Objectives: enable the medical student to understand
a. formation of the heart tube
b. the process of looping

Key words: bulbus cordis, primitive ventricle, primitive atrium, sinus venosus

The cardiovascular system appears in the middle of the third week, it is the first major system to function within the embryo with the heart beginning to function during the fourth week.

Cardiac progenitor cells lie in the epiblast, lateral to the primitive streak. From there they migrate through the streak. Cells destined to form cranial segments of the heart (the outflow tract) migrate first, and cells forming more caudal portions (right ventricle, left ventricle, and sinus venosus, respectively) migrate in sequential order. The cells proceed toward the cranium and position themselves rostral to the buccopharyngeal membrane and neural folds.

Cardiac progenitor cells, reside in the splanchnic layer of the lateral plate mesoderm, are induced by the underlying pharyngeal endoderm to form cardiac myoblasts. Blood islands also appear in this mesoderm, where they will form blood cells and vessels by the process of vasculogenesis.

With time, the islands unite and form a horseshoe-shaped endothelial-lined tube surrounded by myoblasts. This region is known as the cardiogenic field. The intraembryonic cavity over it later develops into the pericardial cavity.

In addition to the cardiogenic region, other blood islands appear bilaterally, parallel, and close to the midline of the embryonic shield. These islands form a pair of longitudinal vessels, the dorsal aortae.

Formation and Position of the Heart Tube
As a result of cephalic folding of the embryo, the Buccopharyngeal membrane is pulled forward, while the heart and pericardial cavity move first to the cervical region and finally to the thorax.

As a result of lateral folding, the caudal regions of the paired cardiac primordia merge except at their caudal most ends. Simultaneously, the crescent part of the horseshoe-shaped area expands to form the future outflow tract and ventricular regions.

After fusion, constrictions and dilations appear in the heart tube, forming the following divisions (listed from cranial to caudal position):
1. Bulbus cordis
2. Primordial ventricle
3. Primordial atrium
4. Sinus venosus

Endocardium The endothelial tube becomes the internal endothelial lining of the heart-endocardium

The myocardium thickens and secretes a thick layer of extracellular matrix, rich in hyaluronic acid, that separates it from the endocardium.

Epicardium or Visceral pericardium is derived from:

Mesothelial cells on the surface of the septum transversum migrate over the heart to form most of the epicardium. The remainder of the epicardium is derived from mesothelial cells originating in the outflow tract region.

This outer layer is responsible for formation of the coronary arteries, including their endothelial lining and smooth muscle.

Formation of the Cardiac Loop
The heart tube continues to elongate and bend on day 23. The cephalic portion of the tube bends ventrally, caudally, and to the right; and the atrial (caudal) portion shifts dorsocranially and to the left. This bending is complete by day 28.
The process of looping was initially suggested that it is due to faster growth of the bulboventricular portion of the heart compared to the pericardial sac. However, it has been shown that the heart will loop even when the pericardial sac is removed as seen when the heart is cultured in vitro. It seems that the process of looping is a genetic property of the myocardium (may be due to cell shape changes) and not related to differential growth.

**Dorsal mesocardium**
Initially, the tube remains attached to the dorsal side of the pericardial cavity by a fold of mesodermal tissue, the dorsal mesocardium. No ventral mesocardium is ever formed. During heart looping, the dorsal mesocardium disappears, creating the transverse pericardial sinus, which connects both sides of the pericardial cavity.

The heart is now suspended in the cavity by blood vessels at its cranial and caudal poles. The atrial portion, initially a paired structure outside the pericardial cavity, forms a common atrium and is incorporated into the pericardial cavity. The atrioventricular junction remains narrow and forms the atrioventricular canal, which connects the common atrium and the early embryonic ventricle. Concurrently, the tubular heart elongates and develops alternate dilations and constrictions: Bulbus cordis, primitive ventricle, Primitive atrium, sinus venosus.

**Bulbus cordis**
The proximal third will form the trabeculated part of the right ventricle. The midportion, the conus cordis, will form the outflow tracts of both ventricles. The distal part of the bulbus, the truncus arteriosus, will form the roots and proximal portion of the aorta and pulmonary artery.

The junction between the ventricle and the bulbus cordis, externally indicated by the bulboventricular sulcus, remains narrow. Internally, it is called the primary interventricular foramen. The primitive ventricle, which is now trabeculated, is called the primitive left ventricle. Likewise, the trabeculated proximal third of the bulbus cordis may be called the primitive right ventricle.

**Abnormalities of Cardiac Looping**

**Dextrocardia:**
The heart lies on the right side of the thorax instead of the left, is caused when the heart loops to the left instead of the right. Dextrocardia may coincide with Situs inversus, a complete reversal of asymmetry in all organs.

**Development of the Sinus Venosus**
In the middle of the fourth week, the sinus venosus receives venous blood from the right and left sinus horns.

Each horn receives blood from three important veins:
(a) the vitelline or omphalomesenteric vein,
(b) the umbilical vein, and
(c) the common cardinal vein.

At first, communication between the sinus and the atrium is wide. Soon, the entrance of the sinus shifts to the right. This shift is caused by left-to-right shunts of blood, which occur in the venous system during the fourth and fifth weeks of development. The left sinus horn rapidly loses its importance with obliteration of the left vitelline vein and the left common cardinal vein. The right umbilical vein is obliterated also. All that remains of the left sinus horn is the oblique vein of the left atrium and the coronary sinus. The right horn, which now forms the only communication between the original sinus venosus and the atrium, is incorporated into the right atrium to form the smooth-walled part of the right atrium. Its entrance, the sinuatrial orifice, is flanked on
each side by a valvular fold, the right and left venous valves. Dorsocranially, the valves fuse, forming a ridge known as the septum spurium. The left venous valve and the septum spurium fuse with the developing atrial septum. The superior portion of the right venous valve disappears entirely. The inferior portion develops into two parts: (a) the valve of the inferior vena cava, and (b) the valve of the coronary sinus.

The crista terminalis forms the dividing line between the original trabeculated part of the right atrium and the smooth-walled part (sinus venarum), which originates from the right sinus horn.

Next lecture: Formation of cardiac septa