Development and teratology of cardiovascular and lymphatic systems

Repetition: Muscle tissue
Beginning of the cardiovascular system development – the 3rd week:

**Hemangiogenesis** (day 15 – 16) – blood islets (insulae sanguinae) in extraembryonic **mesoderm** and splanchnic **mesenchyme** of embryo
Clusters of mesenchyme cells (angiogenic cells) differentiate into:
- angioblasts ⇒ endothelium (at the periphery of blood islets)
- hemoblasts ⇒ primitive erythrocytes (in the center of blood islets)
Clusters of **angiogenic cells** form a "horseshoe-shaped" space between somatic and splanchnic layer of mesoderm = **pericardial cavity**. Two endothelial tubes arise in splanchnic mesoderm. The ventral portion of these tubes forms the **cardiogenic area** with two **heart tubes**, while the lateral portions form the **dorsal aortae**.
Germ disc:

1. prosencephalon
2. eye
3. mesencephalon
4. rhombencephalon
5. heart
6. lateral mesoderm
7. somites
8. small blood vessels
9. primitive streak
10. 8,9 Spine
11. blood islands
12. blood islands
Initially, the cardiogenic area is located anterior to the prechordal plate and the neural plate. The growth of the central nervous system pulls the cardiogenic area and prechordal plate (buccopharyngeal membrane ventrally and caudally (→)).
Cardiogenic region just cranial to the prechordal plate.
The canalization of cardiogenic clusters in the splanchnic mesoderm results in the formation of the paired heart tubes.

Folding of embryo and primitive gut separation from yolk sac.

Fusion of the heart tubes
a single heart tube is, temporarily attached to the dorsal side of the pericardial cavity by the **dorsal mesocardium** (4). The splanchnic mesoderm (5) around the heart tube (3 - future **endocardium**) thickens and forms the heart jelly = myoepicardial mantle (future **myocardium** and **epicardium**).
Heart tube

- Truncus arteriosus + aortic roots
- Bulbus cordis
- Ventricle
- Atrium
- Sinus venosus

Cor tubulare

Cor sigmoideum

Cor quadricameratum

Common cardinal veins

Umbilical veins

Vitelline veins
Looping of the heart tube

- because growth of the heart tube is faster than growth of the pericardial cavity
Cor quadricameratum
Atrioventricular septum

**Endocardial cushions** develop in the dorsal and ventral walls of the heart in the region of the atrioventricular canal. They grow towards each other and fuse, thus **dividing the atrioventricular canal** into right and left orifices. The lateral interventricular cushions appear on the sides of the canal. These proliferations of the mesenchymal tissue subsequently differentiate into **bicuspid** and **tricuspid atrioventricular valves**.
Septum interventriculare
Grows from the heart apex cranily to the endocardial cushions (AV septum)

6 - membranaceous part of septum
7 - IV septum
Atrium

Septum atriorum
-septum primum with ostium primum (obliterates); ostium secundum
-septum secundum with foramen ovale
Atrium
At the end of the 4th week, septum primum grows from the dorsocranial wall of the primitive atrium towards the endocardial cushions. The temporary opening (ostium primum - op) between the lower rim of the septum primum and the endocardial cushions gradually closes. Perforations in the upper part of the septum primum form the ostium secundum - os. Subsequently, another crest (septum secundum) grows from the right side of the septum primum and gradually covers the foramen secundum. The oval opening left by the septum secundum is called foramen ovale.
Sinus venosus

Common cardinal veins
Umbilical veins
Vitelline veins

left veins obliterate and
- left portion of sinus venosus is transformed into sinus coronarius
- right portion becomes to be part of right atrium
Truncus arteriosus + aortic roots

- cranial part of bulbus cordis divides into:
- aortic roots, branched into 6 pairs of aortic arches
Bulbus cordis

- cranial part give rise to truncus arteriosus
- middle part give rice to conus arteriosus distal part participate in formation of ventricle wall
Bulbus cordis and truncus arteriosus

A pair of opposing ridges appear in the walls of the bulbus cordis and truncus arteriosus. These ridges twist around each other, forming a spiral course of the aortico-pulmonary septum. This septum divides the bulbus cordis and truncus arteriosus into two channels, the aorta and the pulmonary artery. It also participates in the closure of the interventricular foramen.
Formation of aorticopulmonary septum

1. Aorta
2. Left pulmonary artery
3. **Pulmonary trunk**
4. Muscular interventricular septum
5. Right ventricle
6. Membranous interventricular septum
1. Aorticopulmonary septum
2. Pulmonary valve
3. Pulmonary artery
4. Aortic valve
5. Aorta
1. Internal carotid artery
2. External carotid artery
3. Common carotid artery
4. Right subclavian artery
5. Arch of aorta
6. Brachiocephalic artery
7. Ductus arteriosus
8. 7th intersegmental artery
9. Pulmonary artery
10. Carotid duct
11. Obliterated right dorsal aorta
Primitive blood circulation

Embryonic Circulation

- Aortic arch arteries
- Ventral aorta
- Dorsal aorta
- Anterior cardinal vein
- Common cardinal vein
- Posterior cardinal vein

Placental Circulation

- Left umbilical vein
- Umbilical artery

Vitelline Circulation

- Vitelline vein
- Vitelline artery
the primitive blood circulation in an embryo.
The fetal circulation
At birth, the circulation of the fetal blood through the placenta is stopped and the lungs begin to function. The foramen ovale, ductus arteriosus, ductus venosus and umbilical vessels subsequently obliterate and transform into corresponding ligaments.
Congenital malformations in CVS
(the most frequent)

• **With left → right shunt** (without cyanosis)
  atrial septum defect
  ventricular septum defect
  ductus arteriosus apertus (patens, persistens)

• **With right → left shunt** (with cyanosis)
  Fallot tetralogy
  transposition of great vessels
  truncus arteriosus (common aorticopulmonal canal)
  tricuspid valve atresia

• **Without shunt**
  coarctation of aorta
  aortic stenosis
  pulmonary stenosis
  dextrocardia (+situs inversus)
  ectopia cordis
Atrial Septal Defects
a group of common congenital anomalies defects occurring in a number of different forms and more often in females.

patent foramen ovale
left-right shunting
Ventricular Septal Defect
occurs in the interventricular septum, and is more frequent in males than females.
Patent Ductus Arteriosus occurs commonly in preterm infants, can close spontaneously (by day three in 60% of normal term neonates) the remainder are ligated simply and with little risk.

left-right shunting
Tetralogy of Fallot

named after Etienne-Louis Arthur Fallot (1888) who described it as "la maladie blue" and is a common developmental cardiac defect. The syndrome consists of a number of cardiac defects possibly stemming from abnormal neural crest migration.

consists of:
1. ventricular septal defect
2. pulmonary stenosis (valvular or infundibular)
3. results in an overriding aorta
4. right ventricular hypertrophy

right-left shunting
Transposition of Great Vessels
Characterized by aorta arising from right ventricle and pulmonary artery from the left ventricle and often associated with other cardiac abnormalities (e.g. ventricular septal defect).

right-left shunting
Tricuspid Atresia
Blood is shunted through an atrial septal defect to the left atrium and through the ventricular septal defect to the pulmonary artery. The shaded arrows indicate mixing of the blood.

right-left shunting
Coarctation of Aorta (preductal or postductal)
before or behind ductus arteriosus
Aortic Stenosis

Pulmonary Stenosis
Hypoplastic Left Heart
Characterized by hypoplasia (underdevelopment or absence) of the left ventricle obstructive valvular and vascular lesion of the left side of the heart.
Double Outlet Right Ventricle
De-oxygenated blood enters the aorta from the right ventricle and is returned to the body.
Pulmonary Atresia
Abnormal blood flow (as indicated by the shaded blue arrow) is from the right atrium and right ventricle through an atrial septal defect to the left side of the heart. Blood can reach the pulmonary arteries only through a patent ductus arteriosus.
Heart
Sinus venosus (R horn): smooth part of right atrium (sinus venarum) and the "valve" of the superior vena cava. The sino-atrial node.
Sinus venosus (L horn): coronary sinus, valve of coronary sinus
Valve of sinus venosus (R): border of smooth part of right atrium (crista terminalis)
Valve of sinus venosus (L): part of atrial septum
Common atrium: rough part of right and left atria and the auricles
Embryonic pulmonary vein: large part of the left atrial wall
Septum primum: left side of the atrial septum
Septum secundum: right side of the atrial septum
Foramen secundum: dimple in the atrial septum seen from left side (fossa ovalis, ok)
Foramen ovale: fossa ovalis
Endocardial cushions: parts of the atrioventricular wall, mitral, and tricuspid valves
Endocardial cushions: membraneous part of ventricular septum, part of arterial trunk
Bulbus cordis: trabeculated part of R ventricle and aortic vestibule of L ventricle
Truncus arteriosus: ascending (ventral) aorta and pulmonary artery
Common ventricle: parts of the right and left ventricle
Arterial System
Aortic sac (R and L sides of sac): brachiocephalic artery (right) and part of the ascending aorta (left), large parts of common carotid arteries
1st aortic arch (R and L): part of the maxillary artery and external carotid arteries
2nd aortic arch (R and L): part of the hyoid and stapedial arteries, part of external carotids
3rd aortic arch (R and L): part of common carotids and first part of the internal carotids
4th aortic arch (R): small proximal part of the right subclavian artery
4th aortic arch (L): small part of arch of the aorta just proximal to the left subclavian artery
6th aortic arch (R): proximal part of right pulmonary artery
6th aortic arch (L=ductus): proximal left pulmonary artery and and ligamentum arteriosum
Ductus arteriosus: ligamentum arteriosum
Dorsal aorta (R and L): part of right subclavian, descending aorta below left subclavian
Unpaired ventral (or vitelline) arteries: celiac, superior mesenteric, and inferior mesenteric arteries
Paired dorsal segmental arteries: intercostal arteries and vertebral arteries
Umbilical arteries: internal iliac, superior vesical arteries, medial umbilical ligaments
Venous System
Ductus venosus: ligamentum venosum
Umbilical vein (L): round ligament (ligamentum teres)
Vitelline vein (R): superior mesenteric vein and the inferior vena cava
Vitelline vein (L): most of the portal vein
Anterior cardinal veins (R and L): internal jugular veins (left brachiocephalic vein is an anastomosis)
Anterior cardinal vein (R): part of superior vena cava and right brachiocephalic vein
Common cardinal vein (R): proximal part of superior vena cava
Common cardinal vein (L): lateral part of coronary sinus and oblique vein of left atrium
Posterior cardinal vein (R): part of azygos vein and common iliac veins
Supracardinal veins: hemiazygos vein (L) and caudal part of azygos vein (R)
Subcardinal vein (R): renal segment of inferior vena cava
Cardiogenic precursors form the linear heart tube.

Mesenchymal cells form the cardiac valves from the conotruncal (CT) and atrioventricular valve (AVV) segments. A – atrium; Ao – aorta; DA – ductus arteriosus; LA – left atrium; LCC – left common carotid; LSCA – left subclavian artery; LV – left ventricle; PA – pulmonary artery; RA – right atrium; RCC – right common carotid; RSCA – right subclavian artery; RV – right ventricle; V – ventricle.
transposition of the great vessels - the aorta exits from the right ventricle, and the pulmonary trunk exits from the left ventricle. This is only compatible with life postnatally if the ductus arteriosus remains patent, allowing communication between the otherwise closed systemic and pulmonary circulations driven by the left and right sides of the heart.
patent ductus arteriosus

coaicntation of the aorta

preductal

postductal

double aortic arch
Sarcomere shortens with contraction

H zone and I band both shorten