In the 3rd week of embryonic development, both the neurulation as well as the development of the cardiovascular system begins. The neurulation denotes the formation of the neural tube in the development of the central nervous system. These complex processes are a combination of numerous factors and interactions. Embryology is always relevant for the understanding of an organ. By understanding the development we can understand the anatomy and possible malformations. The processes relevant for the examination are explained step by step in this article.

The Stages of Neurulation

1st Stage: Induction

At the beginning of the 3rd week of embryonic development, the induction of the neurulation begins. The notochord and paraxial mesoderm secrete signaling molecules. This results in the differentiation of the overlying ectoderm into neuroectoderm.

2nd Stage: Formation of the Neural Plate

The neural plate originates from the neuroectoderm, an area with compressed and increased epithelial cells. It grows in the direction from cranial to caudal. The cranial end initially increases rapidly and is therefore wider than the caudal end. From this histoid, first the brain will originate.
3rd Stage: Formation of the Neural Tube

Approximately on the 18th day the neural plate deepens and forms the neural groove. The margins are increased by the so-called convergent extension. This means that the cell rows shift into one another and thus form the neural folds. Finally, the neural folds merge, cut off the neural groove and thus form the neural tube. This is the basis for the central nervous system.

4th Stage: Closing of the Front and Rear Neuropore

The neural tube resembles a channel which is open at both ends. The end of the head is called anterior neuropore. The brain will develop in this region. The caudal end, the posterior neuropore, will form the spinal cord. The cavity of the neural tube later forms the ventricular system of the central nervous system.

On the 25th embryonic day, the end of the head joins the anterior neuropore. Two days later, the posterior neuropore closes. The neural tube now ends approximately at the height of the later S2 segment. If the closing of the neural tube is disturbed, it leads to neural tube defects or dysraphic disorders.

5th Stage: Cells of the Neural Crest

The neural crests separate at the closed neural folds. The cells of the neural crest are very important in the embryonic development. Although they originate from the ectoderm, they are sometimes even referred to as the fourth cotyledon. The cells of the neural crest have the ability to wander and diversify into numerous cell types. They form the glial and nerve cells, melanocytes of the skin, calcitonin cells of the thyroid gland, cells of the adrenal medulla, and many of the connective tissue cells and bone cells of the skull.

Remember: Many cell types of the central nervous system are formed from the neural tube. Numerous cells of the peripheral nervous system emerge from the neural crest cells.

Primary Neurulation vs. Secondary Neurulation

The primary neurulation refers to the development of the neural tube under the influence of the notochord and the mesoderm. It ends in the 4th week with the closure of the posterior neuropore. This is followed by the secondary neurulation. The caudal end of the neural tube thereby develops into the neural notochord and is then canalized. This process ends in the 6th week.
Neural Tube Defects

When translated, dysraphism means something like “abnormal suture”. The closure of the neural tube, either on the neuropore anterior or posterior, is thus disturbed. It therefore results in the following defects.

**Anencephaly**: The anterior neuropore remains unclosed. As a result, a large part of the skullcap, the cerebrum and the diencephalon, is missing. Anencephaly is incompatible with life.

**Spina bifida**: The neuropore caudalis does not close and the vertebral arches remain open. There are different degrees of severity. This defect is compatible with life, however paralysis often occurs.
Development of the Heart

Like the neurulation, the development of the heart begins in the 3rd week of the embryonic development. The first contractions of the heart can be identified with an ultrasound device already in the 4th week of development.

Cardiogenic Plate

The development of the cardiovascular system begins approximately on the 18th day. A horseshoe-shaped region of the splanchnopleura which lies cranial to the neural plate forms the cell groups. The cardiogenic plate originates from these cells. It consists of endothelium strands (endocardium), coelomic epithelium (myocardium) and coelom pockets (pericardium).

Cardiac Tube

At the end of the 3rd week, a tubular structure i.e. the cardiac tube differentiates itself from the cardiogenic plate. It lies ventrally, partly due to the folding of the embryo. The following structures shape the heart tube through protuberances and constrictions from cranial to caudal:

- **Truncus arteriosus**: The cardiac outflow tract of the heart tube is connected to the aortic sac.
- **Bulbus cordis**: It connects the truncus aorticus. The septum aorticopulmonary therein develops from cells of the neural crest. Through a spiral rotation of the septum by 180 °, the aorta and the pulmonary truncus are separated from each other.
- **Primitive ventricle**
- **Primitives atrium**
- **Sinus venosus**: The blood of the vitelline veins, umbilical vein and cardinal anterior and posterior veins flows in the influx path with two sinus horns.

The first contractions can be detected from about the 22nd or 23rd day.
Cardiac Loop

The cardiac loop forms when the sinus venosus cranial pushes behind the bulbus cordis. The result is an S-shaped structure, which is also known as cor sigmoideum. The primitive ventricle lies caudally.

Atrioventricular Canals

The four endocardial cushions are formed from the subendocardial connective tissues at the constriction between the primitive atrium and the primitive ventricle. Every two endocardial cushions grow towards each other, finally combine and form the atrioventricular canals on the one hand. The remaining two tissue cushions are part of the subsequent mitral and tricuspid valves. These valves will monitor the blood flow between the atria and the ventricles once.

Division of the Atrium

The primitive atrium is divided at the end of the 4th week of development. In order to form the right and left atria, the septum primum grows from the roof of the atrium towards the endocardial cushion. This closes as a falcate and thereby leaves behind the ostium primum as communication between the right and left atrium. Finally, the ostium primum also disappears.

Meanwhile small perforations are formed in the cranial part of the septum. They join together and form the ostium secundum. A second septum, the septum secundum, grows from top to bottom as well. It thereby closes the ostium secundum. There remains a slot-shaped opening between the septa and the endocardial cushion. The foramen ovale remains open until birth.

Division of the Ventricle

The division of the ventricles occurs from the cardiac apex to the atrioventricular canals. The muscular septum is formed by the migration of the myoblasts. The interventricular foramen between the right and left ventricles remains in the cranial portion up to the 7th week of development. This opening is finally closed only by a thin membrane. Therefore, this part of the septum is called the membranous part.
Congenital Malformations of the Heart

If due to a defect of the septa a connection between the atria or the ventricles is made, the result is a mixing of oxygen-rich and oxygen-poor blood.

Atrial Septal Defect

A remaining communication of the atria is called **atrial septal defect (ASD)**. Most commonly, a patent foramen ovale occurs. Less common is an ostium primum- or ostium secundum defect.

Ventricular Septal Defect

Ventricular septal defect (VSD) is the most common congenital heart defect. The membranous part is not formed and there is only an imperfect septum between the ventricles.

The Tetralogy of Fallot

A syndrome which is **often asked in exams** is the tetralogy of fallot. It is a combination of four specific congenital malformations of the heart and the great vessels.

1. Ventricular septal defect
2. Pulmonary stenosis
3. Hypertrophy of the right ventricle
4. The “overriding aorta”
Review Questions

Find the solutions below the references.

1. In which time period of the embryonic development does the secondary neurulation occur?

   A. 1st – 3rd week  
   B. 4th – 7th week  
   C. 15th-17th day  
   D. 25th-27th day  
   E. So far no specific time period has been ascertained.

2. Which cells do not differentiate from the neural crest cells?

   A. Oligodendrocytes  
   B. Schwann cells  
   C. Melanocytes  
   D. Odontoblasts  
   E. Glandular cells of the adrenal medulla

References


**Correct answers:** 1B, 2B

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