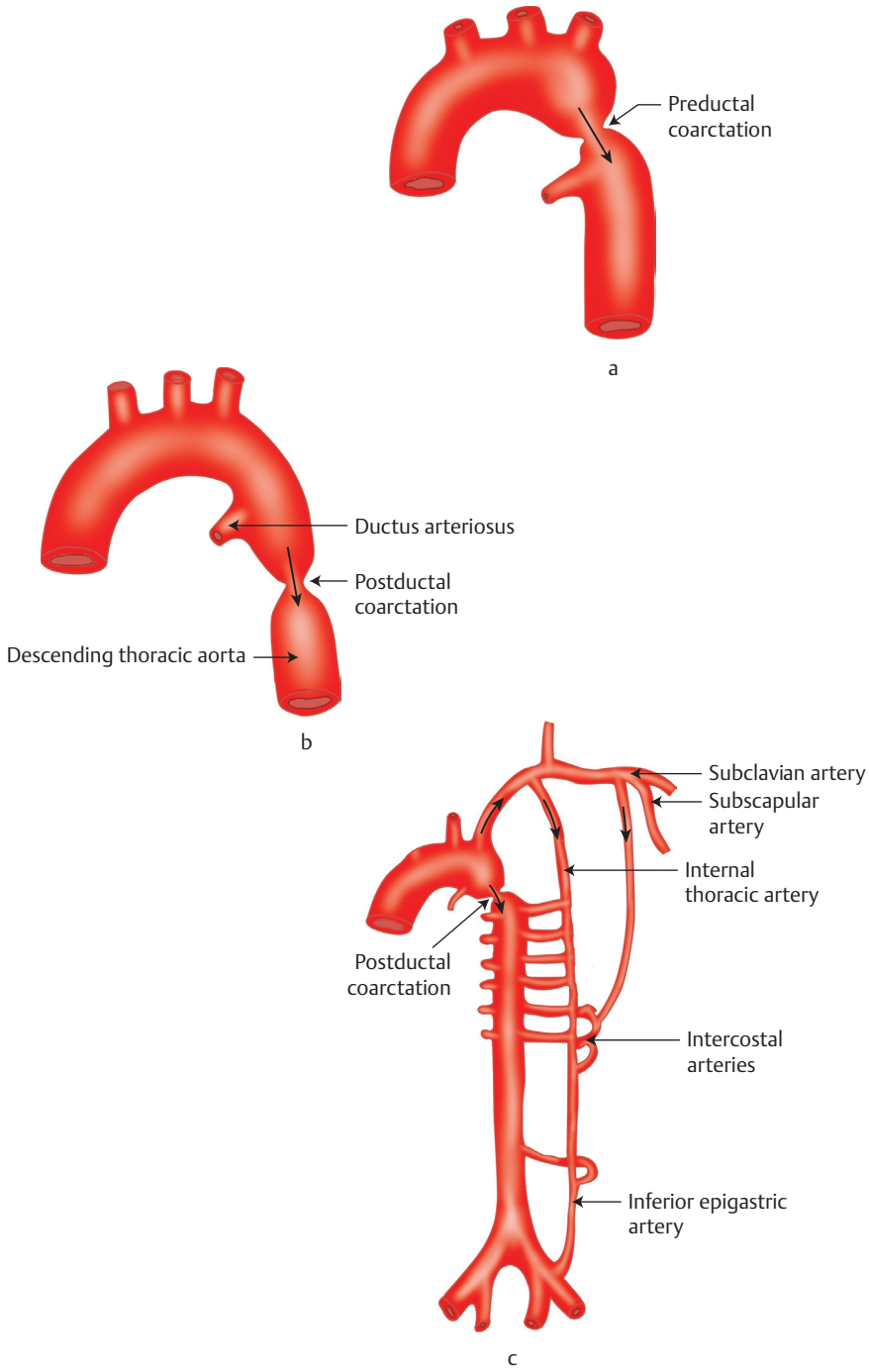

Fig. 14.15 Illustrations showing **(a, b)** pre- and postductal coarctation of aorta, and **(c)** possible route of collateral circulation.

eventually the oblique anastomosis forms the left brachiocephalic vein. The part of the right anterior cardinal vein cranial to the anastomosis forms the right brachiocephalic vein. The SVC is formed from the remaining part of the right anterior cardinal vein along with the right common cardinal vein. The posterior cardinal veins largely disappear except those that form the root of azygos vein and common iliac veins.

Two more pairs of cardinal veins appear gradually replacing the posterior cardinal veins. These are *the subcardinal and supracardinal veins.* The subcardinal veins form the renal veins, suprarenal veins, and gonadal veins, and contribute to the IVC. The supracardinal veins which develop at later stages give rise to azygos and hemiazygos veins and form a part of the IVC.

Formation of the Inferior Vena Cava

It develops from the following four segments:

- **Hepatic segment:** It is derived from the hepatic veins which in turn are formed from the right vitelline vein and the hepatic sinusoids.
- **Prerenal segment:** It is derived from the right subcardinal vein.
- **Renal segment:** It is contributed by the anastomosis between the subcardinal and supracardinal veins.
- **Postrenal segment:** It is formed by the right supracardinal vein (**Fig. 14.16**).

Basically, the primitive veins draining the trunk and caudal part of the embryo exhibit a shift from the left to right side as seen in the development of the IVC.

Anomaly

Double IVC: In this, the IVC below the level of renal veins is represented by two vessels.

Fetal Circulation

The circulatory system of the fetus is designed to serve the needs in prenatal life and to permit necessary modifications at birth so as to establish the postnatal circulatory pattern. The oxygenated blood from the placenta is returned in left umbilical vein (because the right vein degenerates in early prenatal life). It passes through the ductus venosus to the IVC. The ductus venosus does not allow it to pass through hepatic sinusoids to conserve its oxygen content. It is believed that there is a sphincter which regulates the blood flow through ductus. It is more of a physiologic entity.

The flow of blood from the IVC is guided toward the foramen ovale by a valve. It is called the valve of the IVC/eustachian valve. It prevents mixing of deoxygenated blood from the SVC with the oxygenated blood from the IVC. Another factor preventing this admixture of blood from the SVC to the IVC is intervenous tubercle. However, it is said to be well developed in quadrupeds and not so much in humans.

The blood now passes through the foramen ovale into the left atrium. Here it mixes with a small amount of deoxygenated blood returning from the nonfunctional pulmones (lungs) via pulmonary veins. From the left atrium, the blood passes into the left ventricle and leaves it via ascending aorta to be distributed to the heart, head, neck, and the upper limbs. These are supplied with well-oxygenated blood.

The deoxygenated blood in the right atrium coming via the SVC mixes with a small amount of oxygenated blood from the IVC. It then passes to the right ventricle, leaving it via pulmonary trunk; some of it goes to the lungs, but most passes via ductus arteriosus into the aorta (**Fig. 14.17** and **Fig. 14.18**).

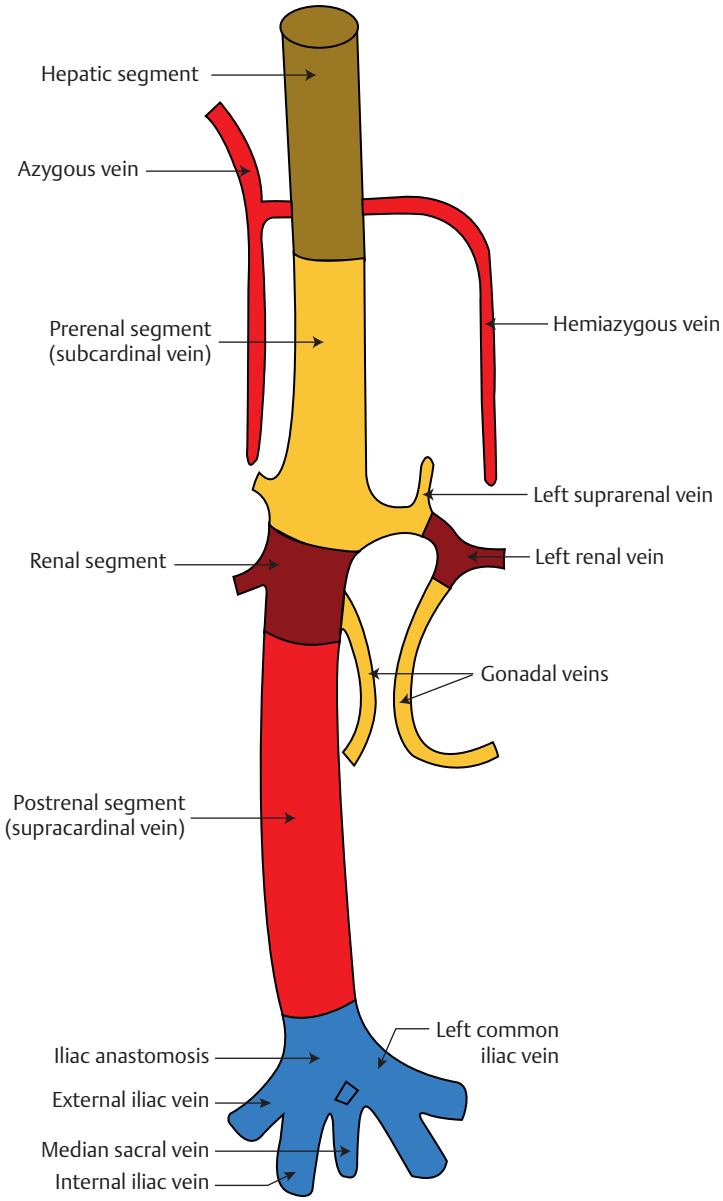

Fig. 14.16 Illustration showing the development of the inferior vena cava.

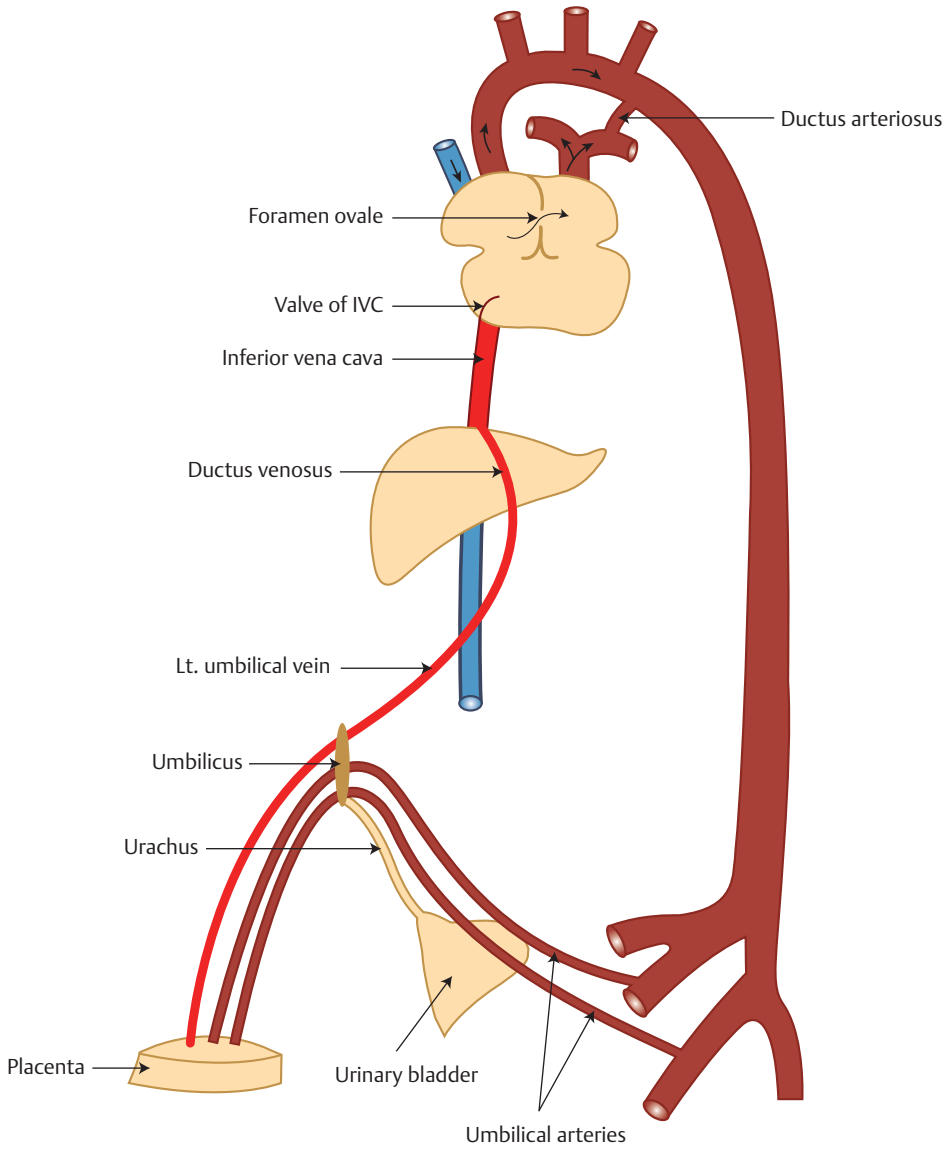

Fig. 14.17 Illustration showing fetal circulation. Note ductus venosus bypassing the liver and ductus arteriosus bypassing pulmonary circulation. IVC, inferior vena cava.

Hemodynamics

- The pulmonary blood flow is low in the fetal life. Only 5 to 10% of the cardiac output is diverted to the lungs, because these (lungs) are nonfunctional.
- About 40 to 50% of the blood passing down the descending aorta enters umbilical arteries to be oxygenated in the placenta.
- The rest of the blood supplies various organs and the lower half of the body.

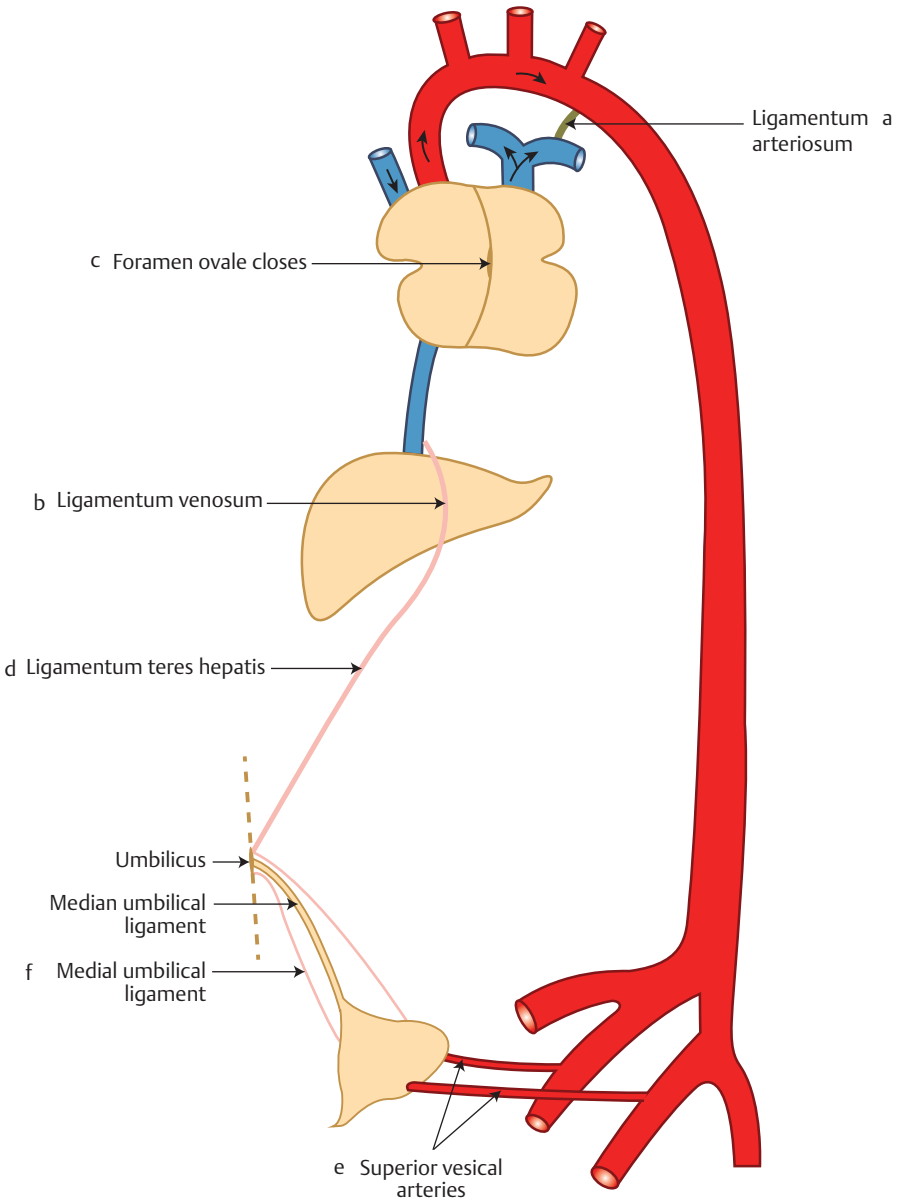

Fig. 14.18 Illustration showing changes in circulation after birth. **(a)** Ligamentum teres (left umbilical vein). **(b)** Ligamentum venosum (ductus venosus). **(c)** Foramen ovale (closes). **(d)** Ligamentum arteriosum (ductus arteriosus). **(e)** Superior vesical artery (patent part of umbilical artery). **(f)** Medial umbilical ligament (obliterated umbilical artery).

Natal Events

Important alterations occur in the circulatory system for the following reasons:

- The placental circulation ceases.
- The lungs start functioning.

These reasons include the following changes:

- The sphincter in a ductus venosus constricts so that blood entering the liver has to pass through the hepatic sinusoids.
- **The lungs become functional:** Their aeration causes fall in the pulmonary vascular resistance and the pulmonary blood flow increases.
- **Valvular foramen ovale closes:** With the increased pulmonary blood flow, more blood returns to the left atrium. The pressure within it increases. The pressure gradient between the two atria is lost, and hence the valvular foramen ovale closes. At birth, there is functional closure of the foramen ovale; it is then followed by the process of fibrosis completing anatomical closure of foramen ovale in around 1 week.
- The valvular foramen ovale lies between the caudal limb of the septum primum and the caudal edge of the septum secundum. The septum primum forms the floor of the fossa ovalis and septum secundum forms limbus fossa ovalis.
- **Ventricular wall:** The right ventricular wall is thicker than the left during the fetal life because the right ventricle has to work harder. By the end of the first postnatal month, the left ventricular wall becomes thicker than the right. In fact, the right ventricular wall undergoes atrophy associated with its lighter workload.
- **The ductus arteriosus:** It constricts at birth giving rise to ligamentum arteriosum. It appears to connect the left pulmonary artery to the arch of aorta. The functional closure of the ductus occurs in approximately 10 to 15 hours after birth. In the premature infants or those with persistent hypoxia, it may remain open for longer duration.
- The ductal closure is mediated through bradykinin released from the lungs on their initial inflation. The prenatal patency of the ductus is controlled by the locally produced prostaglandins. These prostaglandins act on muscle cells in the wall of ductus arteriosus allowing them to relax. Hypoxia causes local production of prostaglandins, which keeps the ductus open. This is probably true because indomethacin, an inhibitor of prostaglandin synthesis, can cause constriction of the patent ductus arteriosus in the premature infants.
- The umbilical arteries constrict at birth: The part of it that obliterates forms medial umbilical ligament, while the unobliterated part forms superior vesical artery.
- Umbilical vein: The intra-abdominal portion of the left umbilical vein obliterates to form the ligamentum teres hepatis (round ligament of the liver).
- The ductus venosus obliterates to form ligamentum venosum, stretching from the left branch of the portal vein to the IVC.

Patent Ductus Arteriosus

Patent ductus arteriosus (PDA) is a common congenital malformation and is about three times more frequent in females as compared with the males. It is frequently associated with maternal rubella infection in the early part of gestation. It is more frequent in premature babies with low birth weight.

Causes

- There is failure of contraction of the muscular wall of the ductus; hence, it does not involute and remains patent.
- The low oxygen content of the blood in babies with neonatal respiratory

distress may have an adverse effect on the closure of the ductus. The fact supporting this hypothesis is that PDA is found more often in people living at high altitude.

- PDA may be associated with other cardiac defects leading to substantial pressure differences between the aortic and the pulmonary pressures. This allows heavy blood flow through the ductus, thus preventing its constriction.

Multiple Choice Questions

1. **The coronary sinus is derived from**
   a. Right horn of sinus venosus
   b. Right sinoatrial valve
   c. Left horn of sinus venosus
   d. Left sinoatrial valve

2. **Interatrial septum is derived from all of the following except**
   a. Septum primum
   b. Septum spurium
   c. Septum secondum
   d. Right sinoatrial valve

3. **Fate of right horn of sinus venosus is**
   a. It gets incorporated into the left atrium
   b. It gets incorporated into the right atrium
   c. It forms superior vena cava
   d. It forms inferior vena cava

4. **Limbus fossa ovalis is a remanent of**
   a. Septum primum
   b. Septum spurium
   c. Septum secondum
   d. Crista terminalis

5. **Arch of aorta is partly formed by contribution of**
   a. Left fourth aortic arch
   b. Right third aortic arch
   c. Right fourth aortic arch
   d. Left third aortic arch

6. **Ligament venosum is formed by obliteration of**
   a. Ductus venosus
   b. Right umbilical vein
   c. Left umbilical vein
   d. Right vitelline vein

7. **Postrenal segment of inferior vena cava is formed by**
   a. Right supracardinal vein
   b. Right subcardinal vein
   c. Left supracardinal vein
   d. Right supracardinal vein

8. **Left umbilical vein obliterates to form**
   a. Ligamentum venosum
   b. Ligamentum arteriosum
   c. Ligamentum teres hepatis
   d. Median umbilical ligament

9. **Membranous part of interventricular system develops from all of the following except**
   a. Right bulbar ridge
   b. Left bulbar ridge
   c. Septum primum
   d. Fused A-V cushion

10. **Outflow tract of right ventricle develops from**
    a. Conus cordis
    b. Bulbus cordis
    c. Truncus arteriosus
    d. Primitive ventricle

Answer Key: 1, c; 2, d; 3, b; 4, c; 5, a; 6, a; 7, c; 8, c; 9, c; 10, a.

Brief Answer Questions

Q1. When and where do the heart tubes develop?

Ans. Around day 18 to 19, cardiogenic area shows formation of cardiogenic cords (by condensation of mesenchymal cells); the cords on canalization form two heart tubes.

Q2. How and when a single heart tube is formed?

Ans. Fusion of the two endocardial heart tubes in a craniocaudal sequence forms a single heart tube on day 22.

Q3. What is the fate of myoepicardial mantle?

Ans. Mesenchyme surrounding the endocardial heart tube forms myoepicardial mantle, which subsequently forms myocardium and visceral pericardium.

Q4. How transverse pericardial sinus is formed?

Ans. It is formed by degeneration of the dorsal mesocardium.

Q5. Enumerate veins received by sinus venosus along with the part they drain.

Ans. Two common cardinal veins draining the embryo.

- Two umbilical veins from placenta.
- Two vitelline veins from the yolk sac.

Q6. What is foramen ovale and when does it close?

Ans. Foramen ovale is a valvular foramen between septum secondum and caudal limb of septum primum. It closes at birth.

Q7. Why the right horn of the sinus venosus enlarges while the left horn regresses?

Ans. The right horn enlarges because of two left to right shunts:

- An oblique anastomosis between two anterior cardinal veins.
- Ductus venosus.

Q8. What is the fate of sinus venosus?

Ans. Its right horn forms sinus venarum (the smooth inflowing) part of the right atrium and the left horn forms coronary sinus.

Q9. What is the fate of left umbilical vein?

Ans. After birth, it is fibrosed and forms ligamentum teres hepatis.

Q10. Which embryonic veins form superior vena cava?

Ans. The extrapericardial part of superior vena cava is formed by right anterior cardinal vein, while the intrapericardial part is formed by the right common cardinal vein.

Q11. Vein of Marshall (oblique vein of left atrium) develops from which vein?

Ans. It develops from left common cardinal vein.

Q12. What is the fate of vitelline veins?

Ans. They form portal vein after anastomosing around duodenum. In the septum transversum, they form hepatic sinusoids and hepatic veins. Remains of the right vitelline vein gives rise to the terminal part of inferior vena cava.

Q13. Enumerate the structures forming right atrium.

Ans.

- Right horn of sinus venosus forms right atrium.
- Common atrium (right part) forms musculi pectinate.
- Right sinoatrial valve forms crista terminalis.
- Right half of atrioventricular (AV) canal forms the most ventral part.
- Septum primum, secondum, and spurium form septal wall.

Q14. How the membranous part of interventricular septum develops?

Ans. It develops from (i) right, (ii) left bulbar ridges, and (iii) fused atrioventricular cushion.

This tissue fuses with aorticopulmonary septum and the muscular part of the interventricular septum.

Q15. What is the fate of the fourth aortic arch artery?

Ans. The fourth aortic arch artery on the left side forms a part of arch of aorta and on the left side it forms the proximal part of the right subclavian artery.

Q16. Why do the recurrent laryngeal nerves on two sides follow different course?

Ans. The right nerve passes beneath the right subclavian (fourth arch artery) because on the right the fifth and sixth arch elements have disappeared while on the left side the distal part of the sixth arch artery forms ductus arteriosus, which retains left recurrent nerve at lower level.

Q17. What leads to the closure of foramen ovale at birth?

Ans. At birth, the lung starts functioning, which increases influx to the left atrium; as a result, the pressure gradient between the atria is lost, and hence the valvular foramen ovale closes.

Q18. Which anatomical changes transform the fetal circulation into the adult pattern?

Ans.

- Obliteration of ductus arteriosus to form ligamentum arteriosum.
- Obliteration of ductus venosus to form ligamentum venosum.
- Closure of foramen ovale.
- Degeneration of the valve of inferior vena cava.

Q19. What causes obliteration of ductus arteriosus at birth?

Ans. The contraction of ductal muscle is caused by bradykinin released from lungs during their initial inflation; this closes ductus arteriosus. The action of bradykinin, however, depends upon high oxygen tension (PO_2) in the aortic blood achieved by ventilation of lungs at the time of birth.

Q20. What is the fate of umbilical arteries?

Ans. The patent part of umbilical artery forms superior vesical artery while obliterated part forms medial umbilical ligament.

Q21. What is ectopia cordis?

Ans. In this condition, the heart is completely or partially outside the body. The cause is a sternal defect owing to the failure of lateral folds to fuse in the fourth week.

Q22. What is Fallot's tetralogy?

Ans. Fallot's tetralogy is characterized by (1) an overriding aorta leading to (2) pulmonary stenosis resulting in (3) right ventricular hypertrophy and (4) high ventricular septal defect.

Q23. What causes coarctation of aorta?

Ans. The following are thought to be instrumental in causing coarctation of aorta:

- Invasion of ductal tissue (muscle) in the wall of aorta.
- An abnormal involution of segment of left dorsal aorta.
- Failure of isthmus to dilate to normal size.

Q24. What is cor triloculare biatriatum?

Ans. It is complete absence of interventricular septum, with the heart presenting with three chambers: one (common) ventricle and two atria.