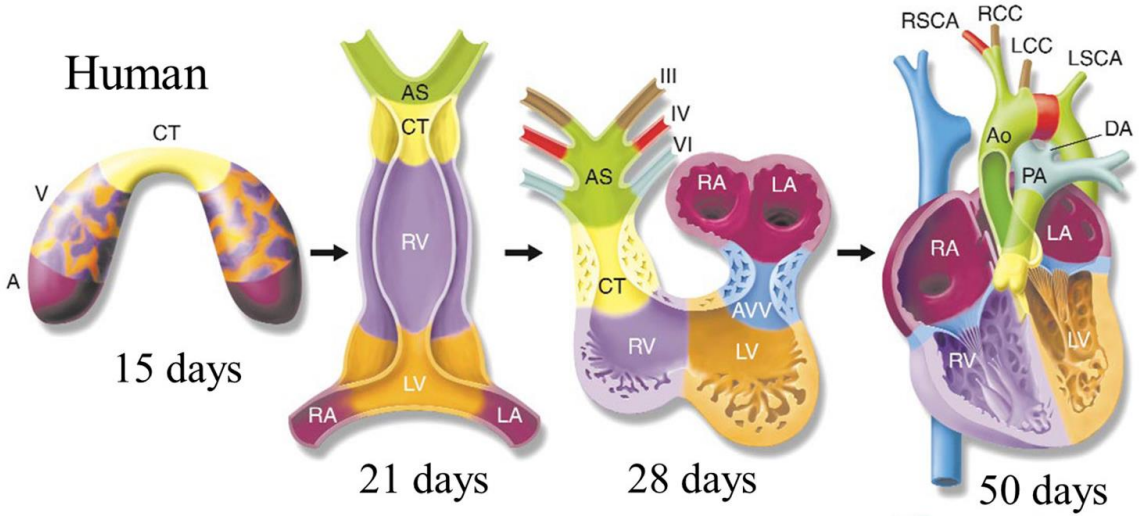
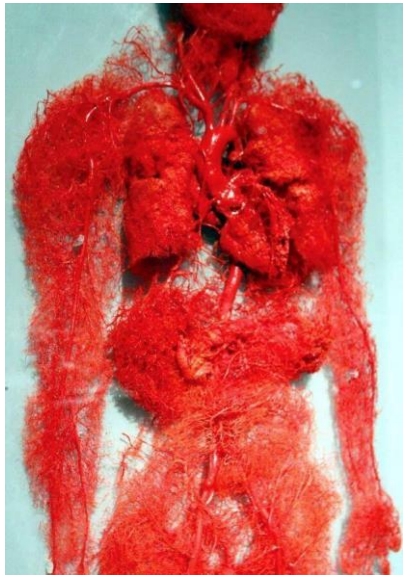
MUNI MED
Ústav histologie a embryologie

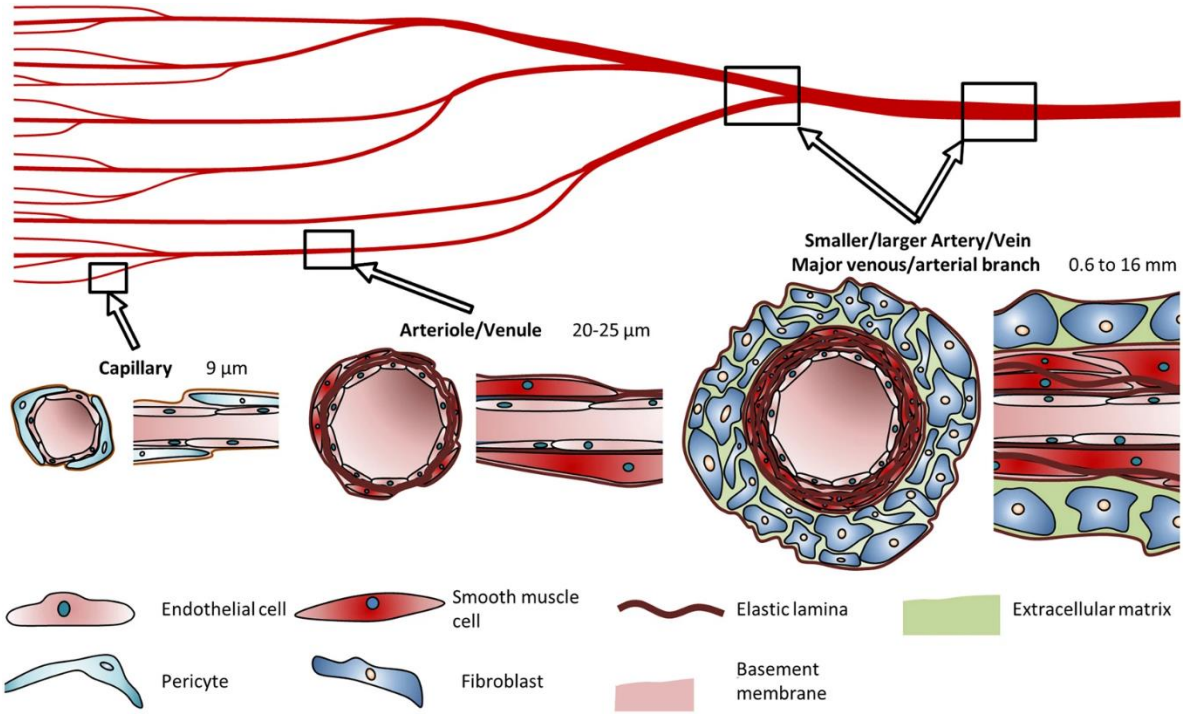
DEVELOPMENT OF CARDIOVASCULAR SYSTEM

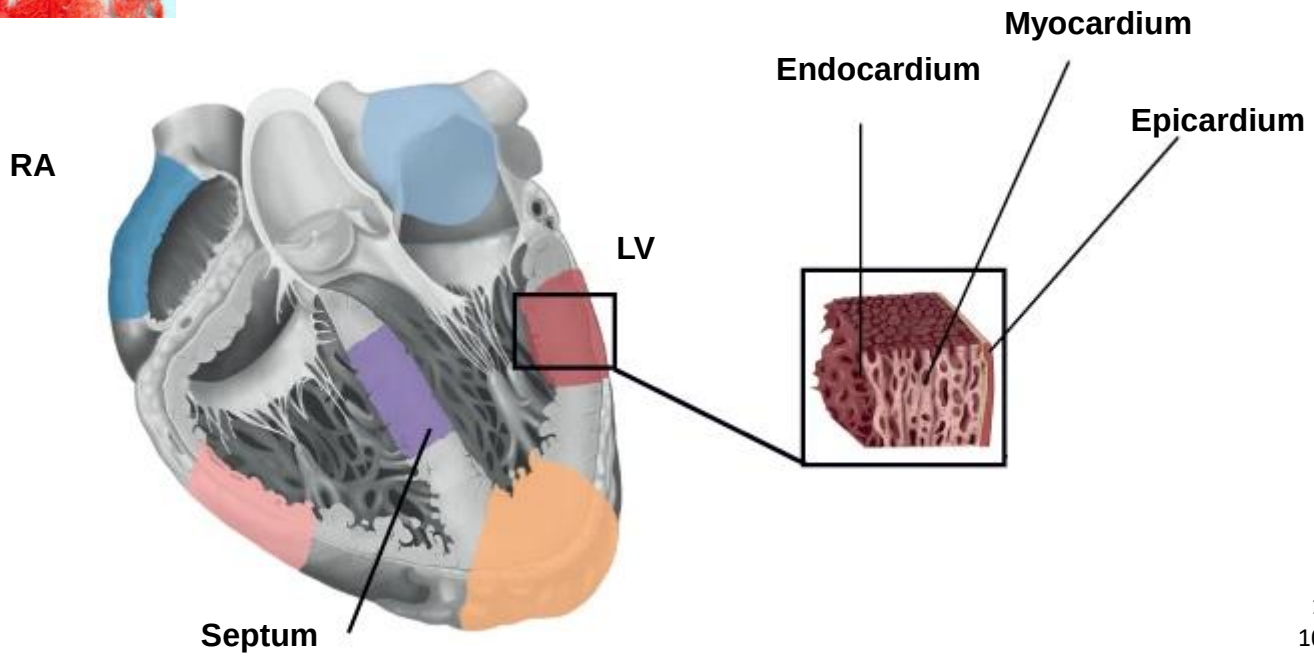


Petr Vaňhara

BLOOD CIRCULATION







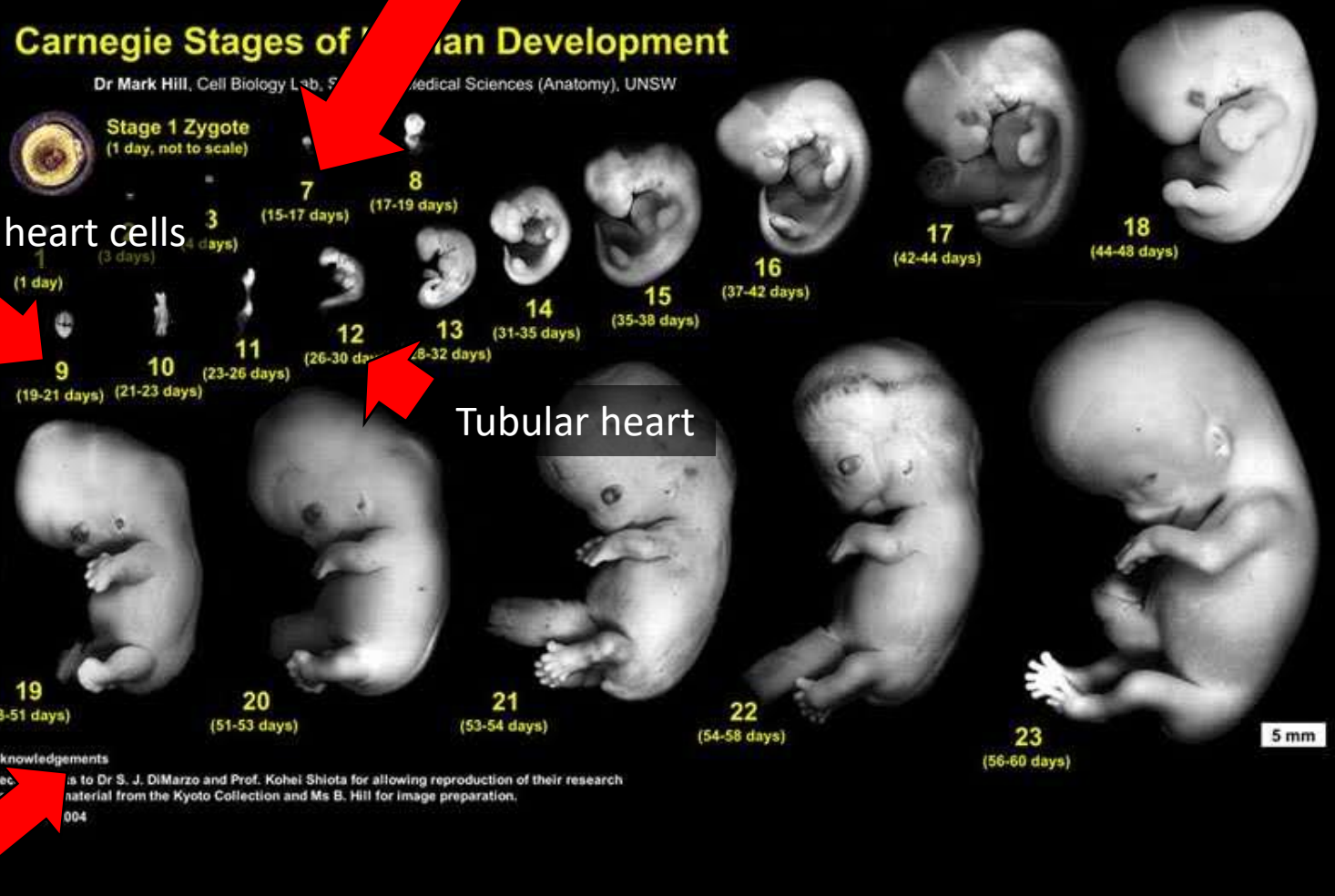
https://www.reddit.com
10.1038/s41586-020-2797-4
10.1038/s41598-018-28715-0

DEVELOPMENT OF CARDIOVASCULAR SYSTEM

Fitst morphological hallmarks of developing heart

First activity of heart cells

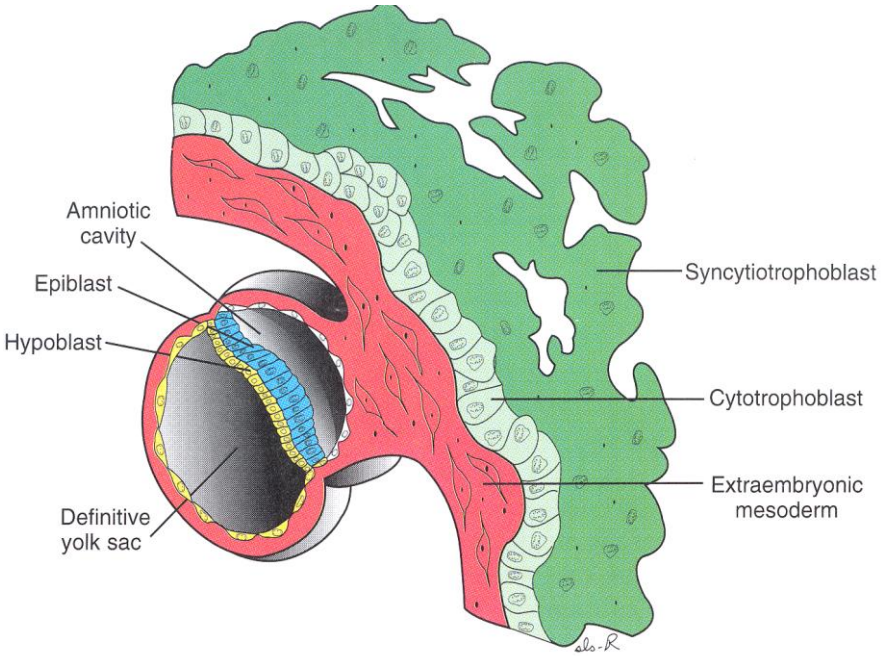
Tubular heart

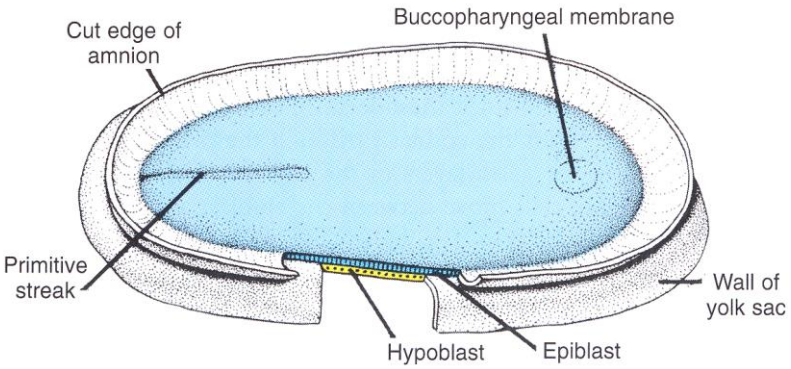


Fully functional heart with four chambers

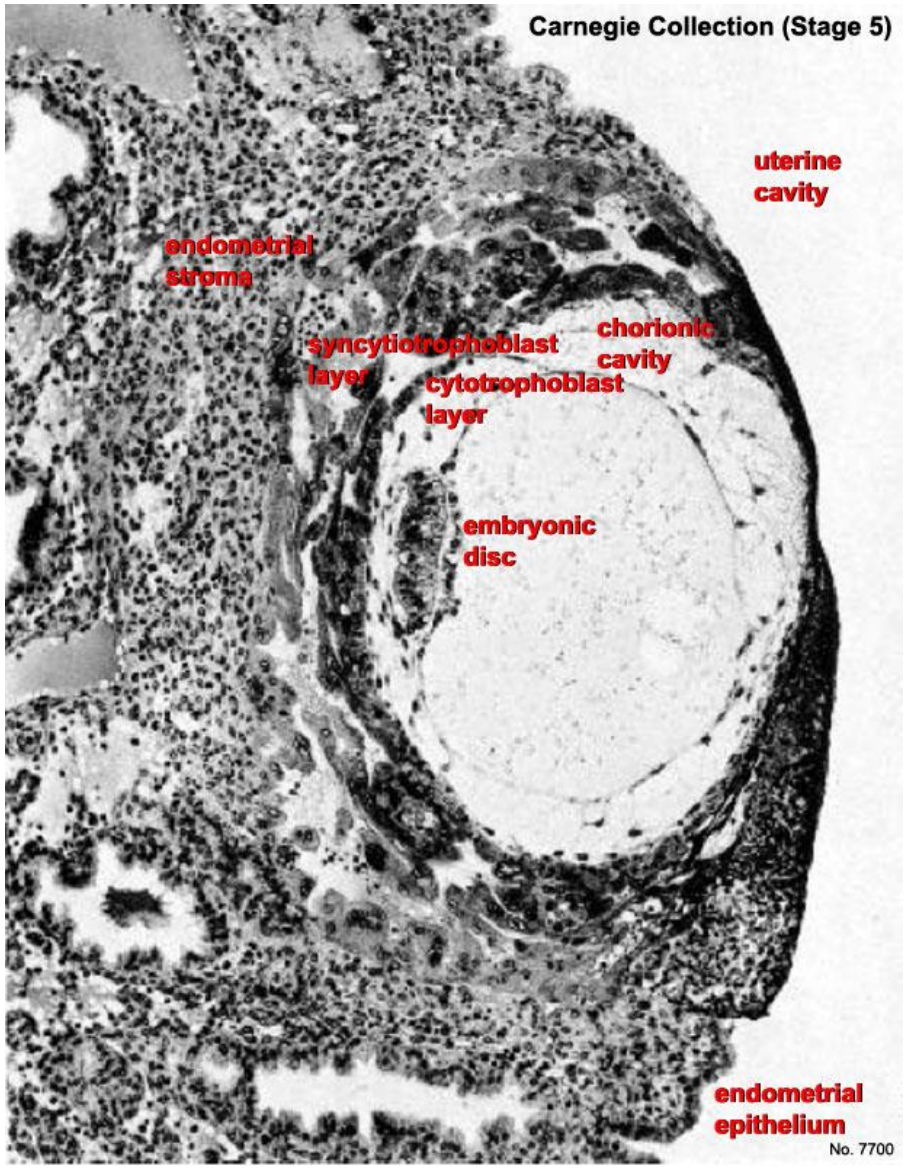
Week 2-3


Carnegie Collection
(Stage 5)
No. 7700


Amniotic cavity
Epiblast
Hypoblast
Definitive yolk sac
Syncytiotrophoblast
Cytotrophoblast
Extraembryonic mesoderm

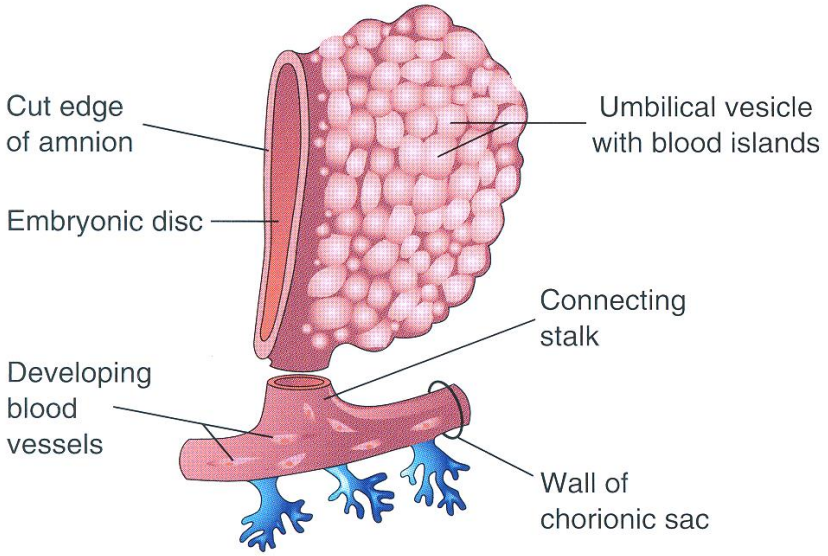

Cut edge of amnion
Buccopharyngeal membrane
Primitive streak
Wall of yolk sac
Hypoblast
Epiblast

DEVELOPMENT OF CARDIOVASCULAR SYSTEM

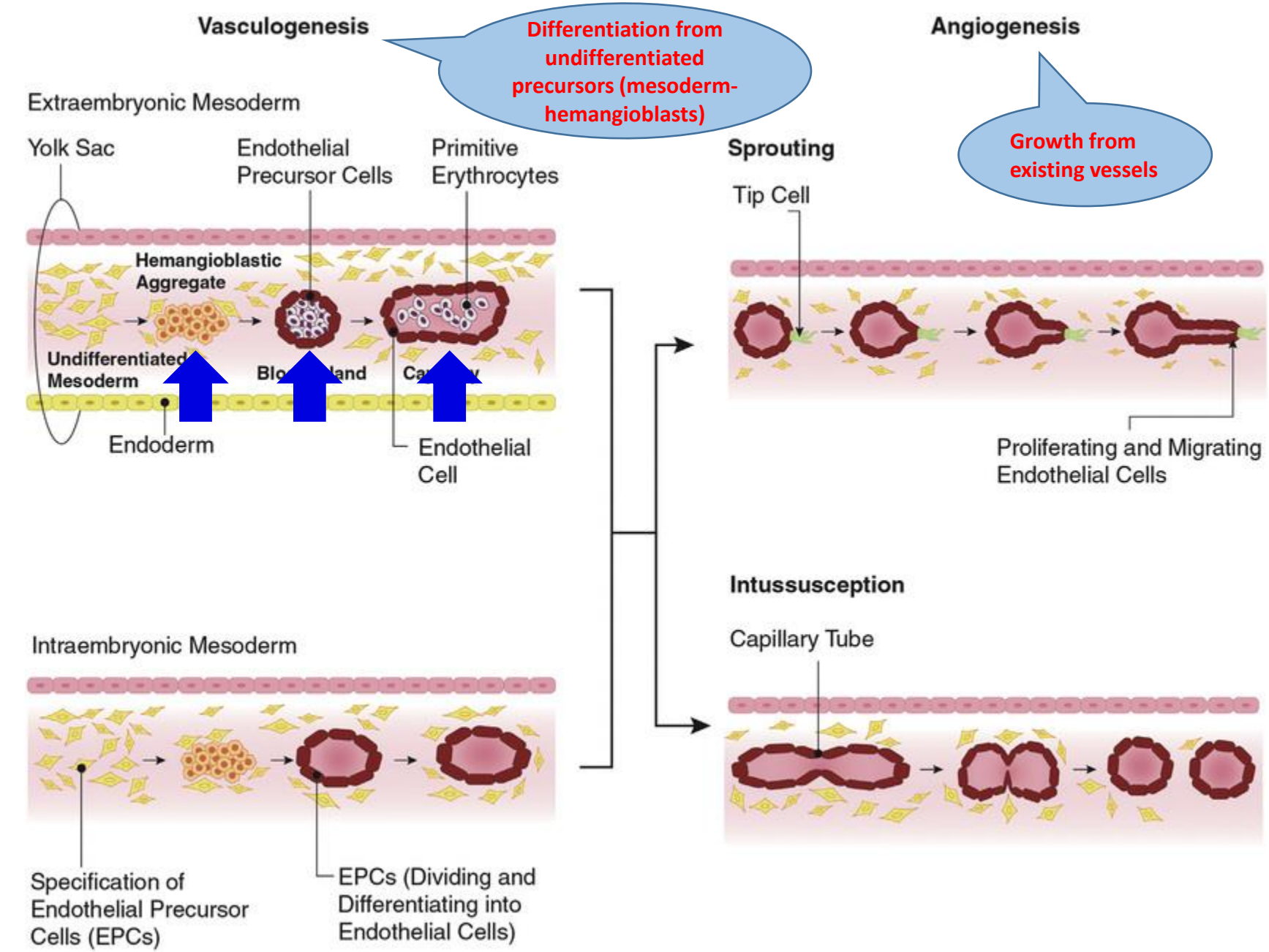


Week 2-3

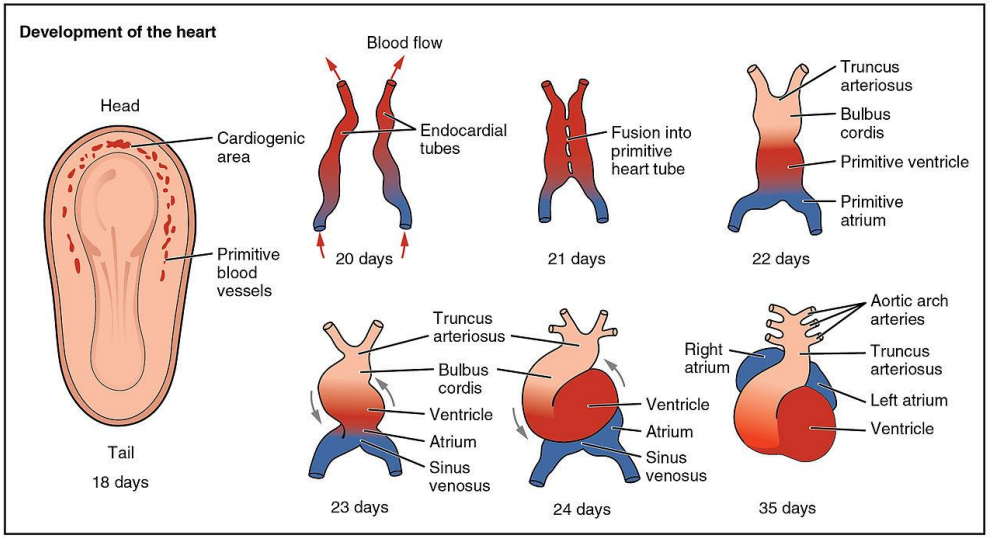
- rapid growth of embryo
- insuffcient supply by diffusion
- first vascularisation develops **outside** embryo – yolk sac, chorion and connecting stalk
- bipotential (hem)angioblasts in blood islands
- vasculogenesis and angiogenesis
- blood cells formation

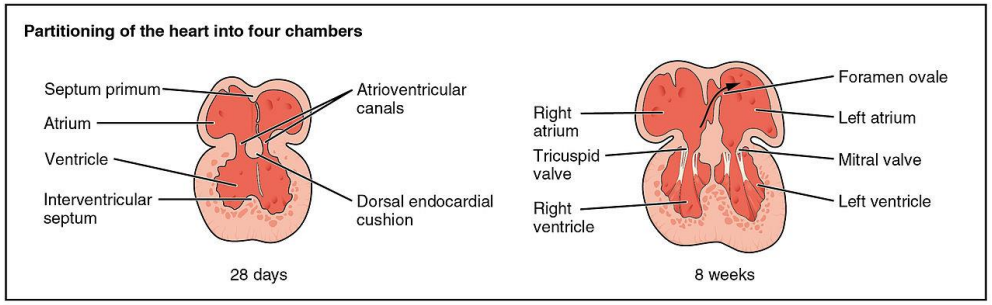


VASCULOGENESIS AND ANGIOGENESIS



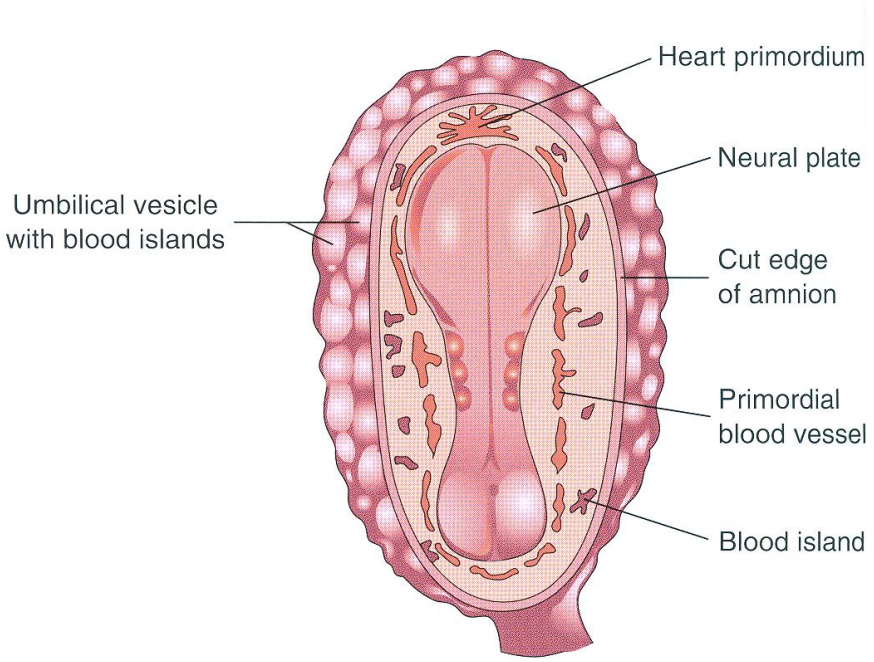
Development of heart and the first embryonic vasculature



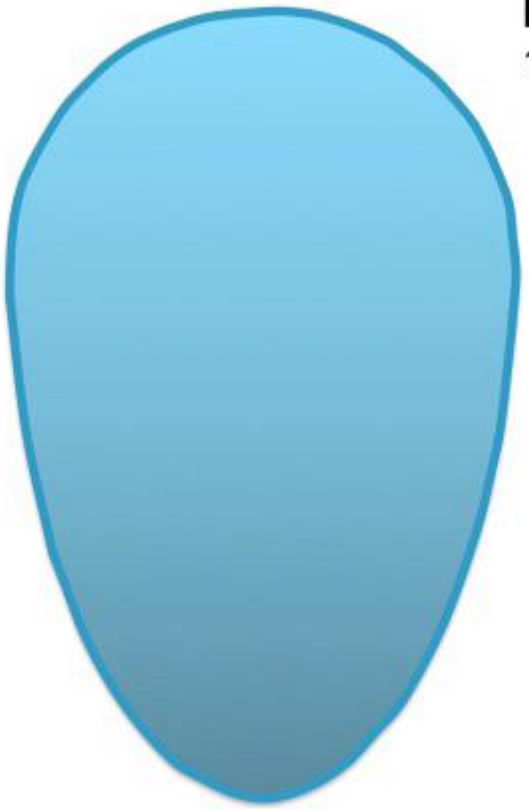


End of week 3

- **embryonic vasculogenesis** approx. 2 days later after establishment of extra-embryonic vessels
- primordial blood vessels
- **heart primordium** in cardiogenic area → **endocardial tubes**
- embryonic hematopoiesis from para-aortic clusters in AGM



Week 3



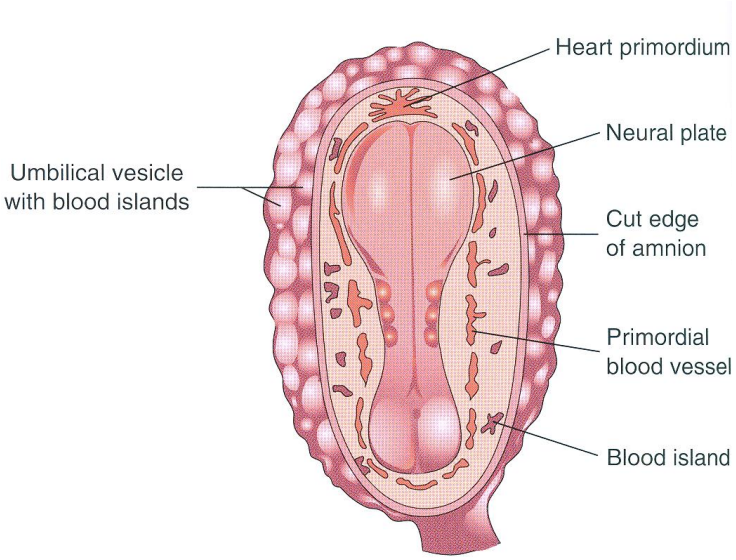
Epiblast

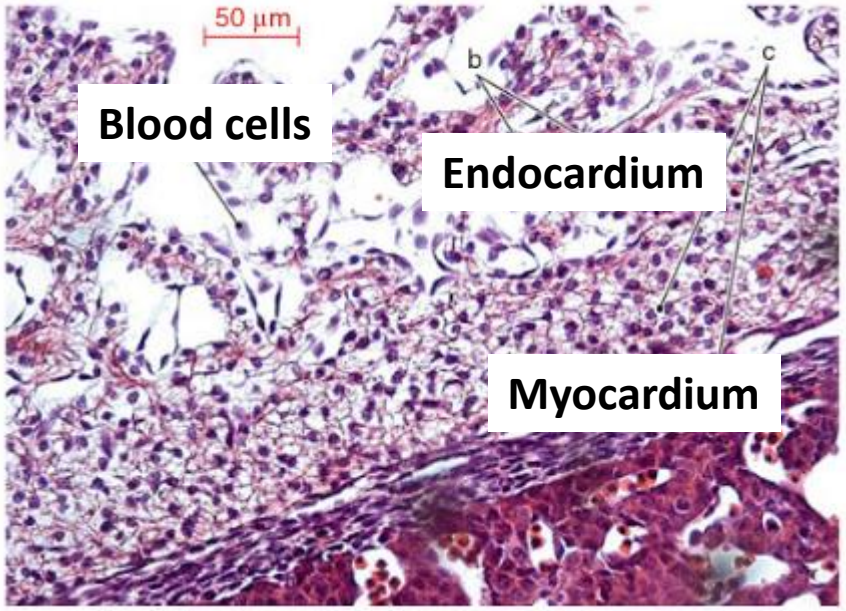
18 days, dorsal surface

Development of primitive heart

Week 3

- paired endocardial **heart tubes** (**cor tubulare duplex**) derived from embryonic splanchnopleura in cardiogenic area
- flexion of the embryo → medial fusion of paired tubes into **simple-tubular heart** (**cor tubulare simplex**)
- visceral mesoderm constitutes **myoepicardial layer**: **myocardium** and **epicardium**
- **cardiac jelly** → subendocardial connective tissue
- heart starts beating day 21-22
- blood starts flow ~week 4th

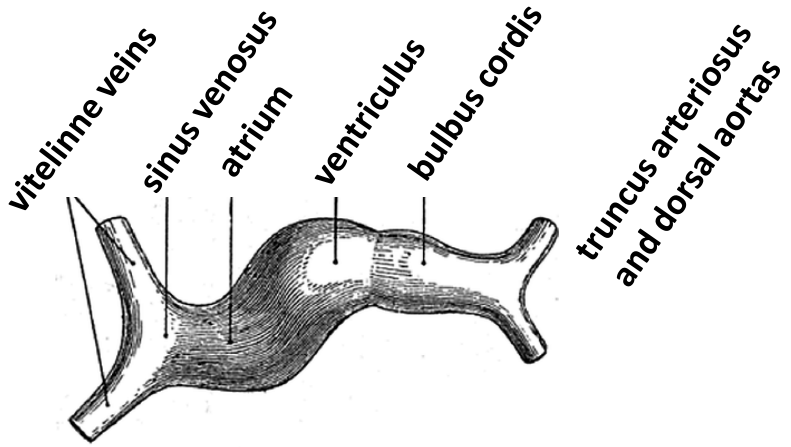




Week 4

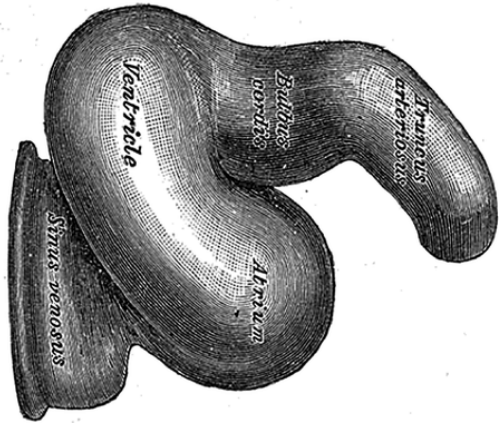
- **simple-tubular heart** (cor tubulare simplex and cor tubulare sigmoideum)
- **sinus venosus → atrium → ventriculus → bulbus cordis→ truncus arteriosus**

cor tubulare simplex



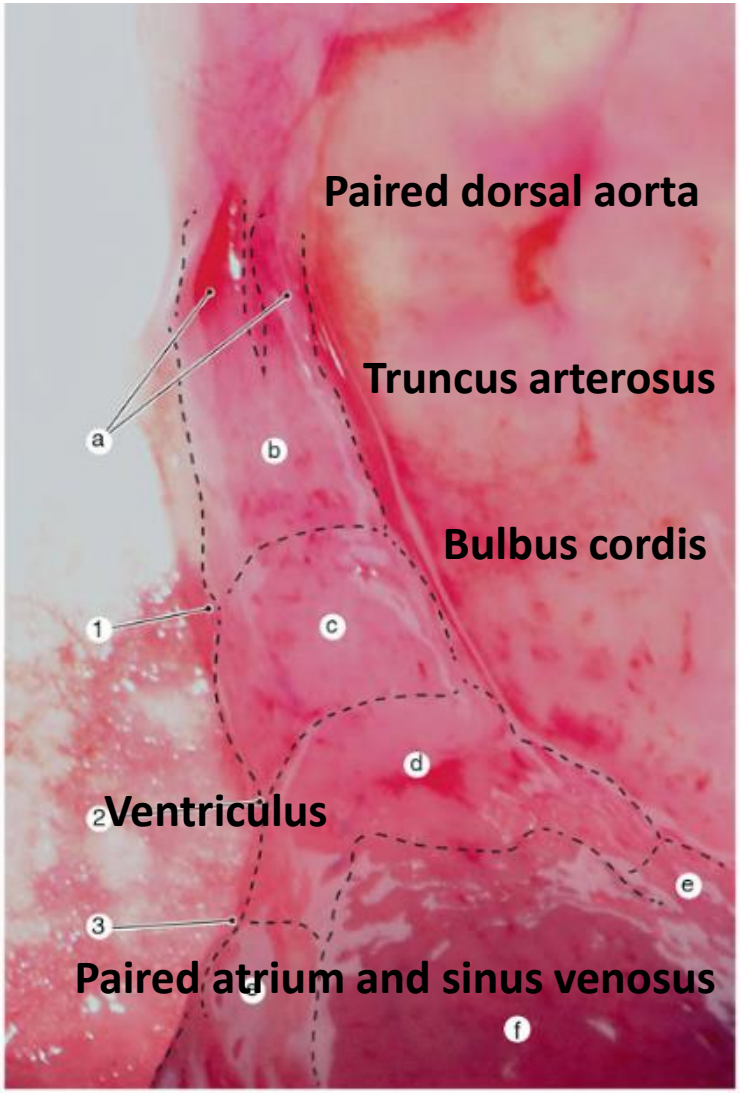
venous end **arterial end**

cor tubulare sigmoideum



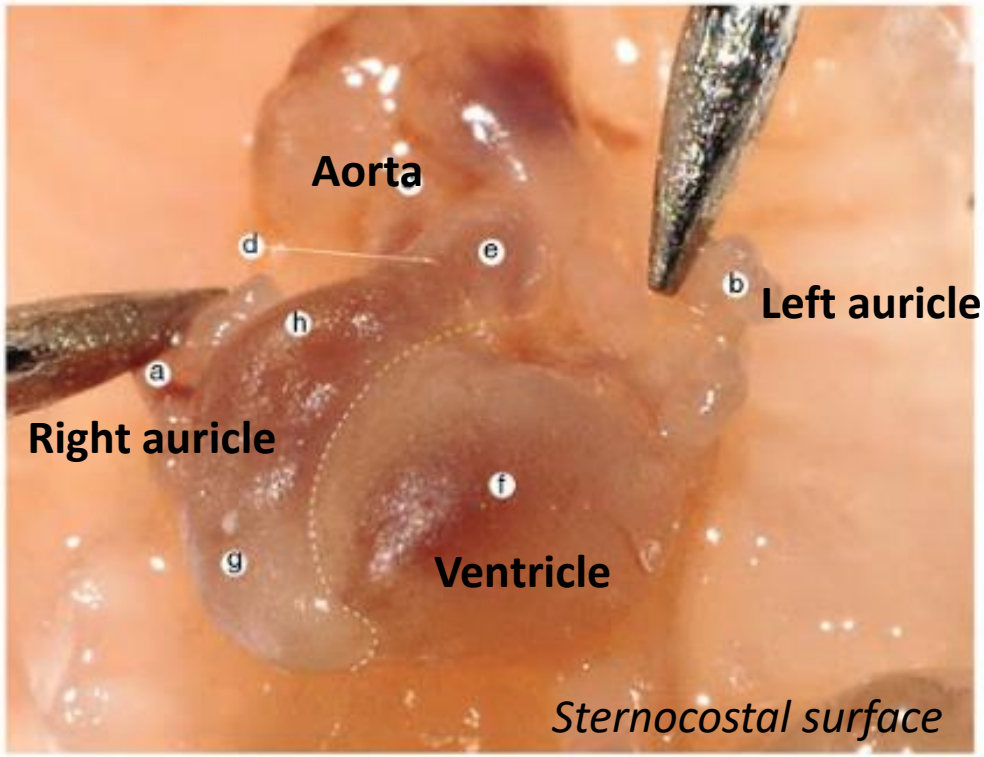
Week 4

Cor tubulare simplex

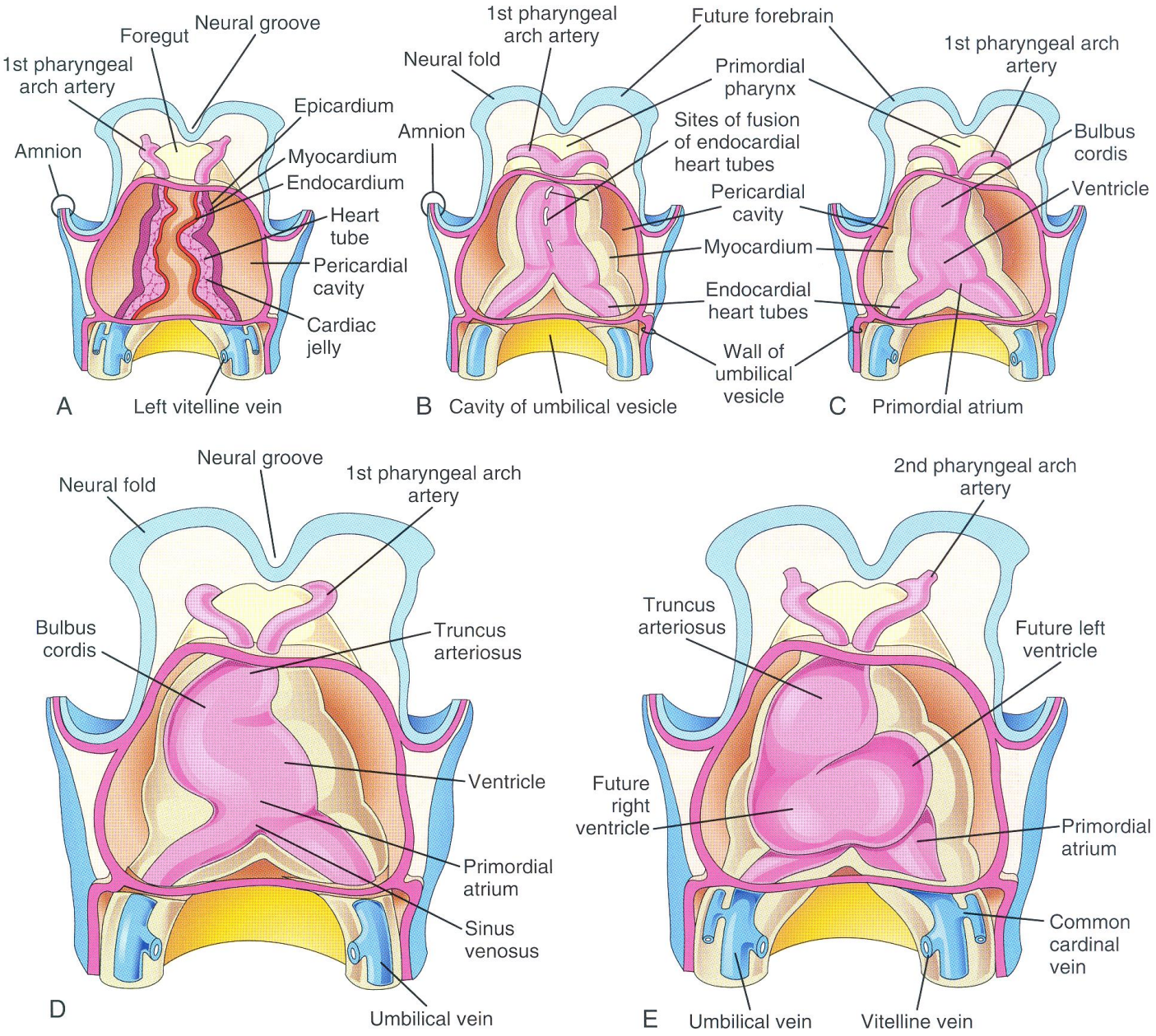


tubular heart is indeed a real structure

Cor tubulare sigmoideum

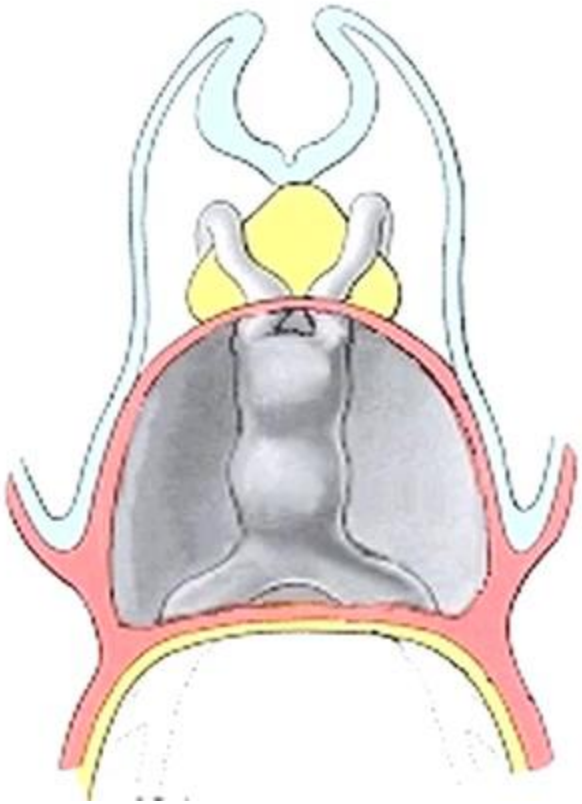


DEVELOPMENT OF HEART



DEVELOPMENT OF HEART

Week 4

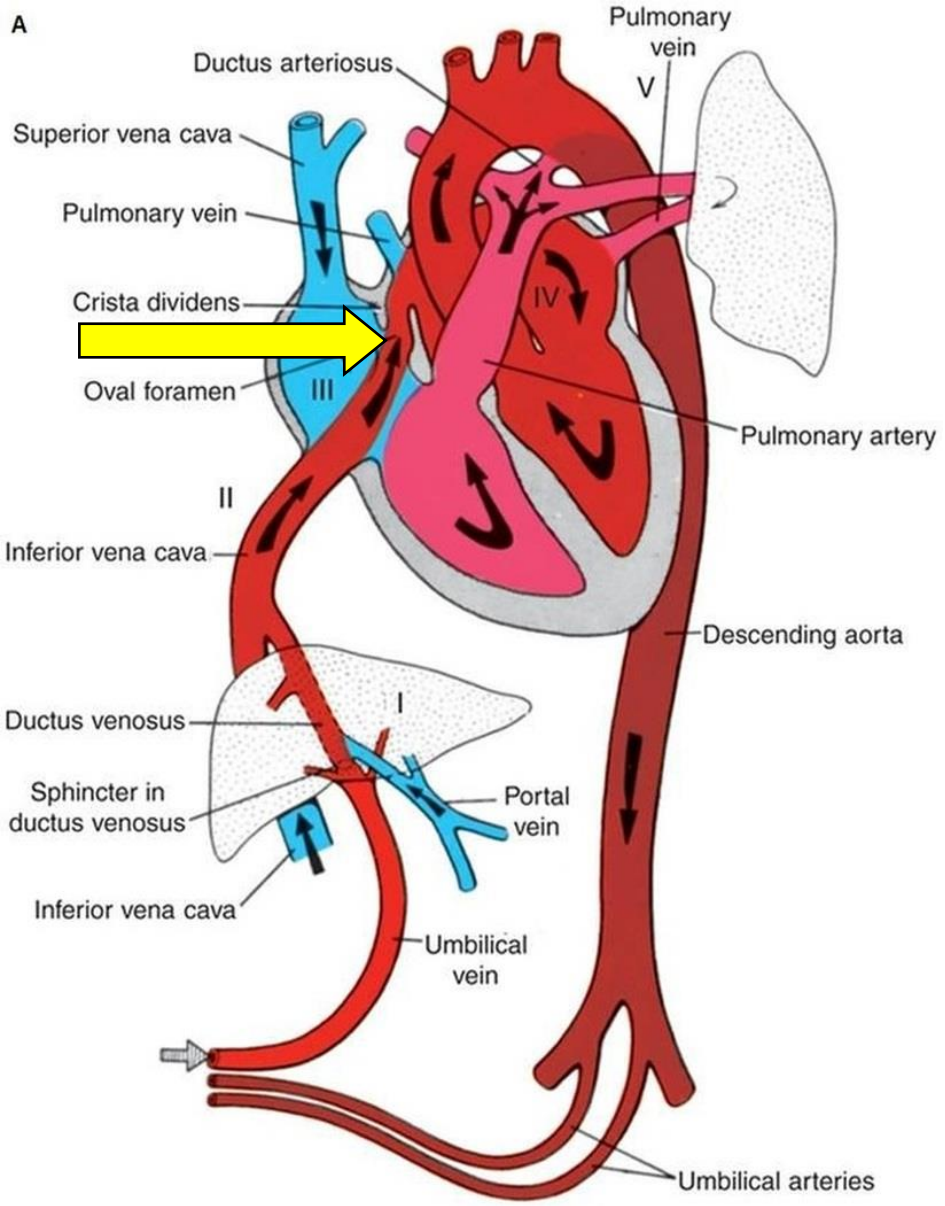


Partitioning of atrium commune

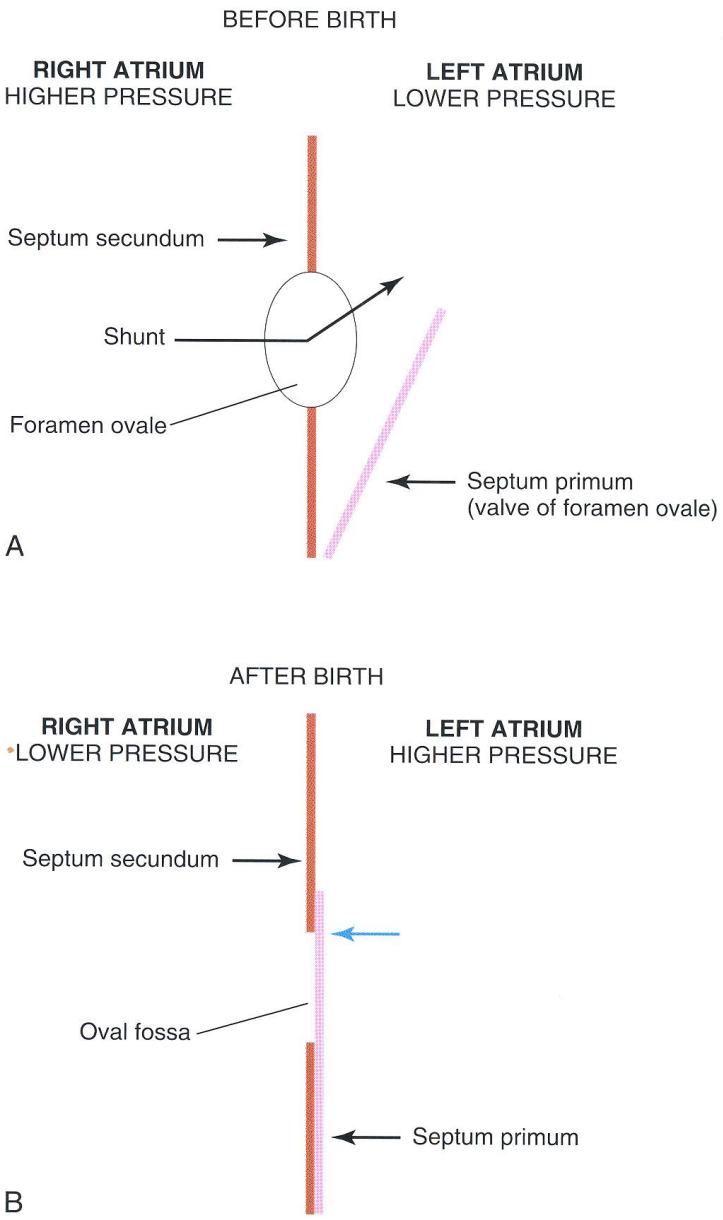
- septum primum grows from dorso-cranial wall towards endocardial cushions
- incoplete closure → **foramen** (ostium) **primum**
- by apoptosis → **foramen secundum**
- **septum secundum** → surrounds **foramen ovale**
- valvula foraminis ovalis from septum primum

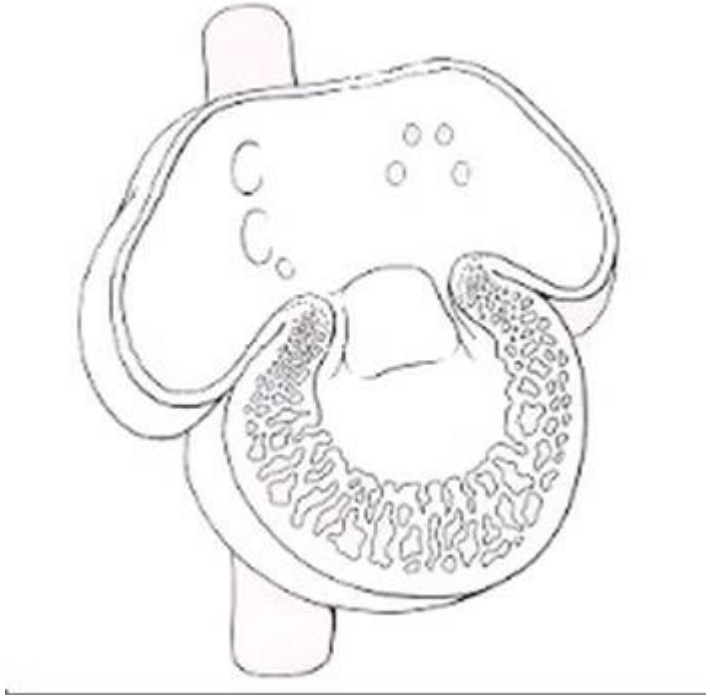
- foramen ovale: crucial embryonic shunt
- foramen ovale patens

- after atrial septation:
- opening of sinus venosus shifts to the right
- rest of sinus venosus → sinus coronarius

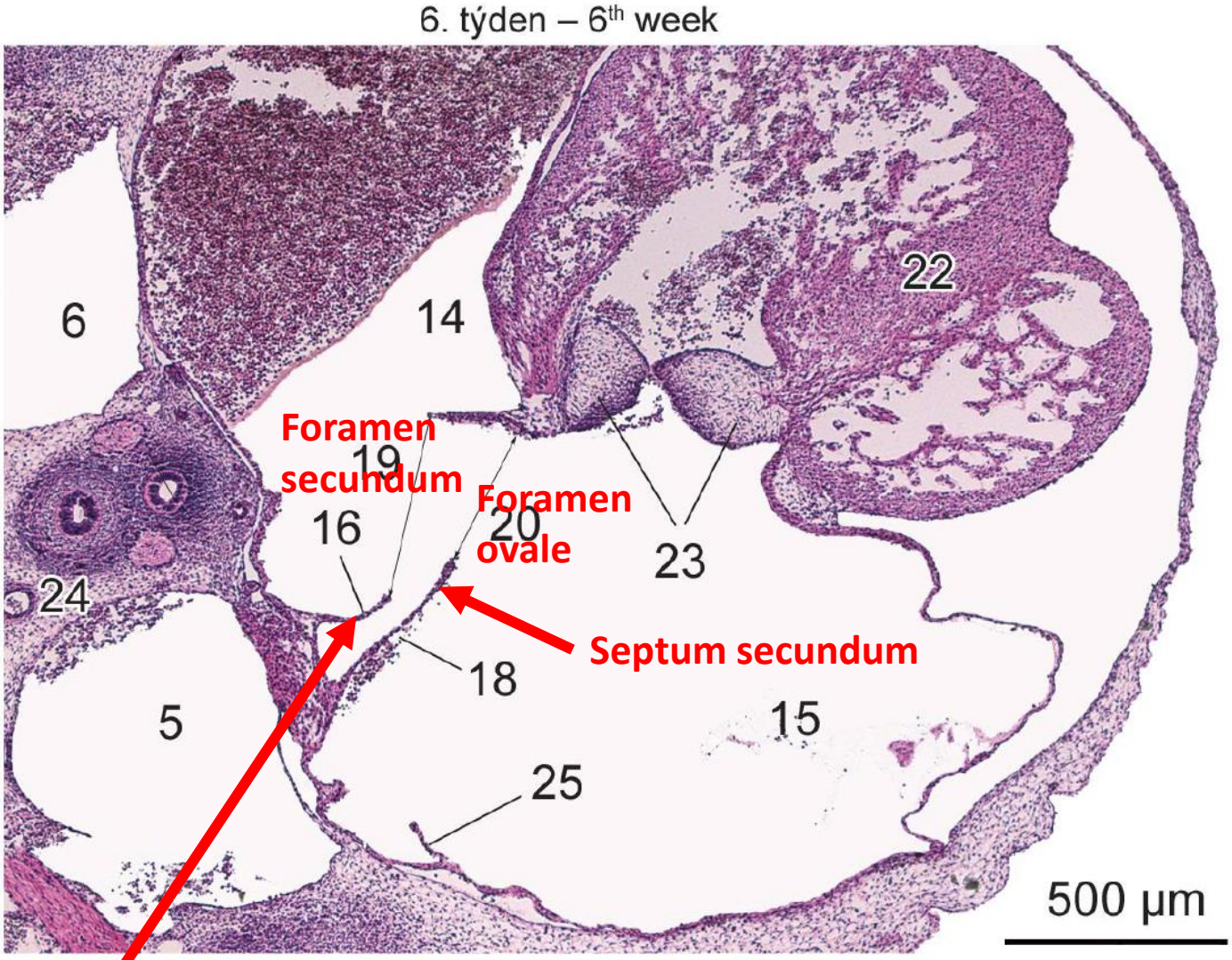


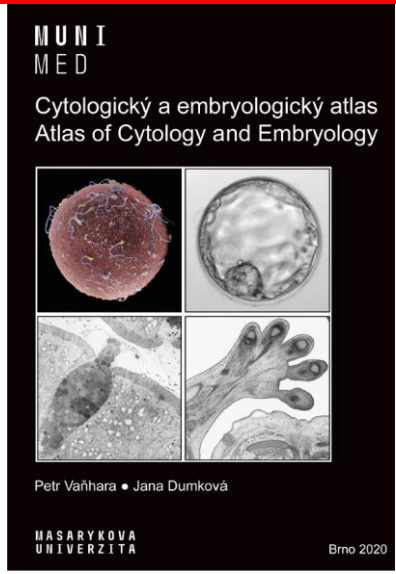
DEVELOPMENT OF HEART





DEVELOPMENT OF HEART



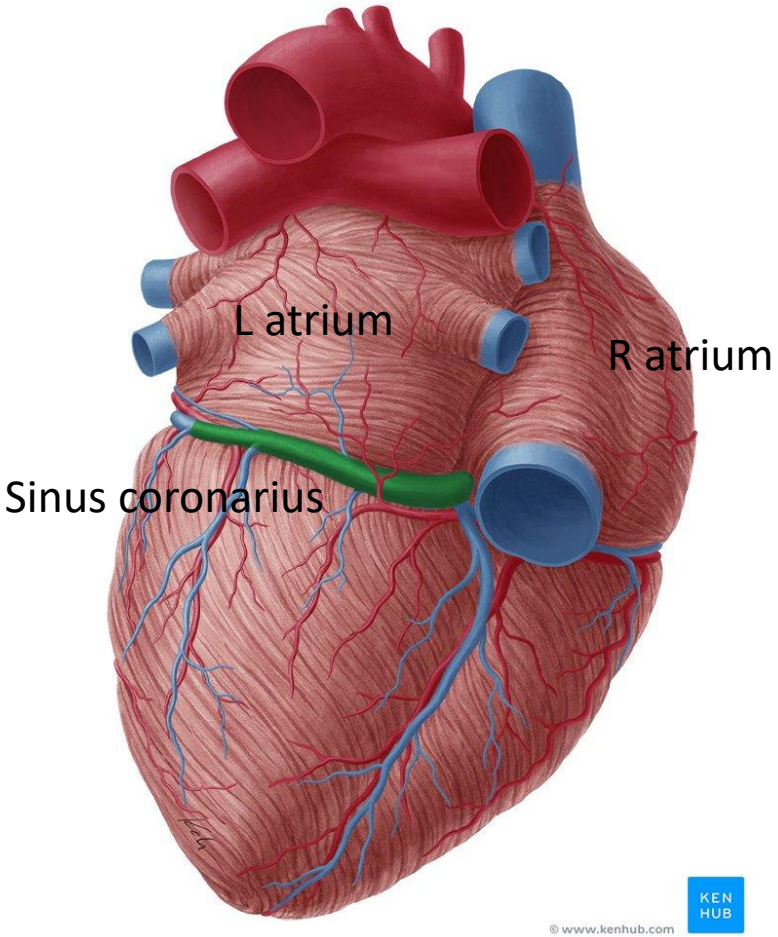


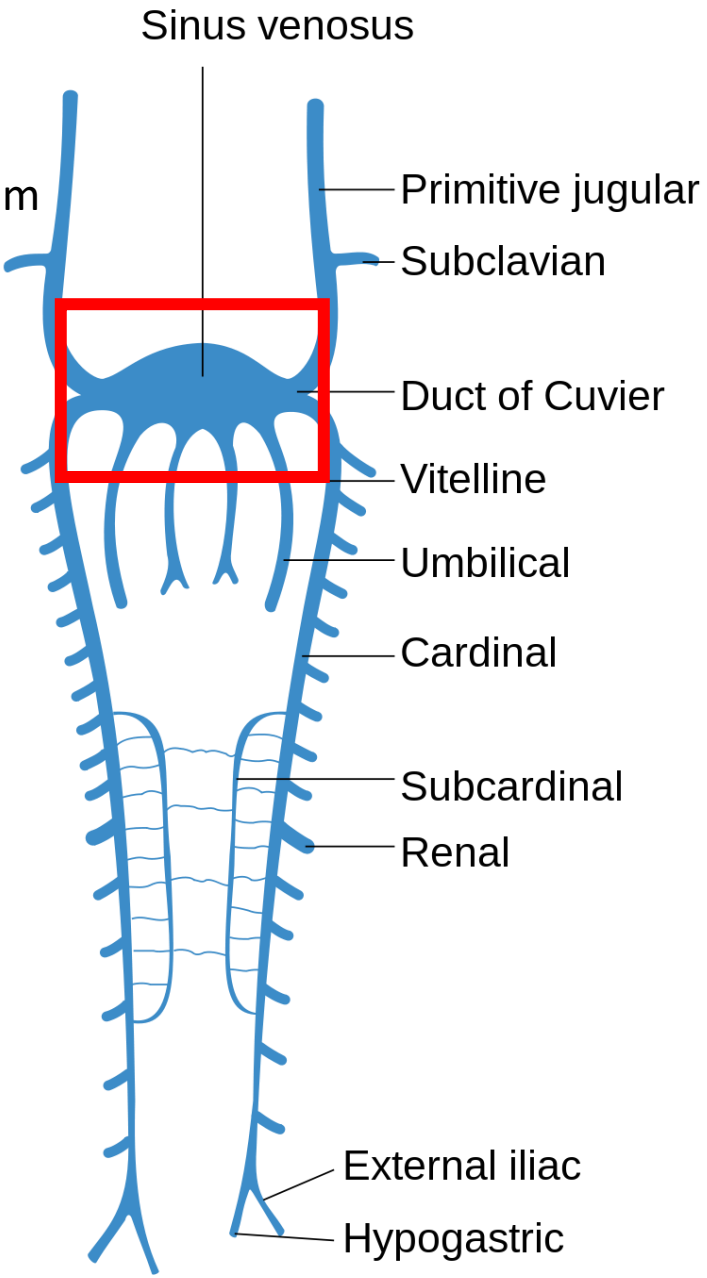
Vývoj srdce – development of heart. (1) perikardová dutina – pericardial cavity, (2) *bulbus cordis*, (3) *ventriculus primitivus*, (4) *atrium commune*, (5) *cornu dx. sinus venosus*, (6) *cornu sin. sinus venosus*, (7) dorsal aortae, (8) *truncus arteriosus*, (9) *conus cordis*, (10) základ pravé komory – developing right ventricle, (11) budoucí 1. faryngová arterie (aortální oblouk) – developing 1st pharyngeal artery (aortic arch), (12) *sulcus bulboventricularis*, (13) základ levé komory – developing left ventricle (14) *atrium sin.*, (15) *atrium dx.*, (16) *septum primum*, (17) *foramen* (*ostium*) *primum*, (18) *septum secundum*, (19) *foramen* (*ostium*) *secundum*, (20) *foramen ovale*, (21) *foramen interventriculare*, (22) *septum interventriculare*, (23) endokardové polštářky (návalky) – endocardial cushions, (24) *mediastinum*, (25) venózní chlopeň – venous valve.

DEVELOPMENT OF HEART

- **sinus venosus** during atrial septation:

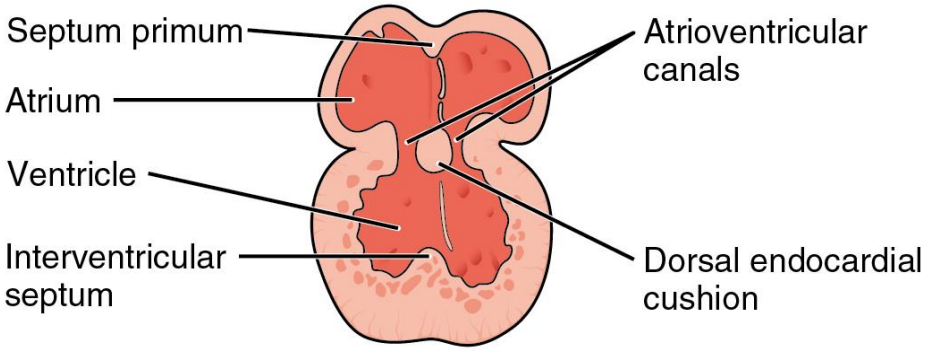
- shift of sinus venosus opening to the right → right atrium
- left part sinus venosus is separated → **sinus coronarius**



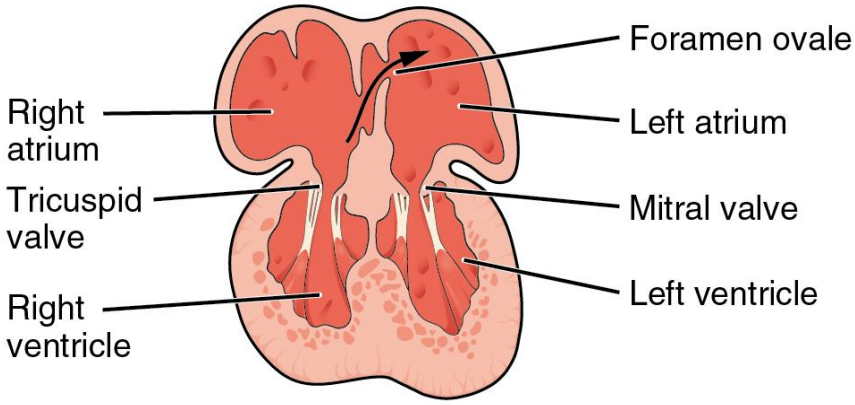


Partitioning of ventriculus communis

- septum interventriculorum primitivum – temporary
- septum interventriculare at the end of week 4 – grows cranially
- foramen interventricualre – closure linked to development of aortico-pulmonary septum
- pars membranacea (septi interventricularis)
- pars muscularis (septi interventricularis) - medial walls of both ventricles



28 days

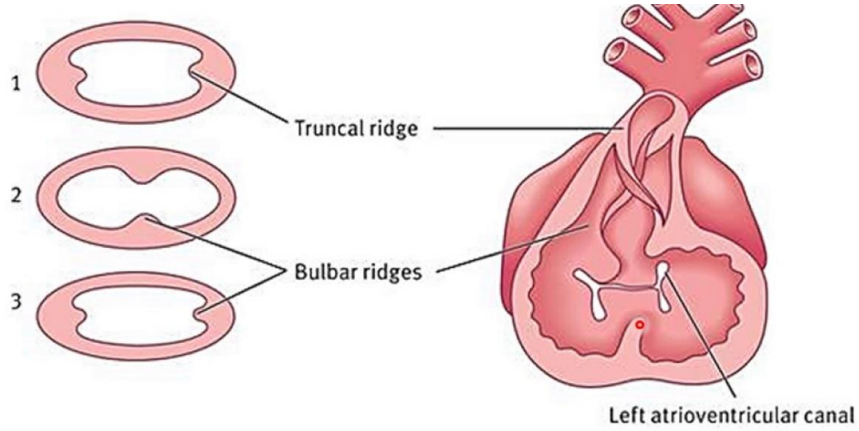


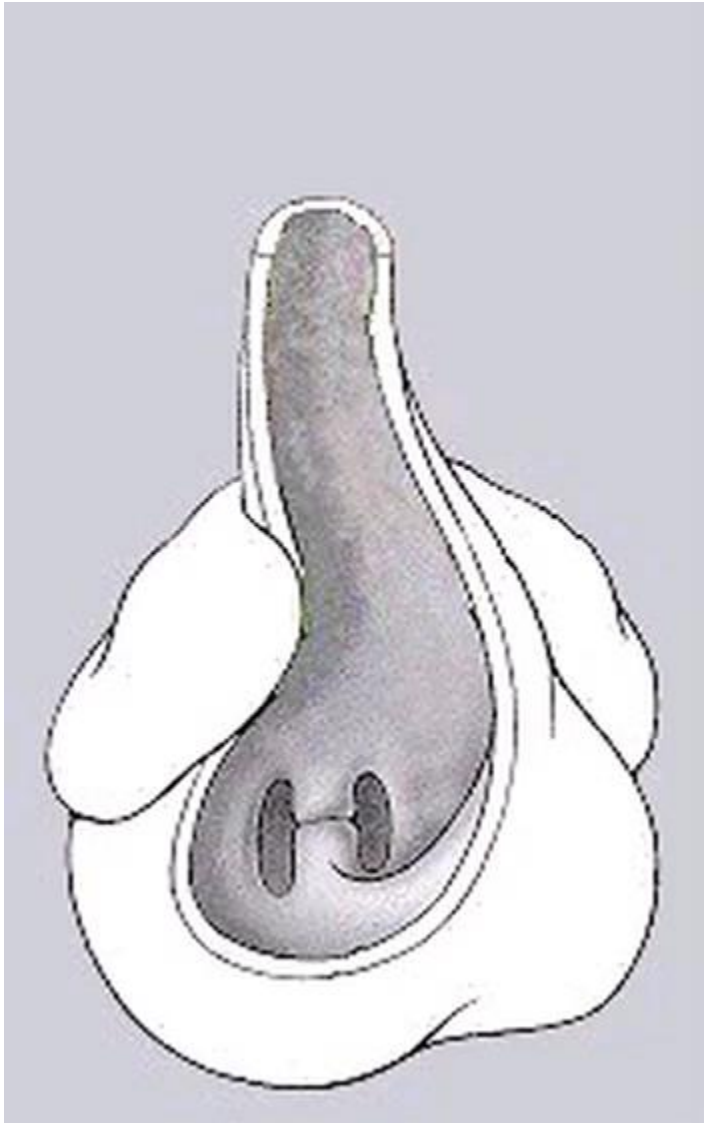
8 weeks

DEVELOPMENT OF HEART

- **Partitioning of bulbus cordis and truncus arteriosus**
- 5th week – ridges in bulbus and truncus from neural-crest mesenchyme
- 180° spiraling – spiral aortico-pulmonary septum
- pulmonary trunk twists around aorta

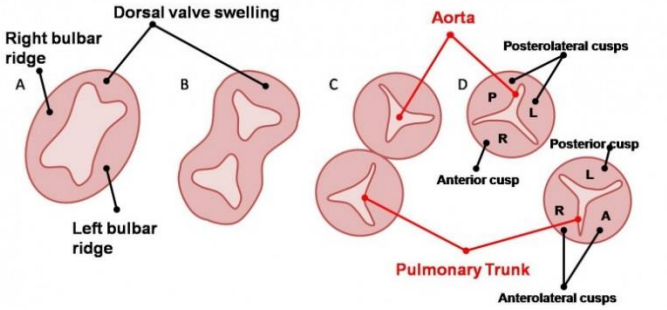
- bulbus cordis is embedded into the definitive ventricles:
- right ventricle: conus arterious (infundibulum) → pulmonary trunk
- left ventricle: aortic vestibule

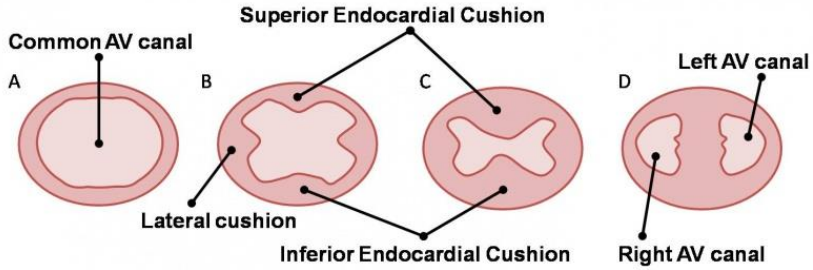


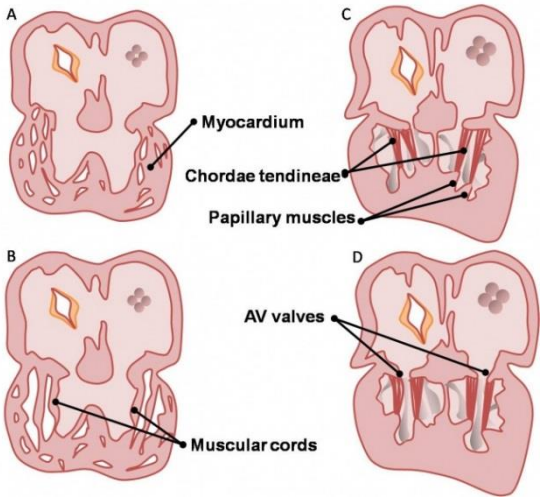


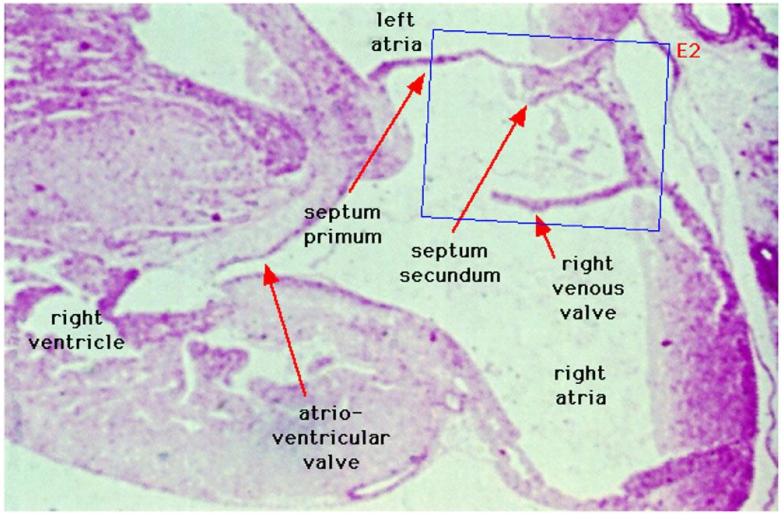
- **Development of cardiac valves**

- **semilunar valves** develop by the partitioning of truncus arteriosus from three swellings of endocardial tissue
- neural crest origin
- **AV valves** (tricuspid and mitral) develop similarly at AV canals





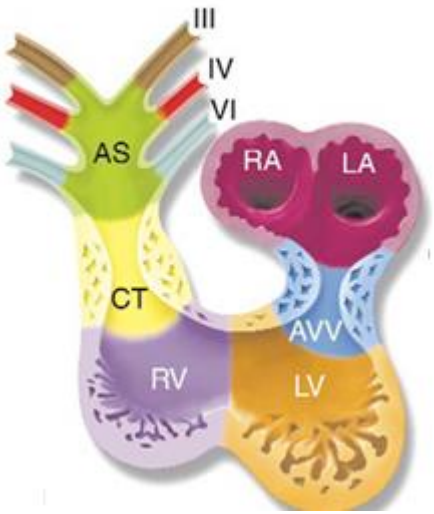


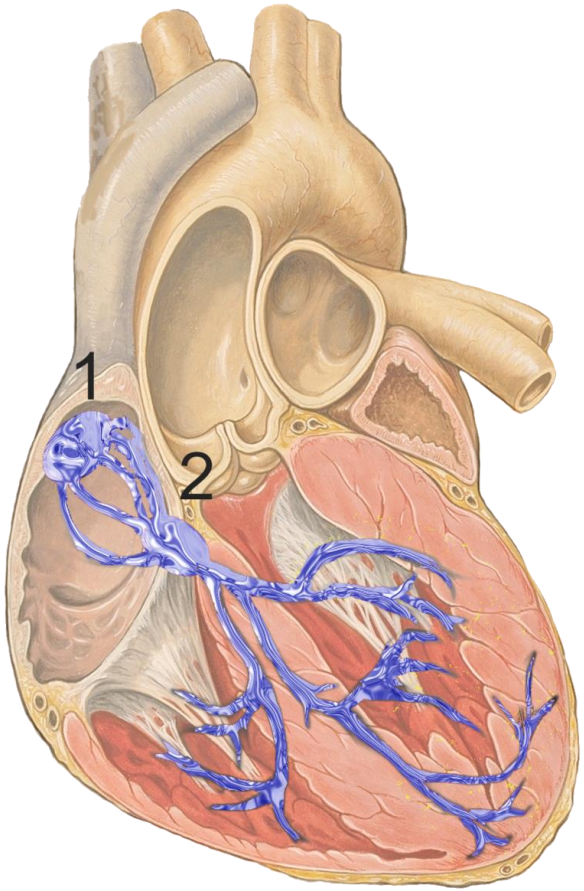


Development of conductive heart system

Definitive conductive heart system provides the electrical conduction between atria and ventricles

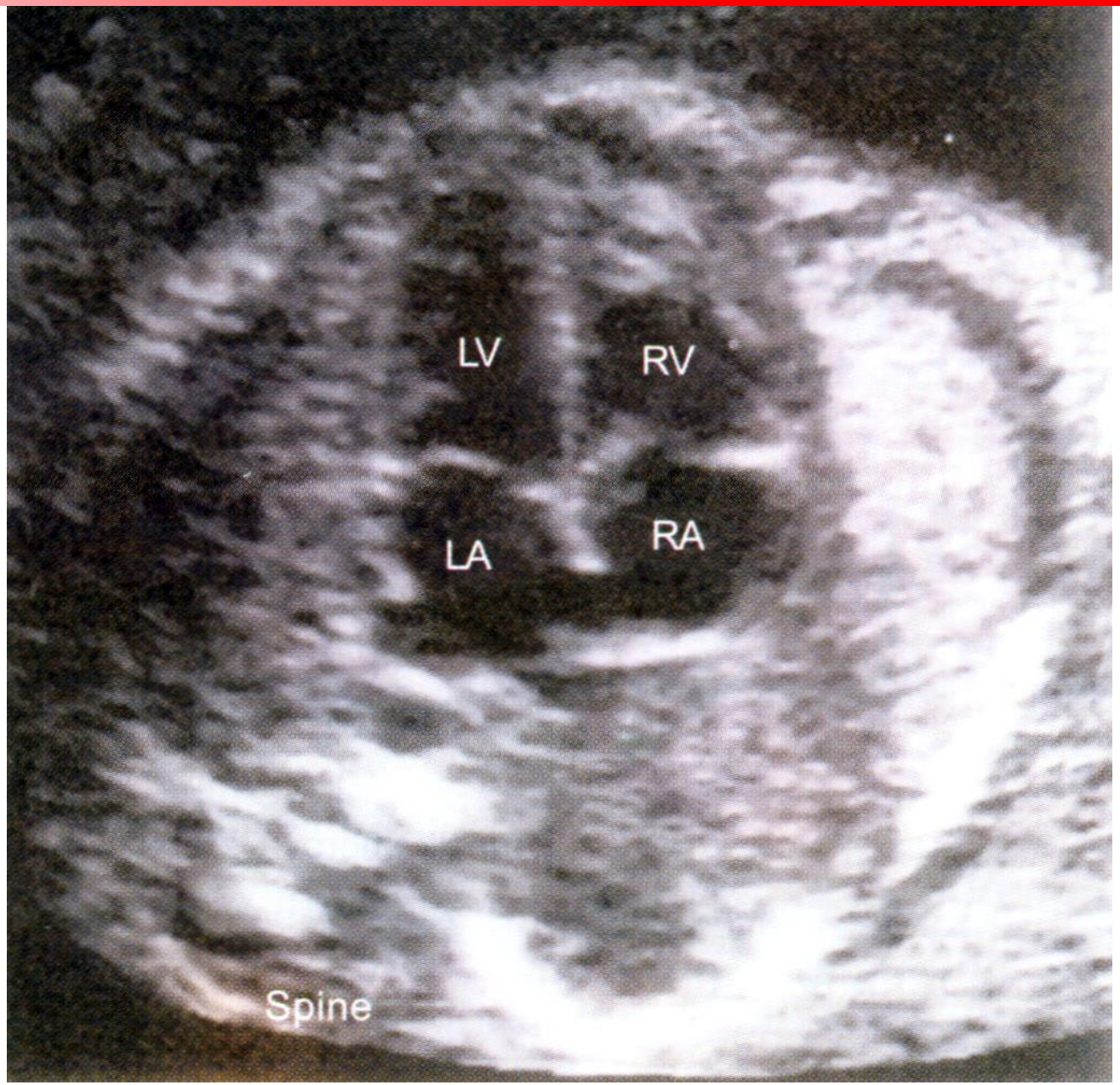
- First all muscular layers are connected
- **Primitive atrium – primary pacemaker**
- **SA node** in 5th weeks develops from tissues of sinus venosus
- Cells of interatrial and atrioventricular septa contribute to formation of **AV node** and fasciculus atrioventricualris → bundle branches → ventricular myocardium





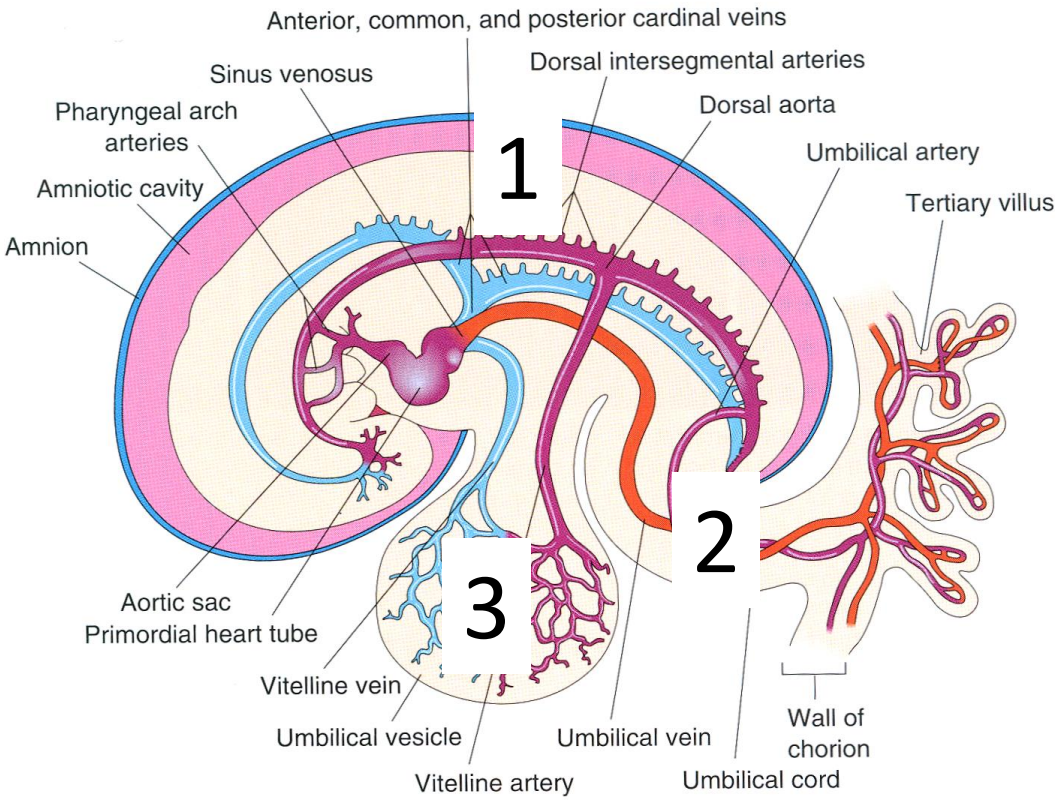
DEVELOPMENT OF HEART

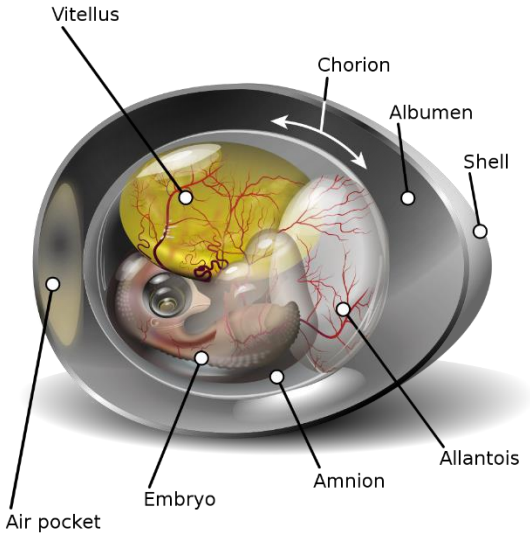
Week 20

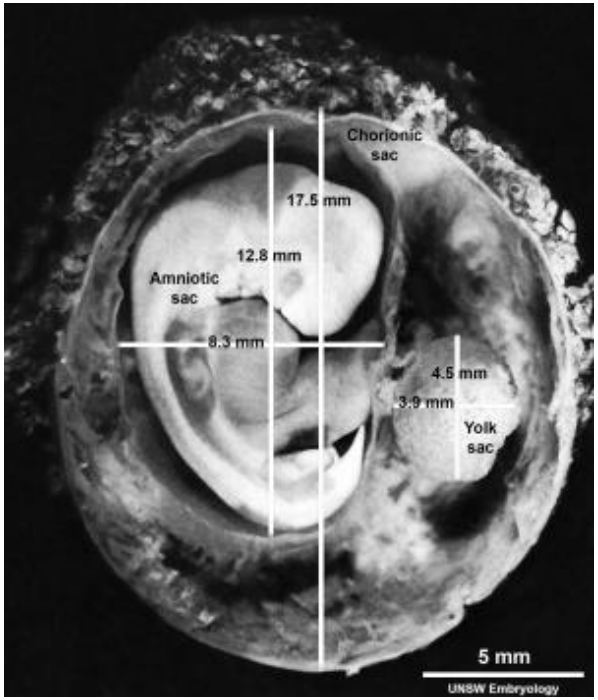


DEVELOPMENT OF VASCULATURE

Week 4

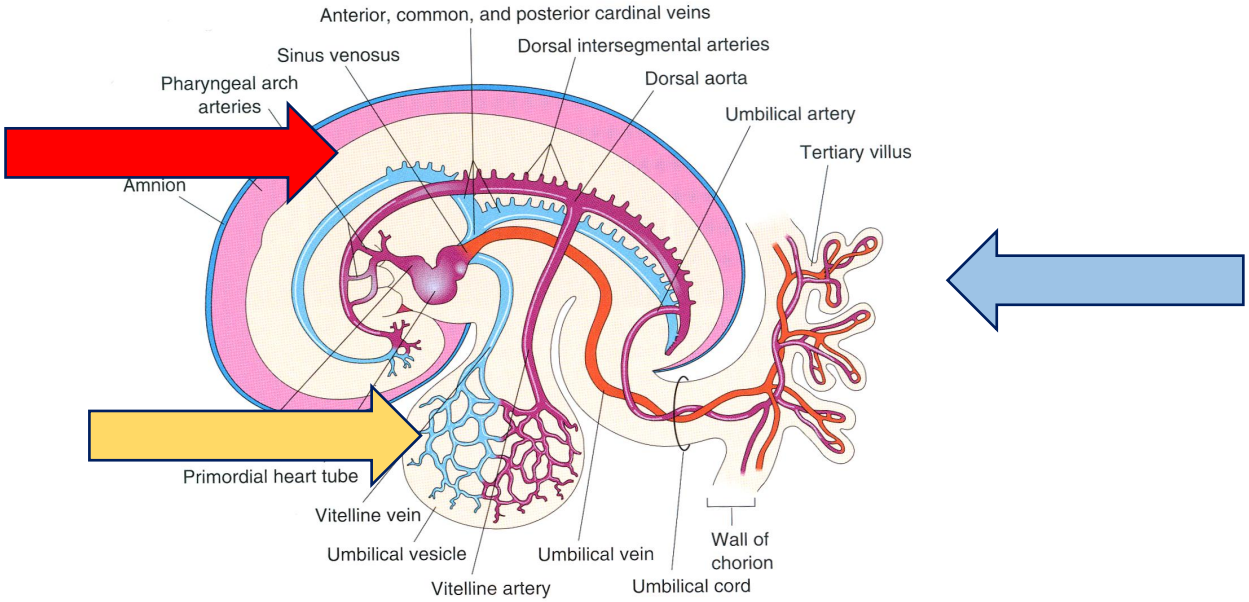




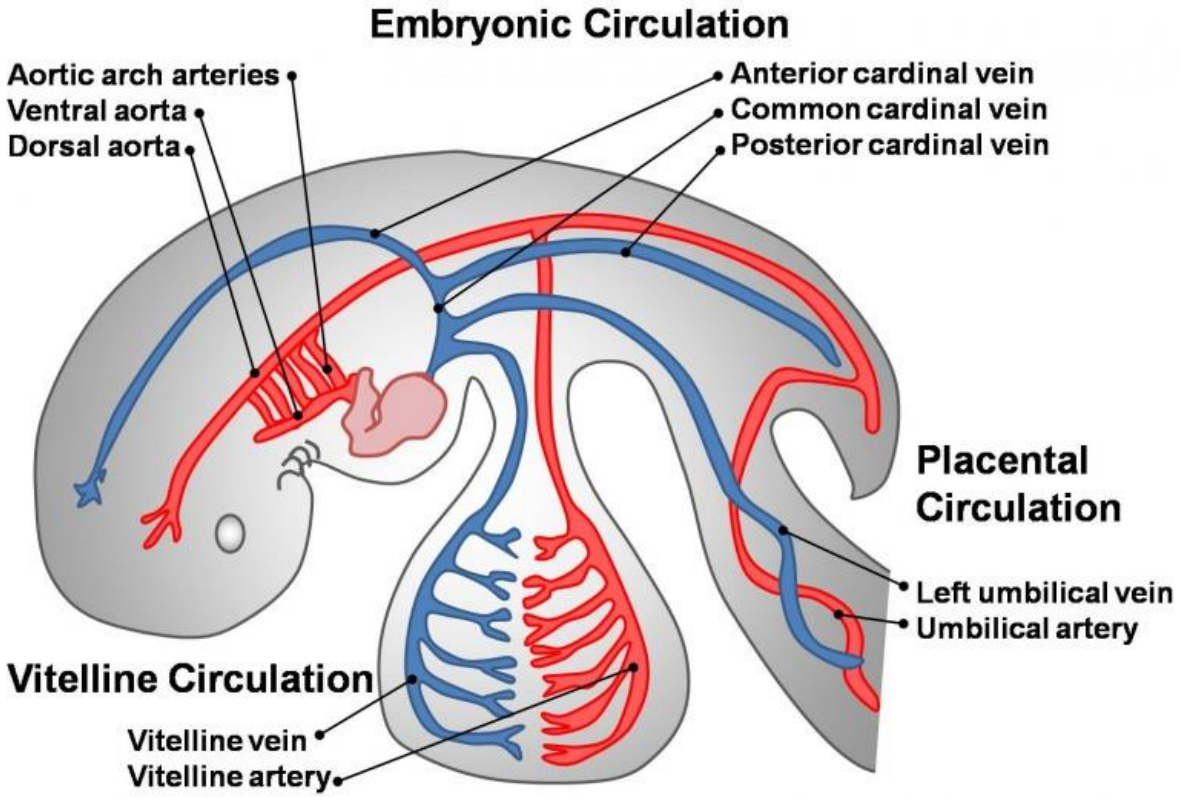


Week 4

- **embryonic circulation**: heart tube → *truncus arteriosus* → aortal arches → paired dorsal aorta → caudally fuse into single aorta dorsalis → capillary beds → paired cardinal veins (drain pre- and postcardinal veins) → *ductus Cuvieri* → *sinus venosus*
- **vitelline circulation**: dorsal aorta → *aa. omphalomesentericae* → fuse into single *a. omphalomesenterica* → *vv. omphalomesentericae + vv. umbilicales* → paired *truncus vitelloumbilicalis* → *sinus venosus*
- **umbilical circulation**: dorsal aorta → *aa. umbilicales* → chorion → *vv. umbilicales* + *vv. omphalomesentericae* → paired *truncus vitelloumbilicalis* → *sinus venosus*



Arteries


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

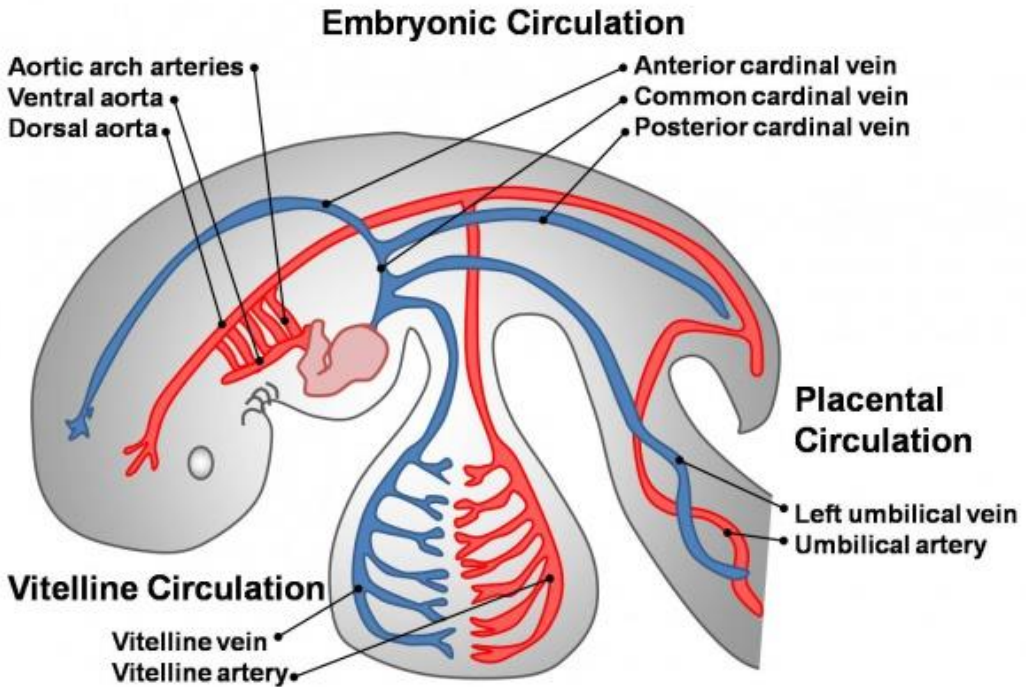
DEVELOPMENT OF ARTERIES

Dorsal aorta

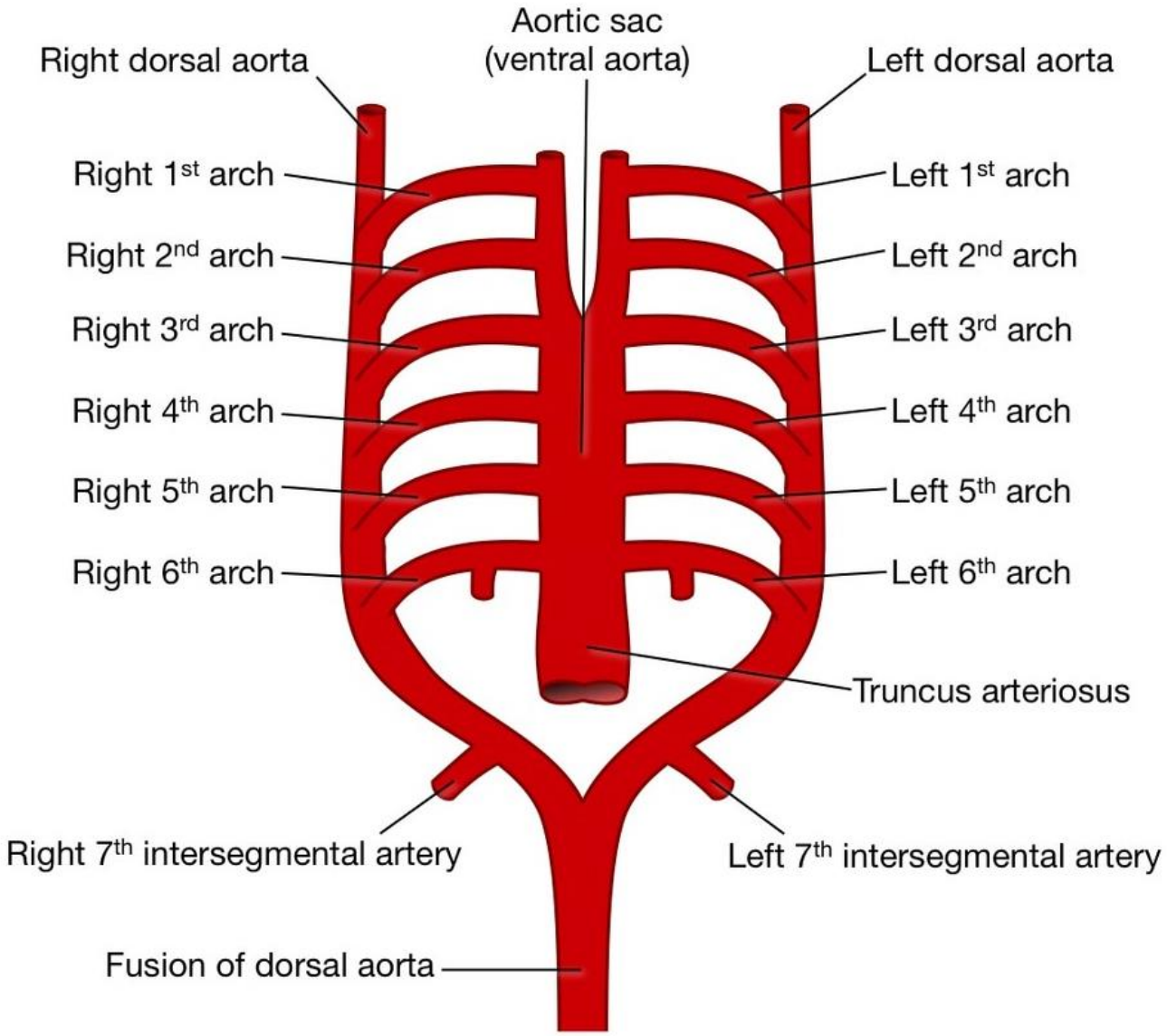
- originally a paired structure - fusion into a single dorsal aorta → a. descendens
- aortal arches

Ventral aorta

- originally a tempory paired structure
- fusion into the aortic sac when embryo folds

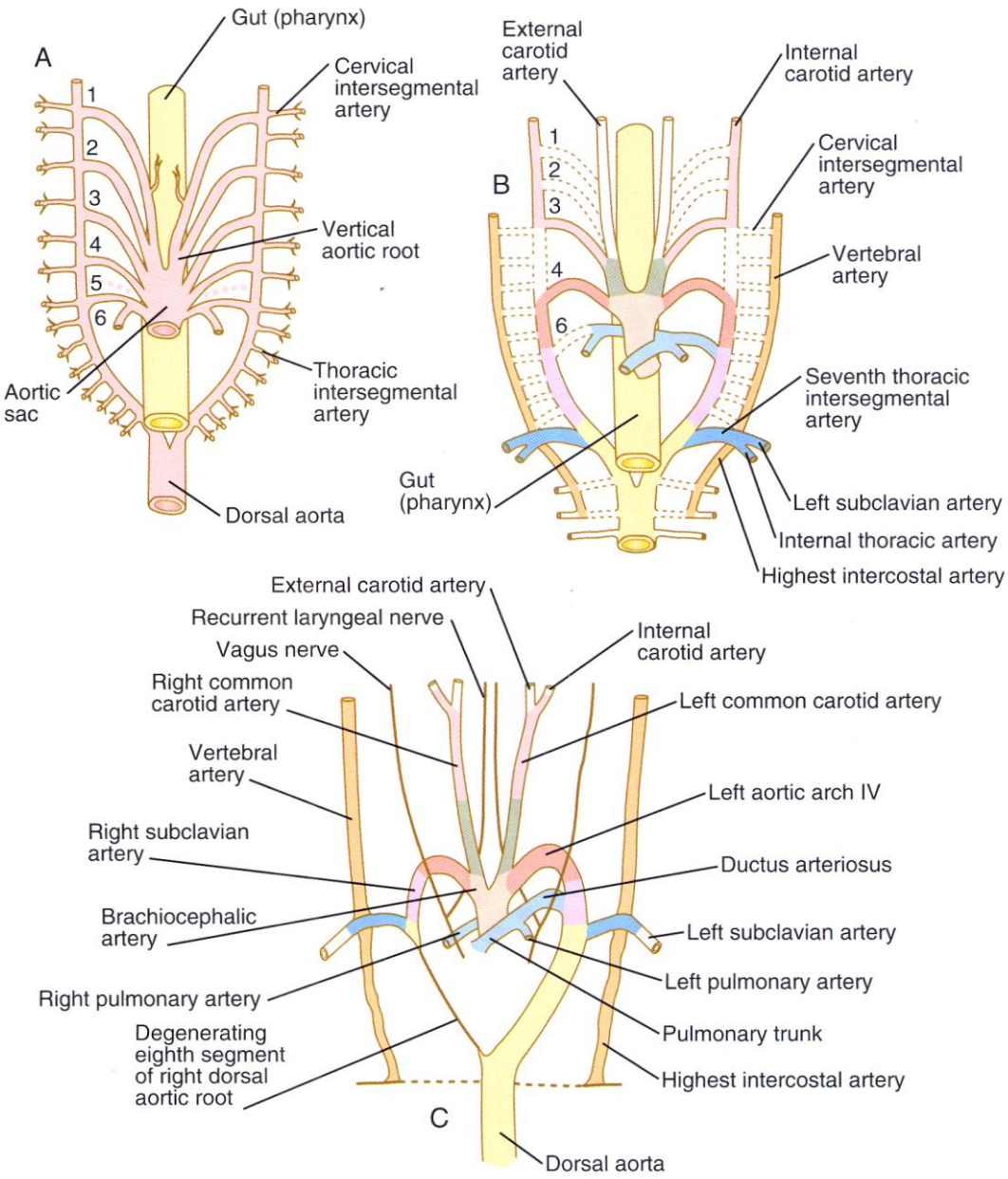


Development of large arteries – aortic arches



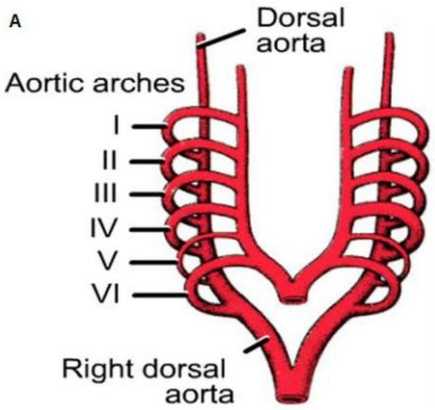
DEVELOPMENT OF ARTERIES

Aortic arches



DEVELOPMENT OF ARTERIES

Aortic arches



1 mostly disappears, **a. maxillaris**

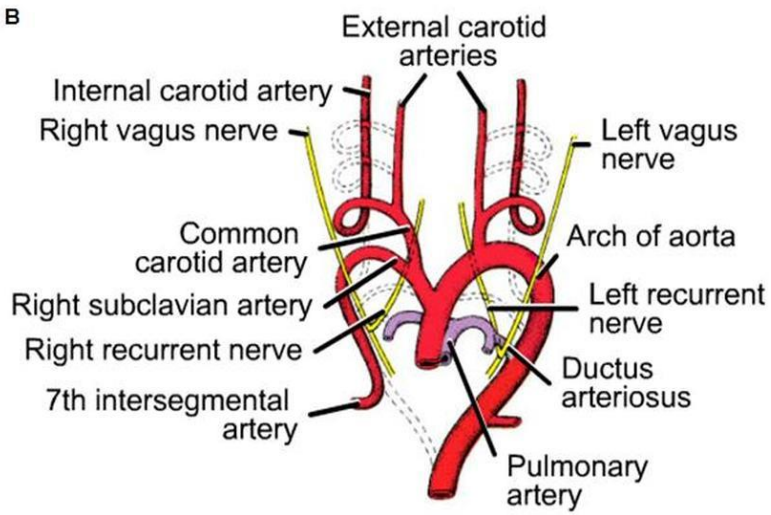
2 mostly disappears, **a. stapedia** and **a. hyoidea**

3 proximal parts **aa. carotides communes**, distal parts of **aa. carotides internae**

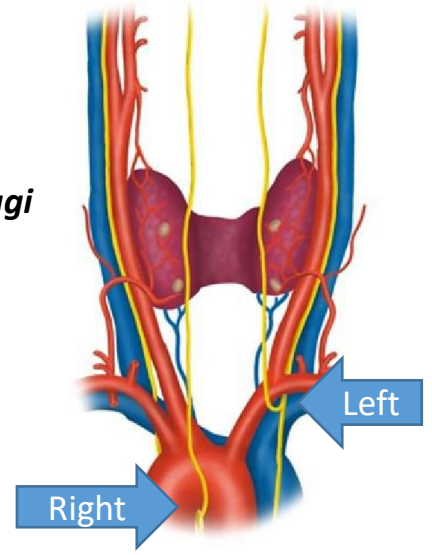
4 right: proximal part of **a. subclavia dextra** (distal part from dorsal aorta and 7th intersegmental artery);
left: **arcus aortae** (aorta develops from aortic sac and left dorsal aorta)

5 do not develop at all or quickly degenerates

6 right: from proximal part: proximal part of **a. pulmonalis dextra**, distal part disappears
left: from proximal part: proximal part of **a. pulmonalis sinistra**, from distal part: **ductus arteriosus**.



Ramus laryngeus reccurens n. vagi
Right: under a.subclavia dx.
Left: under arcus aortae



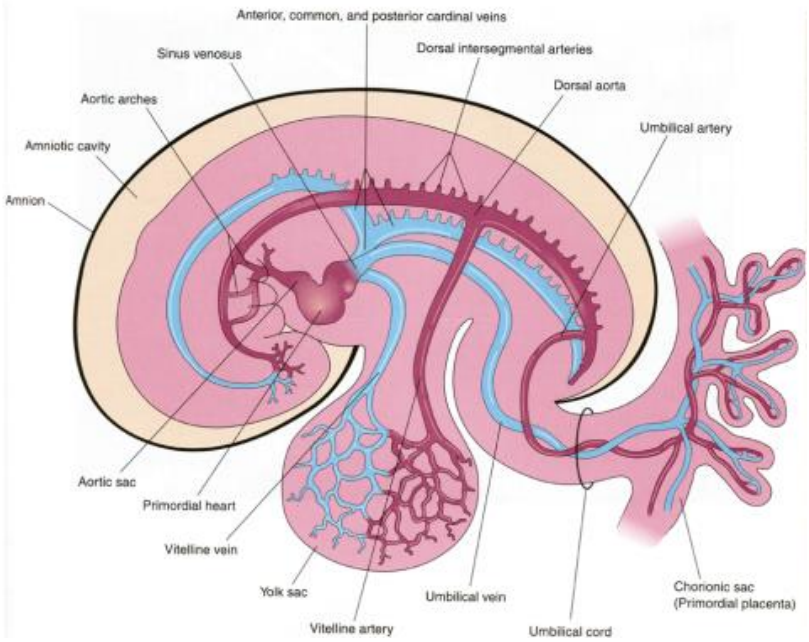
DEVELOPMENT OF ARTERIES

Branches of dorsal aorta

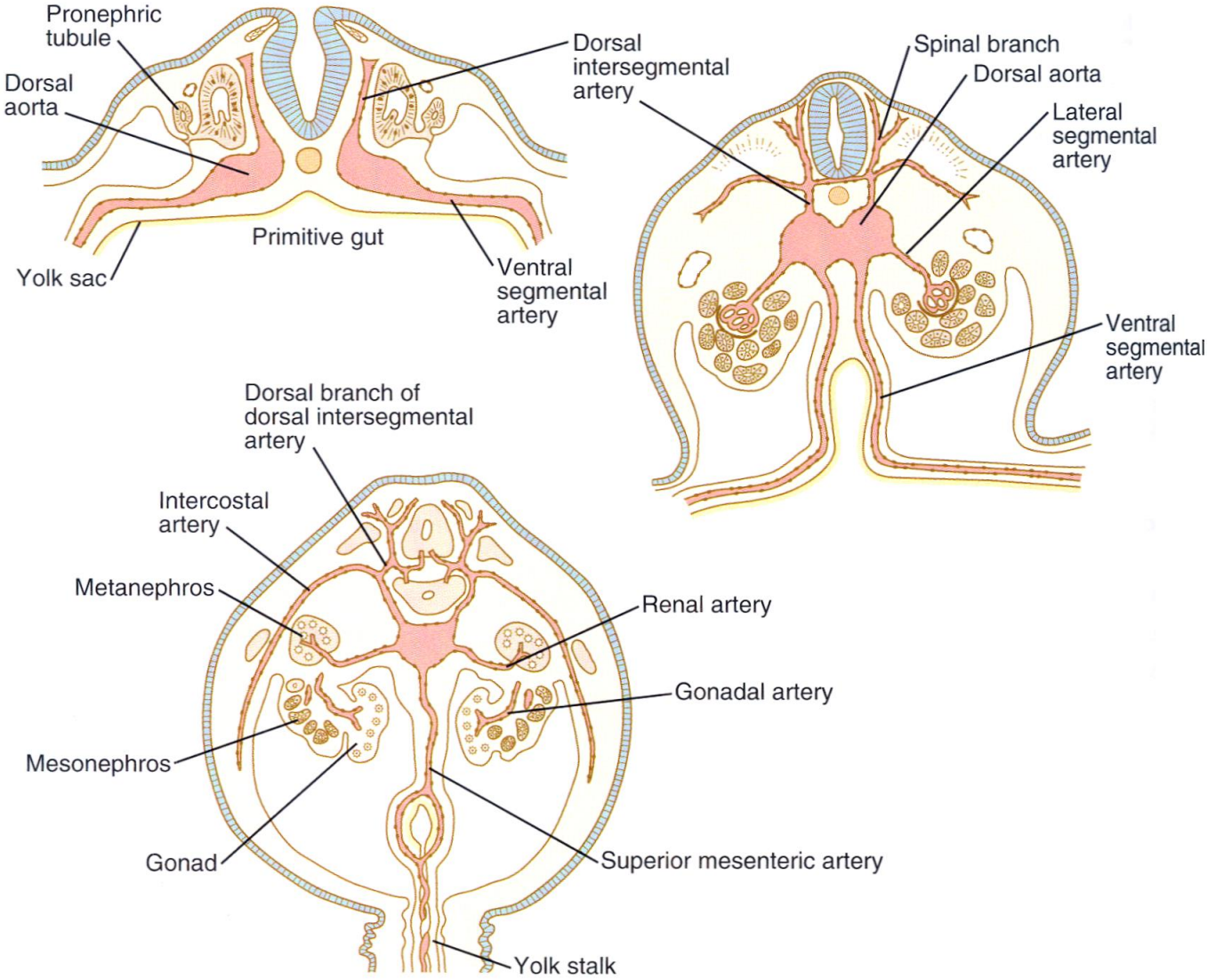
- **intersegmental arteries** (parietal, dorsal) a **visceral** (ventral, towards primitive gut)

- between somites
- vascularisation of somites and their derivatives
- intersegmental arteries:
  - neck → a. vertebralis
  - chest → aa. intercostales
  - abdomen → aa. lumbales
  - sacral → aa. sacrales laterales
- part of 7th intersegmental artery → a. subclavia dx.
- caudal end of dorsal aorta → a. sacralis media

- truncus coeliacus
- a. mesenterica superior
- a. mesenterica inferior

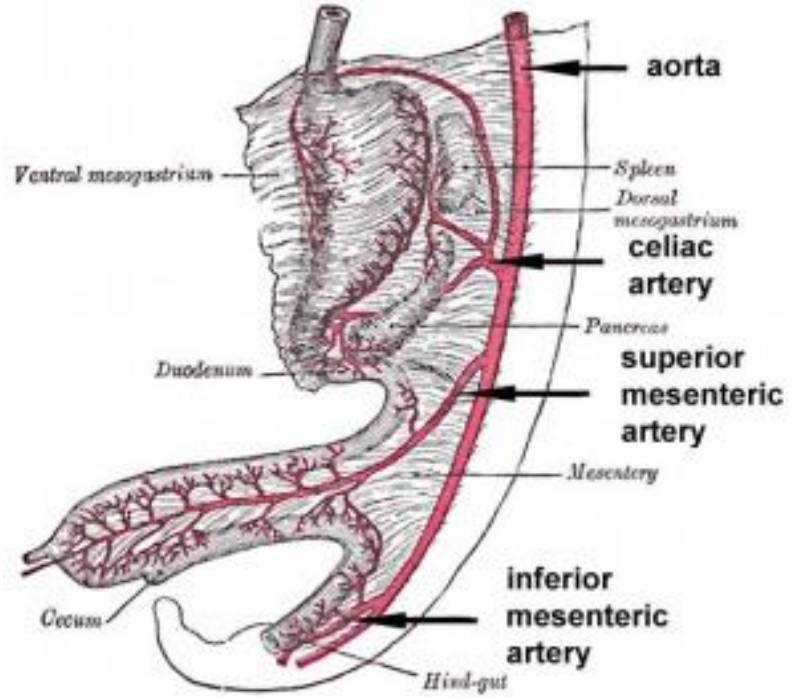


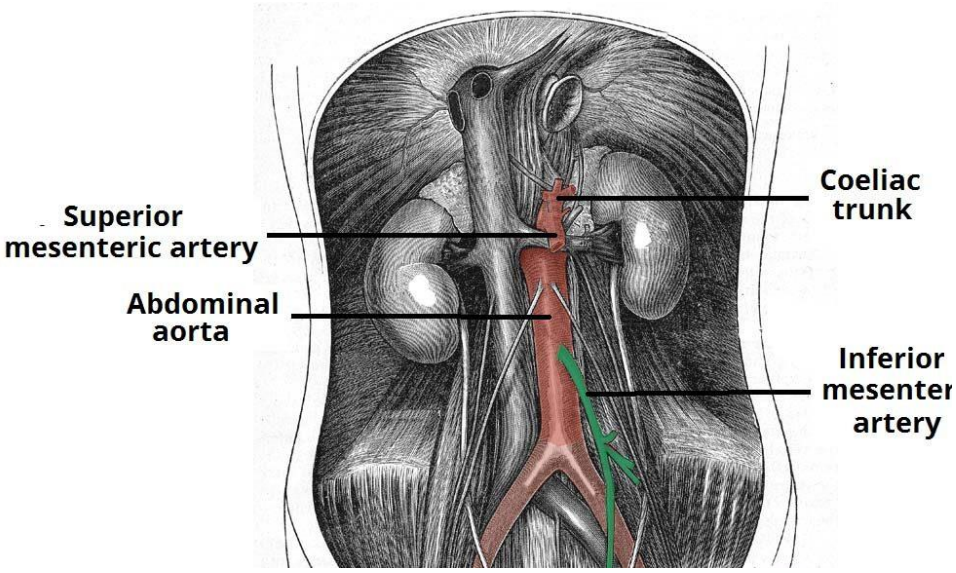
Intersegmental arteries



Vitelline arteries

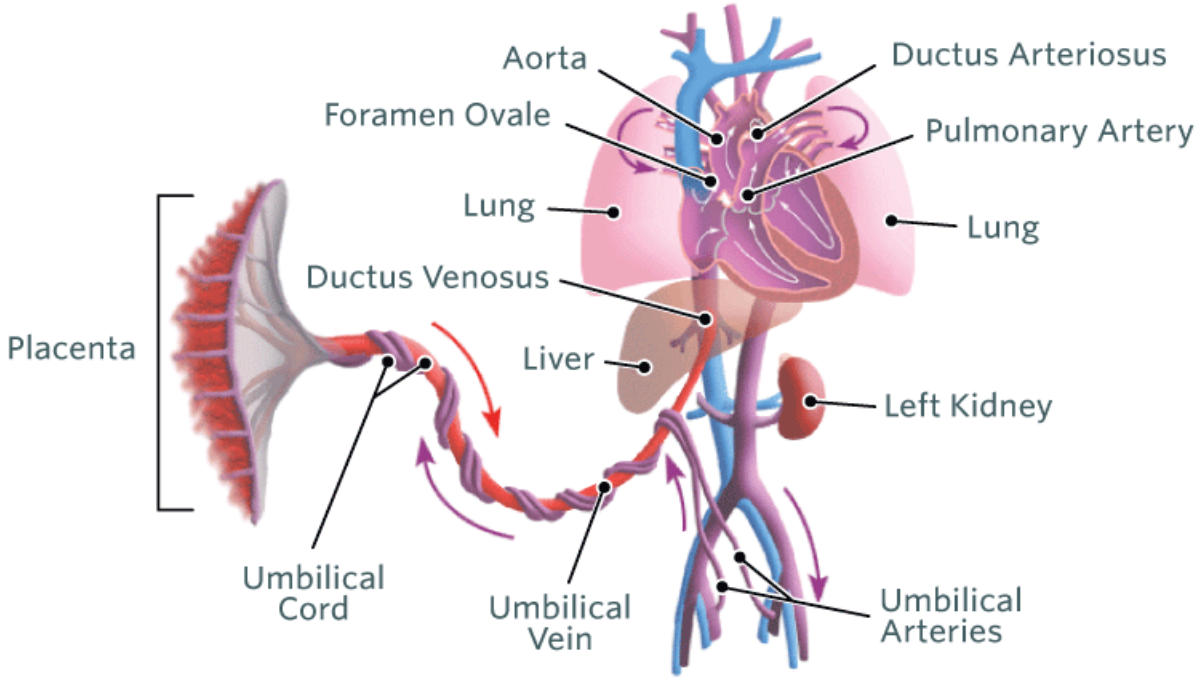
- ventral branches of dorsal aorta
- **aa. vitellinae** (aa. omphalomesentericae) reduced to three principal vessels:
  1. **truncus coeliacus**
  2. **a. mesenterica superior**
  3. **a. mesentrica inferior**



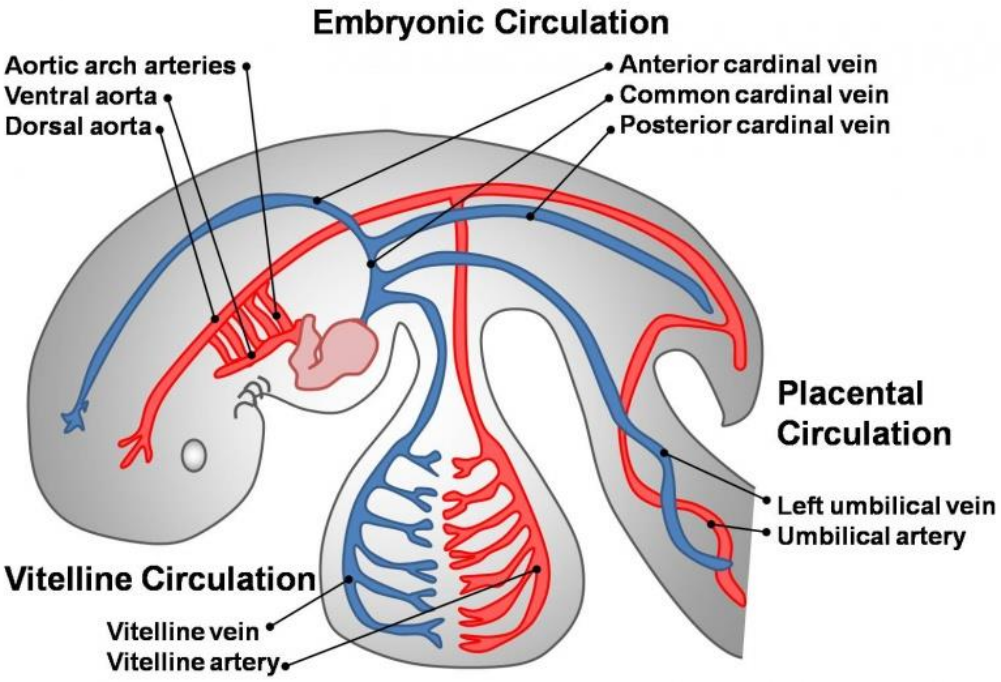


Umbilical arteries

- First, aa. umbilicales are ventral branches of dorsal aorta
- Later, aa. umbilicales are continuations to aa. iliacae communes and aa. communes internae.
- Abnormally, a single a. umbilicalis develop (can result in growth retardation of fetus)
- After birth: proximal parts of aa. umbilicales form aa. iliacae internae and aa. vesicales superiores. Distal parts obliterate.



Veins


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

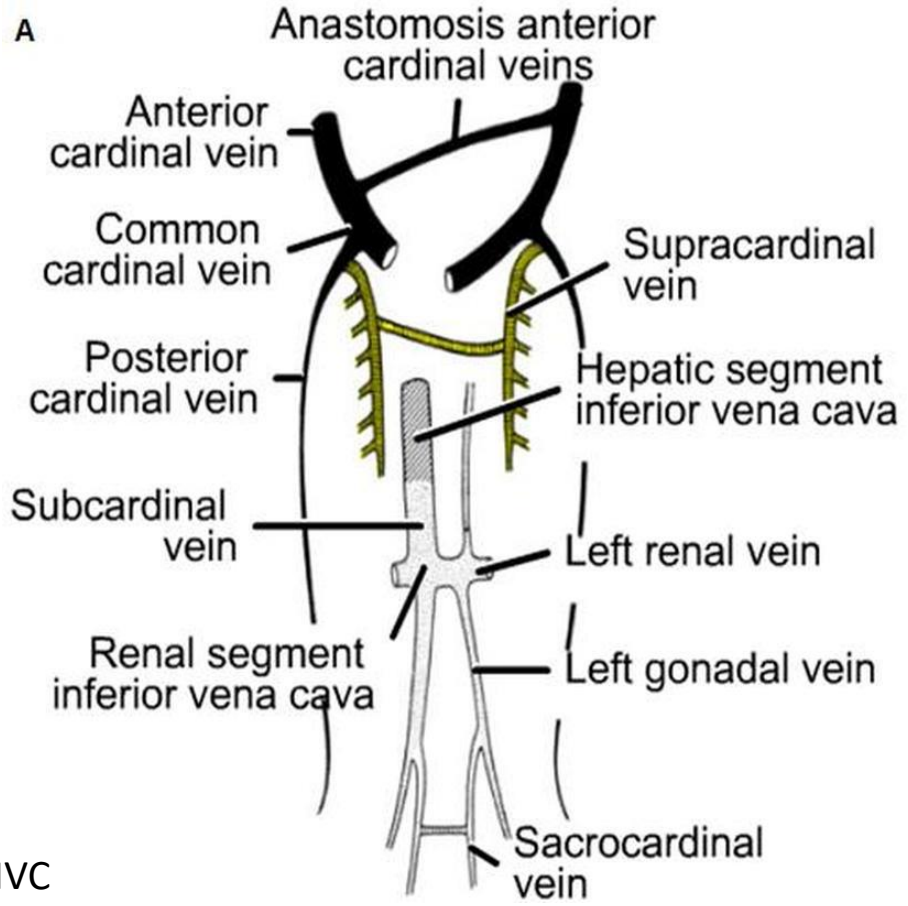
DEVELOPMENT OF VEINS

Cardinal veins

- main venous system of embryo
- **v. cardinales anteriores et posteriores**, → **v. cardinales communes**

- paired v. cardinales anteriores
- 8th week: anastomosis (L→R)
- → **v. brachiocephalica**
- caudal part of left v. card. ant. disappears
- right v. card. ant. + v. card. commun.: **SVC**

- paired v. cardinales posteriores
- primary vessels of mesonephros
- persists as branches of v. hemiazygos and v. azygos
- replaced by subcardinal and supracardinal veins



- paired **v. subcardinales**
- anastomoses also to v. cardinales posteriores
- left: v. renalis, v. suprarenales, gonad veins, part of IVC

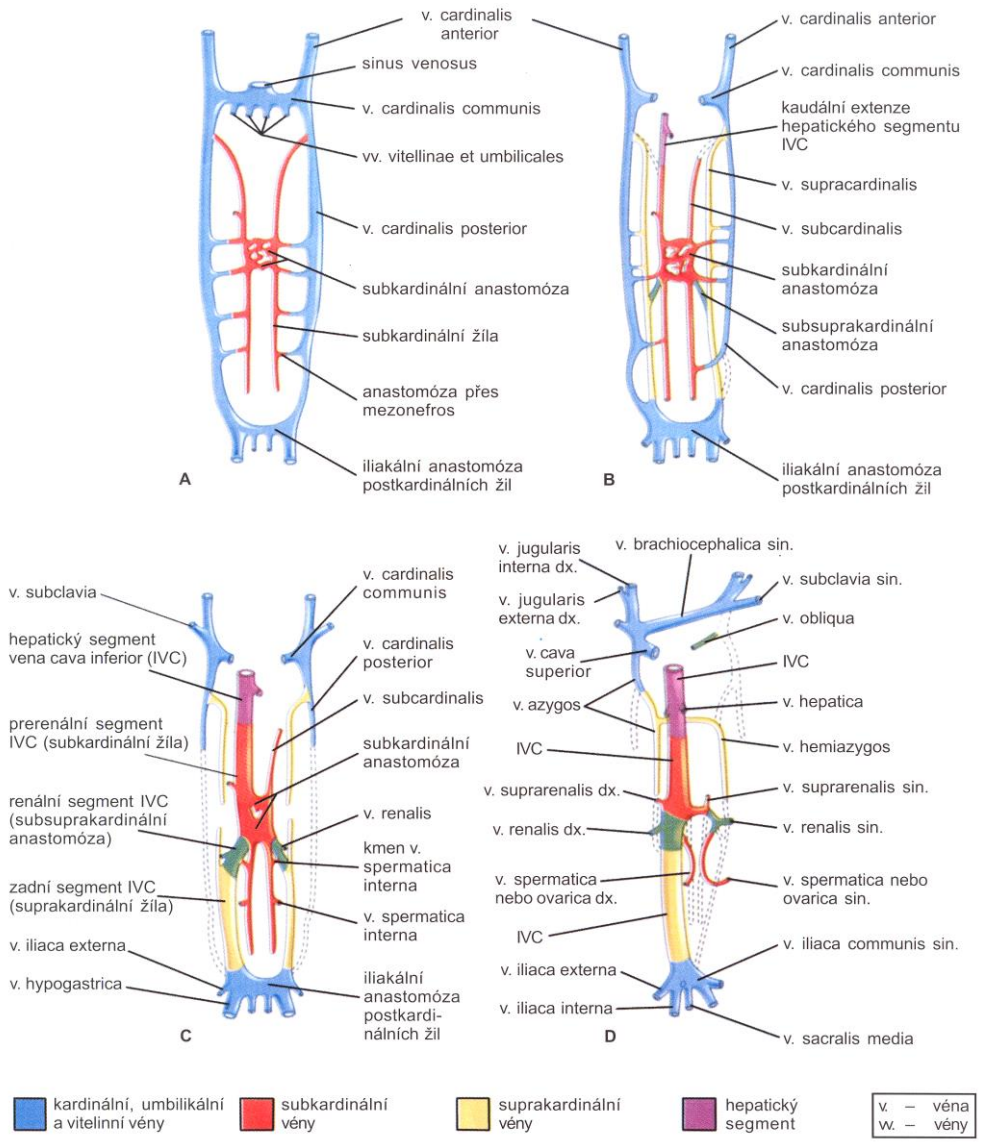
- paired **v. supracardinales**
- cranial – anastomosis – **v. azygos et v. hemiazygos**
- caudal left v. supracardinalis disappears, right – lower part of IVC (anastomosis to v. subcardinalis)

Cardinal veins and development of vena cava inferior

- four principal segments

1 **hepatic segment** (proximal part of v. omphalomesenterica = v. hepatica)
2 **prerenal segment** (right v. subcardinalis)
3 **renal segment** (anastomosis between v. subcardinalis and v. supracardinalis
4 **postrenal segment** (right v. supracardinalis)

Vena cava superior: right v. cardinalis communis and v. cardinalis anterior



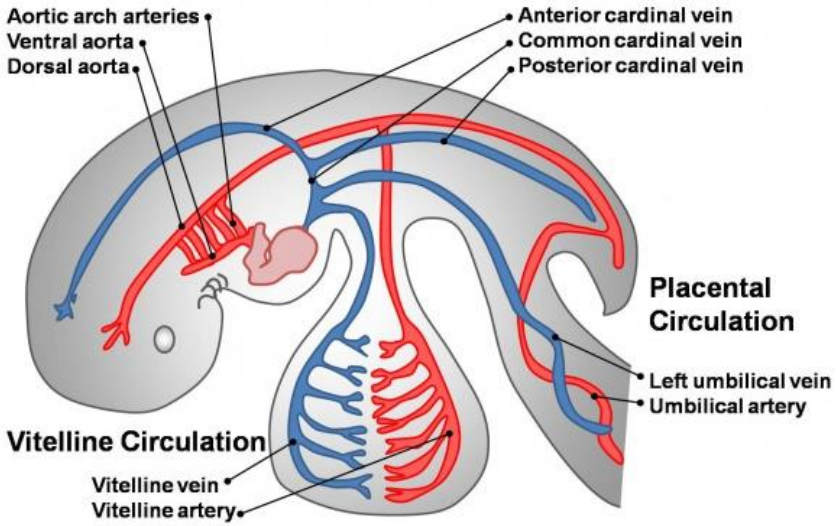
DEVELOPMENT OF VEINS

Vv. omphalomesentericae

- bring blood from yolk sac
- septum transversum
- sinus venosus (together with umbilical veins as trunci vitelloumbilicales)
- growth of liver – separation of omphalomesenteric veins to proximal (yolk sac-liver) and distal parts (liver-heart)
- distal parts form anastomoses and develop into v. portae
- proximal parts form posthepatic part of IVC

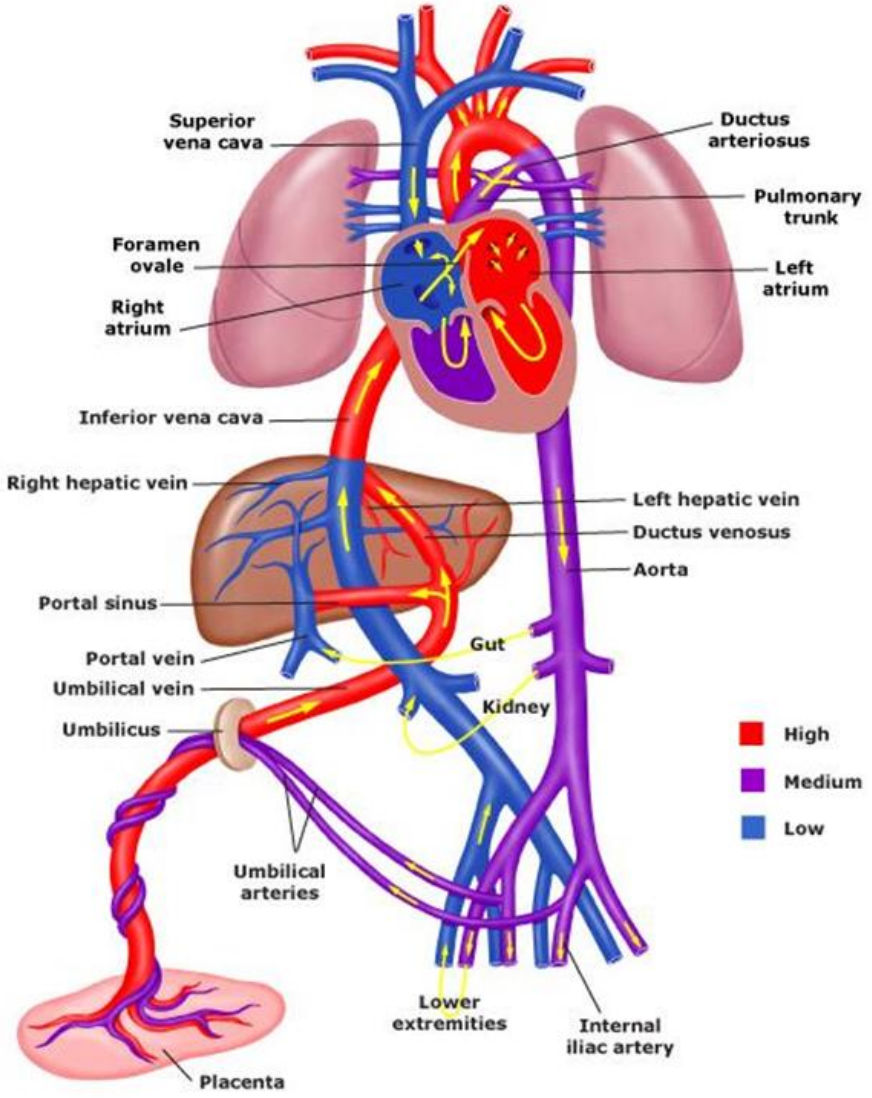
Vv. umbilicales

- begin in chorionic villi
- due to liver growth lose connection with sinus venosus
- right v. umbilicalis disappears
- distal part of left v. umbilicalis forms ductus venosus (ligamentum venosum post natally)

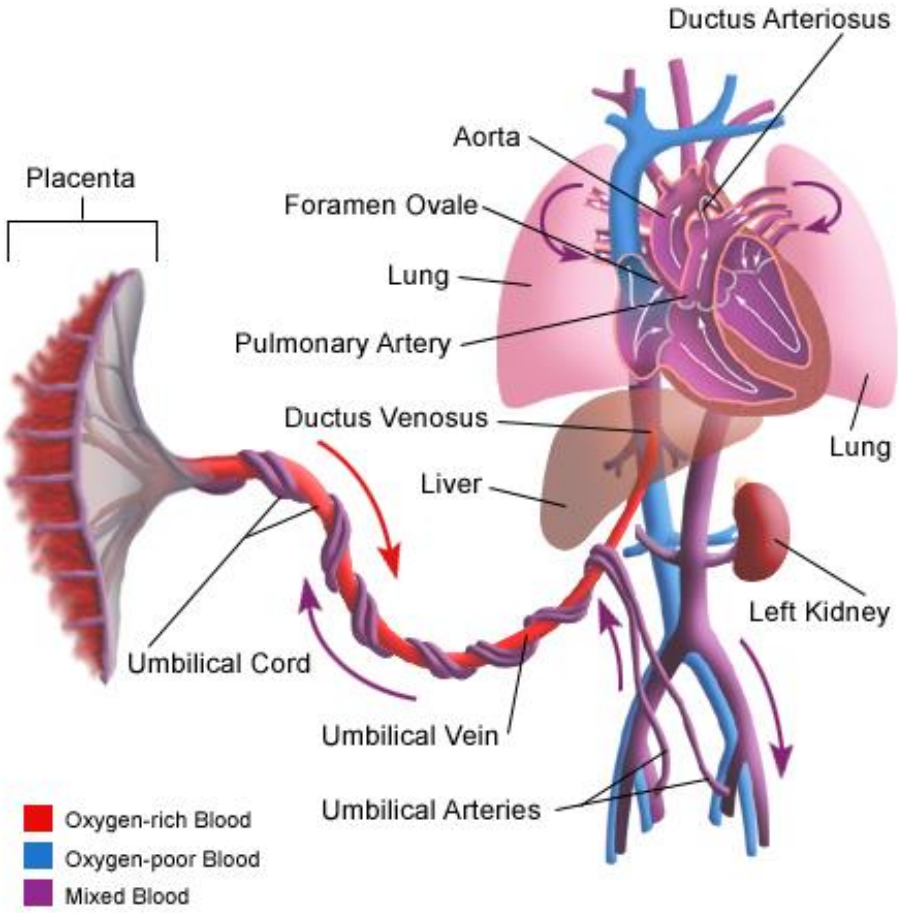


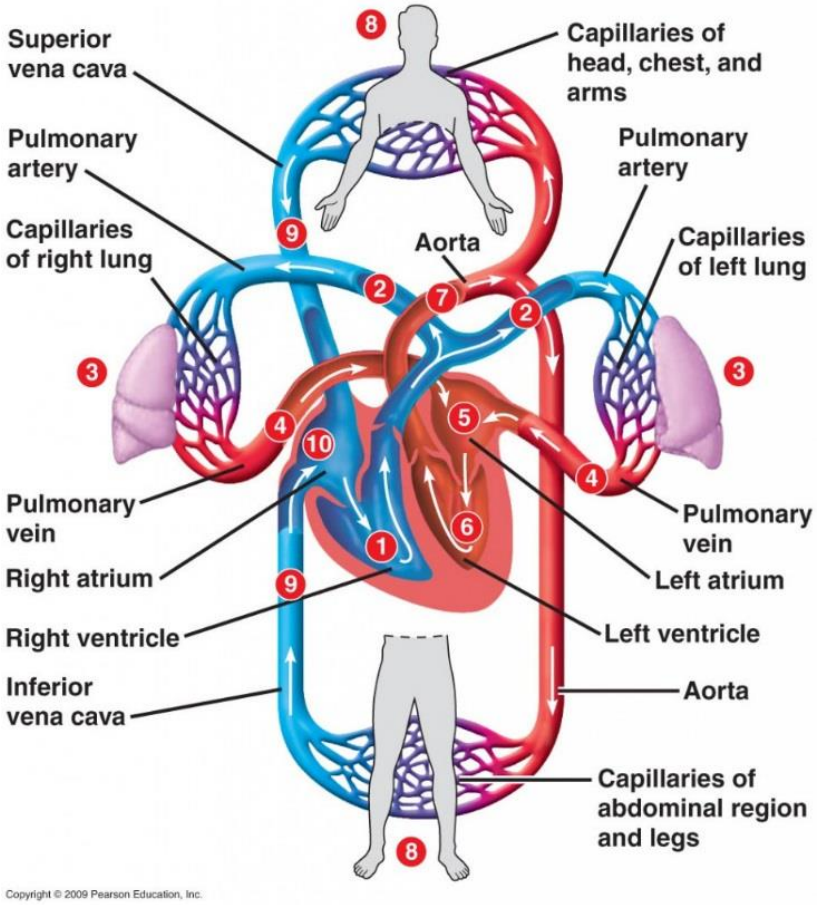
Embryonic circulation

Fetal circulation



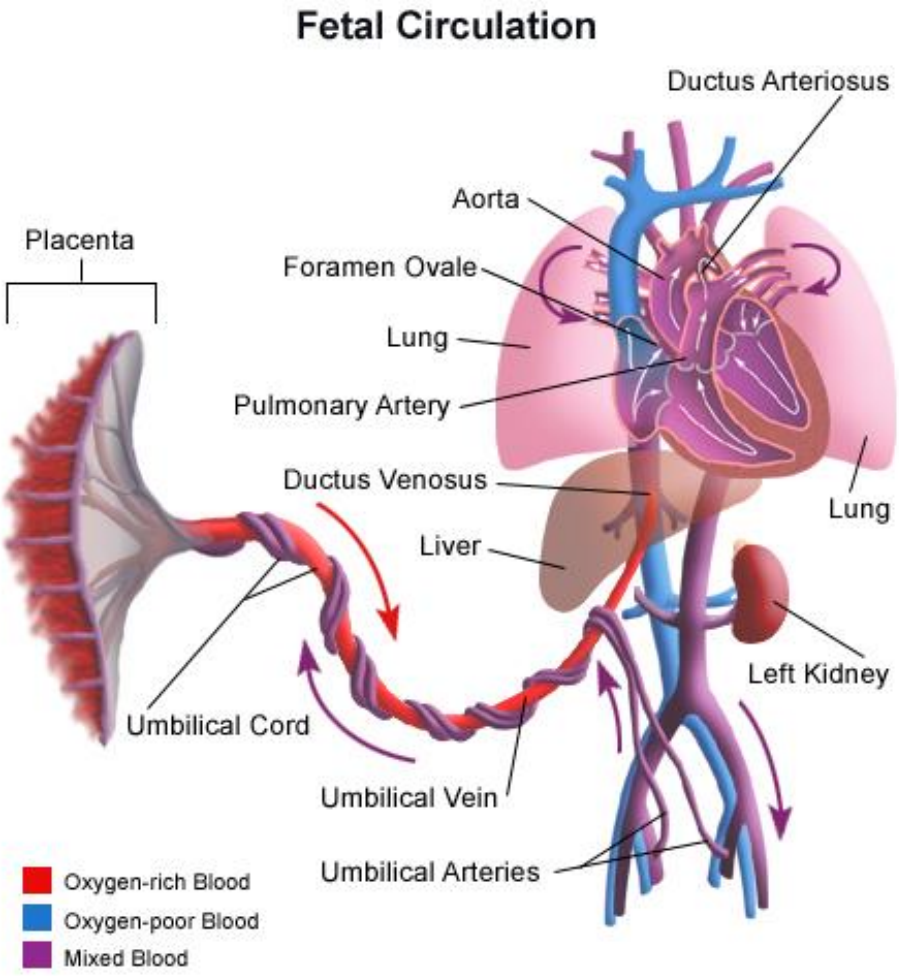
Fetal circulation





Postnatal circulation

Derivatives of fetal vascular structures



Umbilical vein → ligamentum teres
From umbilicus to porta hepatis and left v. portae
Lumen of l. teres might persist

Ductus venosus → ligamentum venosum
(through liver from left v. portae to IVC)

Umbilical arteries → ligamenta umbilicalia medialia (most of intrabdominal part) and **arterie vesicales superiores**

Foramen ovale → fossa ovalis
Adhesion of septum primum (valvula foraminis ovalis) to left part of septum secundum
Bottom of fossa ovalis – septum primum
Lower part of septum secundum – limbus fossae ovalis (anulus ovalis)

Ductus arteriosus → ligamentum arteriosum
(from left pulmonary artery to arcus aortae

Thank you for attention