Lecture Objectives:

- Describe the development of primary and secondary atrial septa and the ventricular septum.
- Explain the changes occurring in the bulbis cordis and truncus arteriosus in its transformation from a single to a double tube.

The major septa of the heart are formed between the 27th and 37th days of development, when the embryo grows in length from 5 mm to approximately 16 to 17 mm.

Septum are formed by:
- Endocardial cushions
- Merging of two expanding portions of the wall of the heart.

Endocardial cushions: (1) two actively growing ridges approach each other until they fuse. (2) a single actively growing cell mass.

Formation of Endocardial cushions depends on:
1. synthesis and deposition of extracellular matrices and
2. cell proliferation.

Endocardial cushions develop in the atrioventricular and conotruncal regions. They assist in formation of the atrial and ventricular (membranous portion) septa, atrioventricular canals and valves, aortic and pulmonary channels.

Merging of two expanding portions of the wall of the heart:

A narrow ridge forms between the two expanding portions of the wall of the heart.

a narrow strip of tissue in the wall of the atrium or ventricle should fail to grow while areas on each side of it expand rapidly.

Such a septum partially divides the atria and ventricles.

Such a septum never completely divides the original lumen but leaves a narrow communicating channel between the two expanded sections. It is usually closed secondarily by tissue contributed by neighboring proliferating tissues.

Partitioning of the Primordial Heart

Partitioning of the atrioventricular canal, primordial atrium, and ventricle begins around the middle of the fourth week and is essentially completed by the end of the eighth week. Although described separately, these processes occur concurrently.

Septum Formation in the Atrioventricular Canal

Initially, the atrioventricular canal gives access only to the primitive left ventricle and is separated from the bulbus cordis by the bulbo(cono) ventricular flange.
Since the atrioventricular canal enlarges to the right, blood passing through the atrioventricular orifice now has direct access to the primitive left as well as the primitive right ventricle.

Toward the end of the fourth week, two endocardial cushions form on the dorsal and ventral walls of the atrioventricular (AV) canal referred to as the superior and inferior cushions respectively. The dorsal and ventral cushions, in the meantime, project further into the lumen and fuse, resulting in a complete division of the canal into right and left atrioventricular orifices by the end of the fifth week.

Two lateral cushions appear on the right and left borders of the atrioventricular canal which later help to form the mitral and tricuspid heart valves.

These canals partially separate the primordial atrium from the primordial ventricle, and the endocardial cushions function as AV valves.

**Atrioventricular Valves**

Each atrioventricular orifice is surrounded by local proliferations of mesenchymal tissue. The blood stream hollows out and thins tissue on the ventricular surface of these proliferations.

Valves form and remain attached to the ventricular wall by muscular cords.

Muscular tissue in the cords degenerates and is replaced by dense connective tissue.

The valves then consist of connective tissue covered by endocardium.

They are connected to the papillary muscles (thick trabeculae in the wall of the ventricle) by means of chordae tendineae.

In this manner two valve leaflets, constituting the bicuspid (or mitral) valve, form in the left atrioventricular canal, and three, constituting the tricuspid valve, form on the right side.

**Persistent common atrioventricular canal**

This abnormality is always accompanied by a septum defect in the atrial as well as in the ventricular portion of the cardiac partitions.

**Partitioning of the Primordial Atrium**

**Septum primum**; a thin crescent-shaped membrane grows from the roof of the common atrium into the lumen. The two limbs of this septum extend toward the endocardial cushions in the atrioventricular canal.

The opening between the lower rim of the septum primum and the endocardial cushions is the Ostium primum.

Extensions of endocardial cushions grow along the edge of the septum primum, closing the ostium primum. Before closure is complete, cell death produces perforations in the upper portion of the septum primum. Coalescence of these perforations forms the Ostium secundum, ensuring free blood flow from the right to the left primitive atrium.
As a result of incorporation of the sinus horn into the right atrium, a new crescent-shaped fold appears. This new fold, the **Septum secundum**, never forms a complete partition in the atrial cavity.

When the left venous valve and the septum spurium fuse with the septum secundum, the free concave edge of the septum secundum begins to overlap the ostium secundum.

The opening left by the septum secundum is called the **oval foramen** (foramen ovale).

When the upper part of the septum primum gradually disappears, the remaining part becomes the **valve of the oval foramen**.

An obliquely elongated cleft, through which blood from the right atrium flows to the left side.

After birth, when lung circulation begins and pressure in the left atrium increases, the valve of the oval foramen is pressed against the septum secundum, obliterating the oval foramen and separating the right and left atria.

In about 20% of cases, fusion of the septum primum and septum secundum is incomplete, and a narrow oblique cleft remains between the two atria. This condition is called **probe patency of the oval foramen**; it does not allow intracardiac shunting of blood.

**Further Differentiation of the Atria**

**Left atrium**  a single embryonic pulmonary vein develops as an outgrowth of the posterior left atrial wall, just to the left of the septum primum. This vein gains connection with veins of the developing lung buds. During further development, the pulmonary vein and its branches are incorporated into the left atrium, forming the large smooth-walled part of the adult atrium. The original embryonic left atrium becomes the trabeculated atrial appendage.

**Right atrium**  The original embryonic right atrium becomes the trabeculated right atrial appendage containing the pectinate muscles, and the smooth-walled sinus venarum originates from the right horn of the sinus venosus.

**Atrial septal defect (ASD)**

- Ostium secundum defect caused by excessive resorption of the septum primum.
- Defect caused by failure of development of the septum secundum.
- Common atrium, or “Cor triloculare biventriculare”, resulting from complete failure of the septum primum and septum secundum to form.

**Premature closure of the oval foramen**

Occasionally, the oval foramen closes during prenatal life. This abnormality leads to massive hypertrophy of the right atrium and ventricle and underdevelopment of the left side of the heart. Death usually occurs shortly after birth.

**Septum Formation in the Ventricles**

By the end of the fourth week, the two primitive ventricles begin to expand.

This is accomplished by
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- continuous growth of the myocardium on the outside and
- continuous diverticulation and trabecula formation on the inside

**Interventricular septum**: The medial walls of the expanding ventricles become apposed and gradually merge, forming the muscular interventricular septum.

The interventricular foramen: the space between the free rim of the muscular ventricular septum and the fused endocardial cushions permits communication between the two ventricles.

The interventricular foramen

- shrinks on completion of the conus septum
- During further development, outgrowth of tissue from the inferior endocardial cushion along the top of the muscular interventricular septum closes the interventricular foramen. This tissue fuses with the abutting parts of the conus septum.

Complete closure of the interventricular foramen forms the membranous part of the interventricular septum.

**Septum Formation in the Truncus Arteriosus and Conus Cordis**

**Truncus cushions (swellings)**

During the fifth week, pairs of opposing ridges appear on the right superior wall (right superior truncus swelling) and on the left inferior wall (left inferior truncus swelling).

The right superior truncus swelling grows distally and to the left, and the left inferior truncus swelling grows distally and to the right.

While growing toward the aortic sac, the swellings twist around each other, foreshadowing the spiral course of the future septum.

After complete fusion, the ridges form the aorticopulmonary septum, dividing the truncus into an aortic and a pulmonary channel.

**Conus swellings——conus septum**

When the truncus swellings appear, similar swellings (cushions) develop along the right dorsal and left ventral walls of the conus cordis.

The conus swellings grow toward each other to unite with the truncus septum.

When the two conus swellings have fused, the septum divides the conus into an anterolateral portion (the outflow tract of the right ventricle) and a posteromedial portion (the outflow tract of the left ventricle).

**Neural crest cells** migrate from the edges of the neural folds in the hindbrain region and contribute to endocardial cushion formation in both the conus cordis and truncus arteriosus.

Abnormal migration, proliferation, or differentiation of these cells results in congenital malformations in this region, such as
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Prof. Dr. Malak A. Al-yawer

- tetralogy of Fallot
- pulmonary stenoses,
- persistent truncus arteriosus
- transposition of the great vessels
- atrial and ventricular septal defects

Since neural crest cells also contribute to craniofacial development, it is not uncommon to see facial and cardiac abnormalities in the same individual.

**Semilunar valves**

These develop at the lower end of the truncus arteriosus. At this level there are four swellings of sub-endocardial tissue - the right and left bulbar swellings and two accessory dorsal and ventral swellings. Separation of the fused bulbar ridges forms the aortic and pulmonary vessels each containing three swellings.

The aorta has one posterior valve and two anterior valves, above which the right and left coronary arteries arise. The pulmonary trunk has one anterior and two posterior valves.

Growth and excavation of the swellings results in the formation of the semilunar valves. Formation of the semilunar valves is complete by the end of the 9th week.

**Clinical Correlates**

**Ventricular septal defect (VSD)**

involving the membranous portion of the septum. Although it may be found as an isolated lesion, VSD is often associated with abnormalities in partitioning of the conotruncal region. Occasionally, the defect is not restricted to the membranous part but also involves the muscular part of the septum.

**Tetralogy of Fallot**

is due to an unequal division of the conus resulting from anterior displacement of the conotruncal septum. The four components of the defect:

- pulmonary stenosis,
- overriding aorta,
- interventricular septal defect, and
- hypertrophy of the right ventricle.

**Persistent truncus arteriosus**

The conotruncal ridges fail to fuse and to descend toward the ventricles

the pulmonary artery arises some distance above the origin of the undivided truncus.

This abnormality is always accompanied by an interventricular septal defect.

The undivided truncus thus overrides both ventricles and receives blood from both sides.

**Transposition of the great vessels**
occurs when the conotruncal septum fails to follow its normal spiral course and runs straight down. As a consequence, the aorta originates from the right ventricle, and the pulmonary artery originates from the left ventricle.

This condition, sometimes is associated with a defect in the membranous part of the interventricular septum. It is usually accompanied by an open ductus arteriosus.

**Valvular stenosis (atresia) of the pulmonary artery**

The trunk of the pulmonary artery is narrow or even atretic. The **patent oval foramen** then forms the only outlet for blood from the right side of the heart.

**The ductus arteriosus, always patent**, is the only access route to the pulmonary circulation.

**Aortic valvular stenosis**

In aortic valvular stenosis(A), fusion of the thickened valves may be so complete that only a pinhole opening remains. The size of the aorta itself is usually normal.

Aortic valvular atresia (B): (1) fusion of the semilunar aortic valves is complete (2) the aorta, left ventricle, and left atrium are markedly underdeveloped. (3) The abnormality is usually accompanied by an open ductus arteriosus, which delivers blood into the aorta.

**Formation of the Conducting System of the Heart**

Initially the pacemaker for the heart lies in the caudal part of the left cardiac tube.

Later the sinus venosus assumes this function. As the sinus is incorporated into the right atrium, pacemaker tissue lies near the opening of the superior vena cava. Thus, the sinuatrial node is formed.

The atrioventricular node and bundle (bundle of His) are derived from two sources: (a) cells in the left wall of the sinus venosus, and (b) cells from the atrioventricular canal. Once the sinus venosus is incorporated into the right atrium, these cells lie in their final position at the base of the interatrial septum.

Abnormalities of the conducting tissue may cause unexpected death during infancy.

Thank you

Next lecture: Vascular system