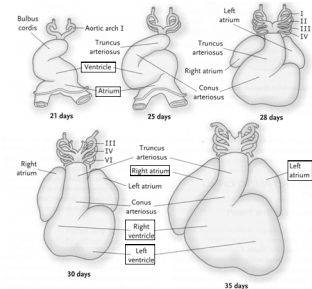


## INTRODUCTION TO HUMAN HEART DEVELOPMENT

Debbie Yelon  
 Developmental Genetics Program  
 Department of Cell Biology  
 Skirball Institute, NYU School of Medicine

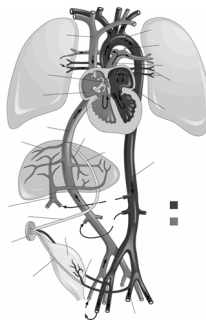
## HUMAN HEART DEVELOPMENT



## POSTNATAL CIRCULATION

PULMONARY CIRCULATION  
 RIGHT CHAMBERS

SYSTEMIC CIRCULATION  
 LEFT CHAMBERS



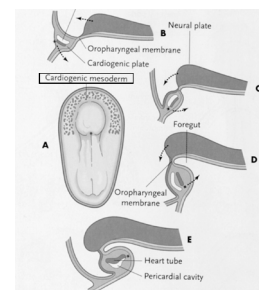
## HUMAN HEART DEVELOPMENT

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

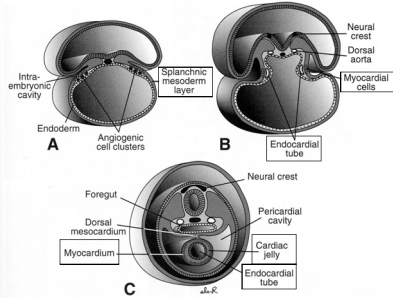
## CONGENITAL HEART DISEASE

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

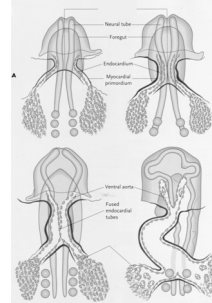
## LONGITUDINAL FOLDING POSITIONS CARDIAC CELLS



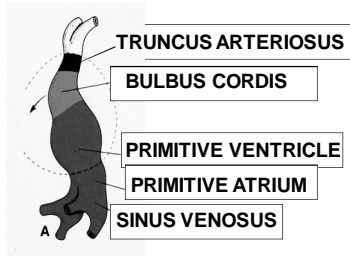
**LATERAL FOLDING FACILITATES TUBE FORMATION**



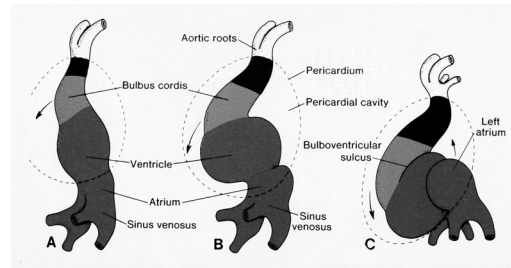
**TUBE FORMATION BEGINS ROSTRALLY**



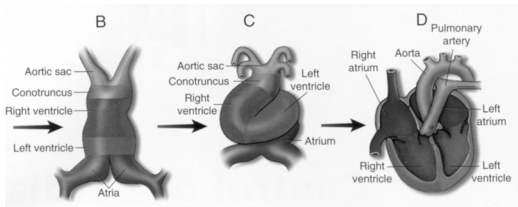
**PRIMITIVE HEART TUBE**



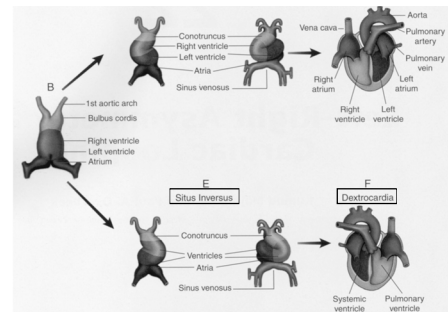
**CARDIAC LOOPING**



**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

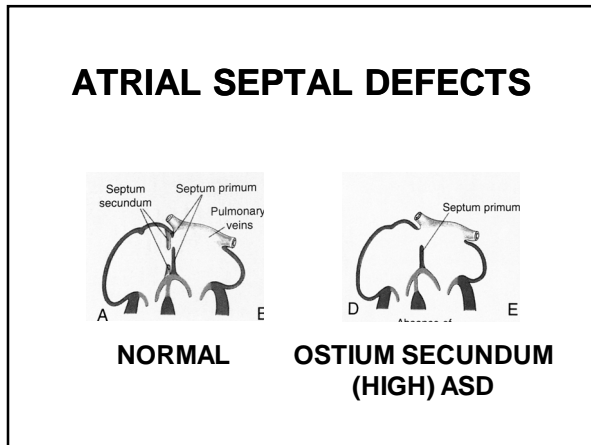
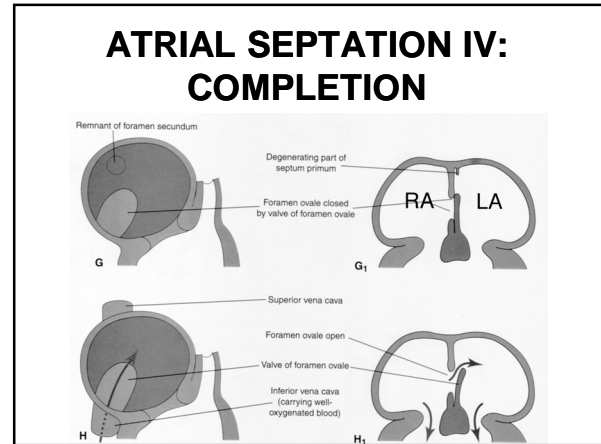
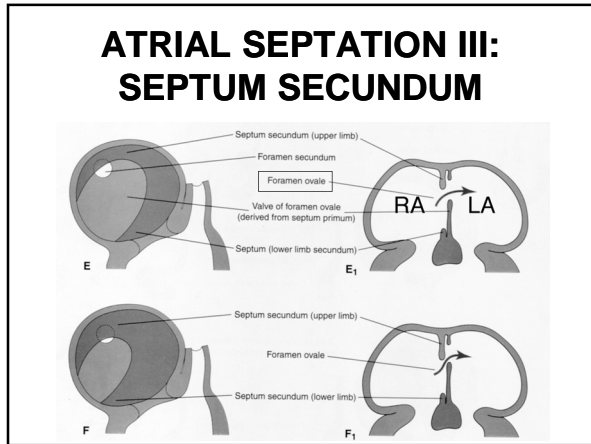
- ATRIAL SEPTATION
- VENTRICULAR SEPTATION
- ATRIOVENTRICULAR VALVE FORMATION
- DIVISION OF THE OUTFLOW TRACT

### SAGITTAL SECTIONS

### CORONAL SECTIONS

### ATRIAL SEPTATION I: SEPTUM PRIMUM

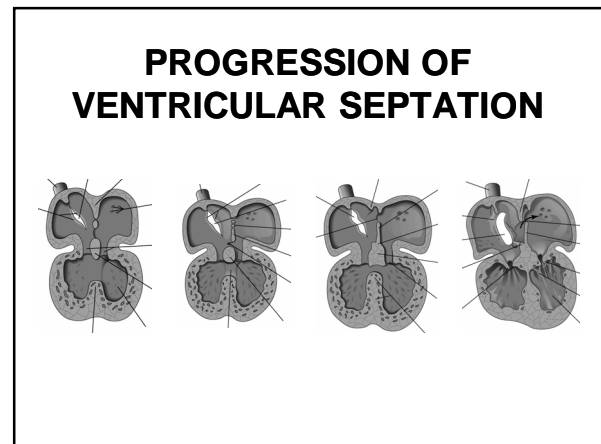
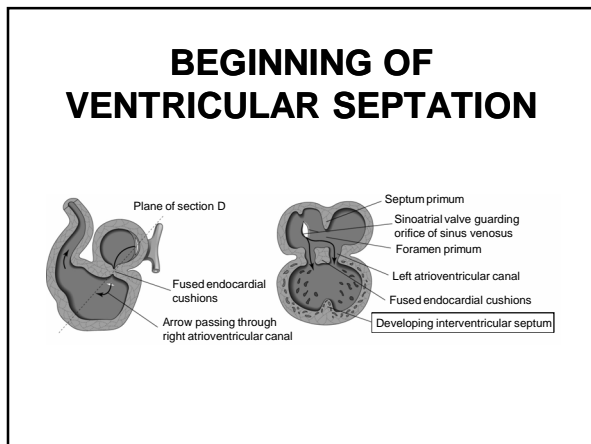
### ATRIAL SEPTATION II: FORAMEN SECUNDUM



### 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)

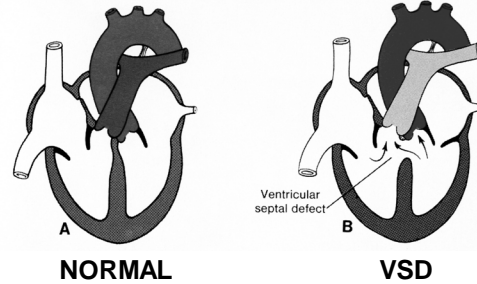


### COMPLETION OF VENTRICULAR SEPTATION

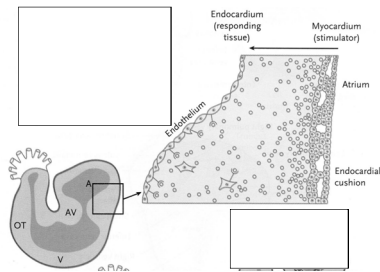
- MUSCULAR SEPTUM
- MEMBRANOUS SEPTUM
- CONOTRUNCAL SEPTUM



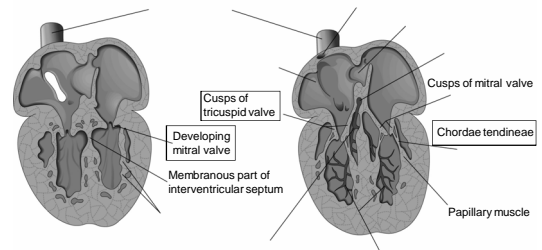
### MEMBRANOUS VSD



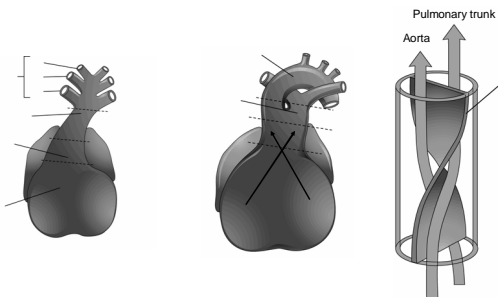
### ENDOCARDIAL CUSHION FORMATION



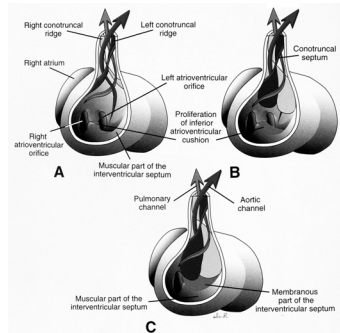
### VALVE FORMATION

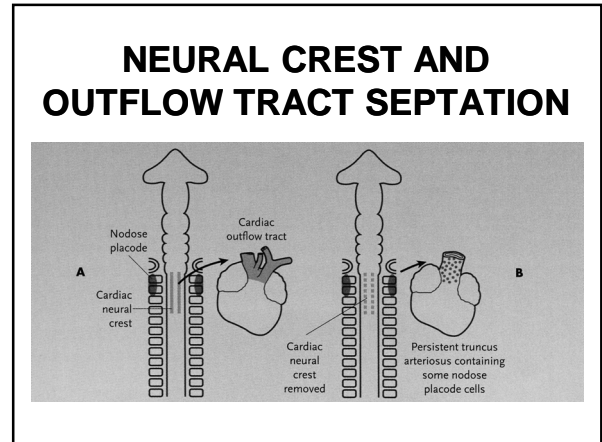
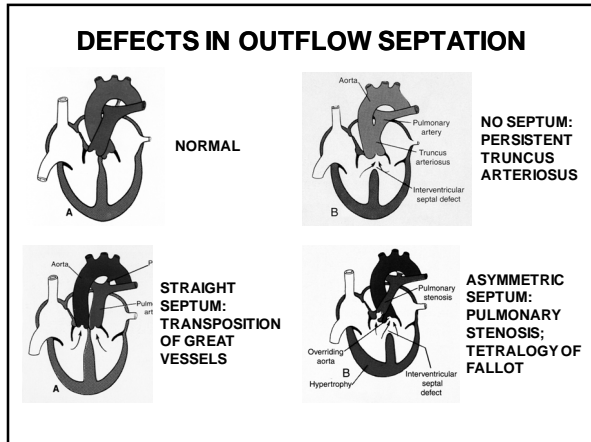


### OUTFLOW SEPTATION



### OUTFLOW SEPTATION



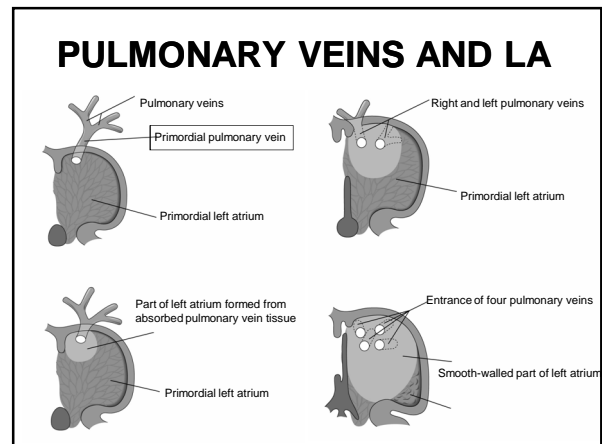
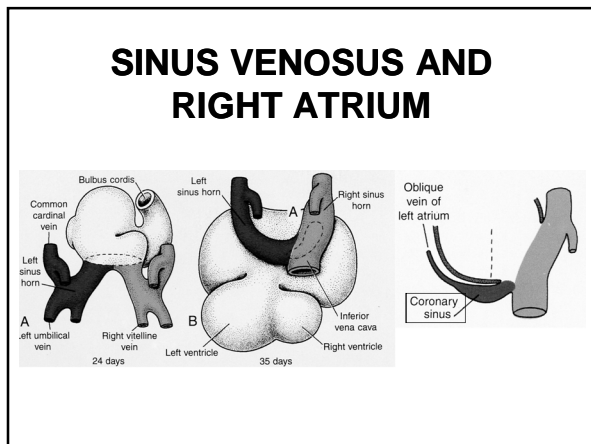


### GENETIC BASIS FOR OUTFLOW DEFECTS

- *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



**ATRIAL SEPTAL DEFECTS**

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

End