DEVELOPMENT OF CARDIOVASCULAR SYSTEM

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Lecture 1, March 2017

Outline -1: General Principles

1. Early development of CVS
2. Sources of cells
3. General events
4. Vasculogenesis
5. Angiogenesis

Outline-2:Cardiogenesis

1. Site and induction
2. Cardiac precursor cells
3. Origin of cardiac mesodermal cells
4. Formation of primitive heart tube
5. Transformation of heart tube
6. Derivatives of heart tubes

Developmental disorders

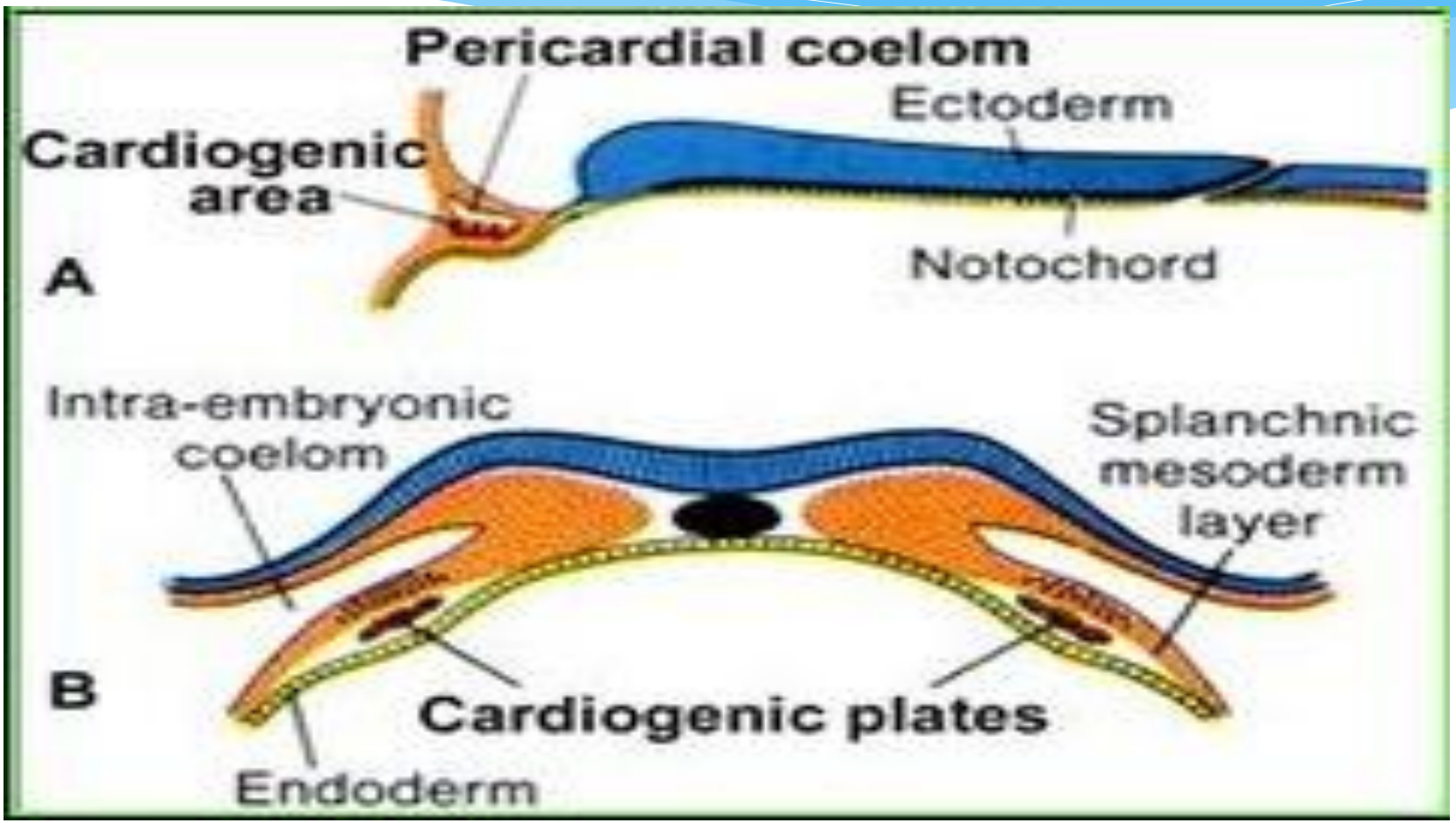
Early Development of CVS

1. Precedes other organs
2. To serves needs of other systems
3. Starts development day 15
4. Heart starts pumping on day 22
5. Essential for embryonic viability

Sources of Cells -1

1. Splanchnic mesoderm
2. Yolk sac
3. Neural crest
4. Coelomic epithelium

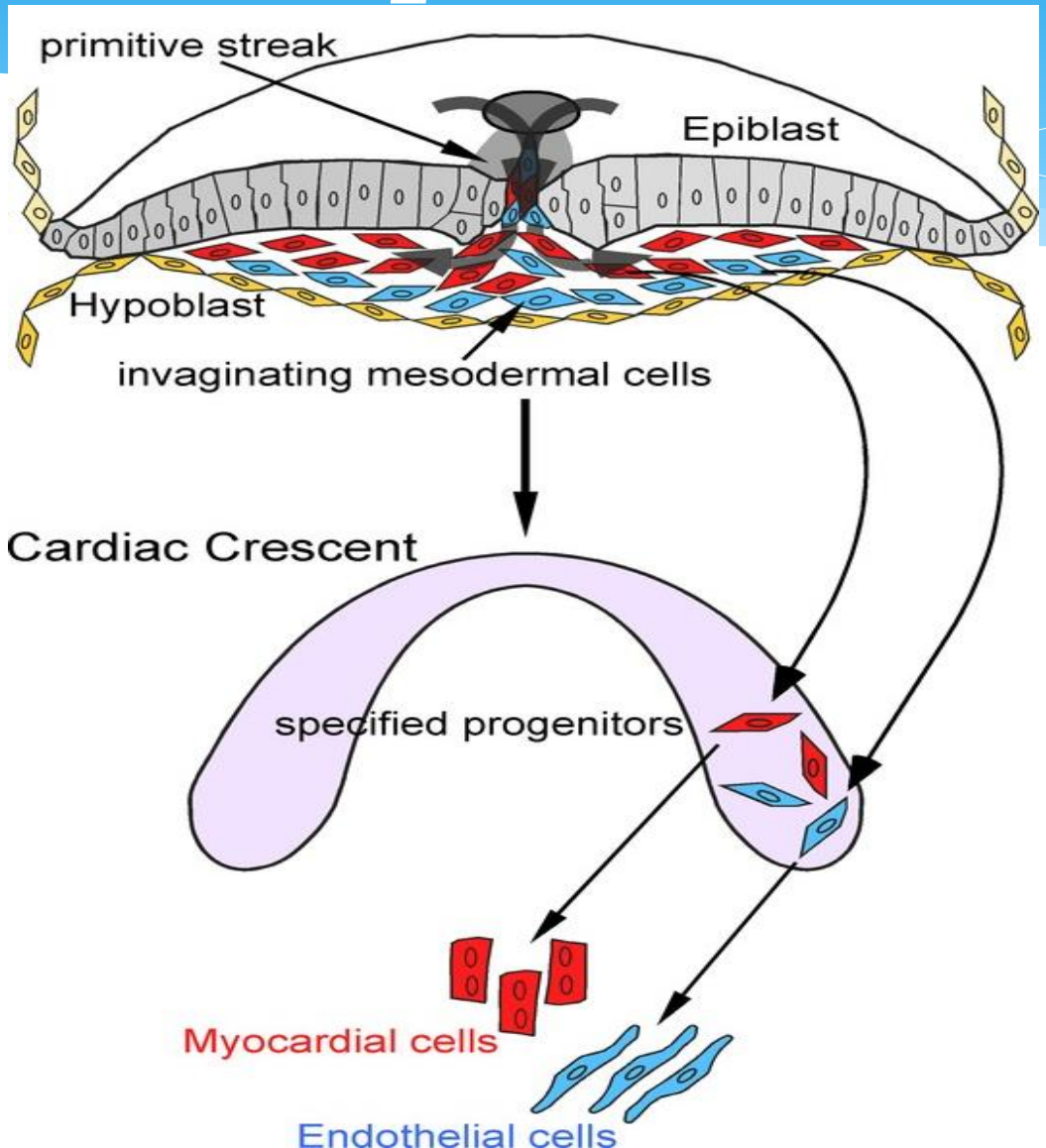
Sources of Cells - 2



General Events of Development -1

1. Specification
2. Differentiation
3. Proliferation
4. Migration and aggregation
5. Morphogenesis
6. Cell – cell and cell – matrix interaction

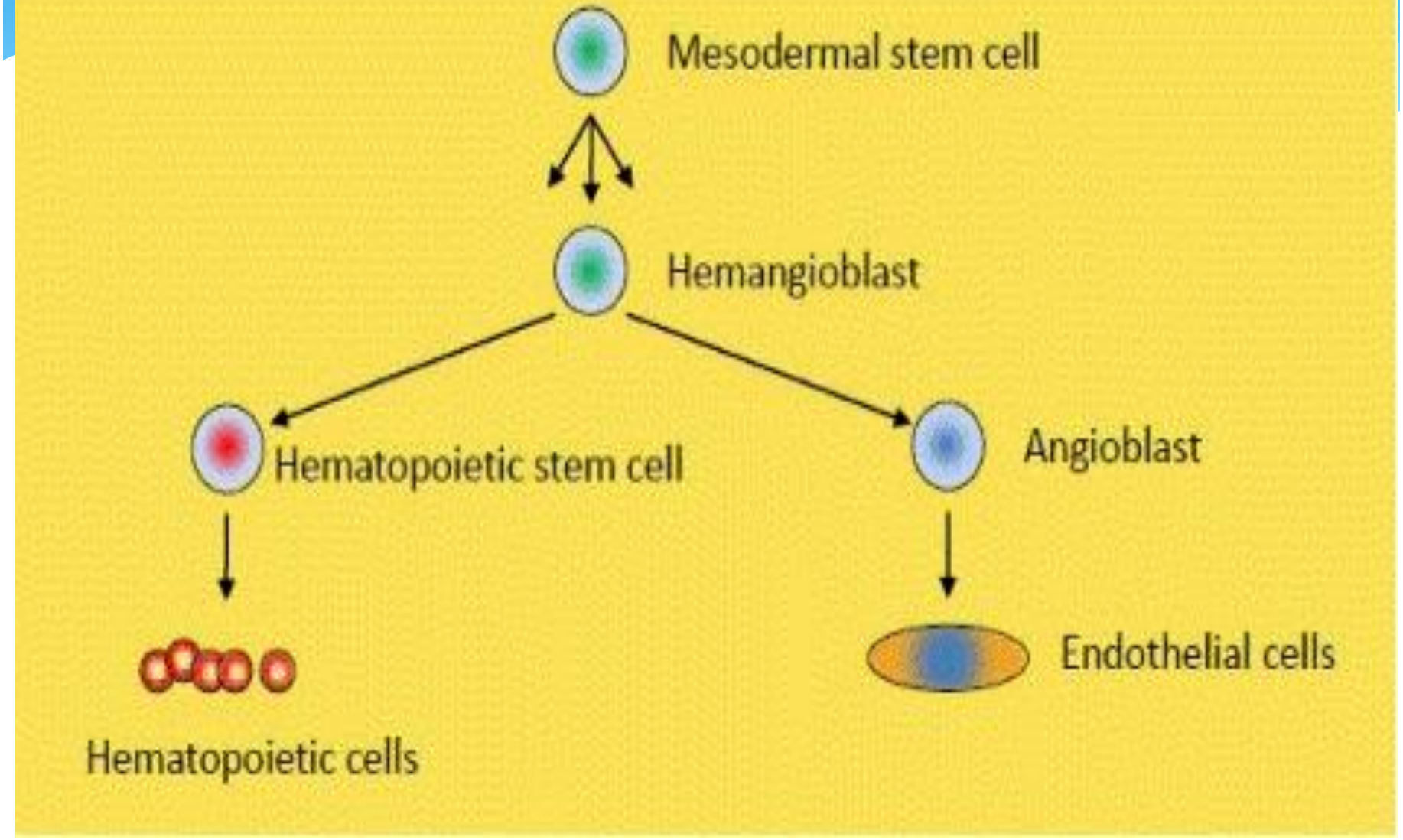
General Events of Development -2



Vasculogenesis - 1

1. De- novo formation of blood vessels
2. Forms the heart and vessels in endodermal and mesodermal derivatives
3. Prenatal and postnatal
4. Regulated by FGF-2, VEGF, PDGF
5. The precursor cell is hemangioblast

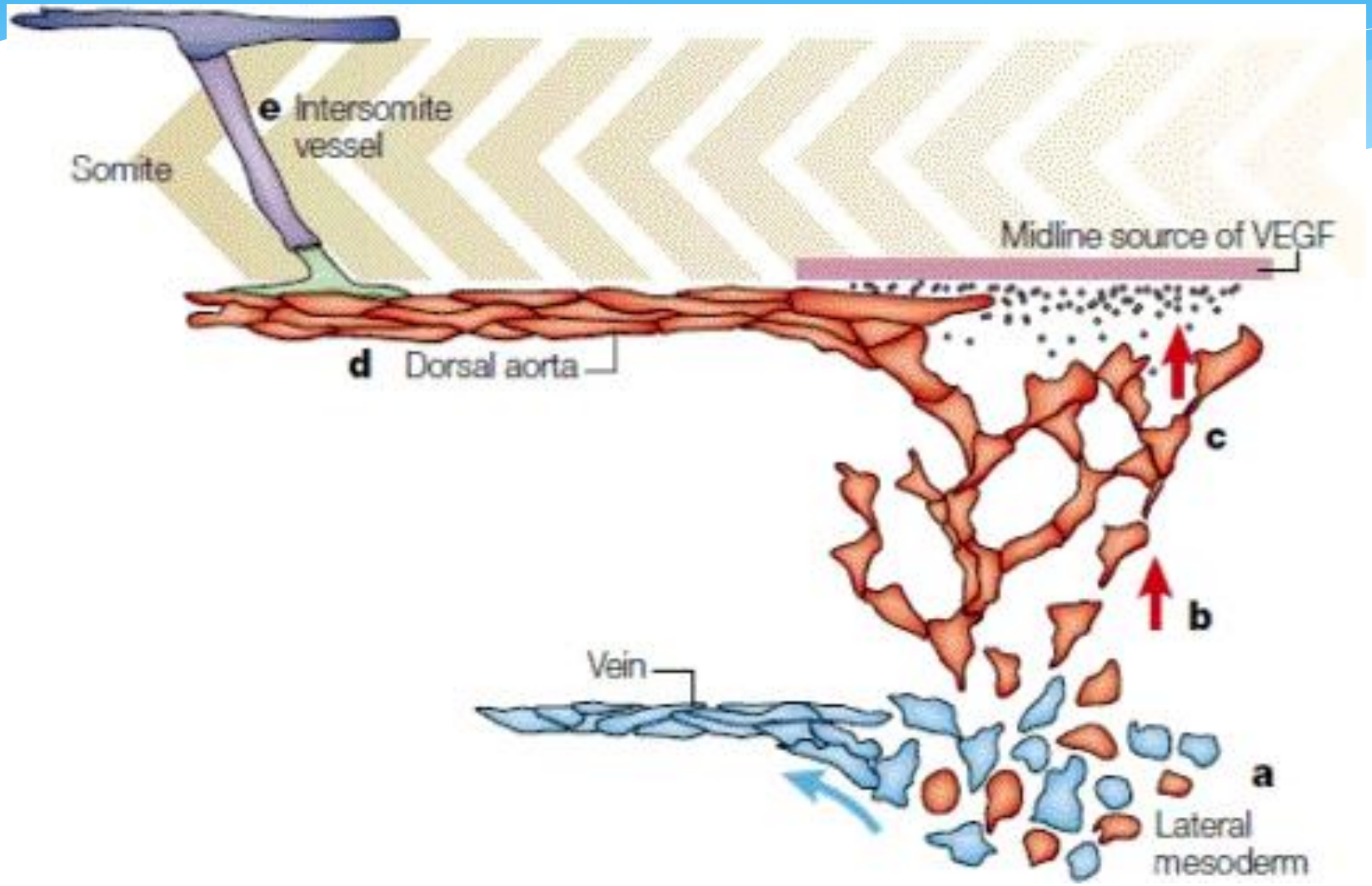
Vasculogenesis - 2



Vasculogenesis - 3: Steps

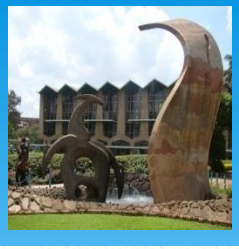
1. Establishment of angioblastic cell lineages
2. Formation of blood Islands
3. Canalization
4. Development of vascular networks
5. Vascular remodeling

Vasculogenesis - 4

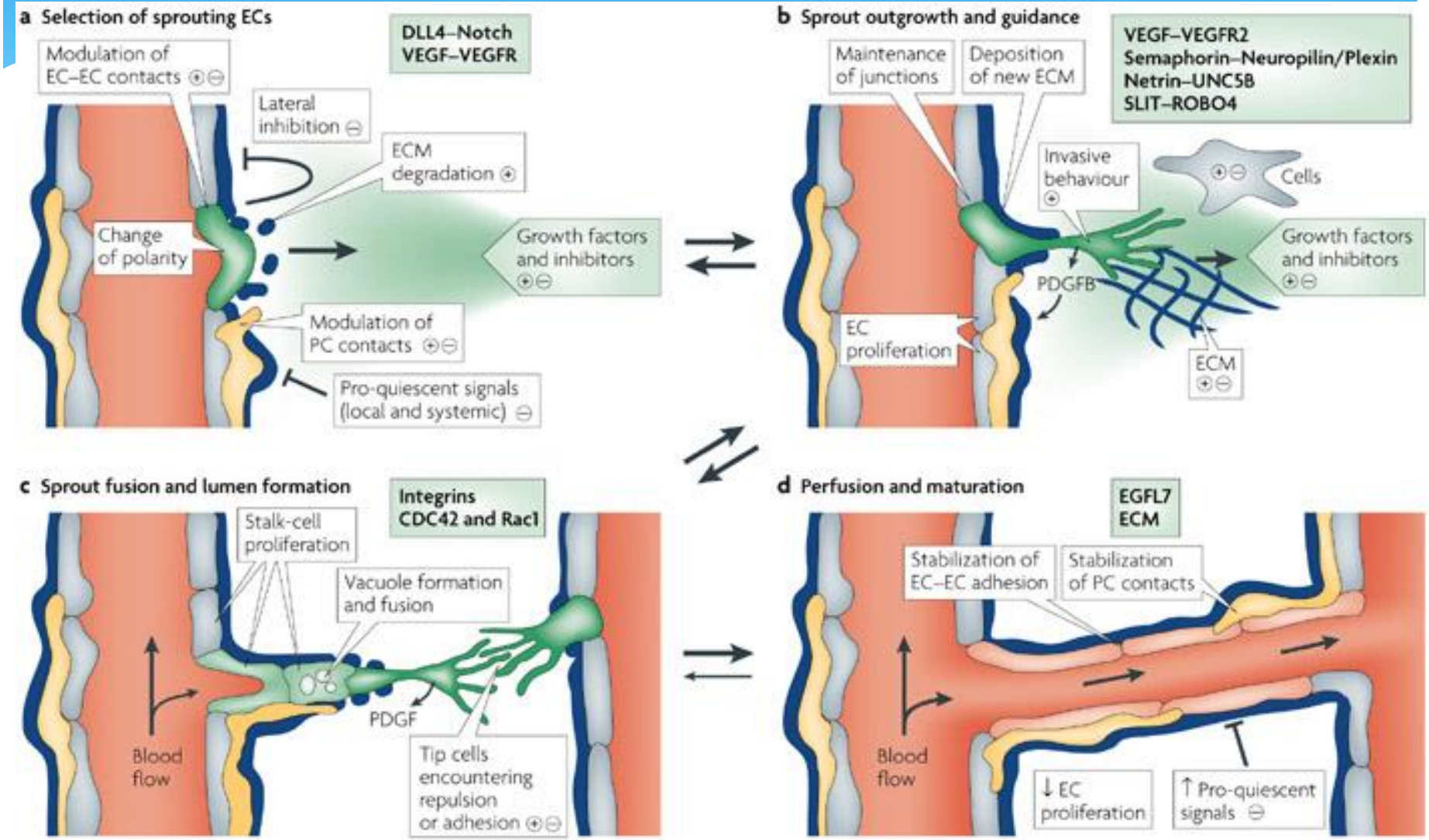


Angiogenesis - 1

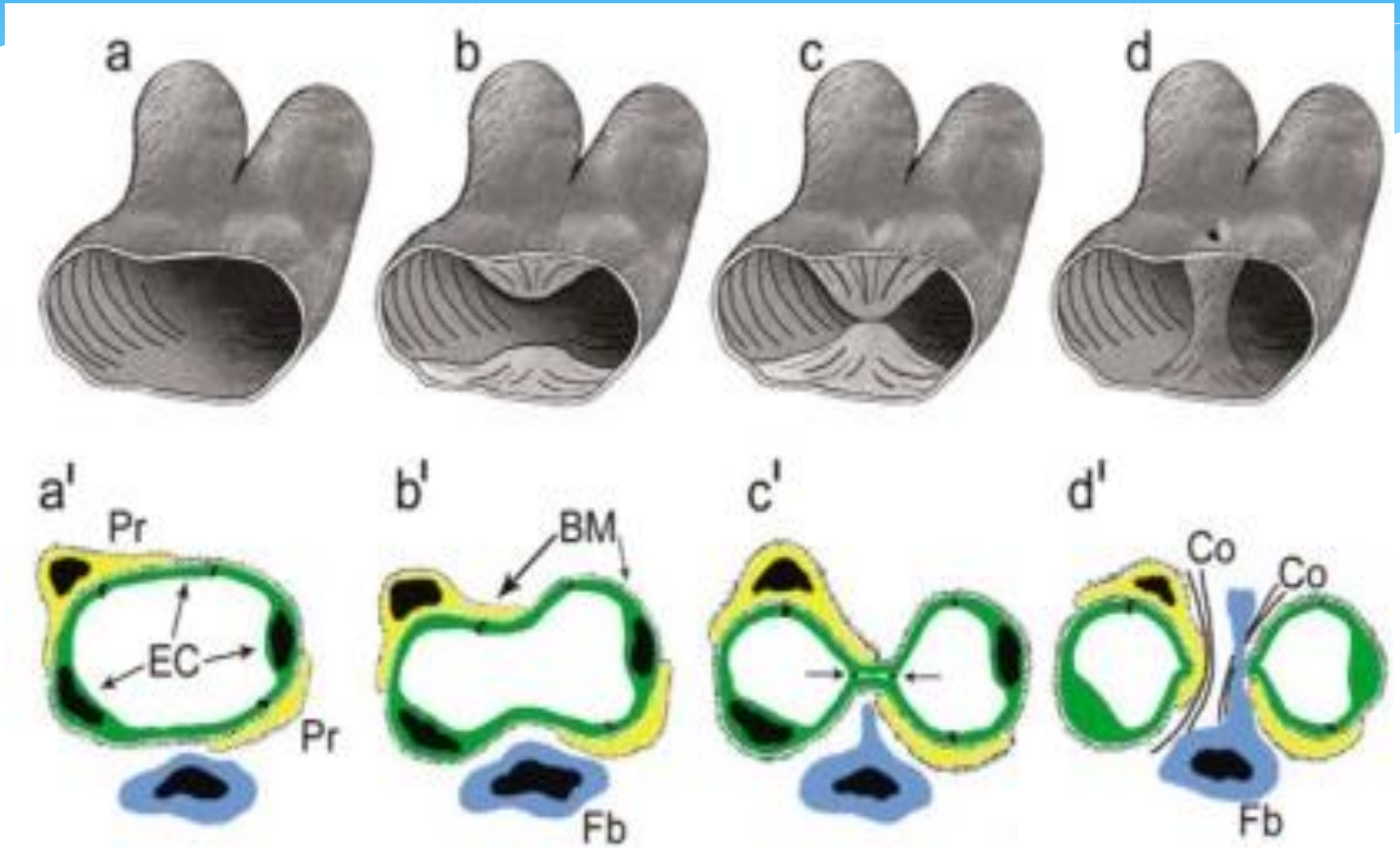
1. New vessels form from pre-existing ones
2. Prenatal and Postnatal
3. Vascularisation of ectodermal / mesodermal organs
4. Stimulated by tissue hypoxia
5. Regulated by FGF, VEGF,TGF, PDGF,Angiopoetins,MMPs, integrins
6. Can be sprouting or spliting (interssusceptive)



Angiogenesis-2: Sprouting



Angiogenesis-3: Splitting



Angiogenesis-4: Steps

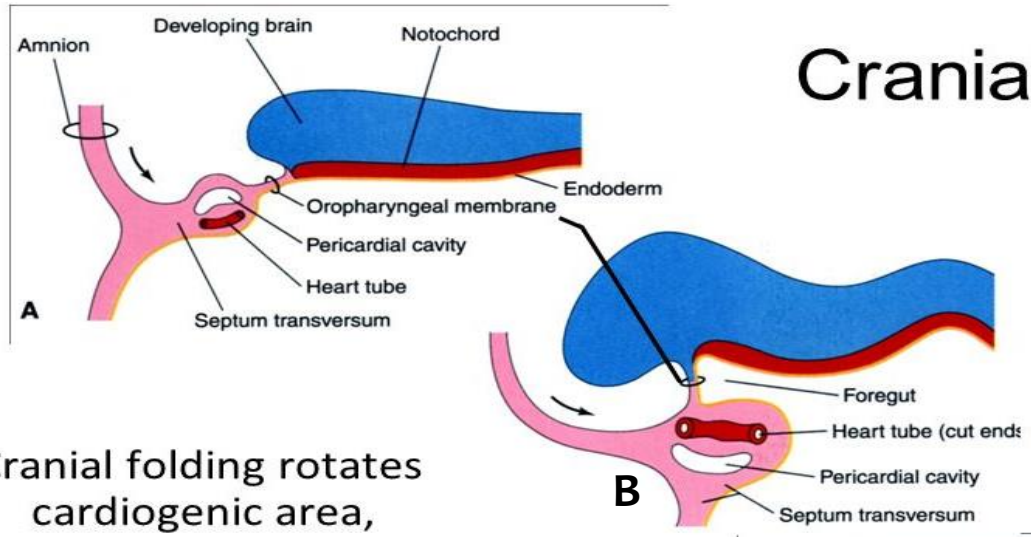
1. Degradation of basement membrane
2. Migration of endothelial cells
3. Alignment of endothelial cells
4. Alignment of muscles cells
5. Re-establishment of basement membrane
6. Vascular remodelling

Cardiogenesis

1. Site and induction
2. Cardiac precursor cells
3. Origin of cardiac mesodermal cells
4. Precursors of the heart tube
5. Formation of primitive heart tube
6. Transformation of heart tube
7. Derivatives of the heart tube

Cardiogenesis: site

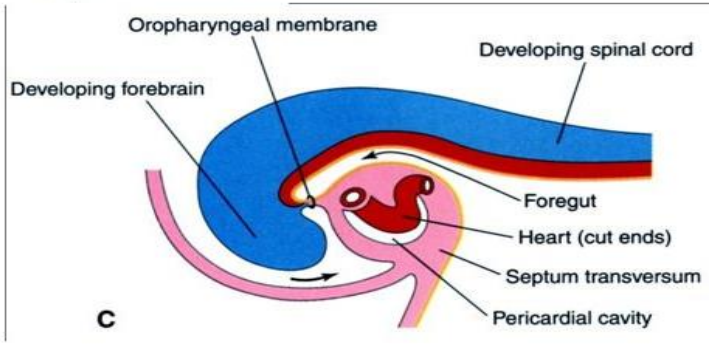
Cardiogenic area: rostral to neural tube and oro-pharyngeal membrane



Cranial folding

Cranial folding rotates cardiogenic area,

moves it ventrally and caudally, and orients **heart tube** and **pericardial cavity**



Moore & Persaud fig 13-9

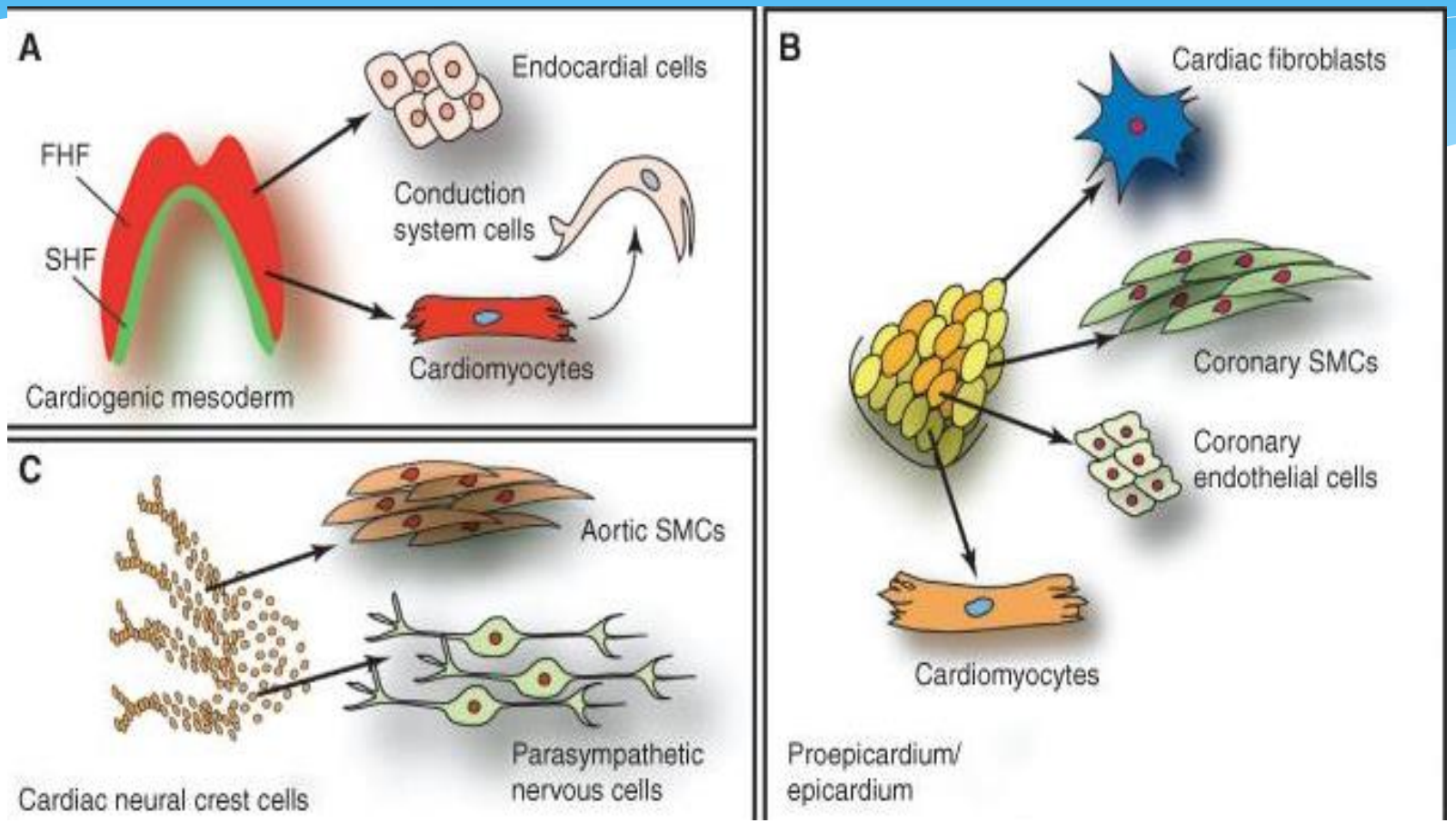
Cardiogenesis: induction

1. Influenced by cross-talk with surrounding layers
2. Induced by anterior endoderm
3. Involves TGF – ß, BMP, FGF- 2, nodal activin
4. Regulation is time and space determined

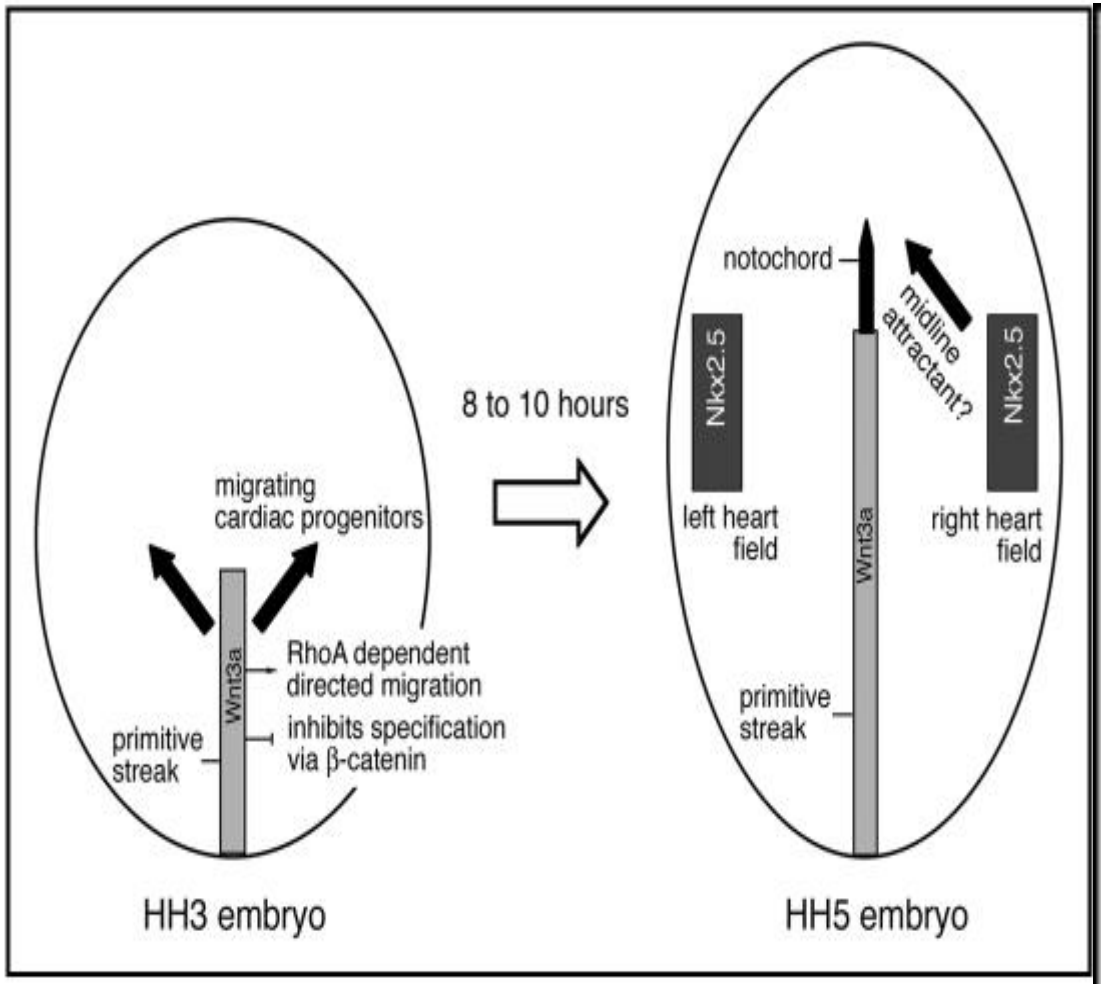
Cardiac precursor cells - Origin

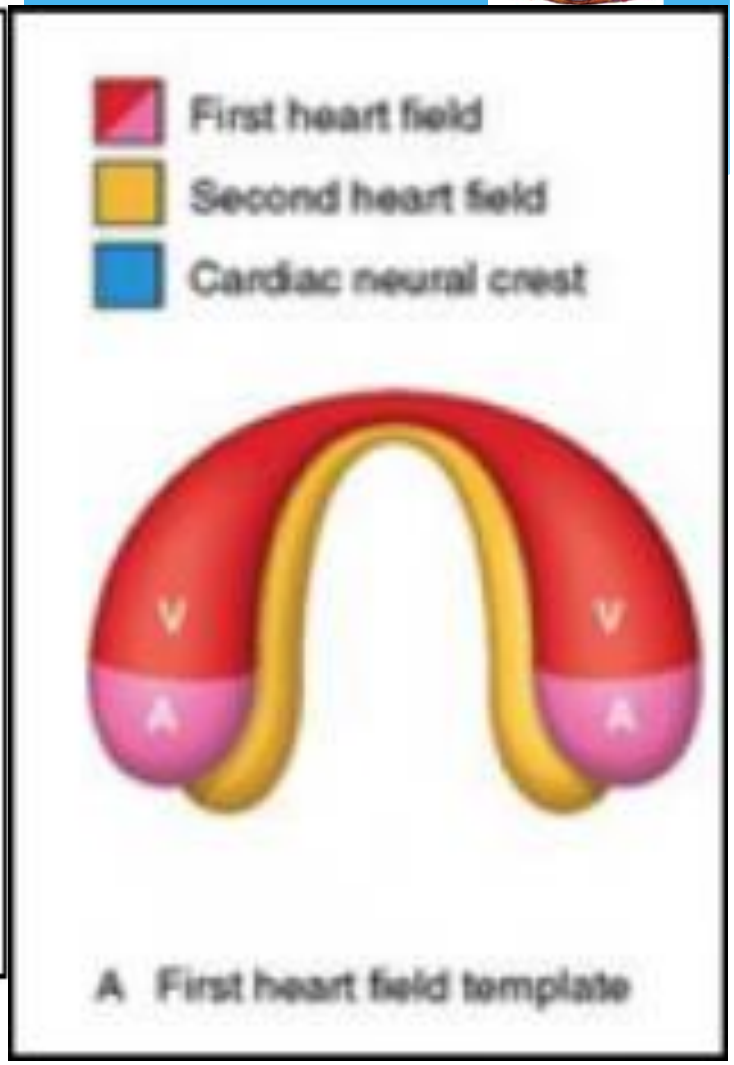
CELL	ORIGIN
• Cardiac mesodermal cell	• Splanchnic Mesoderm
• Pro- epicardium	• Septum transversum, sinus venosus
• Cardiac neural crest cell	• Neural crest

Cardiac precursor cells -Derivatives

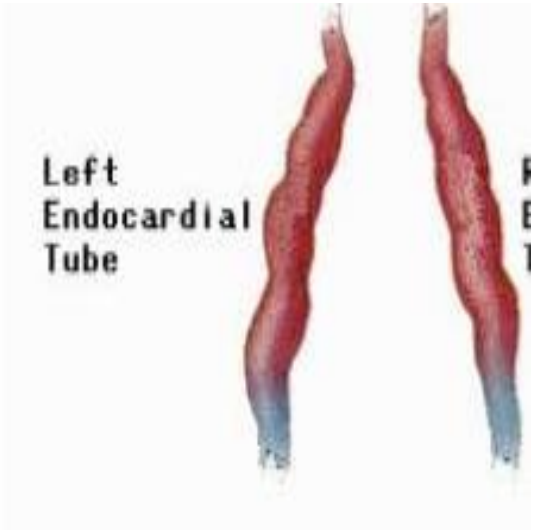


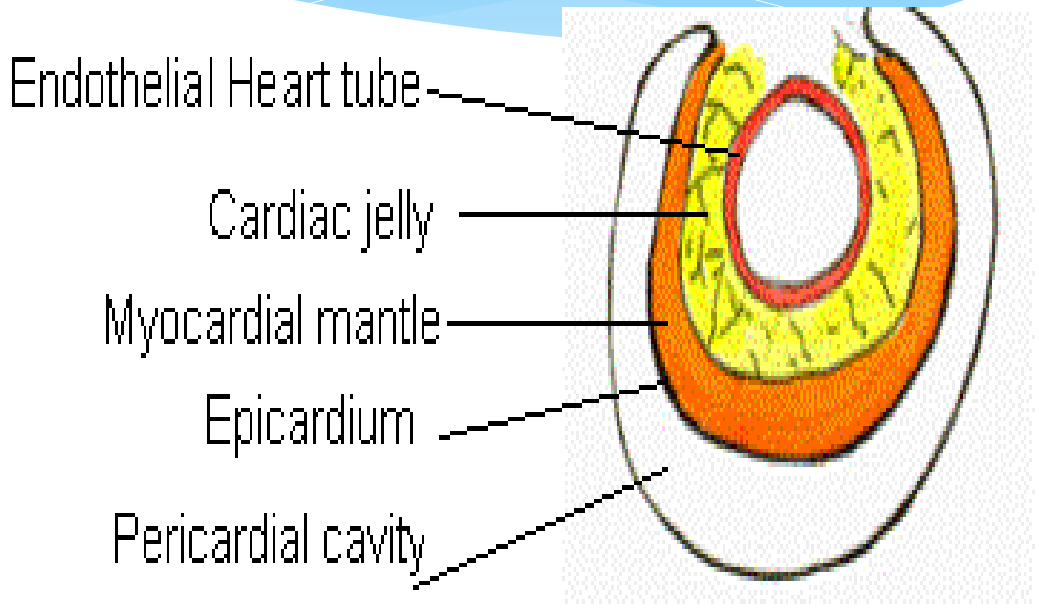
Precursors of primitive heart tube





Formation of heart tube

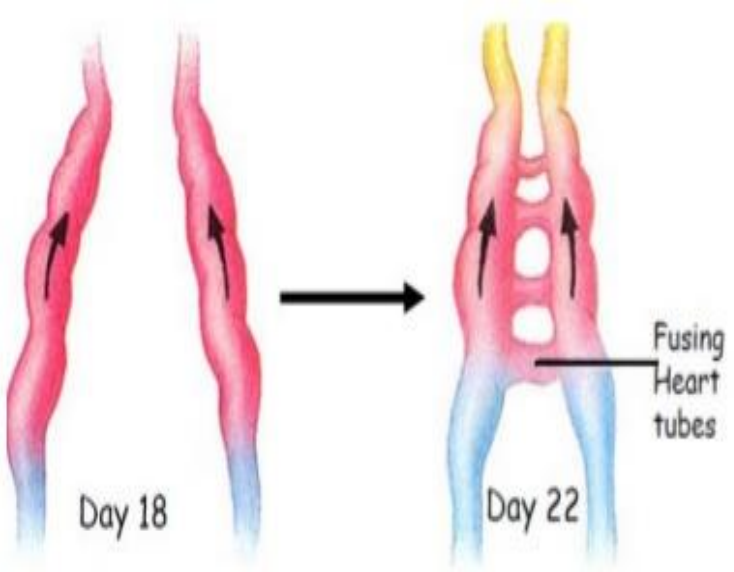


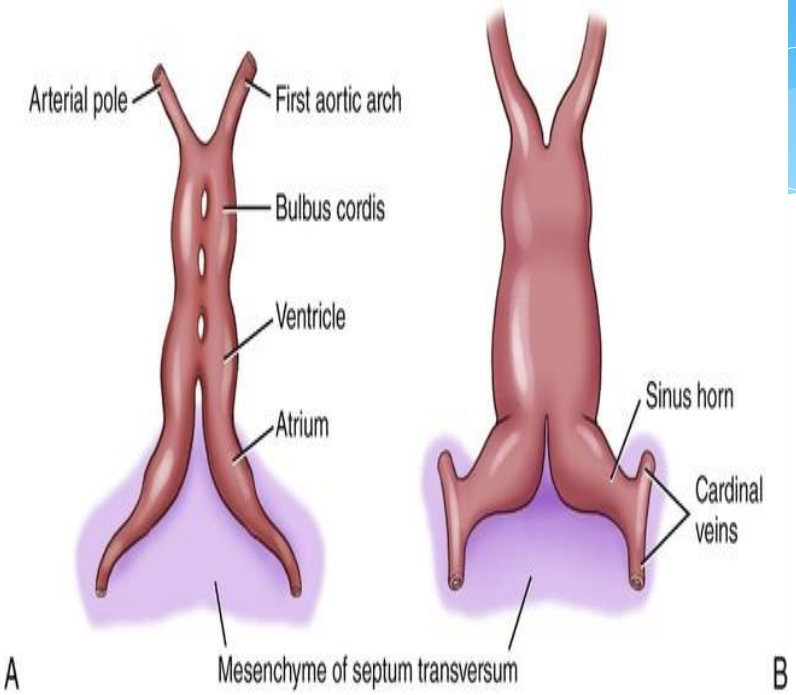


Transformation of Heart Tube

1. Fusion
2. Elongation
3. Constriction
4. Ballooning
5. Looping
6. Partitioning

Fusion

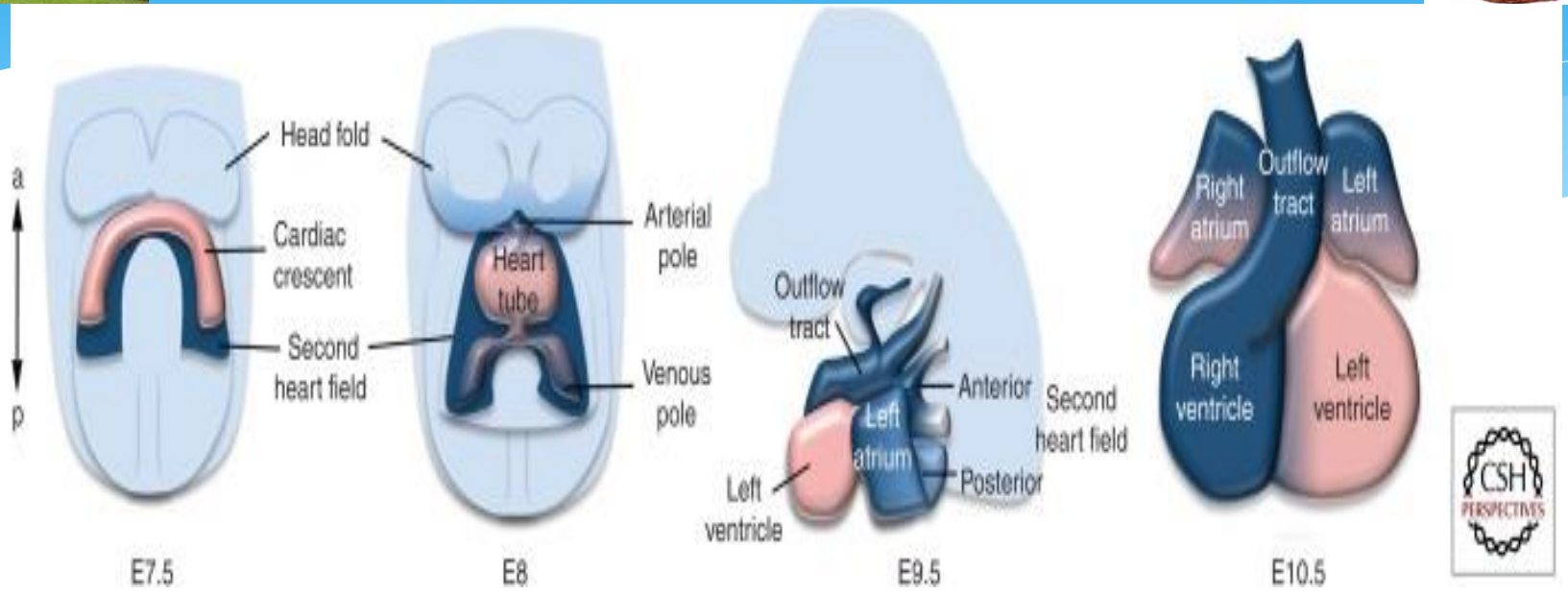

Day 18
Day 22
Fusing
Heart
tubes


Arterial pole
First aortic arch
Bulbus cordis
Ventricle
Atrium
Sinus horn
Cardinal
veins
Mesenchyme of septum transversum
A
B

Elongation -1

1. Proliferation of primary cardiac mesodermal cells
2. Addition of myocardial cells from pharyngeal mesoderm

Elongation -2



Progressive addition of second heart field progenitor cells (dark blue) to the elongating heart tube between 7.5 and 9.5 d of mouse development. In the midgestation heart (*right*), second heart field–derived parts of the heart are indicated in blue. (From Kelly 2012; reproduced, with permission.)

Constrictions / Parts

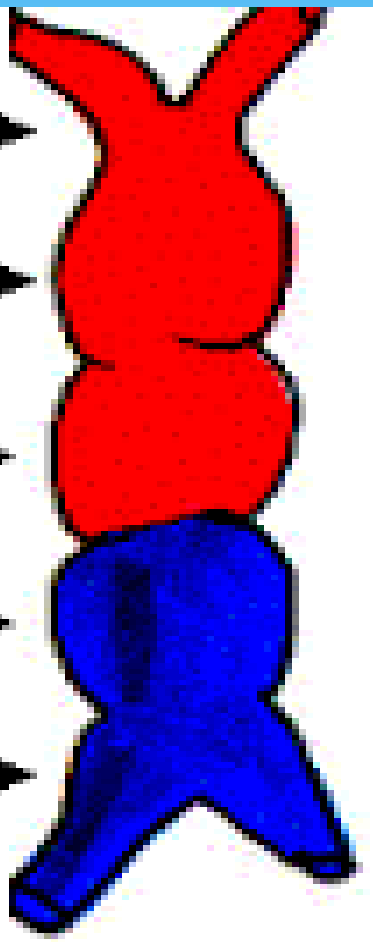
truncus arteriosus

bulbus cordis

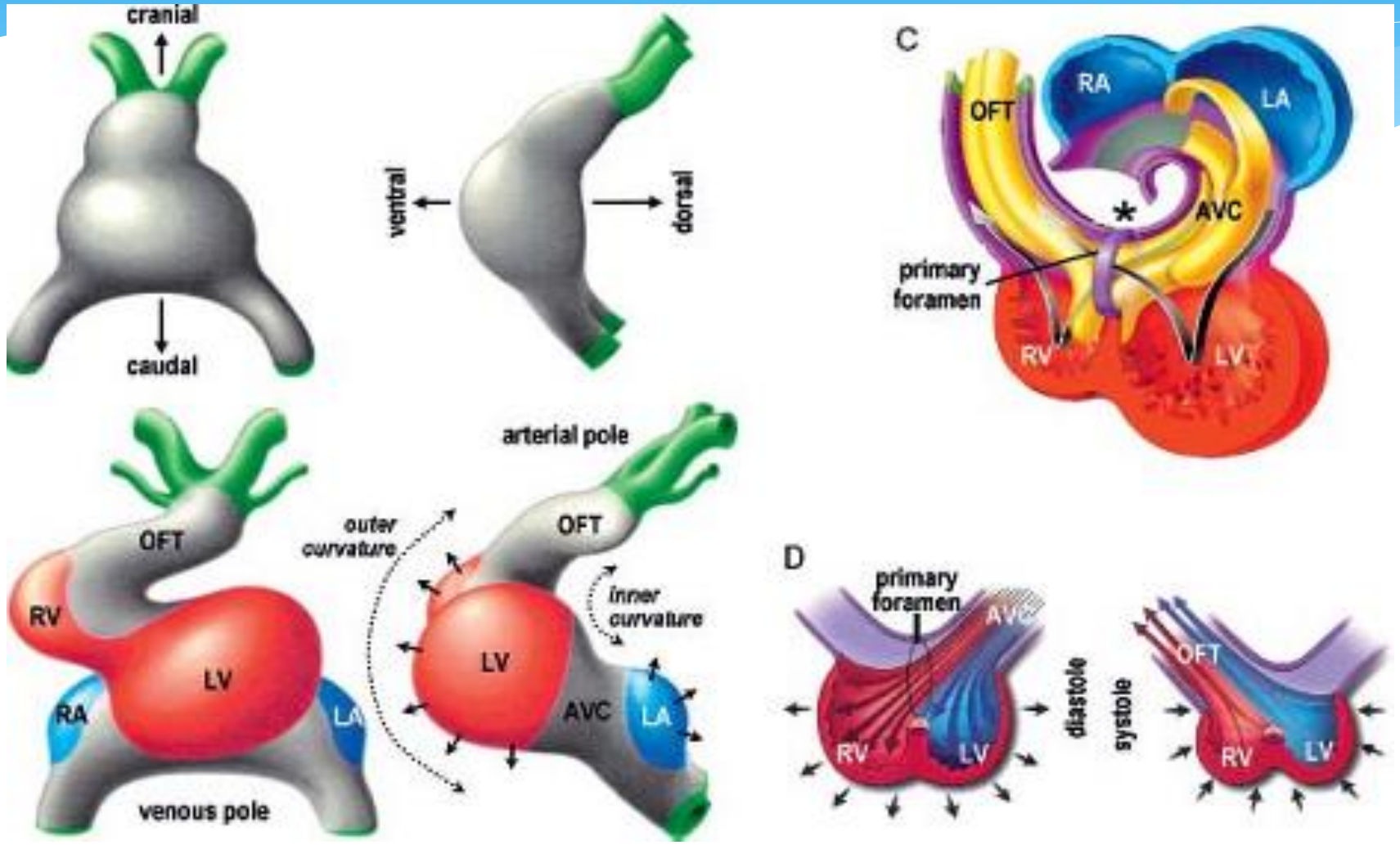
ventricle

atrium

sinus venosus

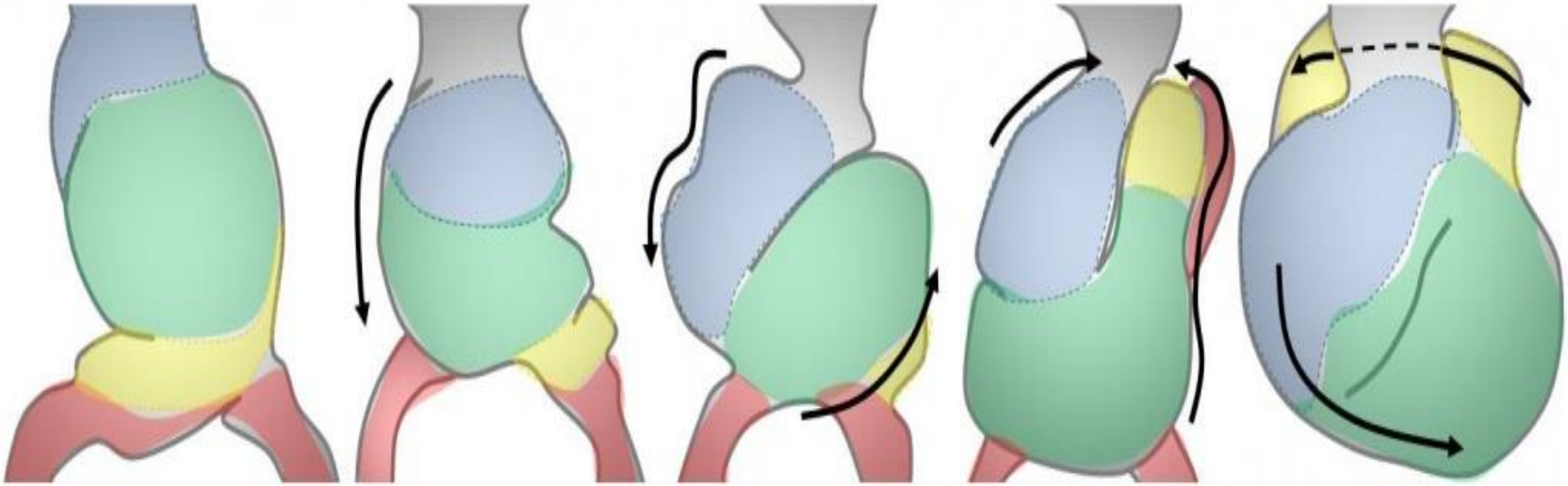


Ballooning


cranial
caudal
ventral
dorsal
C
OFT
RA
LA
AVC
primary foramen
RV
LV
OFT
RV
LV
RA
LA
venous pole
arterial pole
outer curvature
OFT
inner curvature
LV
AVC
LA
D
primary foramen
AVC
RV
LV
diastole
systole
OFT
RV
LV

Looping

Sequence of Events in Looping



Straight Heart Tube C-Shaped Loop S-Shaped Loop

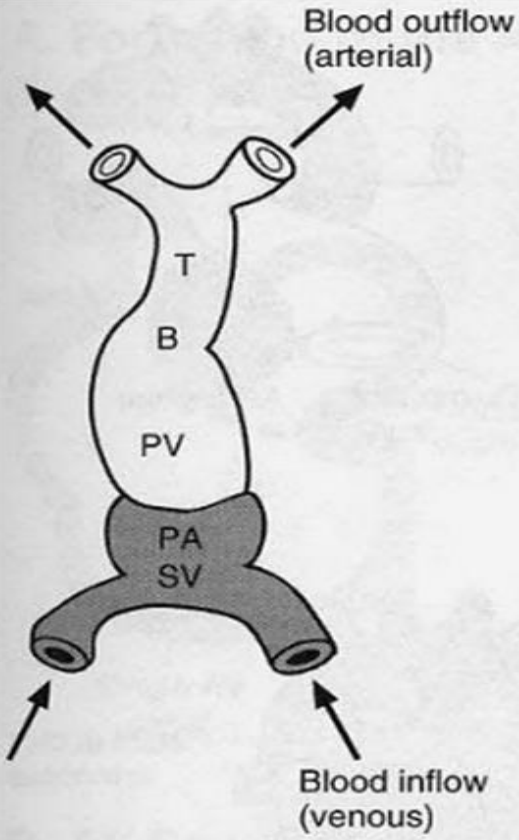
Blue = Bulbus Cordis

Yellow = Atrium

Green = Ventricle

Red = Sinus Venosus

Derivatives of Heart Tube



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.**

Developmental disorders

1. Disorders of Vasculogenesis and Angiogenesis e.g

* Keloids
* Uterine Fibroids
* Tumor growth
* Diabetic retinopathy

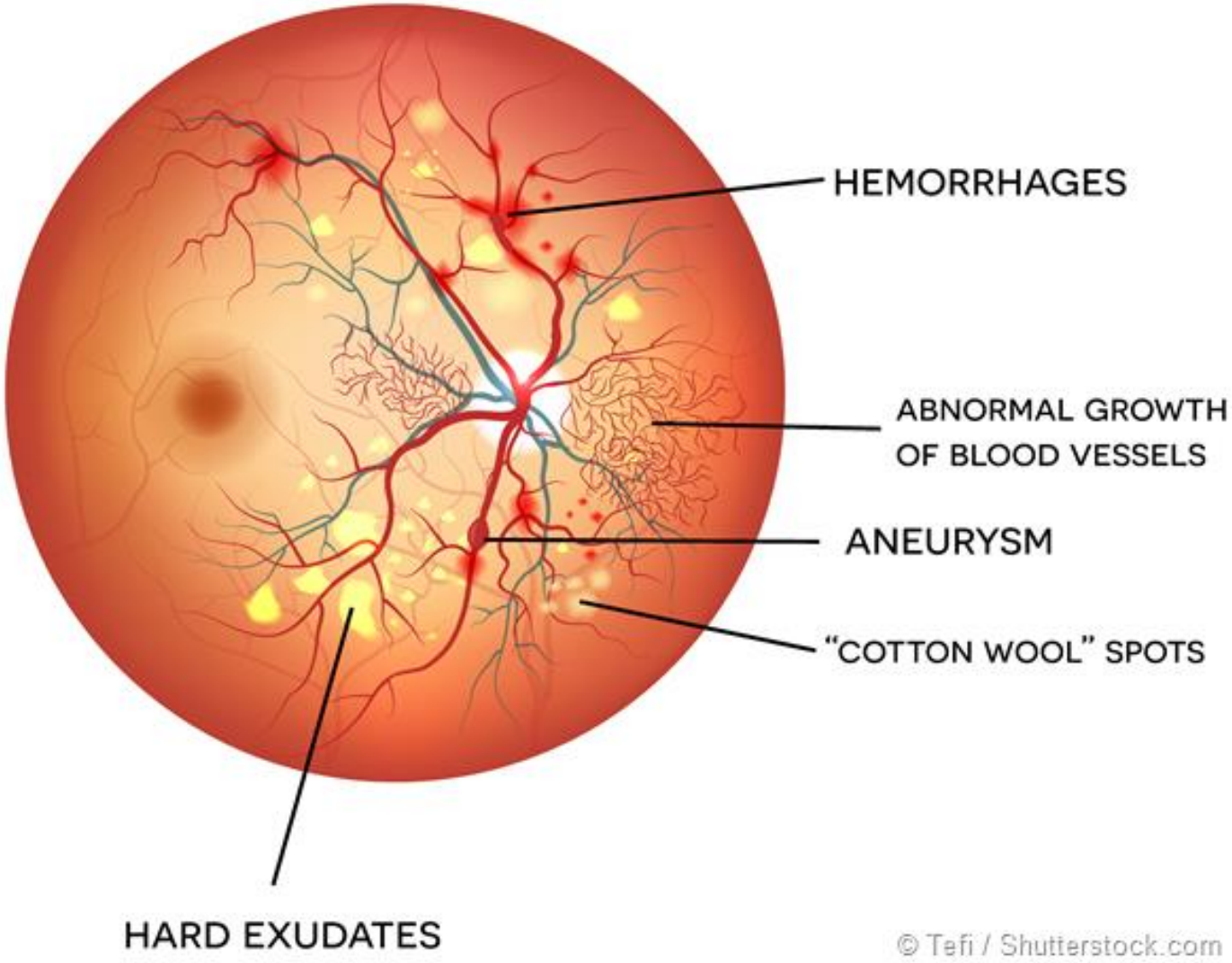
2. Cardiac Bifida

Keloids

Uterine Fibroids

Tumor

Diabetic retinopathy



Cardia bifida