Blood vessel development occurs by two mechanisms:

1. **vasculogenesis**: in which vessels arise by coalescence of angioblasts. The major vessels, including the dorsal aorta and cardinal veins, are formed by vasculogenesis.

2. **angiogenesis**: whereby vessels sprout from existing vessels. The remainder of the vascular system is formed by angiogenesis.

The entire system is patterned by guidance cues involving vascular endothelial growth factor (VEGF) and other growth factors.

**The pharyngeal arches**

They develop during the fourth week. Although six pairs of pharyngeal arch arteries usually develop, they are not all present at the same time. By the time the sixth pair of pharyngeal arch arteries has formed, the first two pairs have disappeared. During the eighth week, the primordial pharyngeal arch arterial pattern is transformed into the final fetal arterial arrangement.

**Aortic Arches** arise from the aortic sac (the most distal part of the truncus arteriosus) which contributes a branch to each new pharyngeal arch as it forms. They are embedded in mesenchyme of the pharyngeal arches. They appear in a cranial to caudal sequence, giving rise to a total of five pairs of arteries. [The fifth arch either never forms or forms incompletely and then regresses]. Consequently, the five arches are numbered I, II, III, IV, and VI. They terminate in the right and left dorsal aorta. (In the region of the arches, the dorsal aortae remain paired, but caudal to this region they fuse to form a single vessel.)

**The aortic sac** then forms right and left horns, which subsequently give rise to the brachiocephalic artery and the proximal segment of the Aortic arch, respectively.

Most of the first aortic arch has disappeared, although a small portion persists to form the maxillary artery.

The second aortic arch soon disappears. The remaining portions of this arch are the hyoid and stapedial arteries.

**The third aortic arch**

- Distal parts of the third pair of aortic arches join with the dorsal aortas to form the internal carotid arteries, which supply the middle ears, orbits, brain and its meninges, and pituitary gland.

- Proximal parts of these arteries form the common carotid arteries, which supply structures in the head.

The external carotid artery is a sprout of the third aortic arch.

**The fourth aortic arch persists on both sides.**

On the left, it forms part of the arch of the aorta, between the left common carotid and the left subclavian arteries. On the right, it forms the most proximal segment of the right subclavian artery, the distal part of which is formed by a portion of the right dorsal aorta and the seventh intersegmental artery.

The left subclavian artery forms from the left seventh intersegmental artery.

As development proceeds, it comes to lie close to the origin of the left common carotid artery.

The left sixth pharyngeal arch artery develops as follows:

The proximal part of the artery persists as the proximal part of the left pulmonary artery.
The distal part of the artery passes from the left pulmonary artery to the dorsal aorta and forms a prenatal shunt, the ductus arteriosus (DA).

The right sixth pharyngeal arch artery develops as follows:

The proximal part of the artery persists as the proximal part of the right pulmonary artery.

The distal part of the artery degenerates

**The course of the recurrent laryngeal nerves differs on the two sides**

These nerves supply the sixth pair of pharyngeal arches and hook around the sixth pair of pharyngeal arch arteries on their way to the developing larynx.

**On the right**, because the distal part of the right sixth artery degenerates, the right recurrent laryngeal nerve moves superiorly and hooks around the proximal part of the right subclavian artery, the derivative of the fourth pharyngeal arch artery.

**On the left**, the left recurrent laryngeal nerve hooks around the DA formed by the distal part of the sixth pharyngeal arch artery.

When the DA involutes after birth, the left recurrent laryngeal nerve remains around the ligamentum arteriosum (remnant of DA), and the arch of the aorta.

**Other changes in the aortic arch system**

(a) The dorsal aorta between the entrance of the third and fourth arches, known as the carotid duct, is obliterated.

(b) The right dorsal aorta disappears between the origin of the seventh intersegmental artery and the junction with the left dorsal aorta.

(c) Cephalic folding and elongation of the neck push the heart into the thoracic cavity:
   
   ✓ the **carotid and brachiocephalic arteries** elongate considerably.
   
   ✓ the **left subclavian artery**, distally fixed in the arm bud, shifts its point of origin from the aorta at the level of the seventh intersegmental artery to an increasingly higher point until it comes close to the origin of the left common carotid artery.

**Vitelline and Umbilical Arteries**

**The vitelline arteries**

Initially a number of paired vessels supplying the yolk sac, gradually fuse and form the arteries in the dorsal mesentery of the gut.

In the adult they are represented by the celiac, superior mesenteric, and inferior mesenteric arteries. These vessels supply derivatives of the foregut, midgut, and hindgut, respectively.

**The umbilical arteries**

Initially paired ventral branches of the dorsal aorta, course to the placenta in close association with the allantois. During the fourth week, each artery acquires a secondary connection with the dorsal branch of the aorta, the common iliac artery, and loses its earliest origin.

After birth, the proximal portions of the umbilical arteries persist as the internal iliac and superior vesical arteries, and the distal parts are obliterated to form the medial umbilical ligaments.

**Coronary Arteries**

are derived from two sources:
angioblasts formed elsewhere and distributed over the heart surface by migration of the proepicardial cells;

(2) the epicardium itself. Some epicardial cells undergo an epithelial to mesenchymal transition induced by the underlying myocardium. The newly formed mesenchymal cells then contribute to endothelial and smooth muscle cells of the coronary arteries.

Neural crest cells also contribute smooth muscle cells along the proximal segments of these arteries.

Connection of the coronary arteries to the aorta occurs by ingrowth of endothelial cells from the arteries into the aorta. By this mechanism the coronary arteries “invade” the aorta.

Intersegmental Arteries
Thirty or so branches of the dorsal aorta, pass between and carry blood to the somites and their derivatives.
The intersegmental arteries in the neck join to form a longitudinal artery on each side, the vertebral artery.
In the thorax, the intersegmental arteries persist as intercostal arteries.
Most of the intersegmental arteries in the abdomen become lumbar arteries, but the fifth pair of lumbar intersegmental arteries remains as the common iliac arteries.
In the sacral region, the intersegmental arteries form the lateral sacral arteries.
The caudal end of the dorsal aorta becomes the median sacral artery.

Clinical Correlates
Arterial System Defects
Under normal conditions the ductus arteriosus is functionally closed through contraction of its muscular wall shortly after birth to form the ligamentum arteriosum. Anatomical closure by means of intima proliferation takes 1 to 3 months.

cocartation of the aorta
the aortic lumen below the origin of the left subclavian artery is significantly narrowed.
The cause of aortic narrowing is primarily an abnormality in the media of the aorta, followed by intima proliferations.
Since the constriction may be above or below the entrance of the ductus arteriosus, two types (preductal and postductal) may be distinguished.

preductal type of coarctation of the aorta
the ductus arteriosus persists
postductal type of coarctation of the aorta is more common
The ductus arteriosus is usually obliterated
collateral circulation between the proximal and distal parts of the aorta is established by way of large intercostal and internal thoracic arteries. In this manner the lower part of the body is supplied with blood.

Abnormal origin of the right subclavian artery
occurs when the artery is formed by the distal portion of the right dorsal aorta and the seventh intersegmental artery. The right fourth aortic arch and the proximal part of the right dorsal aorta are obliterated.
Since the origin of the abnormal right subclavian artery finally settles just below that of the left subclavian artery, it must cross the midline behind the esophagus to reach the right arm. This location does not usually cause problems with swallowing or breathing, since neither the esophagus nor the trachea is severely compressed.

**double aortic arch**

the right dorsal aorta persists between the origin of the seventh intersegmental artery and its junction with the left dorsal aorta.

A vascular ring surrounds the trachea and esophagus and commonly compresses these structures, causing difficulties in breathing and swallowing.

**right aortic arch**

the left fourth arch and left dorsal aorta are obliterated and replaced by the corresponding vessels on the right side.

Occasionally, when the ligamentum arteriosum lies on the left side and passes behind the esophagus, it causes complaints with swallowing.

**interrupted aortic arch**

is caused by obliteration of the fourth aortic arch on the left side.

It is frequently combined with an abnormal origin of the right subclavian artery. The aorta supplies the head; the pulmonary artery, by way of the ductus arteriosus, supplies the rest of the body.

**Venous System**

In the fifth week, three pairs of major veins can be distinguished:

- (a) the vitelline veins, or omphalomesenteric veins, carrying blood from the yolk sac to the sinus venosus;
- (b) the umbilical veins, originating in the chorionic villi and carrying oxygenated blood to the embryo; and
- (c) the cardinal veins, draining the body of the embryo proper.

**Vitelline Veins**

Before entering the sinus venosus, the vitelline veins form a plexus around the duodenum and pass through the septum transversum.

The liver cords growing into the septum interrupt the course of the veins, and an extensive vascular network, the hepatic sinusoids, forms.

With reduction of the left sinus horn, blood from the left side of the liver is rechanneled toward the right, resulting in an enlargement of the right vitelline vein (right hepatocardiac channel). Ultimately the right hepatocardiac channel forms the hepatocardiac portion of the inferior vena cava.

The proximal & distal parts of the left vitelline vein disappears.

The anastomotic network around the duodenum develops into a single vessel, the portal vein.

The superior mesenteric vein, which drains the primary intestinal loop, derives from the right vitelline vein.

**Umbilical Veins**

Initially, the umbilical veins pass on each side of the liver, but some connect to the hepatic sinusoids.
The proximal part of both umbilical veins and the remainder of the right umbilical vein disappear, so that the left vein is the only one to carry blood from the placenta to the liver.

With the increase of the placental circulation, a direct communication forms between the left umbilical vein and the right hepatocardiac channel, the ductus venosus. This vessel bypasses the sinusoidal plexus of the liver. After birth, the left umbilical vein and ductus venosus are obliterated and form the ligamentum teres hepatis and ligamentum venosum, respectively.

**Cardinal Veins**

Initially the cardinal veins form the main venous drainage system of the embryo. This system consists of:

1. the anterior cardinal veins, which drain the cephalic part of the embryo, and
2. the posterior cardinal veins, which drain the rest of the embryo.

The anterior and posterior veins join before entering the sinus horn and form the short common cardinal veins. During the fourth week, the cardinal veins form a symmetrical system.

**During the fifth to the seventh week, a number of additional veins are formed:**

(a) the subcardinal veins, which mainly drain the kidneys;
(b) the sacrocardinal veins, which drain the lower extremities; and
(c) the supracardinal veins, which drain the body wall by way of the intercostal veins, taking over the functions of the posterior cardinal veins

**Formation of the vena cava system**

is characterized by the appearance of anastomoses between left and right in such a manner that the blood from the left is channeled to the right side.

The anastomosis between the anterior cardinal veins develops into the left brachiocephalic vein.

The terminal portion of the left posterior cardinal vein entering into the left brachiocephalic vein is retained as a small vessel, the left superior intercostal vein. This vessel receives blood from the second and third intercostal spaces.

The superior vena cava is formed by the right common cardinal vein and the proximal portion of the right anterior cardinal vein.

The anterior cardinal veins ultimately form the internal jugular veins.

External jugular veins are derived from a plexus of venous vessels in the face and drain the face and side of the head to the subclavian veins.

The anastomosis between the subcardinal veins forms the left renal vein. The left subcardinal vein disappears except at its distal portion which remains as the left gonadal vein. The right subcardinal vein becomes the main drainage channel and develops into the renal segment of the inferior vena cava.

The anastomosis between the sacrocardinal veins forms the left common iliac vein. The right sacrocardinal vein becomes the sacrocardinal segment of the inferior vena cava. With obliteration of the major portion of the posterior cardinal veins, the supracardinal veins assume a greater role in draining the body wall.

The 4th to 11th right intercostal veins empty into the right supracardinal vein, which together with a portion of the posterior cardinal vein forms the azygos vein.
On the left the 4th to 7th intercostal veins enter into the left supra-cardinal vein, and the left supracardinal vein, then known as the hemiazygos vein, empties into the azygos vein.

**Clinical Correlates**

**Venous System Defects**

**Double inferior vena cava**

at the lumbar level arising from the persistence of the left sacrocardinal vein

The left common iliac vein may or may not be present, but the left gonadal vein remains as in normal conditions.

**Absent inferior vena cava**

The lower half of the body is drained by the azygos vein, which enters the superior vena cava.

The hepatic vein enters the heart at the site of the inferior vena cava.

**Left superior vena cava**

is caused by persistence of the left anterior cardinal vein and obliteration of the common cardinal and proximal part of the anterior cardinal veins on the right.

The left superior vena cava drains into the right atrium by way of the left sinus horn, that is, the coronary sinus.

**Double superior vena cava**

is characterized by the persistence of the left anterior cardinal vein and failure of the left brachiocephalic vein to form.

The persistent left anterior cardinal vein, the left superior vena cava, drains into the right atrium by way of the coronary sinus.

**Fetal Circulation**

Before birth, blood from the placenta, about 80% saturated with oxygen, returns to the fetus by way of the umbilical vein.

On approaching the liver, most of this blood flows through the ductus venosus directly into the inferior vena cava, short-circuiting the liver. A smaller amount enters the liver sinusoids and mixes with blood from the portal circulation (I).

A sphincter mechanism in the ductus venosus, close to the entrance of the umbilical vein, regulates flow of umbilical blood through the liver sinusoids. This sphincter closes when a uterine contraction renders the venous return too high, preventing a sudden overloading of the heart.

After a short course in the inferior vena cava (II), it enters the right atrium (III). Here it is guided toward the oval foramen by the valve of the inferior vena cava, and most of the blood passes directly into the left atrium (IV).

A small amount is prevented from doing so by the lower edge of the septum secundum, the crista dividens, and remains in the right atrium.

From the left atrium, blood enters the left ventricle and ascending aorta.

Since the coronary and carotid arteries are the first branches of the ascending aorta, the heart musculature and the brain are supplied with well-oxygenated blood.

Desaturated blood from the superior vena cava flows by way of the right ventricle into the pulmonary trunk. During fetal life, resistance in the pulmonary vessels is high, such
that most of this blood passes directly through the ductus arteriosus into the descending aorta, where it mixes with blood from the proximal aorta. After coursing through the descending aorta, blood flows toward the placenta by way of the two umbilical arteries. The oxygen saturation in the umbilical arteries is approximately 58%.

**Blood in the umbilical vein gradually loses its high oxygen content as it mixes with desaturated blood**

(1) by mixture with a small amount of blood returning from the portal system; (2) in the inferior vena cava (II), which carries deoxygenated blood returning from the lower extremities, pelvis, and kidneys; (3) in the right atrium (III), by mixture with blood returning from the head and limbs; (4) in the left atrium (IV), by mixture with blood returning from the lungs; and (5) at the entrance of the ductus arteriosus into the descending aorta (V).

**Circulatory Changes at Birth**

are caused by

- cessation of placental blood flow and
- the beginning of respiration.

**Closure of the umbilical arteries**

Functionally the arteries close a few minutes after birth, although the actual obliteration of the lumen by fibrous proliferation may take 2 to 3 months. Distal parts of the umbilical arteries form the medial umbilical ligaments, and the proximal portions remain open as the superior vesical arteries.

**Closure of the umbilical vein and ductus venosus**

occur shortly after that of the umbilical arteries. After obliteration, the umbilical vein forms the ligamentum teres hepatitis in the lower margin of the falciform ligament. The ductus venosus, which courses from the ligamentum teres to the inferior vena cava, is also obliterated and forms the ligamentum venosum.

**Closure of the ductus arteriosus**

by contraction of its muscular wall occurs almost immediately after birth; it is mediated by bradykinin, a substance released from the lungs during initial inflation. Complete anatomical obliteration by proliferation of the intima is thought to take 1 to 3 months.

In the adult, the obliterated ductus arteriosus forms the ligamentum arteriosum.

**Closure of the oval foramen**

is caused by an increased pressure in the left atrium, combined with a decrease in pressure on the right side. During the first days of life, however, this closure is reversible. Crying by the baby creates a shunt from right to left, which accounts for cyanotic periods in the newborn. Constant apposition gradually leads to fusion of the two septa in about 1 year. In 20% of individuals, however, perfect anatomical closure may never be obtained (probe patent foramen ovale).
The lymphatic system begins its development later than the cardiovascular system, not appearing until the fifth week of gestation. Lymphatic vessels arise as **saclike outgrowths from the endothelium of veins**.

**Six primary lymph sacs are formed**
- two jugular,
- two iliac,
- one retroperitoneal,
- one cisterna chyli.

**Two main channels, the right and left thoracic ducts**

*The thoracic duct* forms from anastomosis of the right and left thoracic ducts, the distal part of the right thoracic duct, and the cranial part of the left thoracic duct. **The right lymphatic duct** develops from the cranial part of the right thoracic duct.

Thank you

Next lecture: Head and Neck