Where to Get More Information

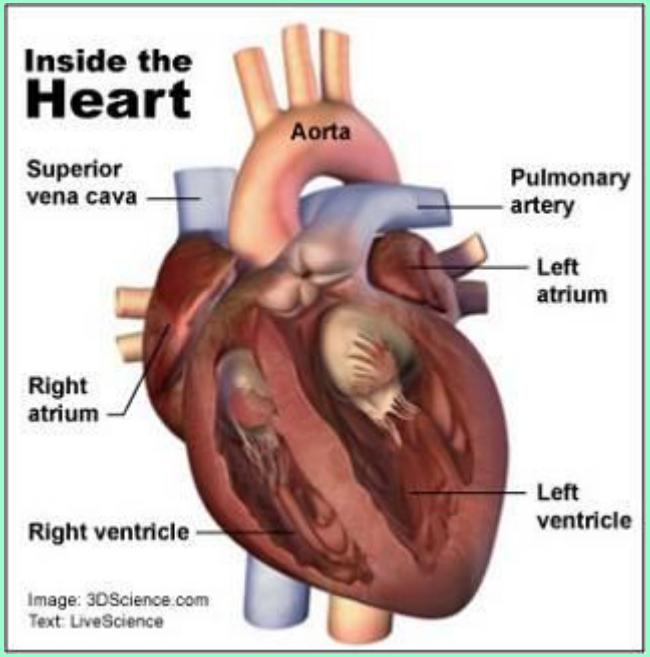
T.W.Sadler : **Langman´s Medical Embryology**

8th edition, Lippincott, Williams, Wilkins, pp.:208-259

K.L.Moore, T.V.N.Persaud : **Before we are born**

6th edition, Saunders, pp.:264-304

Heart (*Cor*)



Histologia

Systema conducens cordis

Embryologia

David Kachlík

Heart wall structure

- *endocardium* (corresponds to *tunica intima*)
  - endothelium
  - subendothelial layer (loose connective tissue with muscle cells, elastic and collagen fibers)
  - subendocardial layer (connective tissue, vessels, conducting system)
- *myocardium* (cardiomyocytes)
- *epicardium* (*mesothelium* + thin connective tissue layer)
  - subepicardial layer with adipose tissue, vessels, nerves and autonomic ganglia
- *pericardium (serous)*
- heart skeleton (dense connective tissue)

Atrial cardiomyocytes

- mechanoreceptors
- ANF production = granule of atrial natriuretic factor
- more GER and larger GA

- Function: diuresis stimulation, antagonist of ADH and angiotensin II
- prevention of water and Na resorption – protects from hypervolemia

Conducting system of heart
Complexus stimulans cordis
Systema conducens cordis; Excitomotor apparatus

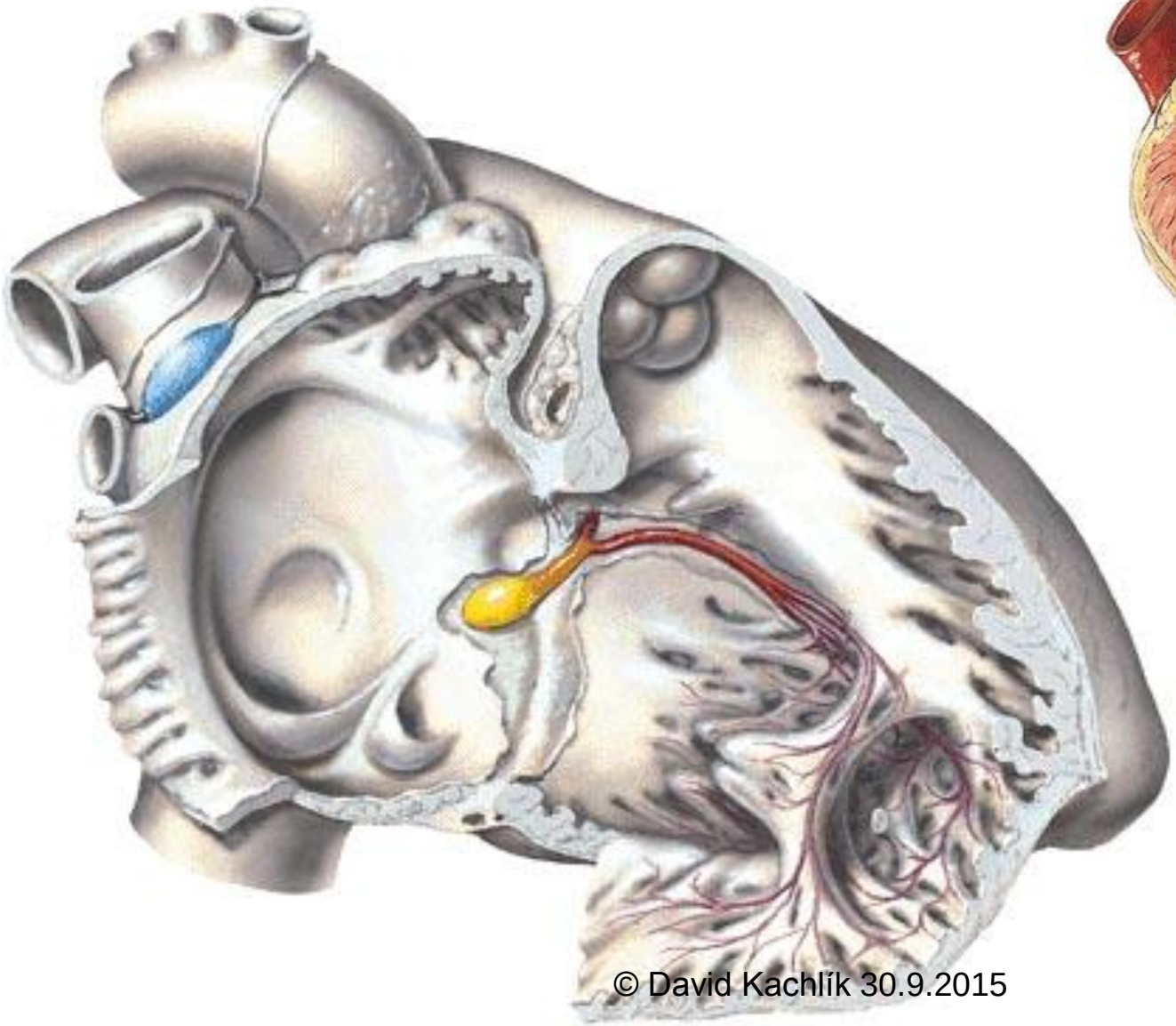
- co-ordination of cardiac activity
- enables generation of heart automatic impulse
- formed with modified cardiomyocytes:
  - less myofibrils placed in periphery
  - no intercalar discs
  - connections by desmosomes and nexuses
  - different size
  - glycogen gathered aroud the nucleus

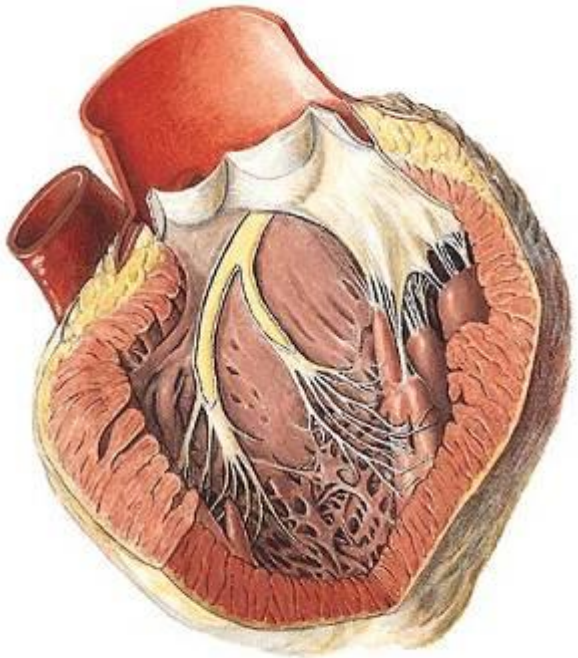
Conducting system of heart
individual parts

- myocytes lesser than those of working myocardium
- rich blood supply
- **nodus sinuatrialis** /*Keith-Flack*/
  - right atrium close to foramen v. cavae superioris
- **interatrial connections (fasciculi atriales)**
  - fasciculus interatrialis (*Bachmanni*)
  - toher fascicles dubious
    - anterior *(James)*, medius *(Wenckebach)*, posterior *(Thorel)*
- **nodus atrioventricularis** (*Aschoff-Tawara*)
  - Koch´s triangle in right atrium

Conducting System of Heart

Right Side



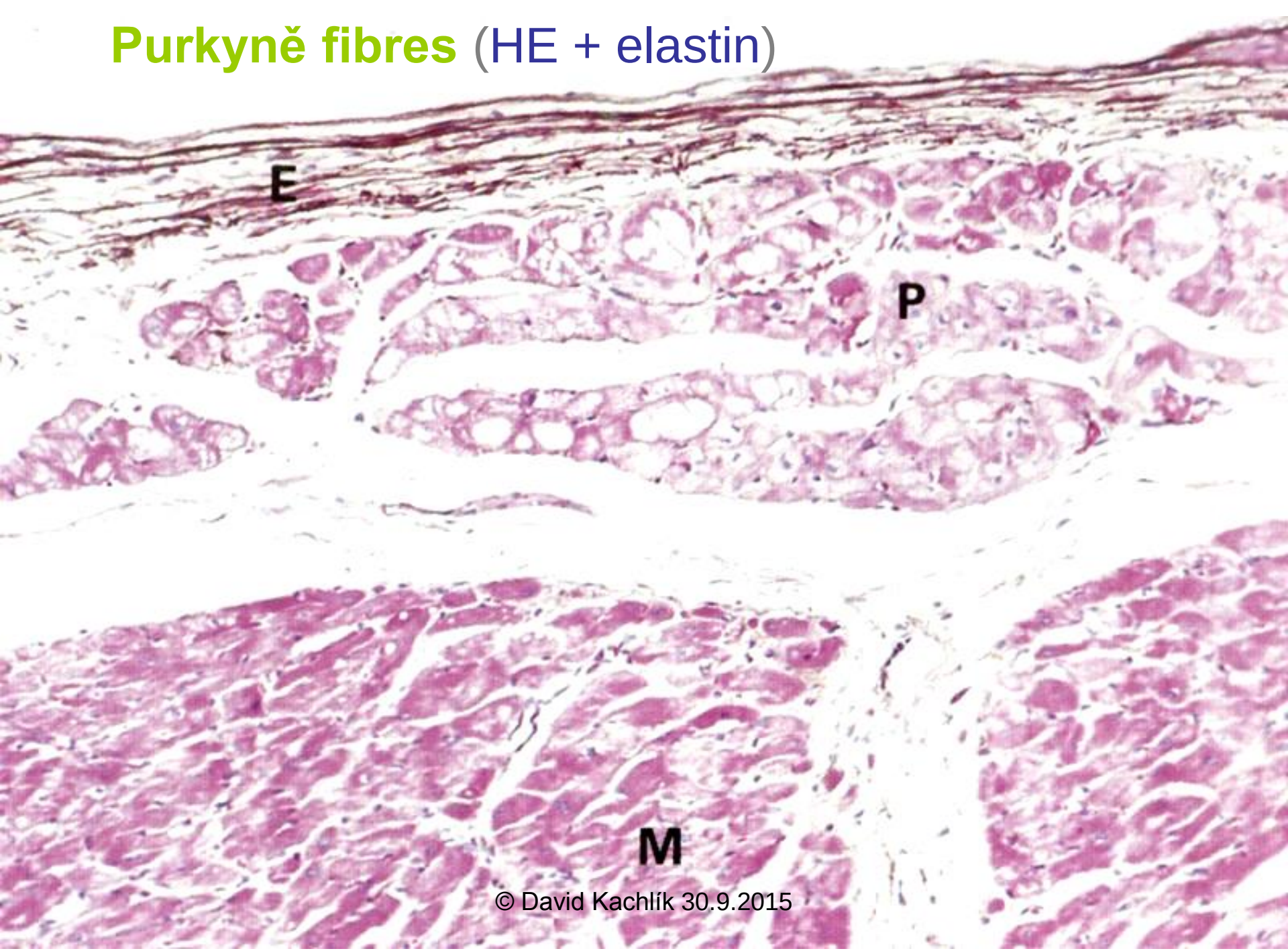


Conducting system of heart

- **fasciculus atrioventricularis** (*His-Kent-Gaskell*)
  = *atrioventricular bundle*
  – *AV blockage of 1st-3rd grade*
  – truncus f.a.
  – crus f.a. (*Tawara) = Tawara´s bundle*
    - dextrum
    - sinistrum
      – limbus anterior
      – limbus posterior
- **rami subendocardiales** */Purkyně/*
  – larger than typical cardiomyocytes
  – with lighter cytoplasma, ↑ glycogene, positive in acetylcholinesterase
  – quick impulse conduction towards heart apex
- ***accessory atrioventricular pathways***

  → *preexcitation syndrome WPW (Wolff-Parkinson-White)*

Purkyně fibres (HE + elastin)



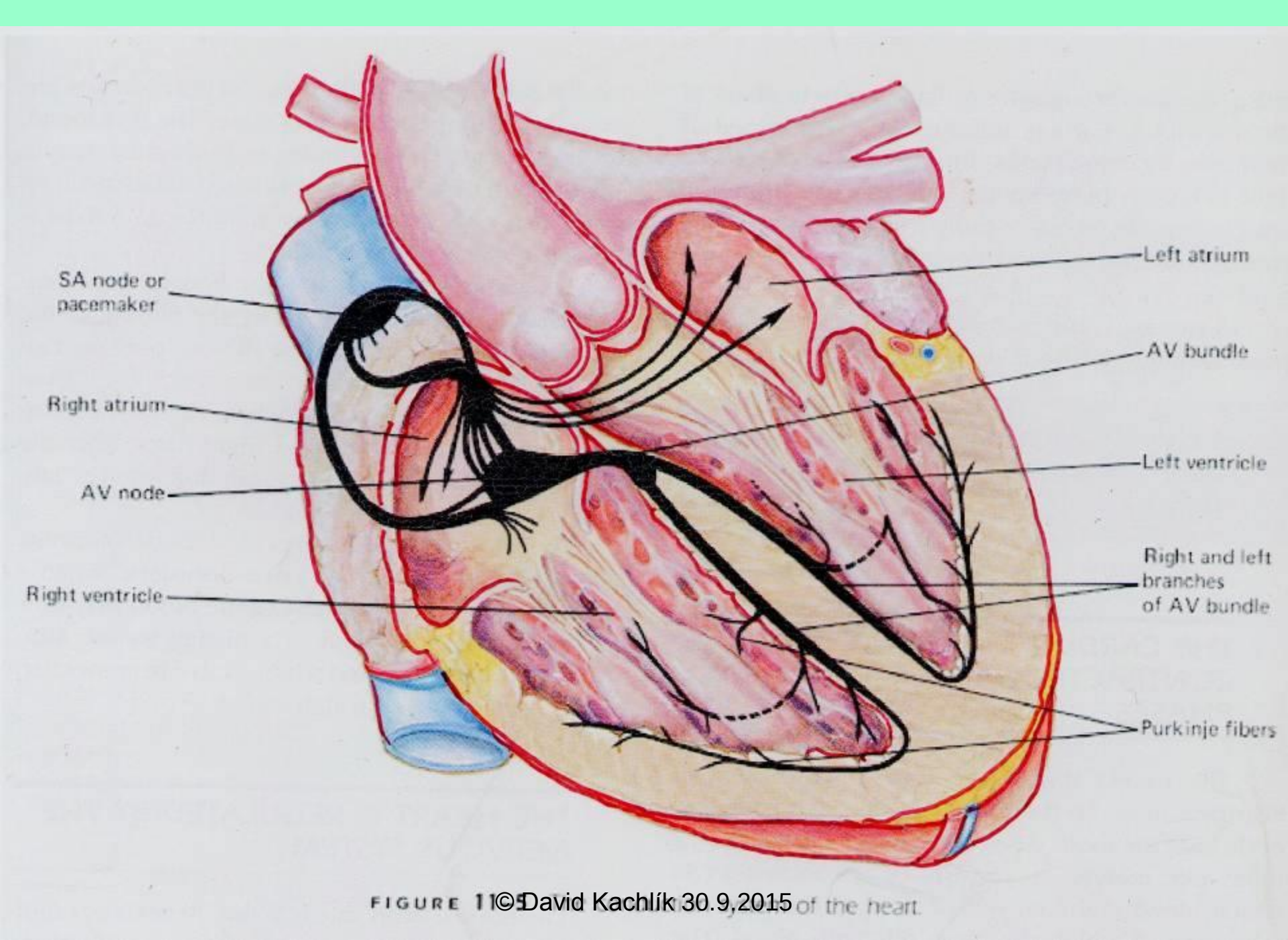
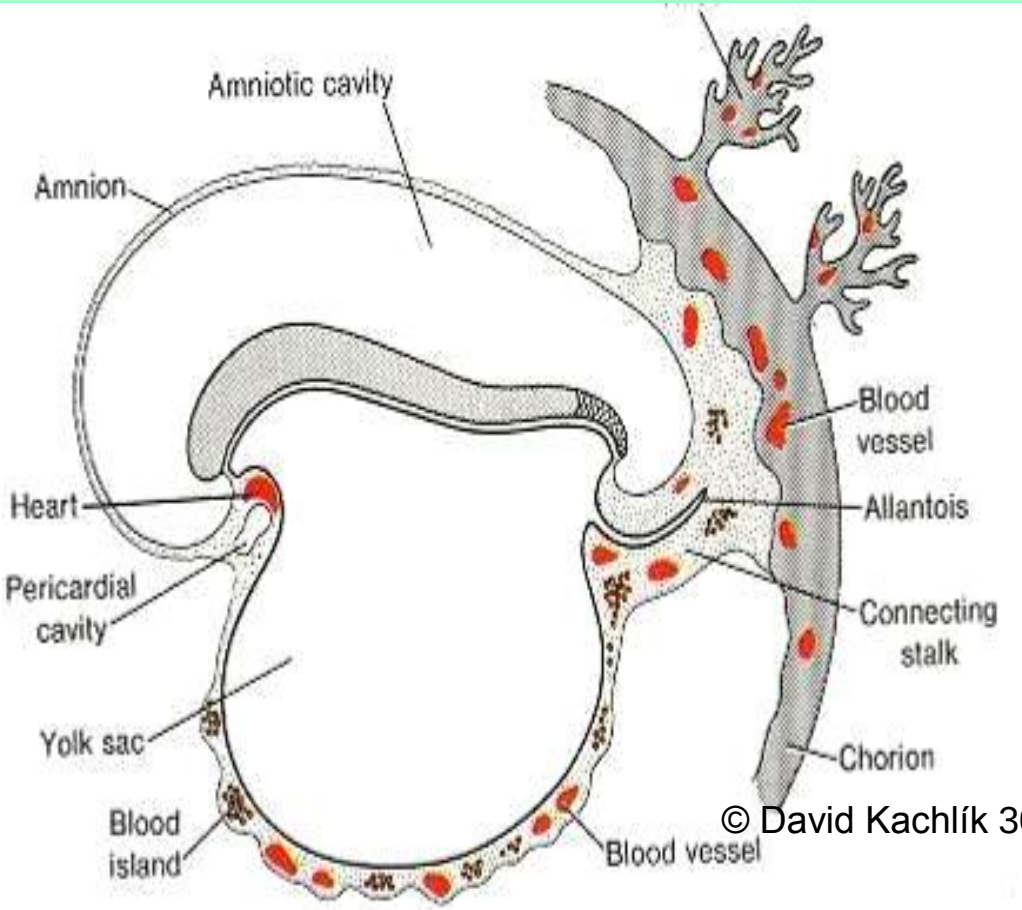
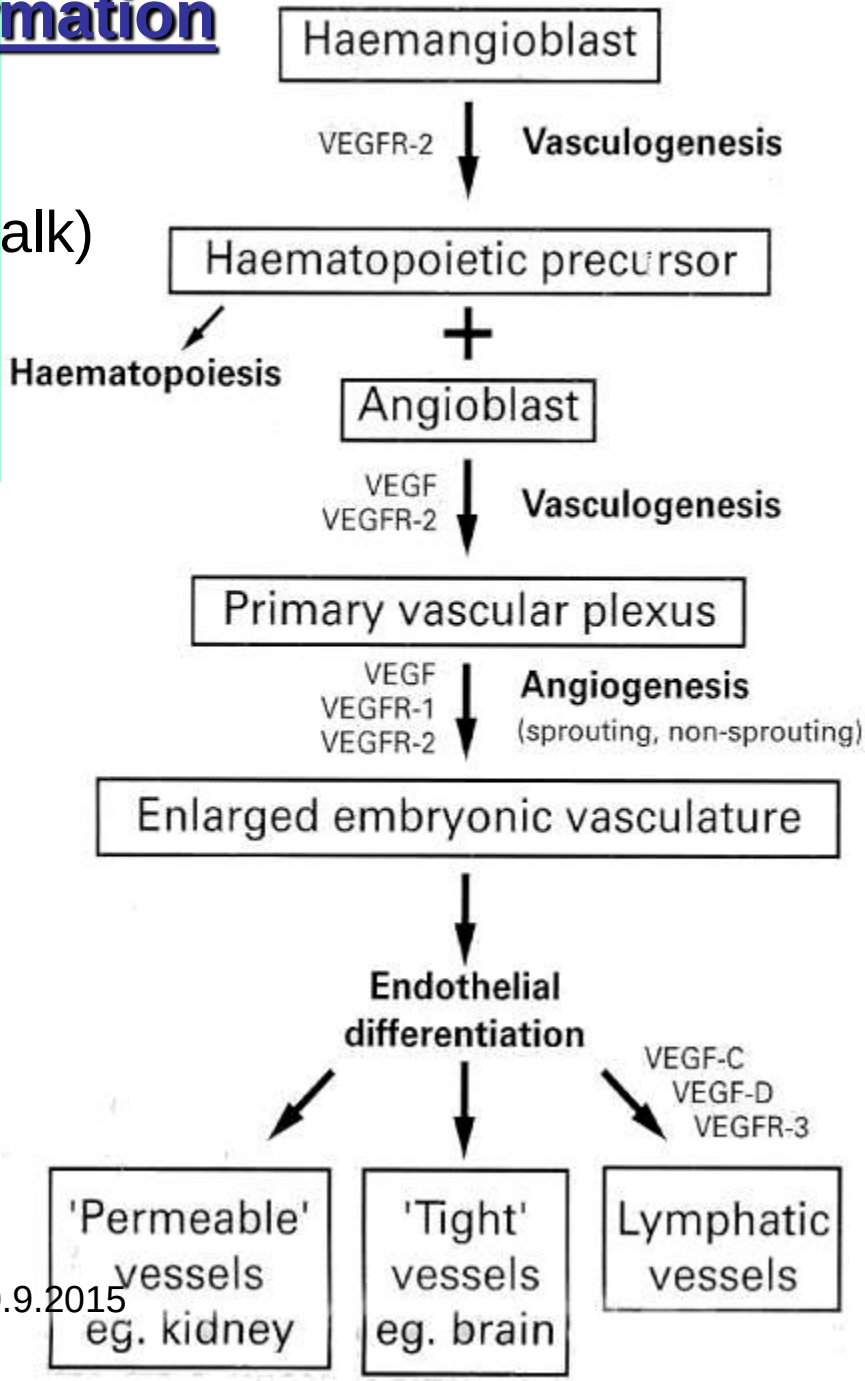


FIGURE 11-5 ... of the heart.

Extraembryonic blood vessel formation

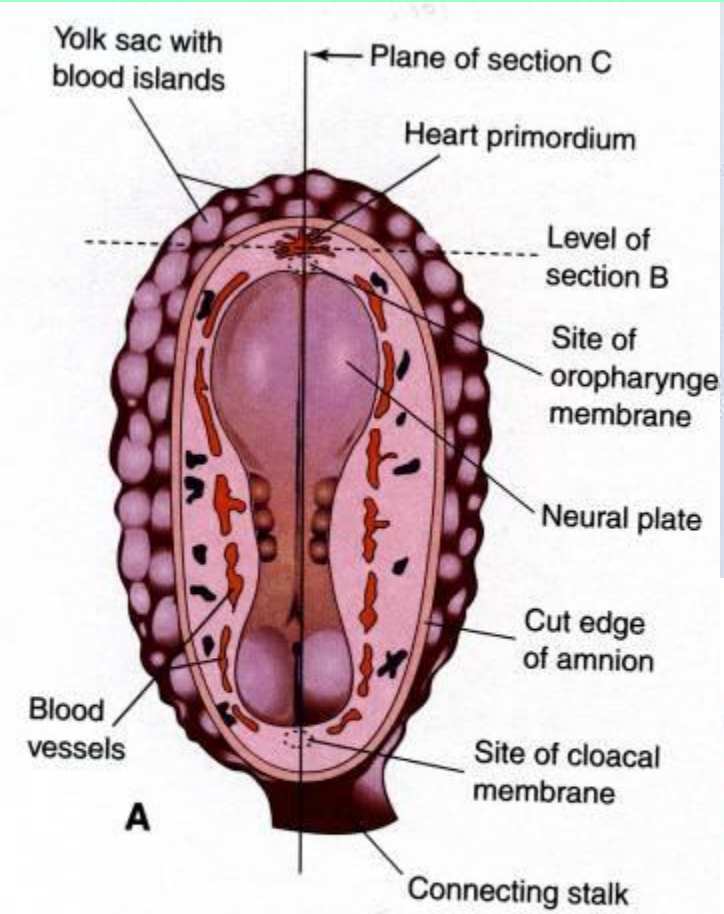
- villi chorionici
- chorion
- pedunculus connectans (connecting stalk)
- wall of the yolk sac
- presomite embryo

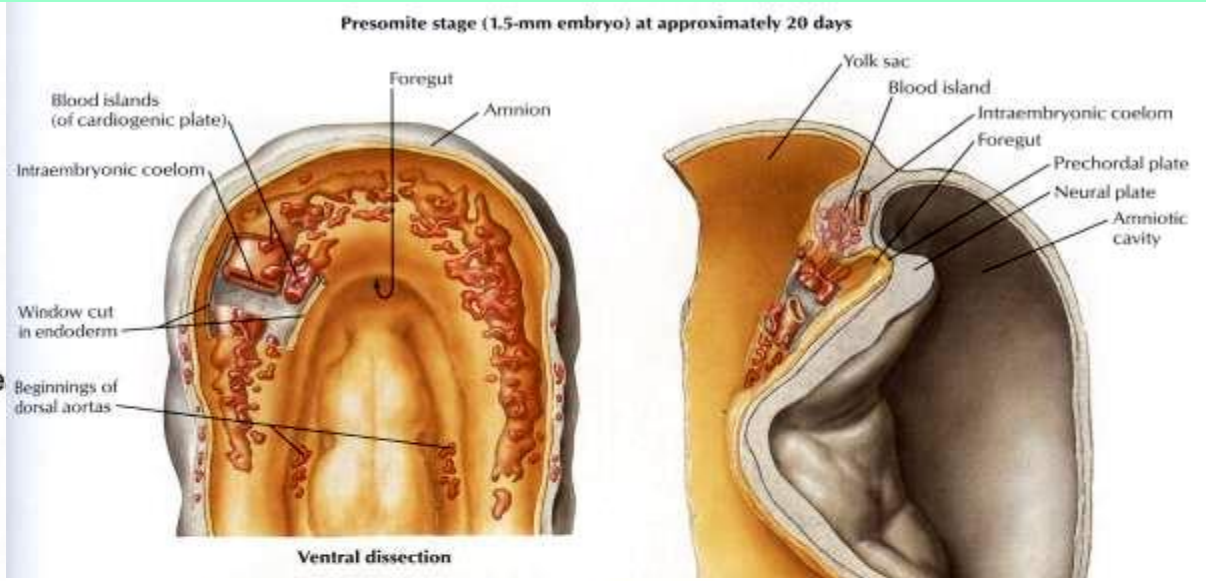




Vasculogenesis

- angioblasts are determined before gastrulation
- angioblasts develop from the blood islands





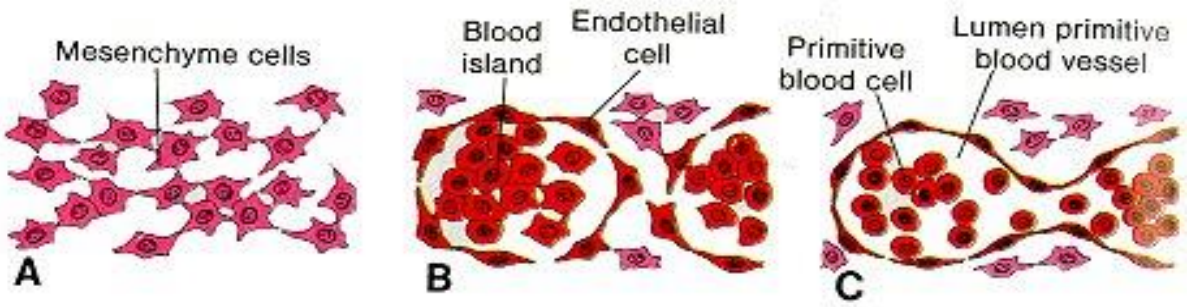
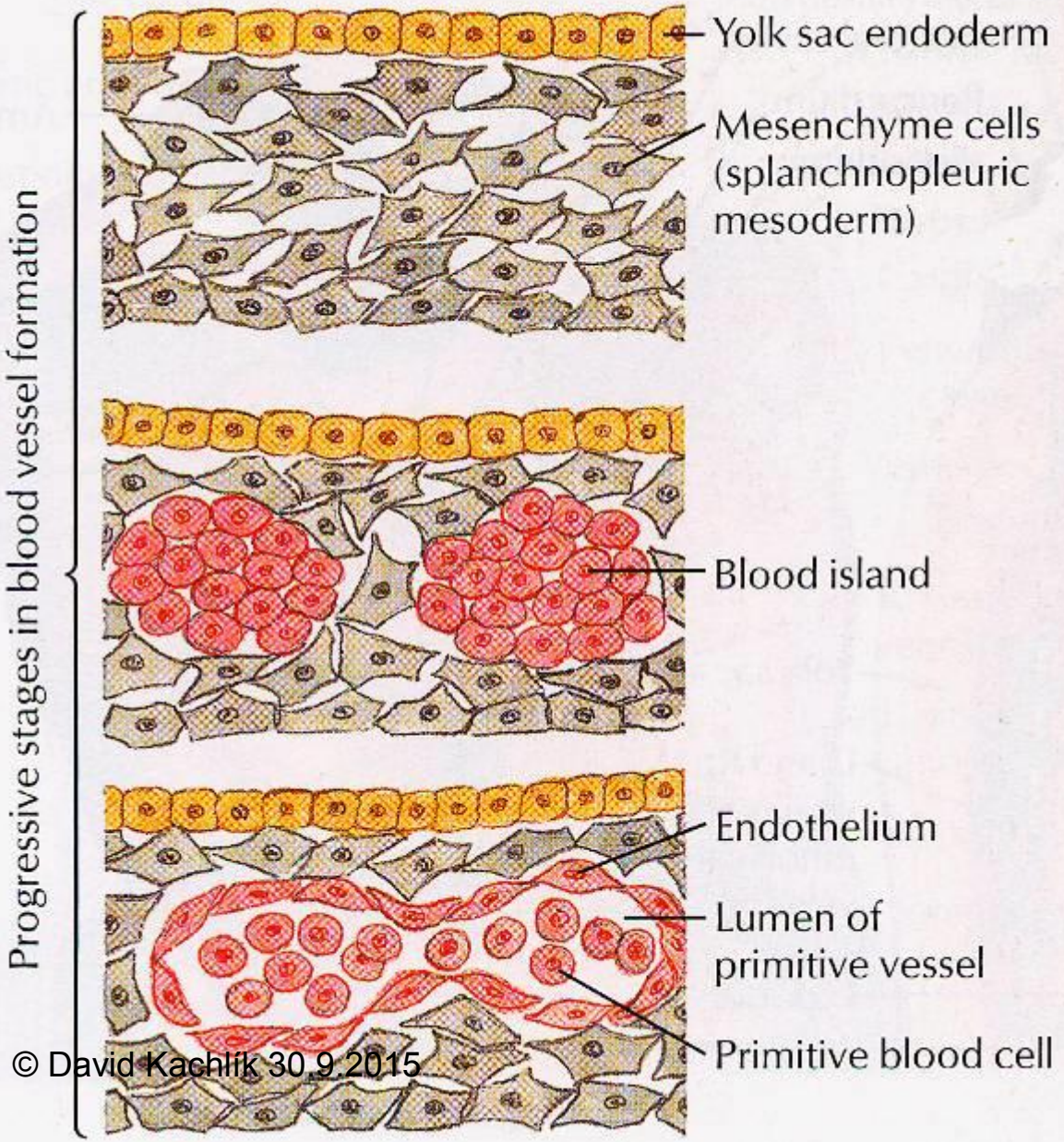


Figure 5-12. Successive stages of blood vessel formation. **A**, Undifferentiated mesenchymal cells. **B**, Blood island formation. **C**, Primitive capillary. Note the differentiation of mesenchymal cells into the primitive blood cells and the endothelial cells.

Vasculogenesis

- blood islands
- mesoderm
- FGF2 + VEGF

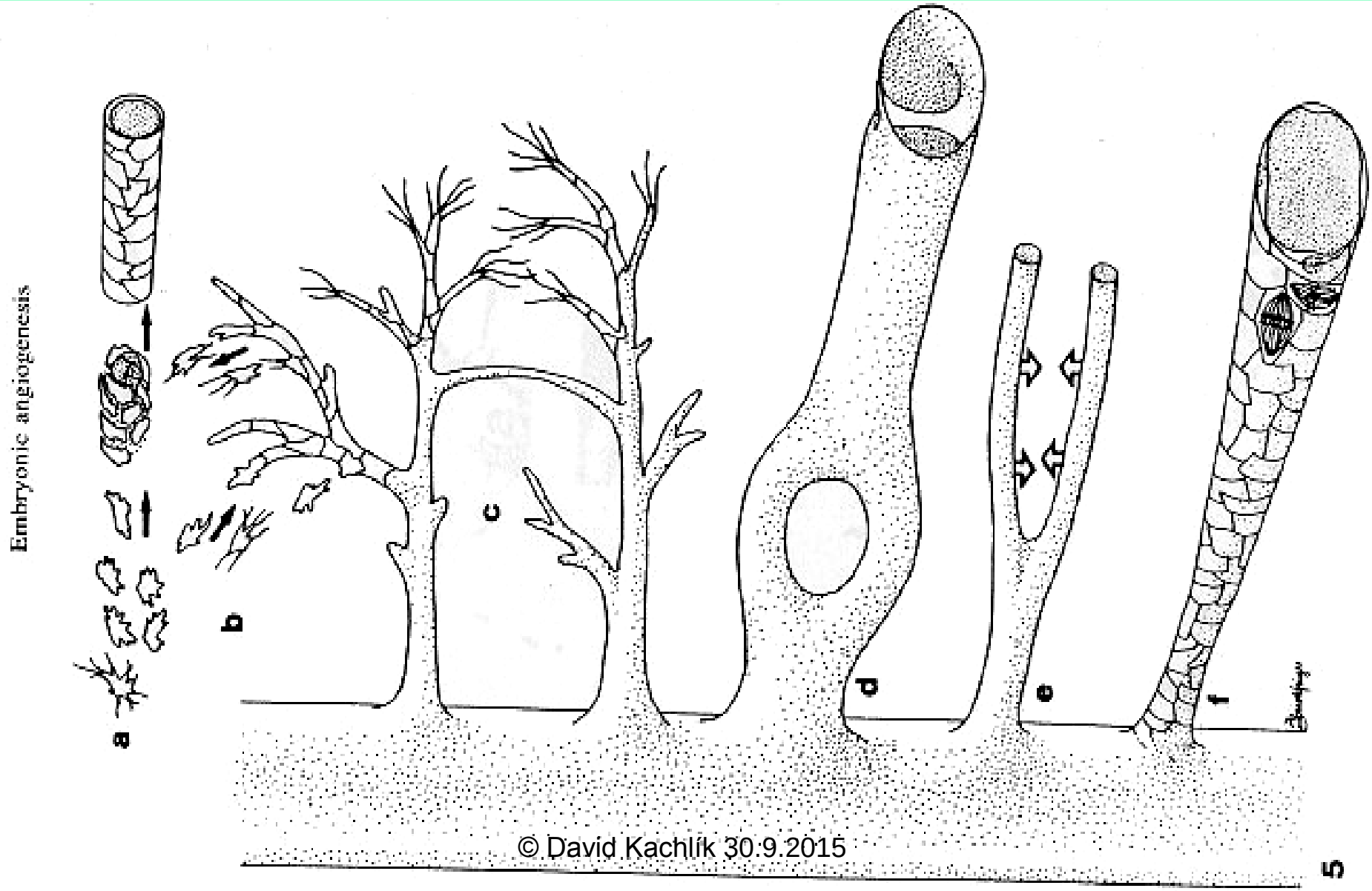
induce differentiation to hemangioblasts (hematopoetic stem cells) and angioblasts (endothelium)



Angiogenesis

- primary vascular bed is established by vasculogenesis
- existing vessels sprout up = angiogenesis (mediated by VEGF)
- first blood islands appear within extraembryonal mesoderm in the wall of yolk sac (**3rd week**) of development
- later in intraembryonal mesoderm in other regions

Angiogenesis



Haematopoesis

- first generation – blood islands of extaembryonal mesoderm - transitory
- second generation of stem cells arises from intraembryonic mesoderm – aorta-gonad-mesonephros region. Stem cells colonize liver and spleen: hepato-splenic period
- later, stem cells colonize bone marrow – definitive blood forming tissue

Heart development - Early stages

source layer: **intraembryonal mesoderm**

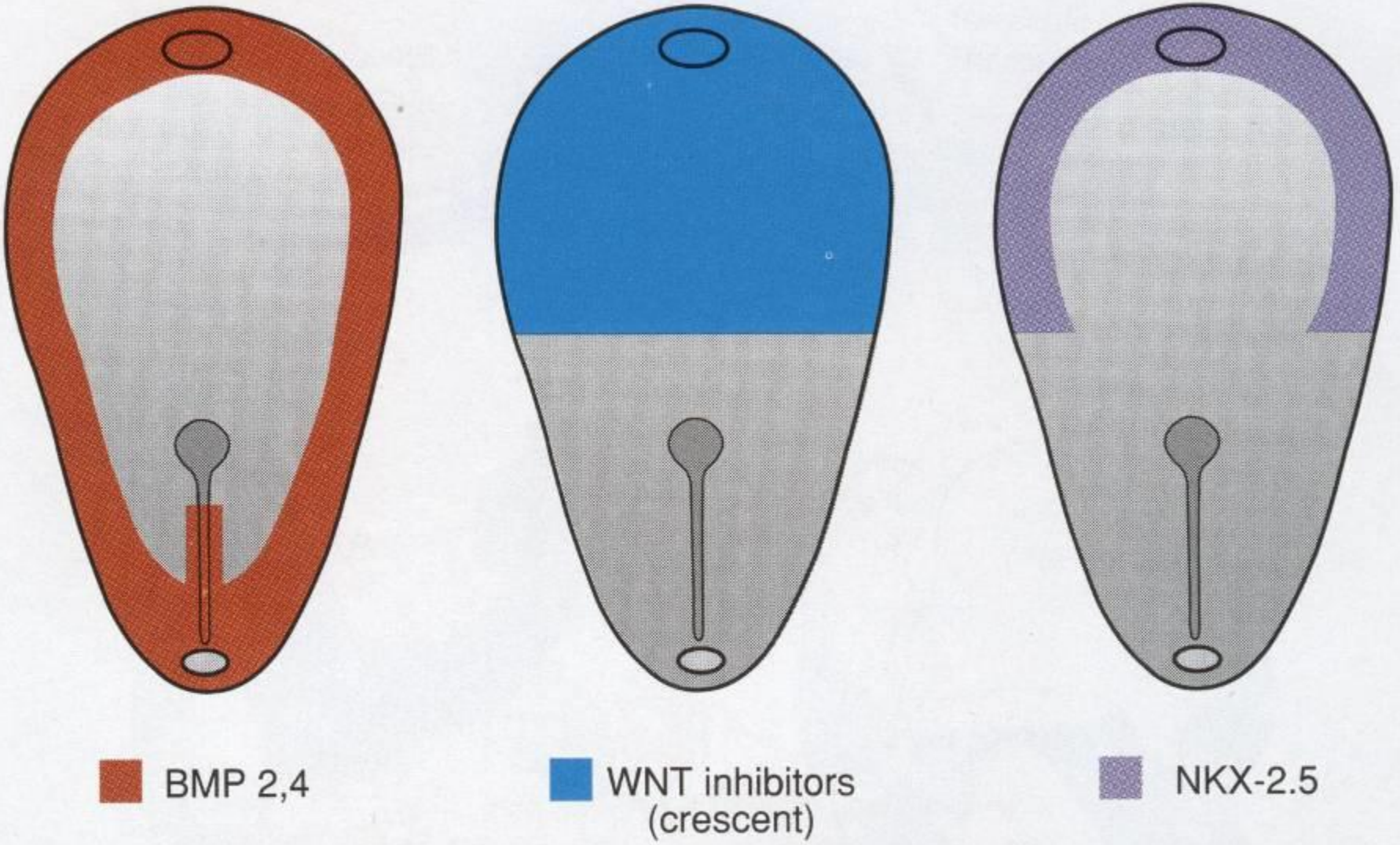
- angioblastic cords

→ form lumen

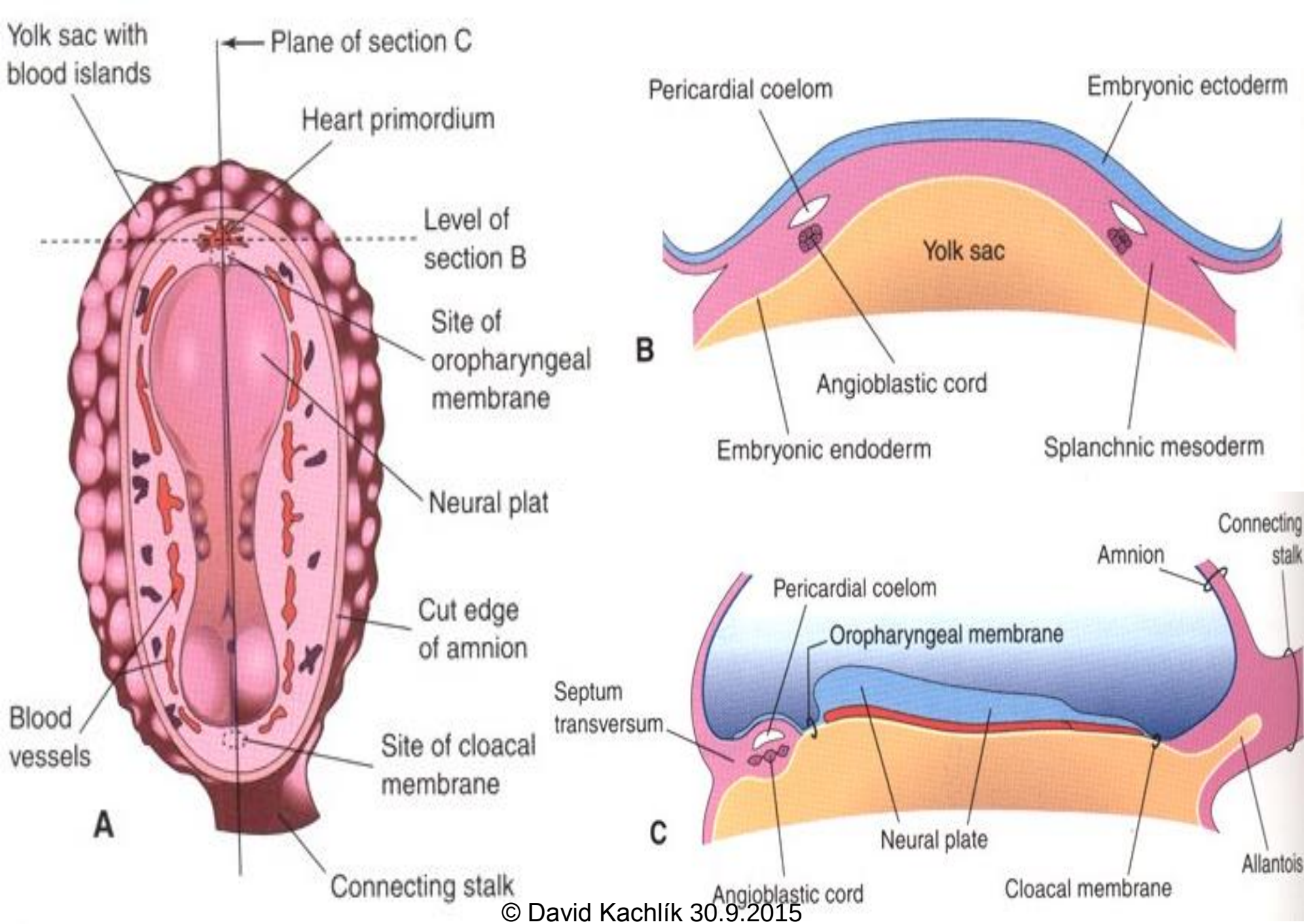
- endocardial heart tubes

→ fuse to form tubular heart

- heart begins to beat on **22nd or 23rd day**
- **cardiogenic area (*lamina cardiogenica*)**
  - in mesoderm in front of oropharyngeal membrane and future brain
- folding of embryo
  - pericardial cavity and heart move to cervical region and later to thorax



Heart induction. BMPs secreted in the posterior portion of the primitive streak and periphery of the embryo, in combination with inhibition of *WNT* expression by *crescent* in the anterior half of the embryo, induce expression of *NKX2.5* in the heart forming region of the lateral plate mesoderm (splanchnic layer). *NKX2.5* is then responsible for heart induction.

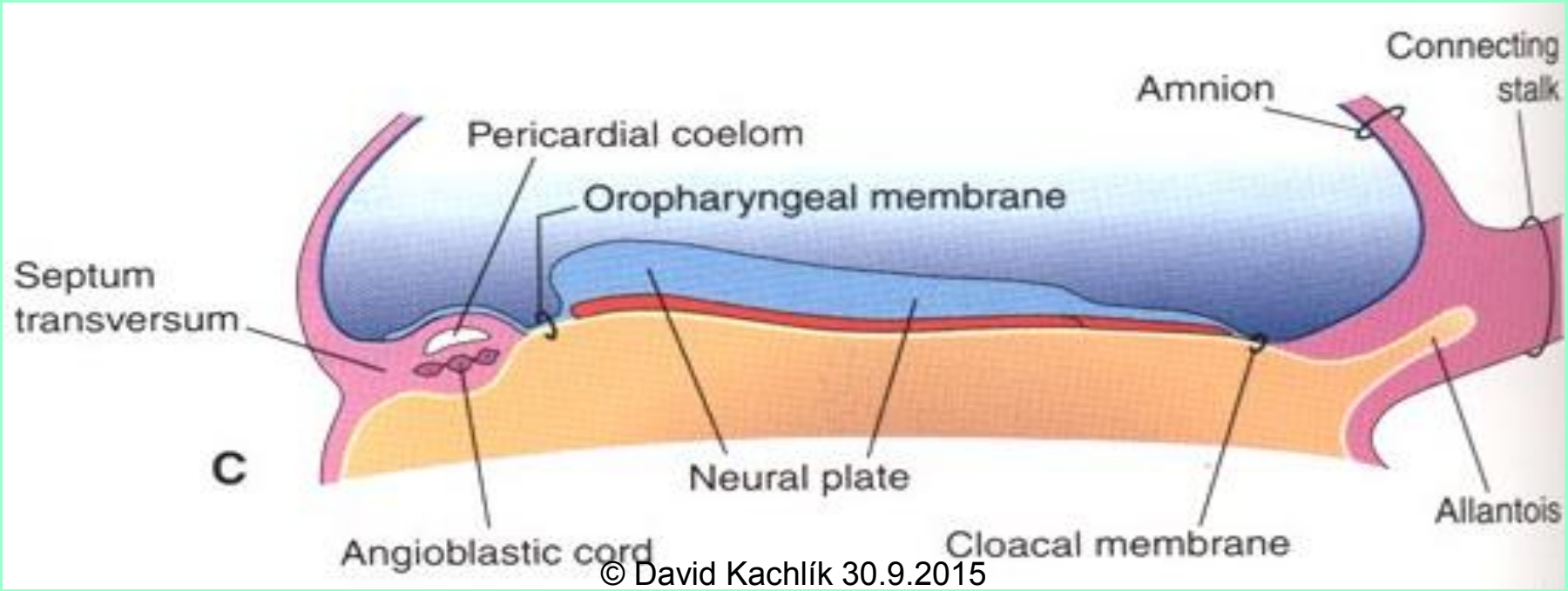


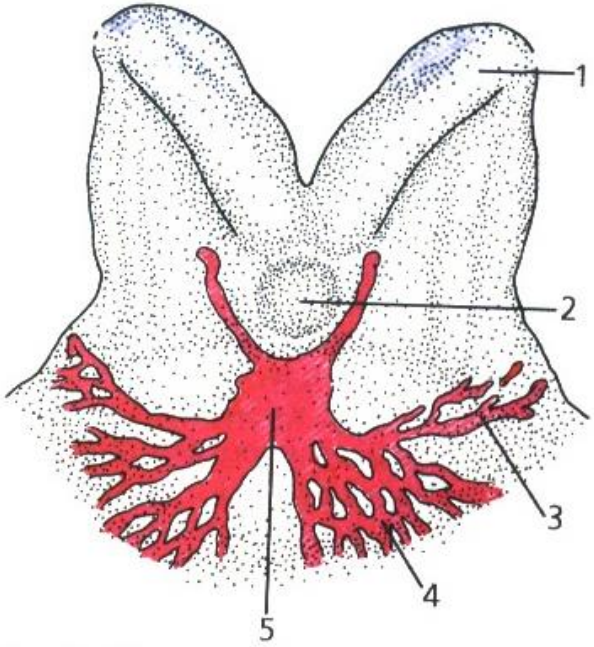
Folding of head region

heart and pericardial cavity come to lie:

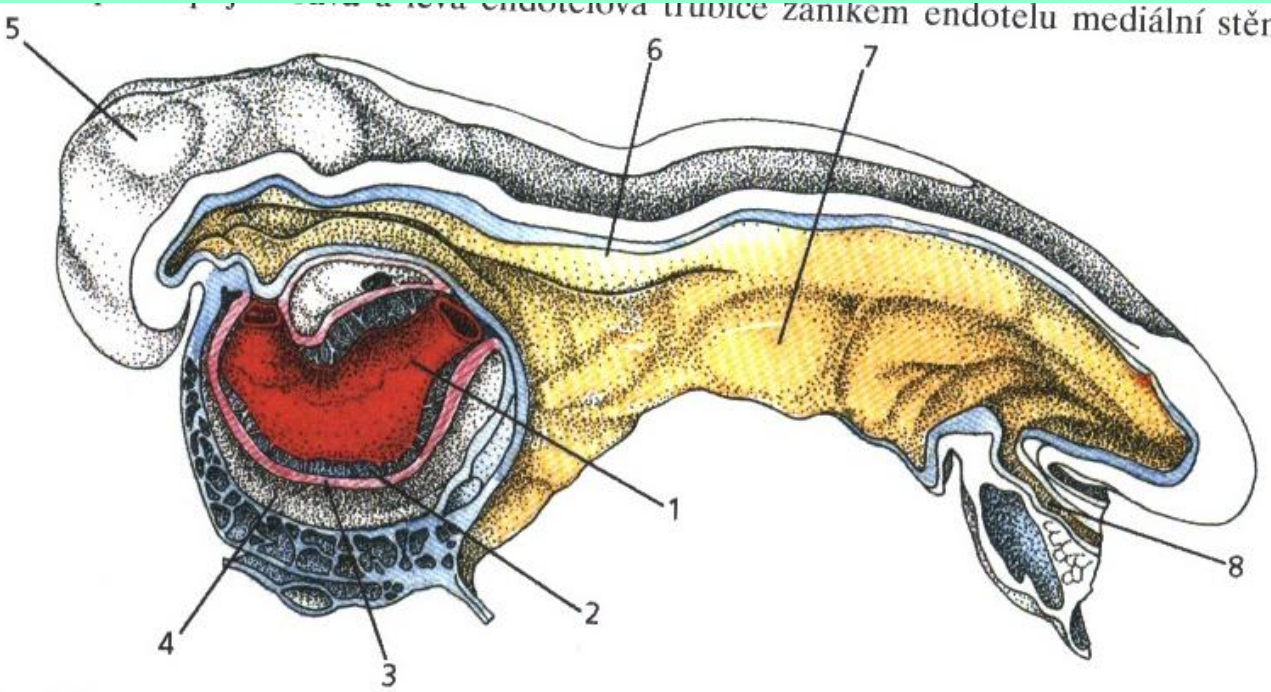
ventral to the foregut

caudal to the oropharyngeal membrane





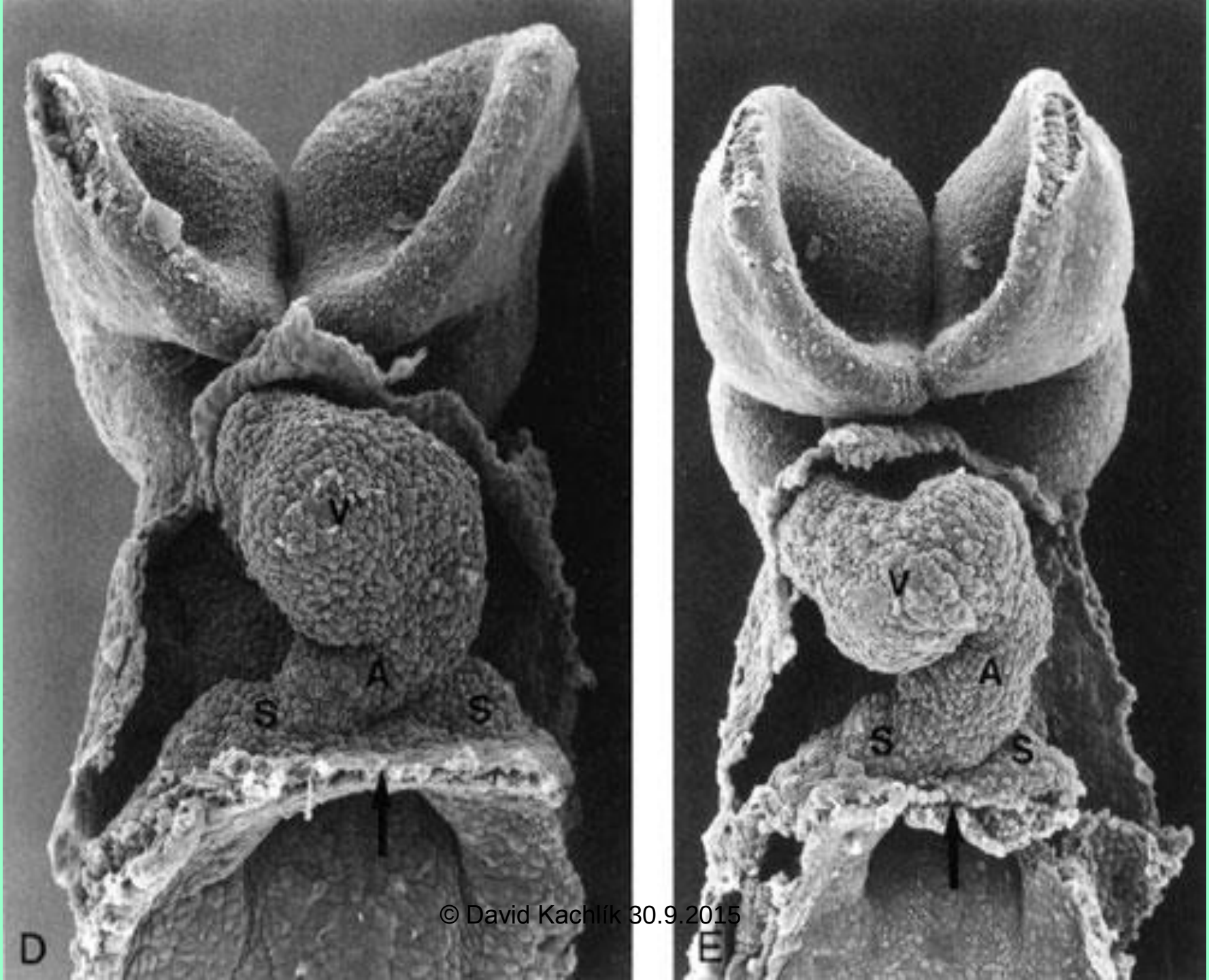
Obr. 8.126 *Schéma vývoje základu srdce. Pohled z ventrální strany na hlavovou část embrya se 6 prvosegmenty, starého asi 20 dnů.*
1 – neuroektodermové valy neurální rýhy, 2 – faryngová membrána, 3–5 endotelové štěrbiny splývající v endotelovou trubici

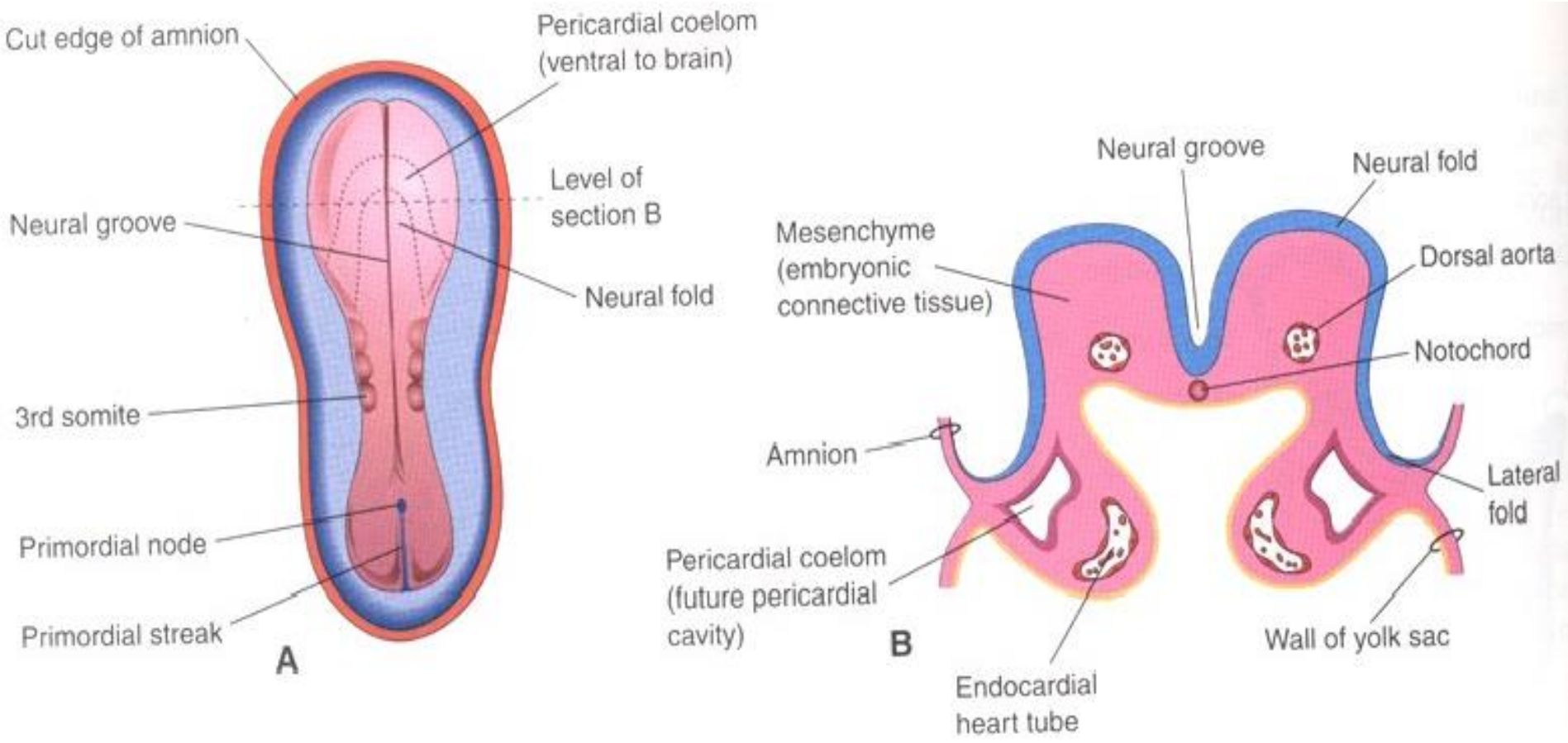


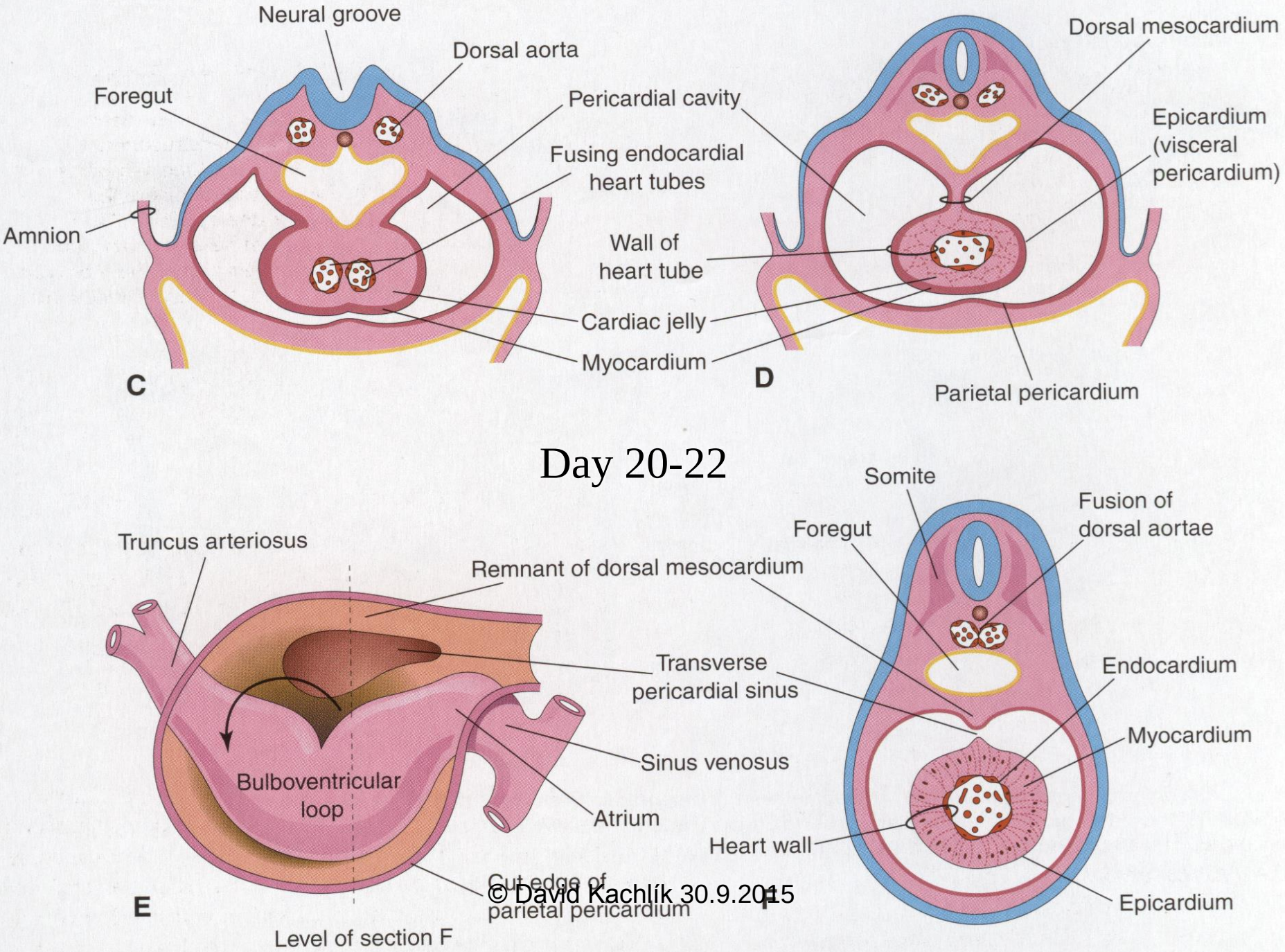
Obr. 8.127 *Schéma vývoje srdce. Sagitální řez tělem embrya s 10 prvosegmenty, starého asi 20 dnů.*
1 – endotelová trubice, 2 – vlákna řídkého mezenchymu, 3 – myoepikard, 4 – základy dutiny perikardové, 5 – hlavová část meduární ploténky se základy mozkových váčků, 6 – střevo, 7 – stěna žloutkového váčku, 8 – allantois a zárodečný stvol.

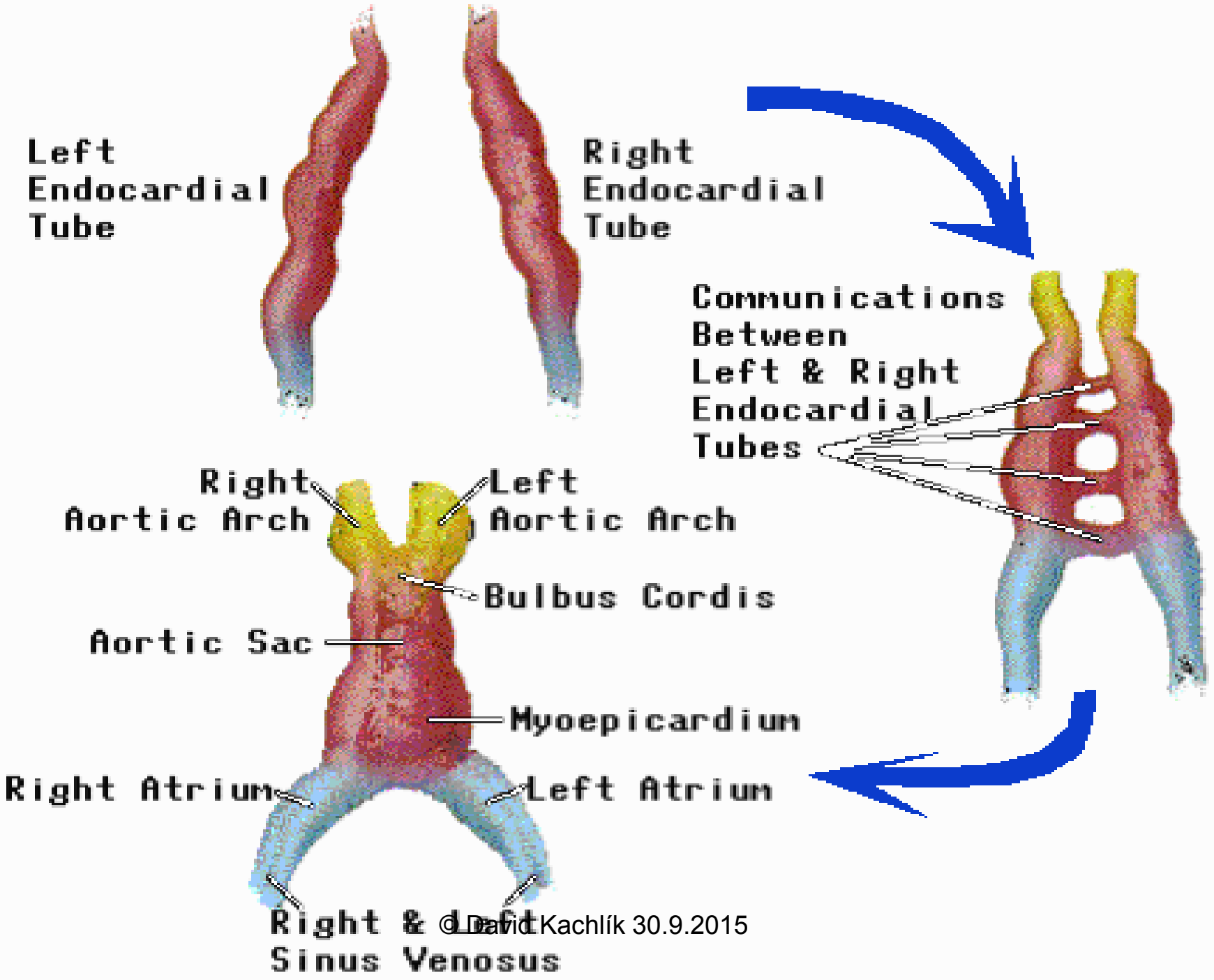
Heart development

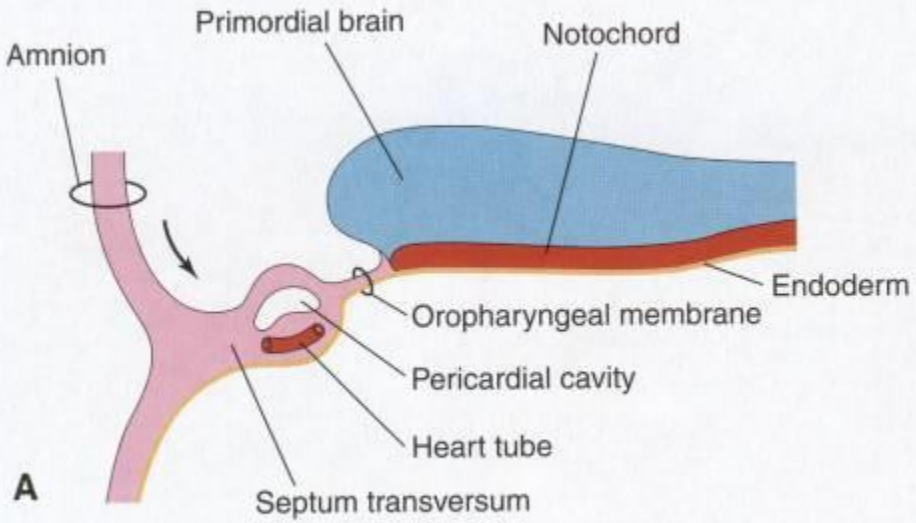
- pair of cardiac primordia fuse
  - except for the most caudal reagion
- longitudinal growth
  - heart tube bulges into the pericardial cavity
  - it is attached to the body wall by dorsal mesocardium
    - which disappears later forming transverse pericardial sinus
- heart is fixed:
  - caudally to septum transversum
  - cranially to the pharyngeal arches (aortal arches)

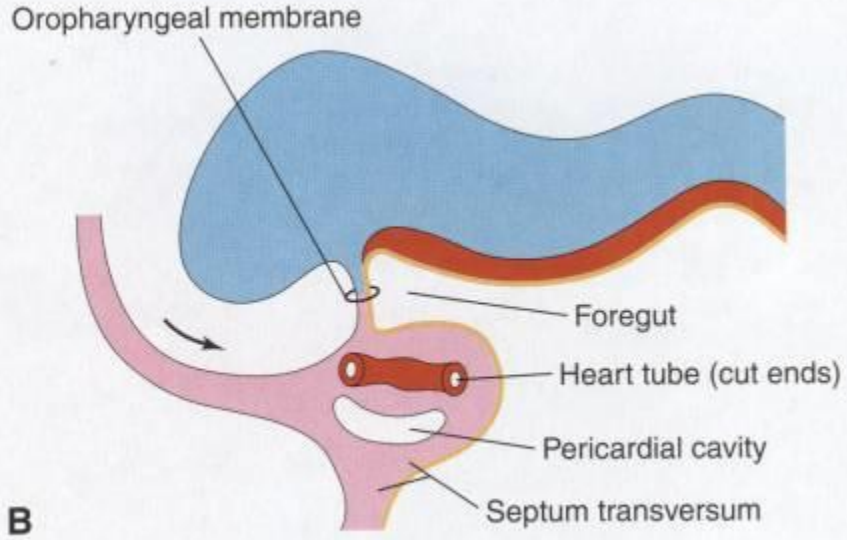












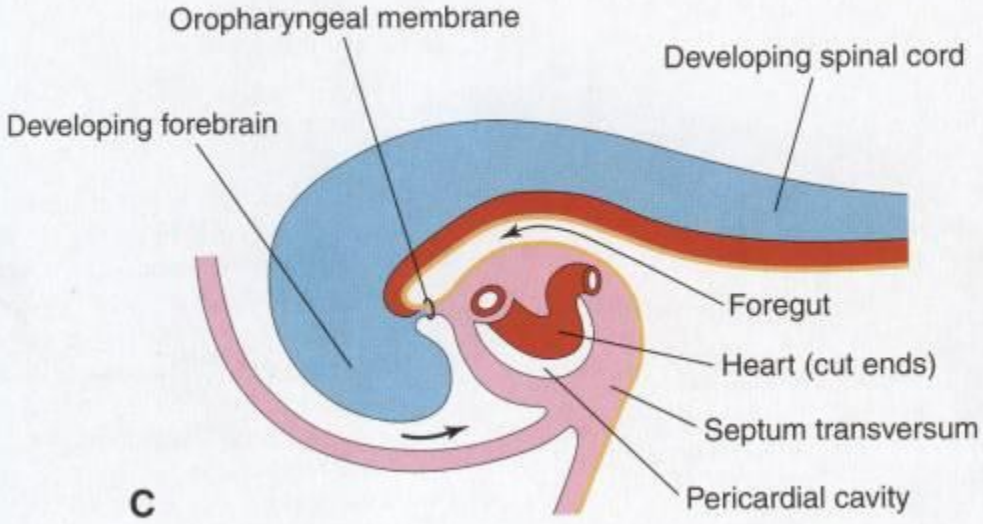
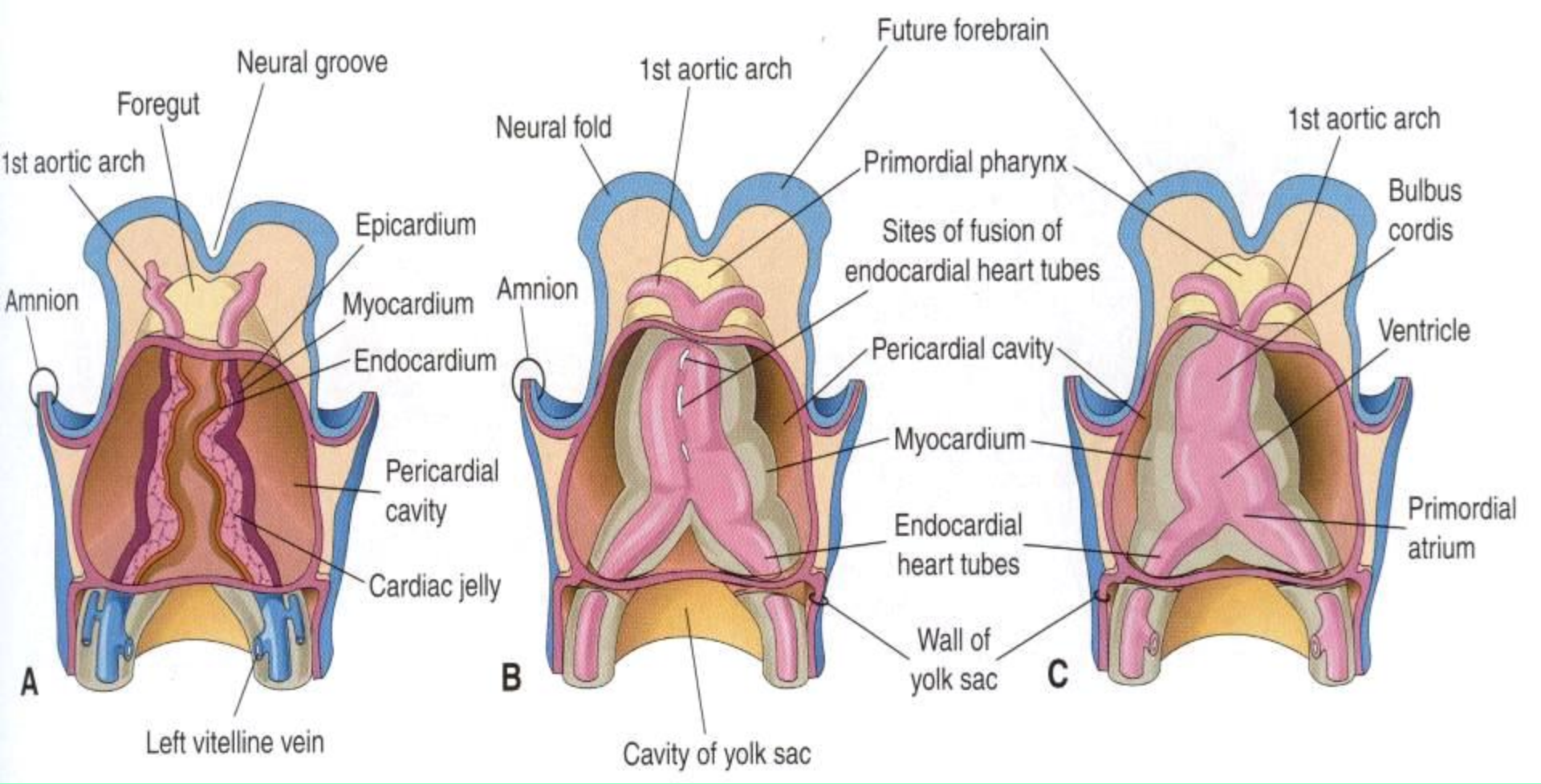
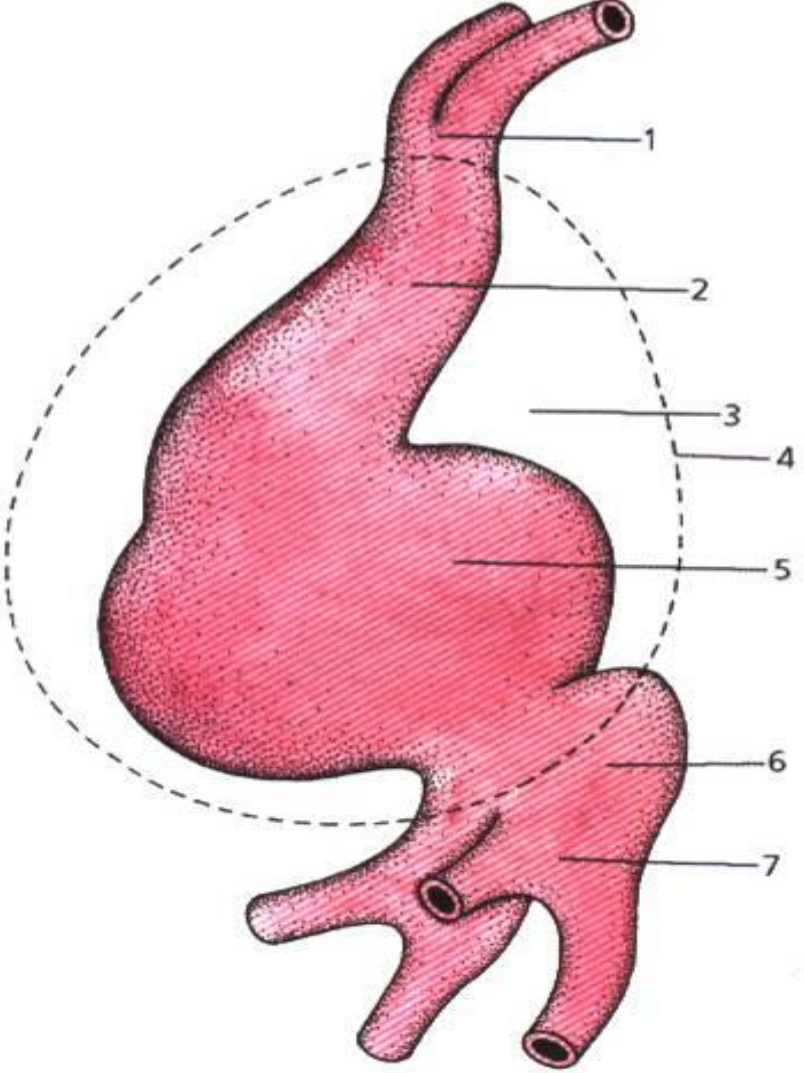


Figure 15 – 7. Drawings of longitudinal sections through the cranial half of human embryos during the fourth week of development. The illustrations show the effect of the head fold (*arrow*) on the position of the heart and other structures. *A* and *B*, As the head fold develops, the heart tube and pericardial cavity come to lie ventral to the foregut and caudal to the oropharyngeal membrane. *C*, Note that the positions of the pericardial cavity and septum transversum have reversed with respect to each other. The septum transversum now lies posterior to the pericardial cavity, where it will form the central tendon of the diaphragm.

Endocardial heart tubes fuse to form primitive heart tube, which develops into **endocardium**



Mesoderm surrounding heart tube develops into **myocardium and epicardium**



Obr. 8.128 *Schéma vývoje srdeční trubice. Pohled z ventrální strany na srdeční trubici embrya s 8 prvosegmenty, starého asi 20 dní.*
1 – truncus arteriosus, 2 – bulbus cordis, 3 – perikardová dutina, 4 – perikard, 5 – ventriculus, 6 – atrium, 7 – sinus venosus.

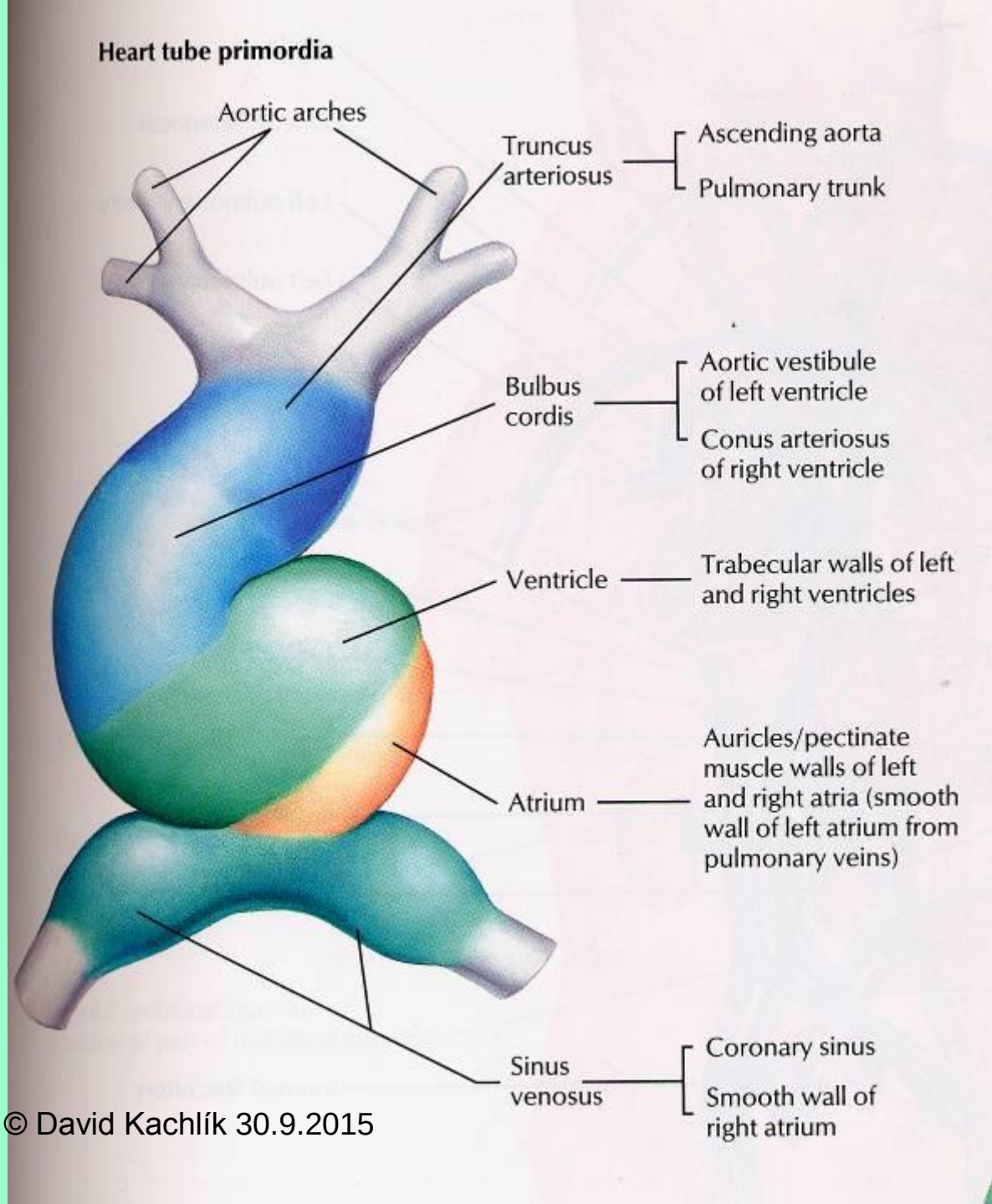
Heart development

- sinus venosus
- primitive atrium
- embryonic ventricle
- bulbus cordis
- truncus arteriosus

- atrium - sinus venarum cavarum
- atrium (separated with *crista terminalis*)
- ventriculus (inflow part)
- ventriculus (outflow part, separated with *crista supraventricularis*)
- aorta + truncus pulmonalis

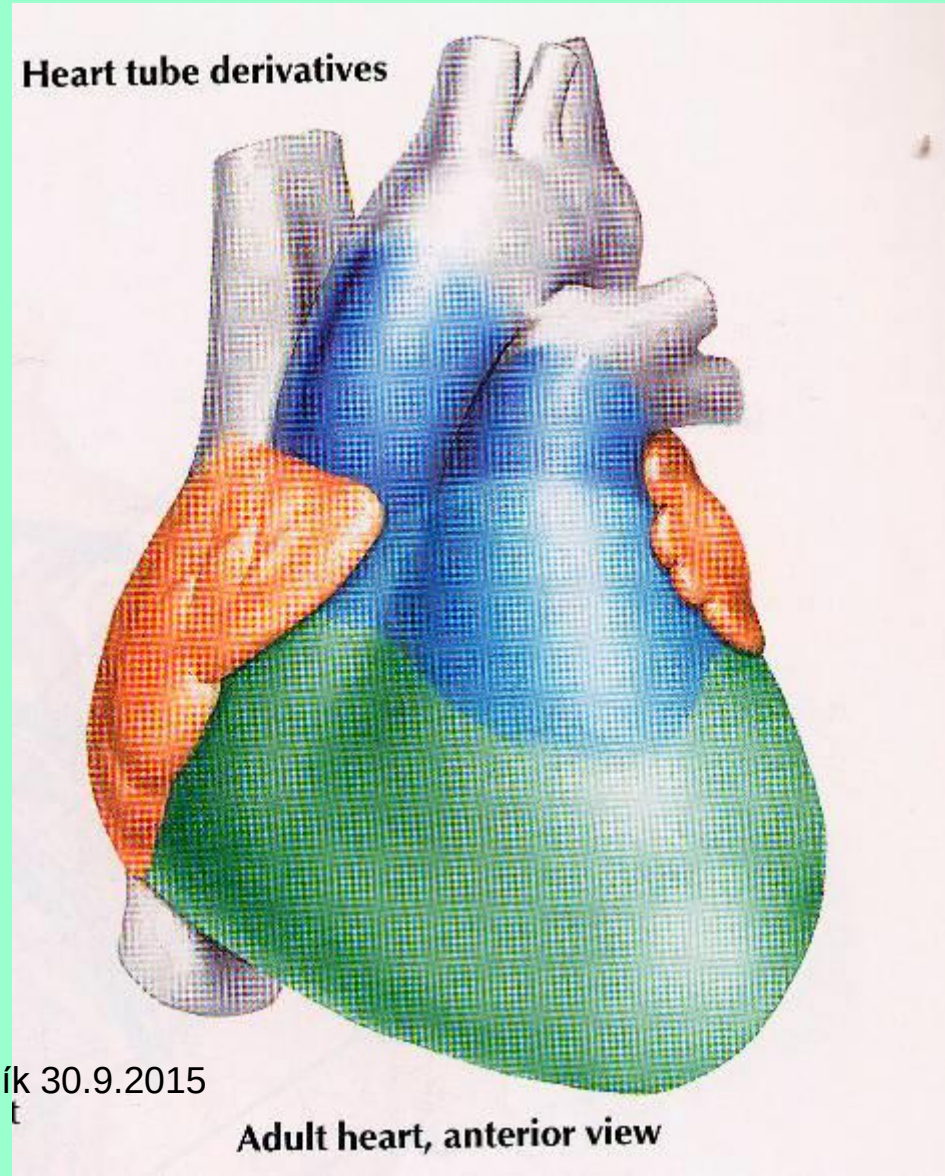
Cardiac loop (*Ansa cordis dextra*)

- truncus arteriosus
- conus cordis
- bulbus cordis
- embryonic ventricle
- atrioventricular canal
- common atrium
- sinus venosus

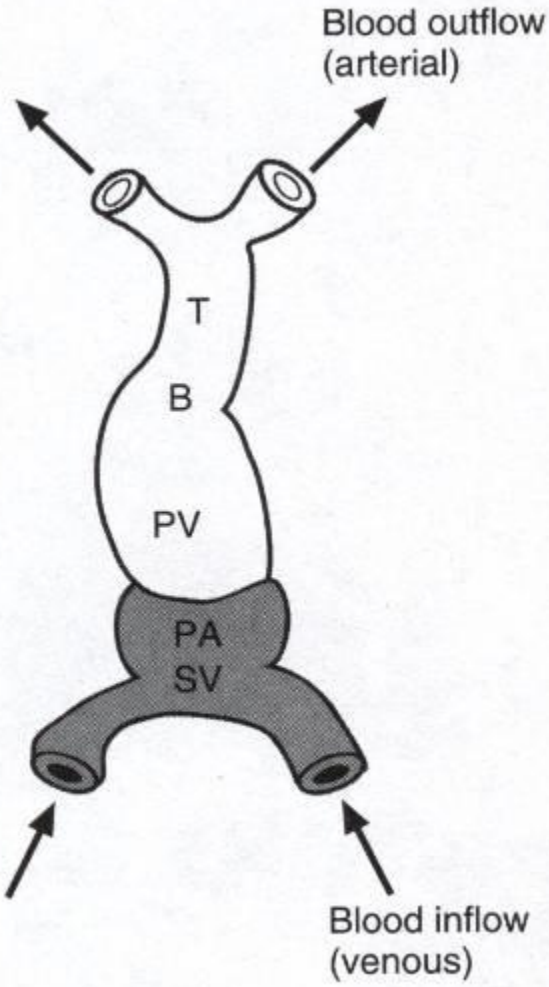


Development of heart tube

- common atrium = atrium
- bulbus cordis = trabecular part of right ventricle
- conus cordis = outflow tract of both ventricles
- bulboventricular sulcus= primary interventricular foramen
- ventricle = left ventricle

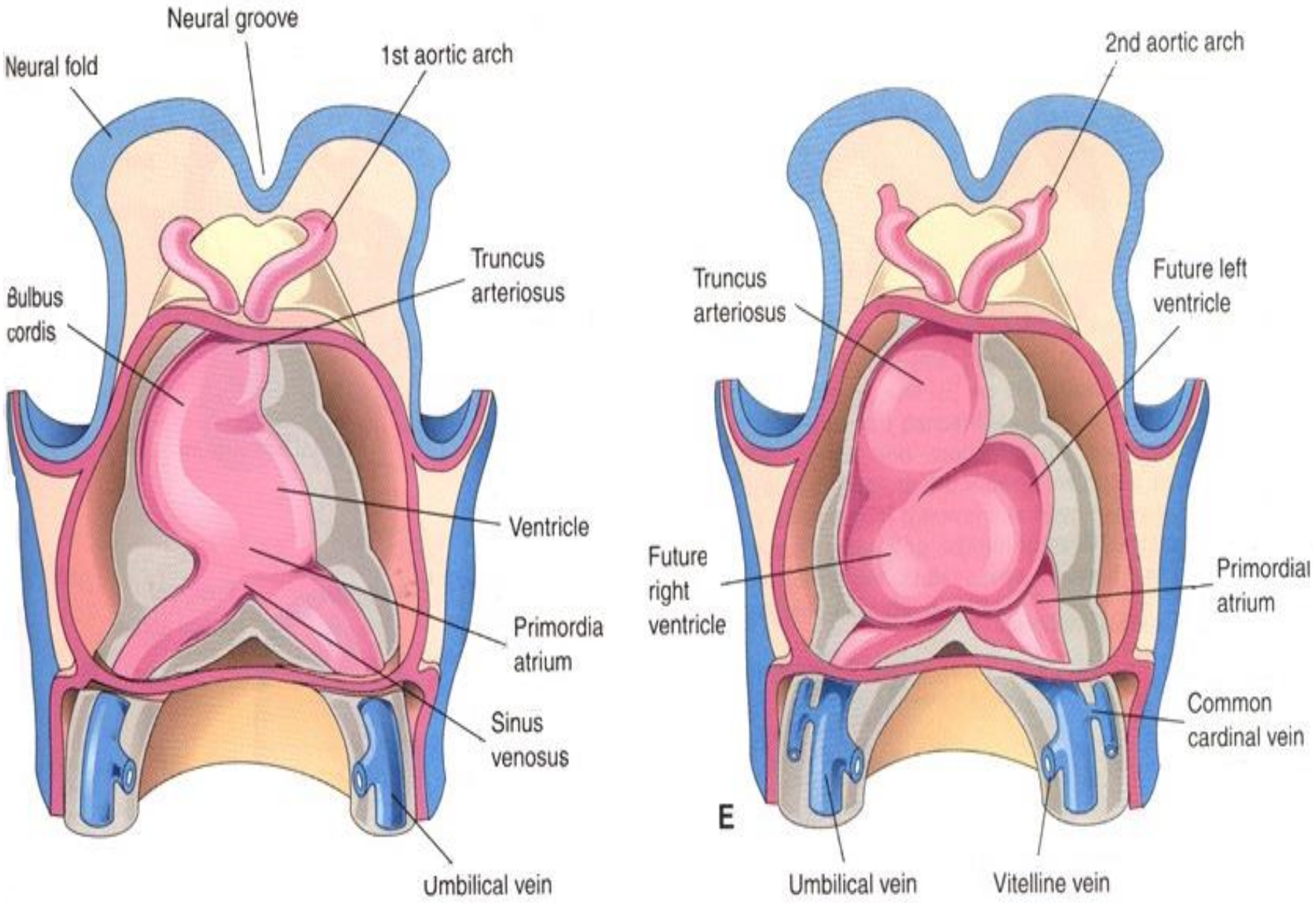


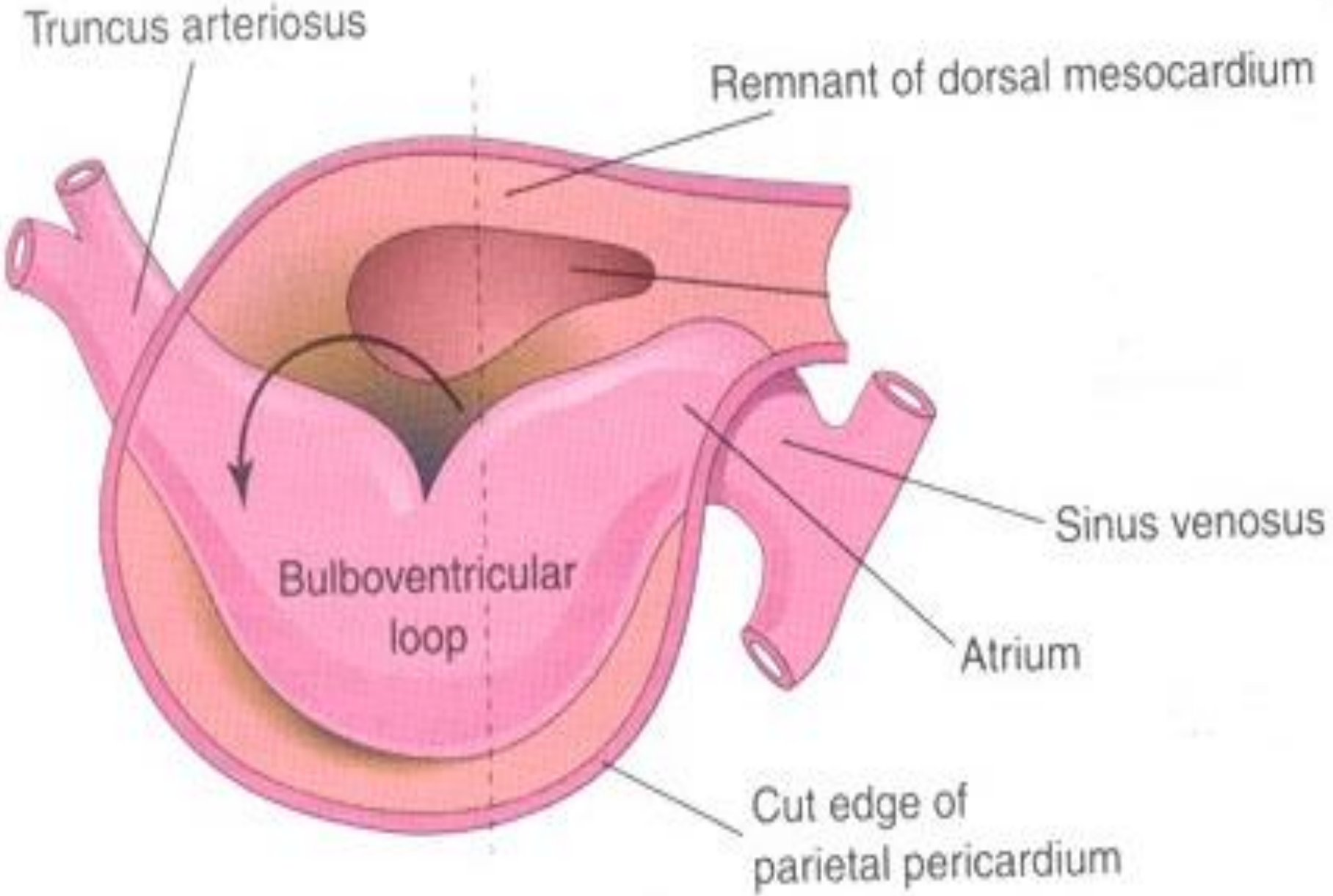
Development of cardiac loop

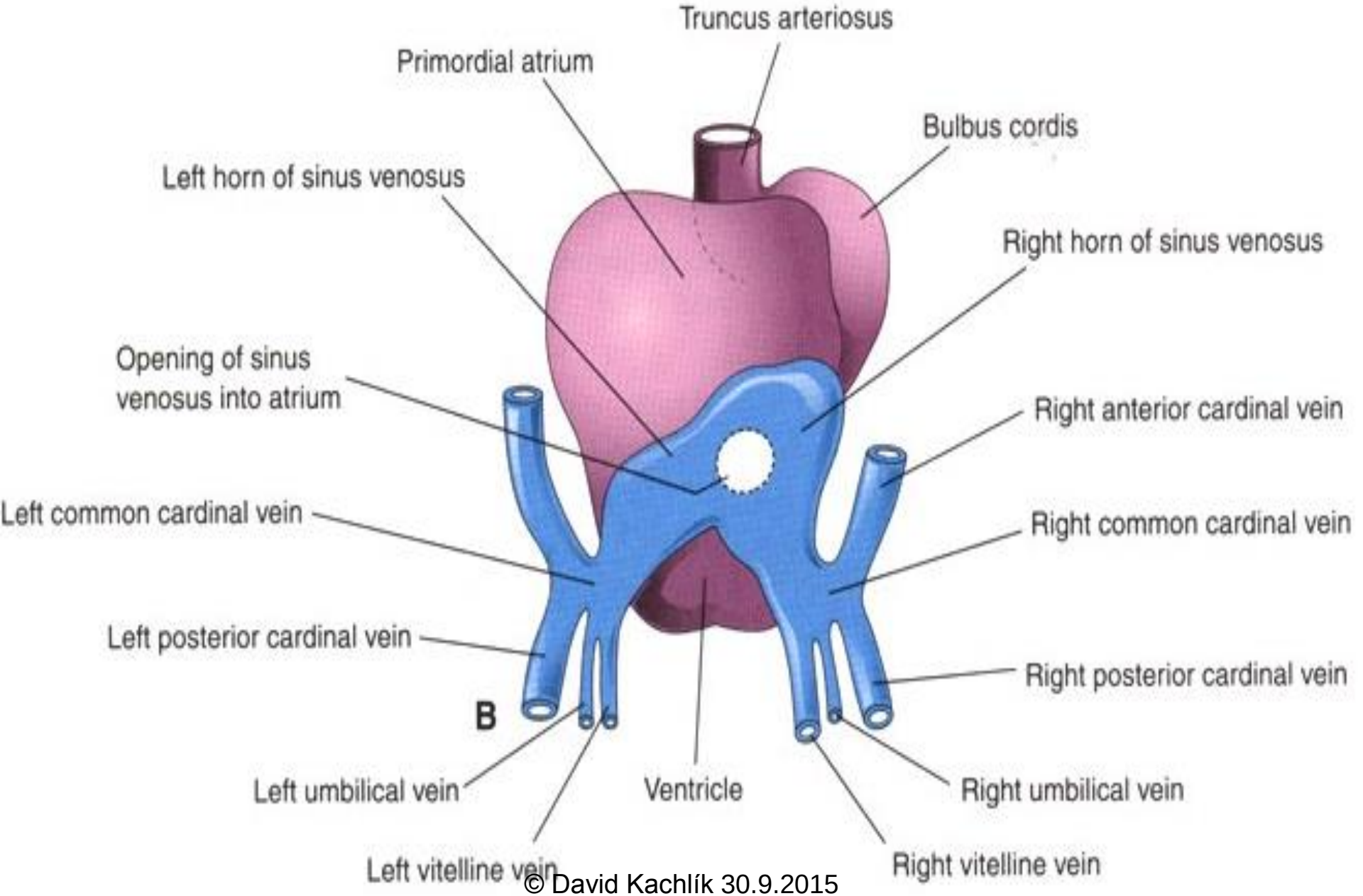


Embryonic Dilatation	Adult Structure
Truncus arteriosus (T)	Aorta Pulmonary trunk
Bulbus cordis (B)	Smooth part of right ventricle **(conus arteriosus)** Smooth part of left ventricle **(aortic vestibule)**
Primitive ventricle (PV)	Trabeculated part of right ventricle Trabeculated part of left ventricle
Primitive atrium (PA)	Trabeculated part of right atrium Trabeculated part of left atrium
Sinus venosus (SV)	Smooth part of right atrium **(sinus venarum)*** Coronary sinus Oblique vein of left atrium

*The smooth part of the left atrium is formed by incorporation of parts of the **pulmonary veins** into the atrial wall. The junction of the trabeculated and smooth parts of the right atrium is called the **crista terminalis.**







Partitioning of primordial heart

- starts around middle of the **4th** week
- completed by the end of the **5th** week

partitioning of:

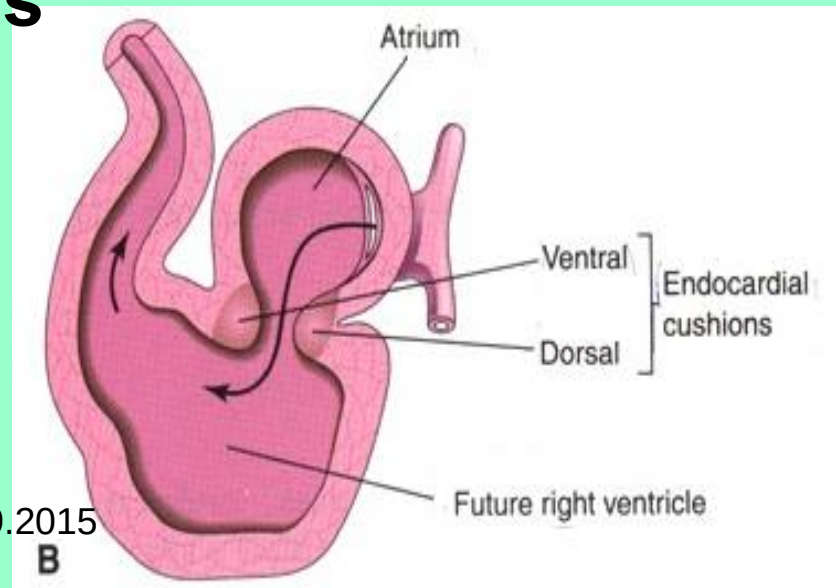
- atrioventricular canal
- common atrium
- embryonic ventricle

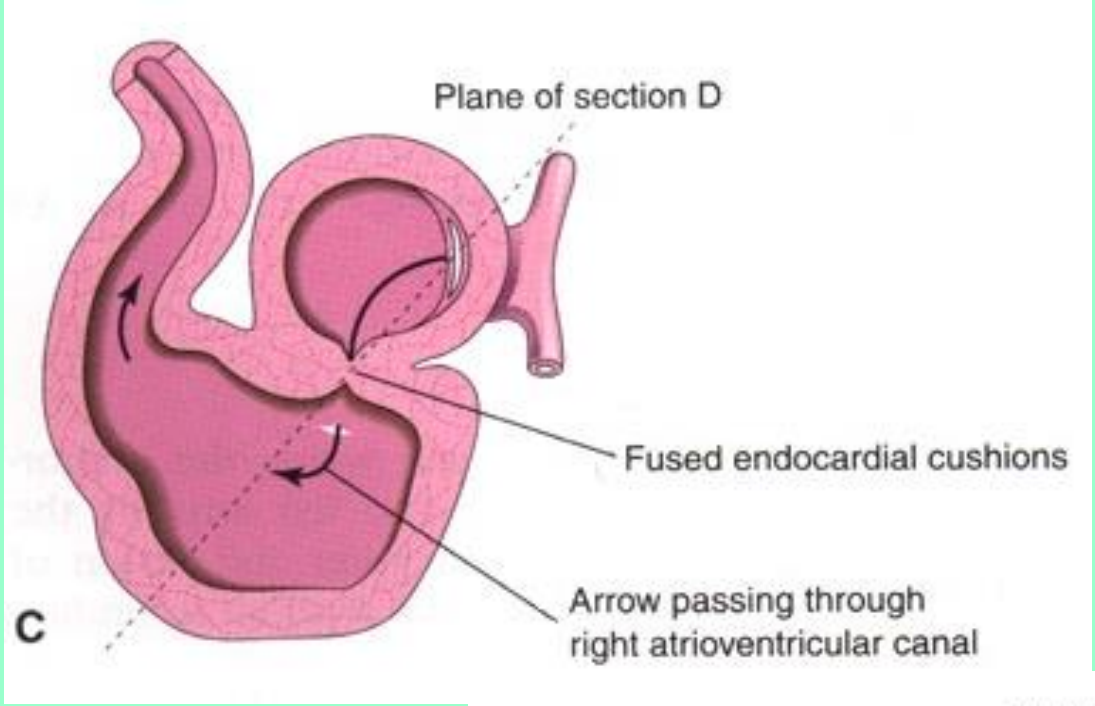
Partitioning of atrioventricular canal

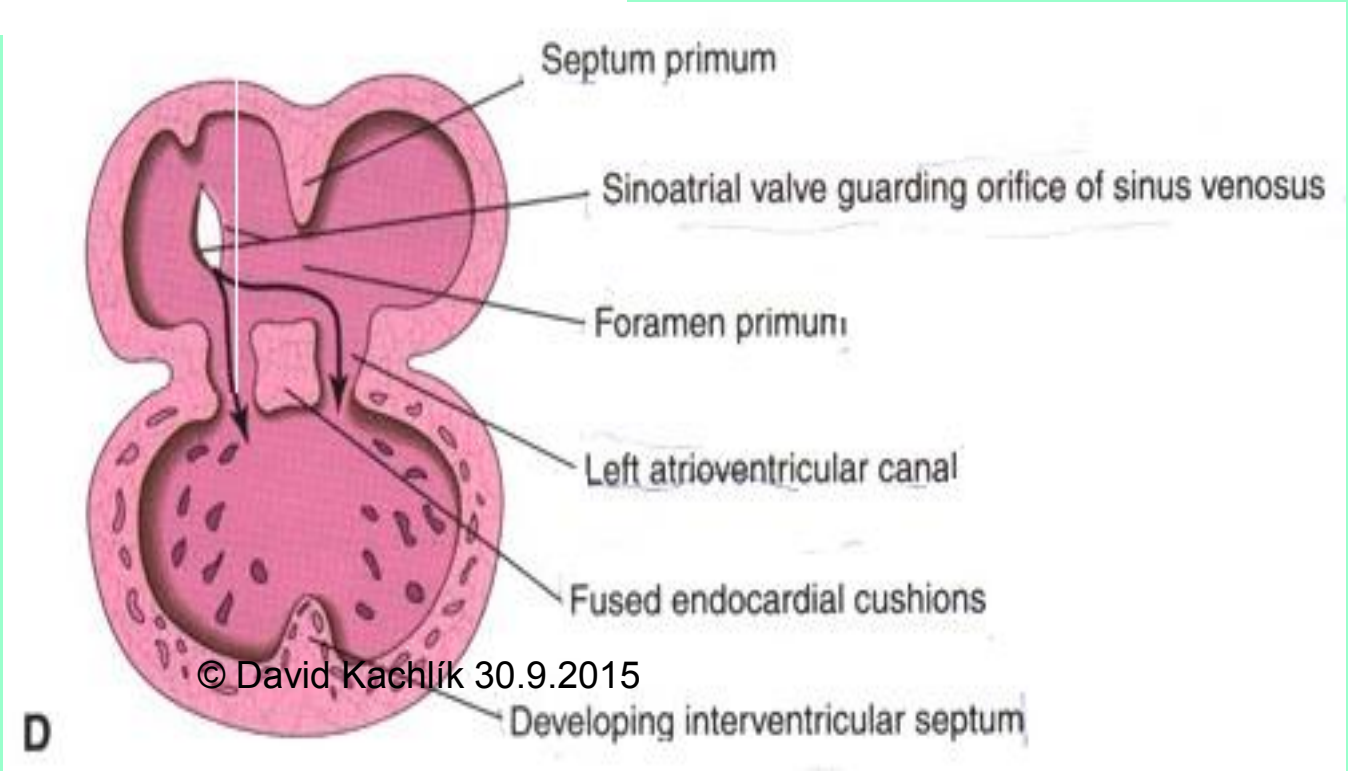
endocardial cushions (*tubera endocardiaca atrioventricularia*)

- dorsal and ventral walls
- right and left
- septum atrioventriculare membranosum

→ **canalis atrioventricularis**



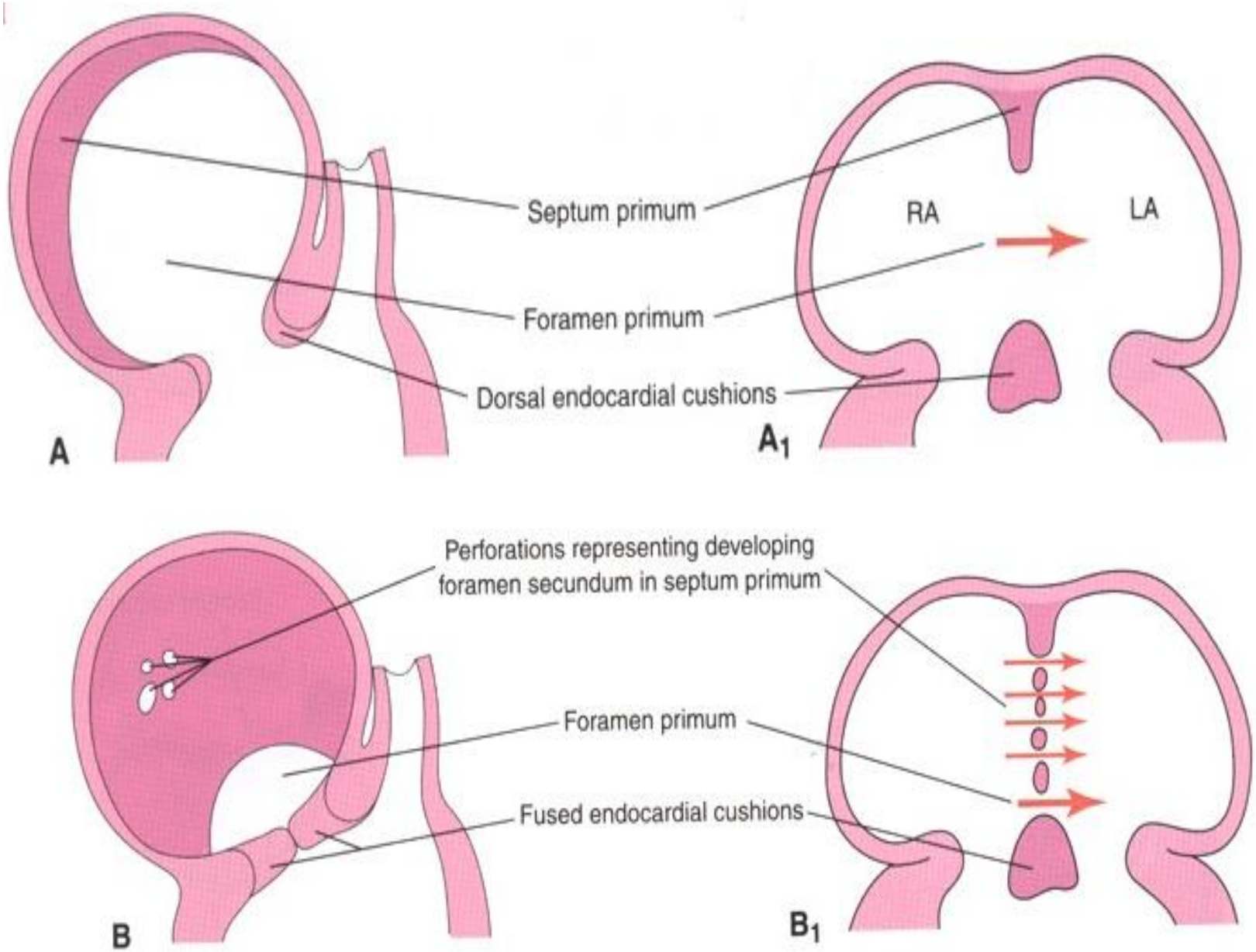


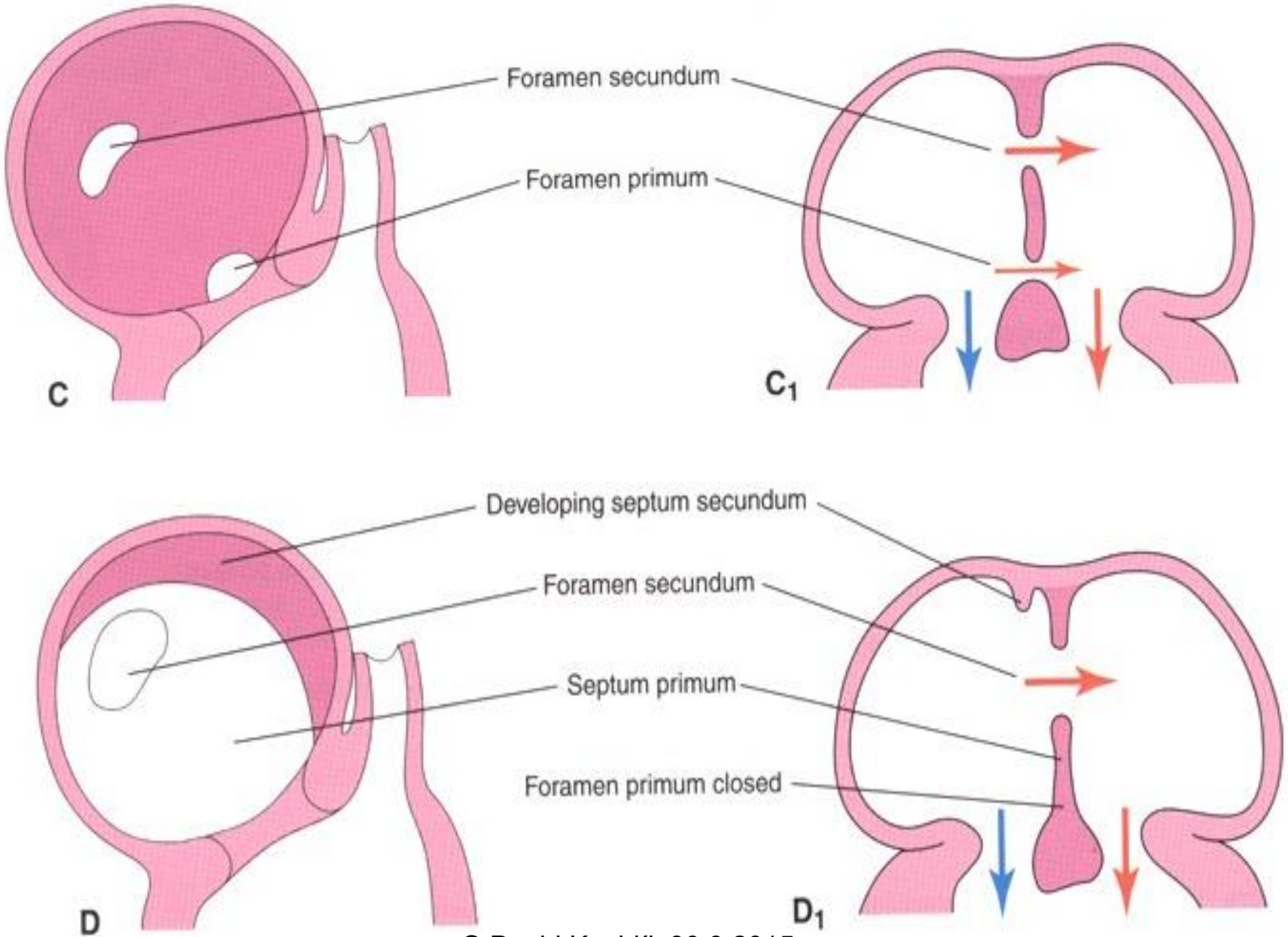


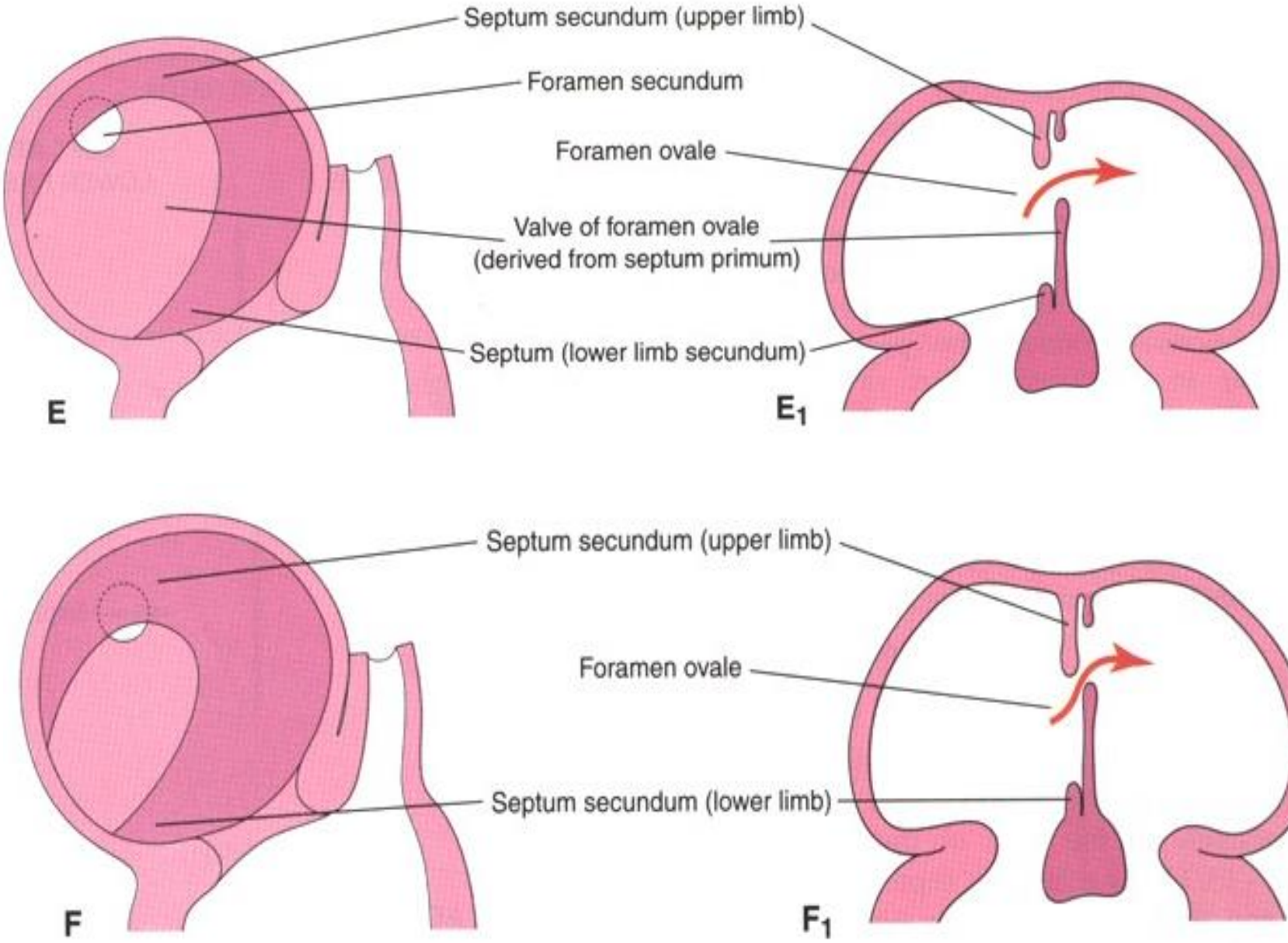
Partitioning of common atrium

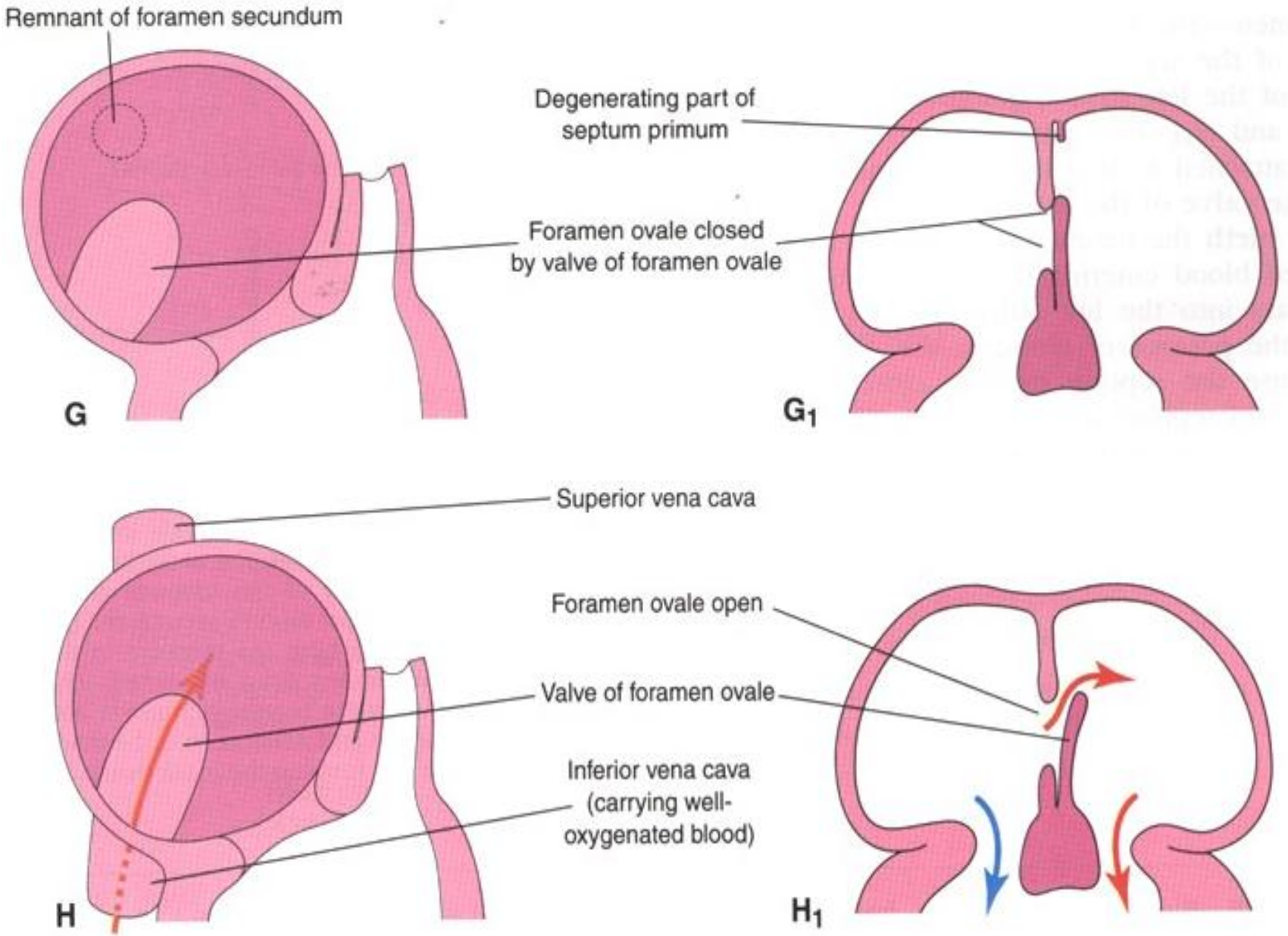
- **septum primum**
  - *foramen (ostium) primum*
  - *foramen secundum*
  - → valvula foraminis ovalis

- **septum secundum**
  - right to septum primum
  - *foramen ovale*
  - → fossa ovalis

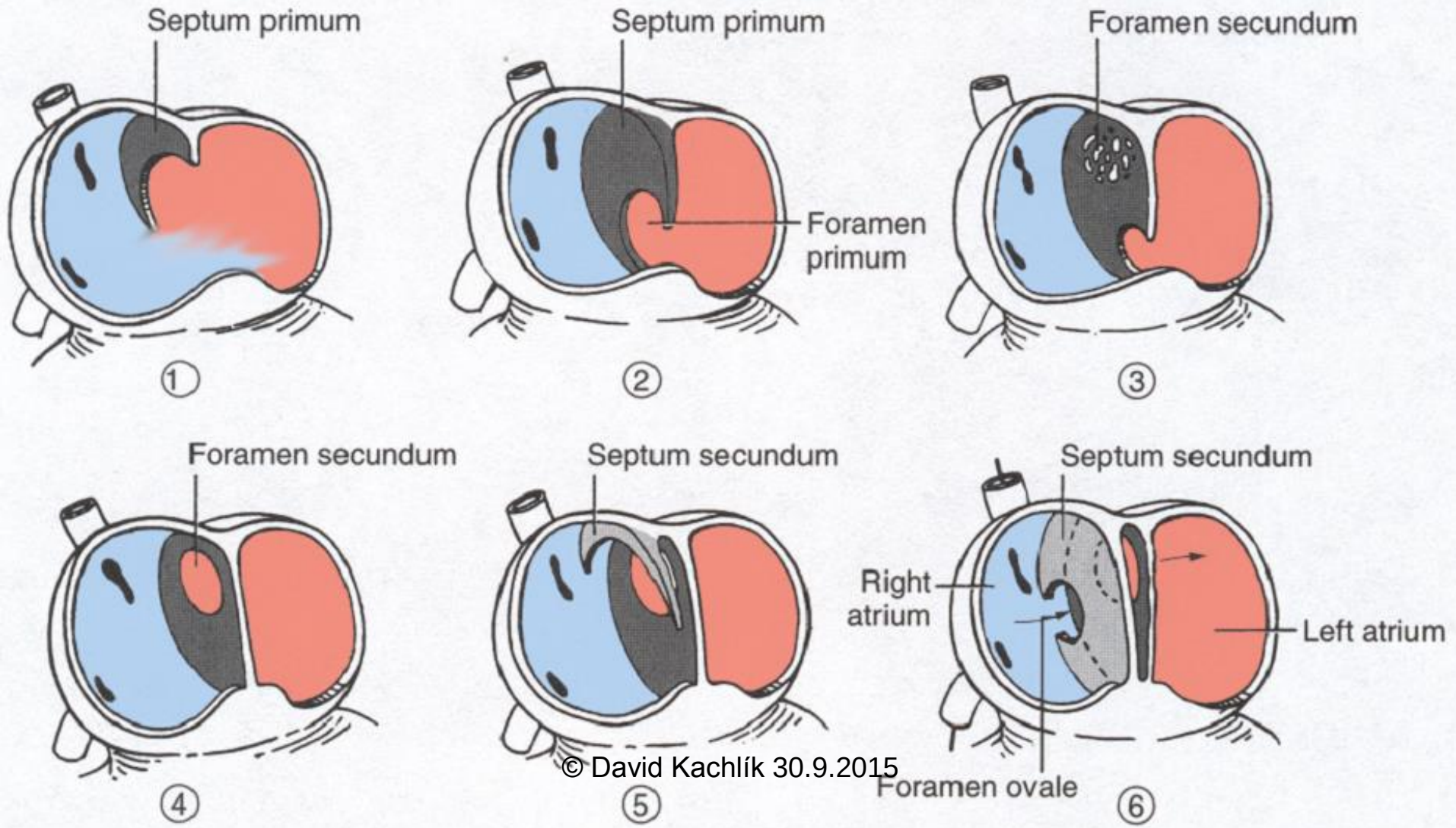


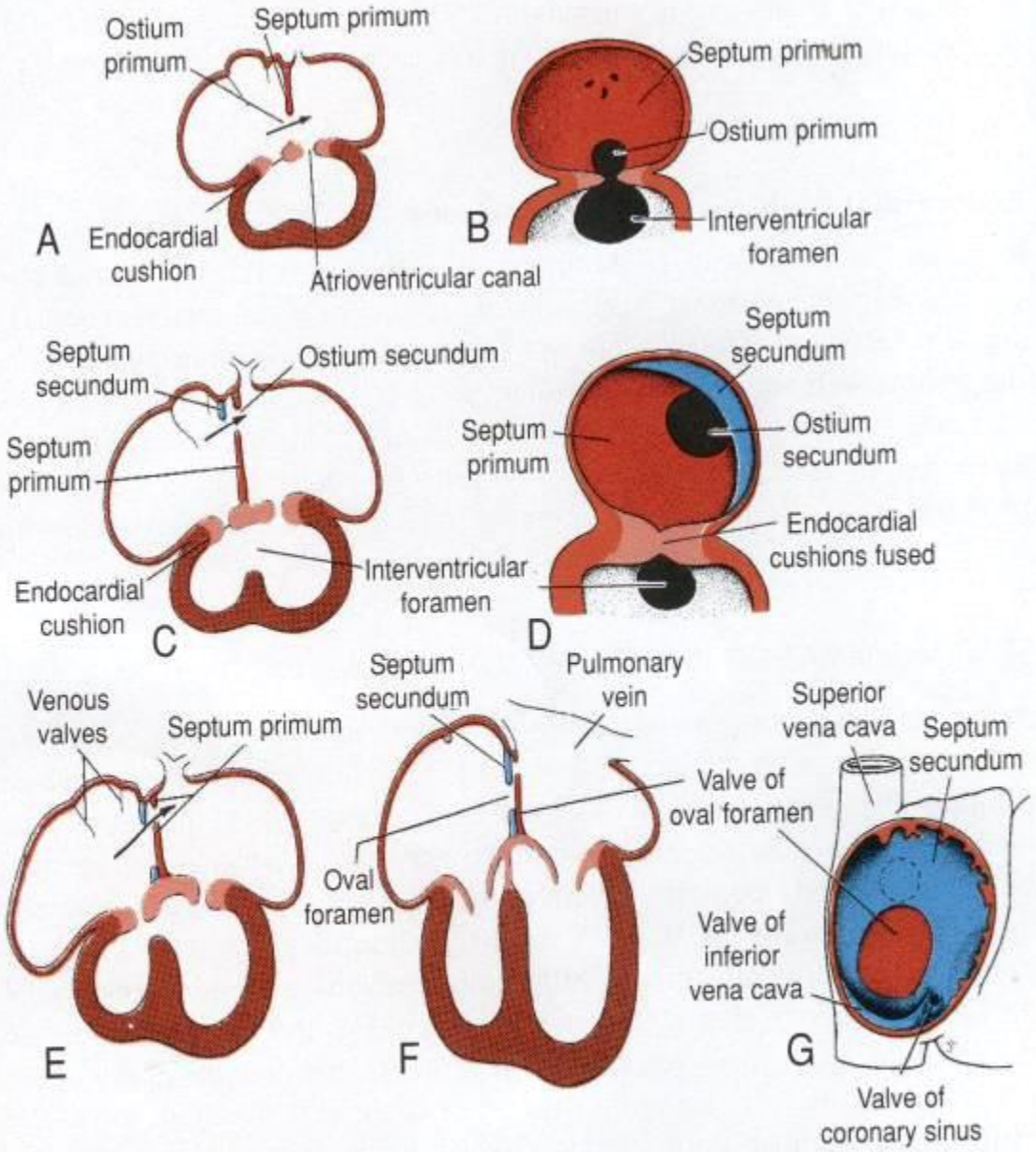




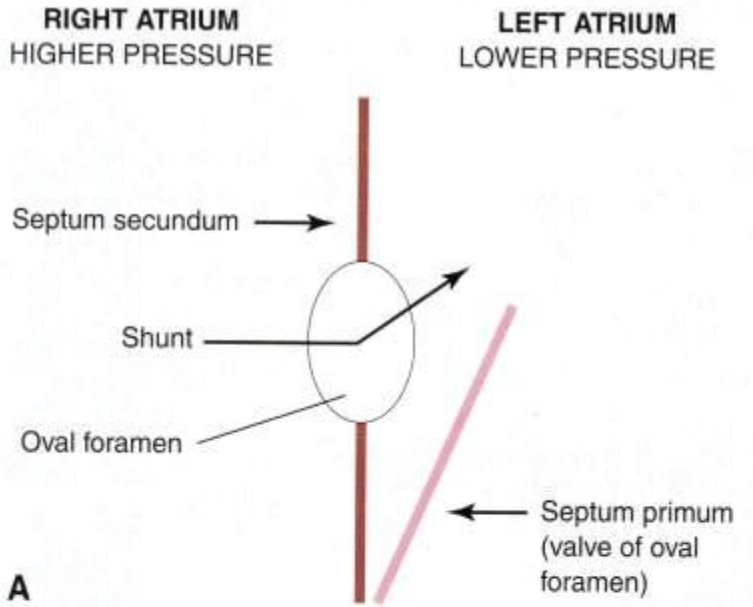


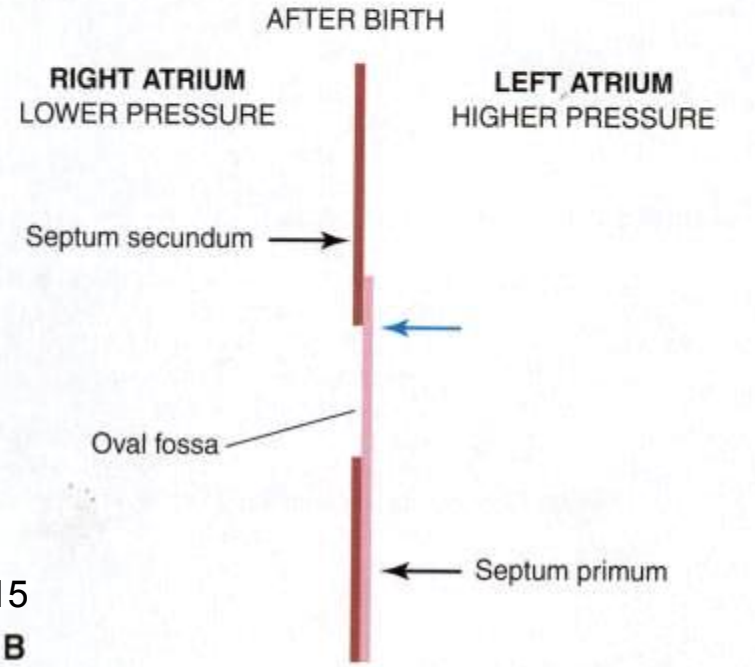
Formation of atrial (interatrial) septum in a common atrium





Atrial septa at various stages of development. **A.** 30 days (6 mm). **B.** Same stage as **A,** viewed from the right. **C.** 33 days (9 mm). **D.** Same stage as **C,** viewed from the right **E.** 37 days (14 mm). **F.** Newborn. **G.** Tricuspid valve from the right; same stage as **F.**

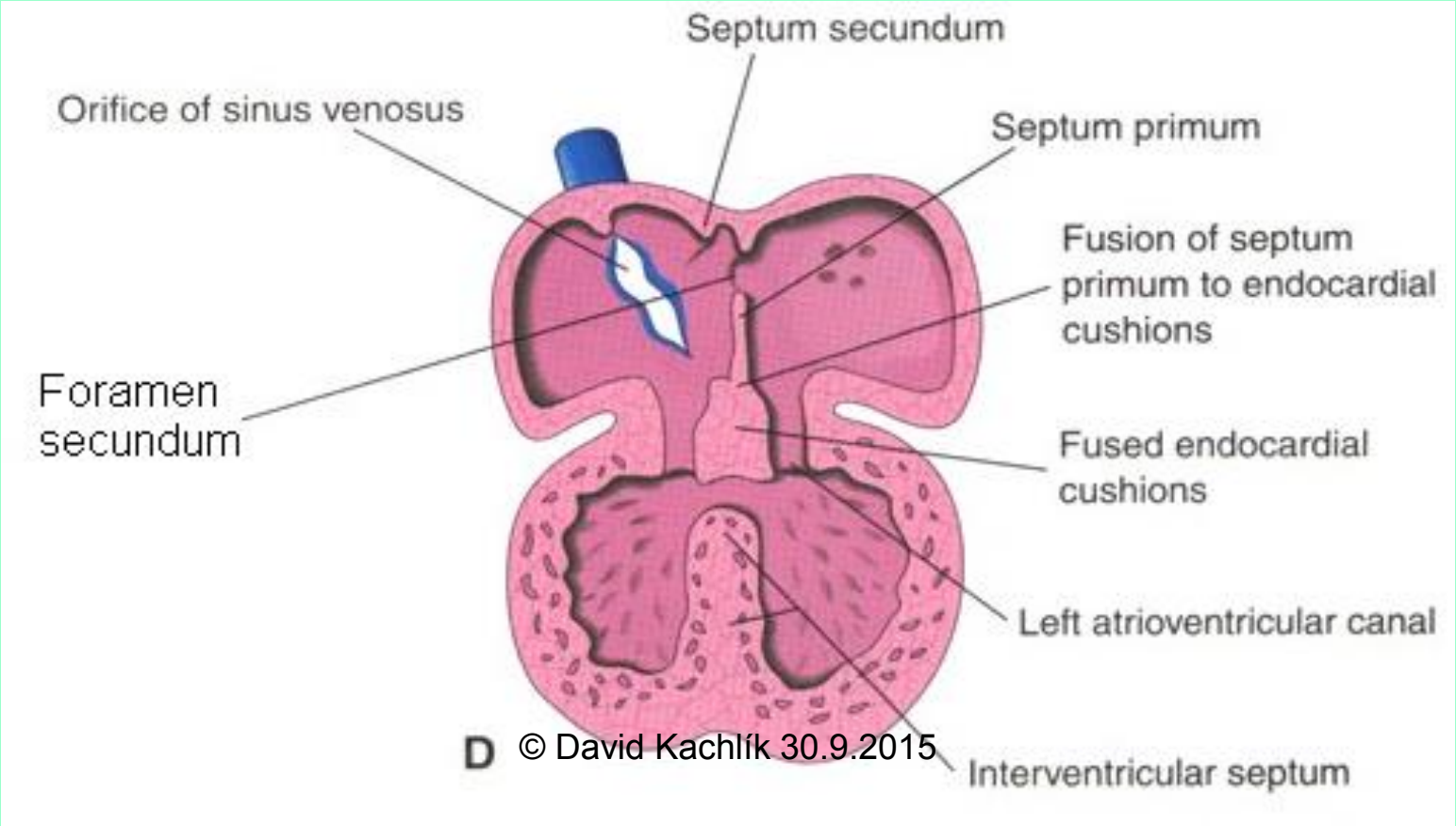




Partitioning of primordial ventricle

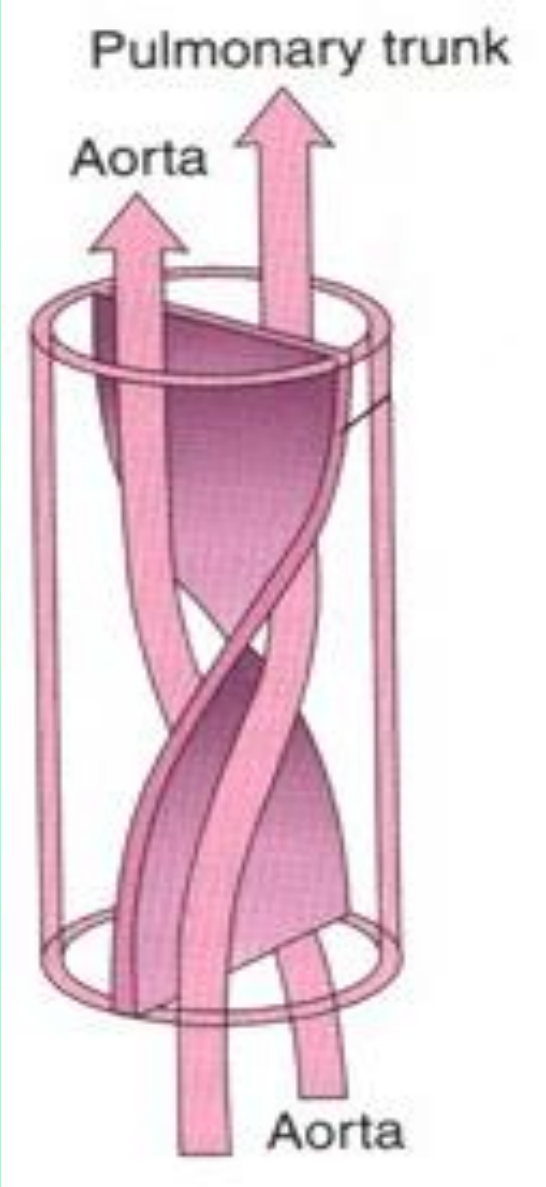
- **Primordial interventricular septum**

Foramen interventriculare (close by end of 7th week)

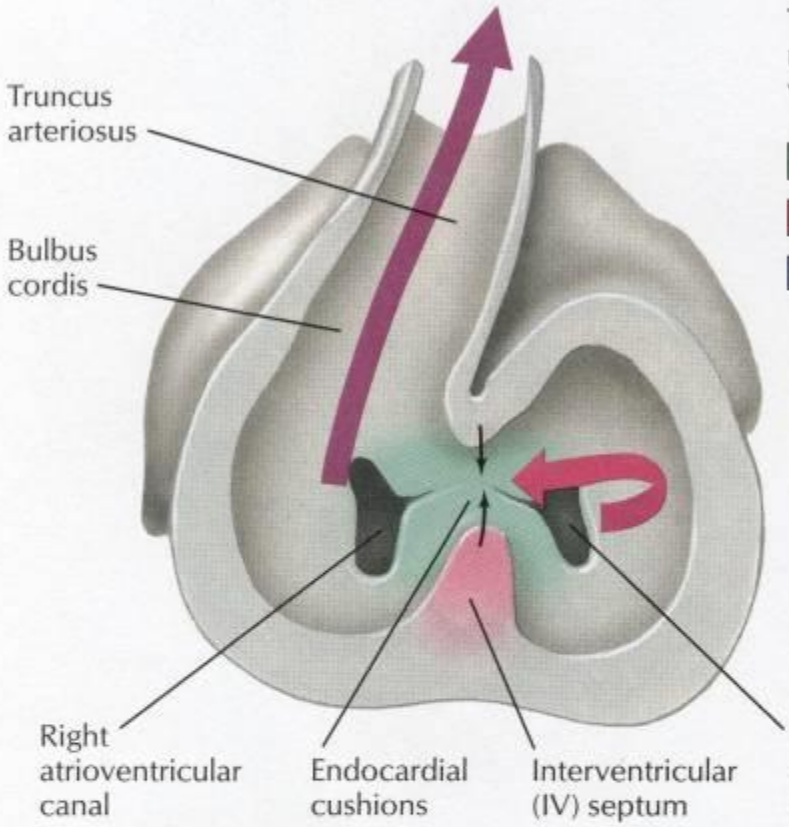


Partitioning of outflow part

- proximal (conus) and distal (truncus) part
- ridges: bulbar and truncal
  - crista endocardiaca septalis (conus) → pars proximalis (ventricles)
  - pars distalis (aorta-truncus pulmonalis)
- migration of neural crest cells
- 180-degree spiraling



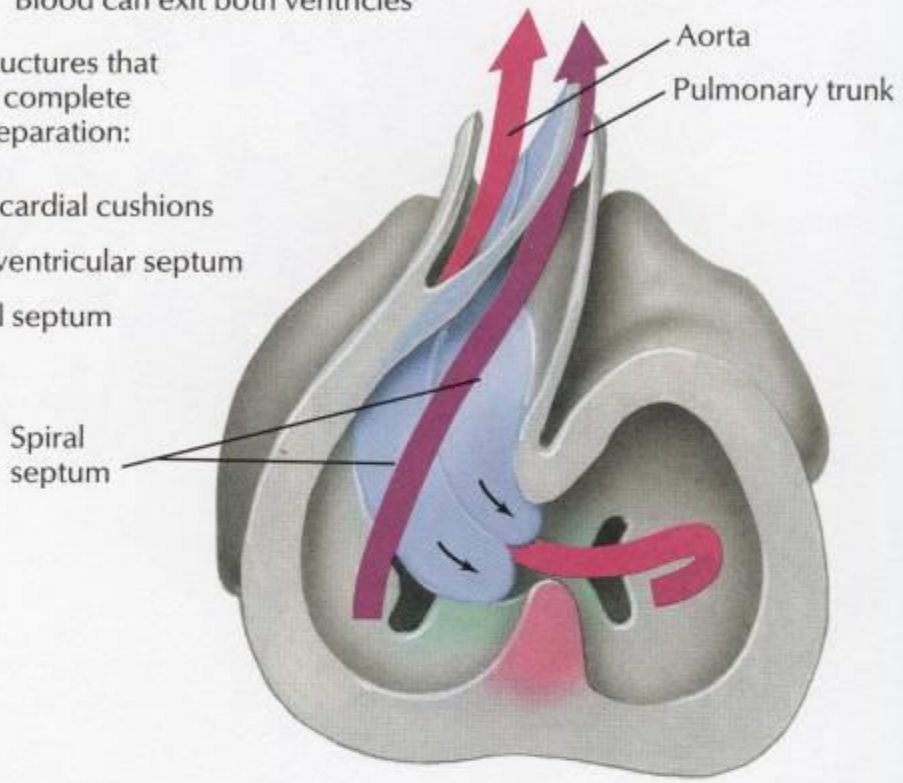
Without the spiral septum
No exit for blood in left ventricle

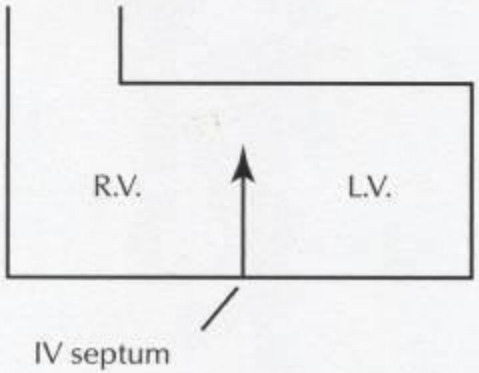


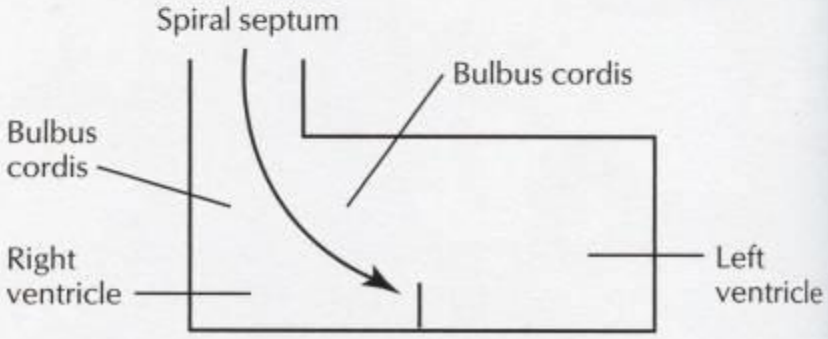
With the spiral septum
Blood can exit both ventricles

The three structures that must fuse to complete ventricular separation:

- Endocardial cushions
- Interventricular septum
- Spiral septum



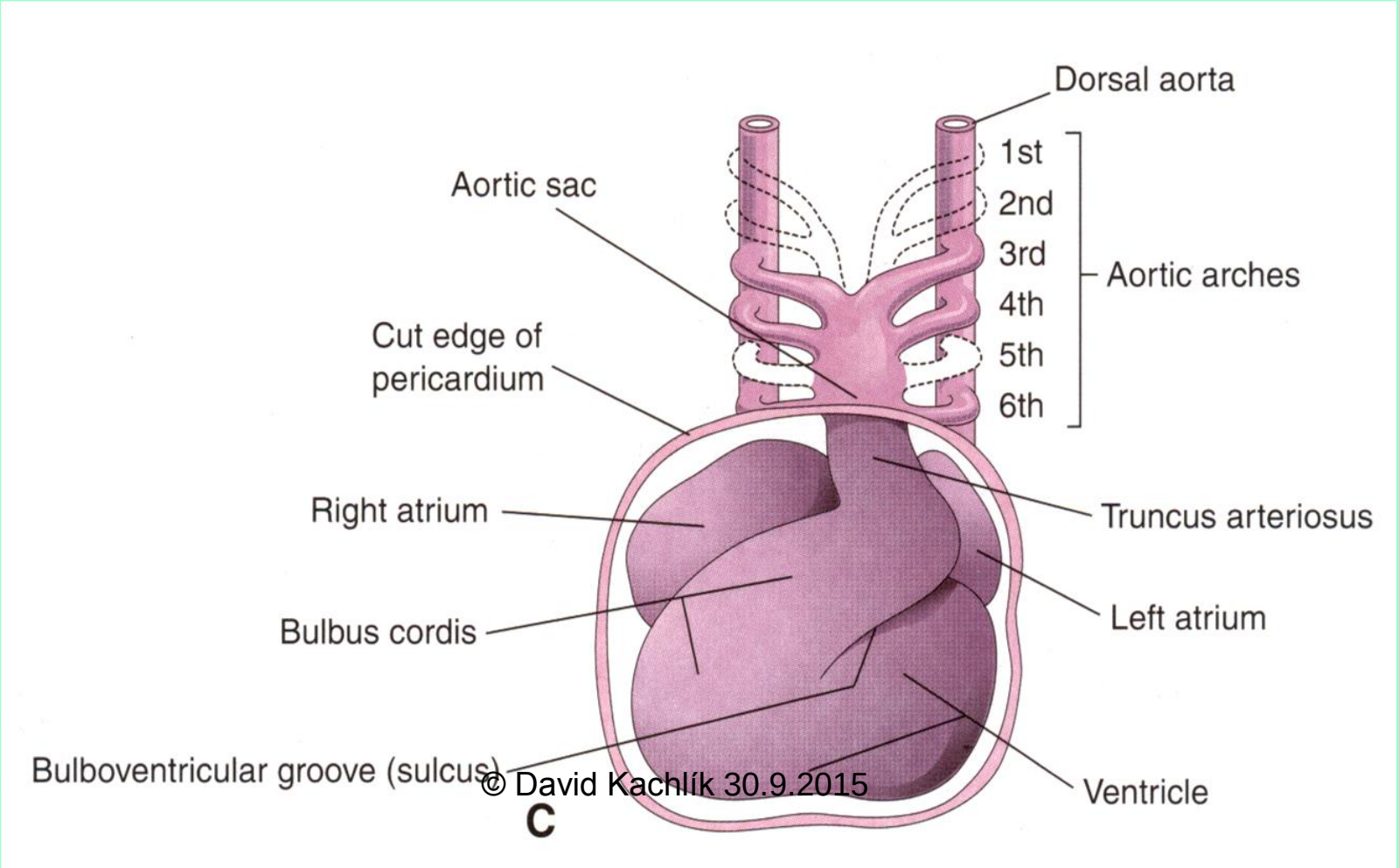




Part of the right ventricle is incorporated into the left

Arteries associated with heart

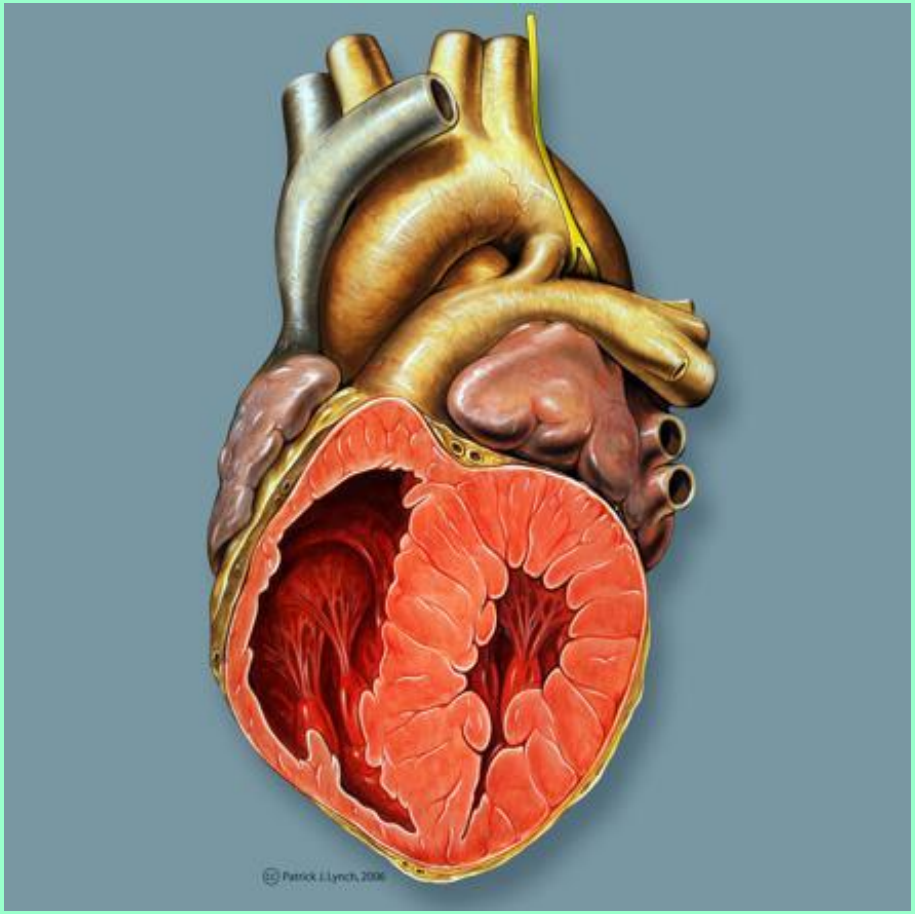
- truncus arteriosus → saccus aorticus → aa. arcuum pharyngeorum (aortal arches)

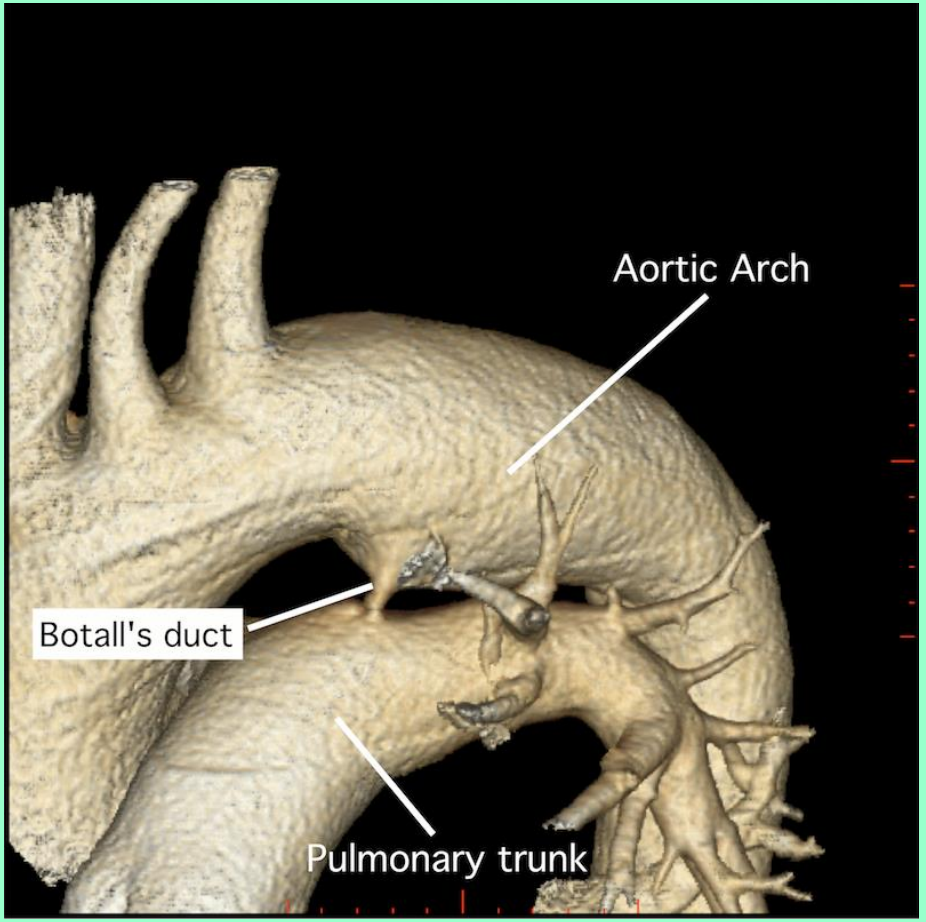


Ductus arteriosus Botalli
Botallo‘s duct

- fetal shunt
  - between the end of truncus pulmonalis (or the beginning of a. pulmonalis sinistra)
  - and isthmus aortae (mild narrowing of arcus aortae at its end after origins of arteries for head and upper limb)
- originates from the 6th aortic arch
- takes deoxygenated blood from truncus pulmonalis into the beginning of aorta descendens
- closes after birth (retraction) and changes into the ligamentum arteriosum

Ductus arteriosus Botalli
Botallo‘s duct





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Veins associated with heart

- ***Venae omphalomesentericae* (*vv. vitellinae*)**
  - poorly oxygenated blood from yolk sac
- ***Venae umbilicales***
  - well-oxygenated from chorionic villi of placenta
- ***Venae cardinales communes* (ductus Cuvièri)**
  - poorly oxygenated blood from body of embryo

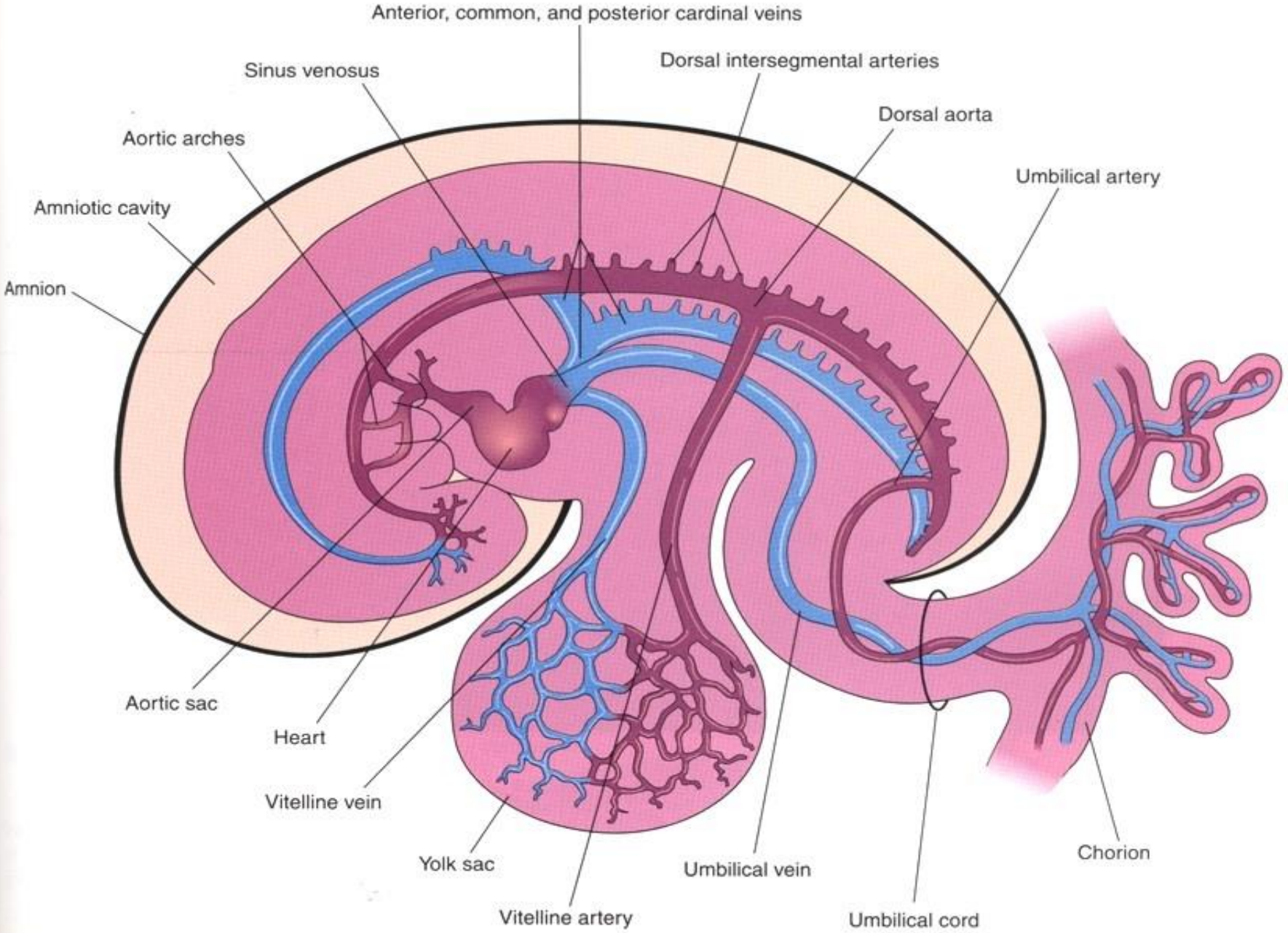
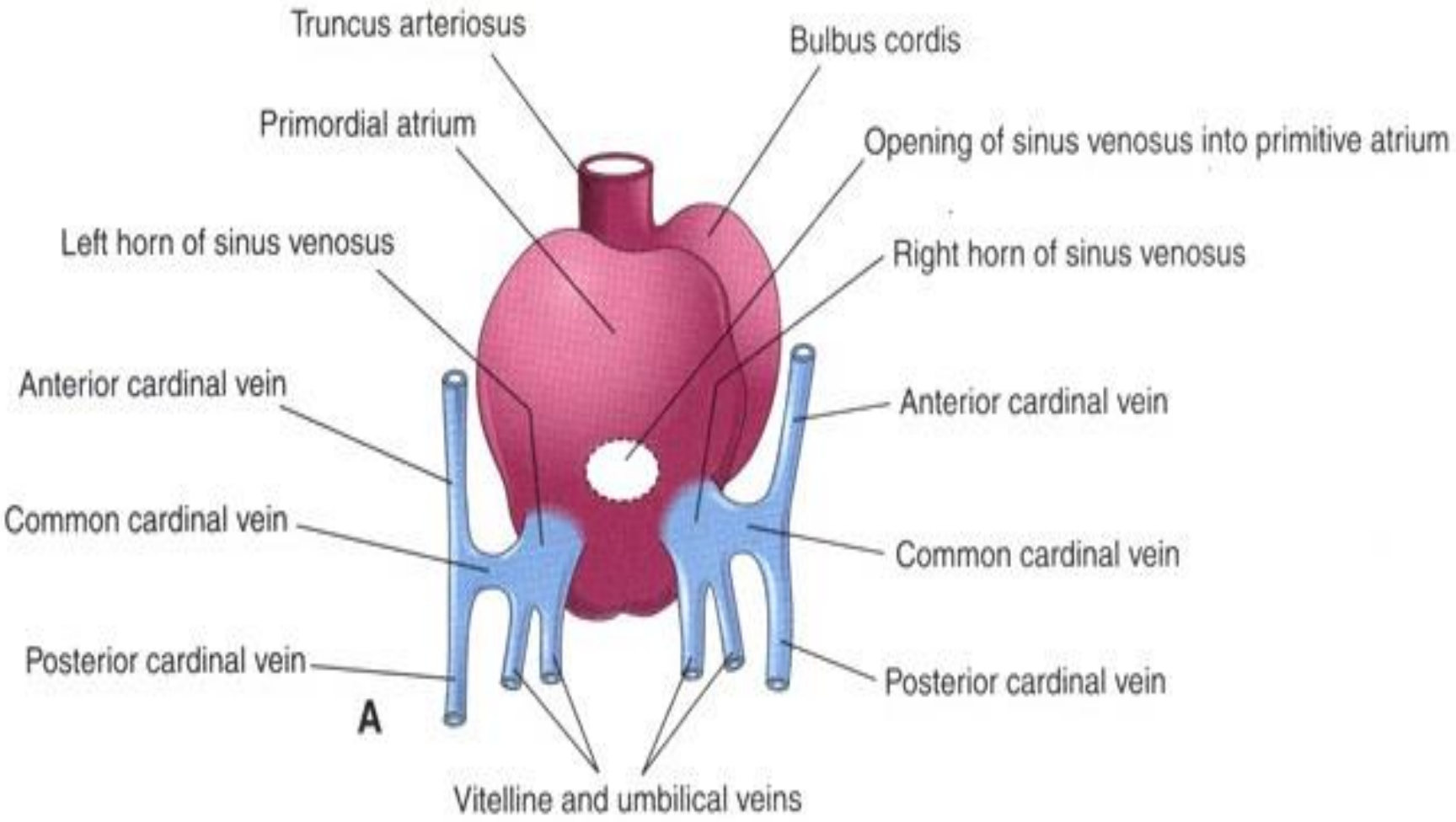


Figure 15–2. Sketch of the embryonic cardiovascular system (about 26 days) showing vessels on the left side only. The umbilical vein carries well-oxygenated blood and nutrients from the chorion (embryonic part of placenta) to the embryo. The umbilical arteries carry poorly oxygenated blood and waste products to the chorion.



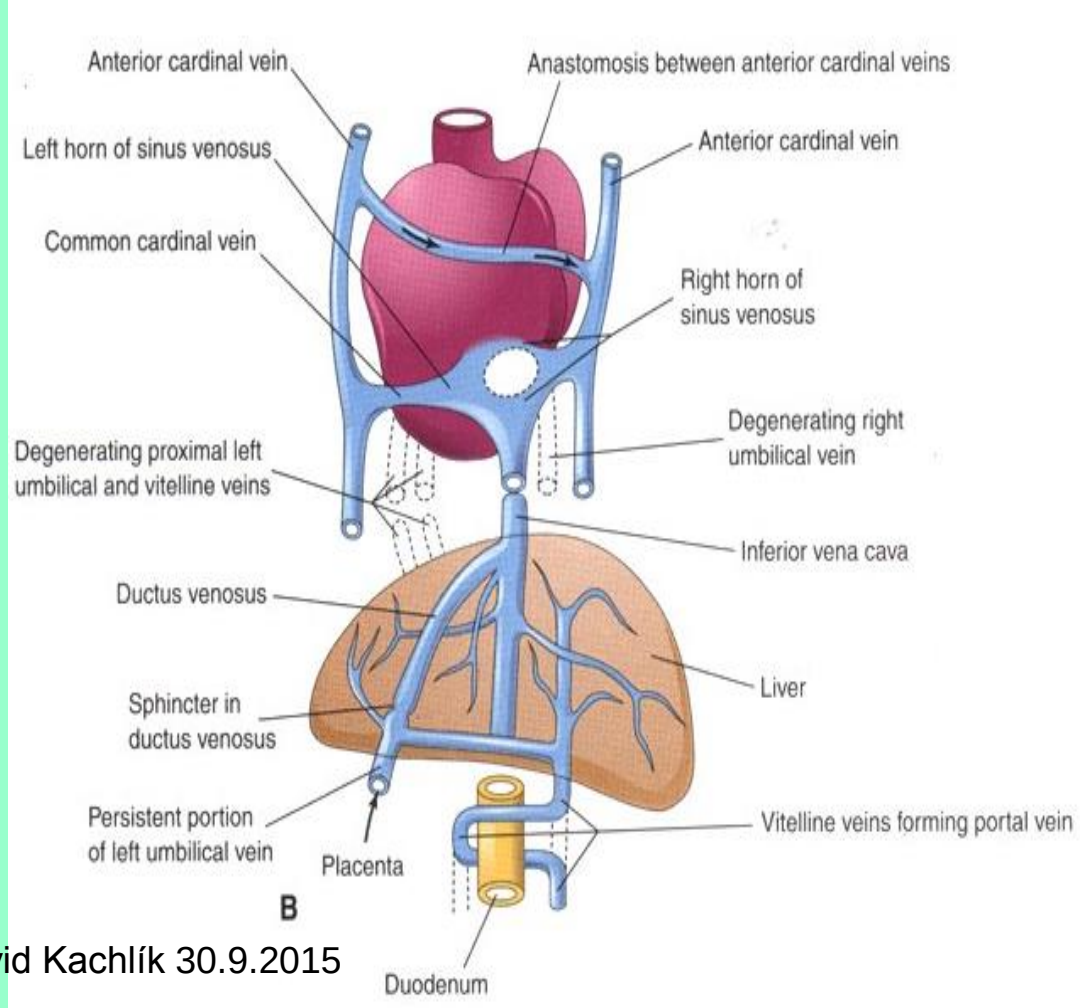
Venae omphalomesentericae

➔ **venae hepaticae**

from remnants of right omphalomesenteric vein

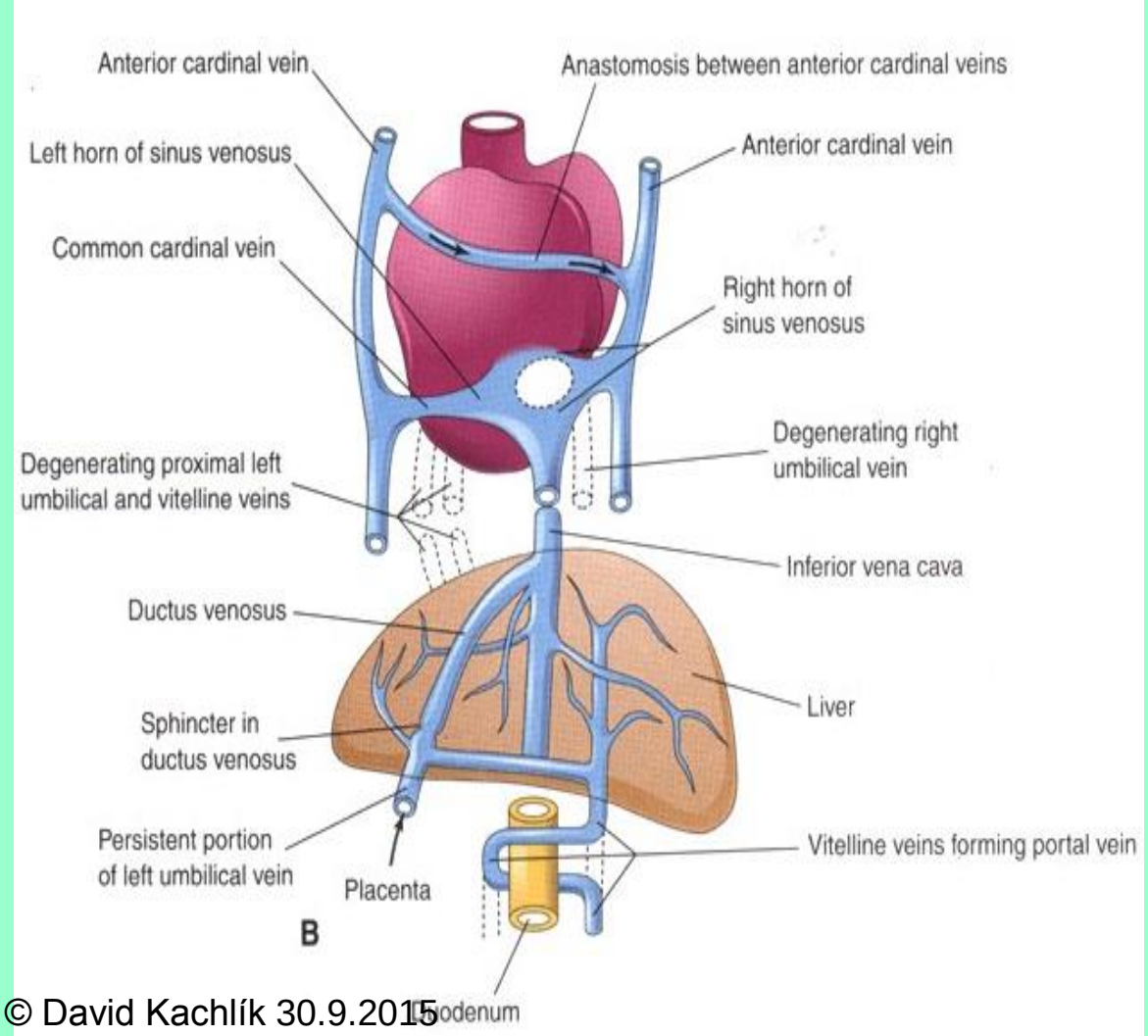
➔ **venae portae**

from an anastomotic network around duodenum



Venae umbilicales

- right and part of left vein degenerate
- persistent part of left vein becomes **vena umbilicalis**
- venous shunt detouring liver – **ductus venosus**

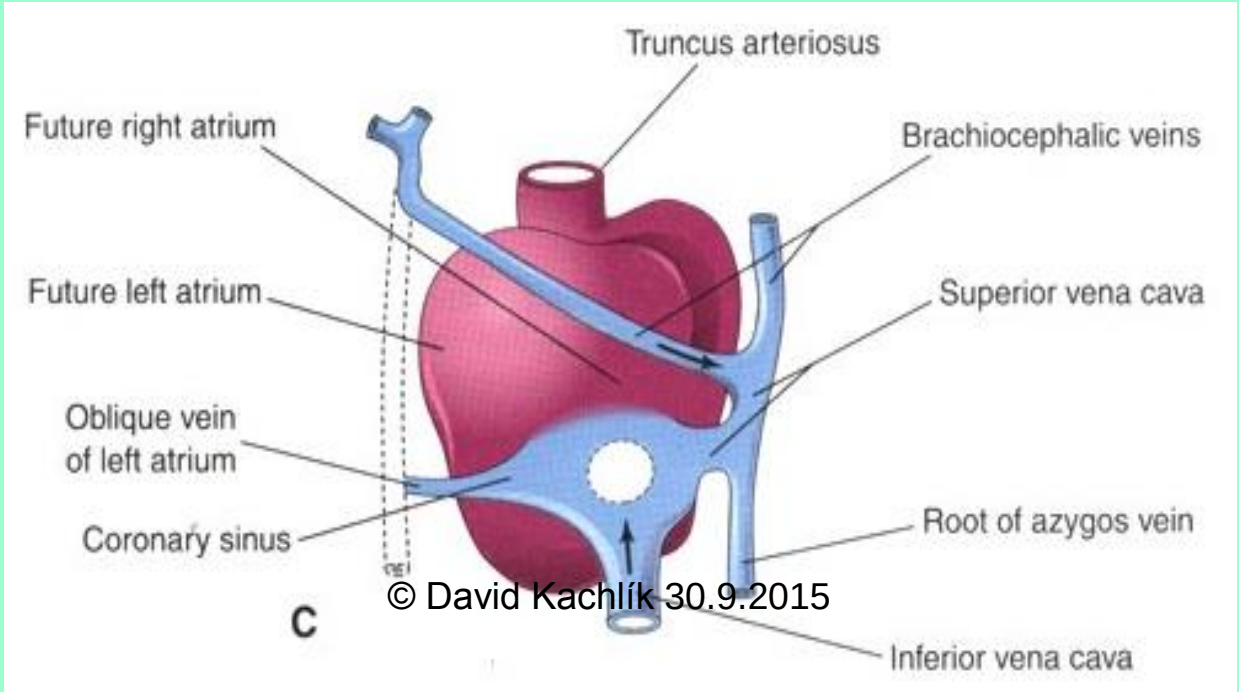


Venae cardinales

- v. precardinalis + v. postcardinalis →

v. cardinalis communis (ductus Cuvieri)

- an oblique anastomosis shunt takes blood from left to right → **v. brachiocephalica sinistra**
- right precardinal vein and right common cardinal vein → **vena cava superior**



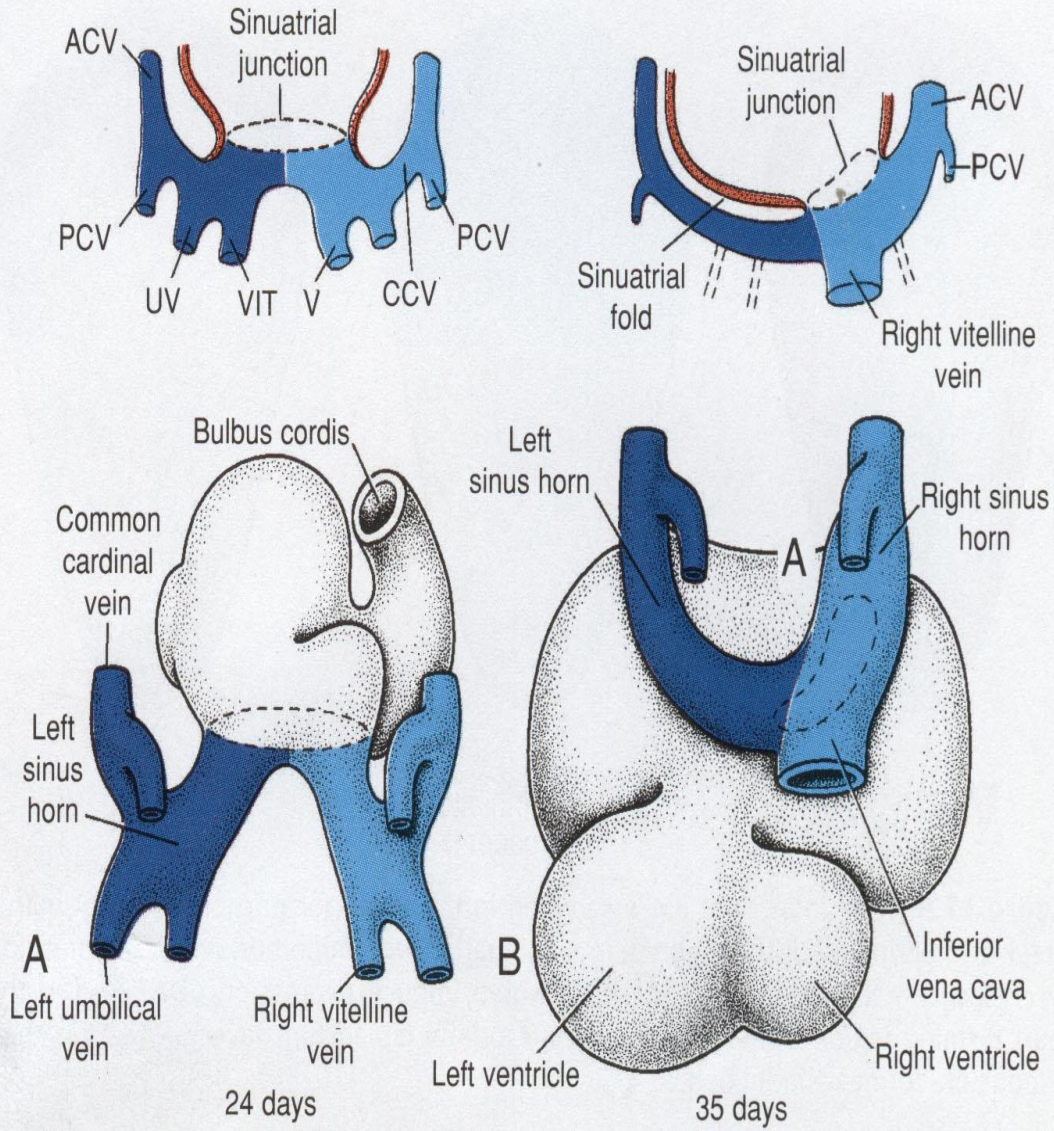
Sinus venosus

- 4th – 5th week
- right and left horn

= smooth part of atrium

- venae pulmonales sprout → their incorporation forms left atrium

trabecular part of atrium = auricles

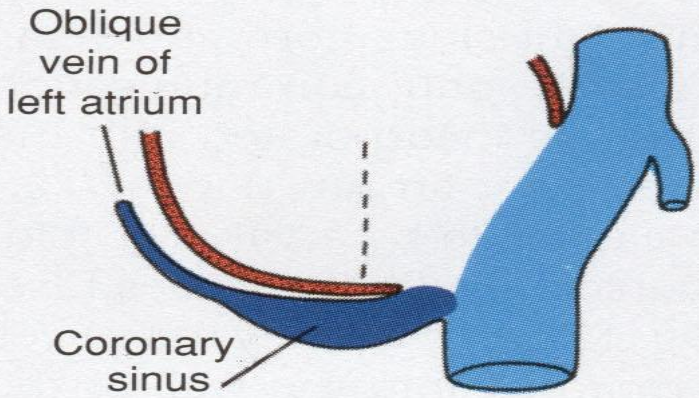


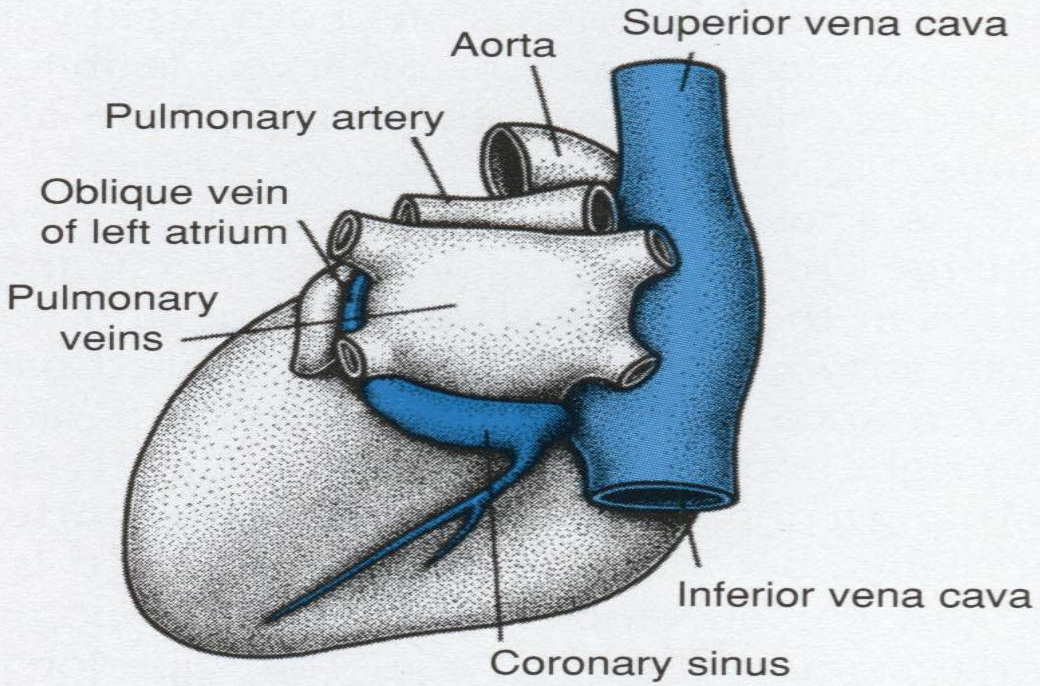
Dorsal view of two stages in the development of the sinus venosus at approximately 24 days **(A)** and 35 days **(B).** *Broken line*, the entrance of the sinus venosus into the atrial cavity. Each drawing is accompanied by a scheme to show in transverse section the great veins and their relation to the atrial cavity. *ACV*, anterior cardinal vein; *PCV*, posterior cardinal vein; *UV*, umbilical vein; *VIT V*, vitelline vein; *CCV*, common cardinal vein. (See also Fig. 11.41.)

Changes in sinus venosus

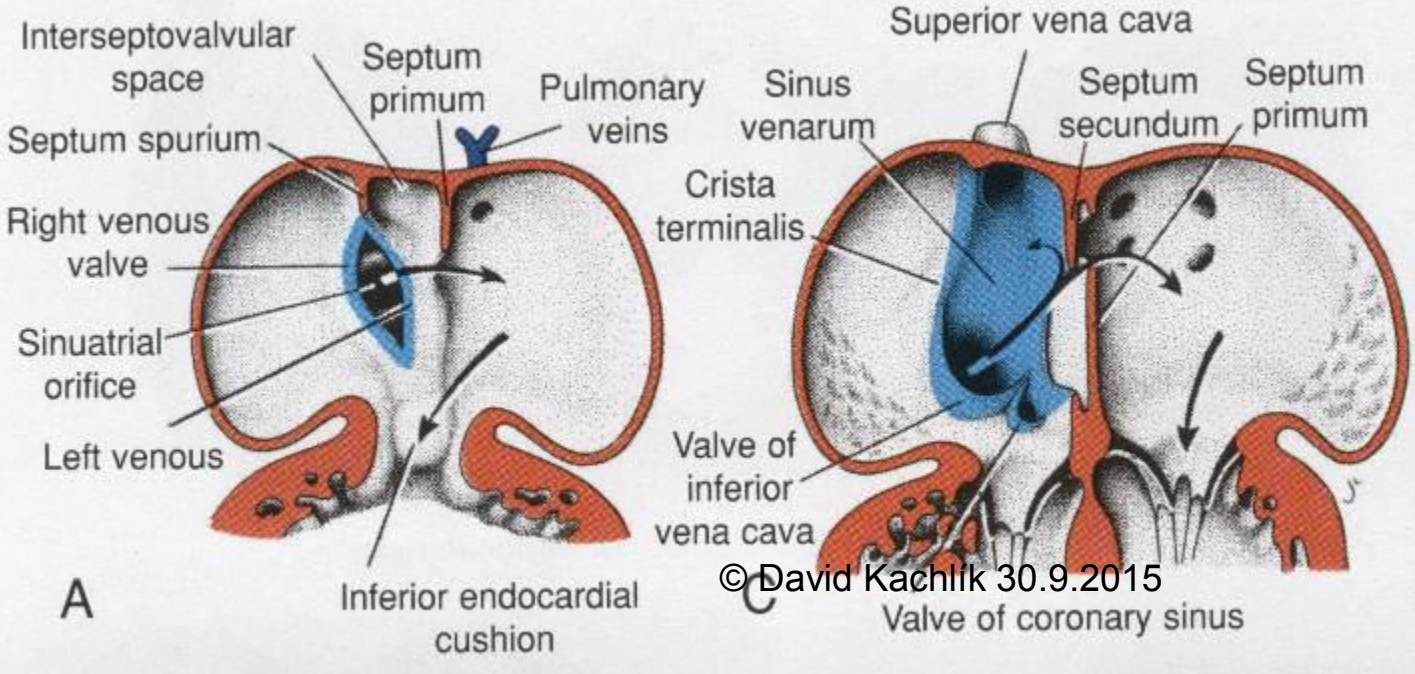
- right horn
  - enlarges, receives all the blood from cranila regions of body (VCS), from placenta and caudal regions of body (VCI)
  - becomes incorporated into wall of right atrium
- left horn
  - decreses in size and importance
  - becomes ***sinus coronarius***
- valvulae sinuatriales
  - dx: valvula VCI + valvula SC
  - sin: part of interatrial septum

Week 5





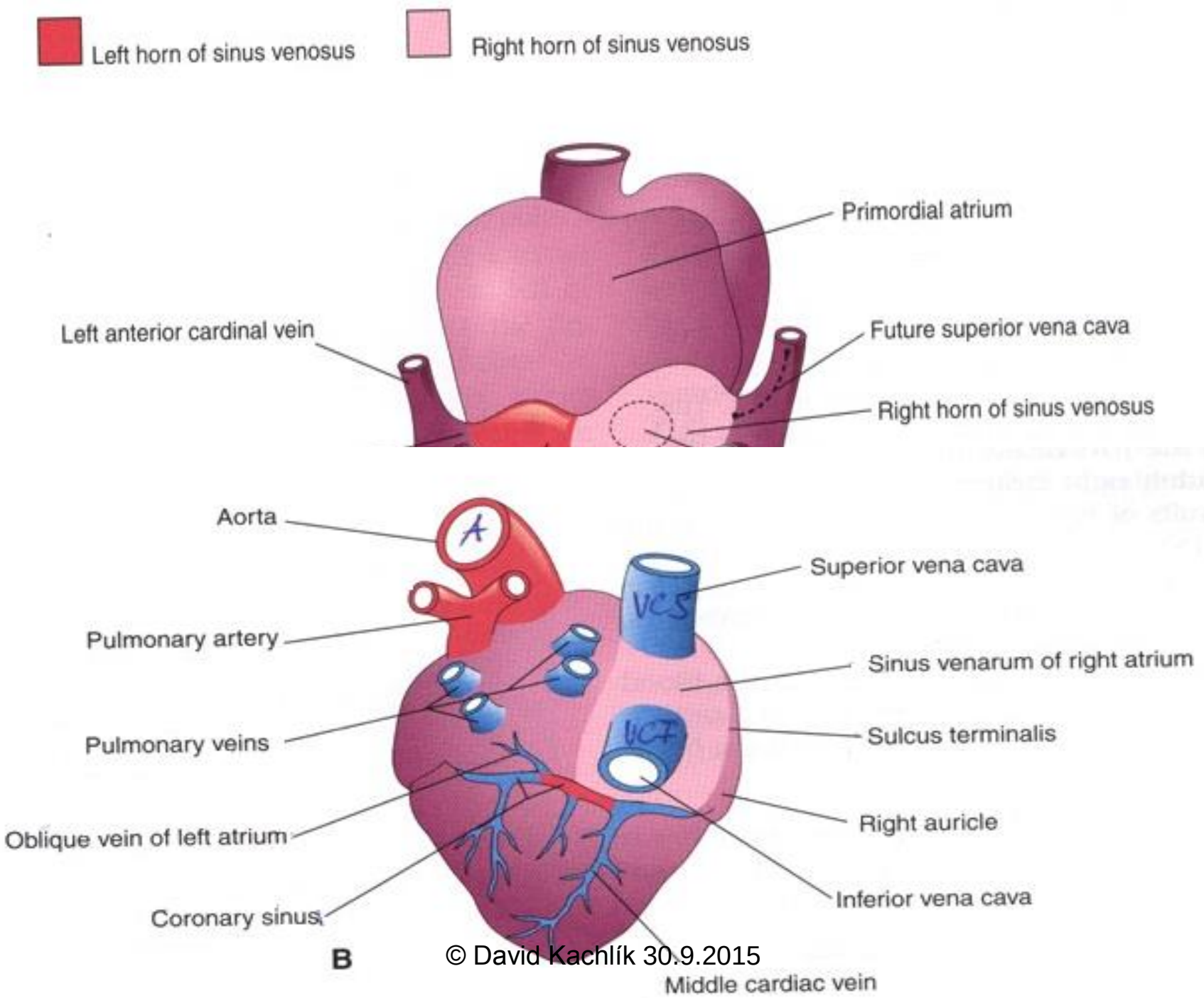
Final stage in development of the sinus venosus and great veins.



Atrium

smooth walled part (sinus venarum)

trabeculated part (auricle)



Adult Derivatives of Fetal Vascular Structures

- vena umbilicalis → ligamentum teres hepatis
- ductus venosus → ligamentum venosum
- aa. umbilicales → ligg. umbilicalia medialia, proximal parts persist as arteriae vesicales superiores

Heart in motion

Heart malformations

0.6 - 0.8%

critical period - from 3th to 6th week

Heart malformations

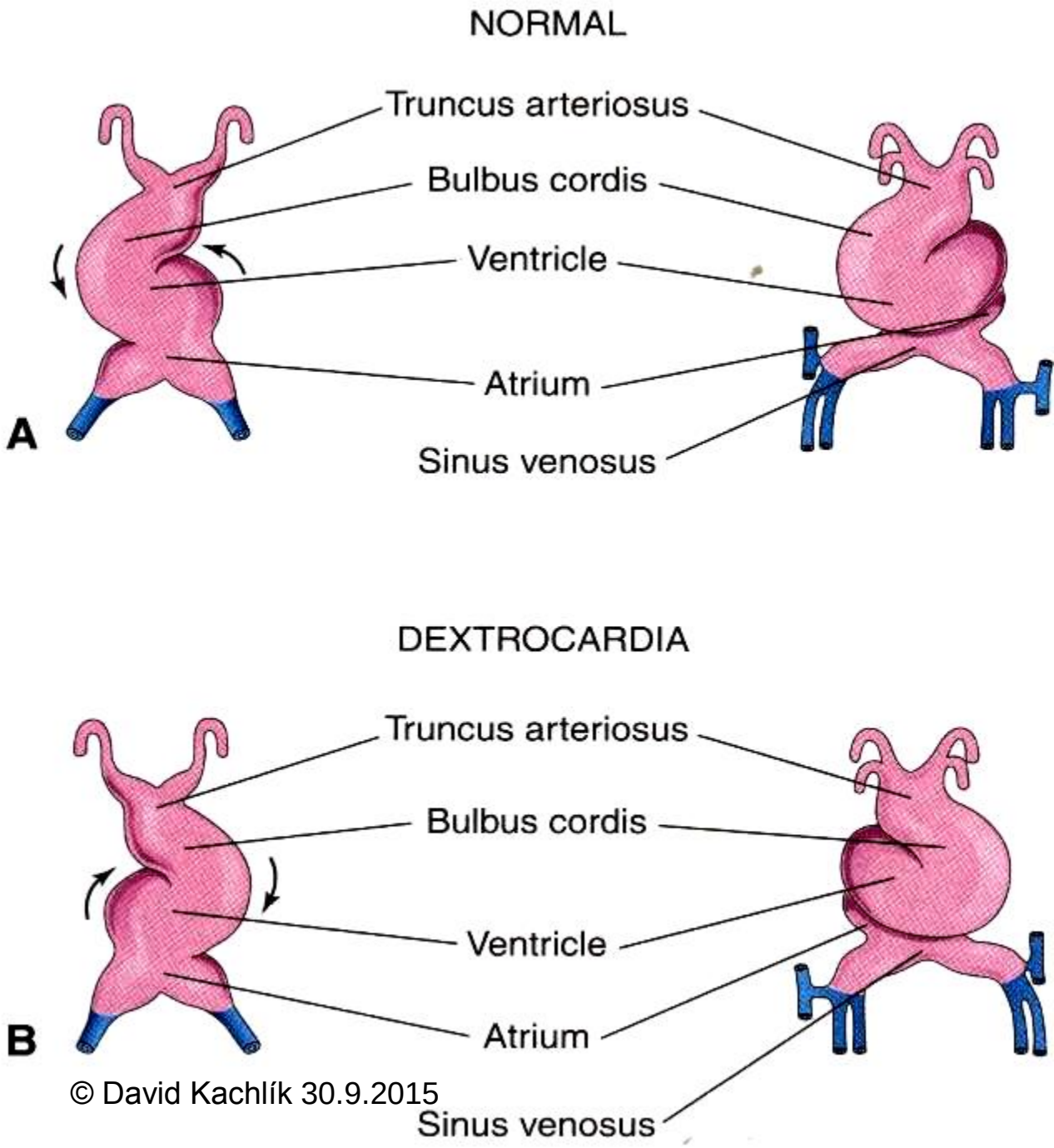
- abnormaities of heart partioning
  - cor biloculare, triloculare
  - **atrial septal defect** (*second most common*)
  - **ventricular septal defect** (*most common*)
  - transposition of great vessels
    - tetralogy of Fallot (trilogy, pentalogy)
  - persistent ductus arteriosus Botalli

Heart malformations

- principal abnormalities
  - acardia, diplocardia, ectopia cordis
- abnormalities of cardiac looping
  - situs inversus, heterotaxia (dextrocardia)
- valve anomalies
  - stenosis, atresia, dysplasia
    - dysplasia of tricuspid valve and right ventricle (of Ebstein)

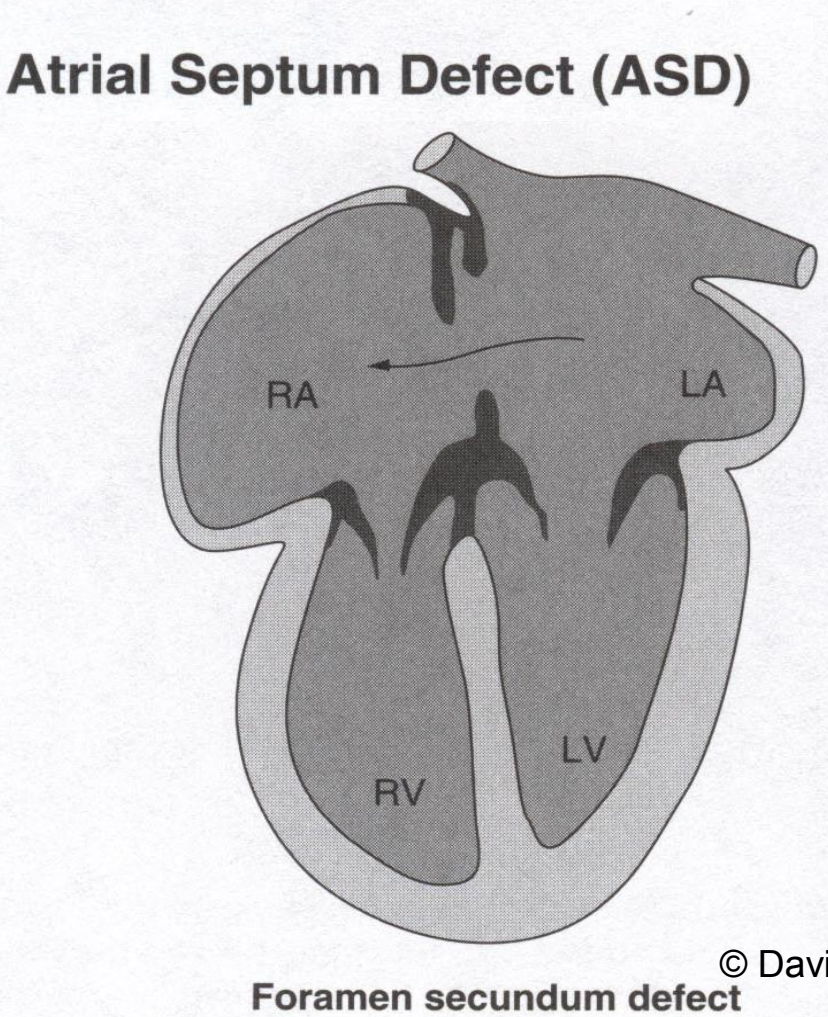
Abnormality in looping process

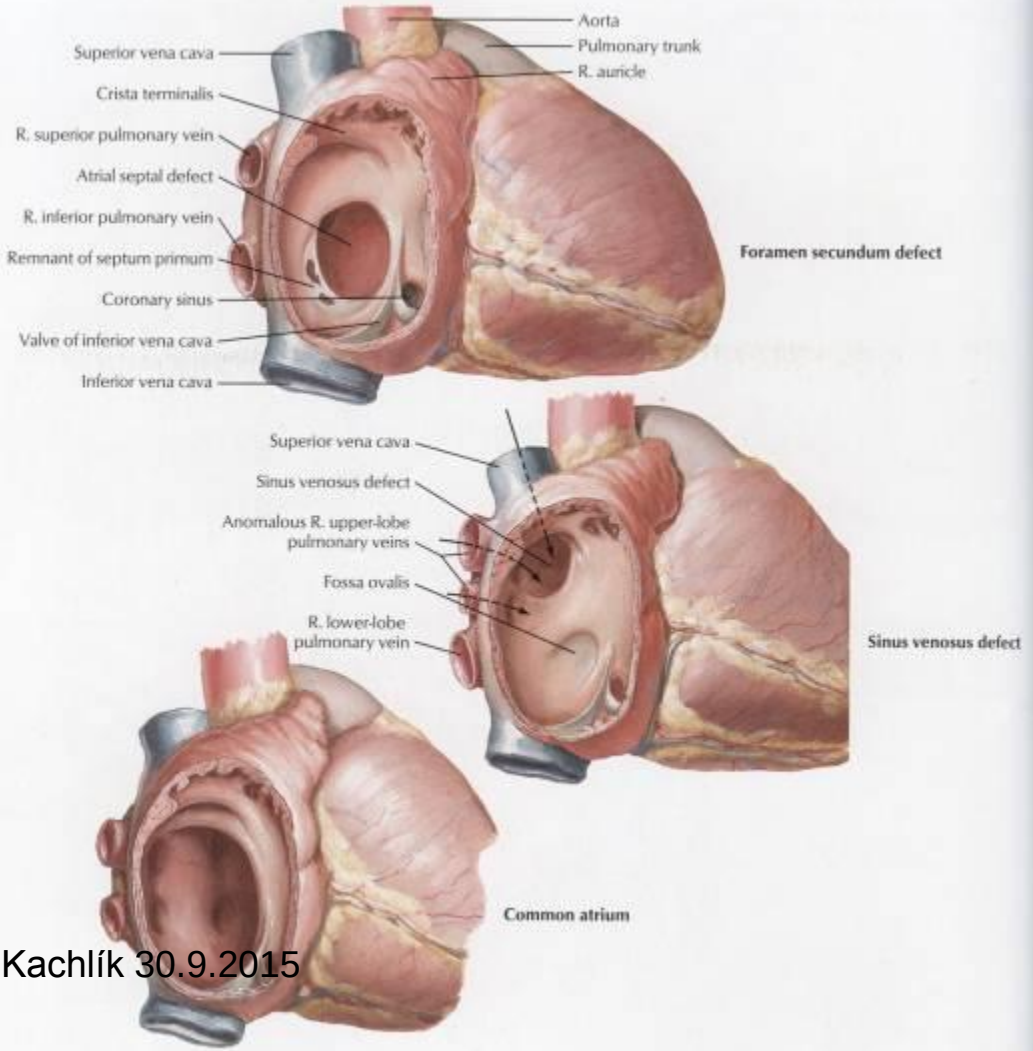
dextrocardia



Atrial septal defect

Small defects - clinical symptoms may be delayed as age 30
Premature closure of foramen ovale results in hypertrophy of the right side of the heart

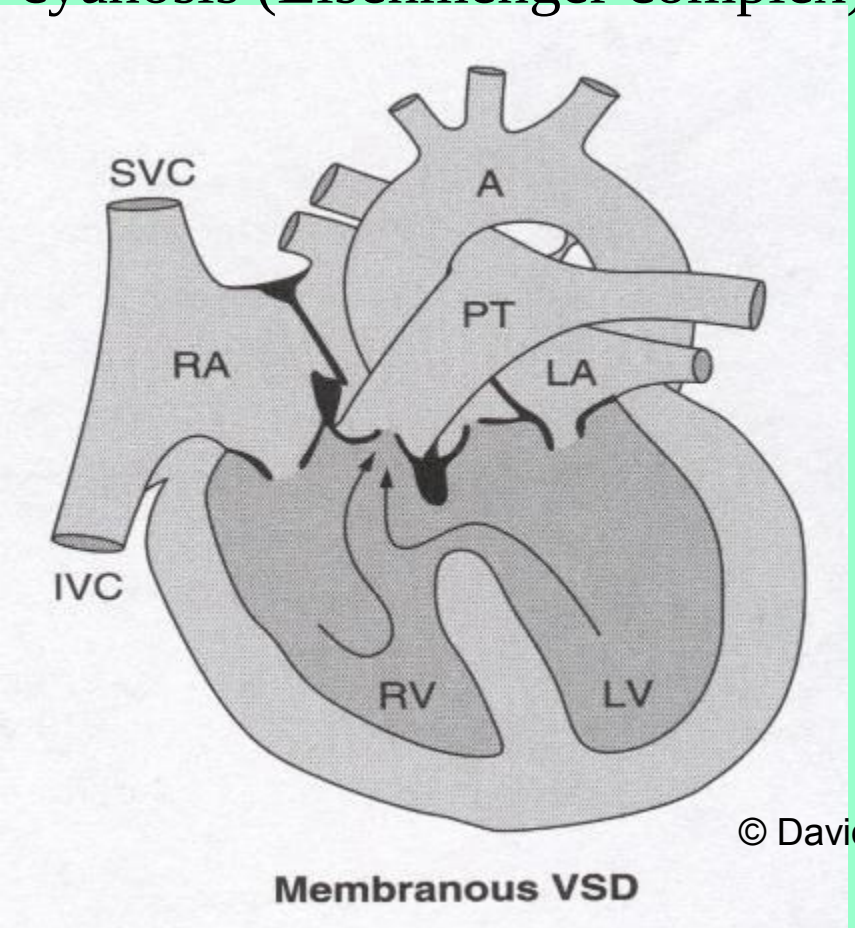


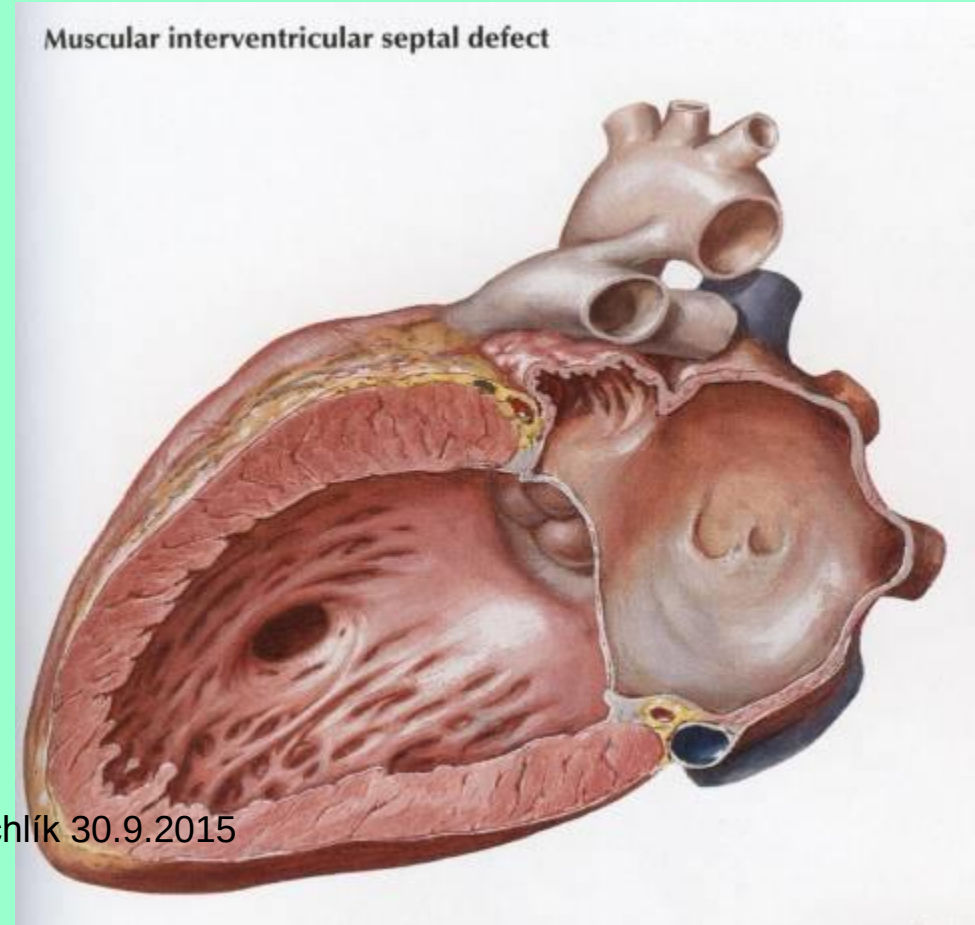


Ventricular septal defect

left to right shunting of blood, excessive fatigue upon exertion

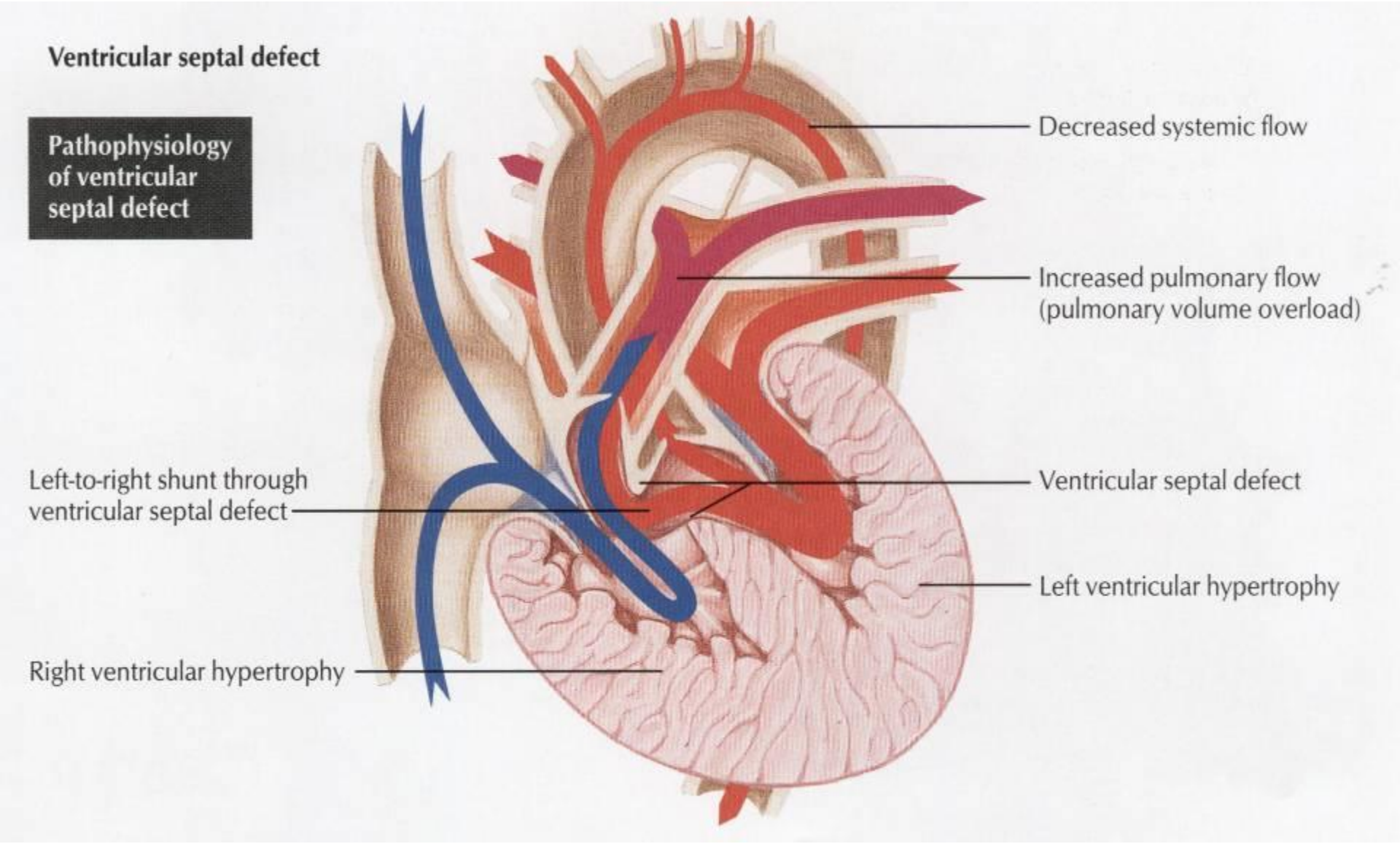
- pulmonary blood flow is increased resulting in pulmonary hypertension
- intima and media proliferate → lumina of pulmonary arteries narrower
- later pulmonary resistance causes right to left shunting of blood and cyanosis (Eisenmenger complex)





Ventricular septal defect

Pathophysiology of ventricular septal defect

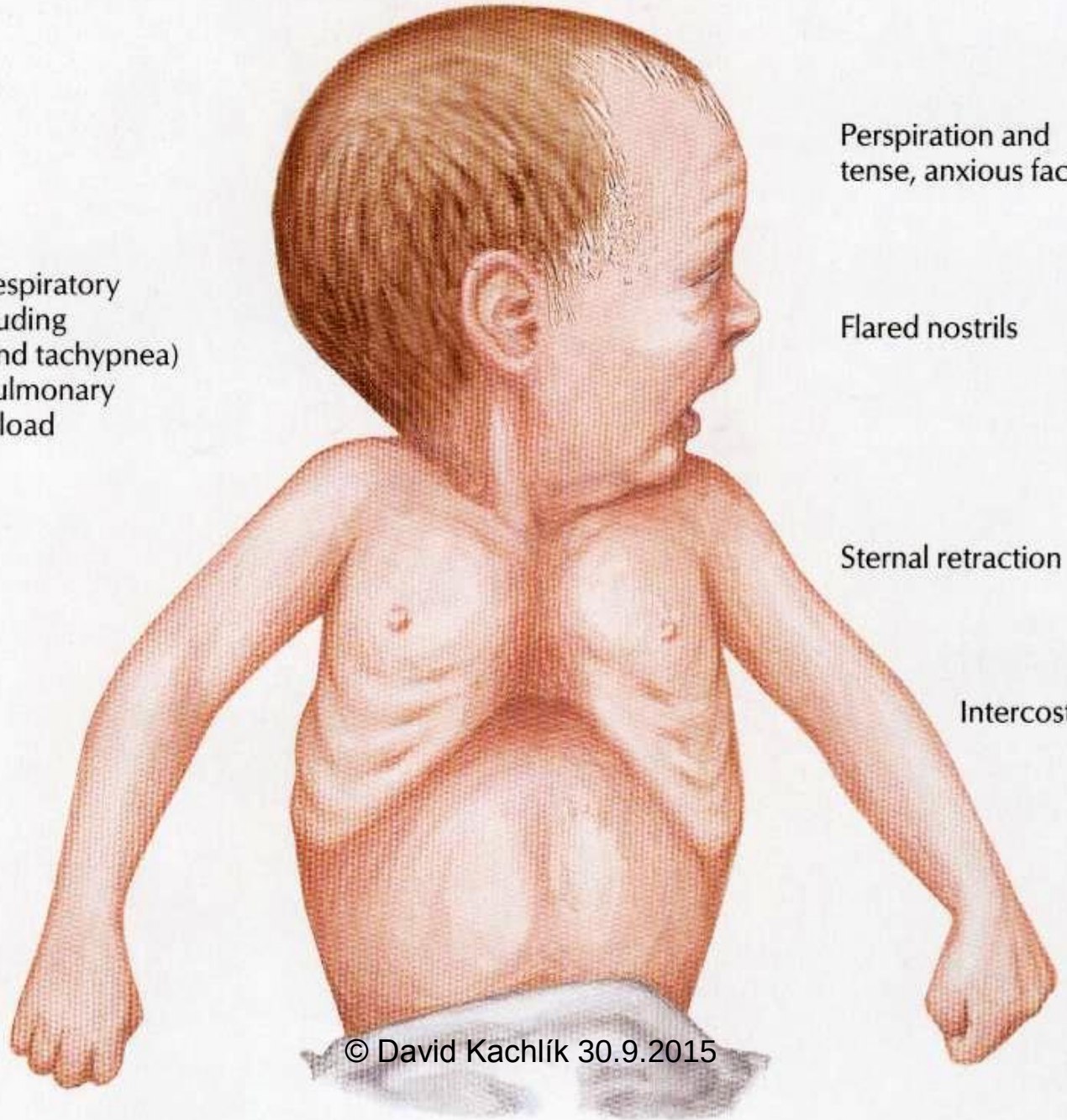


Clinical characteristics of too little pulmonary flow

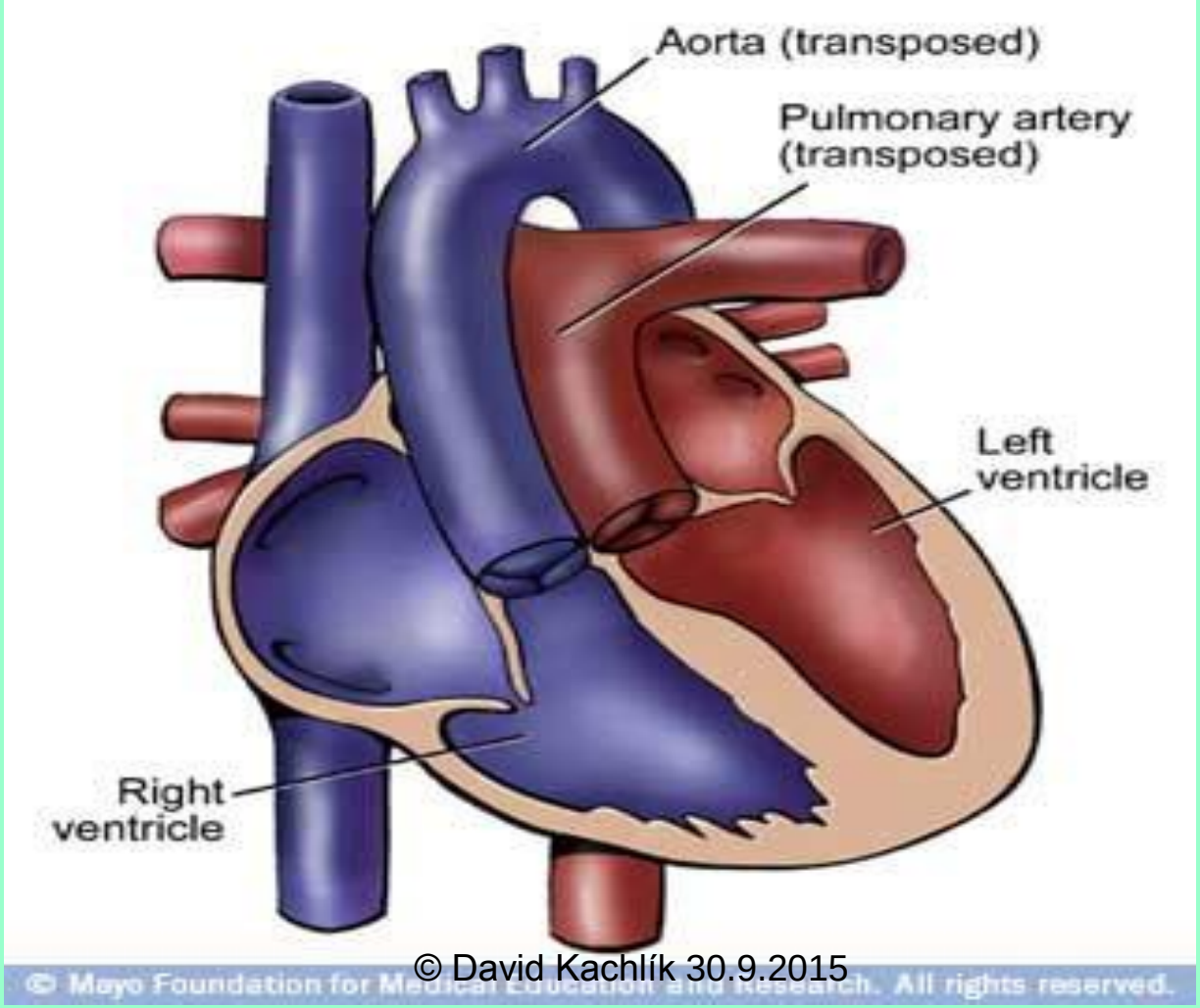
Cyanosis

Clubbing of fingers

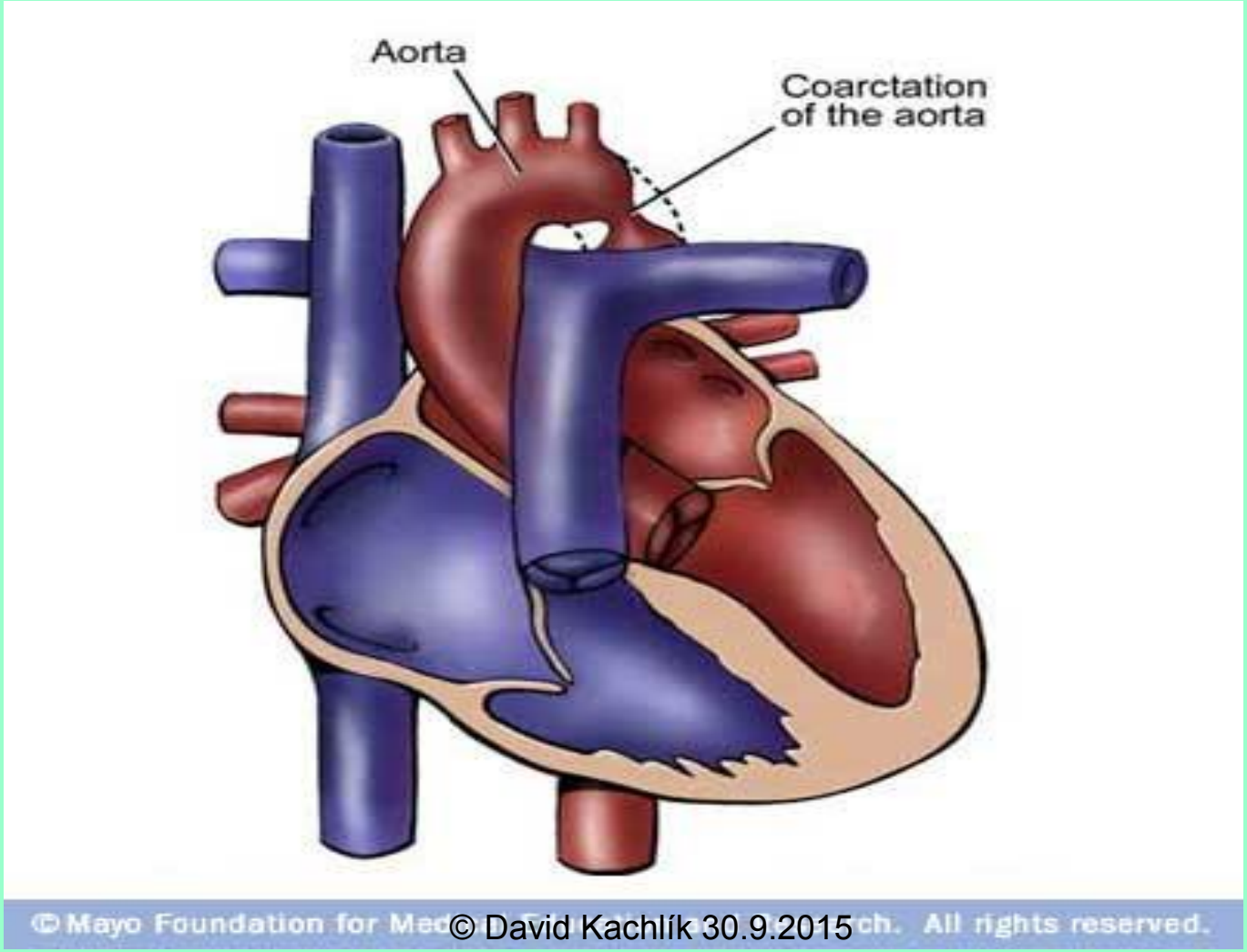
Clinical characteristics of too much pulmonary flow (pulmonary volume overload)



Transposition of great arteries



Coarctation of aorta



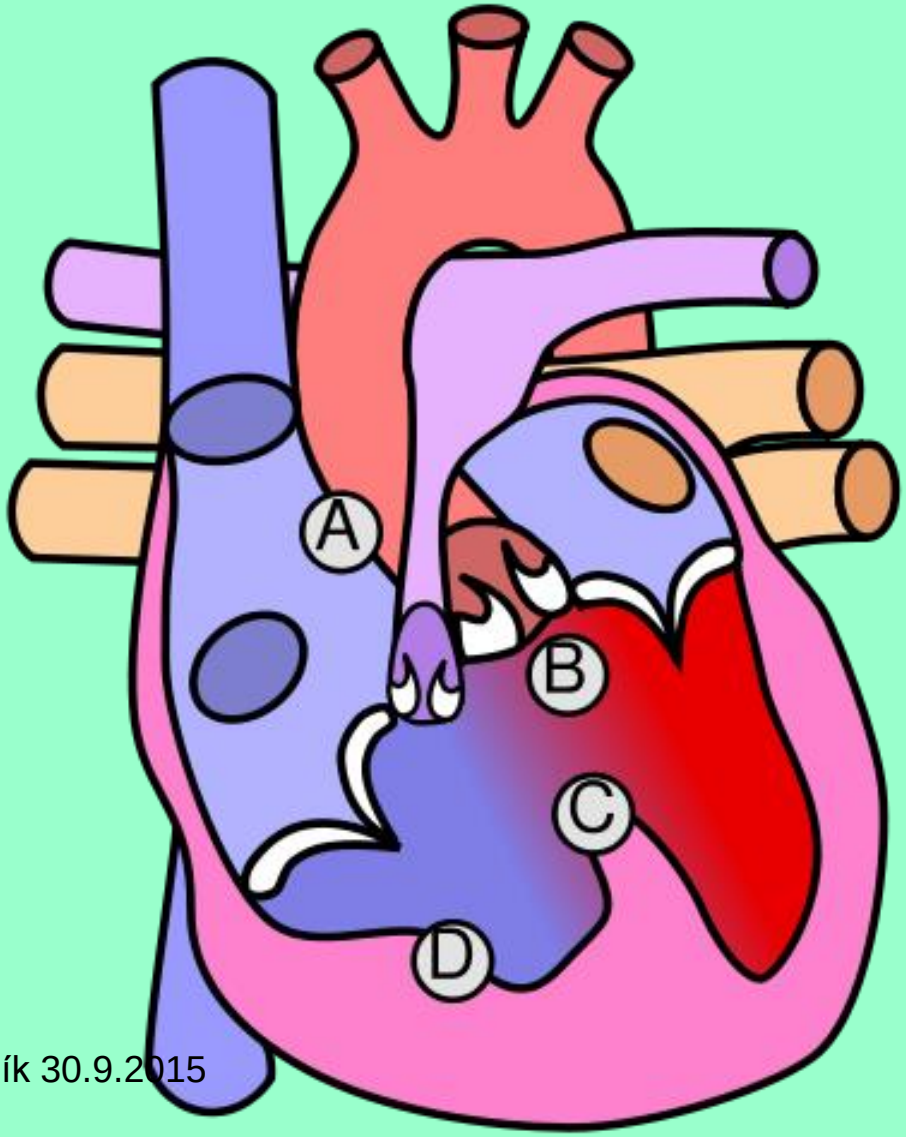
Tetralogy of Fallot

A – dextroposition of aorta (overriding aorta)

B – pulmonary stenosis (obstruction to right ventricle outflow)

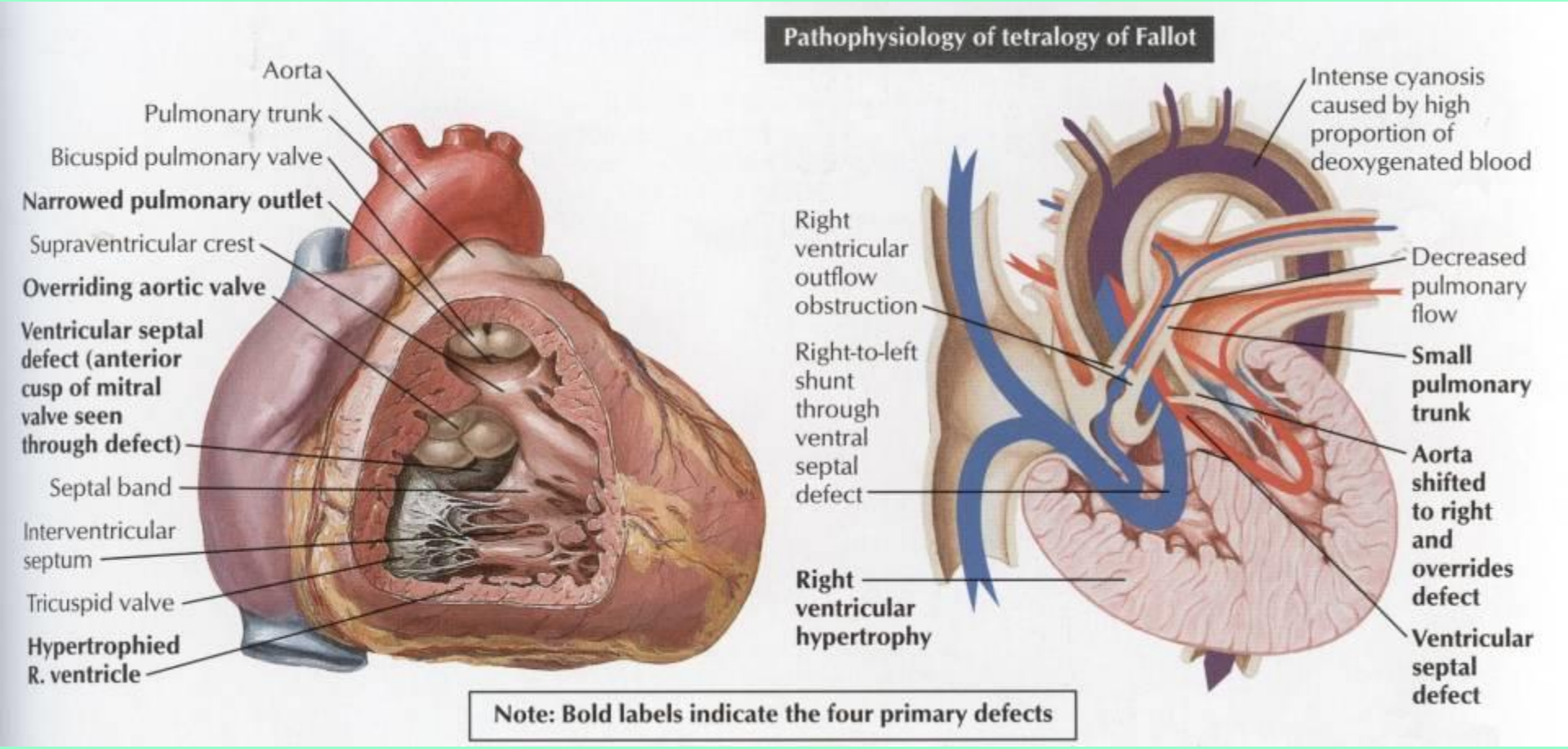
C – ventricular septal defect

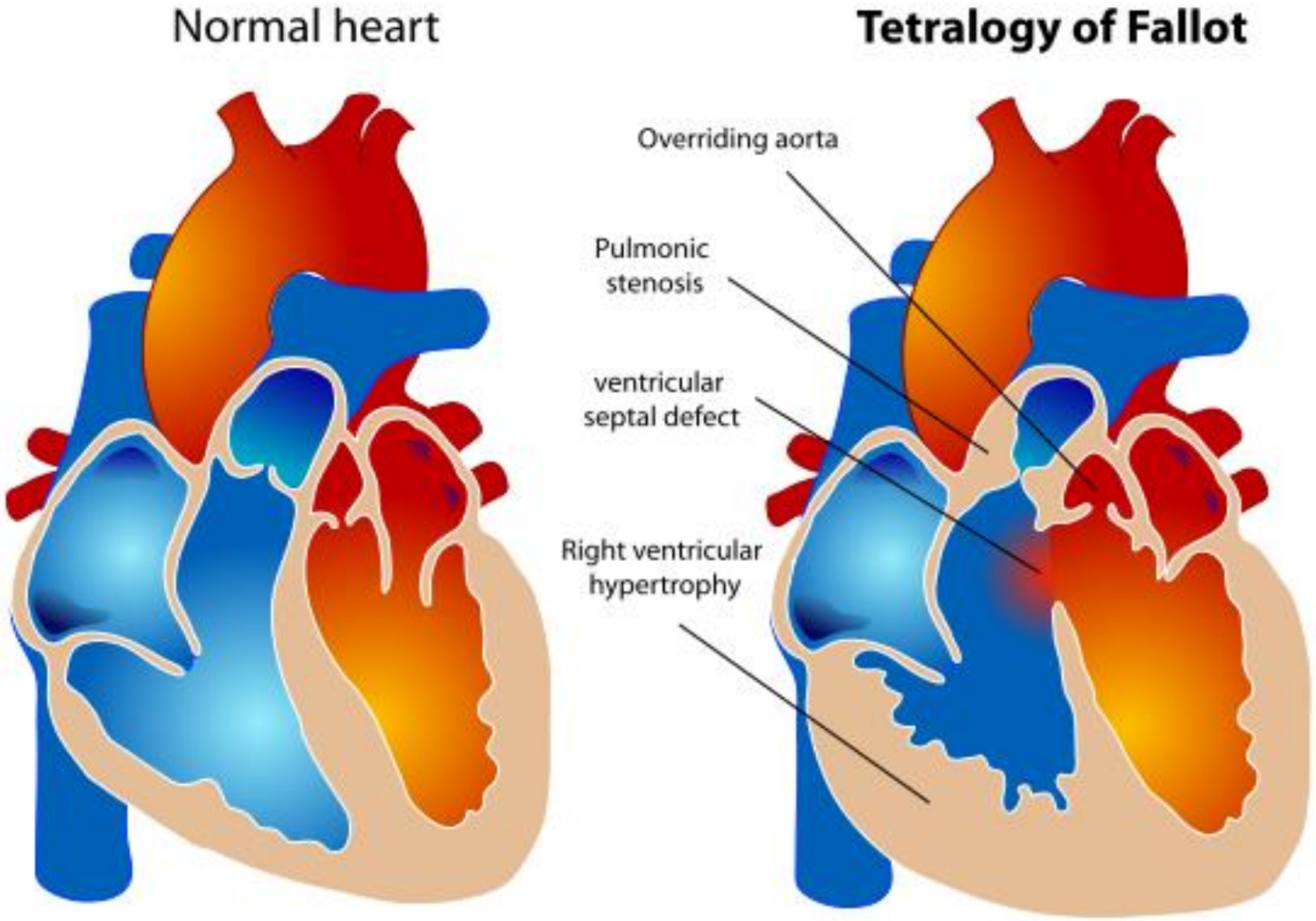
D – right ventricular hypertrophy



Tetralogy of Fallot

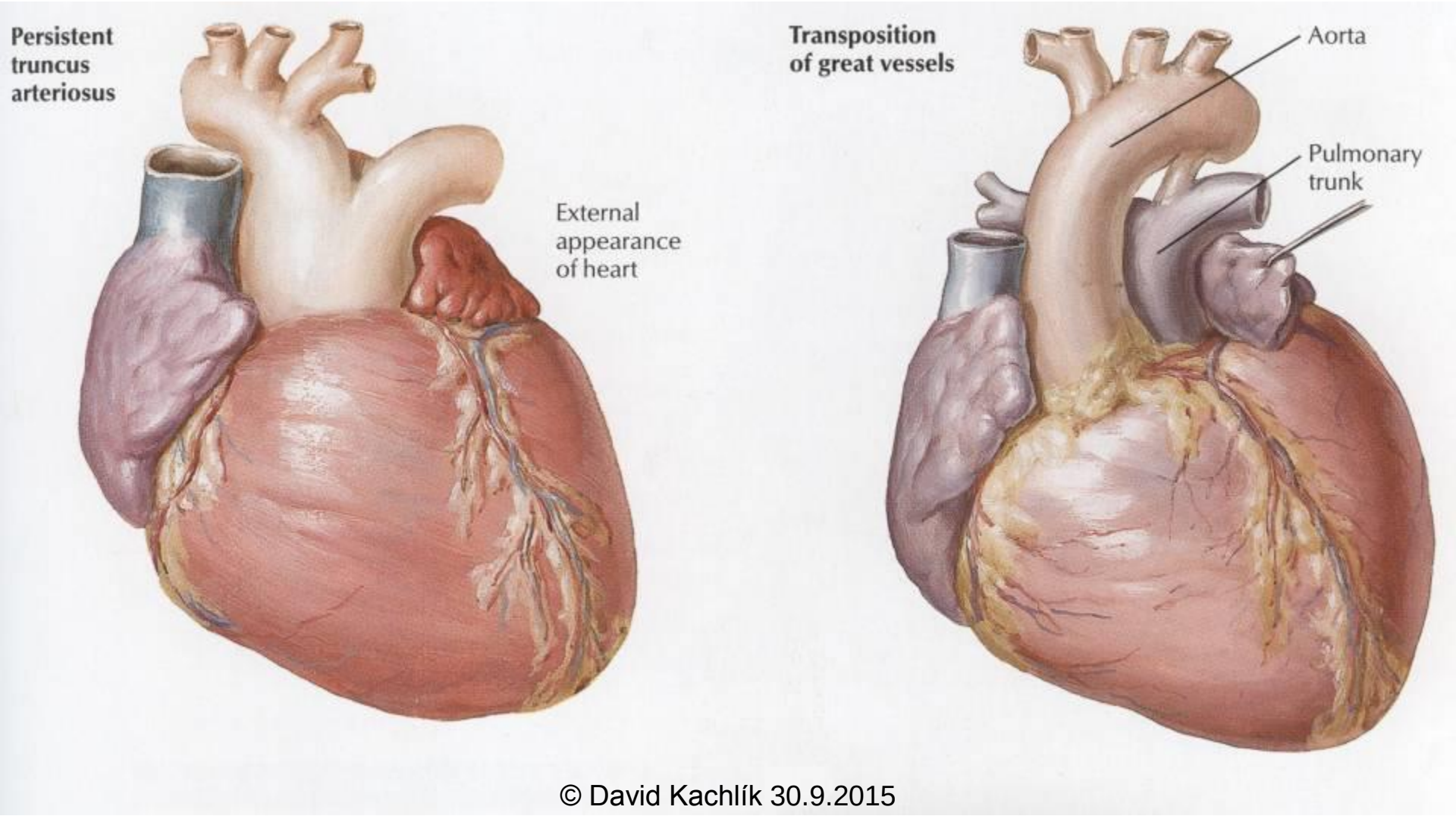
1 ‰



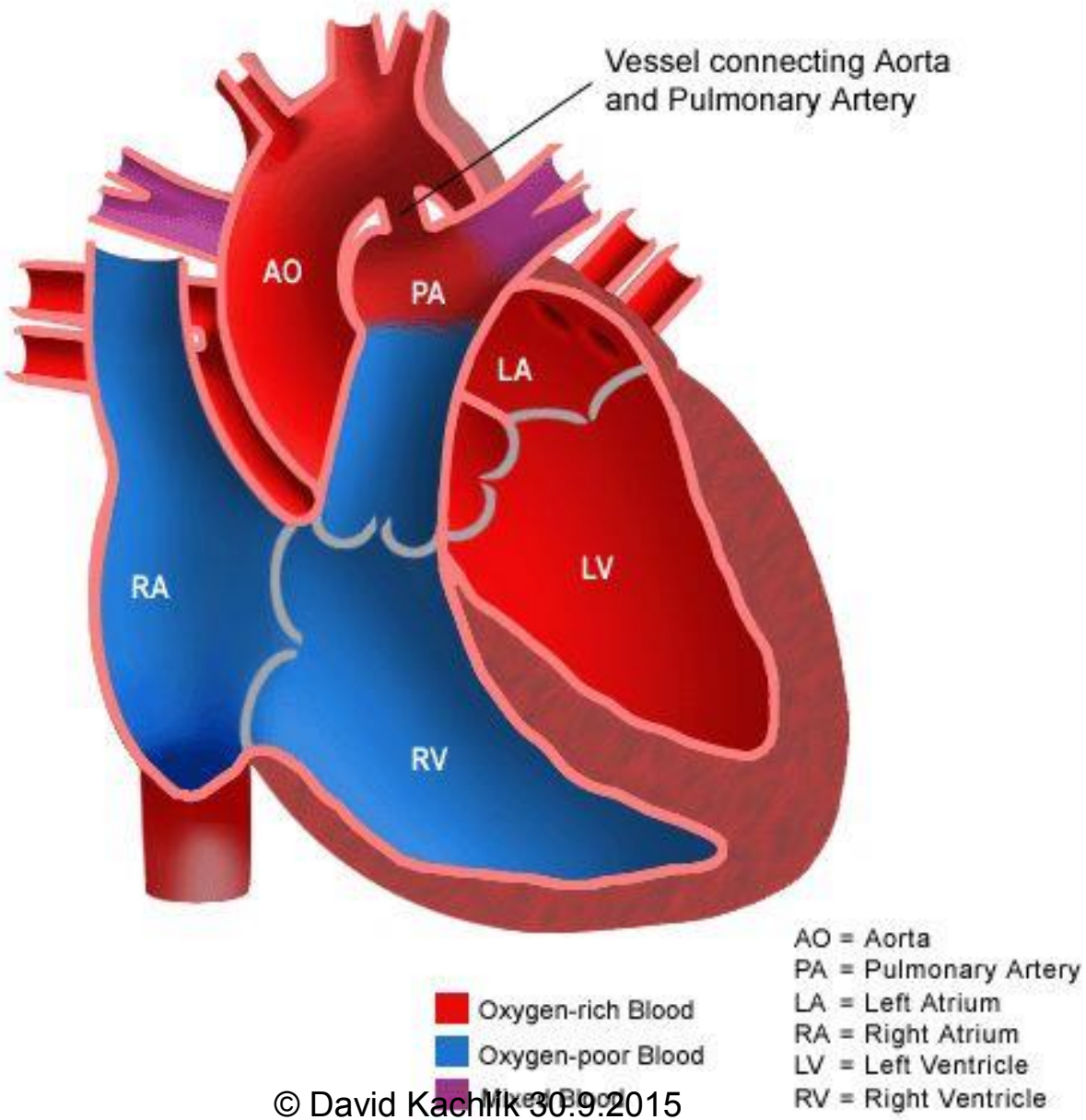


Persistent truncus arteriosus

Transposition of great vessels



Patent Ductus Arteriosus (PDA)

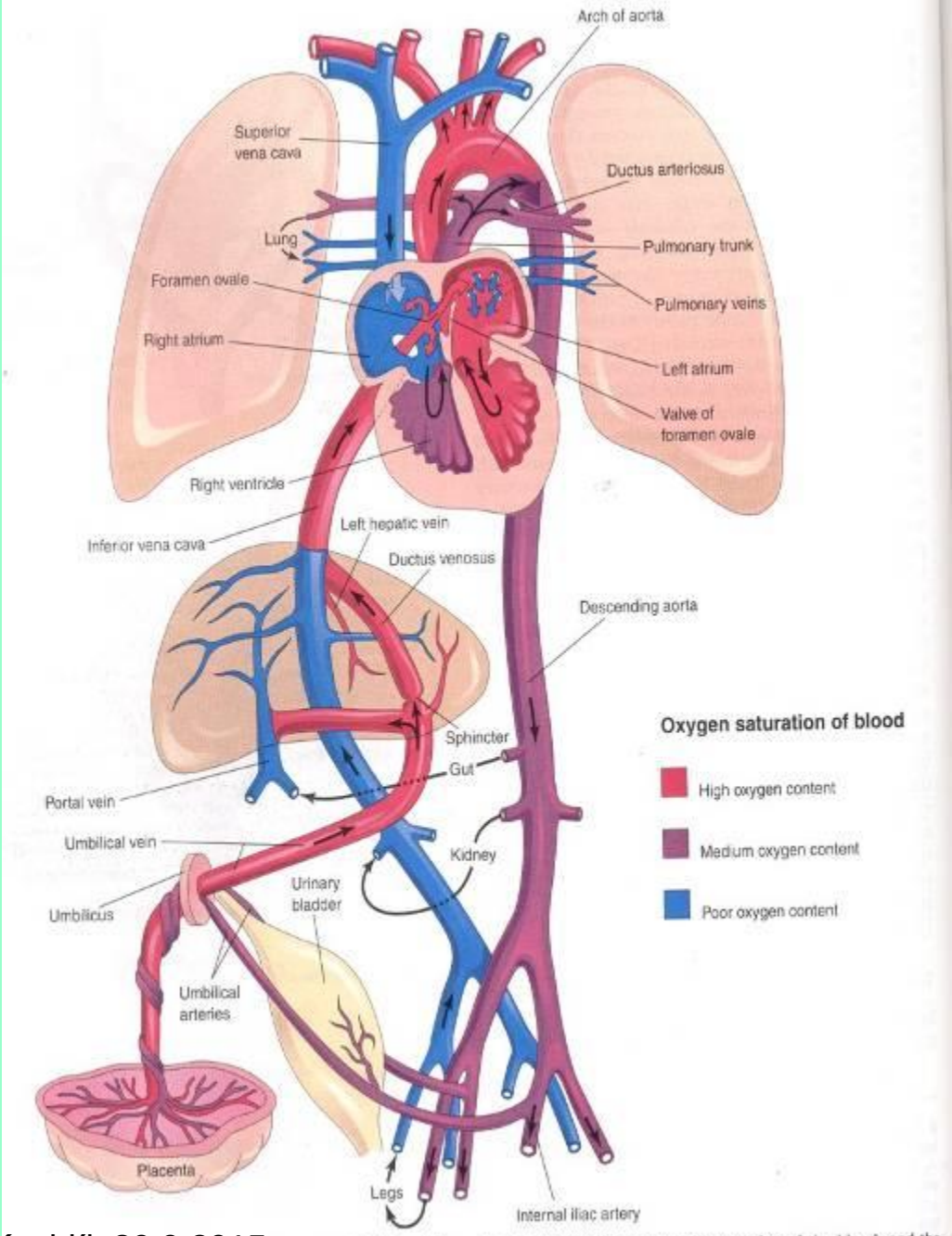


Causes of heart defects

- multifactorial
- teratogenes
  - rubella, thalidomide, vitamine A, alcohol, diabetes
- genetic
  - 33% children with chromosomal abnormalities have a heart defect,
  - 100% with trisomy of chromosome 18

Fetal circulation

- ductus venosus (Arantii)
- foramen ovale
- ductus arteriosus (Botalli)



arrows show the course of the blood from the placenta to the heart. The organs are not drawn to scale. Observe that three shunts permit most of the blood to bypass the liver and lungs: (1) ductus venosus, (2) foramen ovale, and (3) ductus arteriosus. The poorly oxygenated blood returns to the placenta for oxygen and nutrients through the umbilical arteries.

Neonatal circulation

- aeration of lungs
- sphincter in ductus venosus constricts
- foramen ovale closes
- ductus venosus and umbilical arteries constrict
- ductus arteriosus constricts

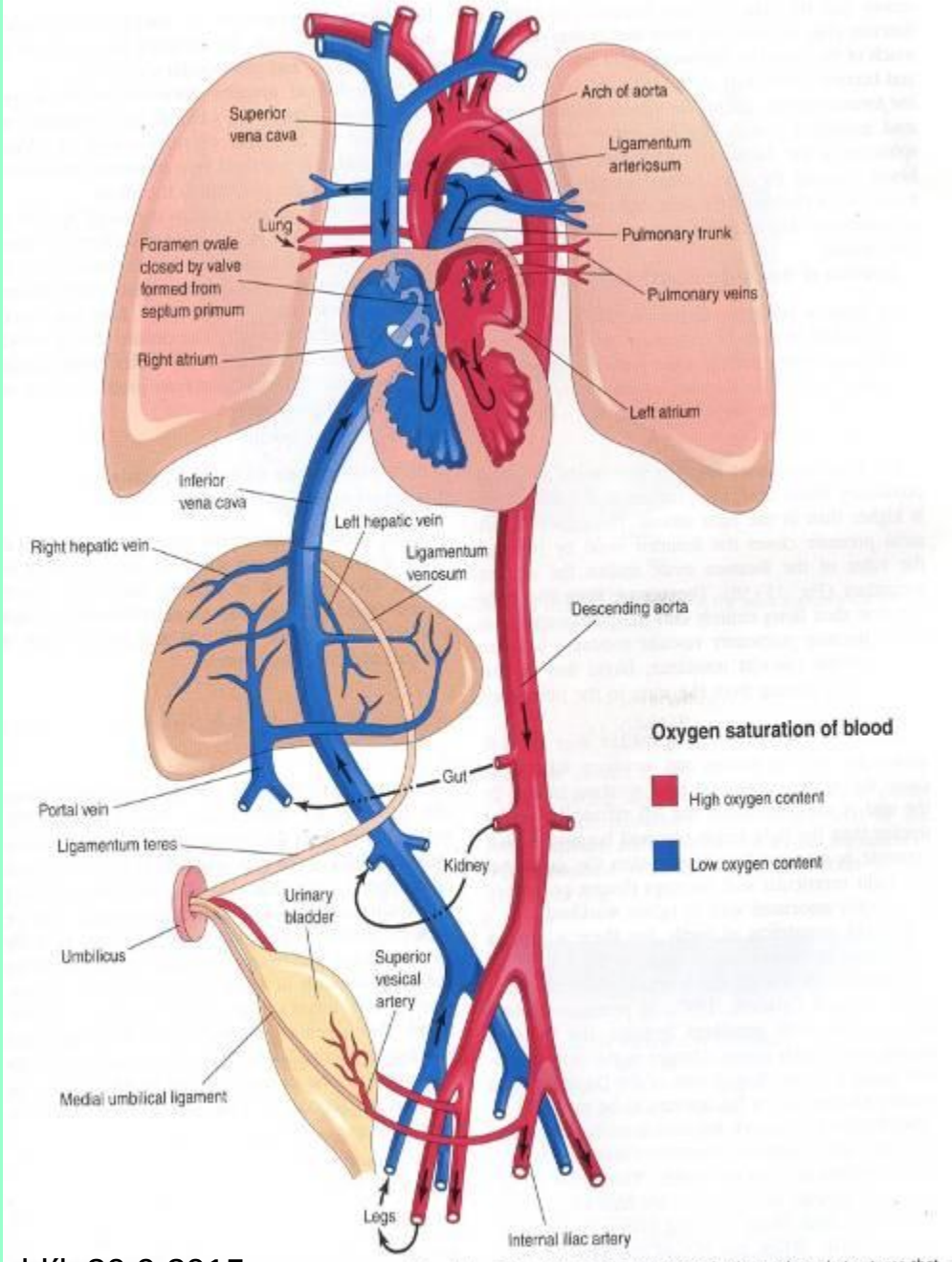


Figure 15-38. Schematic illustration of the neonatal circulation. The adult derivatives of the fetal vessels and structures that become nonfunctional at birth are also shown. The arrows indicate the course of the blood in the infant. The organs are not drawn to scale. After birth the three shunts that short-circuited the blood during fetal life cease to function, and the pulmonary and systemic circulations become separated.