

INTRODUCTION TO HUMAN HEART DEVELOPMENT

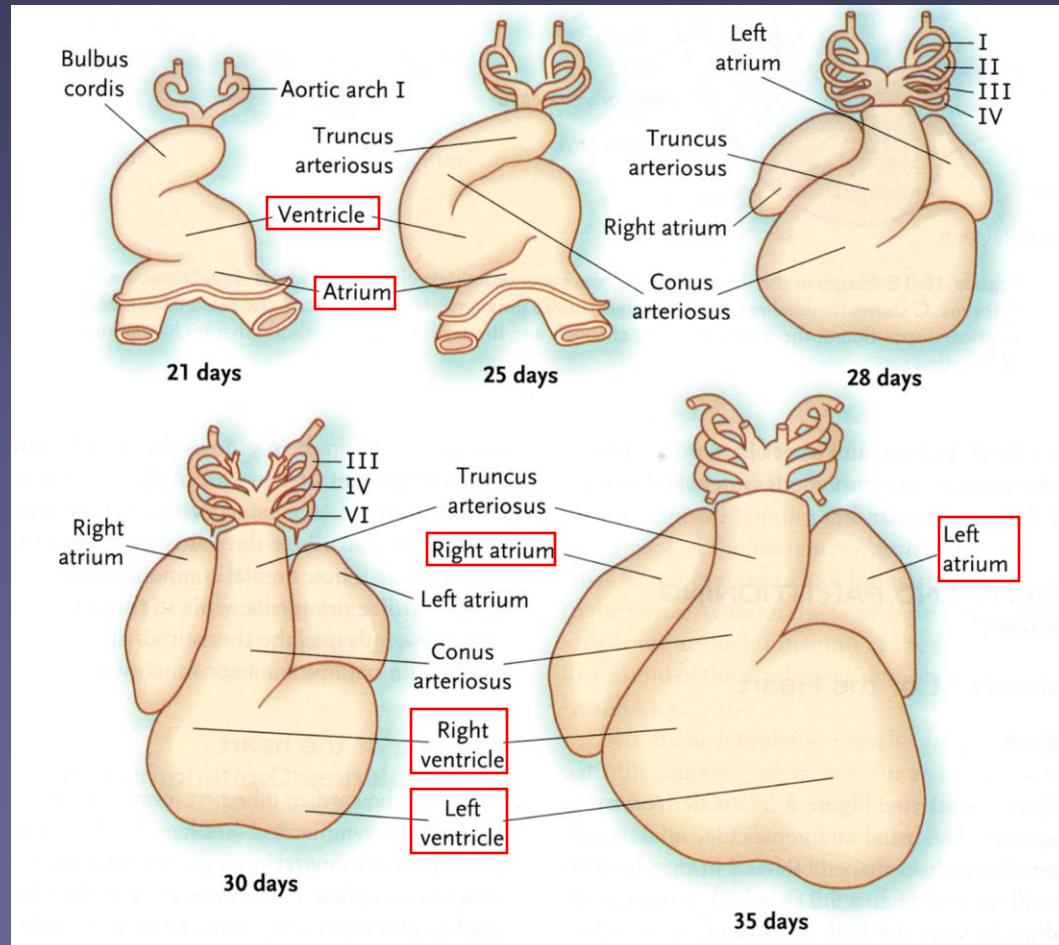
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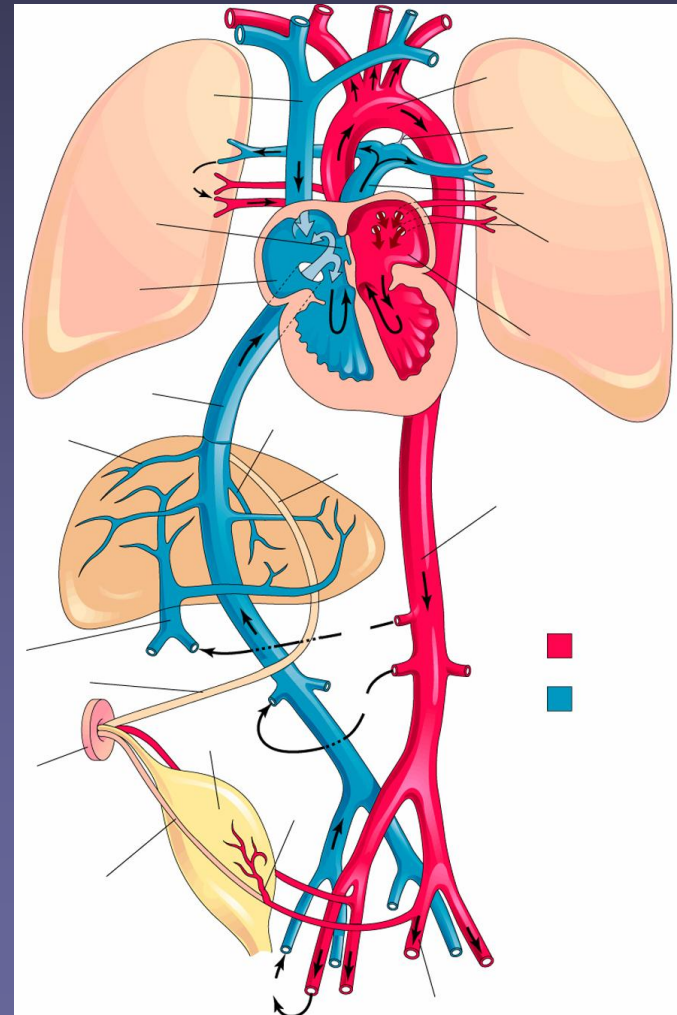
HUMAN HEART DEVELOPMENT



POSTNATAL CIRCULATION

**PULMONARY CIRCULATION
RIGHT CHAMBERS**

**SYSTEMIC CIRCULATION
LEFT CHAMBERS**



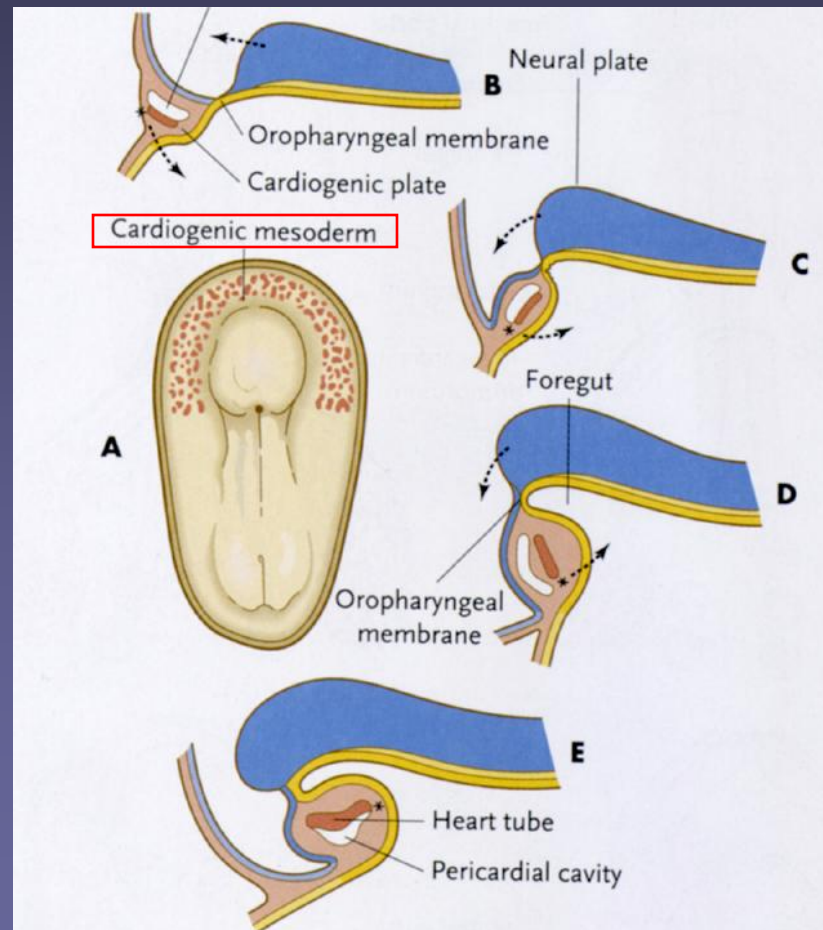
HUMAN HEART DEVELOPMENT

- HEART TUBE FORMATION
- CARDIAC LOOPING
- CHAMBER SEPTATION
- VALVE AND OUTFLOW FORMATION

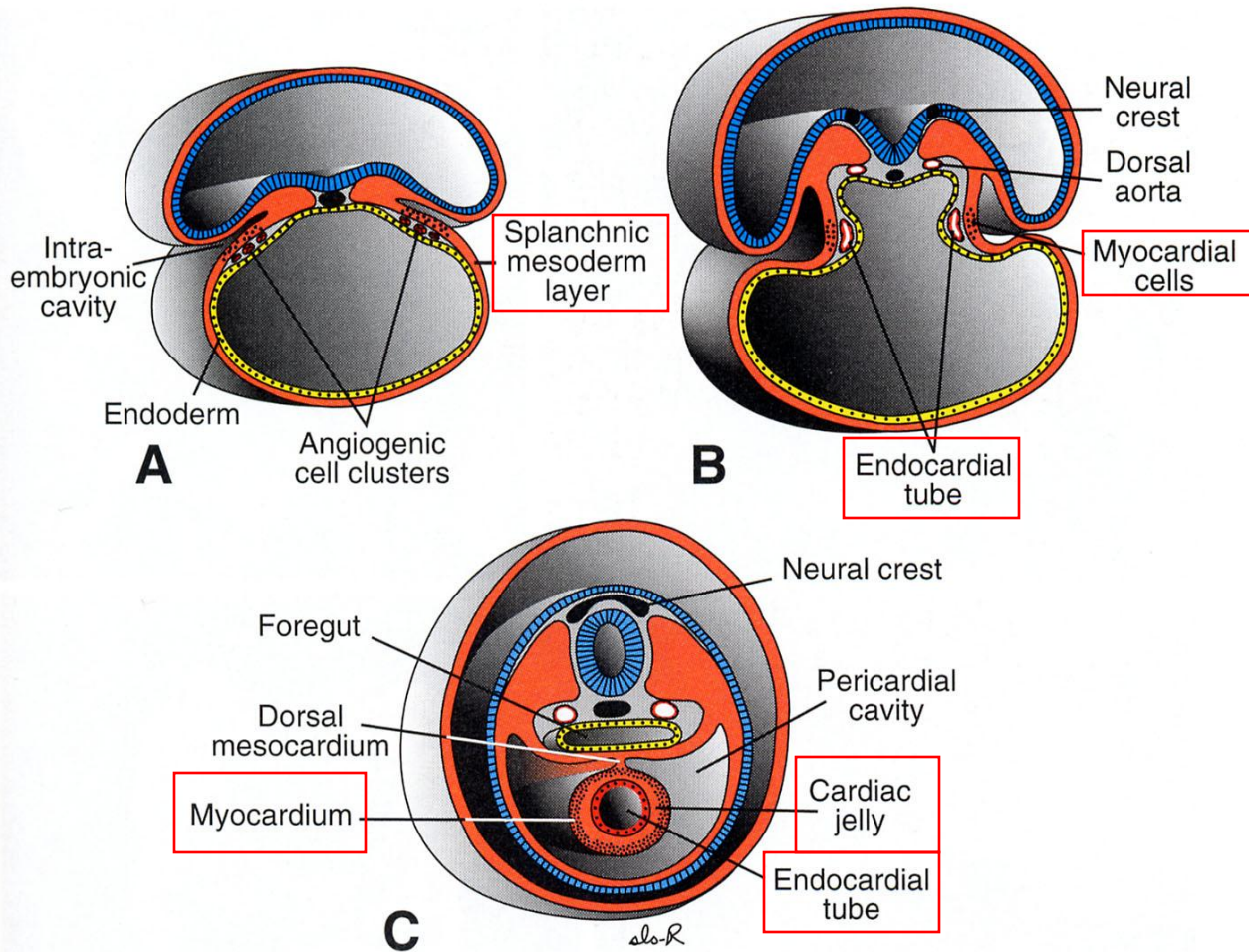
CONGENITAL HEART DISEASE

- RELATIVELY COMMON
- GENERALLY INITIATED BY EARLY DEVELOPMENTAL ERRORS
- CAN BE CAUSED BY EXPOSURE TO TERATOGENS
- CAN ORIGINATE WITH GENETIC DEFECTS

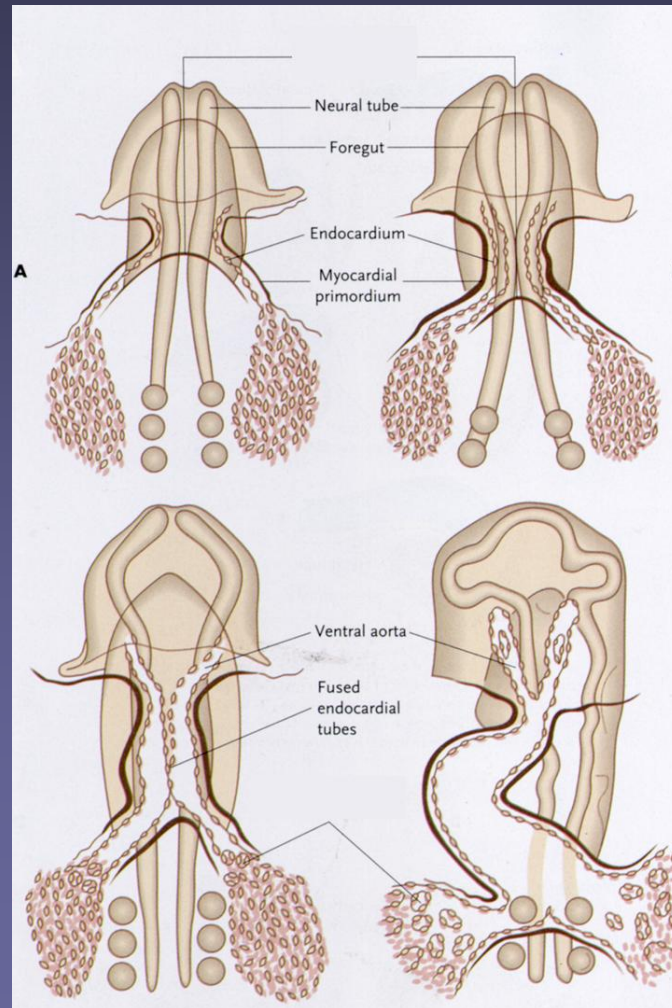
LONGITUDINAL FOLDING POSITIONS CARDIAC CELLS



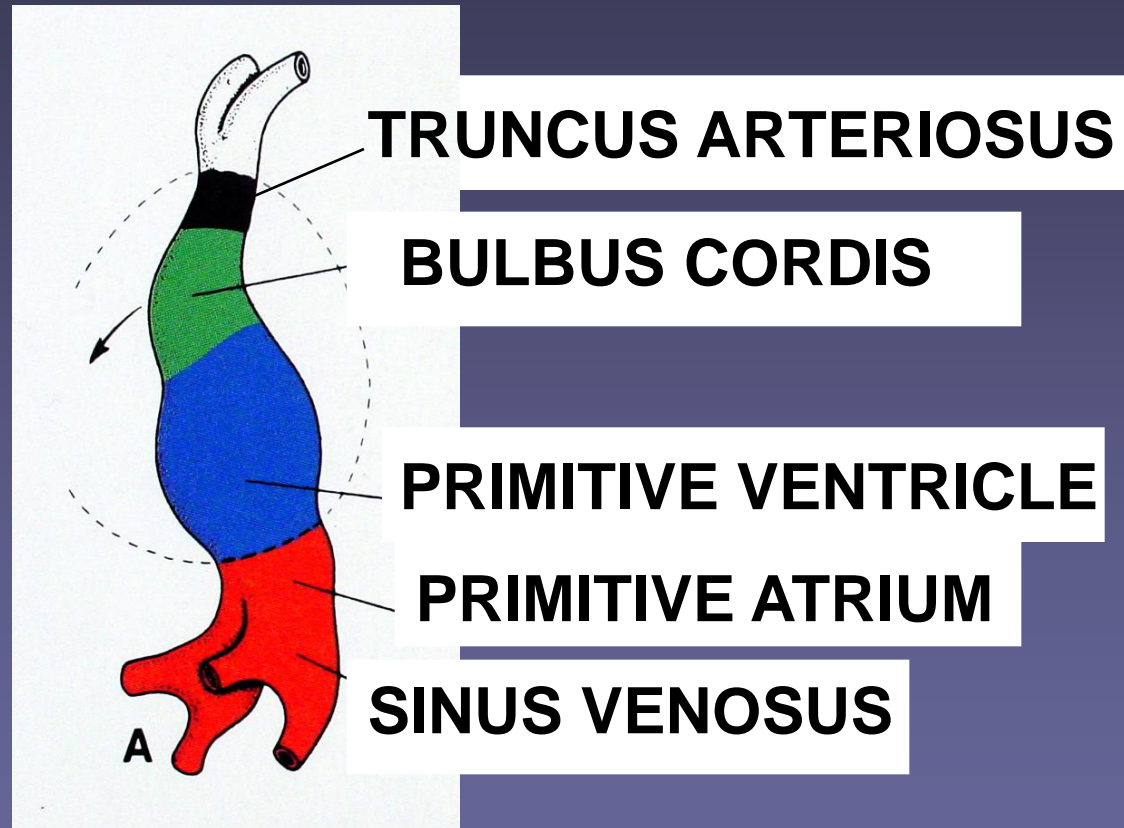
LATERAL FOLDING FACILITATES TUBE FORMATION



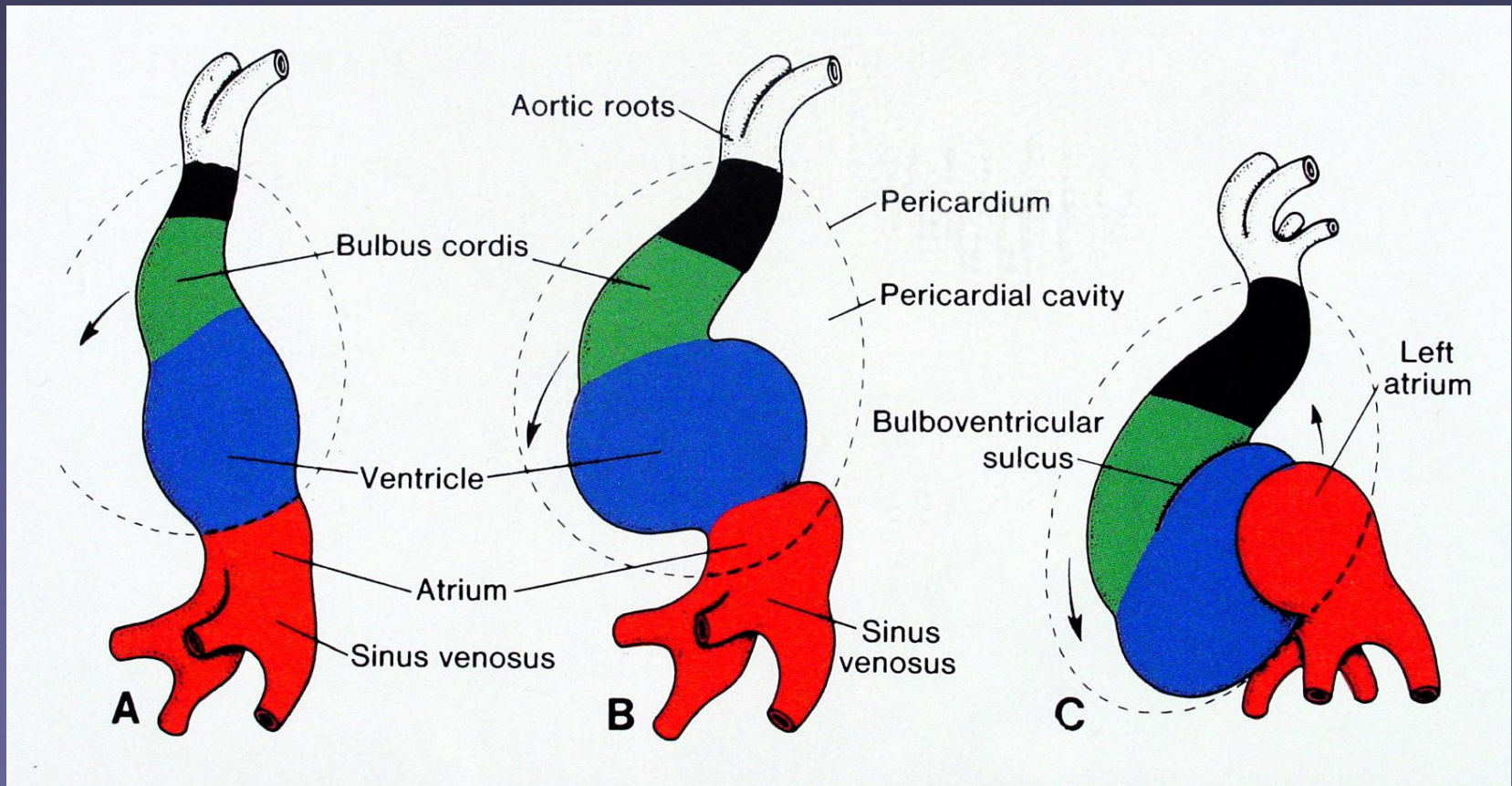
TUBE FORMATION BEGINS ROSTRALLY



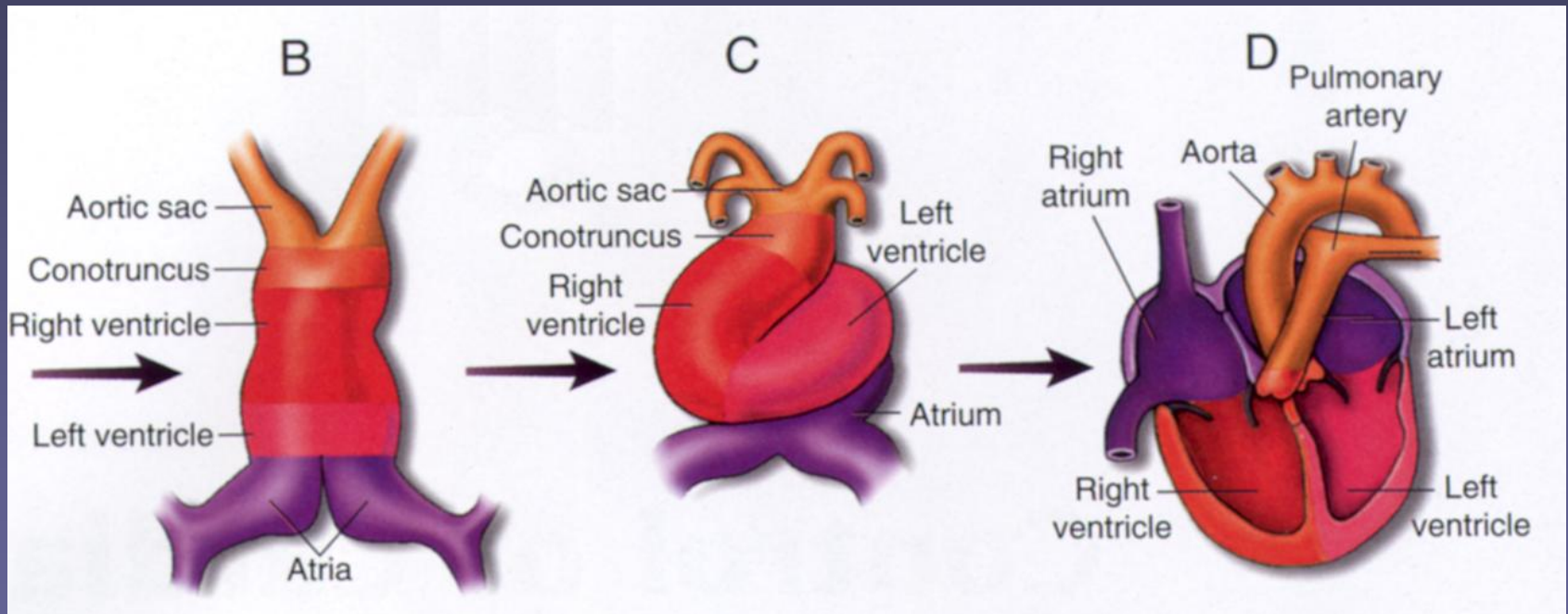
PRIMITIVE HEART TUBE



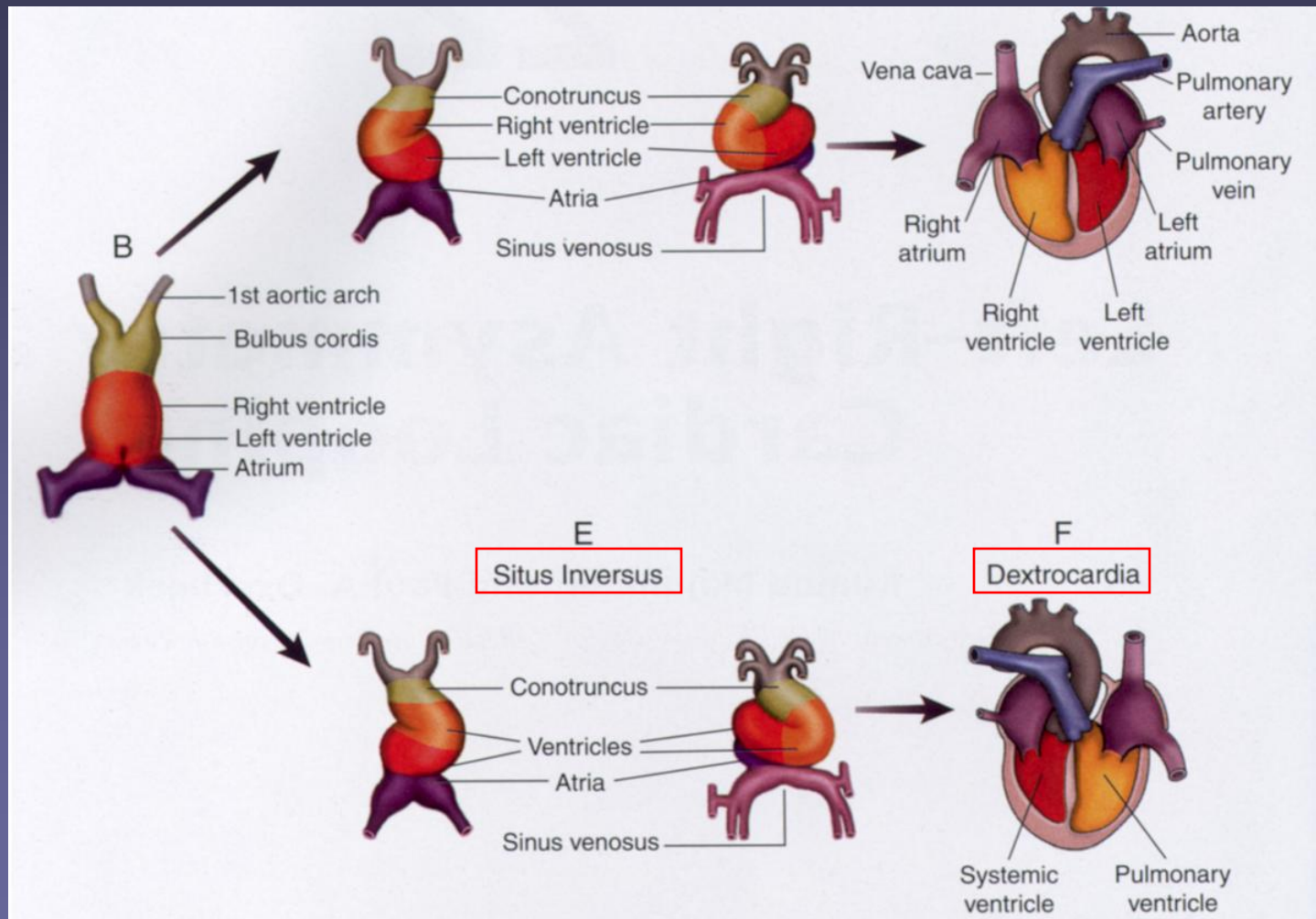
CARDIAC LOOPING



CARDIAC LOOPING



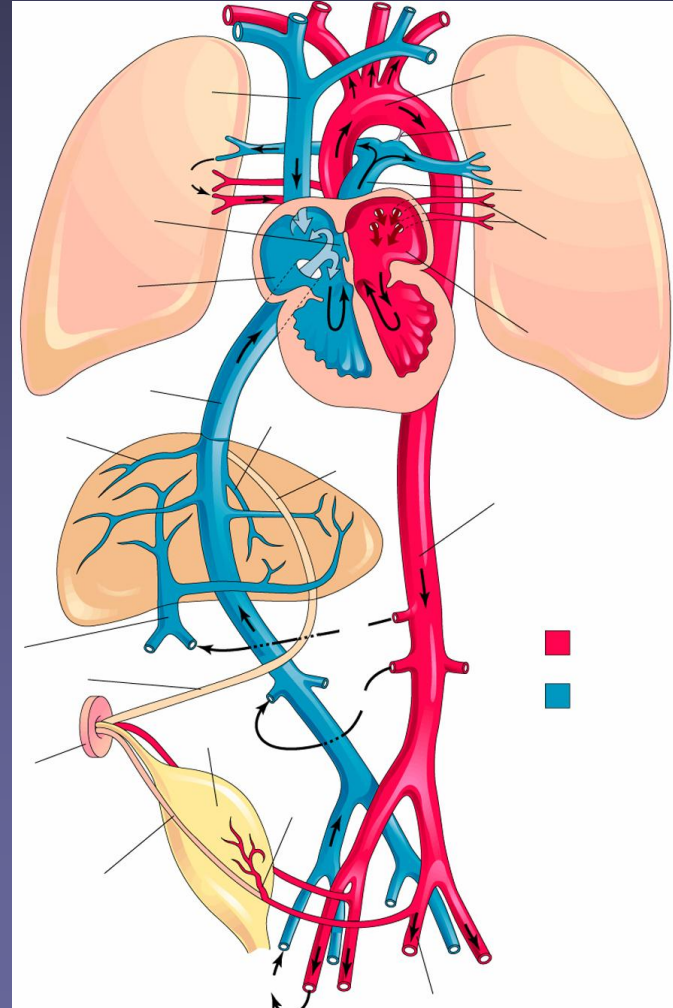
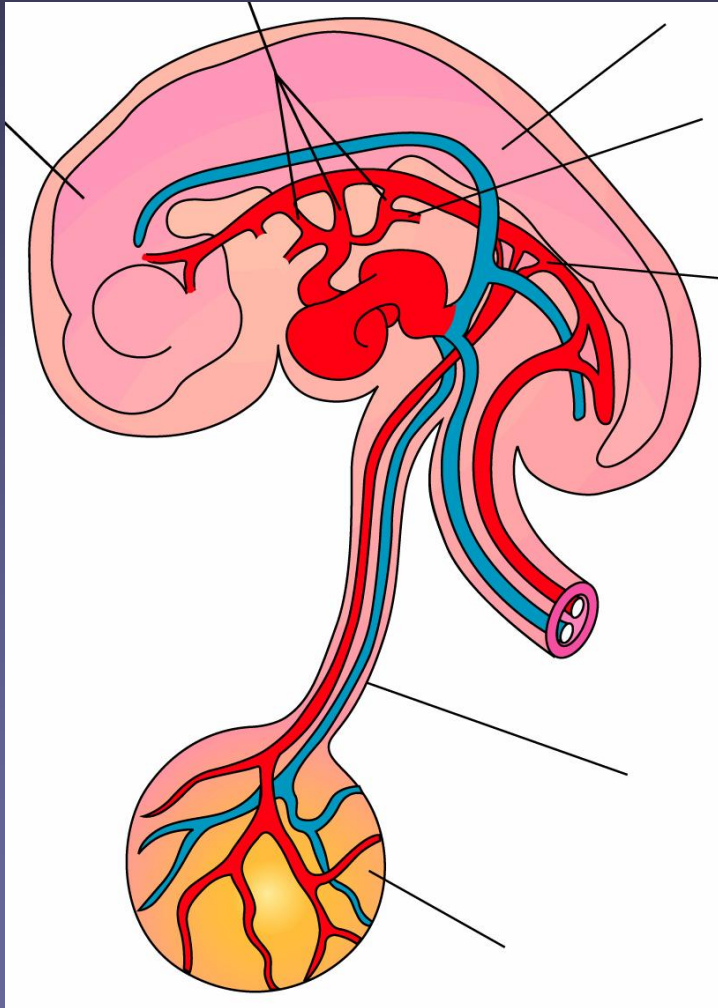
DEXTROCARDIA AND SITUS INVERSUS



GENETIC BASIS FOR HETEROTAXY

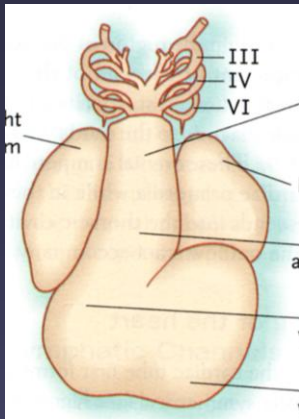
- NODAL FAMILY OF GROWTH FACTORS REQUIRED FOR ESTABLISHMENT OF LEFT-RIGHT AXIS
- *CFC1* GENE ENCODES A COMPONENT OF THE RECEPTOR FOR NODAL FACTORS
- MUTATIONS IN *CFC1* CAUSE HETEROTAXY

FROM FETAL TO POSTNATAL CIRCULATION



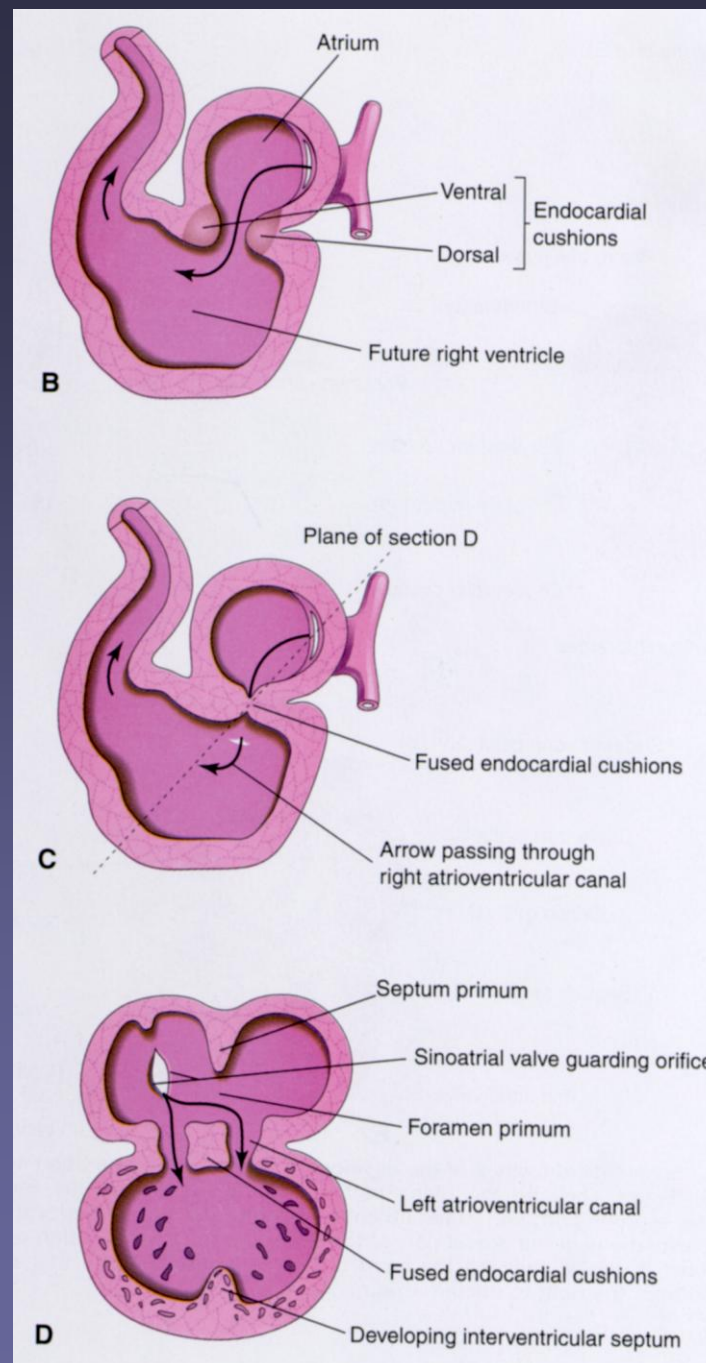
PARTITIONING THE HEART

- **ATRIAL SEPTATION**
- **VENTRICULAR SEPTATION**
- **ATRIOVENTRICULAR VALVE FORMATION**
- **DIVISION OF THE OUTFLOW TRACT**

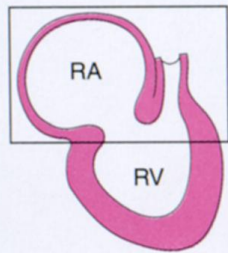


SAGITTAL SECTIONS

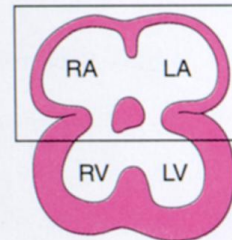
CORONAL SECTIONS



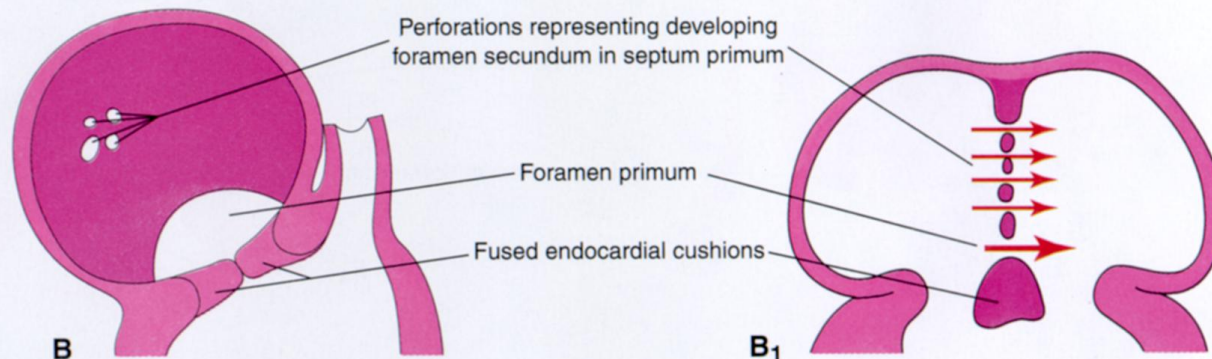
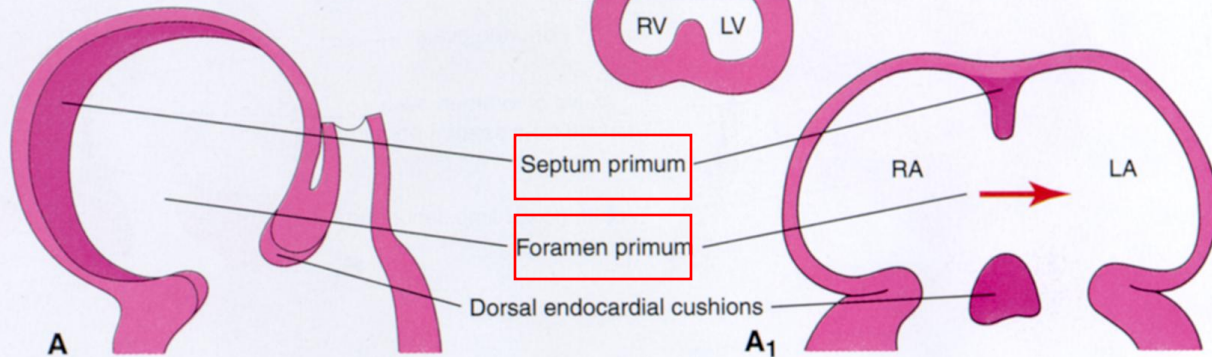
ATRIAL SEPTATION I: SEPTUM PRIMUM



RA, right atrium
RV, right ventricle

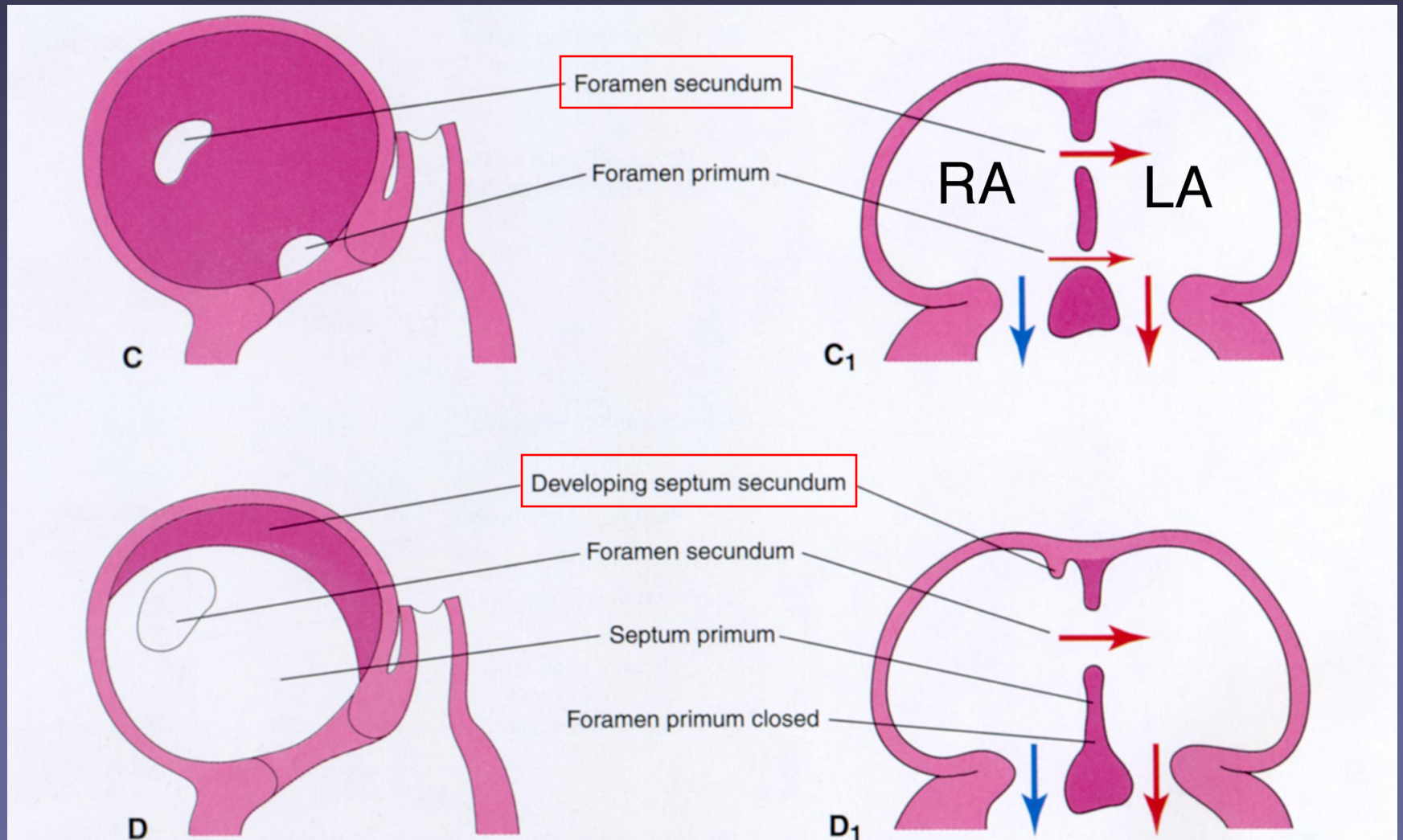


LA, left atrium
LV, left ventricle

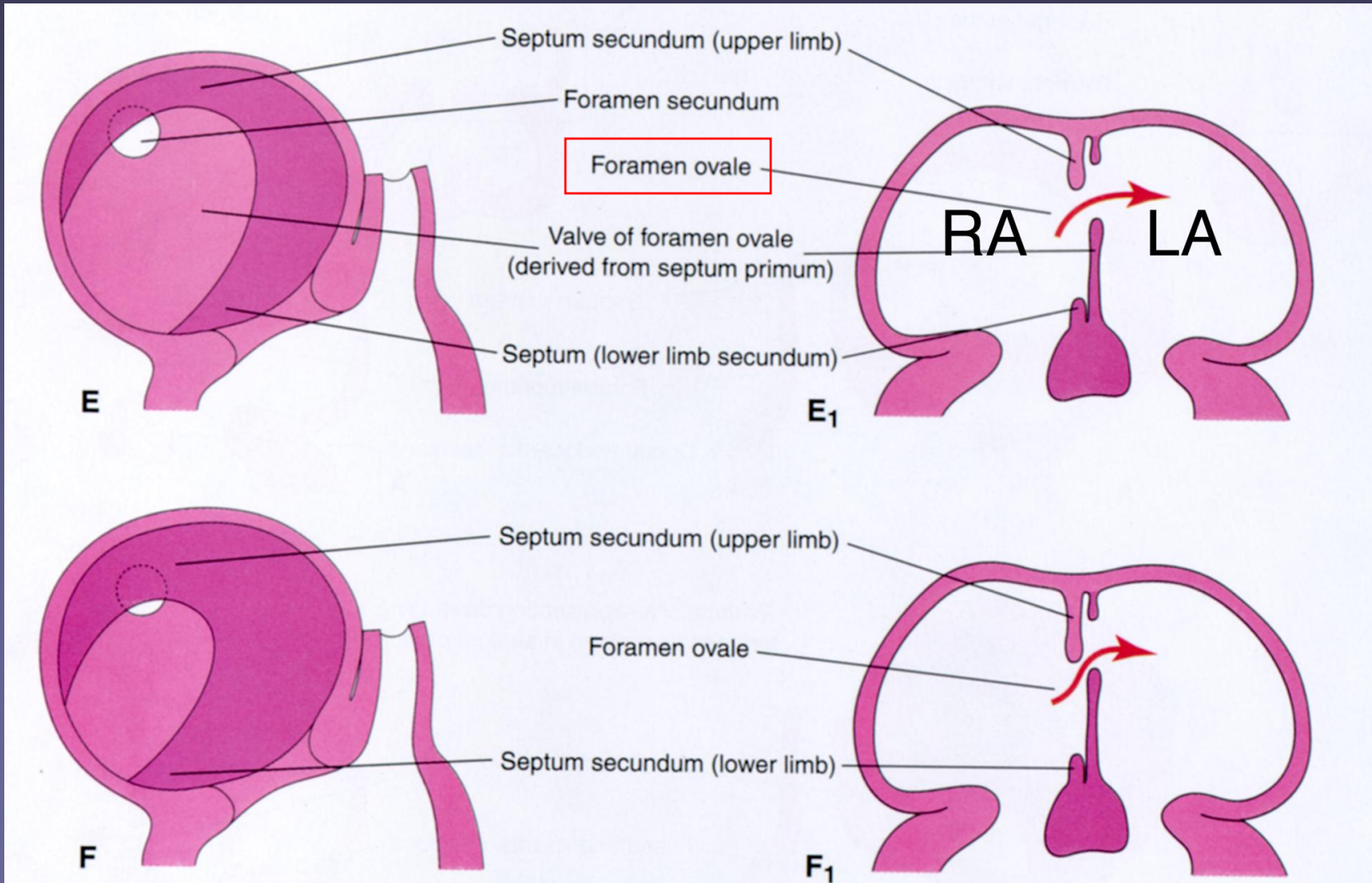


Red arrows—well oxygenated blood Blue arrows—poorly oxygenated blood

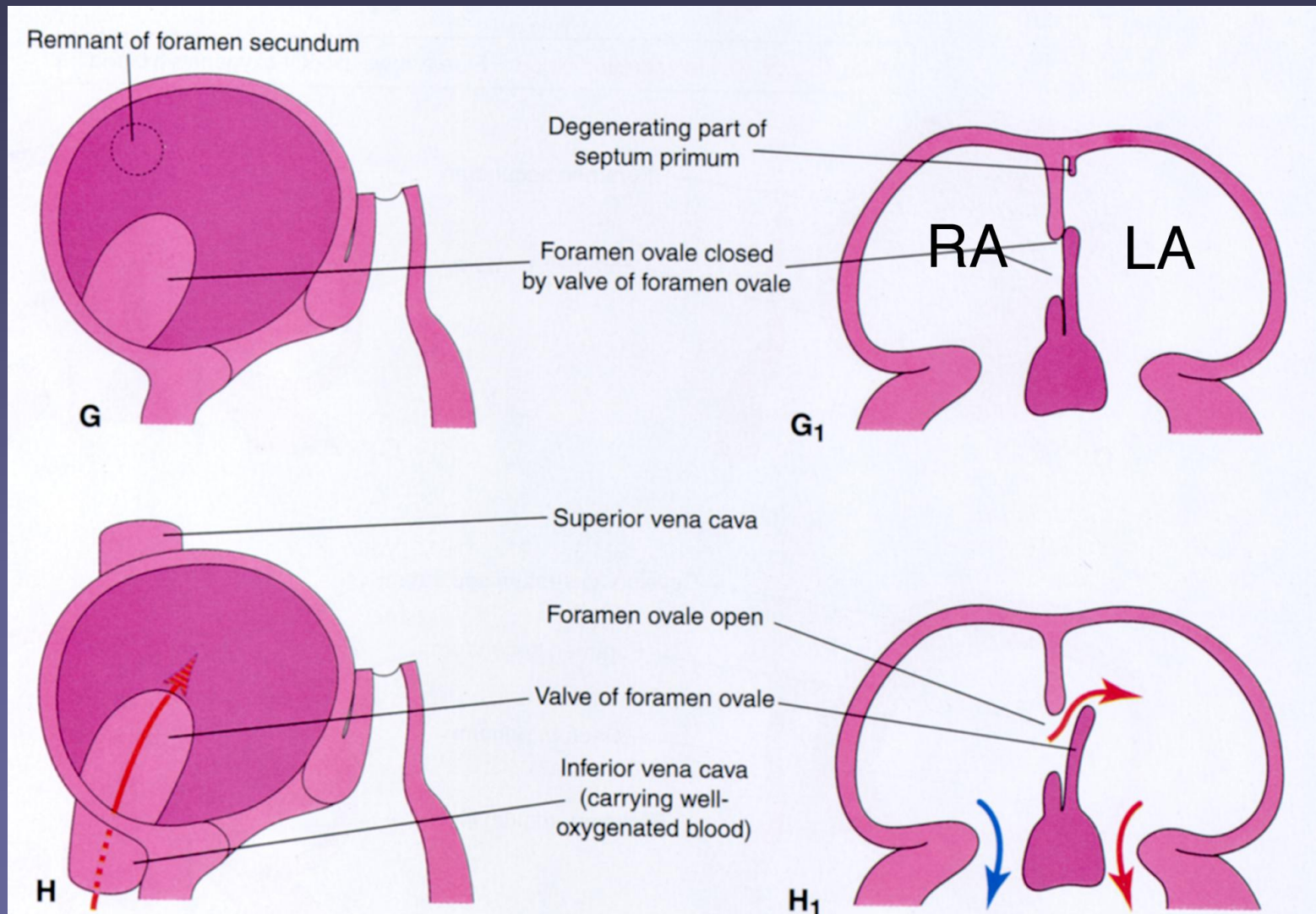
ATRIAL SEPTATION II: FORAMEN SECUNDUM



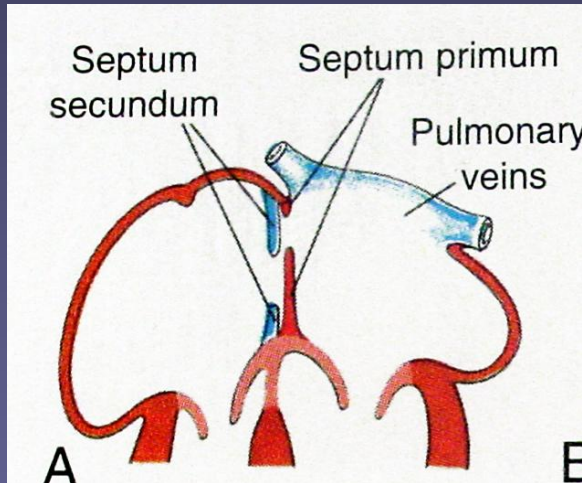
ATRIAL SEPTATION III: SEPTUM SECUNDUM



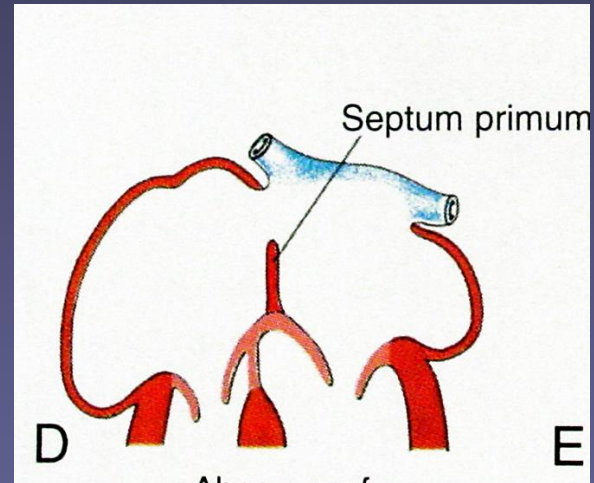
ATRIAL SEPTATION IV: COMPLETION



ATRIAL SEPTAL DEFECTS



NORMAL



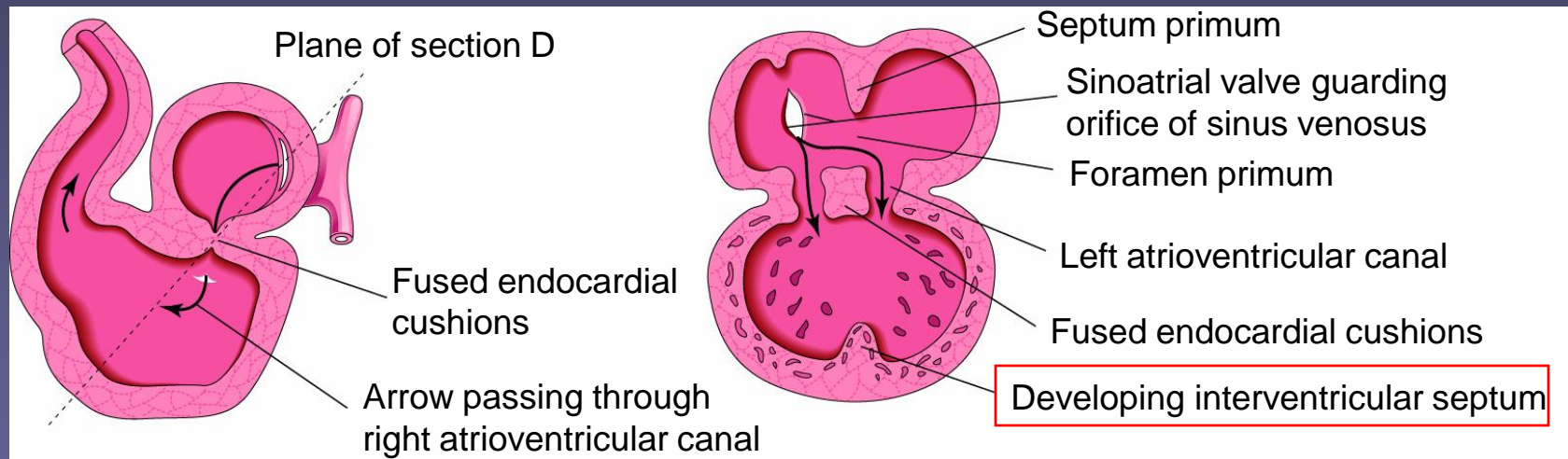
**OSTIUM SECUNDUM
(HIGH) ASD**

GENETIC CAUSES OF ASD

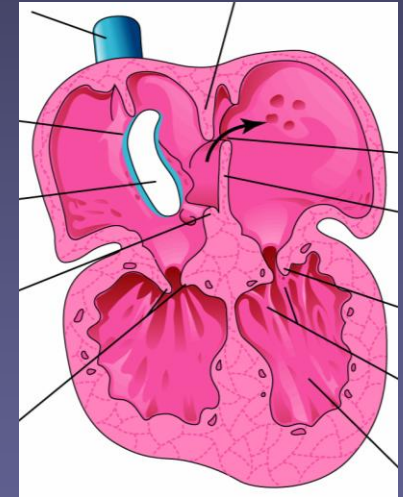
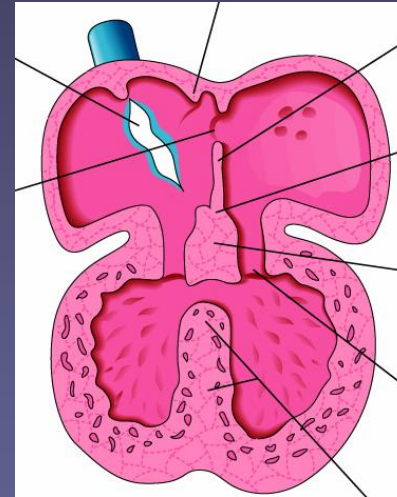
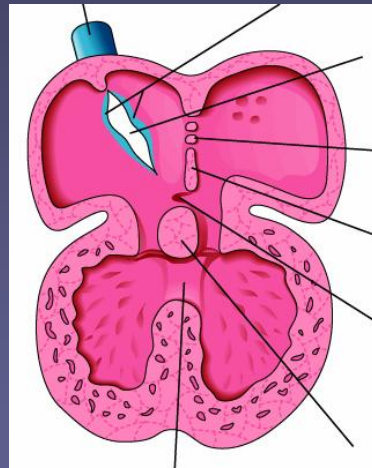
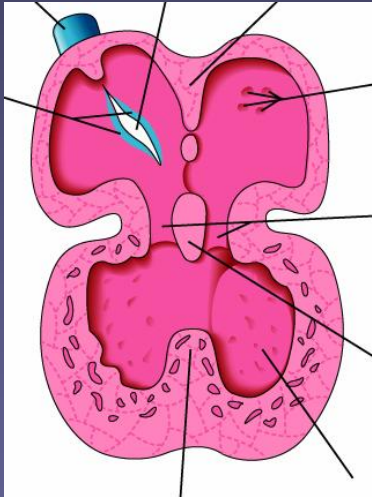
HETEROZYGOSITY OF MUTATIONS IN GENES LIKE:

- *Nkx2-5*, ENCODING A HOMEODOMAIN TRANSCRIPTION FACTOR
- *TBX5*, ENCODING A T-BOX TRANSCRIPTION FACTOR (HOLT-ORAM SYNDROME)

BEGINNING OF VENTRICULAR SEPTATION



PROGRESSION OF VENTRICULAR SEPTATION

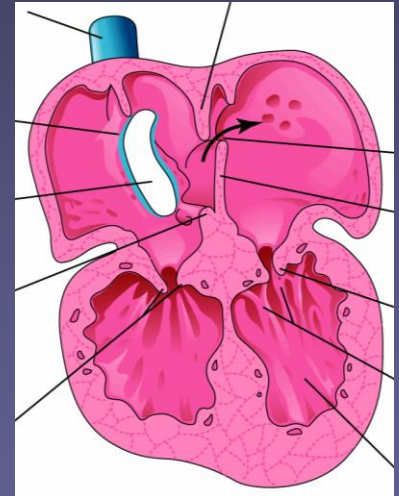


COMPLETION OF VENTRICULAR SEPTATION

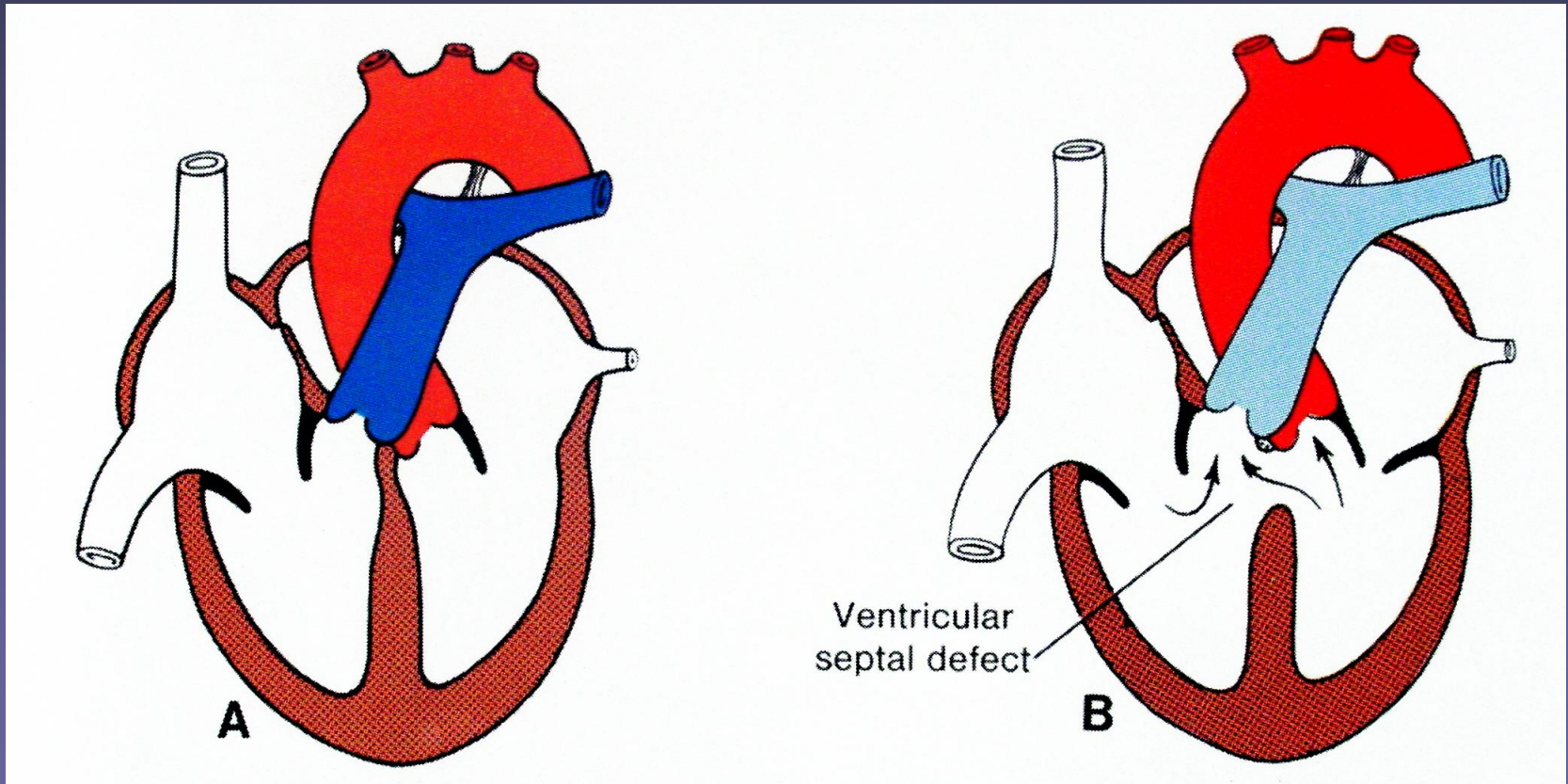
MUSCULAR SEPTUM

MEMBRANOUS SEPTUM

CONOTRUNCAL SEPTUM



MEMBRANOUS VSD



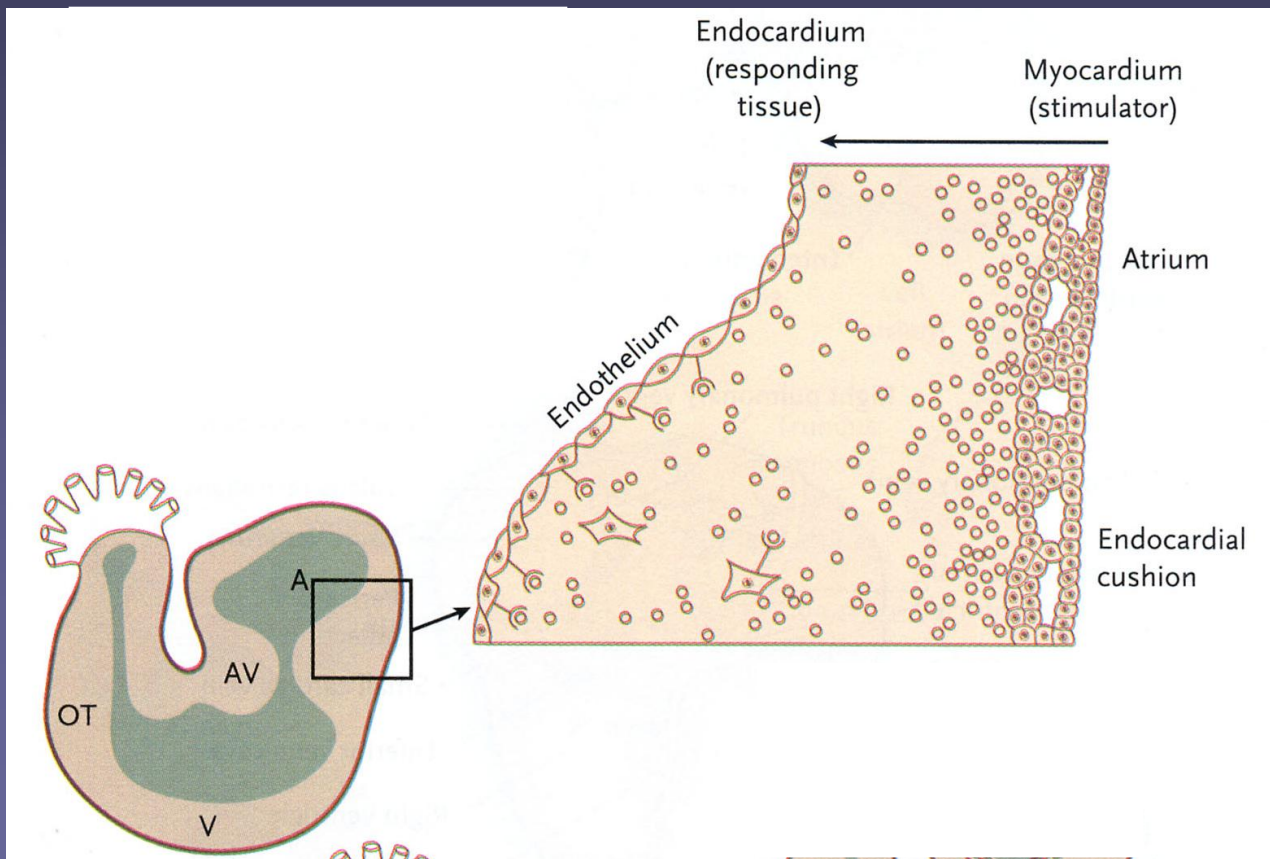
A
NORMAL

Ventricular
septal defect

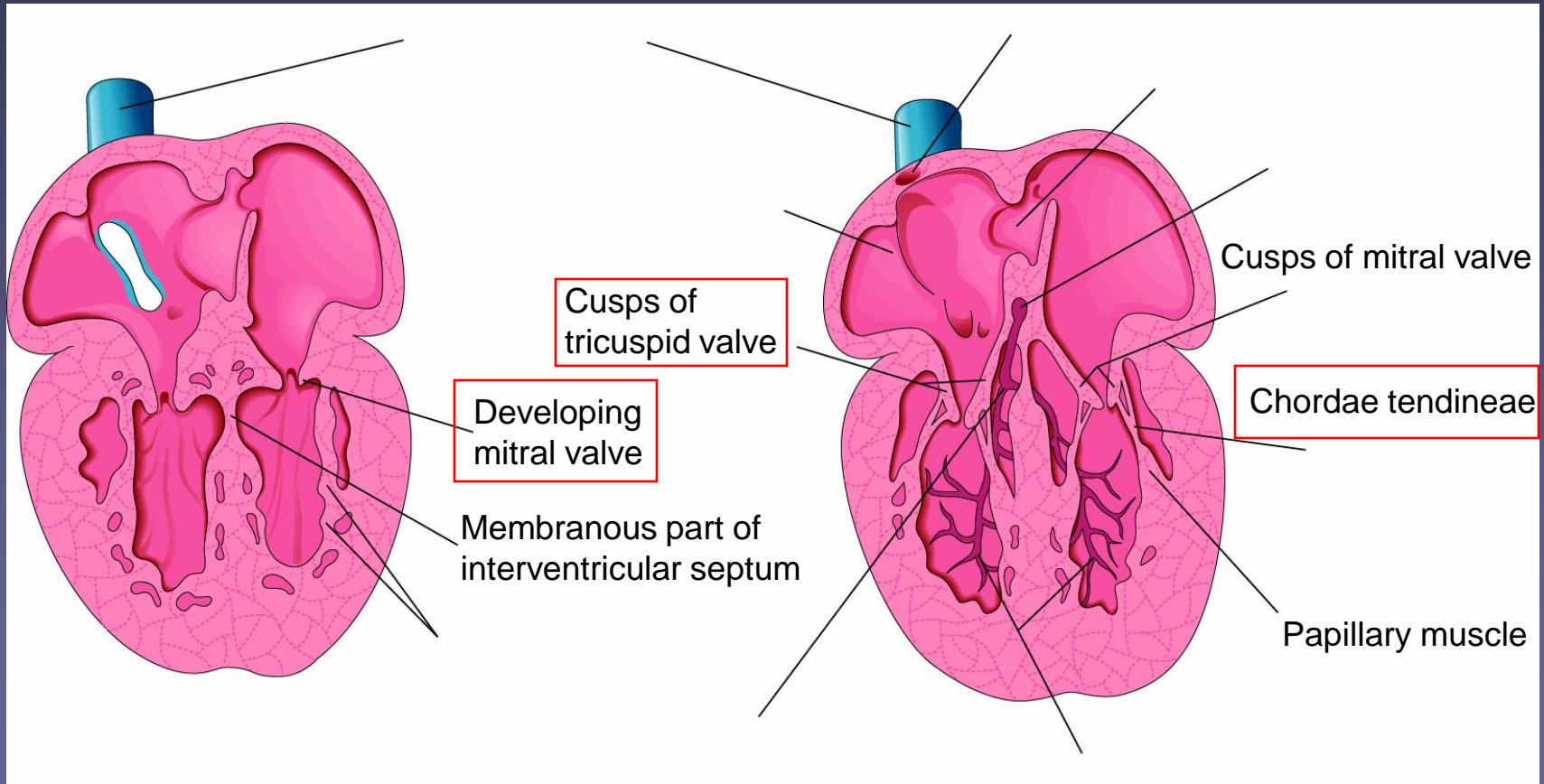
B

VSD

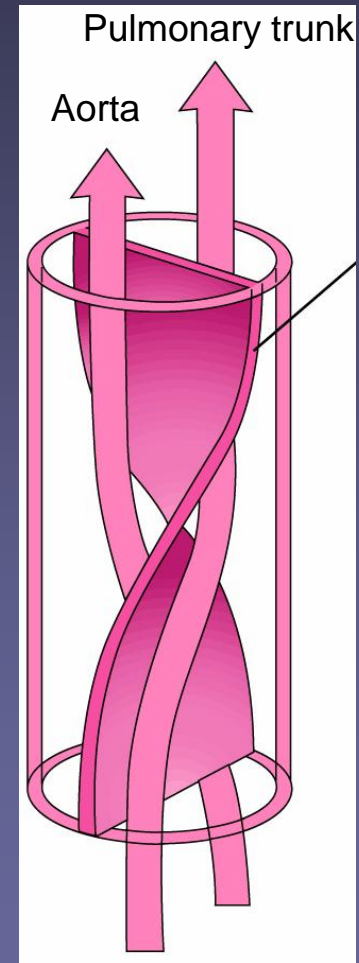
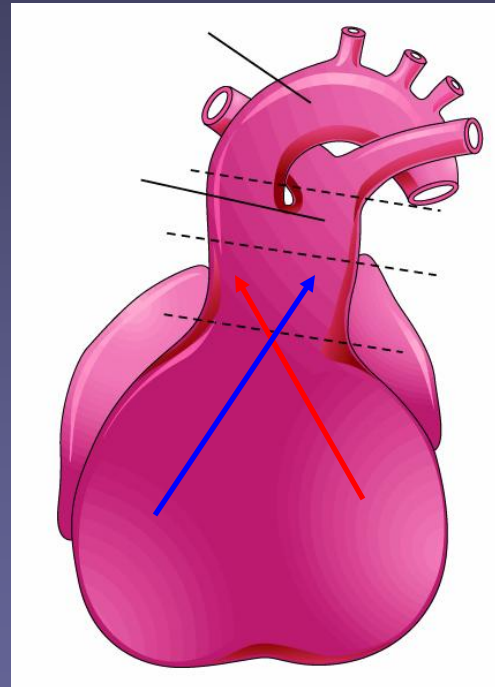
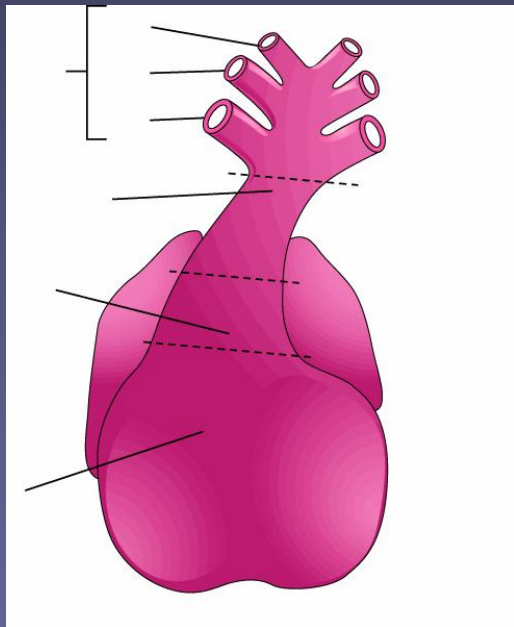
ENDOCARDIAL CUSHION FORMATION



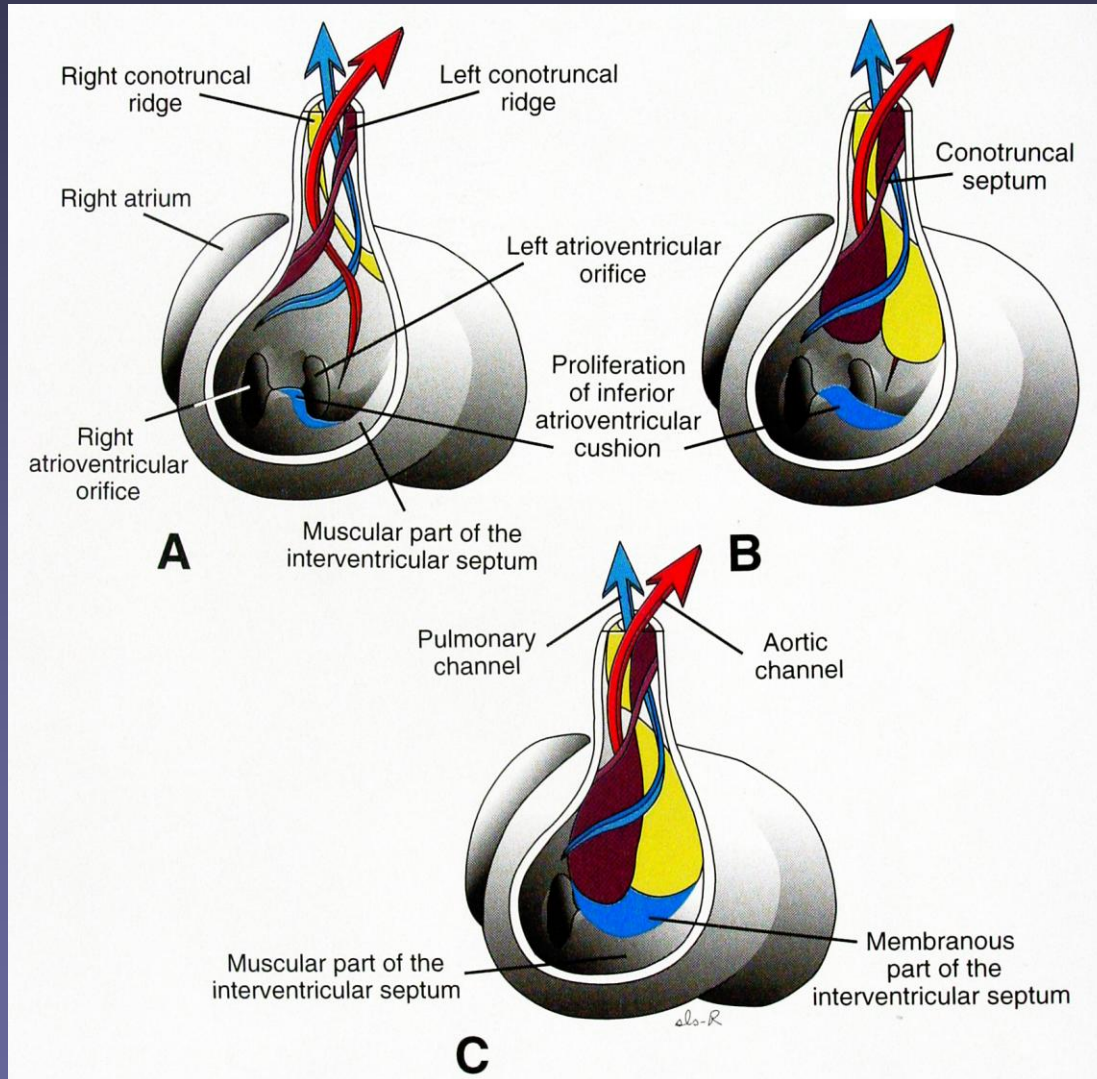
VALVE FORMATION



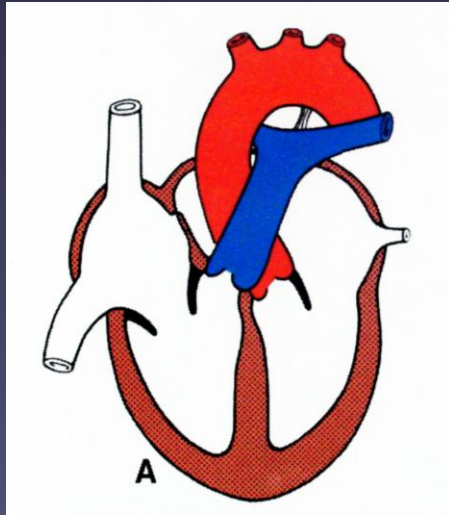
OUTFLOW SEPTATION



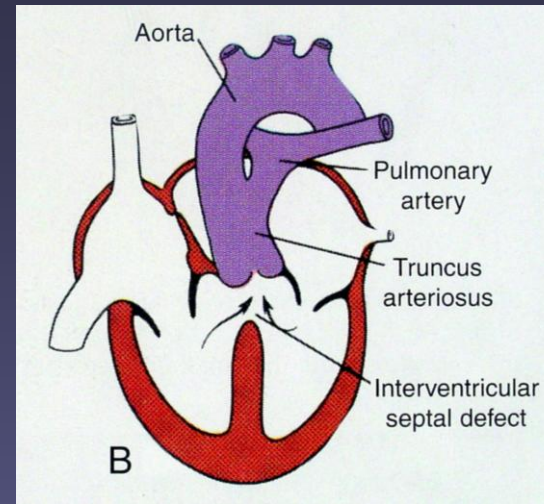
OUTFLOW SEPTATION



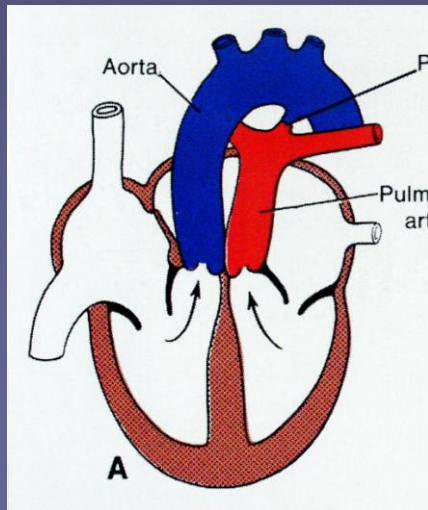
DEFECTS IN OUTFLOW SEPTATION



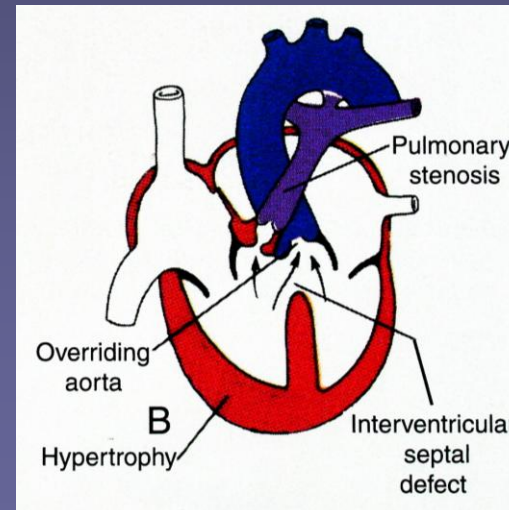
NORMAL



**NO SEPTUM:
PERSISTENT
TRUNCUS
ARTERIOSUS**

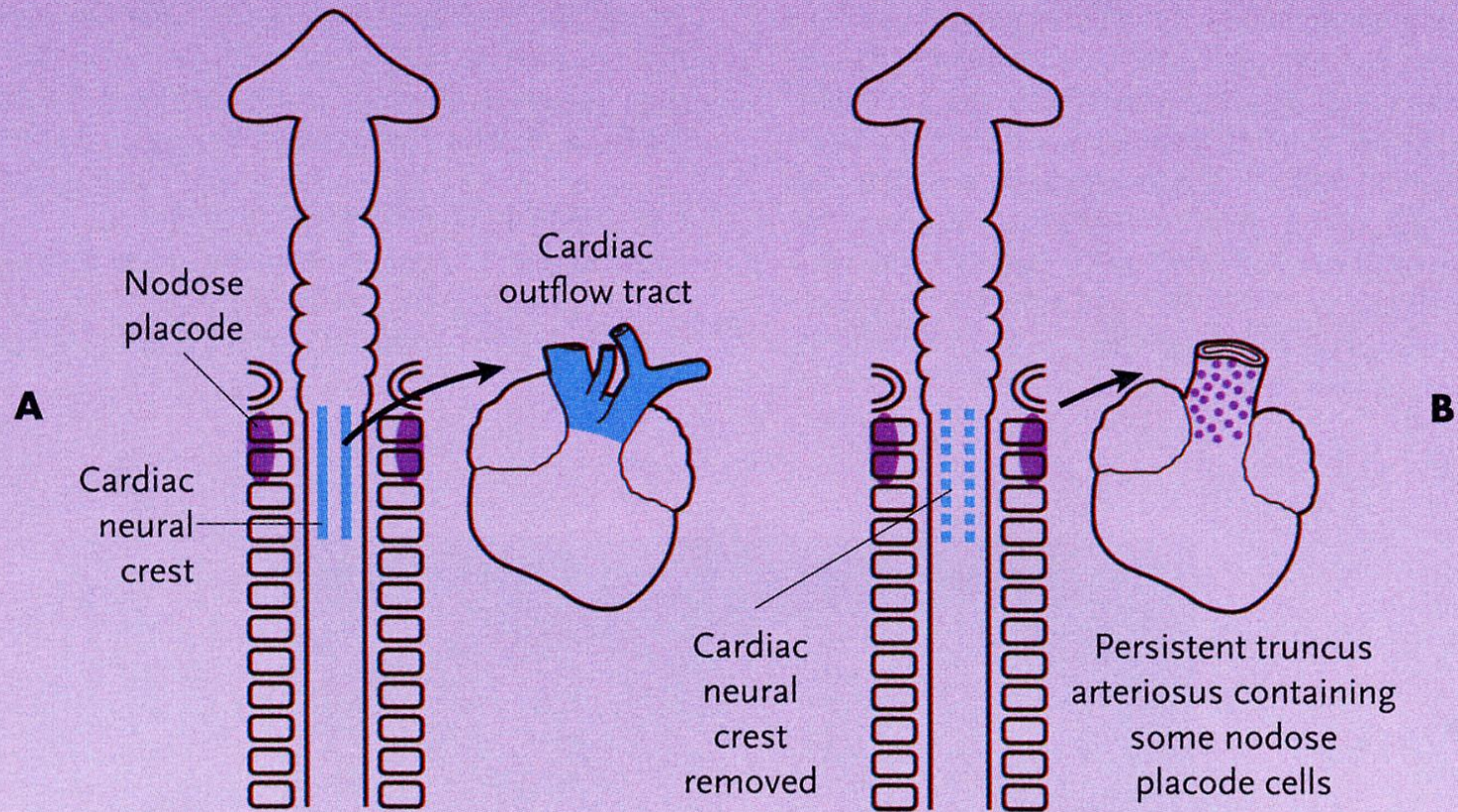


**STRAIGHT
SEPTUM:
TRANSPOSITION
OF GREAT
VESSELS**



**ASYMMETRIC
SEPTUM:
PULMONARY
STENOSIS;
TETRALOGY OF
FALLOT**

NEURAL CREST AND OUTFLOW TRACT SEPTATION



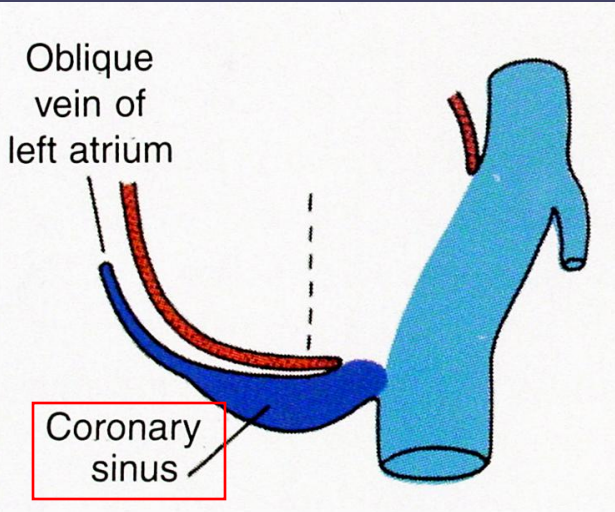
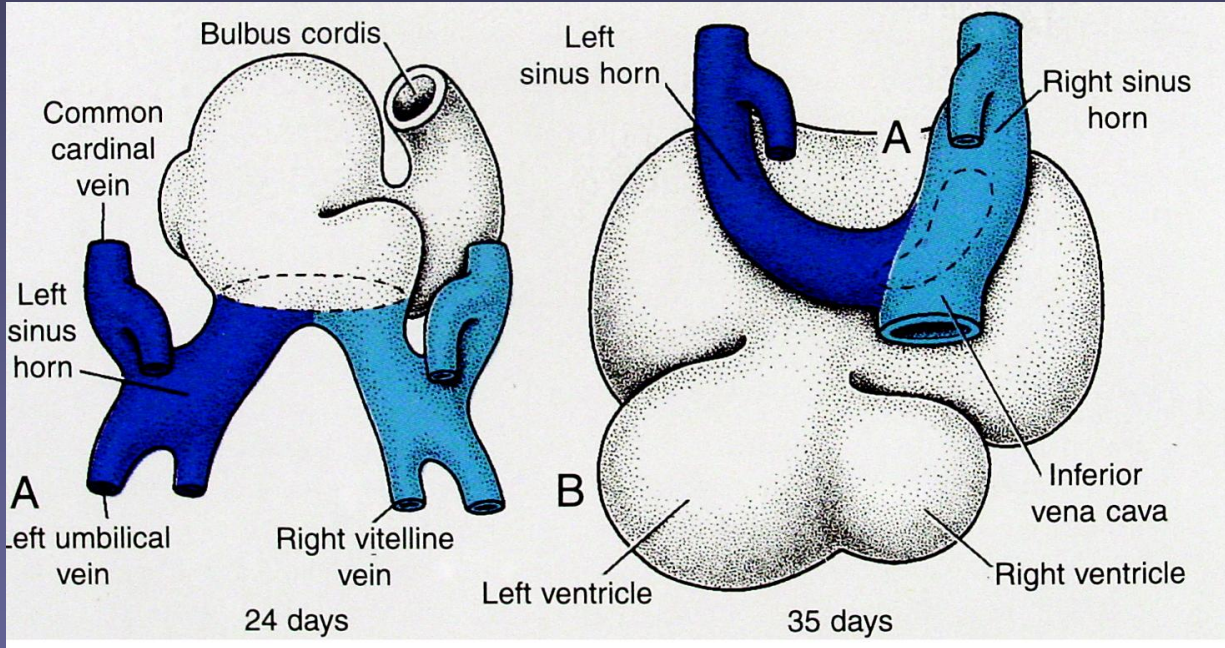
GENETIC BASIS FOR OUTFLOW DEFECTS

- ***TBX1* ENCODES A TRANSCRIPTION FACTOR EXPRESSED NEAR MIGRATING NEURAL CREST CELLS**
- ***TBX1* MUTATION IN MICE CAUSES DEFECTS RESEMBLING DIGEORGE SYNDROME**
- **DELETION OF *TBX1* FOUND IN MANY DIGEORGE SYNDROME PATIENTS**

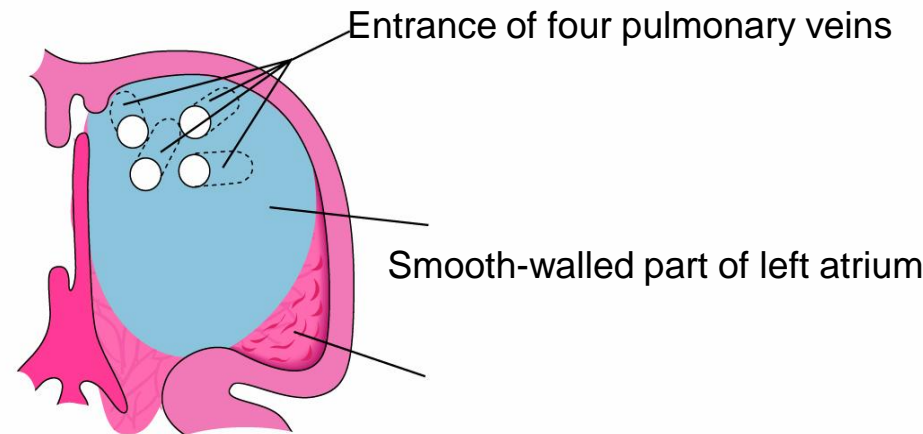
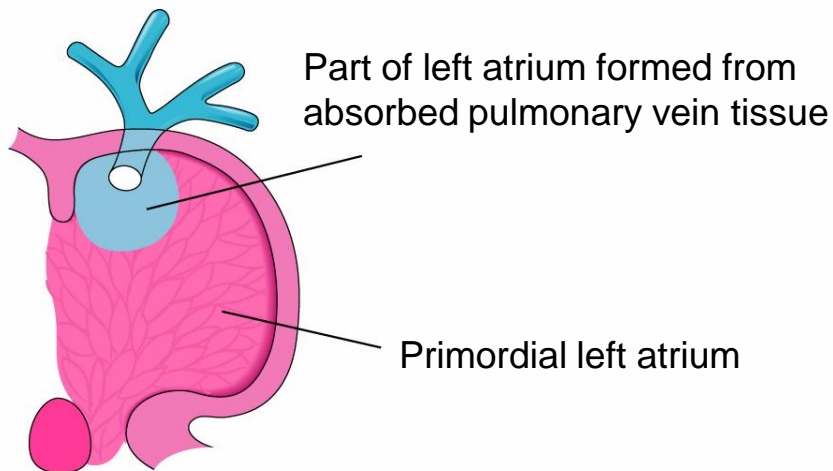
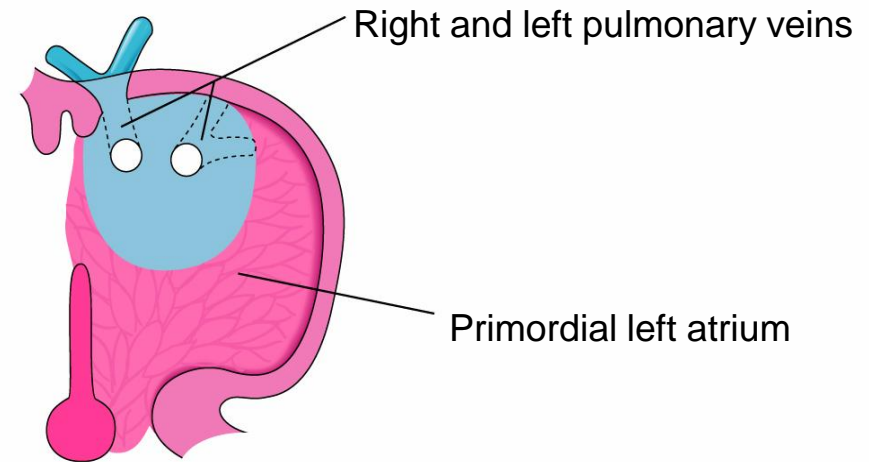
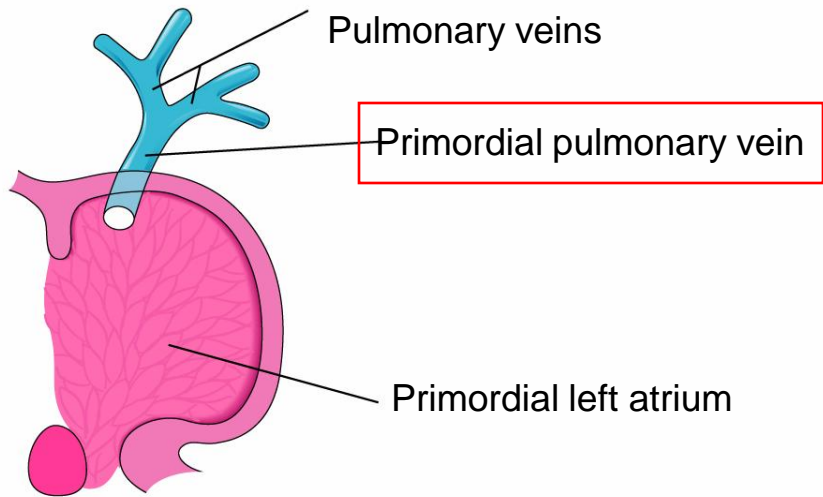
HUMAN HEART DEVELOPMENT

- **HEART TUBE FORMATION**
- **CARDIAC LOOPING**
- **CHAMBER SEPTATION**
- **VALVE AND OUTFLOW FORMATION**

SINUS VENOSUS AND RIGHT ATRIUM



PULMONARY VEINS AND LA



ATRIAL SEPTAL DEFECTS

- OSTIUM PRIMUM (LOW) ASD
- OSTIUM SECUNDUM (HIGH) ASD
- SINUS VENOSUS ASD

End