



MINISTRY OF HEALTH OF THE RUSSIAN FEDERATION
PIROGOV RUSSIAN NATIONAL RESEARCH MEDICAL UNIVERSITY

Department of Biology. Pediatrics Faculty

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A.G. Mustafin

INTRODUCTION TO DEVELOPMENTAL BIOLOGY OF CHORDATA

STUDENT WORKBOOK

Edited by prof. A.G.Mustafin



Moscow
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The workbook is intended for students of medical universities enrolled in the educational programs "General Medicine", "Pediatrics", and "Dentistry" to master the discipline "Biology". It includes basic information and practical tasks that help to better understand ontogenesis of chordates and general processes of animal development. The workbook is prepared in accordance with the requirements of the Federal state educational standard of higher professional education in the areas of training 31.05.02 "Pediatrics", 31.05.01 "General medicine", 31.05.03 "Dentistry".

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TABLE OF CONTENT

TOPIC 1. REPRODUCTION. GAMETOGENESIS. TYPES OF EGG CELLS.....	4
TOPIC 2. CLEAVAGE IN CHORDATA.....	9
TOPIC 3. GASTRULATION.....	16
TOPIC 4. PRIMARY ORGANOGENESIS IN CHORDATES. MECHANISMS AND ABNORMALITIES OF ORGANOGENESIS.....	22
TOPIC 5. EXTRAEMBRYONIC MEMBRANES IN AMNIOTES.....	28
QUESTIONS TO COLLOQUIUM.....	36

TOPIC 1. REPRODUCTION. GAMETOGENESIS.

TYPES OF EGG CELLS

General notes

Ontogeny, or ontogenesis is the process of individual development of an organism from fertilization to death.

Periodization of ontogeny

Ontogenesis can be divided into **three periods**: pre-reproductive, reproductive and post-reproductive, or aging.

- The **pre-reproductive period** is the most important one. The pre-reproductive period continues until puberty.
- The **reproductive period** is the period of active sexual reproduction.
- The **post-productive period** is the period of slow extinction of all body functions.

Another periodization divides the ontogeny into **embryonic and post-embryonic periods**.

- The **embryonic period** is the development of the embryo inside the egg shells. It includes: (a) rapid cell division or cleavage; (b) formation of the germ layers or gastrulation; (c) differentiation and growth of the organs and organ systems (organogenesis).
- **Postembryonic development** begins after the emergence of the embryo from the egg and embryonic membranes, when the organism becomes capable of active feeding and locomotion. Upon transition to the postembryonic state the organism either immediately possesses the principal pubertal morphological characteristics (direct development) or essentially differs from the pubertal form, in which case the larva that hatches out of the egg must undergo a metamorphosis (indirect development) before it reaches its adult state.

Since human beings belong to the phylum Chordata, we will study the evolution of ontogenesis in this phylum.

General features of Chordates

- Single, hollow nerve cord beneath dorsal surface; in vertebrates, it differentiates into brain and spinal cord.
- Notochord: flexible rod on the dorsal side of gut, present at early stage in all chordates; displaced in vertebrates by vertebral column that forms around the nerve cord.
- Pharyngeal slits (pouches) connect pharynx (between mouth and esophagus) with outside gills in fish; present in terrestrial animal embryos but disappear later except Eustachian tube (connecting throat and middle ear).
- Postanal tail extends beyond anus; present at least in embryo; regresses into coccygeal bone in humans.
- Segmentation: reflected in arrangement of muscles (somites) and in vertebral column.
- Closed type of circulatory system: 1 or 2 circles of circulation, the heart in vertebrates on the ventral side.

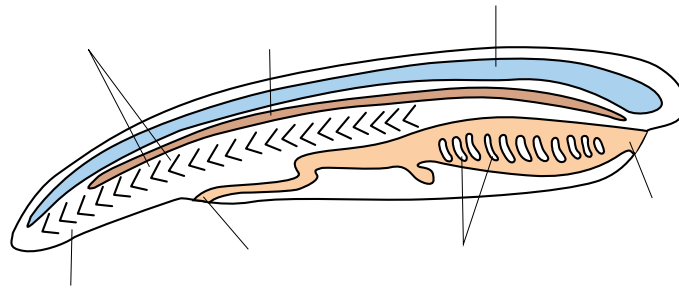
If the development of vertebrates occurs on the dry land, the embryogenesis is accompanied by the formation of **extra-embryonic membranes**. Reptiles, birds and mammals have this evolutionary adaptation and are grouped together as **amniotes**. Other vertebrates who develop in water and do not possess these provisory organs are referred to as **anamniotes** (Tab.1).

Table 1. Taxonomy of phylum Chordata

Phylum	Subphylum	Classes	Group
Chordata	Urochordata	Ascidia (sea-squirt)	
	Cephalochordata	Amphioxus (lancelet)	
	Vertebrata	Cyclostomata (lampreys, hagfish), Pisces (fish), Amphibia	Anamniotes
		Reptilians, Aves (birds), Mammalia	Amniotes



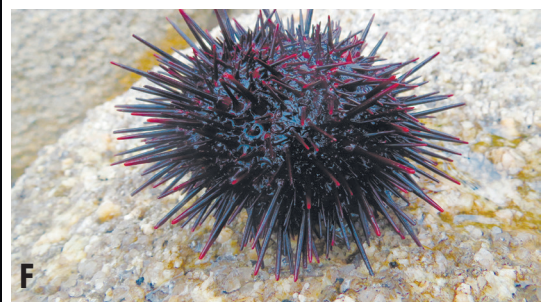
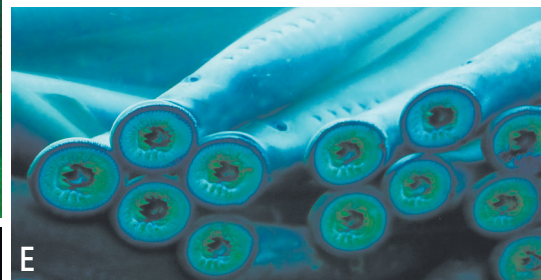
Task 1.1. Label the scheme of a Chordate animal using the following list of terms: 1 – muscle segments, 2 – notochord, 3 – dorsal nerve cord, 4 – anus, 5 – mouth, 6 – pharyngeal slits or clefts, 7 – muscular postanal tail.



Basically, the development of an organism begins with the formation of germ cells in its parents.



Task 1.2. Decide which subtype and class these animals belong to:



	Subtype	Class
A		
B		
C		
D		
E		
F		

Reproduction is the biological process by which new individual organisms – “offspring” – are produced from their “parents”. Reproduction is a fundamental feature of all known life; each individual organism exists as the result of reproduction. There are two forms of reproduction: **asexual** and **sexual**.

In **asexual reproduction**, an organism can reproduce without the involvement of another organism. By asexual reproduction, an organism creates a genetically similar or identical copy of itself.

Sexual reproduction typically requires the sexual interaction of two specialized cells, called gametes, which contain half the number of chromosomes of normal cells and are created due to meiosis, with typically a male fertilizing a female of the same species to create a fertilized zygote. This produces offspring organisms whose genetic characteristics are derived from those of the two parental organisms.



Task 1.3. Complete the table “Sexual and asexual reproduction in animals” below:

Characteristics	Asexual reproduction	Sexual reproduction
Number of parents		
Gamete formation (yes or no)		
Types of cell division		
Difference between offsprings		
Examples	binary, fission, schizogony, budding, fragmentation.	copulation, conjugation, parthenogenesis.

Gametogenesis and fertilization

Gametogenesis is the process of gamete formation precedes ontogenesis. From gametogonia, male and female gametes develop differently: males – by **spermatogenesis** and females – by **oogenesis**.

Fertilization is the fusion of gametes to initiate the development of a new individual organism. There are two mechanisms by which fertilization can take place. The first is **external fertilization** (the eggs are fertilized outside of the body), and the second is **internal fertilization** (the eggs are fertilized within the female reproductive tract). Examples of external fertilization can be seen in frogs, some marine invertebrates and many types of fish. Internal fertilization occurs most often in land-based animals (reptiles, birds and mammals), although some aquatic animals also use this method.



Task 14. Match each of the key terms (column A) with its corresponding definition (column B):

COLUMN A

- (1) Anamniotes
- (2) Amniotes
- (3) Spermatogonia
- (4) Spermatids
- (5) Budding
- (6) Parthenogenesis
- (7) Schizogony
- (8) Notochord
- (9) Oogenesis
- (10) Internal fertilization

COLUMN B

- (a) Flexible rod on the dorsal side of gut in Chordates
- (b) Production of egg cells in animals
- (c) Multiple fission in Protozoa, a type of asexual reproduction
- (d) A type of asexual reproduction in which a new organism develops from an outgrowth at one particular site
- (e) These vertebrates reproduce in water
- (f) These cells are formed as a result of meiosis during spermatogenesis
- (g) A type of sexual reproduction which does not require fertilization
- (h) These cells divide mitotically during gametogenesis
- (i) These vertebrates reproduce on dry land and develop extra-embryonic membranes
- (j) It occurs mostly in land-based animals

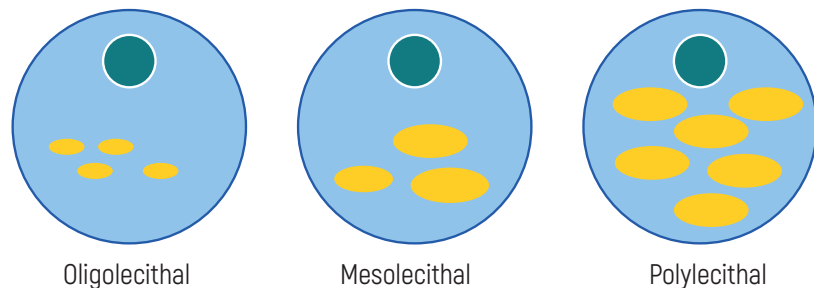
A	1	2	3	4	5	6	7	8	9	10
B										

Types of egg cells in Chordates

Mature egg (ovum) contains all the material necessary for the beginning of the growth and development of the embryo. During the oogenesis developing egg accumulates yolk proteins, energetic material, mRNAs, rRNAs, synthesizes ribosomes, manufactures specialized secretory vesicles known as the cortical granules. Cortical granules spread just beneath the egg's plasma membrane. **Two hemispheres (poles) in egg – animal and vegetal – are formed.** There are more proteins, RNAs into the animal hemisphere. Nucleus and organelles are frequently displaced toward the **animal** pole, whereas the **vegetal** pole contains a lot of yolk.

In the series from lancelet via amphibians to birds, the eggs become larger and the amount of yolk increases. Increased yolk size enables the embryo to attain a higher degree of organization prior to hatching or birth. Egg cells of placental mammals are **is secondarily poor in yolk**, as mammalian embryogenesis occurs in the uterus and mother provides developing organism with everything it needs. There are special terms to that. The egg cell that has little amount of yolk is referred to as **oligolecithal**, medium amount of yolk – **mesolecithal**, large amount of yolk – **polylecithal**. If the yolk is distributed equally the egg is named isolecithal, if the yolk granules are located mostly at the vegetal pole of egg cytoplasm – **telolecithal**.

Fig. 1. Types of Chordates' egg cells



Home work

Answer the questions using information from textbook «ESSENTIAL MEDICAL BIOLOGY», Chapters 22 and 23 (pp.106–110).

1. What three periods of ontogeny do you know? _____
2. Compare direct and indirect postembryonic development: _____
3. What patterns of reproduction do you know? _____
4. Why parthenogenesis is an example of sexual reproduction? _____
5. What is the function of the yolk in vertebrate eggs? _____
6. How are these eggs classified according to the amount of yolk within them? _____

7. What are the animal pole and the vegetal pole of vertebrate eggs? _____

8. Why is it said that mammalian egg is secondarily poor in yolk? _____

9. Who has a bigger egg cell: a little bird or a whale? Why? _____

10. What are the general features of Chordates? _____

11. What axial organ of Chordates (neural tube, notochord or intestine) is positioned dorsally? ventrally?
between them?

TOPIC 2. CLEAVAGE IN CHORDATA

Cleavage is a series of successive mitotic divisions of zygote. Forming daughter cells are named **blastomeres**. Result of cleavage is formation of a **blastula** that is multicellular single-layer embryo. This single layer of cells is referred to as **blastoderm**. Blastula has a cavity – **blastocoel**.

Mitotic divisions during cleavage are rapid whereas the blastomeres don't grow. The G1 and G2 phases are not present in the mitotic cycles, and the volume of cell cytoplasm does not increase. The blastomeres become progressively smaller until they acquire the size of most of the somatic body cells. The normal **nucleus to cytoplasm volume ratio** is restored. That is why this stage of development is termed segmentation or cleavage, but not division. DNA replication in S-period of mitotic cycle occurs at a rapid rate due to the fact that number of replication origin increases and replication in all ones carries out synchronously.

Pattern of cleavage depends on amount and distribution of yolk within the egg cytoplasm. In zygotes with relatively little yolk (isolecithal and mesolecithal eggs) **cleavage is complete or holoblastic**. It means that cleavage furrows extend through the entire egg. The blastomeres are equal in size (**equal holoblastic cleavage**). Cleavage furrows pass through the animal and vegetal poles. This cleavage pattern (in lancelet or in sea urchin) results in formation of a blastula with a single-layered wall (**coeloblastula, or hollow blastula**). Amphibians have telolecithal egg so after the third equatorial division the cells at the vegetal pole contain more yolk and are named **macromeres**, ones at animal pole contain less yolk and are named **micromeres**. This pattern is **holoblastic unequal cleavage**. The forming blastula is referred to as **amphiblastula**. In giant bird egg the clear cytoplasm of animal pole is separated from the yolk-filled cytoplasm. Cleavage is restricted to this yolk-free cytoplasmic region at the animal pole. It is a **meroblastic discoidal cleavage pattern**. The blastula in birds is referred to as **discoblastula**.

Cell egg of a placental mammalian is secondarily poor in yolk so cleavage is holoblastic. There are some characteristic features of mammal cleavage. The first cleavage is a normal meridional division; however, in the second cleavage, one of the two blastomeres divides meridionally and the other divides equatorially. Moreover, blastomeres divide at different time and may be even or odd in number. It is **asynchronous cleavage** and due to this fact cleavage is **unequal**. The mammalian blastula named blastocyst consists of two parts: an outer cell layer – the **trophoblast**, and an inner cell mass – the **embryoblast**. The inner cell mass (embryoblast) will develop into the embryo proper and part of extraembryonic membranes, and the outer cell mass (trophoblast) will take part in placenta formation.



Task 2.1. Fill in the table "Eggs and cleavage features":

Eggs and cleavage features	Lancelet (or sea urchin)	Amphibia	Reptiles, birds, egg-laying mammals	Placental mammals
Type of egg: a.yolk amount; b.yolk distribution	Oligolecithal, isolecithal			
Cleavage pattern: complete or incomplete; equal or unequal, discoidal	Holoblastic (complete), equal			
Blastula type	Coeloblastula			



Task 2.2. Examine types of cleavage in fig. 2 and fig. 3. Mark following structures:

- (a) blastula of a lancelet (coeloblastula): 1 – blastomeres, 2 – blastocoel, 3 – blastoderm;
- (b) amphibian blastula (amphiblastula): 1 – blastoderm, 2 – blastocoel, 3 – macromeres, 4 – micromeres;
- (c) avian blastula (discoblastula): 1 – blastomeres, 2 – yolk;
- (d) mammalian blastula (blastocyst): 1 – blastomeres, 2 – trophoblast, 3 – embryoblast, 4 – blastocyst cavity.

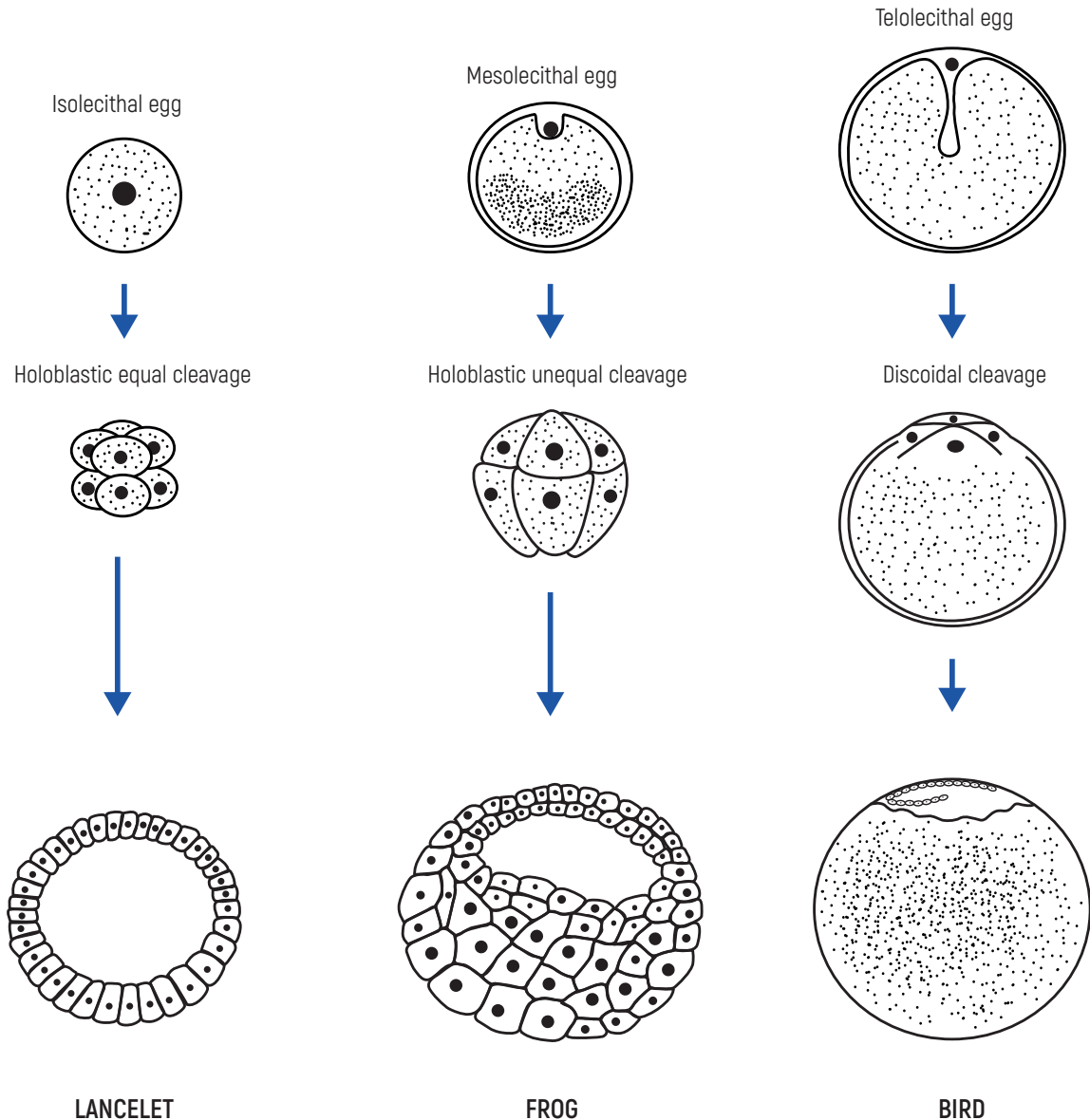


Fig. 2. Types of egg cells and cleavage

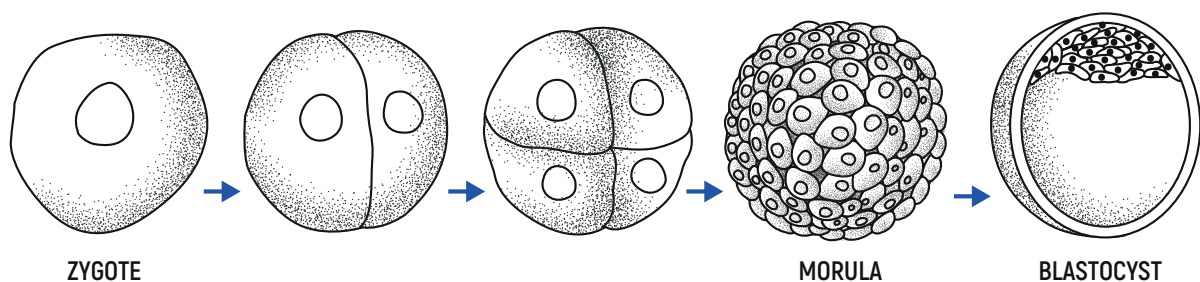


Fig. 3. Cleavage in placental mammals is complete unequal and leads to blastocyst formation

In human, the ovulation occurs at the metaphase II of meiosis. Then oocyte enters fallopian tube (oviduct) and fertilization takes place in upper part of it approximately 12 to 24 hours after ovulation. After fertilization cleavage begins and proceeds for 3 days and **morula** — a solid ball of 12 to 16 blastomeres that looks like a mulberry — is formed. During cleavage embryo moves toward uterus. As the morula enters the uterus on the fourth day after fertilization, a cavity begins to appear, and the **blastocyst** forms. The blastocyst starts to fix and embeds in the endometrium along the wall of uterus. This process known as implantation occurs on about sixth or seventh day after fertilization. Thus, embryo before implantation develops autonomously. Owing to this fact, it is possible to carry out fertilization and early development in vitro (IVF). Then at the morula stage the embryo can be placed into uterus where it gets implantation and grows to full term.

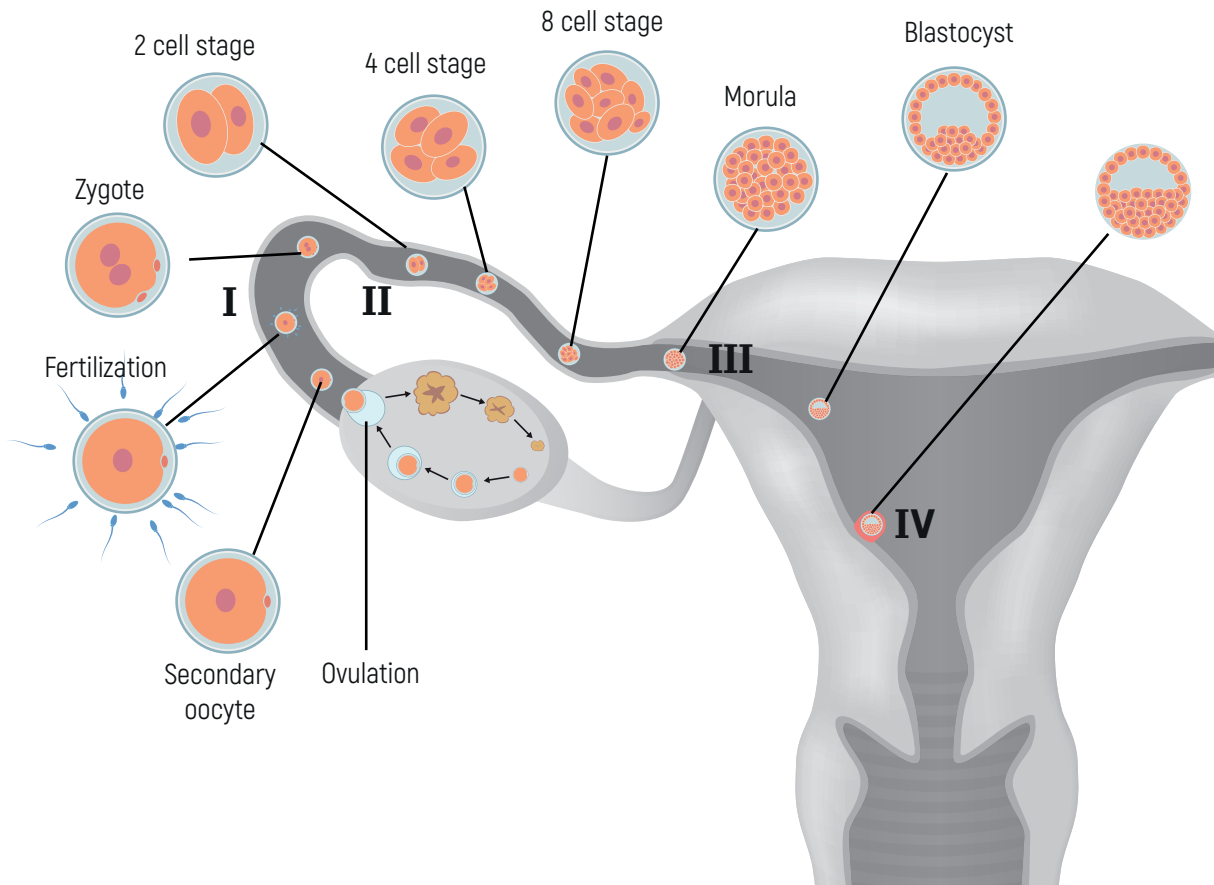


Fig. 4. Fertilization and cleavage in human



Task 2.3. Match each of the key terms (column A) with its corresponding definition (column B):

COLUMN A

- (1) Blastula
- (2) Micromere
- (3) Macromere
- (4) Totipotency
- (5) Oligoethital
- (6) Animal pole
- (7) Vegetal pole
- (8) Blastomere
- (9) Blastocoel
- (10) Coeloblastula
- (11) Discoblastula

COLUMN B

- (a) Embedding of the blastocyst in the uterine wall
- (b) Multicellular single-layer embryo
- (c) Lots of yolk is situated at this hemisphere
- (d) Birds, reptiles and egg-laying mammals have this type of blastula
- (e) The ability to give rise for all types of cells
- (f) Small blastomeres of animal pole in amphiblastula
- (g) Cavity inside blastula
- (h) It happens when the embryo cannot get in the uterus
- (i) A cell during cleavage period
- (j) Blastomeres of vegetal pole during frog's cleavage
- (k) Blastula typical of lancelet or sea urchin

- (12) Implantation

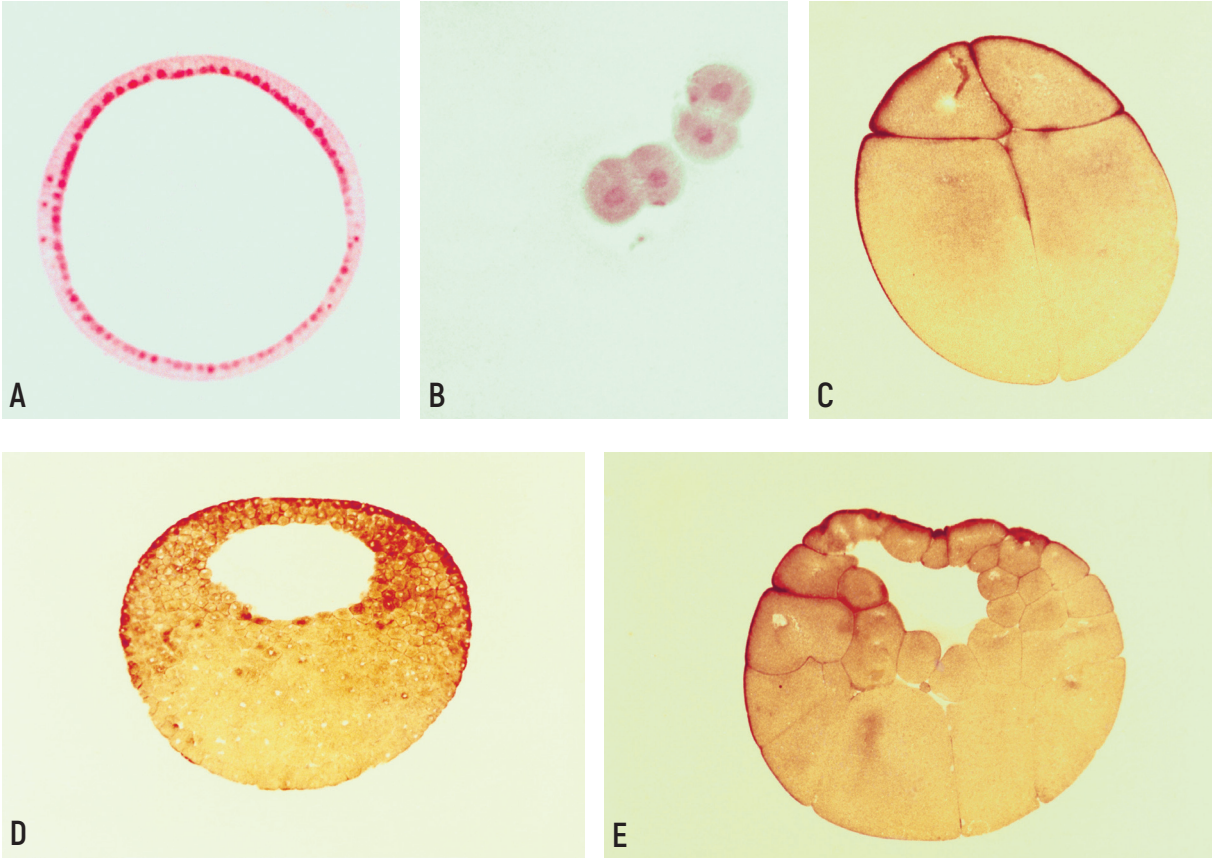
(13) Ectopic pregnancy
- (l) Very few yolks can be found in this egg cell

(m) Here the cleavage furrow begins

A	1	2	3	4	5	6	7	8	9	10	11	12	13
B													



Task 2.4. Determine development stage and type of the cleavage in photographs below. What classes of animals is this type of development typical for?



	Type of cleavage	Stage	Classes of animals
A			
B			
C			
D			
E			



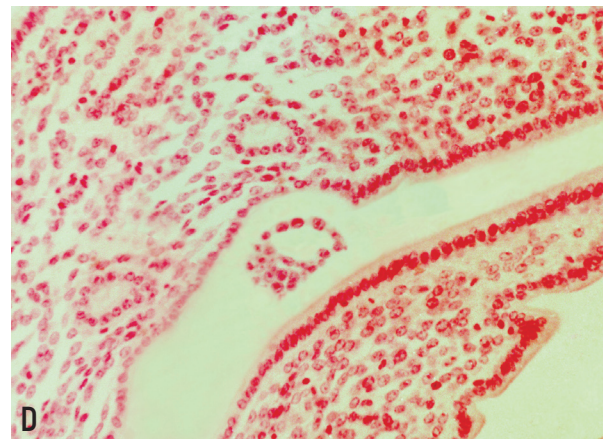
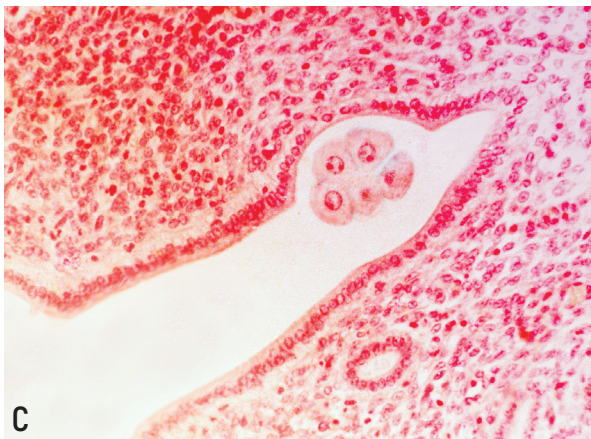
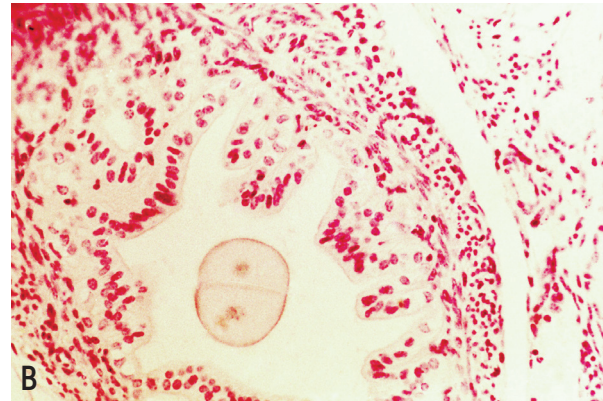
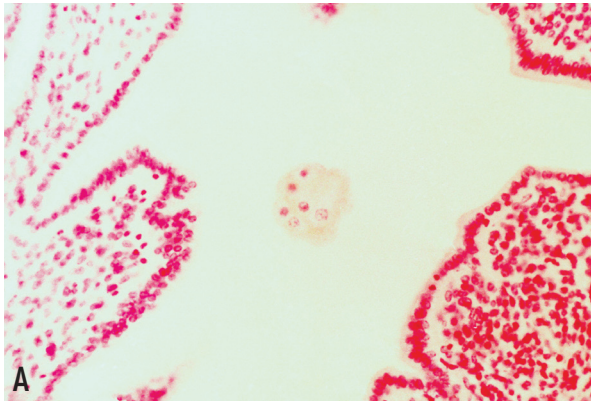
Task 2.5. In fig. 4, decide what I, II, III and IV stand for:

I	
---	--

II	
III	
IV	



Task 2.6. Determine development stages of mouse development in photographs. In each case indicate organ where embryo is located?



	Stage of development	Embryo location
A		
B		
C		
D		

Abnormalities of cleavage in human

1. **Siamese twins.** Blastomeres have totipotency, it is that they can form all tissues and are even capable to give rise to the entire organism. Thus, identical twins appear and in some cases also Siamese twins.
2. **Extrauterine pregnancy** (ectopic pregnancy, also known as tubal pregnancy) happens if the embryo attaches outside the uterus.

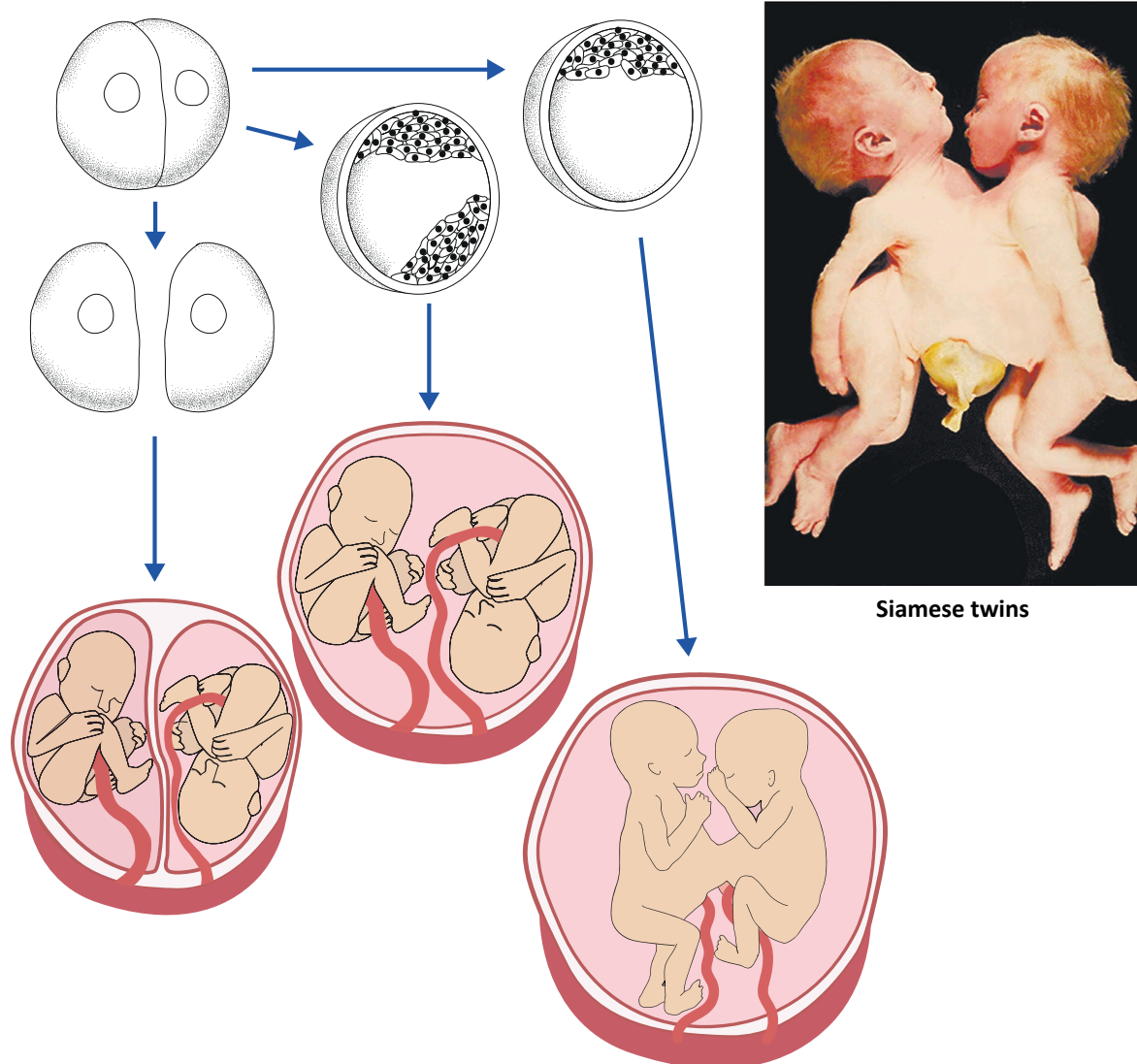
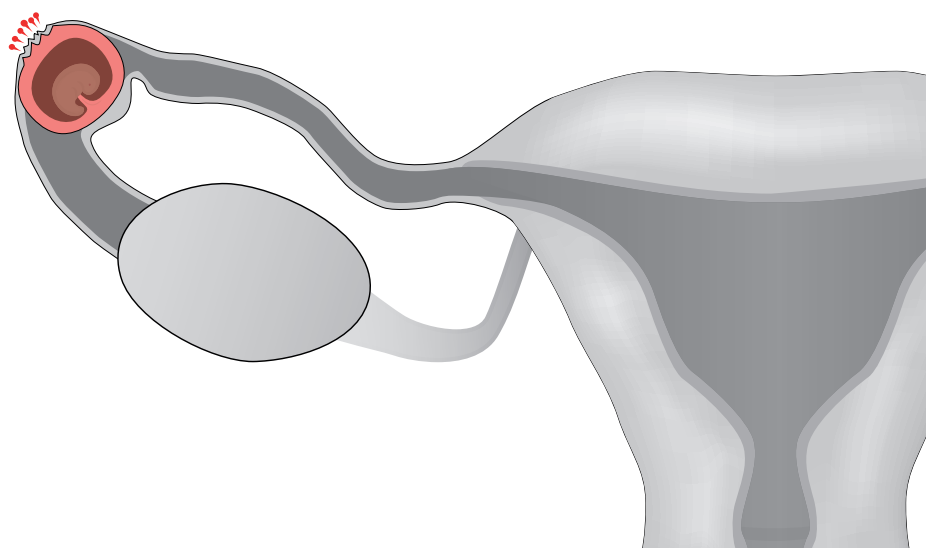


Fig. 5. Siamese twins are the result of an incomplete separation of embryoblast cells



Task 2.7. Examine example of ectopic pregnancy with an embryo developing in the uterine tube. Mark: 1 – uterine (Fallopian) tube, 2 – uterus, 3 – ovary.





Home work

Answer the questions using information from textbook «ESSENTIAL MEDICAL BIOLOGY», Chapter 24 (pp. 111–113):

1. Give characteristics of cleavage process: _____

2. What factors does the cleavage depend on? _____

3. What patterns of cleavage do you know? Compare patterns of cleavage in different classes of Chordates.

4. What blastula types do you know? _____

5. What are the cells produced during the first stage of embryonic development called? _____

6. In humans, what is the next stage after morula? What morphological feature determines this stage?

7. A woman has had several bouts of pelvic inflammatory disease and now wants to have children. However, she has been having difficulty becoming pregnant. What is likely to be the problem, and what would you suggest to help her?

8. To prevent low success rate of IVF four or five eggs are collected, fertilized and placed in the uterus. What can this strategy lead to? Are these twins identical or fraternal?

9. What is the cleavage pattern of a duckbill platypus? of a crocodile? _____

10. A human egg cell was fertilized by a spermatozoon having both sex chromosomes. What is the consequence of such fertilization?

TOPIC 3. GASTRULATION

Gastrulation is a process of formation of a multilayer embryo which is named **gastrula**. Gastrula can have a cavity — **gastrocoel**, or primitive gut.

All chordates are triploblastic (three-layer) organisms and develop from three germ layers: **ectoderm** (outer layer), **endoderm** (inner one), **mesoderm** (interstitial one). Amphioxus gastrula at first has two germ layers only (ectoderm and endoderm). Mesoderm is formed later during organogenesis. In vertebrates all germ layers are formed during gastrulation.

There are some modes of gastrulation:

1. **invagination** — infolding of cell sheet into embryo,
2. **involution** — inturning of cell sheet over the basal surface of an outer layer,
3. **ingression** — migration of individual cells into the embryo,
4. **delamination** — splitting or migration of one sheet into two sheets,
5. **epiboly** — the expansion of one cell sheet over other cells.

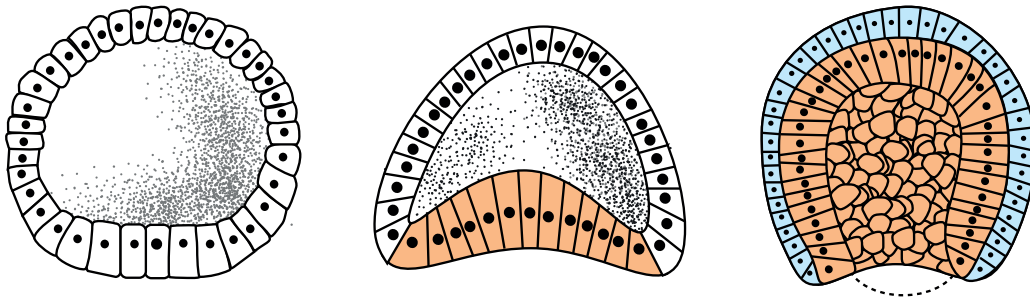
The gastrulation of any particular organism is a combination of several of these modes.

Gastrulation in Chordates

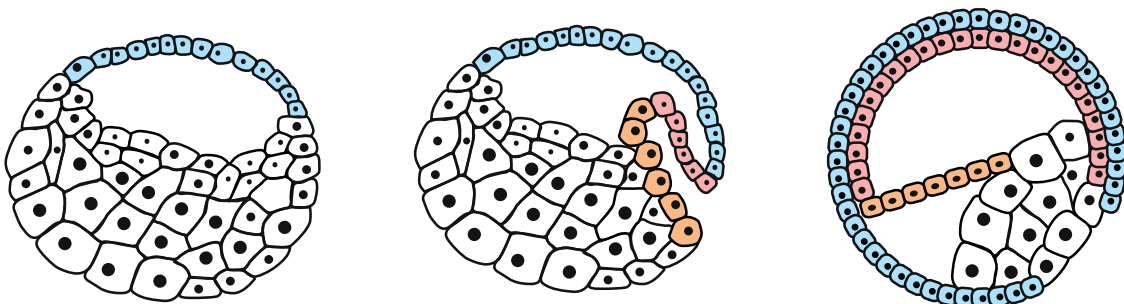
In lancelet (or sea urchin) the cells at the vegetal pole of the blastula **invaginate** into blastocoel. Due to this movement two-layers gastrula having ectoderm and endoderm forms. Invaginated region forms the **gastrocoel**, or **archenteron**, or **primitive gut** and the opening of the archenteron at the vegetal region is called the **blastopore**, or **primitive mouth**. This opening corresponds to the mouth opening of Protostomes. As all Chordates belong to Deuterostomes their definitive mouth is located at opposite site of their gastrula.



Task 3.1. Study lancelet gastrulation. Mark: 1 – ectoderm, 2 – endoderm, 3 – gastrocoel, 4 – blastopore, 5 – blastocoel, 6 – blastoderm, 7 – vegetal pole, 8 – animal pole.



Task 3.2. Study frog gastrulation. Mark: 1 – ectoderm, 2 – endoderm, 3 – mesoderm, 4 – prospective notochord, 5 – gastrocoel, 6 – dorsal lip of blastopore, 7 – ventral lip of blastopore, 8 – yolk plug.



Gastrulation in reptiles, birds and mammals proceeds in a very similar way. First of all, blastomeres that form discoblastula delaminates into a bilaminar embryo disk. The upper layer is called epiblast and the lower - hypoblast. Then the epiblast only takes part in further gastrulation and gives rise to all three germ layers of embryo (ectoderm, mesoderm, and endoderm). Intensive cell movement on the surface of epiblast leads to formation of so-called primitive node and primitive streak. After that, individual epiblastic cells begin to move through these structures into narrow cavity between epiblast and hypoblast. This mode of cell movement is called ingression. Epiblastic cells migrate through the primitive streak and form the mesoderm and endoderm. The cells of hypoblast become extra-embryonic endoderm. Cells remaining in the epiblast are referred to as the ectoderm. Thus, as a result of the gastrulation the three-layers embryo is formed. The primitive node and primitive streak are considered to correspond to the dorsal lip of blastopore and the blastopore itself of amphibian gastrula. Cell movements during placental mammals' gastrulation are delamination and ingression as well as during bird's and reptilian's ones.

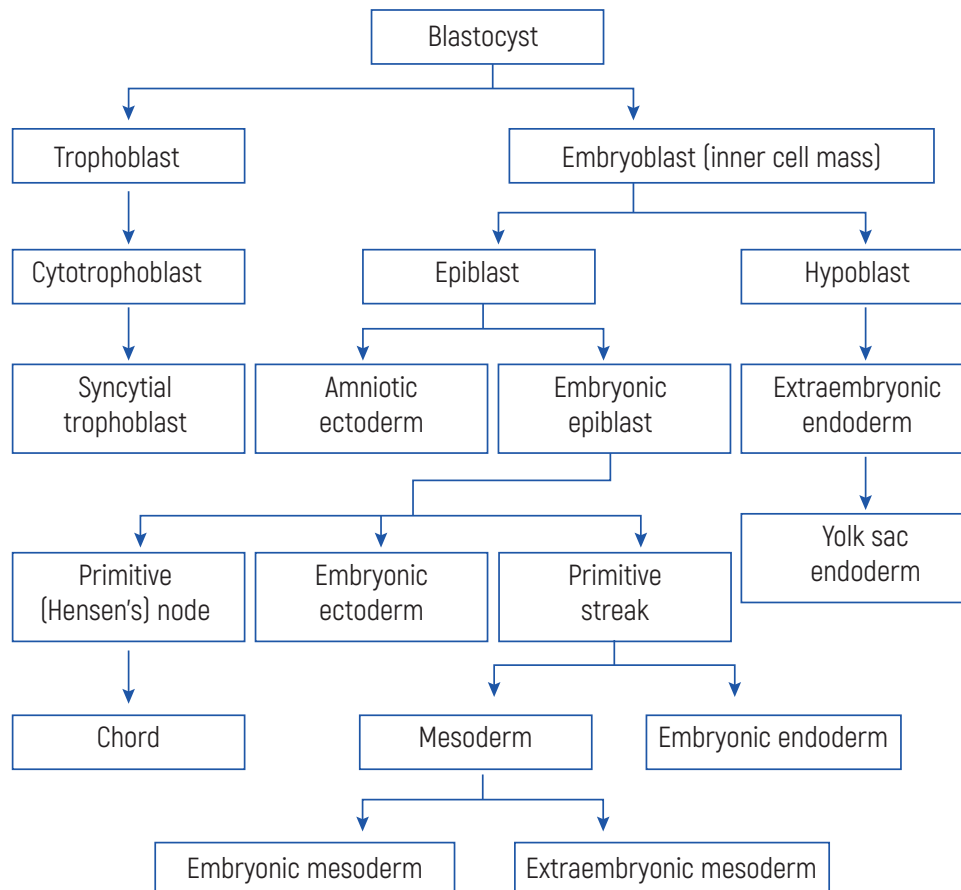


Fig. 6. Cell and tissue lineages in the mammalian embryo

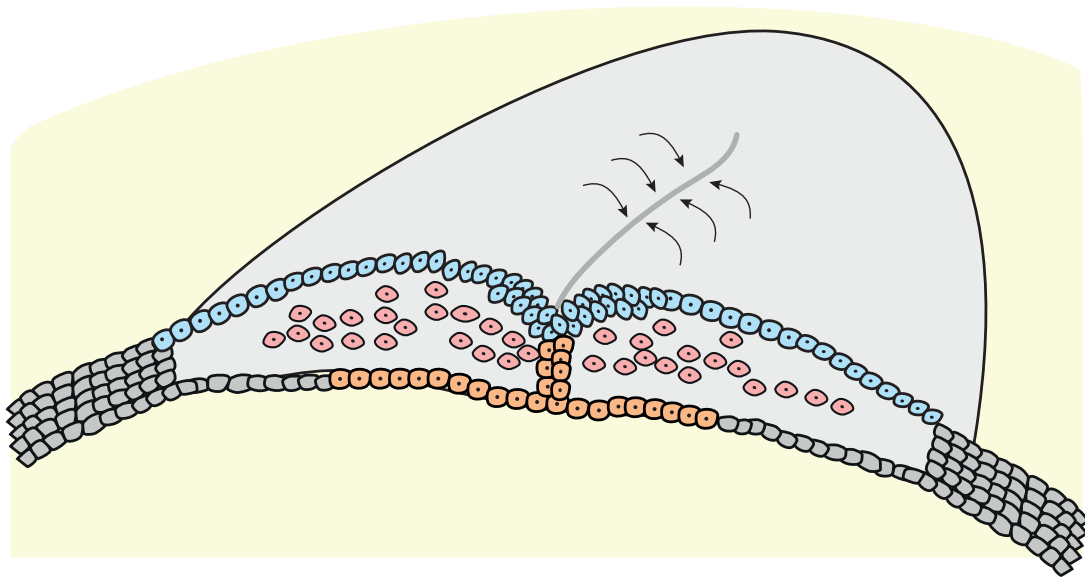


Task 3.3. Fill in the table:

Classes	Modes of gastrulation
1. Lancet	a.
2. Amphibians	a.
	b.
	c.
3. Birds, reptiles, mammals and human	a.
	b.



Task 3.4. Study ransversal cut of chicken embryo through the primitive streak. Mark: 1 – epiblast, 2 – hypoblast, 3 – primitive streak, 4 – migrating cells.



Task 3.5. Match each of the key terms (column A) with its corresponding definition (column B):

COLUMN A

- (1) Delamination
- (2) Invagination
- (3) Ingression
- (4) Epiboly
- (5) Involution
- (6) Blastopore
- (7) Spemann organizer
- (8) Gastrocoel, or archenteron
- (9) Competence
- (10) Ectoderm
- (11) Endoderm
- (12) Mesoderm
- (13) Primitive streak

COLUMN B

- (a) infolding of the vegetal pole of the blastula like a soft rubber ball when poked
- (b) cells of the animal pole spread over the vegetal and enclose them
- (c) the primary gut
- (d) the primary mouth
- (e) splitting of one cellular sheet into two parallel sheets
- (f) migration of individual cells from the surface layers into the interior of the embryo
- (g) the interning of the expanding outer layer so that it spreads over the internal surface of the remaining external cells
- (h) the ability of cells to respond to inductive signal
- (i) this structure in chick or human embryo is analogous to the blastopore in frog or lancelet
- (j) the dorsal lip of the blastopore at early gastrula stage
- (k) This is a middle germ layer
- (l) This is an inner germ layer
- (m) This is an outer germ layer

A	1	2	3	4	5	6	7	8	9	10	11	12	13
B													

Embryonic induction in gastrulation

The development of entire organism is determined by mechanisms of integration. Those are: **intercellular contacts**, **inductive interactions** and, later in development, **neuro-hormonal regulation**.

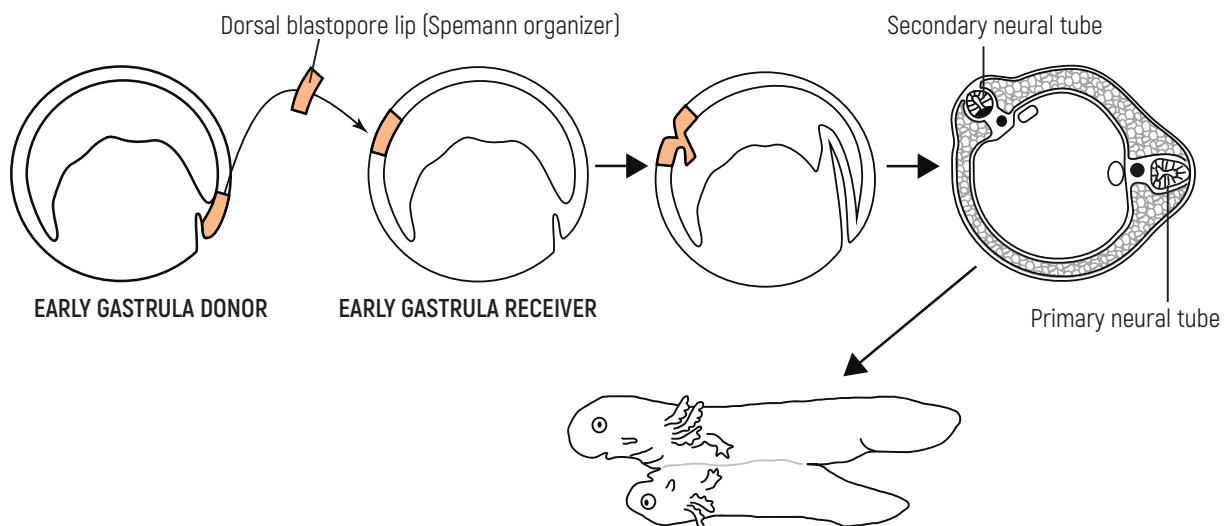


Fig. 7. Spemann-Mangold organizer experiment

Beginning from the blastula stage the main integrative mechanism of development is **embryonic induction**. Embryonic induction is a process of early determined embryo structures influence on the other ones to direct their development in specific way. The influencing structure is called the **inductor** or **organizer** and the reacting on this influence structures are called **competent tissues**. The competence of tissue is a temporary status.

George Spemann and Hilde Mangold in their classic experiment demonstrated that in early amphibian gastrula stage **prospective notochord** that invaginates through the dorsal lip of the blastopore **induces neural tube development**. The dorsal lip of the blastopore in amphibians corresponds to the primitive node in birds and reptiles. In the blastocoel of the host (pigmented) embryo, the transplant comes to lie in the region of the future ventral body wall. In this place it induces the formation of a second neural tube. The transplanted tissue becomes integrated into the corresponding notochord-mesoderm complex. The result is an embryo with two complete embryonic axial systems.

This organizer experiment is successive in the beginning of gastrulation only because of the fact that competent tissue (ventral body wall) has **labile determination**. It means that competent tissue can change the developmental direction. At later gastrula stage transplantation of dorsal lip material doesn't lead to formation of second embryonic axial system due to **irreversible determination** of competent tissue.

Abnormalities of gastrulation

Gastrulation abnormalities lead to malformations or even loss of embryo viability. Since gastrulation and neurulation often overlap, neurulation disorders are often associated with gastrulation abnormalities. This is the case, for example, with a violation of the development of hemimyelocoele. It is also worth mentioning two other disorders during gastrulation: sirenomelia and coccyx teratoma. Remnants of a primitive nodule often develop into tumors known as sacrococcygeal teratomas and coccyx teratomas, which are some of the most common neonatal tumors. In the case of sirenomelia, the formation of a primitive stripe is disrupted, which leads to insufficiency of the mesoderm in the posterior half of the embryo. Sirenomelia is associated with malformations such as fused limbs, spinal anomalies, missing kidneys, or deformed genitals.

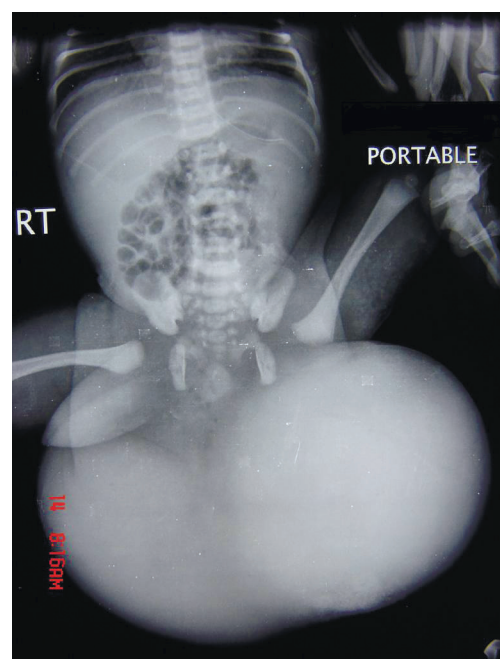


Fig. 8. Sacrococcygeal teratoma
(source: <https://radiopaedia.org/cases/sacrococcygeal-teratoma-4>. Case contributed by Dr. F.M. Ebouda)



Fig. 9. Sirenomelia (Source: Ježová M et al. *Diagnostic Pathology* 2008, 3. doi:10.1186/1746-1596-3-S1-S9)



Home work

Answer the questions using information from textbook «ESSENTIAL MEDICAL BIOLOGY», Chapter 24 (pp. 114–116):

1. After the blastula stage, what is the following stage of embryonic development? What is the passage from the blastula to the next stage called?

2. What is the essence of gastrulation? What are the germ layers forming in process of gastrulation?

3. Explain the difference between ingression, involution and invagination: _____

4. What are the archenteron and the blastopore? At what stage of embryonic development are these structures formed?

5. How are animals classified according to the germ layers present during their embryonic development?

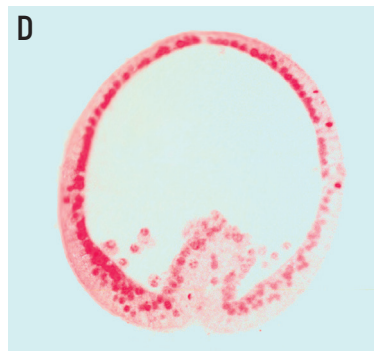
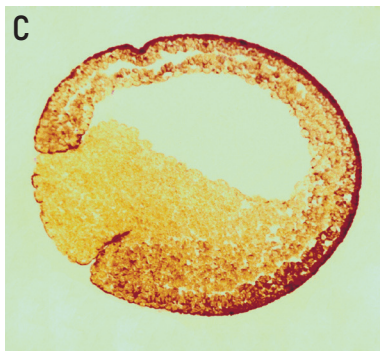
6. What is embryonic induction? _____

7. Give the definition of inductor and competent tissue: _____

8. At what stage of embryogenesis is the Spemann's organizer experiment successive? _____

9. The notochord induces the overlying ectoderm to develop into the (chose one answer): (a) skin, (b) eye, (c) primitive streak, (d) primitive node, (e) neural tube?

10. Determine the development stage and the class of animals shown in the photographs:



	Stage	Classes of animals
A		
B		
C		
D		
E		

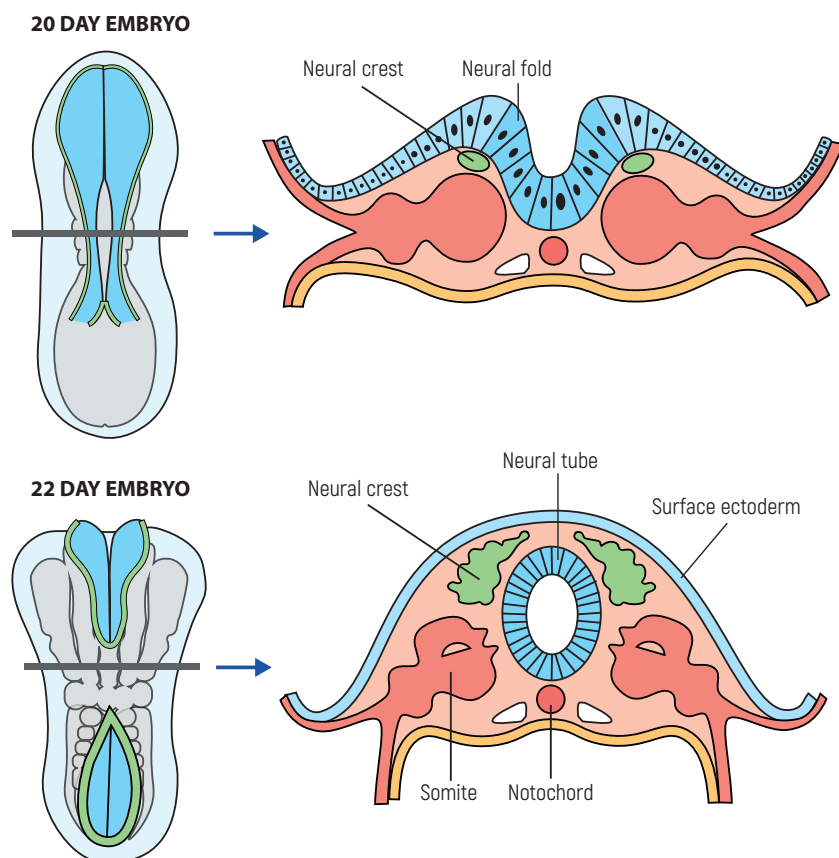
TOPIC 4. PRIMARY ORGANOGENESIS IN CHORDATES. MECHANISMS AND ABNORMALITIES OF ORGANOGENESIS

Primary organogenesis is a process of formation of so called **axial structures** of the Chordates: **neural tube**, **notochord**, **secondary gut tube** and the most important derivatives of mesoderm: segmented dorsal **somites** and the **lateral plate**, located on the lateral sides of the embryo. As far as the neural tube is forming in this period of embryonic development, the other name of this stage is **neurulation**. Primary organogenesis proceeds identically in all the Chordates. It leads to formation of typical chordates design or their general structure plan. The typical chordates design depends on the fact, that the developing **notochord** material is playing a role of so-called **organizer center** and it is inducing formation of the most essential structures of the embryo around itself. So, **notochord directs the dorsal ectoderm to form neural tube**.

Then, mesoderm is forced to differentiate into segmented somites or dorsal mesoderm, intermediate mesoderm (nephrogonotome) and unsegmented lateral plate. Lateral plate cell masses spread under the skin ectoderm in ventral direction. They form two cell-sheets: **parietal** and **visceral** with the **secondary body cavity**, or **coelom**, between them. **Neural crest cells** are a temporary group of cells unique to vertebrates that arise from the embryonic ectoderm cell layer, and in turn give rise to a diverse cell lineage—including melanocytes, craniofacial cartilage and bone, smooth muscle, peripheral and enteric neurons and glial cells.

Three germ layers (**ectoderm**, **mesoderm**, and **endoderm**) give rise to all cells and tissues of the embryo. The neural crest is called sometimes the “fourth germ layer”, because of giving rise to numerous derivatives, such as connective tissue of head and neck, glands (pituitary, salivary, lachrymal, thymus, thyroid), peripheral nervous system, chromaffin cells of the adrenal medulla, odontoblasts, melanocytes and many others.

Fig. 10. Neurulation and the neural crest formation



Task 4.1. Examine the photo of neurula. Mark the following structures: 1 – skin ectoderm, 2 – endoderm, 3 – area of intestinal wall, 4 – notochord, 5 – somite, 6 – lateral plate, 7 – neural tube, 8 – intermediate mesoderm, 9 – neurocoele, 10 – parietal sheet of lateral mesodermal plate, 11 – visceral sheet of lateral mesodermal plate, 12 – coelom.



Task. 4.2. Match derivatives to the germ layer:

Germ layer	derivatives
(1) Ectoderm	(a) epidermis of skin
	(b) heart
	(c) liver cells
	(d) enamel of teeth
(2) Mesoderm	(e) eye cornea
	(f) cerebellum
	(h) dermis of skin
	(g) spleen
(3) Endoderm	(i) kidneys
	(j) m. quadriceps femoris
	(k) lung epithelium
	(l) epithelium of the pancreas

a	b	c	d

e	f	h	g

i	j	k	l

Cellular mechanisms of development

In general, there are five cellular mechanisms of development: cell proliferation; cell migration; cell adhesion; cell differentiation and programmed cell death.

At period of cleavage cell proliferation begins, and then cell migration is important during gastrulation process. Cell adhesion is seen in neurulation (notochord and somite formation). Cell differentiation may be illustrated by the differentiation of somites into dermatome, myotome and sclerotome, and cell death by apoptosis is very important in the CNS and morphogenesis of cavities and openings of the body.

Mechanisms of integration in embryogenesis. Embryonic induction in primary organogenesis

Embryo is developing as an integrated system through the whole embryogenesis. Mechanisms of integration are different in different periods of development. They are **inter-cell contacts**, **embryonic inductions**, **nervous and humoral regulation**. The most important integrative mechanism of embryogenesis is embryonic induction.

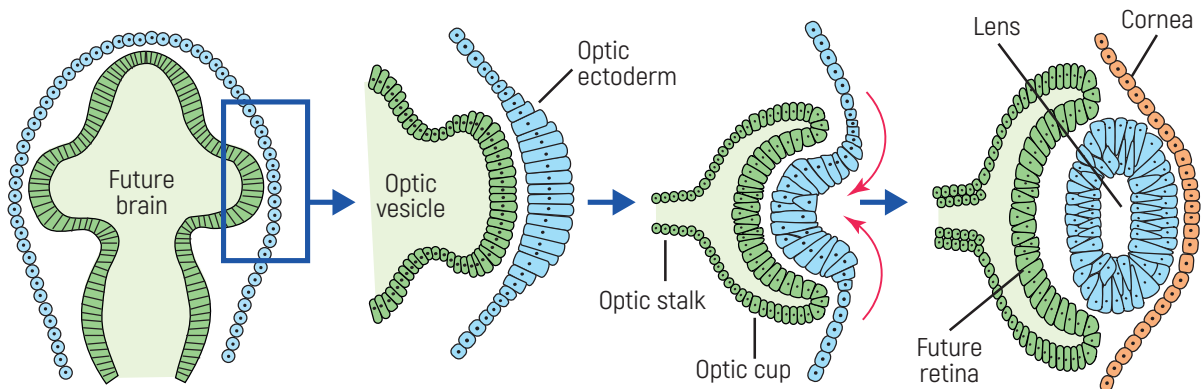


Fig. 11. Example of a secondary embryonic induction – eye formation

Genetic mechanisms of development

The basis of differentiation is **differential genes activity**. Each cell contains a complete gene set established in the zygote during fertilization. As cells develop, the genetic material does not change but part of genes become repressed (inactivated) and tissue- (or cell-) specific genes are expressed (activated). Only a small percentage of the genome is expressed in each terminally differentiated cell (about 3–10 %). In diverse specialized cell types different groups of genes are activated.

Totipotency is the ability of a single cell to divide and produce all the differentiated cells in an organism, including extraembryonic tissues. This is true for the zygote and for early embryonic blastomeres up to at least the 4-cell stage in human embryo. Due to differential genes activity totipotency gives way to **pluripotency**, then to **multipotency** and in the end to **oligo-** or **unipotency** (cell group is able to give rise to one cell type only). For example, cell group of mesoderm can give rise to bones, cartilage, blood cells and vessels and so on at early gastrulation stage. Then, during development the potency of this cell group is restricted and it can give rise to, for example, erythrocytes only (one cell type).

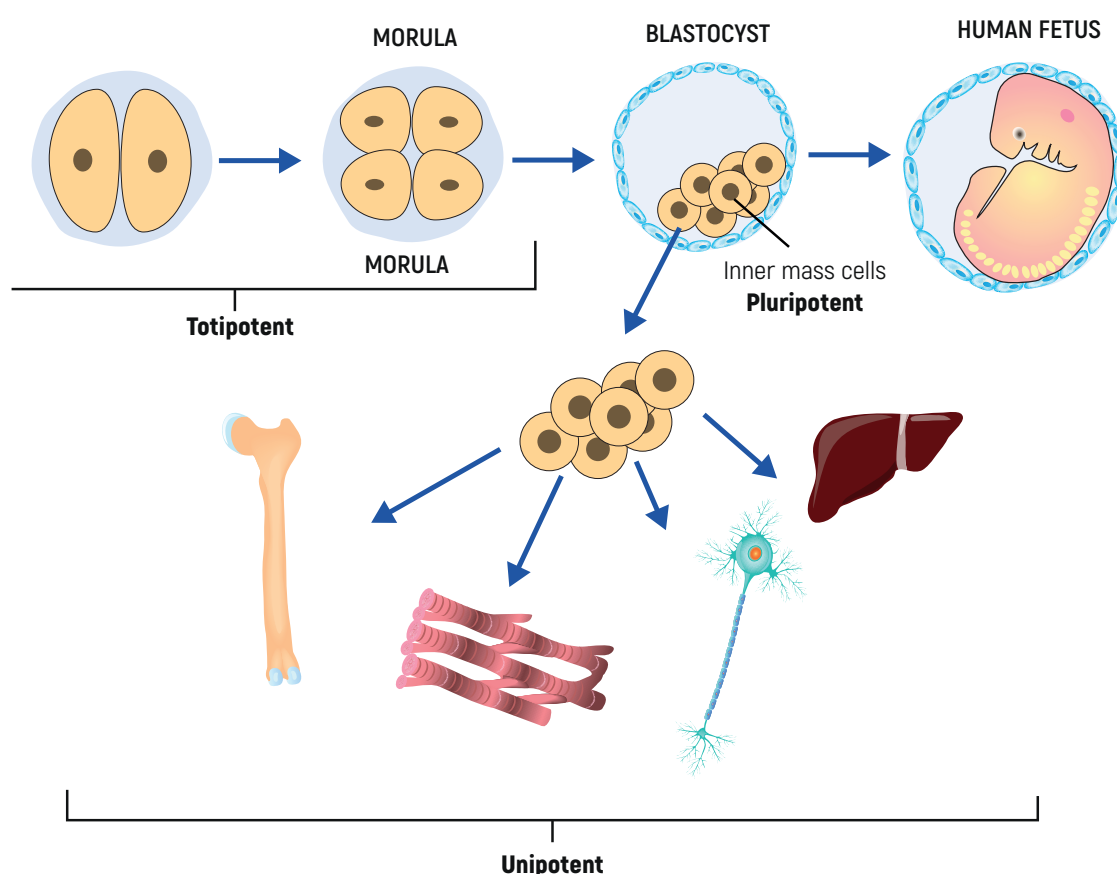


Fig. 12. Restriction of cell potency in ontogenesis

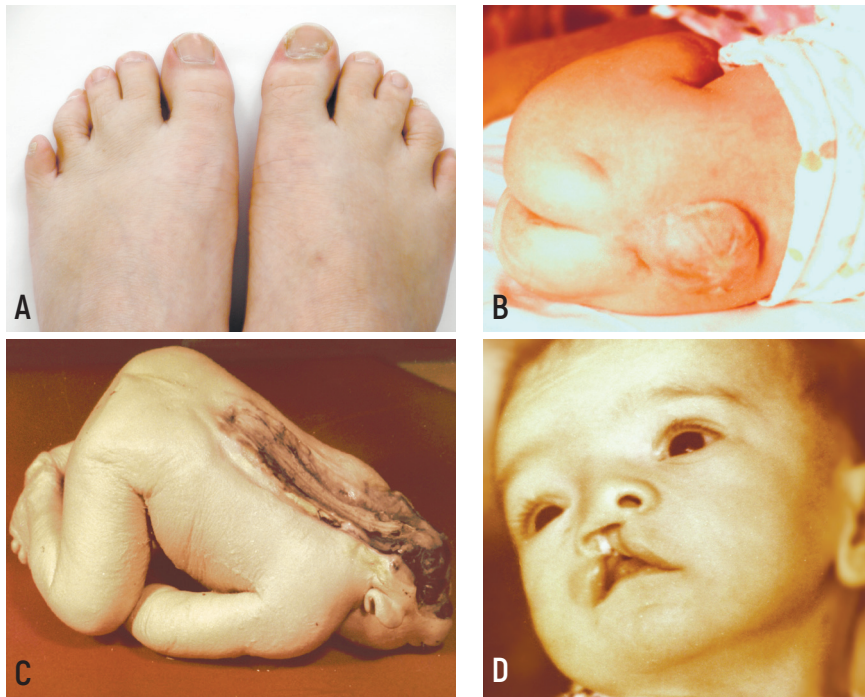
Abnormalities of organogenesis

There are five main cell mechanisms of development (**proliferation, migration, adhesion, differentiation** and **programmed cell death**) and each of them can be broken.

For example, insufficient cell proliferation leads to underdevelopment of tissue or organ, excessive proliferation may lead to overdeveloped organ. Abnormal cell migration leads to ectopy of a particular structure, abnormal adhesion – to clefts or dysraphism. Lack of programmed cell death is the cause of excessive tissue, for example between fingers or toes. Abnormal cell differentiation may give rise to development of a different cell type or even a cancer cells.



Task. 4.3. Study photos of embryonic abnormalities. Make a guess which embryonic mechanisms are disrupted in the first place: A. Syndactyly [Source: <http://commons.wikimedia.org/wiki/User:AzaToth>]; B. Spina bifida; C. Platineuria and anencephaly; D. Cleft lip and palate.



A	
B	
C	
D	



Task 4.4. Match each of the key terms (column A) with its corresponding definition (column B):

COLUMN A

- (1) Neurocoele
- (2) Notochord
- (3) Coelom
- (4) Intermediate mesoderm
- (5) Apoptosis
- (6) Spina bifida
- (7) Neural crest
- (8) Totipotency
- (9) Somite
- (10) Neurula

COLUMN B

- (a) The cavity between two sheets of lateral mesoderm
- (b) Segmented part of mesoderm. There are 44 in human, 50 in chick embryo and 500 in snake
- (c) The cavity inside the neural tube
- (d) It is situated between the neural tube and the gut
- (e) The "4th germ layer"
- (f) The axial complex of organs is formed at this stage
- (g) Programmed cell death
- (h) This part of mesoderm gives rise to gonads and kidneys
- (i) The ability to give rise to all embryonic or extraembryonic cell types. Is seen in zygote and early blastomeres
- (j) This anomaly develops mainly due to the lack of cell adhesion

A	1	2	3	4	5	6	7	8	9	10	11
B											



Home work

Answer the questions using information from textbook «ESSENTIAL MEDICAL BIOLOGY», Chapter 25 (pp. 116–119):

1. How is the neural tube formed? What is the embryonic origin of the nervous system in vertebrates?

2. What is the notochord? What is the role of this structure in neurulation? _____

3. What is the coelom? Where is the coelom in the body of an adult? _____

4. What are somites? What are the derivatives of somite? _____

5. From which germ layer are the epidermis and the nervous system produced? What other organs and tissues are made from that germ layer?

6. From which germ layer are the blood cells produced? What other organs and tissues are made from that germ layer?

7. From which germ layer are the liver and the pancreas cells produced? What other organs and tissues are made from that germ layer?

8. What are the derivatives of the neural crest? _____

9. List the five cellular mechanisms of embryonic development: _____

10. What cell mechanism failure can lead to syndactily? _____

11. Eye formation is an example of secondary embryonic induction. Name the inductor tissue and competent tissue in this case.

TOPIC 5. EXTRAEMBRYONIC MEMBRANES IN AMNIOTES

Provisory organs are larval organs that play important role in embryonic adaptation to specific environmental conditions. So, gills develop in tadpoles that live in water. During metamorphosis the gills disappear.

Provisory organs of reptiles, birds and mammals are: **yolk sac**, **amnion**, **chorion** and **allantois**. Last three of them are referred to as **extraembryonic**, or **fetal membranes**. These membranes provide adaptation of an embryos to terrestrial development.

According to absence or presence of extra embryonic membranes all Vertebrates are divided in two groups: **Anamniotes** and **Amniotes**. Anamniotes have only a yolk sac, that provides nutrition and, also, is the first hematopoietic organ. Amniotes have a yolk sac, amnion, chorion and allantois.

Amnion is a kind of "inner sea" and provides a protective environment for the developing embryo. **Chorion** is the outermost fetal membrane around the embryo. The main function of the chorion is protection of the embryo and gas exchange. The function of the **allantois** is to collect liquid waste from the embryo and to help with the exchange of gases.

Formation of extraembryonic membranes in egg-laying Amniotes (chick embryo)

At the stage of late neurula formation of so-called **body folds** around the whole embryo can be observed. They are getting deeper, surrounding the embryo and isolating it from underlying yolk. Simultaneously extraembryonic ectoderm and outer sheet of extraembryonic somatic mesoderm are forming **amniotic folds**, which are growing toward one another and finally fuse above the embryo, forming **amnion** and **chorion**. So, wall of amnion and chorion are made of ectoderm and somatic mesoderm (**somatopleura**). At the same time extraembryonic endoderm and mesoderm are surrounding yolk and fuse under it. A part of the posterior gut forms allantois. So, the walls of the yolk sac and the allantois consist of endoderm and splanchnic mesoderm (**splanchnopleura**).



Task. 5.1. Study formation of amnion and chorion in chick embryo and label following elements: 1 – embryonic ectoderm, 2 – neural tube, 3 – dermatome, 4 – sclerotome, 5 – myotome, 6 – nephrogonotome, 7 – notochord, 8 – one of two dorsal aortas, 9 – coelom, 10 – amniotic fold, 11 – extraembryonic ectoderm, 12 – extraembryonic somatic mesoderm, 13 – body fold, 14 – extraembryonic splanchnic mesoderm, 15 – endoderm, 16 – blood vessels, 17 – wall of forming chorion, 18 – wall of forming amnion.



Extraembryonic membranes in placental mammals

As placental mammals and humans develop inside the uterus, some important changes in the functions and formation of their extraembryonic membranes occur. The most important among them is the formation of **placenta**. It is formed when fetal tissues acquire contact with maternal tissue for physiological exchange. In mammals this always involves chorion and either yolk sac or allantois. The amnion remains avascular, and its function is chiefly mechanical. Placenta has **fetal and maternal parts**. It attaches to the wall of uterus, and fetus umbilical cord develops from the placenta. Placenta provides oxygen and nutrients to growing fetuses and removes waste products from fetus blood. What is more, it produces **hormones which support pregnancy**. Hormones produced by placenta are – beta-human chorionic gonadotropin, relaxin, estrogen, progesterone, and many others.

Extraembryonic membranes in humans

In humans, as in all placental mammals, **chorion and amnion are derived from somatopleure** (i.e., trophoblastic ectoderm and extraembryonic somatic mesoderm). **Yolk sac and allantois are derived from splanchnopleure** (endoderm and extraembryonic splanchnic mesoderm).

Human amnion begins its development just after blastocyst stage by splitting of the inner cell mass. It takes place on the 8th day after fertilization.

Chorion is developed from trophoblast of the blastocyst. In human it starts forming on the 12-13 days of development. The chorionic villi emerge from the chorion, invade the endometrium (epithelium of the uterus), and allow the transfer of nutrients from maternal blood to fetal blood.

Yolk sac is formed from hypoblast endoderm and extraembryonic mesoderm. In human, yolk sac provides very limited nutritive function, and regresses early, but it is still important in respect to other functions. Yolk sac mesoderm is a major site of **hematopoiesis**, and yolk sac endoderm is the source of **primordial germ cells**. Yolk sac is connected with middle gut of embryo by **vitellointestinal duct**.

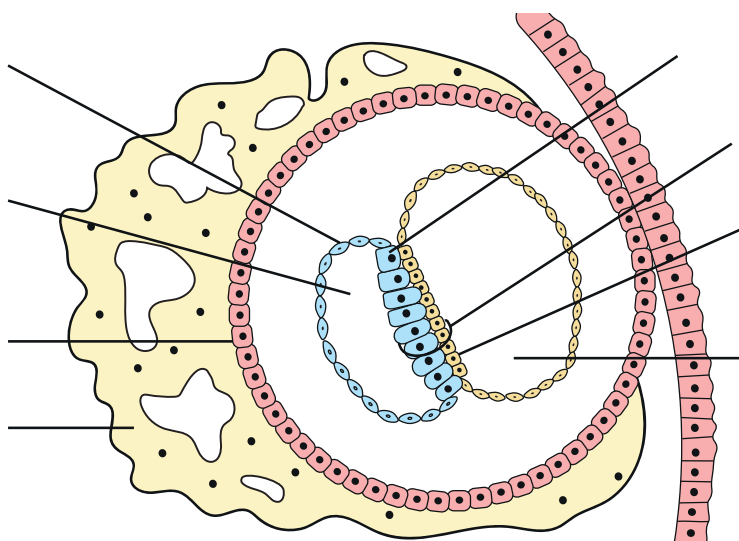
Allantois is also formed from hypoblast endoderm and extraembryonic mesoderm. It is connected with the posterior gut (which later becomes a part of urinary bladder) by the **urachus**.

Both, yolk duct and urachus together with two umbilical arteries and umbilical vein are parts of the **umbilical cord**. In humans, allantois, as yolk sac, is vestigial, but in a functional sense, human placenta is a **chorioallantoic type**. Vessels of allantois vascularize chorion, with allantoic arteries as branches of the two dorsal aortae. Allantoic veins or umbilical veins drain into the caudal (inferior) vena cava through sinus venosus.

Fetal membranes originate from the same zygote as the fetus, so they are used for **invasive fetal tissue sampling techniques in prenatal diagnosis**. These techniques include amniocentesis, chorionic villus sampling (CVS), percutaneous umbilical blood sampling (PUBS, chordocentesis).

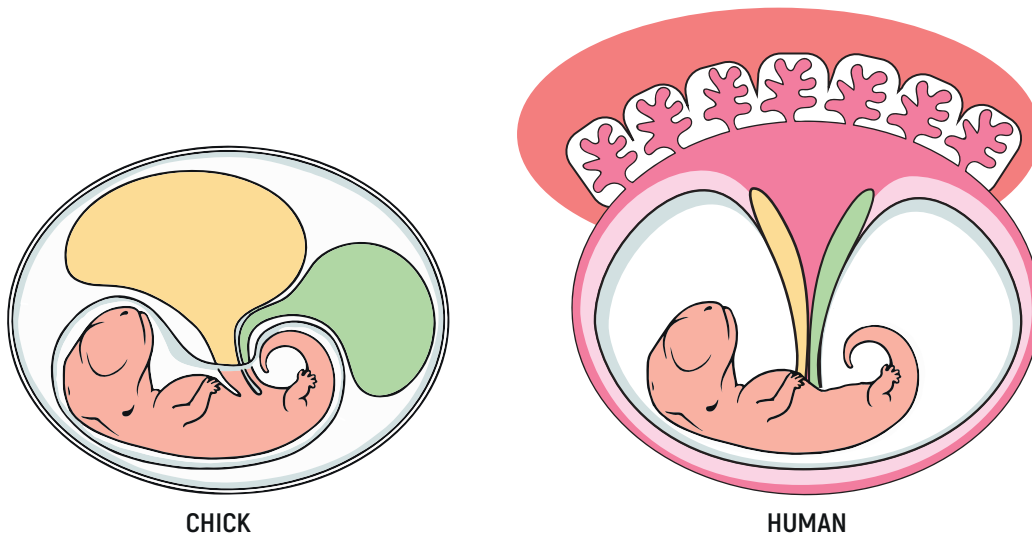


Task. 5.2. Study organization of human embryo at 11th day of development. Mark: 1 – amnion, 2 – epiblast, 3 – amniotic cavity, 4 – yolk sac cavity, 5 – bilaminar embryonic disc, 6 – symplastotrophoblast, 7 – hypoblast, 8 – cytotrophoblast.





Task. 5.3. Study extraembryonic membranes of egg-laying and placental amniotes. Mark: 1 – amnion, 2 – chorion, 3 – embryo, 4 – yolk sac, 5 – allantois, 6 – umbilical cord, 7 – fetal portion of placenta, 8 – maternal portion of placenta (image source: [https://commons.wikimedia.org/wiki/user:Petter Bøckman](https://commons.wikimedia.org/wiki/user:Petter_Bøckman), with modifications).



Task. 5.4. Fill in the table:

Extraembryonic membranes of Amniotes	What are they built of	Functions of the extraembryonic membrane
1. Yolk sac	Splanchnopleura	
2.		
3.		
4.		

5. Placenta		
Fetal part		
Maternal part		

Anomalies of provisory organ reduction in human

Anomalies of reduction of yolk sac remnants are especially well known. A wide variety of anomalies may occur as a result of the **vitellointestinal duct (VID)** failing to obliterate completely. Normally this duct closes long before birth. The failure of its reduction produces anomalies, most common of which is Meckel's diverticulum (about 5% of all people). Meckel's diverticulum is usually about 5 cm in length. It can be connected to umbilicus by a fibrous cord which is the remnant of obliterated part of vitellointestinal duct.

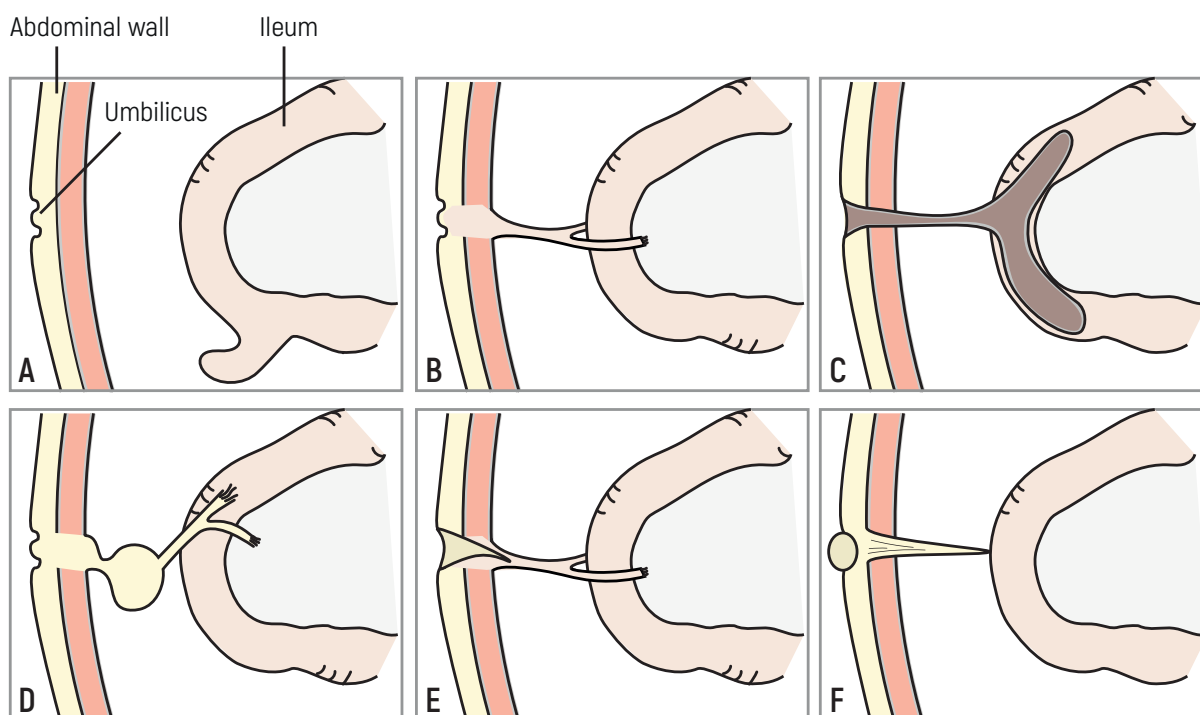


Fig. 13. Vitelline duct abnormalities: A. Meckel's diverticulum. B. Fibrous cord to the ileum. C. Umbilical intestinal fistula. D. Enterocystoma. E. Umbilical sinus. F. Enteroteratoma.

Anomalies of reduction of allantois duct (urachus): During development, lumen of the urachus closes and in adults it forms median umbilical ligament. If the urachus fails to close it is referred to as patent urachus. In this case urine may leak from umbilicus (urachal fistula), or it might be urachal sinus or cyst.

Anomalies of amnion: Amniotic fluid serves as a cushion for the embryo and fetus, and prevents attachments between the skin of the embryo and surrounding tissues. In a condition called **oligohydramnios**, the volume of amniotic fluid is too low, resulting in compression of the fetus by the uterine wall.

If the amniotic fluid is in excess, then a **polyhydramnios** results.

Tears or ruptures in the amnion result in **amniotic bands** forming which can surround limbs and may result in various fetal anomalies. Amniotic bands can constrict limbs, fingers and other body parts.

Abnormalities of chorion: The most dangerous anomaly is a **complete hydatiform mole**. It happens if the embryo dies and the trophoblast begins to grow uncontrollably. **Choriocarcinoma** is a malignant tumor of the trophoblast.

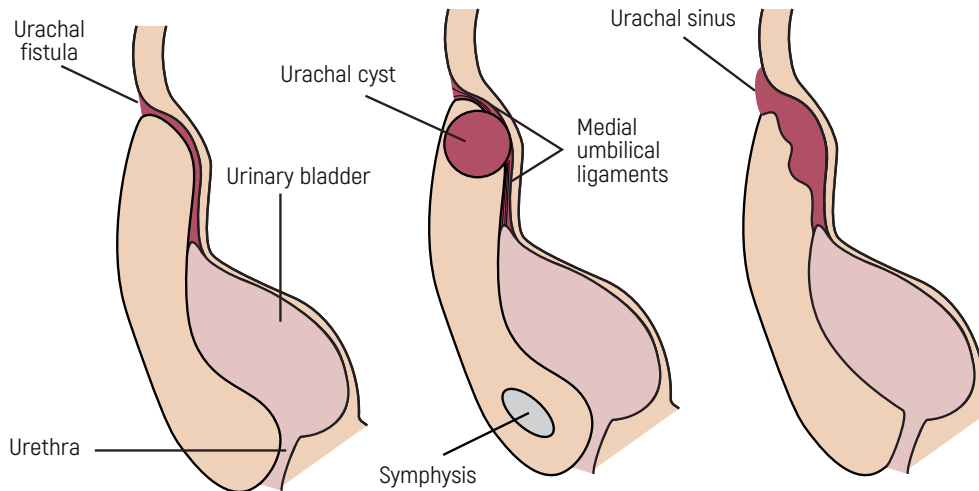


Fig. 14. Patent urachus

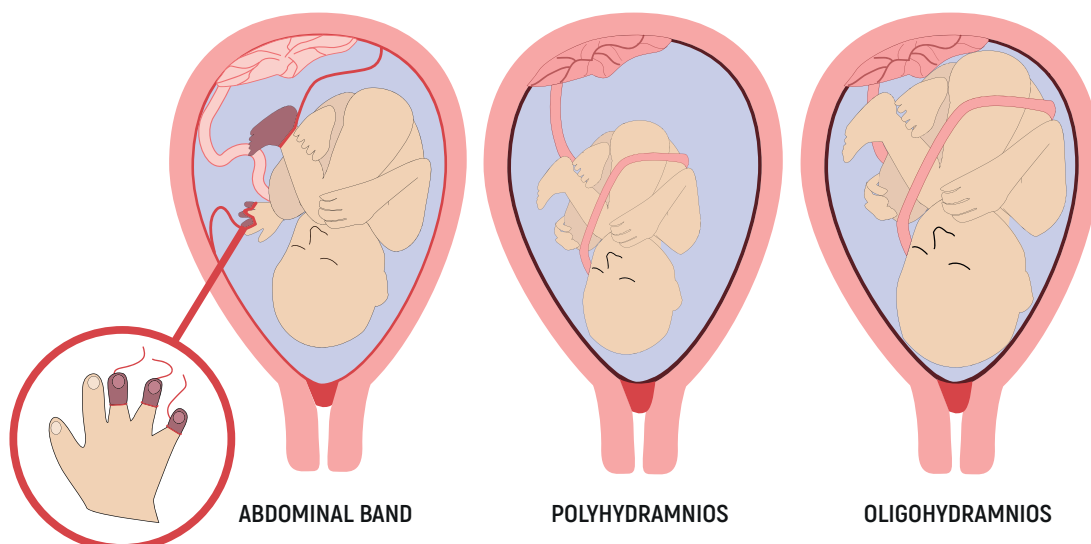


Fig. 15. Anomalies of amnion

Twinning

Twins are the two (or more) offspring produced in the same pregnancy. Therefore, they can be either monozygotic (identical) or dizygotic (fraternal).

All dizygotic twins have two separate placentas (sometimes fused but still separate) and are in different amniotic sacs (Di-Di twins).

One-third of monozygotic twins have two separate placentas and sacs, similar to dizygotic twins (**dichorionic**). With di-di MZ twins, the fertilized egg has split within 2-3 days after fertilization.

2/3 of monozygotic twins share a placenta (**monochorionic-diamniotic** or mono-di). With mono-di MZ twins, the fertilized egg has split within 3-8 days after fertilization.

About 1% of monozygotic twins will share their inner sac (**monochorionic, monoamniotic** or mono-mono). With mono-mono MZ twins the fertilized egg has split within 8-13 days after fertilization.

In very rare circumstances, the fertilized eggs split 13+ days after fertilization, and this result in **conjoined twins**, twins that are joined at certain body parts.

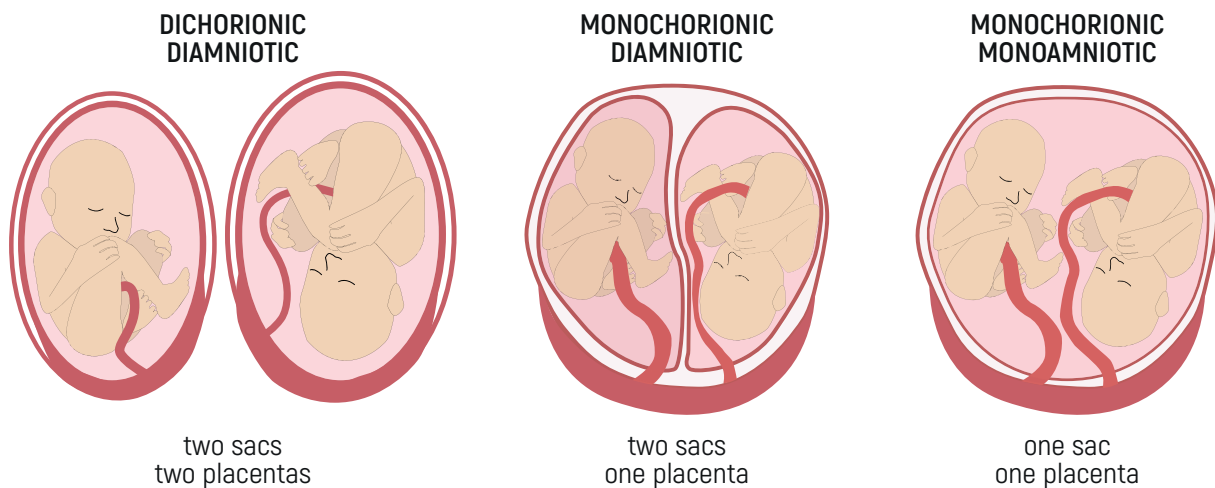


Fig. 16. Placentation in twins



Task. 5.5. Match each of the key terms (column A) with its corresponding definition (column B):

COLUMN A

- (1) Extraembryonic membranes
- (2) Splanchnopleure
- (3) Amniotic bands
- (4) Somatopleure
- (5) Anamniotes
- (6) Fraternal twins
- (7) Allantois
- (8) Yolk sac
- (9) Urachus
- (10) Amniocentesis
- (11) Meckel's diverticulum
- (12) Chorion
- (13) Umbilical cord
- (14) Placenta

COLUMN B

- (a) It consists of the endoderm and the inner layer of mesoderm, and gives rise to the yolk sac and allantois
- (b) It is the remnant of duct between intestine and the yolk sac
- (c) Inside it one can find two arteries, one vein, the duct of yolk sac and the duct of allantois
- (d) It consists of parietal sheet of mesoderm and ectoderm
- (e) They have two placentas and two amniotic sacs.
- (f) Tears or ruptures in the amnion may result in these
- (g) This fetal membrane is analyzed during CVS
- (h) Inside this structure the first blood cells appear
- (i) "Embryonic urinary bladder"
- (j) Amphibians and fish belong to this group
- (k) In embryo, it is between the bladder and the umbilicus. In adults, it forms plica umbilicalis mediana
- (l) It has fetal and maternal parts and is able to produce hormones
- (m) They originate from the embryo, but are not considered part of it.
- (n) Invasive technique for prenatal diagnosis that includes taking amniotic fluid for testing

A	1	2	3	4	5	6	7	8	9	10	11	12	13	14
B														

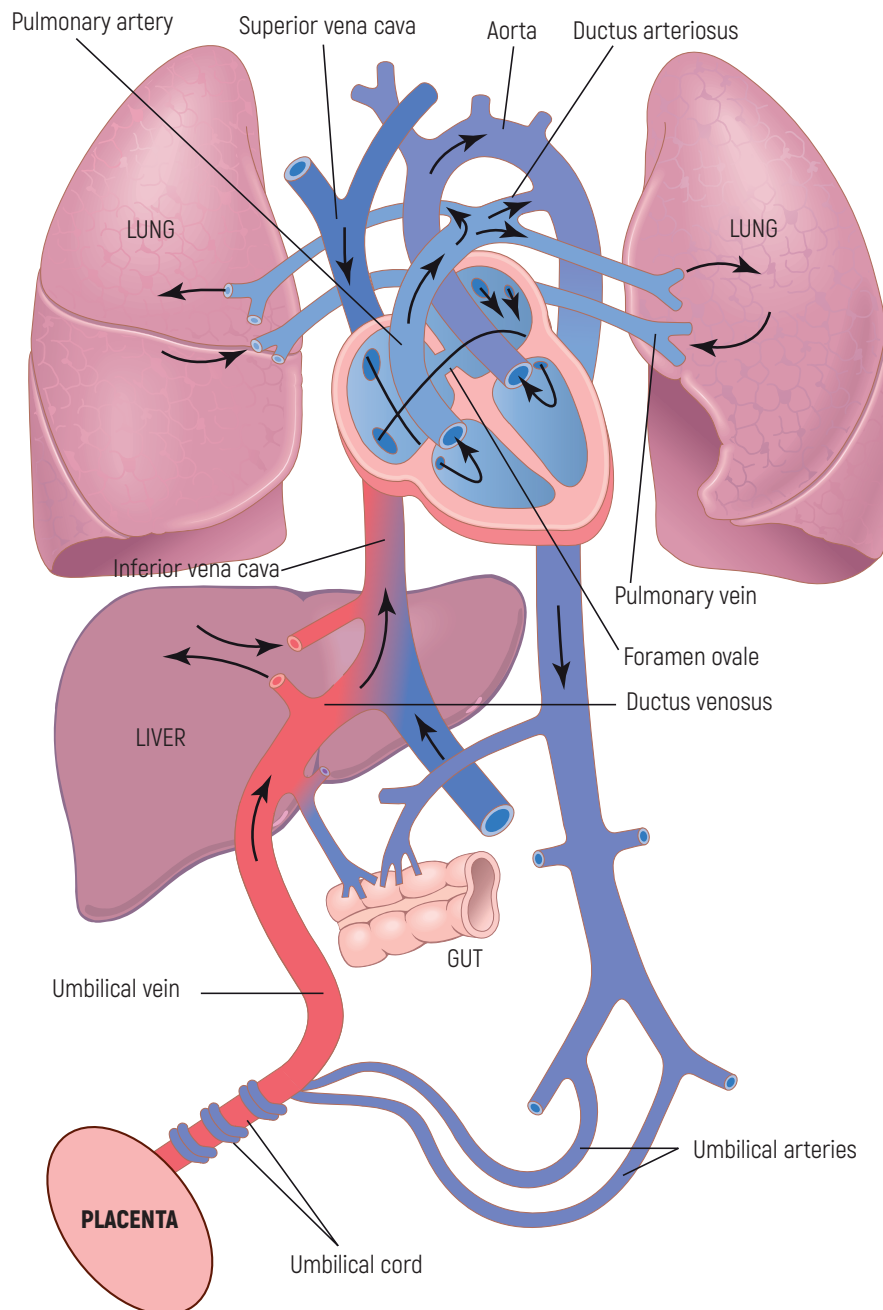


Home work

Answer the questions using information from textbook «ESSENTIAL MEDICAL BIOLOGY», Chapter 26 (pp. 120–125):

1. What are extraembryonic membranes? _____

2. Are extraembryonic membranes the same among all vertebrates? _____
- _____
3. Explain the difference between Amniotes and Anamniotes: _____
- _____
4. How is the yolk sac forming? What are the functions of the yolk sac? _____
- _____
5. Which extraembryonic membrane has the function of storing the nitrogen wastes of the embryo? Is this function necessary in the embryos of placental mammals?
- _____
- _____
6. Why can the amnion be considered an adaptation to terrestrial life? _____
- _____
7. What group of vertebrates develops a placenta? What are its main functions? _____
- _____
8. What are the main substances transferred from the mother to the fetus through placenta? And from the fetus to the mother?
- _____
- _____
9. Study the scheme of human fetal circulation and answer the following questions:
- a. The umbilical arteries are an extension of the arteries of one of the extraembryonic membrane. Which one?
- _____
- b. Lungs of the fetus do not work. How does the fetus get oxygen?
- _____
- _____
- c. Find foramen ovale and ductus arteriosus at the scheme. What purpose do they serve?
- _____
- _____
- d. What may happen if the foramen ovale and ductus arteriosus are still open in the postnatal period?
- _____
- _____
- _____



10. Do mother and fetus normally exchange cells through the placenta? _____

11. What are the endocrine functions of the placenta? _____

12. What is the umbilical cord? What structures does it contain? _____

13. Is it possible for MZ twins to have separate placentas and amniotic sacs? _____

QUESTIONS TO COLLOQUIUM

1. Connections between onto- and phylogeny.
2. Characteristics and periods of animal development (ontogenesis).
3. Sexual and asexual reproduction. Gametogenesis. Structure of gametes.
4. Egg structure. Amount and position of yolk.
5. Fertilization. Gamete fusion and prevention of polyspermy.
6. Cleavage. Patterns of embryonic cleavage.
7. Types of holoblastic cleavage. Types of blastula.
8. Meroblastic cleavage. Discoblastula and its morphology.
9. Cleavage in placental mammals and examples of abnormalities of cleavage in human.
10. Gastrulation. Types of cell movements during gastrulation.
11. Gastrulation in lancelet (or sea urchin) and frog.
12. Gastrulation in birds and mammals.
13. Primary embryonic induction at early gastrula stage. Spemann's organizer.
14. Neurulation. Morphology of a vertebrate embryo at neurula stage.
15. Derivatives of ectoderm, mesoderm and endoderm.
16. Genetic, cellular and integrative mechanisms of development.
17. Anamniotes and Amniotes. Fetal membranes of Amniotes.
18. Formation of extraembryonic membranes in chick and human.
19. Placenta and umbilical cord. Structure and functions.

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