BIOLOGY

FOR INTERNATIONAL STUDENTS

studying «Pharmacy»

Text-book

Minsk BSMU 2016

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ
БЕЛОРУССКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ
КАФЕДРА БИОЛОГИИ

БИОЛОГИЯ

ДЛЯ ИНОСТРАННЫХ СТУДЕНТОВ
по специальности «Фармация»

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FOR INTERNATIONAL STUDENTS
studying «Pharmacy»

Учебно-методическое пособие

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для иностранных студентов по специальности «Фармация»

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for international students studying «Pharmacy»

Учебно-методическое пособие
На английском языке

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Topic 1. MAGNIFYING DEVICES. METHODS OF STUDYING CELLS

The subject, tasks and methods of cytology. (Latin *cytos* — a cell, *logos* — a science) is a science studying the structure, chemical composition and functions of cells, their multiplication, development and interaction in a multicellular organism.

The tasks of cytology:

– studying the structure and function of cells and their components (membranes, organelles, inclusions and nuclei);

– studying cellular division and possibilities of their adaptation to environmental changes;

– studying interrelations between cells in a multicellular organism.

Methods of cytology:

1. *Microscopic* methods help to study morphology of cells and their components (light and electron microscopy).

2. *Cytochemical (histochemical)* methods help to determine chemical composition or location of substances in the cell (in tissue sections). They are based on special staining stuff.

3. *Biochemical* methods are used for studying the chemical composition of cells, determination of substance concentration in tissues. They are based on the property of different biochemical compounds to absorb light waves of a definite length.

4. *The method of differential centrifugation* helps to study to the composition and properties of cell organelles: a tissue specimen is fragmentized to destroy cell membranes, then placed into the centrifuge, where it is divided into separate fractions.

5. *The method of autography* is used for studying the dynamic of metabolic processes in cell compnents. It is based on introduction of radioactive isotopes into the cell. Molecules marked with radioactive isotopes (^{3}H, ^{32}P, ^{14}C) participate in exchange reactions. Their location, movement, accumulation and excretion are determined by radiation registered with a photoplate.

1. *Rhoentgenostructural analysis* is performed for studying the spatial structure and arrangement of molecules in the substance. This method is based on diffraction of X-rays passing through a substance crystal.

2. Magnifying devices and their purpose. Structure of a light microscope.

A biological microscope is intended for studying micro-objects in the current of passing light. A light microscope (fig. 1) consists of 3 parts: mechanical, illuminating and optical.

The *mechanical* part includes a base, a stage, a cremaliera (or macrometric knob), a micrometric knob, a draw-tube and a revolver.

The support consists of a draw-tube holder (column) and a base. The column contains:

– a revolver — a rotating mechanism for changing objectives;

– a draw-tube — a hollow tube for fixing an ocular;

– a system of knobs for coarse (the macrometric one) and fine (the micrometric one) adjustment of the microscope;

– a stage for placing an investigation object;

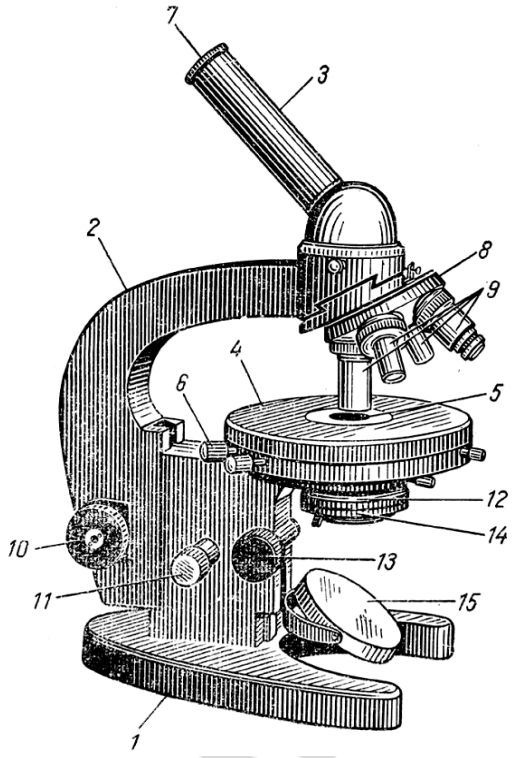


Fig. 1. Structure of a light microscope:
1 — base; *2* — draw-tube holder; *3* — draw-tube; *4* — stage; *5* — aperture of the stage; *6* — knobs for moving the stage; *7* — ocular; *8* — revolving nosepiece; *9* — objectives; *10* — cremaliera; *11* — micrometric knob (in some models it is located in the base); *12* — condenser; *13, 14* — knob and diaphragm of the condenser respectively; *15* — mirror

The *illuminating* part includes a mirror (or an electric illuminator) and a condenser.

The *mirror* of the microscope is double-sided — with a flat and concave surfaces. The concave surface is used under natural illumination, while a flat one — under artificial illumination.

The condenser is a lens system collecting light rays into a band. The diameter of the light band can be regulated with a special level, changing the diaphragm lumen.

The *optical* system consists of an ocular lens and objective lenses.

The *ocular lens* (*oculus* — an eye) is a lens system directed towards the eye. The magnification is indicated on it. A training microscope uses spare oculars with magnification 7×, 10× and 15×.

The *objective lens* is located at the lower end of the draw-tube. It is a lens system directed to the investigated object. Two kinds of objective lenses are used: with small (8×) and a high magnification (40×).

The total magnification of the microscope is determined by multiplying the magnifications of the objective and ocular lenses. For example, the total magnification of the microscope with 40× objective lens magnification and 7× ocular lens magnification is equal to 280.

3. Rules of working with the microscope:

1. Put the microscope approximately a palm width from the edge of the table. Column should be directed towards you and the mirror towards the light source.

2. Set the objective 2–3 cm from the surface of the stage rotating the *macrometric* knob.

3. Check fixation of the objective lens with small magnification (8×) until it clicks, it should be fixed opposite the aperture on the stage.

4. Put the condenser into a neutral position and open the diaphragm completely.

5. *Looking into the ocular*, direct the mirror surface to the light source for even illumination of the *field of vision*.

6. Place the micropreparation on the stage, the cover glass should be directed towards the objective!

7. *Looking on the side* (!), lower the objective lens to 0.5 cm from the surface of the cover glass with a macrometric knob (the focal distance of the objective with 8× is *about 1 cm*).

8. Looking into the ocular, rotate *the macrometric knob* slowly (!) and get a clear image of the object.

9. Study the object. Move the preparation manually.

Note: If the object is too small and is not seen at small magnification, then adjust the microscope to an edge of the cover glass. Having obtained a clear image of the glass edge, move it further to a working field in search of the object.

Rules of working with a high magnification (7 × 40):

1. Center the needed area of a micropreparation — move it to the center of the field of vision.

2. Turn the high-magnification objective lens (×40) using a revolver mechanism until it clicks.

3. Put the condenser into an upper position. Looking from the side, *carefully* lower the large magnification objective lens with the macrometric knob until it touches the surface of the cover glass (the focal distance of 40× objective is approximately 1–2 mm).

4. Looking into the ocular, turn the *macrometric knob* slightly (!) until the object outlines appear.

5. Use a *micrometric knob* for getting a better image turning it towards yourself or from yourself *no more than 0.5 turn*.

6. Study the needed area of the micropreparation.

Terminating the work with the microscope:

1. Having finished studying the object, rise the draw-tube 2–3 cm using the macrometric knob and take off the preparation from the stage.

2. Set a small magnification objective lens until it clicks by turning the revolver and fix it against the aperture on the stage.

3. Lower the objective to the stage level with a macrometric knob.

Basic terms and concepts:

1. Immersion — liquid that fills the space between the cover glass and the immersion objective (90×).

2. Condenser — a lens system collecting light rays into a bundle.

3. Cremaliera — a macrometric knob.

4. Objective lens — a lens system, which are screwed into the revolver and are directed to the stage.

5. Ocular lens — a lens system inserted into an upper aperture of the draw-tube and directed to the eye.

6. Resolution — the ability of the optic device to differentiate small details: a minimum distance between two adjacent points (lines), which are possible to differentiate.

7. Revolving mechanism — a rotating mechanism for changing objectives, which is fixed on the column of the support.

8. Draw-tube — a hollow tube, which connects the ocular and the objective.

Topic 2. BIOLOGY OF THE CELL. THE FLOW OF SUBSTANCE AND ENERGY IN THE CELL

1. The present state of the Cell Theory.

1. The cell is an elementary structural, functional and genetic unit of all living things; it is an open self-regulating system and flows of substances, energy and information continuously pass through it (fig. 2).

2. Cells of all organisms have similar structure, chemical composition and processes of vital activity.

3. New cells are formed as result of the mother cell's division.

4. Cells of a multicellular organism differentiate and form tissues for performing various functions.

2. Differentiating signs of pro- and eukaryotic cells (tab. 1).

Table 1

Pro- and eukaryotic cells

Prokaryotes	Eukaryotes
Differences	
Mycoplasms, bacteria, cyanobacteria	Protozoans, plant and animal cells
Sizes: 1–10 μm	10–100 μm
There is no nucleus, but a nucleoid	There is a nucleus
DNA is not bound with proteins-histones	DNA is bound with proteins-histones
There is no mitosis and membrane-bound organelles, their functions are performed by mesosomes — ingrowths of the membrane	There is mitosis and membrane-bound organelles (fig. 3)

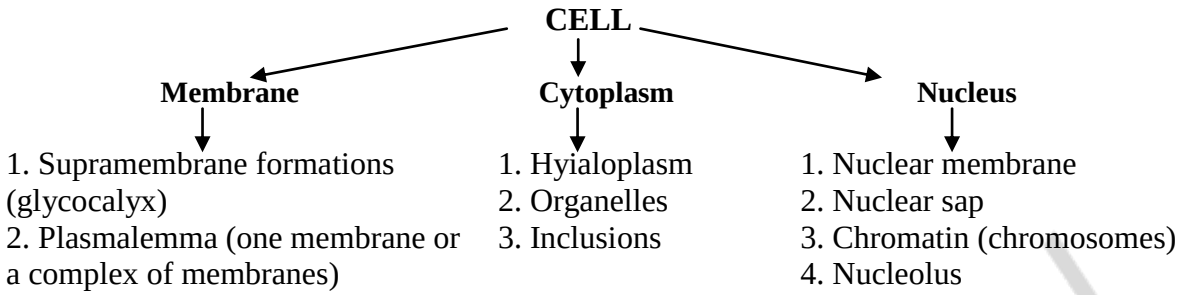


Fig. 2. The diagram of the cell structure

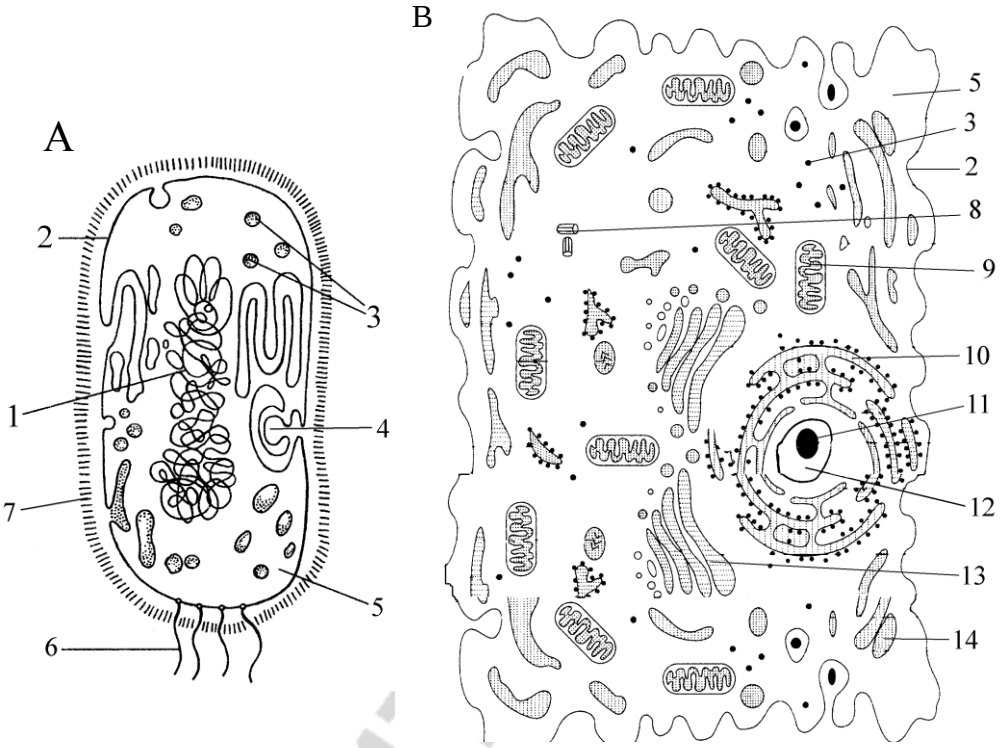


Fig. 3. Structure of prokaryotic and eukaryotic cells:
a — prokaryotic cell, *b*, *c* — eukaryotic cells: *1* — nucleoid; *2* — plasma membrane; *3* — ribosomes; *4* — mesosome; *5* — cytoplasm; *6* — flagellum; *7* — cell wall; *8* — centrosome; *9* — mitochondria; *10* — rough ER; *11* — nucleolus; *12* — nucleus; *13* — Golgi complex; *14* — smooth ER

3. The structure of (a model) elementary membrane, its properties and functions. In 1943 N. Davson and P. Danielli proposed the first model of plasma membrane. It was a **sandwich model**. Two layers of lipid molecules are located between two layers of protein molecules.

Every lipid molecule has two ends: the *hydrophilic* «head» (water-soluble) and the *hydrophobic* «tail» (water insoluble). Hydrophobic ends of molecules are directed towards each other, hydrophilic ones — towards proteins (fig. 4).

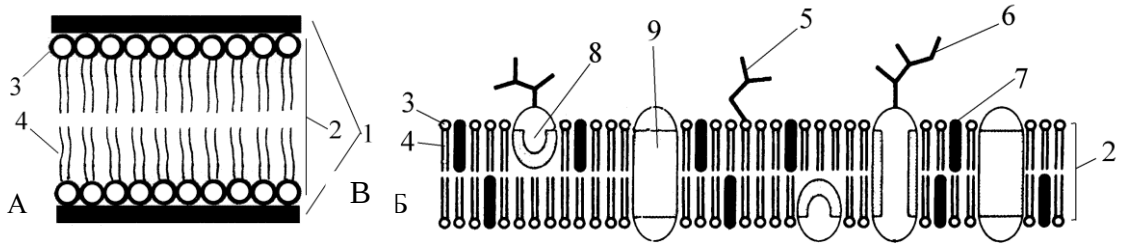


Fig. 4. Models of plasma membrane:
a — sandwich model, *b, c* — fluid mosaic model: *1* — solid protein layers; *2* — bilipid layer; *3* — hydrophilic heads of phospholipids; *4* — hydrophobic tails of phospholipids; *5* — glycolipid;*6* — glycoprotein; *7* — cholesterol; *8* — semi-integral protein; *9* — integral protein

The **fluid mosaic model** is better; it corresponds to the properties and functions of plasma membrane. It was proposed in 1972 by S. Singer and G. Nicolson.

The basic membrane components are lipids. They compose from 20 to 80 % of its mass. They are phospholipids, lecithin and cholesterol.

Protein molecules are in a double layer of lipid molecules that form «lipid sea».

Protein molecules, which penetrate 2 layers of lipid molecules, are *integral*. Those protein molecules, which are immersed into one layer, are *semi-integral*. *Peripheral proteins* lay on the surface of lipids.

The third component of an plasma membrane are *glycoproteins* and *glycolipids* forming a receptor apparatus on its surface (*glycocalyx*).

Properties of the plasma membrane:

– plasticity (it restores quickly after impairment and also stretches and constricts in cell movements);

– semi-permeability (passes molecules selectively);

– ability for self-locking (forms vesicles and vacuoles).

Functions of the plasma membrane:

– structural (membranes are components of all cell organelles except ribosomes and centrosomes);

– barrier (protects the cell from external factors and sustains its composition);

– metabolic (many enzymes are located on membranes);

receptor (receives signals, recognizes substances).

4 Methods of passing substances into the cell:

1. *Passive transport* runs according to the concentration gradient without spending energy. Water and small molecules can pass into the cell by filtration, diffusion, through pores or by of solution in lipids.

2. *Facilitated diffusion* is associated with participation of carrier proteins (permeases) in transport of molecules. Amino acids, sugar, fatty acids get into the cell in this way.

3. *Active transpoprt* demands energy expenditure, because it follows against the concentration gradient. Such transport demands enzymes, ATP molecules and special ion canals. A sodium-potassium pump is an example of such transport.

4. *Endocytosis* is participation of the membrane in catching particles or molecules and transporting them into the cell. Endocytosis is changing architectonics (outlines) of the membrane. Transport of macromolecules or hard particles is *phagocytosis*, while transport of fluid is *pinocytosis*.

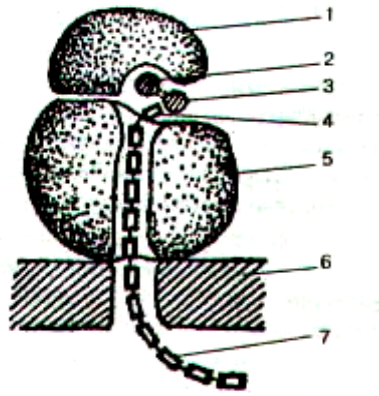


Fig. 5. Structure of a ribosome: *1* — small subunit; *2* — mRNA; *3* — tRNA, *4* — amimo acids; *5* — large subunit;*6* — membrane of ER, *7* — protein

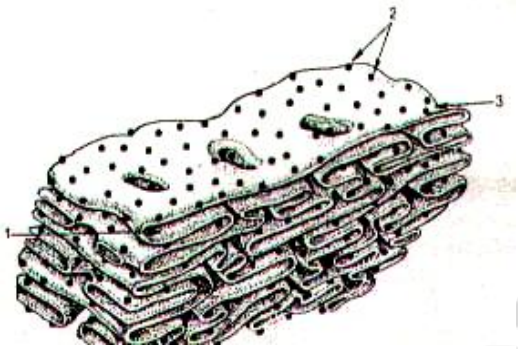


Fig. 6. Structure of granular ER: *1* — canal; *2* — ribosomes; *3* — membrane

5. Anabolic system of the cell. The anabolic system performs reactions of plastic exchange, or assimilation.

Organelles are differentiated areas of the cytoplasm. They have a constant structure and perform specific functions

Ribosomes are spherical bodies (15–35 nm in diameter) consisting of two subunits. They may be in hyaloplasm, on the external membrane of the nucleus, on membranes of the ER. A *large subunit* of the ribosome contains three different molecules rRNA and 40 molecules of proteins, a *small subunit* — one rRNA molecule and 33 protein molecules (fig. 5). Ribosome subunits are synthesized in nucleoli. The information about the rRNA structure is contained in «*nucleolar-organizers»* (DNA molecule areas in the region of secondary constrictions of satellite chromosomes). The final assembly of ribosomes in subunits occurs in the process of translation.

The function of ribosomes is assembling protein molecules (translation).

Endoplasmic reticulum (ER) is a system of canals located throughout the cell. It connected with the perinuclear space of the nucleus and cavities of Golgi complex (fig. 6). Its wall is plasma membrane. ER canals perform compartmentalization of the cell cytoplasm (division into areas, where various biochemical reactions take place). The granular ER (ribosomes are placed on its membranes) participate in biosynthesis of proteins, which are later transported to the Golgi complex.

Carbohydrates and lipids are synthesized on membranes of the smooth ER (which does not contain ribosomes). It takes part in synthesis of steroid hormones, detoxication of toxic substances (in liver cells).

Golgi complex consists of vesicles, tubules, sacs. Dictyosomes are basic elements of the complex.

Dictyosomes are piles of closed sacs composed of 10–15 plasma membranes that have widenings on the ends. These widenings form vesicles that separate and transform into lysosomes and vacuoles (fig. 7). A number of these vesicles excrete secretes and metabolites from the cell.

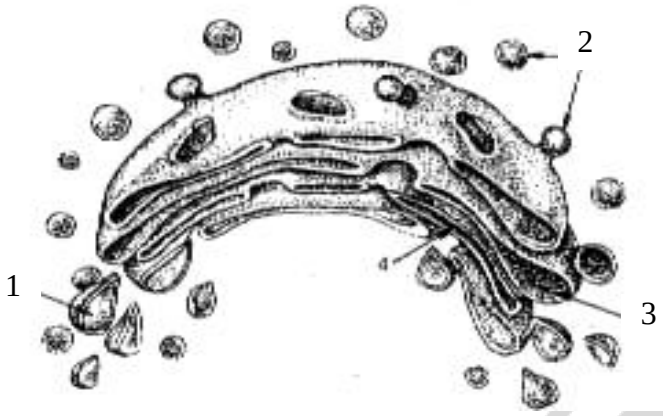


Fig. 7. Structure of Golgi complex:
1 — vacuole; *2* — vesicles; *3* — membrane; *4* — canal

Functions of Golgi complex:
– sorting and packing substances synthesized in ER;
– synthesis of complex compounds (lipoproteins, glycoproteins);
– assembling plasma membranes;
– forming lysosomes, glyoxysomes and vacuoles;
– taking part in substance secretion.

6. The catabolic system of the cell. The catabolic system performs energy exchange, or dissimilation.

Primary lysosomes are formed in Golgi complex. They are spheroidal bodies (0.2–2 μm in diameter) covered with an plasma membrane. They contain approximately 50 different hydrolytic enzymes. *Secondary lysosomes* (phagolysosomes) contain digested substances.

Functions of lysosomes:
– breaking up substances passed into the cell by phagocytosis;
– destroying impaired structures and organelles of the cell.

Peroxisomes are formed in ER. Their enzymes (oxidazes) oxidize amino acids with formation of peroxide (H_2O_2).

Glyoxysomes are formed in Golgi complex, their enzymes transform fats into carbohydrates.

Mitochondria have a shape of rods, filaments and granules. The sizes of mitochondria are from 0.5 to 7 μm (fig. 8). Their number is not same in cells with different activity. A mitochondrion wall consists of an external and internal membranes. Ingrowths of the internal membrane form *cristae*. There is the matrix containing enzyme systems of an oxygen stage of energy exchange and an autonomous system of protein biosynthesis (ribosomes, RNA and ring DNA molecules) under the inner membrane. The interspace between mitochondrion membranes is *perimitochondrial space*.

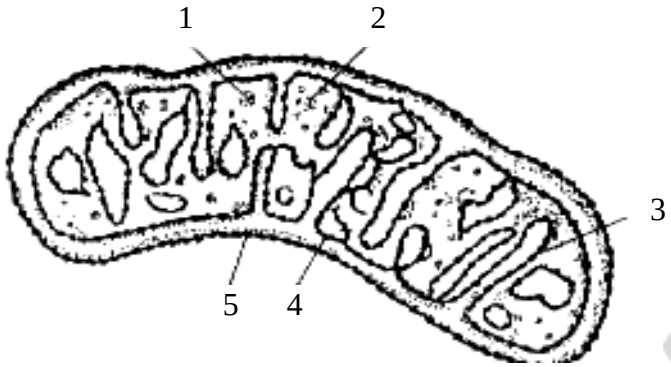


Fig. 8. Structure of a mitochondrion:
1 — ribosome; *2* — matrix; *3* — cristae; *4* — internal membrane; *5* — external membrane

Functions of mitochondria:

– ATP synthesis;

– Synthesis of specific proteins and participating in synthesis of steroid hormones.

7. Energy exchange in the cell. Enzyme systems of mitochondria.

Energy exchange is the sum of enzymatic breaking-down reactions of complex organic compounds followed by releasing energy used for ATP synthesis.

The preparatory stage goes in the digestive system and in phagosomes of cells, where breaking up of complex organic compounds into simple ones occurs. Polysaccharides are split into monosaccharides, proteins into amino acids, fats into glycerol and fatty acids. The released energy is dissipated as warmth.

The anaerobic (anoxic) stage (glycolysis) occurs in the cytoplasm of cells. Ten enzymes participate in it. Glucose breaks down into pyruvic (lactic) acid and 2 ATP molecules are formed. The pyruvic acid passes into mitochondria for further transformations.

Aerobic stage of energy exchange occurs in mitochondria.

There are 3 enzyme systems in mitochondria:

– enzymes of Krebs cycle (citric acid cycle) in the internal matrix;

– enzymes of tissue respiration on the internal membrane;

– enzymes of oxidative phosphorilation on ATP-somes (mushroom-shaped bodies).

Pyruvic acid comes into the internal matrix of the mitochondrion and interacts with co-enzyme A (CoA), when Acetyl CoA (an activated form of Acetic acid) forms. CO_2 and H^+ chip off Acetyl CoA.

CO_2 is excreted by mitochondria, H^+ and electrons (from hydrogen atoms) pass through the enzyme system of tissue respiration.

Protons accumulate on the external surface of the internal membrane and electrons on the internal one. Having reached a critical potential (200 mv), protons pass through canals of ATP-somes.

Electrons give the energy away for adding the residue of phosphoric acid to ADP (ATP synthesis) and join protons. Hydrogen atoms are formed, they interact with oxygen and form water molecules. 1 mol of glucose gives the cell 38 mol of ATP during all reactions of energy exchange.

Basic terms and concepts:

1. Glycocalyx — a receptor apparatus of an animal cell membrane.

2. Glycolysis — a process of breaking down glucose without oxygen.

3. Concentration gradient — the difference of substance concentrations.

4. Enzymes of oxidative phosphorilation — are enzymes of mitochondria located on ATP-somes.

5. Enzymes of tissue respiration — enzymes of mitochondria located in cristae.

6. Enzymes of Krebs cycle — enzymes of mitochondria located in the matrix.

7. Mesosomes — ingrowths of plasmalemma which perform a role of membrane organelles in prokaryotic cells.

8. Nucleoid — a genetic apparatus of prokaryotes.

9. Plasmalemma — a membrane, which is a part of cell envelope.

10. Peroxisomes — organelles, where oxidation of amino acids occurs and hydrogen peroxide is formed

Topic 3. THE FLOW OF genetic information IN THE CELL

1. Structure and functions of the nucleus.

The basic genetic information is in the nucleus. The nucleus (Latin — *nucleus*; Greek — *karyon*) was described in 1831 by R. Brown. The shape of the nucleus depends on the shape and functions of the cell.

The *envelope* of an interphase nucleus (*karyolemma*) consists of an external and internal membranes.

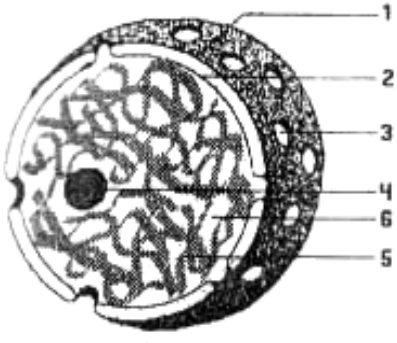


Fig. 9. Structure of the nucleus: *1* — internal membrane; *2* — external membrane; *3* — pore; *4* — nucleoli; *5* — chromatin; *6* — nuclear sap

Perinuclear space is between those membranes. There are openings in membranes *(pores)* with protein molecules forming *pore complexes*. When the cell is active, the majority of pores are open. The substance flow passes through them from the cytoplasm into the nucleus and back.

The number of pores in one nucleus reaches 3–4 thousand. The external nucleus membrane is linked with endoplasmic reticulum canals. *Ribosomes* are usually placed on it.

Proteins of the internal nuclear membrane form a *nuclear lamina*. It sustains a constant shape of the nucleus and chromosomes are attached to it (fig. 9).

Nuclear sap, or *karyolymph*, is colloid jelly-like solution that contains proteins, lipids, carbohydrates, RNA, nucleotides and enzymes.

Nucleolus is a temporary component of the nucleus: it disappears in the beginning of cell division and restores in the end. Chemical composition of nucleolus: protein (~90 %), rRNA (~6 %), lipids, enzymes.

Nucleoli form in the site of secondary constrictions of satellite chromosomes. Its function is assembling ribosome subunits.

Chromatin of the nucleus is chromosomes during the interphase. It contains DNA, proteins-histones and RNA in ratio 1:1.3:0.2. DNA together with protein form *deoxiribonucleoprotein* (DNP). DNP condenses to form chromosomes during mitosis.

Functions of the nucleus:

1) store hereditary information of the cell;
2) takes part in cellular division (multiplication);
3) regulates metabolic processes in the cell.

2. Types of chromosomes. Structure of a metaphase chromosome. Chromosomes (Greek — *chromo* — color, *soma* — body) are condensed chromatin. The chromosome length is 0.2–5.0 μm, diameter — 0.2–2.0 μm.

A metaphase chromosome consists of 2 *chromatids* linked in the area of a *centromere (primary constriction)*. It divides the chromosome into 2 *arms*. Some chromosomes have *secondary constrictions*. The area they separate is a satellite, and such chromosomes are called *satellite chromosomes*. Terminal areas of chromosomes are *telomeres* (fig. 10). Each chromatid includes one DNA molecule bound with proteins-histones. Chromosome areas with intense staining are areas of strong condensation (*heterochromatin*). Lighter areas are areas of weak condensation (*euchromatin*).

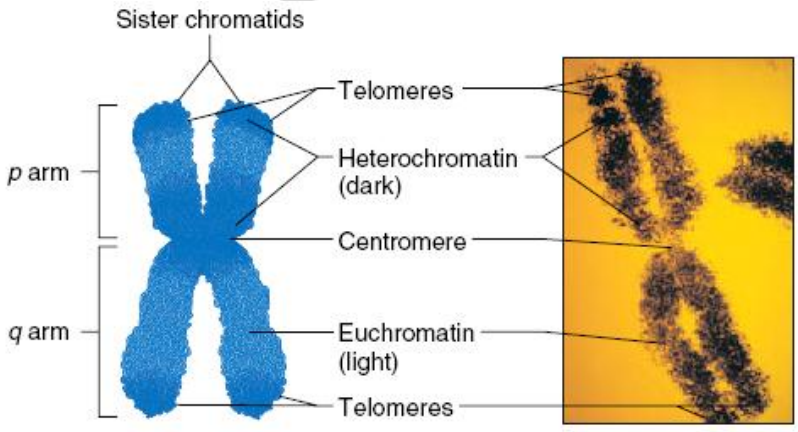


Fig. 10. The diagram of chromosome

Types of chromosomes according to the centromere position (fig. 11):

1. *Metacentric* — the centromere is in the middle, arms are of approximately same length.

2. *Submetacentric* — the centromere is biased from the center, the arms are of different length.

3. *Acrocentric* — the centromere is far from the center, one arm is very short, and the other is very long.

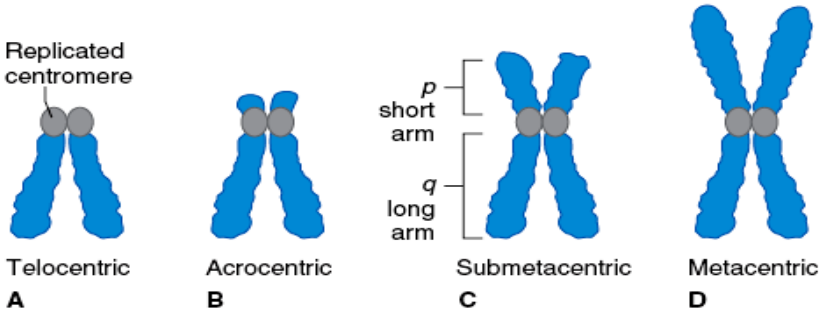


Fig. 11. Types of chromosomes

Theae are giant, *polytene chromosomes* in cells of insects (Drosophila) salivary glands.

There are four rules for chromosomes of all organisms:

1. *The rule of a constant number of chromosomes*. Organisms have a constant number of chromosomes typical for the species. For example, in the human — 46, in the dog — 78, in Drosophila — 8.

2. *Parity of chromosomes*. Normally, every chromosome in a diploid set has a pair — a chromosome with identical shape and size.

3. *Individuality of chromosomes*. Chromosomes of different pairs differ in shape, structure and size.

4. *Continuity of chromosomes*. When genetic material is doubled, a chromosome originates from a chromosome.

Function of chromosomes is storing, reproduction and transmission of genetic information, when cells and organisms multiply.

3. Cell and mitotic cycles. There are a cell and mitotic cycles in life of cells (fig. 12).

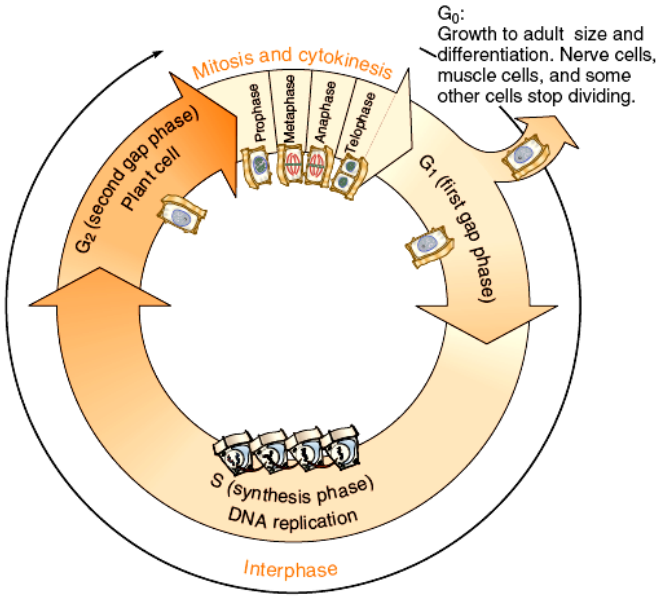


Fig. 12. The diagram types of cellular cycle

Cell cycle or life cycle of the cell is a period from the appearance of the cell until its death or to the end of next cell division. *The period of life cycle of somatic cells*: growth and differentiation, performing specific functions, preparation for division (multiplication), division. The majority of cells can undergo mitotic cycle. It includes a period of its preparation for division (interphase) and the division itself (mitosis).

4. Interphase. Characteristics of periods. Causes of mitosis.

The interphase includes three periods: G_1 — *pre-synthetic period (post-mitotic)*, S — *synthetic period* and G_2 — *post-synthetic period (pre-mitotic)*. The content of genetic material in the cell changes during the interphase. Keys used to denote it are: «*n*» is a set of chromosomes, «*chr*» is the number of chromatids in each chromosome, «*c*» is the number of DNA copies.

Pre-synthetic period. During this period, the cell grows, performs its functions, accumulates RNA, proteins, DNA nucleotides, ATP. The number of ribosomes increases. The period may last 12 hours or sometimes take several months. The content of genetic material is *2n1chr2c*.

During the *synthetic period*, replication of DNA molecules occurs: each chromatid adds one more identical to itself. The content of genetic material becomes *2n2chr4c*. Centrioles duplicate. RNA, ATP and proteins-histones are synthesized. The cell continues performing its functions. The duration of the period is up to 8 hours.

During the *post-synthetic period* energy of ATP accumulates; RNA, nuclear proteins and proteins-tubulines necessary for chromatin division spindle are actively synthesized. The content of genetic material does not change: *2n2chr4c*. By the end of the period all synthetic processes become slower and the cytoplasm viscosity changes.

Causes of mitosis:

– changing of the nuclear-cytoplasmatic ratio from $^1/_6$–$^1/_7$ to $^1/_{69}$–$^1/_{89}$;

– presence of «mitogenetic rays» which stimulate division of adjacent cells;

– action of «wound hormones» released from impaired cells to stimulate division of unimpaired cells.

5. Characteristic and significance of mitosis.

The basic way of cell division is mitosis. Mitosis has four stages: a *prophase*, *metaphase*, *anaphase* and *telophase* (fig. 13).

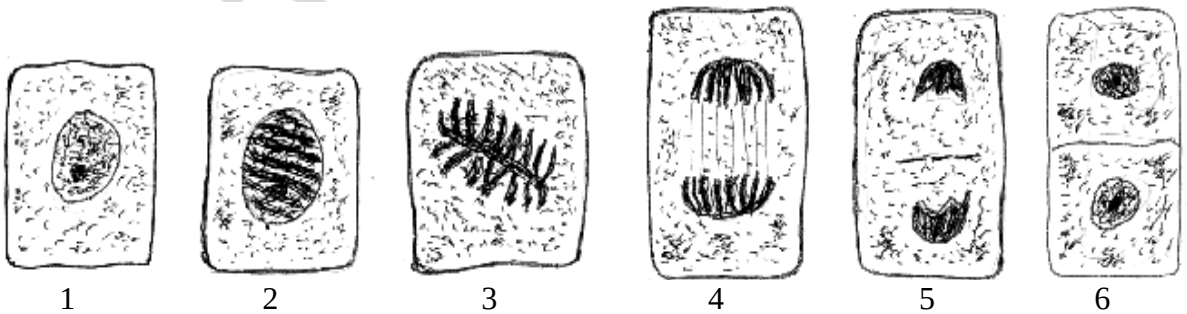


Fig. 13. Mitosis:
1 — interphase*; 2* — prophase*; 3* — metaphase*; 4* — anaphase*; 5* — telophase, *6* — daughter cells

The *prophase* starts with condensation of chromatin. Long chromatin fibers are shortened and thickened to form chromosomes. Centrioles move to cell poles and filaments of the division spindle are formed. Nucleoli and nuclear membrane dissolve, the nucleus volume enlarges. The content of genetic material is 2n2chr4c.

During the *metaphase*, chromosomes are located at the cell equator forming a *metaphase plate*. Filaments of the division spindle are attached to the centromeres of chromosomes. It is clearly visible that each chromosome consists of two chromatids. The content of genetic material does not change — 2n2chr4c.

During the *anaphase*, filaments of the division spindle constrict. Chromosomes divide into two chromatids in the region of centromeres and chromatids diverge to cell poles. Now they are called *daughter chromosomes*. The content of genetic information at each pole of the cell is 2n1chr2c.

During the *telophase*, the formation of daughter nuclei occurs. Nuclear membranes are formed, chromosomes decondense and lose their clear outlines, and nucleoli are restored. The final stage of mitosis is cytokinesis (division of the cytoplasm). Two cells are formed with the content of genetic material 2n1chr2c.

The significance of mitosis:

– sustaining the constancy of the chromosome number, providing genetic succession in cellular populations;

– even distribution of chromosomes and genetic information between daughter cells.

6. Characteristic and significance of meiosis.

Meiosis is a variety of mitosis. Meiosis is division of somatic cells of gonads that leads to the formation of gametes. Meiosis consists of two divisions — meiosis I and meiosis II. Each division has four phases: prophase I and prophase II, metaphase I and metaphase II, anaphase I and anaphase II, telophase I and telophase II (fig. 14).

The prophase of meiosis I is most complicated. It has 5 stages:

1. *Leptotene*: chromatin condenses forming thin chromatin filaments that start moving to each other with centromere parts; genetic material is 2n2chr4c.

2. *Zygotene*: *chromosomal synapsis* starts. Homologous chromosomes bounds together along the whole length; genetic information does not change — 2n2chr4c.

3. *Pachytene*: homologous chromosomes are tightly joined along the whole length; the formed figures are *bivalents* of chromosomes or *tetrads* of chromatids; genetic material can be recorded as ln_{biv}4chr4c; by the end of the stage antagonizing forces start acting in the area of centromeres and *crossing-over* occurs, exchange of homologous chromosomes parts.

4. *Diplotene*: antagonizing forces continue their action, but chromosomes stay bound in the area of chiasm (crossings); the content of genetic material is same - ln_{biv}4chr4c;

5. *Diakinesis*: chromosomal condensation finishes, the nuclear membrane and nucleolus disappear; chromosomal bivalents linked with their ends come into the cytoplasm and move towards the center of the cell; filaments of the division spindle attach to centromeres of chromosomes; $ln_{biv}4chr4c$.

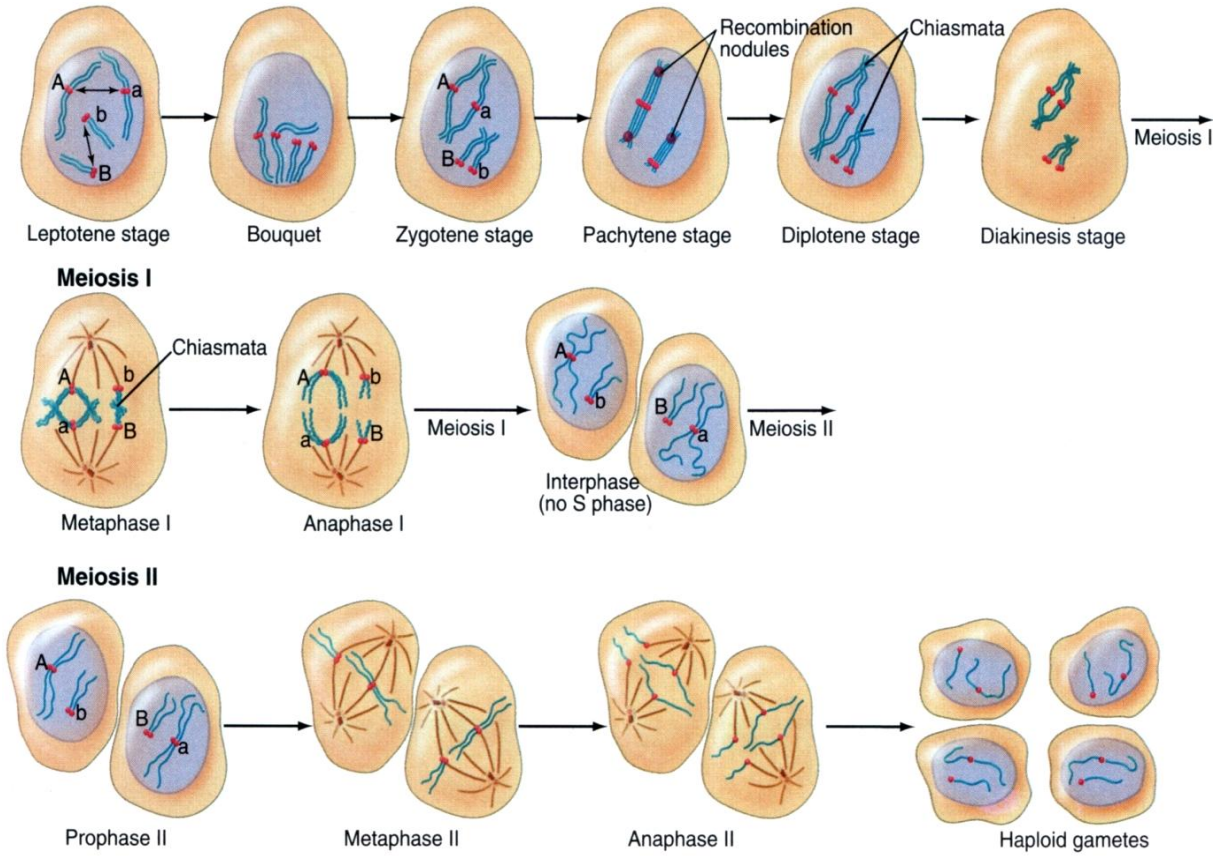


Fig. 14. Meiosis

In the **metaphase of meiosis I,** bivalents are located along the equator of the cell; chromosomes are clearly seen; genetic material — $ln_{biv}4chr4c$.

Anaphase I: bivalents are divided into homologous chromosomes. Filaments of the division spindle constrict, that is why chromosomes diverge to cell poles. Each chromosome is still composed of 2 chromatids. The content of genetic material at each cell pole is ln2chr2c. During this phase the reduction (decrease) of the chromosome number occurs: a diploid complement of chromosomes becomes a haploid one.

In the **telophase of meiosis I,** cytokinesis takes place, and, unlike mitosis in this phase, two-daughter *haploid* cells form — ln2chr2c. Decondensation of chromosomes does not occur.

Interkinesis follows the meiosis I. It is a short interval between two divisions. DNA replication does not occur. Meiosis II starts after interkinesis.

Meiosis II almost does not differ from mitosis. During *prophase II*, condensation of chromosomes (ln2chr2c) does not occur, and in *anaphase II* chromatids (but not chromosomes!) diverge to cell poles. Each daughter cell gets a complement of genetic information 1n1chr1c.

During meiosis one mother diploid cell forms 4 haploid cells (gametes).

The significance of meiosis: it is a mechanism of gamete formation; it sustains the constancy of the number of chromosomes; provides combinative variation.

Basic terms and concepts:

1. Bivalents — two homologous chromosomes, conjugated with each other during the prophase of meiosis I. Their number is equal to a haploid complement of chromosomes.

2. Karyolymph — nuclear sap.

3. Cell cycle — a period from the appearance of the cell to its death or to the end of next cellular division.

4. Synapsis of chromosomes — connection of homologous chromosomes in length.

5. Crossing-over — exchange of identical parts of chromatids of homologous chromosomes during pachitena of the prophase of meiosis I.

6. Meiosis — division of somatic cell of gonads, when gametes are formed.

7. Mitotic cycle — a period of the cell preparation for division (interphase) and division itself (mitosis).

8. Telomeres — terminal parts of chromosome arms.

9. Chiasms — cross of chromatids of homologous chromosomes in synapsis.

10. Chromatin — a complex consisting of DNA and histone proteins.

11. Nuclear-cytoplasmatic ratio — is a physiologically and morphologically regular ratio of the mass (volume) of the nucleus to the mass (volume) of the cytoplasm in every cell

Topic 4. ORGANIZATION OF HEREDITARY MATERIAL

1. Structure and functions of nucleic acids (DNA and RNA). Chargaff's rules.

In 1870 Friedrich Miescher described macromolecules in the nucleus and called them **nucleic acids** (from Latin *nucleus* — nucleus). DNA (deoxyribonucleic acid) and RNA (ribonucleic acid) refer to nucleic acids. The structure of a DNA molecule was decoded in 1953 by James Watson, Francis Crick and Maurice Wilkins.

The nucleic acids are biopolymeres. Their monomeres are *nucleotides*. A nucleotide consists of a nitrogenous base, 5-carbon sugar and residue of *phosphoric acid*. Nitrogenous bases are adenine, guanine, cytosine, thymine, uracyl. A, G are purine nitrogenous bases while T, C, U are pyrimidine bases. Five-carbon sugars are *deoxyribose* or *ribose*.

The **DNA** molecule consists of two strands which are coiled as spirals. Each strand is a polynucleotide. A DNA nucleotide consists of a nitrogenous base (adenine, guanine, cytosine or thymine), deoxyribose and a residue of phosphoric acid (fig. 15). The nucleotide sequence is linked by *phos-*

phodiester bonds between deoxyribose of one nucleotide and the residue of the phosphoric acid of the other nucleotide. Nitrogenous bases of one strand are bound to bases of other strand according to the principle of *complementarity*: A = T — 2 hydrogen bonds G ≡ C — 3 hydrogen bonds.

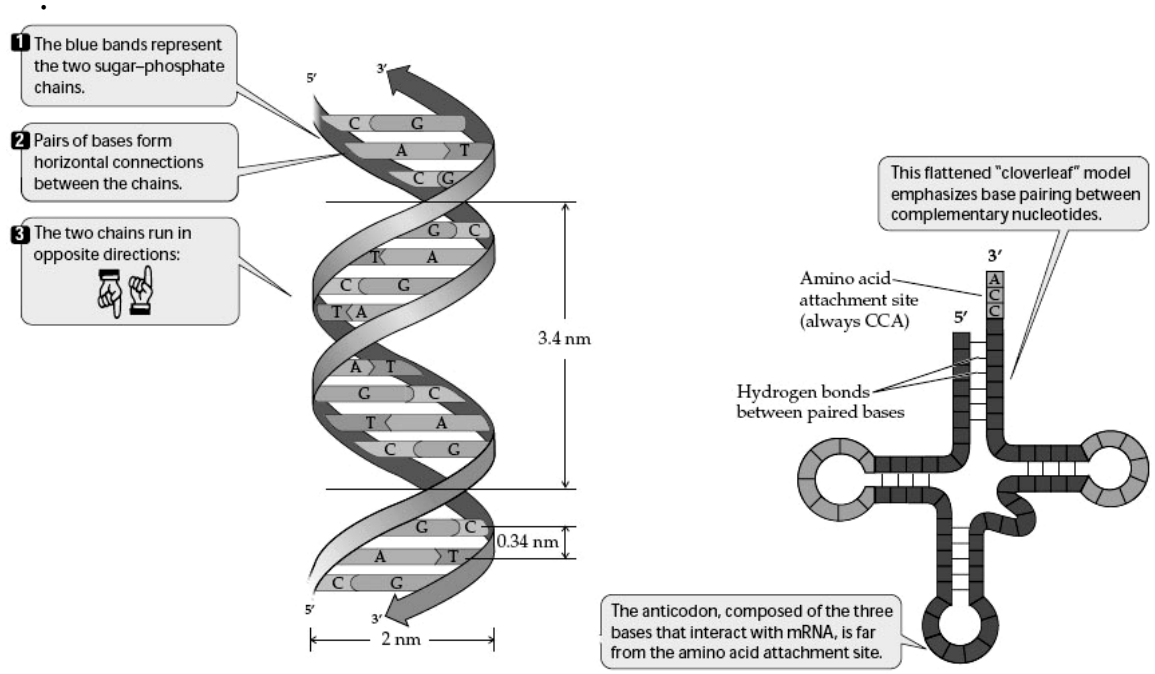


Fig. 15. Structure of a DNA molecule and tRNA

The complementarity property of nitrogenous bases is expressed in Chargaff's rules:

– the number of purine bases in a DNA molecule is equal to the number of pyrimidine bases: A + G = C + T;

– the amount of adenine in a DNA molecule is equal to the amount of thymine (A = T), the amount of guanine is equal to the amount of cytosine (G = C).

DNA molecules are in the nucleus, mitochondria and plastids. DNA properties are *replication* (self-reproduction) and *ability to repair* (restoration of the structure after impairment of the molecule). DNA functions are storing and transmitting genetic information during multiplication of cells and organisms.

The **RNA** molecule is a polynucleotide consisting of one strand. In comparison with a DNA, it includes uracil instead of thymine and sugar ribose instead of deoxyribose. In some viruses, RNA has two strands.

The cell has 3 types of RNA in the nucleus, cytoplasm, mitochondria and plastids. 3–4 % of the whole RNA are *messenger RNA* (mRNA). It «writes out» the genetic information from DNA and carries it into ribosomes where protein molecules are assembled. The *ribosomal RNA* (rRNA) composes 80–85 % of the whole cell RNA. It is included into ribosomes and provides spacial interposition of mRNA and rRNA. The *transport RNA* (tRNA) comprises 10–20 % of the whole RNA of the cell. It transports (transfers) aminoacids from the cytoplasm to ribosomes.

2. Properties of genes.

The *gene* is a part of a DNA molecule coding for a definite polypeptide. Genes are characterized by the following properties:

1. *Specificity* — a unique sequence of nucleotides for every structural gene.

2. *Integrity* — being considered as a functional unit, the gene is indivisible (during protein synthesis).

3. *Discretion* — the gene includes subunits: a muton — a subunit responsible for mutations; a recon responsible for recombination. Their minimal length is equal to a pair of nucleotides.

4. *Stability* — genes are relatively stable. The frequency of spontaneous mutations of a gene is approximately 10^{-5} per a generation.

5. *Lability* — genes are able to modify, mutate.

6. *Pleiotropy* — multiple gene action (one gene is responsible for several characters).

7. *Expressivity* — the degree of phenotypic manifestation of the gene. It depends on environmental factors and effect of other genes.

8. *Penetrance* — frequency of gene manifestation: a ratio (per cents) of the number of individuals having the character to the number of individuals having the gene.

3. DNA replication.

Genes perform two primary functions in the cell. A *heterosynthetic* function is programming of protein biosynthesis in the cell. An *autosynthetic* function is replication of DNA (self-doubling of DNA).

Replication of DNA occurs during the synthetic period of the interphase. Synthesis of the DNA molecule is semi-conservative: one strand is mother strand (old), a new synthesized strand is daughter strand. The new strand is assembled on the mother strand according to complementarity principle. The main enzyme of synthesis is a DNA-polymeraze (fig. 16).

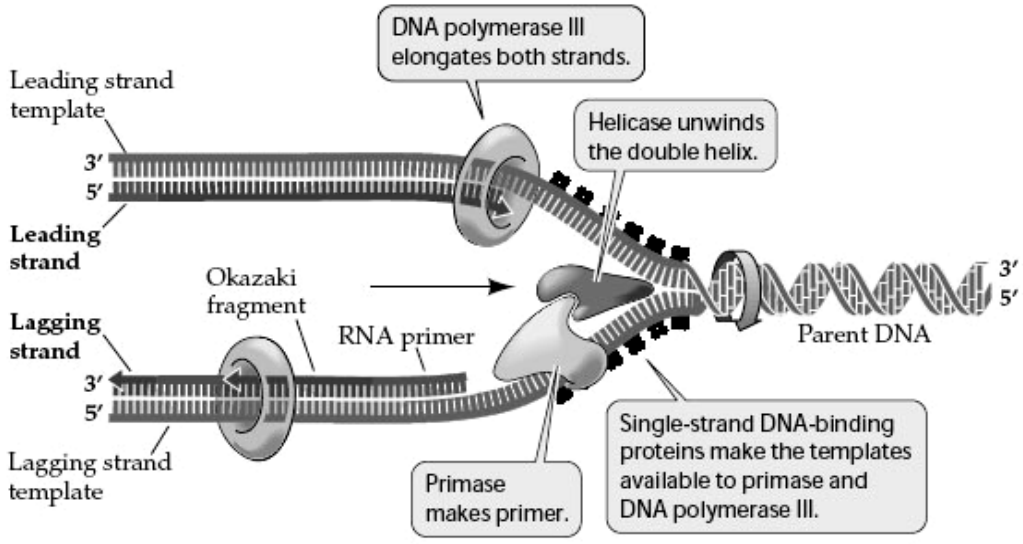


Fig. 16. Replication of a DNA molecule

The spiral of a DNA molecule is uncoiled under the action of the enzyme DNA-helicase. Each strand performs a matrix role. Replication starts in definite points of the DNA molecule. The site of DNA from the start of one replication to the start of the other one is a *replicon*. Chromosomes of eukaryotes have many replicons, while bacterial nucleoid has only one replicon. Doubling in all replicons goes simultaneously. A replication site is called a *replication fork*.

DNA-polymerase can move along the mother strand only from 3' end to 5' end. That is why assembling of daughter strands is *anti-parallel* (goes in opposite directions). Several DNA polymerases work simultaneously in every replication fork. One DNA strand (the leading one) is continuously duplicated. The second strand (the lagging one) is duplicated by short fragments of 150–200 nucleotides under the action of DNA-polymerase, which moves in direction opposite to the first enzyme. These parts are called *Okasaki fragments*. All synthesized fragments of a polynucleotide sequence are «sewn» together by an enzyme *ligase*. The whole genome of the cell is replicated once during a mitotic cycle.

4. The genetic code and its properties. Protein biosynthesis.

Recording of genetic information as a nucleotide sequence in DNA and mRNA is a *genetic code*. A nucleotide triplet coding a specific amino acid is a *codon*. The codon is an elementary functional unit of the gene.

Properties of the genetic code:

– *tripletness* — one amino-acid is coded by a triplet (three nucleotides); such triplet is called a *codon*;

– *universality* — one codon defines same amino acid in all organisms;

– *no overlapping* — one nucleotide belongs to only in one triplet;

– *redundancy (degeneration)* — one amino acid can be coded by several triplets (there are 64 triplets for 20 amino acids);

– *continuity* — there are no disjunctive symbols between codons;

– *unidirectionality (absence of feedback)* — enzymes can move along the DNA only from its 3' end to its 5' end;

– *presence of codons-terminators* (they determine the end of protein biosynthesis).

The correspondence of the nucleotide order in a DNA molecule to the order of amino acids in the polypeptide molecule is **co-linearity**.

Protein biosynthesis in the cell. Protein biosynthesis is an enzymatic process, where nucleic acids play the main role. An mRNA is synthesized in the nucleus on one of DNA strands (coding strand). RNA-polymerase transcribes the order of nucleotides from a DNA molecule (according to the complementarity rule). This process is called *transcription*. The mRNA enters the cytoplasm through the pores of the nucleus and goes to ribosomes.

Recognition (recognizing of corresponding amino acid by tRNA) occurs in the cytoplasm. The transport RNA has a specific structure: there is a nucleotide triplet called an *anti-codon* at the one end of the molecule. It corresponds to a def-

inite amino acid. There is a site for adding amino acid at the other end of the tRNA. A definite amino acid joins corresponding tRNA with help of the enzyme *amino-acyl-tRNA-synthetase* and ATP. The tRNA with corresponding amino acid forms a complex *amino-acyl-tRNA* (fig. 17).

The process of *translation* occurs in ribosomes. Nucleotide order of mRNA determines the amino acid order in the polypeptide molecule. In the cytoplasm, mRNA associate with a small ribosome subunit and then with the large one. The complex of ribosomes, united by one mRNA, is called a polyribosome. Starting translation is called *initiation* (provided by start-codon AUG), finishing translation is called *termination* (provided by stop-codons UAA, UGA, UAG). The formation of peptide bonds between amino acids is *elongation*. There are two mRNA codons in the ribosome simultaneously. The first one is in the *amino-acyl site*, the second one is in the *peptidyl site*.

If a tRNA anti-codon and an mRNA codon, which is in the amino-acyl site, are complementary, then amino-acyl-tRNA forms a temporary bond with an mRNA codon. A peptide bond sets between the first and second amino acids. The ribosome moves by one triplet, and the amino-acyl-tRNA passes into the peptidyl site. The second tRNA with the amino acid comes to the amino-acyl site. The ribosome moves by one triplet, the released tRNA leaves the ribosome and the second tRNA passes into the peptide center. The process repeats many times. Termination of polypeptide synthesis is determined by stop-codons.

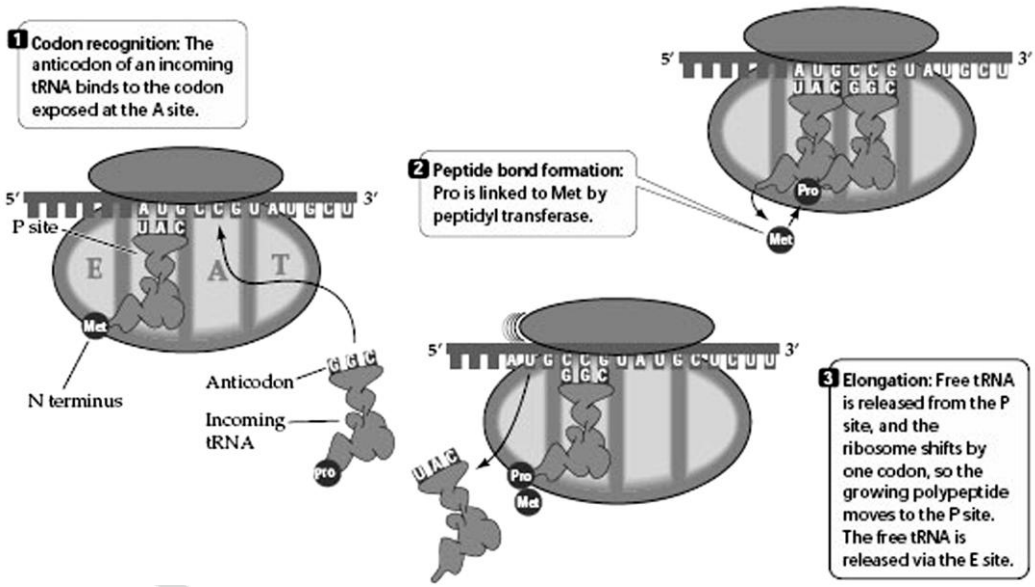


Fig. 17. Elongation

Basic terms and concepts:

1. **Anti-codon** — ia tRNA nucleotide triplet, which is complementary to an mRNA triplet in the process of translation.
2. **Gene** — a fragment of a DNA molecule coding a definite polypeptide.
3. **Initiation** — an initial stage of translation.
4. **Codon** — a nucleotide triplet, the least functional unit of the gene.

5. Complementarity of nitrogenous bases — correspondence of nitrogenous bases to each other in a DNA molecule.

6. Lability of the gene — ability of the gene to mutate.

7. Nucleotide — a monomere of nucleic acids consisting of a nitrogenous base, sugar (pentose) and a residue of the phosphoric acid.

8. Stability of the gene — ability of the gene to preserve its structure.

9. Termination — finishing the polypeptide synthesis.

10. Elongation — the process of translation from formation of the first peptide bond to joining the last amino acid.

Topic 5. INHERITANCE REGULARITIES. INTERACTION OF GENES

1. Genetics as a science. Basic concepts of Genetics.

Genetics is a science about laws of heredity and variation. The term «genetics» was introduced into Biology by William Bateson in 1906.

Genotype is a sum of all genes of the organism.

Phenotype is a sum of all characters and properties of the organism, which are determined by the *genotype* and *environmental factors*.

Alternative characters are incompatible characters.

Allelic genes are genes occupying same loci of homologous chromosomes and determine development of one alternative character.

Non-allelic genes are genes occupying different loci of homologous or non-homologous chromosomes and determine the development of different characters.

Homozygous organism is an organism which contains identical allelic genes, form one type of gametes and characters segregation does not occur in crossing it with individual that have identical genotype.

Heterozygous organism is an organism containing different allelic genes; it forms two types of gametes; in case of its crossing with an individual that have identical genotype segregation occurs.

Dominant characters are characters that manifest both in a homozygous or heterozygous state.

Recessive characters are characters that manifest only in homozygous state.

The basic hereditary laws were described by G. Mendel (1822–1884) in his work «Experiments on vegetative hybrids» (1865).

G. Mendel used a **hybridological method**.

Hybridization is crossing of individuals differing on genotype and phenotype, followed by further analysis of individuals obtained in filial generations (hybrids).

2. Peculiarities of the hybridological method:

1. Crossing of pure lines (homozygotes).
2. Inheritance of particular characters in hybrids of several generations is analyzed.
3. Precise quantitative account of hybrids with different characters..

3. Inheritance regularities in monohybrid cross.

Monohybrid cross is a cross, when one pair of alternative alleles is analyzed.

1st law - the law of hybrid uniformity: if homozygous individuals differing in one pair of alternative characters are crossed, uniformity of hybrids on phenotype and genotype is observed.

P AA x aa P (parents)

G (A) (a) G (gametes)

F_1 Aa F (hybrids)

G. Mendel crossed a homozygous plant of pea with yellow seeds and a homozygous plant of pea with green seeds. As a result of such cross Mendel obtained plants only with yellow seeds. These plants were heterozygous on genotype.

2nd law - the law of segregation: if heterozygous individuals are crossed and analyzed by one pair of alternative characters, then segregations of characters ratios 3:1 for phenotype and 1:2:1 for genotype are observed. **Phenotypic ratio**: 3 groups of individuals having the dominant character and 1 group with the recessive character. **Genotypic ratio**: 1 group of individuals includes dominant homozygotes (AA), 2 groups are homozygotes (Aa), 1 group is composed of recessive homozygotes (aa).

P (F_1) Aa x Aa

G (A)(a) (A)(a) P (F_1) — hybrids of the 1st generation are parental

F_2 AA, Aa, Aa, aa

4. Hypothesis of purity of gametes and its cytological foundation.

W. Bateson proposed a **hypothesis of purity of gametes** in 1902 to explain the results of crossing performed by G. Mendel: genes in hybrids are not hybridized and are in a pure allelic state. The mechanism of meiosis is a cytological basis of Mendel's laws. Homologous chromosomes separate during meiosis that is why only one gene from an allelic pair gets into a gamete.

5. Analyzing cross. The concept of a phenotypic radical.

Analysing cross is crossing of an individual having a dominant character, with a recessive homozygote for determining its genotype. If uniformity of hybrids is observed as the result of analyzing cross then the initial organism is homozygous (AA); if segregation of characters occurs then the initial organism is heterozygous (Aa).

Phenotypic radical is a short record of the genotype made on the basis of the phenotype. Record A-B- means that the phenotype does not depend on the second allelic gene that can be written instead of dash (a dominant or a recessive one): a dominant character will be always revealed.

6. Inheritance regularities in polyhybrid cross. The law of independent assortment of characters.

Dihybrid cross is a cross, when two pairs of alternative characters are analyzed. If more than two pairs of genes are analyzed, crossing is called **polyhybrid.**

3rd Mendel's law — a law of independent assortment: if homozygous individuals are crossed and analyzed by several pairs of alternative characters, independent assortment of genes and characters is observed.

In dihybrid crossing when plants differed in two pairs of alternative characters, G. Mendel got the following results:

Gene	Character
A	Yellow color of seeds
a	Green color of seeds
B	Smooth surface of seeds
b	Wrinkled surface of seeds

P. AABB x aabb

G. (AB) (ab)

F_1. AaBb - 100 %

P. AaBb x AaBb

G. (aB) (ab) (aB) (ab) (AB) (Ab) (AB) (Ab)

G	*AB*	*Ab*	*aB*	*ab*
AB	*AABB*	*AABb*	*AaBB*	*AaBb*
Ab	*AABb*	*AAbb*	*AaBb*	*Aabb*
aB	*AaBB*	*AaBb*	*aaBB*	*aaBb*
ab	*AaBb*	*Aabb*	*aaBb*	*aabb*

The Punnett square is used for recording results of dihybrid cross:

All in all we get 16 combinations: 9 combinations A-B-, 3 combinations A-bb, 3 combinations aaB-, 1 combination aabb. If we estimate the ratio of each character apart from the second one in gene pairs 12 A- and 4 aa- or 12 B- and 4bb-, we'll get the ratio 3:1 in both cases. On the bases of obtained results we can make a conclusion that in crossing of heterozygous individuals which are analyzed by several pairs of alternative characters, segregation ratio on the phenotype in filial generation $(3:1)^n$ is observed (n is the number of characters in a heterozygous state).

The significance of Mendel's laws:

1. The laws are universal; they are applicable for all living organisms.

2. G. Mendel introduced a mathematical method into Biology. His laws are statistical.

7. Conditions limiting the manifestation of Mendel's laws. Pleiotropy. Semi-lethal and lethal genes.

***Conditions limiting the manifestation of Mendel's laws*:**

1. Different probability of formation of various types of gametes and zygotes.

2. Different survival of individuals with different phenotypes (the presence of lethal and semi-lethal genes). *Lethal genes* cause organism's death at the moment of birth or before. *Semi-lethal genes* reduce life span of the organism.

3. Gene interactions of (except complete dominance).

4. Genetic linkage.

5. Cytoplasmic heredity.

P Aa x Aa

G (A) (a) (A) (a)

F_1 ~~AA~~ Aa Aa aa

An example of the *lethal gene's action*. A dominant gene **A** determines grey wool color in sheep but in homozygous state it is lethal (cause underdevelopment of the stomach in lambs). A recessive gene **a** determines black

wool color. Instead of an expected ratio 3:1 we get the ratio 2:1 on the phenotype and genotype.

Pleiotropy of the gene — one gene is responsible for development of several characters. An example is the syndrome of «blue sclera»: a gene causes a blue color of the sclera, breakable bones and congenital deafness.

8. Intra-allelic gene interactions.

Intra-allelic interactions of genes are interactions between a pair of allelic genes:

1. *Complete dominance*: color of peas, brown and blue eyes or straight and curly hair in humans and other characters. They are called mendelizing — segregation obeys Mendel's laws.

2. *Incomplete dominance* or intermediate inheritance.

Gene A — red flowers.

Gene a — white flowers.

P AA x aa → Aa

Red white pink

3. *Super-dominance*. Action of the gene that is in heterozygous state is stronger than that of a homozygous one. For example, Drosophila flies have a recessive lethal gene. Homozygotes on this gene die but vitality and fertility of heterozygotes is higher than that of dominant homozygous individuals.

4. *Co-dominance*. An example is inheritance of blood groups on the AB0 system. There are 2 equivalent allelic genes (I^A, I^B). Being together in the genotype, they both show their action and cause appearance of a new character - (IV (AB) blood group).

9. Inheritance of blood groups.

Inheritance of blood groups in the human on the AB0 system occurs due to the gene I. Alleles of gene I are I^0, I^A, and I^B. Presence of the gene I^0 does not cause synthesis of anti-genes in erythrocytes (group I).

Genes I^A and I^B are dominant to gene I^0. Being in the genotype in homozygous (I^A I^A; I^B I^B) or heterozygous (I^AI^0; I^B I^0) states they cause synthesis of anti-genes, either A or B in erythrocytes: A — blood group II, B — group III. If they both are in the genotype, then 2 types of anti-genes are synthesized in erythrocytes: A and B — blood group IV(AB).

Multiple alleles are alleles that present in the population by more than 2 states (alleles of the gene I — I^0, I^A, I^B).

Inheritance of the Rh-factor. Gene D provides presence of protein rhesus-factor in erythrocytes.

The blood of such people is Rh-positive (Rh^+). When the Rhesus-factor (d) is absent, the blood is Rhesus-negative (Rh^-).

Inheritance of blood groups on system MN. This system exists due to alleles L^N and L^M. Gene L^M causes the presence of anti-gene M in human erythrocytes (blood group M), and gene L^N — of anti-gene N (blood group N).

Presence of both alleles in the genotype causes the presence of both anti-genes M and N in erythrocytes (blood group MN).

10. Inter-allelic gene interactions.

Inter-allelic interaction is the interaction of *non-allelic* genes.

1. **Complementation** is a gene interaction, when a gene of one allele complements the action of a gene of the other allele. Color of flowers in sweat pea plants is determined by a combination of dominant genes of two alleles A and B. The absence of one or two dominant genes in the genotype determines the development of white flowers.

Red flowers: A – B –; white flowers: A-bb, aaB-, aabb

P AaBb x AaBb

Red flowers Red flowers

G (AB) (Ab) (AB) (Ab)

(aB) (ab) (aB) (ab)

F_1 9A-B-; 3A-bb; 3aaB-; 1aabb

Red White White White

(According to Mendel's law, phenotypic segregation ratio is 9:3:3:1 but obtained ratio is 9:7).

2. **Epistasis** is a gene interaction, when a dominant (recessive) gene of one allele suppresses the gene of the other allele. The suppressing gene is called *epistatic* (inhibitor or suppressor); the suppressed gene is called *hypostatic*. An example of epistasis is feathering color in hens. Colored feather is determined by gene **C** whiles the dominant gene **I** suppresses its action.

P CcIi x CcIi

White hens White hens

F_1 9C-I- 3C-ii: 3ccI- 1ccii

White Colored White White

Phenotypic segregation ratio according to the Mendel's law is 9:3:3:1 while obtained ratio is13 white : 3 colored.

Genotype of hens with colored feathering is C – ii.

Genotypes of hens with white feathering are C-I-, cc-I-, ccii.

3. **Polymeria** is a gene interaction when several non-allelic genes increase the manifestation degree of a character. Some human quantitative characters are inherited in this manner: body mass, height, skin pigmentation, blood pressure. Polymeric genes are usually denoted by one letter but with different numeral indices.

For example, skin pigmentation in the human: negroids — $P_1P_1P_2P_2P_3P_3$; europeoids — $p_1p_1p_2p_2p_3p_3$; mulattos — $P_1p_1P_2p_2P_3p_3$. The more dominant genes are in the phenotype, the stronger is the character expressed.

Basic terms and concepts:

1. Allelic genes — genes occupying identical loci of homologous chromosomes, they determine development of different states of one character.

2. Genome — sum of all genes in a haploid complement of chromosomes.

3. Genotype — sum of all genes in the organism.

4. Homozygous organism — organism that has identical variants of one allele in somatic cells (AA, aa).

5. Complementation — inter-allelic gene interaction, when a gene of one allele complements the action of a gene of the other allele.

6. Multiple allelism — phenomenon when a gene has more than two allelic states in the population

7. Polygenic inheritance —inheritance of characters that are determined by polymeric genes.

8. Super-dominance — interaction of genes when a dominant gene in a heterozygous state shows its action stronger than in a homozygous one.

9. Phenotypic radical — a short record of the genotype made on the basis of the phenotype.

10. Phenotype — sum of characters and properties of the organism.

Topic 6. GENETIC LINKAGE

1. Experiments of Thomas Morgan. Complete and partial genetic linkage.

In Experiments on Drosophila were performed in Morgan's laboratories in 1911–1912. That fly is convenient for genetic investigations because of:

– it has few chromosomes (4 pairs);

– early sex maturation, fast alternation of generations;

– a great number of offspring

- it is easy to make similar conditions for Drosophila flies.

Two pairs of alternative characters were analyzed on crossing Drosophila.

Gene B — grey body Gene V — normal wings

Gene b — black body gene v — vestigial wings

The 1st cross of flies was done according to Mendel's scheme:

P BBVV x bbvv

F_1 BbVv — grey with normal wings — 100 %

To clear out the genotype of hybrids an analyzing cross of a male of the 1st generation was performed. It is crossing of an individual that have dominant characters with a recessive homozygote.

According to 3rd Mendel's law, Morgan expected to get equal number of hybrids for each phenotype — per 25 %. But he got just two phenotypes (per 50 %) with characters of parents. Morgan proposed that genes of the body color and wings length was located in one chromosome and was inherited together, i. e. linked. **Genetic linkage** is a joint transmission of genes located in one chromosome pair.

A male Drosophila has a **complete genetic linkage.** One chromosome of a pair contains 2 dominant genes (**BV**), and the other — 2 recessive (**bv**). During the meiosis one chromosome (with genes **BV**) gets into one gamete, and the other (with genes **bv**) in the other gamete. Thus, there form not 4 but 2 types of gametes in a diheterozygous organism. Hybrids also have same characters as their parents.

In the 3rd experiment T. Morgan crossed a hybrid female Drosophila with a recessive male. He got 4 types of hybrids: 2 types (83 %) with parental characters and 2 types (17 %) with a new combination of characters. Per 8.5 % of individuals were formed in the process of crossing-over and they are called *crossover individuals*. The total number of crossover individuals is 17 %, that corresponds to the distance between genes of the body color and wing length — 17 centimorgans.

II P(F_1) bbvv x B-V-
F_2 bbvv B-V-
50 % 50 %

III P(F_1) B-V- x bbvv
F_2 B-V- bbV- B-vv bbvv
41.5 %; 8.5 %; 8.5 %; 41.5 %

In a female Drosophila, unlike a male, crossing-over breaks genetic linkage and stimulates recombination of genetic material.

Linkage is *complete* if crossover individuals are not formed (a male Drosophila). If they are formed (a female Drosophila), linkage is *partial (incomplete)*

2. Autosomal and gonosomal linkage groups.

Genes located in one chromosome (a pair of homologous chromosomes) are transmitted together and are a *linkage group*. The number of linkage groups is equal to the *haploid number of chromosomes*. Linkage can be *autosomal* (the linkage groups of autosomes) and *gonosomal* (linkage groups of sex chromosomes). There are 22 *autosomal* and 1 *gonosomal* linkage groups in the human.

3. Crossing-over, crossover and non-crossover gametes.

Linkage Genetic linkage is broken by a biological phenomenon — *crossing-over*, which occurs in the prophase of meiosis I. Crossing-over is formation of a cross and following exchange of identical chromatid regions of homologous chromosomes in a bivalent. It does not occur in a male Drosophila and a female silkworm. *Crossover gametes* are gametes containing chromatids that have undergone crossing-over. *Non-crossover gametes have* not changed chromatids. less The number of crossover individuals is usually less than the number of non-crossover ones because crossing-over occurs not always.

The linkage force between genes (frequency of crossing-over) depends on the distance between them: the more the distance, the less the linkage forces and the more frequently crossing-over.

4. Basic concepts of the chromosome theory of inheritance.

1. Genes are arranged in chromosomes in a linear order in definite loci. Allelic genes are in identical loci of homologous chromosomes.

2. All genes of one chromosome compose a linkage group and are inherited together. The number of linkage groups is equal to the number of pairs of homologous chromosomes.

3. Crossing-over (exchange of allelic genes) is possible between homologous chromosomes.

4. The percentage of crossing-over depends on the distance between genes in the chromosome. 1% of crossing-over is equal to 1 centimorgan — a unit of the distance between genes called to honor T. Morgan.

5. Chromosome maps of eukariots (genetic and cytological).

Knowing the distance between chromosomes, one can make their maps.

A genetic map is a line where a sequence of genes and distance between them are marked according to the results of analyzing crosses.

A cytological map is a precise picture or a photograph of a chromosome. The arrangement order of genes is determined during comparison of analyzing cross results and chromosomal reconstructions.

Basic terms and concepts:

1. Crossover gametes are gametes that contain chromatids that have undergone the crossing-over.

2. Non-crossover gametes are gametes that contain chromatids that have not undergone the crossing-over.

3. Genetic map of a chromosome is a straight line where the order of genes arrangement and distance between them are marked.

4. A cytological map of the chromosome is a photo or a picture of the chromosome where the order of genes arrangement is marked.

5. Recombinants are the organisms that were formed as result of the fusion of crossover gametes.

6. Genetic linkage is joint transmission of genes of one chromosome.

Topic 7. VARIATION

1. Variation and its types.

Variation is a property of living organisms to obtain characters distinguishing them from their parents during their ontogenesis (fig. 18).

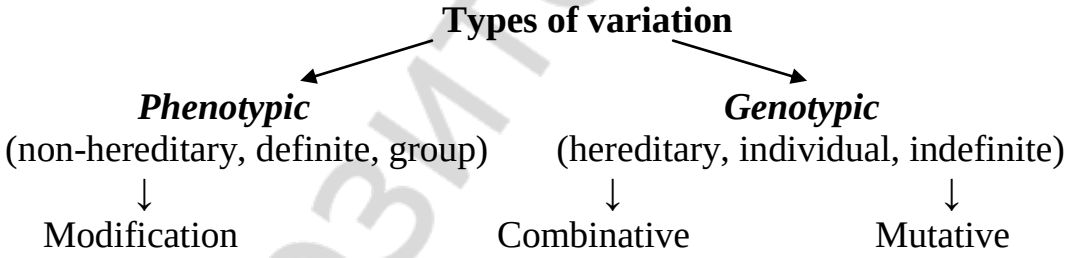


Fig.18. Types of variation

2. Phenotypic variation. Reaction norm.

A phenotypic or modification variation is modification of the phenotype without changing the structure of the genotype. That is why it is non-hereditary. Modifications occur under the action of environmental factors, changes can be predicted for a whole group of individuals. As a rule, modifications have an adaptive character (enhancing of skin pigmentation (suntan) under ultra-violet rays). *Reaction norm* determines the limits of modification variation. It is controlled by the genotype and is inherited. If the character has a narrow reaction norm, it changes insignificantly (fat content of milk). The character with a wide reaction norm changes in wide limits (body mass).

3. Genotypic variation and its types.

Genotypic variation is modification of the phenotype due to changing the genotype. It is inherited. It includes a *combinative* and *mutational* variation.

Combinative variation is associated with recombination of parental genes in filial generations without changing the structure of genetic material. For example, appearance of a blue-eyed child in heterozygous brown-eyed parents.

Mechanisms of combinative variation:

1. Free random combination of chromosomes and chromatids during meiosis.
2. Crossing-over in meiosis (recombination of genes).
3. Random combination of different types of gametes during fertilization.

Mutational variation (mutations) is a sudden uneven changing of genetic material under the influence of environmental factors. It is inherited.

Difference between mutations and modifications (fig. 19).

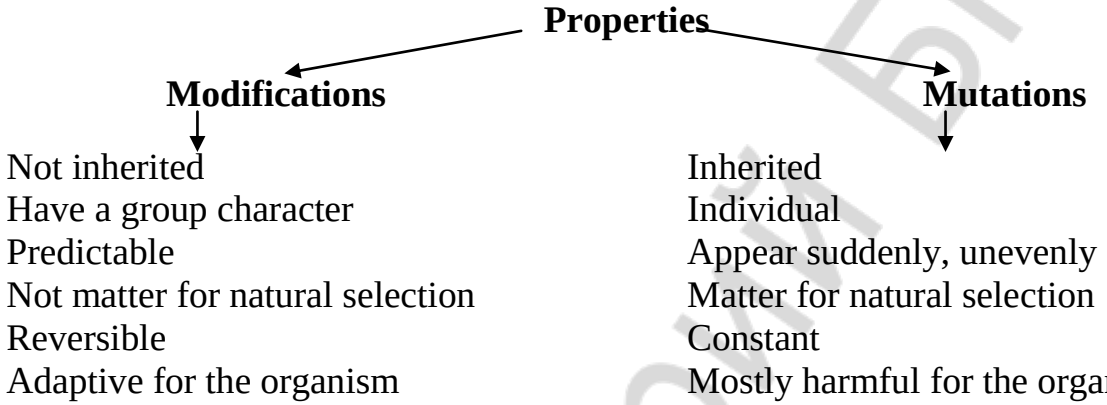


Fig. 19. Differentiation of mutations from modifications

4. Mutagenic factors.

Mutagenic factors are factors causing mutations. Mutagenic factors are divided into physical, chemical and biological

Physical mutagens are various kinds of radiation, temperature, humidity, etc.

They cause structural impairments of genes and chromosomes; formation of free radicals interacting with DNA; cuts of the division spindle threads; formation of dimeres of adjacent pyrimidine bases of one DNA strand (T-T), etc.

Chemical mutagens are some medicines, formalin, sulphur mustard (yperite), colchicine, food preservation agents, etc.

They cause desamination and alkylation of DNA molecule nucleotides; replacement of nitrogenous bases for their analogues (substances with similar structure); suppress synthesis of precursors of nucleic acids (nucleotides, ribose, deoxiribose).

*Biological mutagen*s are viruses, bacteria, metabolites, protozoans and helminthes.

They cause impairments of DNA synthesis, divergence of chromosomes and chromatids in the anaphase of meiosis and mitosis; waste products of parasites act as chemical mutagens, destroy chromosome telomeres and impair the process of crossing-over.

5. Classification of mutations.

The formation process of mutations is called *mutagenesis*.

According to etiological factors:

1. Spontaneous — appear under the influence of natural factors (mutagens) without participation of the human.

2. Induced — the result of directed effect of definite mutagenic factors.

According to mutated cells:

1. Gametic — occur in sex cells and are transmitted during sexual reproduction.

2. Somatic — occur in somatic cells, show in the individual itself and are inherited only in vegetative reproduction.

According to the outcome for the organism:

1. Negative: lethal (incompatible with life) and semi-lethal (reducing vitality).
2. Neutral, affecting the vitality inconsiderably.
3. Positive, increasing the vitalality.

According to modification of the phenotype:

1. Morphological (small eyes, 6 fingers on the hand).
2. Biochemical (albinism, hemophylia).

According to modification of the genotype:

1. Genome.
2. Chromosome.
3. Gene.

6. Genome, chromosome and gene mutations.

Genome mutations is changing of the number of chromosomes. **Haploidy** is a chromosome complement ln. It occurs in drones (males in bees). The vitality of such organisms is decreased, as all recessive genes show in them. *Polyploidy* is increase of a haploid chromosome complement (3n, 4n, 5n). Polyploidy is used in plant cultivation. It increases fruitfulness. For the human, haploidy and polyploidy are lethal mutations.

Heteroploidy is a change of the number of chromosomes indivisible by a haploid one ($2n \pm 1$, $2n \pm 2$ and so on). *Trisomy*: an X-chromosome is added to a pair of sex chromosomes of a female organism, the trisomy X syndrome develops (47, XXX); if it is added to sex chromosomes of a male organism, the Klinefelter syndrome develops (47, XXY). *Monosomy*: absence of one chromosome in the pair — 45, X0 — syndrome of Shereshevsky–Turner. *Nullisomy*: absence of a pair of homologous chromosomes (for humans, it is a lethal mutation).

Chromosome mutations (or chromosomal aberrations) are modifications of the of chromosomal structure (interchromosomal or intrachromosomal).

Rearrangements **inside one chromosome**: inversions, losses (deficiency and deletion), duplications. *Deletion* is loss of a middle region of the chromosome; *deficiency* — of a terminal end; *duplication* is doubling of a chromosomal region; *inversion* is changing of the genes arrangement order in the chromosome. In deletion of telomere regions of both chromosome's arms, fu-

sion of the remaining structure into a ring may occur and forming of *ring chromosomes* may be observed.

Interchromosomal mutations are translocations. Translocations can be: *reciprocal* — 2 chromosomes exchange with their parts; *non-reciprocal* — parts of one chromosome are relocated on the other one; *Robertsonian* — 2 acrocentric chromosomes are linked with their centromeres.

Losses and duplications are always revealed phenotypicly, because a complement of genes changes. Phenotypic inversions and translocations are not always revealed. In these cases conjugation of homologous chromosomes becomes difficult and the distribution of genetic material between daughter cells is impaired.

Gene mutations, or point mutations, transgenations. They are associated with changes of the structure of genes and cause the development of metabolic diseases.

Mutations of structural genes:

1. *Reading frame shift*— deletion or insertion of one or several pairs of nucleotides into a DNA molecule.

2. *Transition* — is a mutation that changes a purine nucleotide to another purine or a pyrimidine nucleotide to another pyrimidine (A ↔ G or C ↔ T). Such mutation change the codon where it occur.

3. *Transversion* — is a mutation that changes a purine nucleotide to a pyrimidine or a pyrimidine nucleotide to purine (A ↔ C; G ↔ T). It results in changing codons. Changing of structural genes results in *missense-mutations* (changing of the codons meaning). If senseless codons are formed (UAA, UAG, UGA), they cause *nonsense-mutations*. These codons do not determine amino acids but are terminators — they determine the end of information reading.

Mutations of functional genes:

1. The protein-repressor is modified and it does not suit the gene-operator. In this case structural genes are not switched off and work permanently.

2. The protein-repressor is tightly bound with the gene-operator and is not released by the inductor. Structural genes do not work permanently.

3. Impairment of alternation of repression and induction. If the inductor is absent but specific protein is synthesized, in the presence of the inductor it is not synthesized. Such impairments of transcripton actions are observed in mutations of a gene-regulator or a gene-operator.

In the majority of cases genic mutations are revealed phenotypicly.

7. Stability and repair of genetic material, anti-mutagens.

Anti-mutagenesis is the impact on the cell or organism, which blocks or reduces the probability of mutations occurrence. Stability of genetic material provides anti-mutagenic mechanisms.

1. **Natural barriers**: a diploid complement of chromosomes (parity of chromosomes), double DNA spiral, redundancy (degeneration) of the genetic code, iteration of some genes.

2. **DNA repair** is an intercellular process of an impaired DNA molecule restoration.

In 1962 C. Rupert described photoreactivation or light repair. He established that irradiation with ultra-violet rays depress vitality of phages, bacteria and protists. But if they are exposed to visible light, their vitallity restores. Ultraviolet rays formed *dimeres* in the DNA (chemical bonds between bases T-T of one strand). This reduced reading of information. Visible light activated enzymes, which destroyed dimeres.

The most common is an **excision repair** (A. Herren) Four groups of enzymes take part in it:

a) *endonuclease* «recognizes» an impaired part of DNA and cuts the strand;

b) *exonuclease* removes the impaired part;

c) *DNA polymerase* synthesizes a DNA fragment instead of a destroyed one according to a complementarity principle;

d) *ligase* links the ends of an inserted part with the main DNA strand.

The impairment of the repair process may result in the development of diseases such as *Xeroderma pigmentosum* and *Fankoni anemia*.

3. **Antimutagens**. These are substances of various origins, which's small concentrations are able to stabilize a mutation process; biologically active substances — histamine and serotonin, antioxidants, sulphanilamide drugs, fresh vegetable juices, α-tocopherol, which decreases the number of both gene and chromosome mutations).

8. Biological basis of cancerogenesis

Cancerogenesis is a process of formation and development of tumors.

1. *Mutation concept* — the basis of cancerogenesis is genomic or chromosomal mutations of somatic cells (G. de Freeze, 1901)**.**

2. *Virogenetic concept* — viruses are causative agents of malignant tumor. Mutagens and cancerogens stimulate the activity of viruses; their genome includes into the cell DNA and changes its properties (L. A. Zilber, 1946).

3. *Epigenomic concept* — the basis of transformation of a normal cell into a tumor are persistent impairments of the structure of functional genes (Yu. M. Olenov, 1967, and A. Yu. Bronovitsky, 1972).

4. *Oncogene concept*. Cell DNA contains definite parts — *protooncogens*. They can be received from parents or introduced into the cell by viruses. Protooncogens are activated by mutations or when a viral promoter gets into the cell. They pass into an active form — oncogens, the cell transforms into a tumor (R. Hubner, 1969.; G. I. Abelev, 1975).

Basic terms and concepts:

1. Deletions — intrachromosomal mutations associated with a loss of a middle part of the chromosome.

2. Duplications — intrachromosomal mutations associated with doubling of a part of the chromosome.

3. Inversion — intrachromosomal mutations, when the gene arrangement order impairment occurs.

4. Cancerogenesis — a process of tumor cells formation.

5. Ring chromosomes — chromosomes, which are formed during deletion of telomere parts and fusion of the remaining structure into a ring.

6. Reaction range — limits of modification variation.

7. Reading frame shift — a mutation of structural genes, when an insertion or deletion of nucleotides occurs.

8. Transitions — a mutations of structural genes, when a replacement of bases occurs: A for G or T for C.

9. Transgenations — genome mutations.

10. Translocations — exchange of non-homologous chromosomes parts.

Topic 8. BIOLOGY AND GENETICS OF SEX

1. Sex as a biological character. Sexual characters.

Sex is a complex of morphological, physiological, biochemical and behavioral characters of the organism that provide the process of reproducing their own selves and transmission of genetic information from generation to generation.

Primary sexual characters — external and internal sex organs. They take a direct part in the process of reproduction, are germinated in the embryogenesis and are formed by the moment of birth.

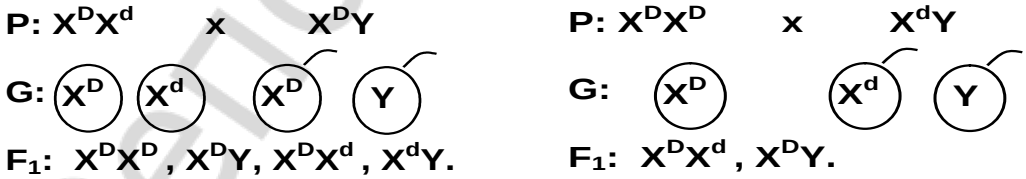
Secondary sexual characters appear in the period of puberty. They include peculiarities of the bony-muscular system, distribution of the adipose tissue and hairy integument, voice timbre, peculiarities of the nervous system and behavior and other characters.

2. Sex-controlled and sex-limited characters

Genes determining *sex-limited characters* present in autosomes of individuals of both sexes but manifest only in individuals of one sex (a gene of lactation manifests in females of the cattle; a gout gene manifests only in men).

Genes determining *sex-controlled characters* are also in autosomes of individuals of both sexes, but the degree and frequency of their manifestation is different (a gene of baldness is differently manifests in men and women).

3. X-linked and holandric characters.



Characters *linked with sex chromosomes (sex-linked)* are divided into characters linked with an X-chromosome and holandric. Genes located in the non-homologous region of the X-chromosome determine *X-linked* characters *(sex-linked)*. They are about 200 (hemophilia, daltonism). They are inherited from father only to daughter and from mother both to son and daughter.

Genes located in the non-homologous region of the Y-chromosome determine holandric characters; 6 of them are described (ichthyosis, membranes between toes) they are inherited from males and are revealed only in men.

4. Peculiarities of sex determination in humans and its impairments.

In the human, the *primordia* of internal and external sex organs form till the 4^{th} week of embryogenesis. On the initial stage, it is provided by only one X-chromosome. The primary gametes in humans can be revealed on the 3^{rd} week of the embryonic development in the ectoderm of the yolk sac.

Differentiation of primordia into sex glands and sex organs in the embryo and fetus occurs from the 4^{th} to 12^{th} weeks of intrauterine development. At this stage, it completely depends on the second sex chromosome. If it is an X-chromosome, primary sex cells develop into ovogonia and the whole sex system develops according to a female type. The development of primary sex primordia according to a male type is determined by the presence of the Y-chromosome in the complement. Primary sex cells are differentiated in spermatogonia, forming testes and external sex organs.

Physical sex determinants: genetic sex, gonadal sex, gametic sex, hormone sex and morphological sex. *Physical (morphophysiological) determinants of sex* are common for humans and the majority of animals.

An Intermediate determinant: civil sex.

Social-psychological determinants: sex of brining up, sex of self-conscious, sex role, choice of a sexual partner. *Social-psychological determinants* have a great significance in the formation of sex consciousness and ideas about sex role in the human. A choice of a sexual partner depends on them. In the majority of cases it is an opposite sex (*heterosexualism*), sometimes — *homosexualism* (identical sex).

Transsexualism is a persistent discrepancy of sexual self-conscious and its true genetic and gonad sex and a wish to change one's sex.

Transvestism is sexual perversion when the excitement and satisfaction are reached during putting on clothes of the opposite sex. In humans a *Morris's syndrome may occur. It is manifestation of* a female phenotype in genotype XY (*testicular feminization*). Male sex hormones are excreted after germination of testes, but in embryos protein-receptor making cells sensitive to these hormones is not formed. The development according to a male type stops and a female phenotype develops.

5. M. Lion's hypothesis.

In 1962 Mary Lion suggested a hypothesis about inactivation of one X-chromosome in mammal females (diagram 10). Every cell of a female embryo contains two X-chromosomes: one maternal (X_m) and the other — paternal (X_f). Up to the 16^{th} day of embryogenesis 2 active X-chromosomes get into every cell during splitting. On the 16^{th} day, inactivation of one X-chromosome takes place (maternal or paternal with equal probability). The process of inactivation is random, that is why in one-half of all cells the paternal X-chromosome stays ac-

tive, and in the other half of cells the maternal X-chromosome is active. Maternal and paternal X-chromo-somes contain allelic genes (dominant and recessive). Two variants of enzymes can be synthesized in cells; they differ in their relation to the substrate or according to pH-indices. It helps female organisms better adapt to the environment. The essence of *female mosaicism according to sex chromosomes* is the content of different active X-chromosomes in different cells — from father and mother.

6. Sex chromosome disorders.

If moving sex chromosomes to the cell's poles during the meiosis is impaired then the human may develop chromosomal sex disorders:

1. XX and XY — a normal male and female organism.

2. XX* — a normal female organism that got both sex chromosomes from mother.

♂ \ ♀	X	XX	0
X	XX	XXX	X0
Y	XY	XXY	Y0
XY	XXY	XXXY	XY*
0	X0	XX*	0

3. XY* — a normal male organism that got both sex chromosomes from father.

4. Y0, 0 — inviable organisms.

5. XXX — the trisomy X syndrome. Karyotype is 47, XXX. The phenotype is female. Incidence frequency 1:800–1:1000. Nuclei of somatic cells have two Barr bodies. Tall height. The constitution corresponds to a male type. In 75% of cases mental retardation is marked. Secondary and primary sex characters are underdeveloped, the function of ovaries is impaired. Sometimes they may have children.

6. X0 — Shereshevsky-Turner syndrome. Karyotype is 45, X0. Female phenotype. Incidence frequency 1:2000–1:3000. Nuclei of somatic cells have no Barr body. A height of an adult is 135–145 cm. Specific characters: a short neck; a skin fold from the nape to the shoulders, a low position of ears, a low growth of hair at the occiput, changed joints of fingers and toes; 15 % have congenital defects of the heart and renal function anomalies. Ovaries and secondary sexual characters are underdeveloped. Such patients are sterile. The intellect does not suffer in this syndrome. Treatment: early hormonotherapy.

7. XXY, XXXY — Klinefelter syndrome. Karyotype — 47,XY, 48,XXXY. A male phenotype. Incidence frequency 1:400–1:500. Nuclei of somatic cells contain one or two Barr bodies. Tall height. Female type of constitution. Gynecomastia — mammary glands are enlarged. Integumentary hair is poorly developed, testes are underdeveloped, the process of spermatogenesis is impaired (individuals are sterile), but sex reflexes are retained. The intellect is decreased. The more are X-chromosomes in the genotype, the stronger suffers the intellect.

Basic terms and concepts:

1. **Hermaphroditism** — the presence of sexual characters of both sexes in one organism.

2. **Holandric characters** — characters determined by genes located in the non-homologous region of the Y-chromosome.

3. **Sex-controlled characters** — characters that manifest with various frequency and degree in individuals of different sex.

4. **Sex-limited characters** — characters that manifest only in individuals of one sex.

5. **X-linked characters** — characters determined by genes located in the non-homologous region of the X-chromosome.

6. **Klinefelter syndrome** — a chromosome disorder due to the presence of an additional X-chromosome in a male organism,

7. **Morris syndrome** — formation of a female phenotype in XY genotype.

8. **Trisomy X syndrome** — a chromosome disorder in women, when an additional X-chromosome is present.

9. **Shershevsky-Turner syndrome** — a chromosome disease in women, when one X-chromosome is absent.

10.**Transsexualism** — a persistent discordance of sexual self-conscious in the human to his genetic and gonad sex (sensation of belonging to an opposite sex).

11. **Physical sex determinants** — morphophysiological sex determinants.

Topic 9. FUNDAMENTALS OF HUMAN GENETICS

1. The human as an object of genetic investigations.

The human as an object of genetic investigations has its peculiarities and a number of difficulties.

Peculiarities of human genetics:

1) impossibility to apply a hybridological analysis and experimentation on humans;

2) a complex karyotype — many chromosomes and linkage groups;

3) late sexual maturation, a small number of hybrids in the family, slow change of generations;

4) a great variety of ecological and social conditions; impossibility to create identical living conditions.

Advantages of the human as a genetic object:

1) a great number of individuals in populations, the possibility of analyzing characters on vast material;

2) international co-operation of geneticists;

3) the human is better clinically studied than other objects;

elaboration of special methods for overcoming difficulties during studying human genetics.

2. Clinical-genealogical method.

A genealogic analysis was proposed by F. Galton in 1883. The **clinical-genealogical method** was developed on its basis; it is making up geneologys (genealogy) and analyzing the transmission mechanism of a character through generations. This method allows determining:

– the type of inheritance;

– whether the character is hereditary or non-hereditary;
– zygosity of the members (homozygotes or heterozygotes);
– penetrance of a gene (frequency of its appearance);
– manifestation probability of the character (genetic risk).

Designations (legend) used for making up a geneology, are shown in the fig. 20.

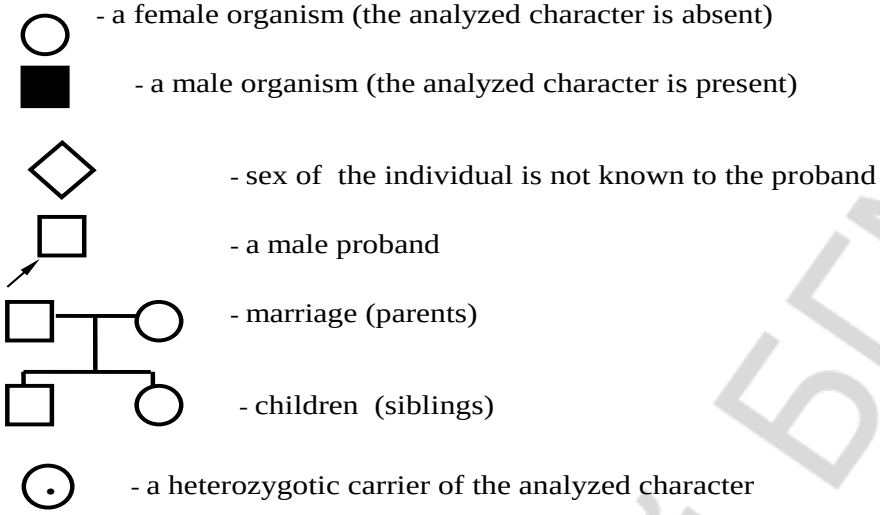


Fig. 20. Designations used in a genealogy

A person from whom making up the geneology starts is a *proband* and is marked with an arrow.

Genealogic analysis stages:
– taking information about relatives of the proband;
– making up a geneology;
– analyzing the geneology and conclusions.

Types of character inheritance.

Autosomal-dominant type of inheritance:
– both men and women fall ill in an equal degree;
– sick persons are in every generation;
– a sick child born by sick parents;
– if one of the parents is homozygous, the probability of inheriting the character is 100 %; if both parents are heterozygous — 75 %, if one parent is heterozygous and the other is homozygous on the recessive gene —50 %.

Autosomal-recessive type of inheritance:
– men and women fall ill in equal degree;
– sick persons are not in every generation;
– a sick child born by healthy parents is possible;
– if both parents are heterozygous, the probability of inheriting the character is 25 %; if one parent is heterozygous and the other is homozygous on a recessive character, it is 50 %; if both parents are recessive homozygotes - 100 %.

X-linked dominant type of inheritance is similar to an autosomal-dominant one, except the fact that a male passes this character (with an X-chromosome) only to daughters.

X-linked recessive type of inheritance:

– predominantly men fall ill;

– sick persons in every generation; a sick child born by healthy parents is possible

– a probability of inheriting the character is 25 % of all children or, if both parents are healthy, in boys — 50 %, in girls — 0 %.

Holandric type of inheritance:

– sick persons in all generations;

– only men fall ill;

– if the father is sick, all his sons are sick.

3. Twin method.

In 1876 F. Galton proposed a **twin method**. The method allows determining a role of heredity and environment for revealing a character in the human. The frequency of giving birth to twins is 1 %. Twins can be *monozygotic* (MT). They develop from one zygote and have an identical genotype. If the twins are *dizygotic* (DT), they develop from different simultaneously fertilized ova. They have a similar but not identical genotype as in siblings.

Zygosity criteria in twins: MT always have same sex, blood group and fingerprints; in DT these factors may differ.

Similarity of twins on the studied character is called *concordance*, differences on this character — *discordance*.

To reveal the roles of heredity and environment in the development of a definite character a Holzinger's formula is used:

$$H = \frac{CMT\,\% - CDT\,\%}{100\,\% - CDT\,\%},$$

where H — role of heredity in determining character; CMT — concordance of monozygotic twins; CDT — concordance of dizygotic twins. If H=1.0, only heredity is responsible for the character development; if the amount of H tends to 0, the environment is mainly responsible for the character development.

4. Cytogenetic method.

The cytogenetic method is based *studying the karyotype* with microscope. Lymphocytes or cells of bone marrow are obtained and grown on culture medium. Mitosis is stimulated and stopped at the metaphase. The cells are treated with NaCl hypotonic solution and then chromosomes are stained. They are studied under microscope, their pictures are taken and ideograms are analyzed. Fluorescent analysis is used for determining the karyotype and mapping chromosomes. The method reveals *genome and chromosome mutations*. Special designations are assumed to record mutations: q — a long chromosomal arm, p — a short chromosomal arm, «+» — redundancy of genetic material, «–» — insufficiency of genetic material. The record of a male karyotype with Down's syndrome — 47,XY,21+.

5. Biochemical methods.

Biochemical methods are used for revealing hereditary metabolic diseases in enzyme activity or the quantity of the reaction product that is catalyzed by the en-

zyme. Chromatography, fluorometry, radio immunological assay and other methods are used for revealing gene mutations (causes of metabolic diseases). For example, phenylketonuria — the impairment of phenylalanine exchange (PhA). Phenylketonuria can be revealed by the content of phenylalanine in blood: in healthy people it is 1–2 mg %, in sick ones — 50–60 mg %. Every 30–40th person is a carrier of a phenylketonuria gene.

Heterozygosity can be revealed after injection of phenylalanine into the organism and determining its amount in the blood. If the curve of PhA content returns to norm slowly after its injection then a person is heterozygous on a phenylketonuria gene.

6. Methods of a recombinant DNA. The Human genome project.

Methods of a recombinant DNA (**molecular-genetic**) allow determining a pathologic gene in the genome. Stages of the methods:

1. DNA specimen are cut by restrictases into short fragments having a point of recognition.

2. Obtained fragments are separated by electrophoresis in an agar gel into fractions differing in size (a molecular mass).

3. A needed number of copies of DNA fractions is obtained with a PCR.

4. Two-strand DNA of a multiplied fraction is heated and denaturize into single-strand fragments.

5. These fragments are placed into the medium with a radioactive probe (a single-sequenced DNA corresponding to a pathologic gene). If there is a probe that is complementary to the pathologic gene among these fragments, a two-strand DNA is formed.

6. The result is registered with an X-ray sensitive film.

In 1990 an international project on making a genetic human map (Human Genome Project) was started. The tasks of the Human genome project included decoding of a nuicleotide sequence (sequencing) of a human DNA molecule. In 2000 the human genome was sequenated.

7. Express-methods.

Express-methods are methods of fast preliminary diagnosis of human hereditary diseases. These methods must be economical, safe and diagnostically accurate; the material for investigation should be in small amounts and be easily accessible (blood, urine).

Guthrie microbiological test (neonatal heel prick). A drop of blood of the newborn is put on blotting paper and then to the agar medium containing anti-metabolite of phenylalanine and bacterial culture. This anti-metabolite inhibits bacterial growth. But if the blood contains a lot of phenylalanine, anti-metabolite is destroyed, and microbes start their growth.

Determination of X- and Y-sex chromatin — the cheek epithelial cells or leukocytes are investigated. X-chromatin is determined during staining with acetoorseine, and Y-chromatin — with acrichine yperite. This method allows determining the genetic sex and chromosomal diseases of sex.

Biochemical and chemical (colored reactions) methods are used for fast preliminary diagnosis of hereditary metabolic diseases (10 % $FeCl_3$ solution for diagnosing phenylketonuria).

8. Methods of prenatal diagnostics of hereditary disorders.

Indirect methods of prenatal (before birth) diagnostics — examination of a pregnant woman (obstetric-gynecological, genealogical, biochemical) and *direct* methods — examination of the fetus.

α-fetoprotein (AFP) is an embryo-specific protein; it is produced by fetal cells and the placenta and passes into the mother's blood. Reducing of *α-fetoprotein* at the 13–15th weeks of embryonic development is characteristic of chromosomal diseases. Its concentration increase in a threatened miscarriage, intrauterine death of the fetus, plural pregnancy, nerve tube defects, congenital nephrosis.

Ultrasonography is referred to *direct non-invasive methods* (without tissues injury), it is the usage of ultrasound for obtaining an image of the fetus and its membranes. It is done for all pregnant women because it is safe for the fetus and can be repeated. This method reveals vitality of the fetus, twin pregnancy and severe development defects of the skeleton, the brain and spinal cord.

Indications for diagnosis using *direct invasive methods*:

– a hereditary disease in the family;

– mother's age over 37 years; an X-linked recessive disease in the mother;

– cases of spontaneous abortions in women at early stages of pregnancy, stillbirths, children with multiple congenital anomalies and chromosome pathology;

– heterozygosity of both parents on a pair of genes with an autosomal-recessive type of inheritance.

Direct invasive methods (with tissue injury):

1. *Chorion biopsy* is taking chorion cilia through the uterine cervical canal for cytogenetic and biochemical investigations and DNA analysis. It is performed under control of ultrasonography at the 8–13th weeks of gestation. The method allows revealing gene, chromosome and genome mutations.

2. *Amniocentesis*. At the 15–17th weeks, a puncture of the amniotic sac is made through the abdominal wall under control of ultrasonography. 15–20 ml of amniotic fluid with fetal cells is taken with a syringe for diagnosis of various hereditary diseases. Complications in this method arise in 1 % of cases.

Basic terms and concepts:

1. Dizygotic twins — develop from two different ova fertilized by different spermatozoa.

2. Monozygotic twins — develop from one fertilized ovum.

3. Discordance — a degree of twins' difference on a studied character.

4. Concordance — a degree of twins' similarity on a studied character.

5. Proband — a person, from whom making a genealogy starts.

6. Sequencing — determination of a nucleotide sequence in the gene.

7. Geneology (genealogy) — a genealogic map, where all relatives of the proband and relativities between them are denoted by symbols.

8. Amniocentesis — a method of prenatal diagnosis: taking of amniotic fluid with fetal cells for biochemical and cytogenetic investigations.

9. α-fetoprotein —protein contained in the amniotic fluid and blood serum of a pregnant woman.

10. Guthrie test — a preliminary method for diagnosis of phenylketonuria in neonates.

11. Ultrasonography — a diagnostic method using ultrasound for obtaining an image of the fetus and its membranes.

12. Chorion biopsy — a method of prenatal diagnosis — taking epithelium of chorion's cilia for cytogenetic and biochemical investigations and DNA analysis.

Topic 10. GENETIC ENGINEERING

1. Purpose of genetic engineering is designing of genetic structures according to a plan (creation of organisms with a new genetic program by translocation of genetic information from one organism to the other).

Stages of genetic engineering methods:

1. Obtaining genetic material.
2. Insertion of DNA fragments into a vector molecule.
3. Incorporation of a recombinant DNA into a cell-recipient.
4. Selection of cell clones containing molecules of a hybrid DNA.

2. Obtaining genetic material.

Chemical-enzymatic synthesis of genes. Short (8–16 nucleotides) single-strand DNA fragments are synthesized *in vitro*, then they are linked with ligases and treated with high temperature for the formation of double-strand DNA molecules. The gene should be **sequenced** before using this method.

Enzymatic synthesis of complex genes. It is performed by reverse transcription. An obtained mRNA is used as a matrix. Using an enzyme revertase, a DNA strand is synthesized on it and then it is replicated. The obtained genes do not function in cells as they have no promoter and other regulatory sites. Before injection into a bacterium, a promoter is added to the structural gene to make it work*Obtaining natural genes with restictases*. Restrictases are enzymes causing DNA hydrolysis with formation of short fragments of the molecule. They interact with DNA of any organisms if it has restriction sites (usually they recognize very specific parts for every enzyme with 4–6 pairs of nucleotides in length). These parts are called *palindromes*.

At present, there are over 500 restrictases are known, they are able to cut the DNA in approximately 120 sites and form *blunt* (double-thread) ends or *sticky* (single-thread) ends in the DNA fragments.

Gene obtaining with restrictases has a number of disadvantages:

– it is not always possible to select restrictases, which allow to cut out a DNA part with a required gene;

– if the cut out DNA fragment contains introns, then recombinant DNA will not be able to work in prokaryotic cells due to its disability for processing and splicing.

Polymerase chain reaction K. Mullis (1987) elaborated a method, which was called a polymerase chain reaction (PCR). PCR is performed in vitro using the enzyme *DNA-polymerase* of a bacterium Thermus aquaticus, 4 *nucleotides* (A, T, G and C) and short *primers*. The enzyme is marked by its persistence to high temperature.

Thanks to primers the DNA fragment that might be copied by DNA polymerase is exactly determined. The PCR has 3 stages:

1. *Denaturation* — the mixture, which contains a specimen of a needed DNA, is heated to 90 °C. During 15 seconds, hydrogen bonds between DNA strands are destroyed and two single-strand molecules are formed.

2. *Hybridization of primers* — the temperature is lowered to +50 °C and primiers jon the DNA. This stage lasts about 30 seconds.

3. *Polymerization* — the mixture is heated again to +70 °C. At this temperature the Taq-polymerase lengthens both primers from their 3' ends. The primers grow up to the matrix sizes forming a new strand. This process takes 90 sec.

As a result, the number of DNA increases by many times. During 20 cycles the number of DNA copies reaches to 10^6.

3. Insertion of DNA fragments into a vector molecule.

Vector is a small autonomously replicated DNA molecule, which provides multiplication and work of the inserted gene.

Vector molecules should:

– contain replication origin points and replicate autonomously;

– be inherited by a host cell;

– be contained in a great number of copies in the cell;

– have enough capacity that allows cloning big genes;

– have convenient sites of restriction;

– have selective markers, which could be used for selecting cells that have received a cloned DNA copy with these markers.

The most high-usage vector-host systems are systems where the host is *bacteria E. coli* and the vectors are **plasmids**.

Plasmids are autonomously replicated circular DNA molecules that are normally present in bacterial cells.

Phage vectors are phage genome particles containing a recombinant DNA. Vectors for E. coli are constructed on the basis of **phage λ and phage M 13**.

Phage λ contains a double-strand DNA that consists of 48 500 nucleotide pairs. It is packed into the head as a linear molecule with sticky ends. After penetrance into the cell, sticky ends attach each other, the molecule closes into a circle and are

sewn by a DNA-ligase. It is possible to clone fragments with the length 15 000 nucleotide pairs in vectors made on the basis of phage λ.

Cosmids are vectors made on the basis of plasmids and phage λ. Cosmids have *cos-sites* from phage λ (sticky ends) at both ends. These sites are complementary single-strand fragments of 12 nucleotides long. Linear phage DNA bind to each other through cos-sites and form a long sequence of hundreds of phage DNA that is called *concatamer*.

Phasmids are hybrid vectors that can develop both as a phage and a plasmid. The capacity of plasmids is comparable to that of phage vectors.

4. Incorporation of recombinant DNA in the cell-recipient.

The following methods are used:

1. Conjugation — in bacteria, transmission of genetic material may occur by direct intercellular contact. Genetic material is transmitted only in one direction.
2. Transformation — transmission of genes by a free soluble DNA (by plasmids), isolated from cells-donors;
3. Transduction — bacteriophages able to the transmit the DNA from a cell-donor to a cell-recipient;
4. Transfection — infection with phages λ, ψ X174 and T4;
5. Competence — ability of cells to absorb a DNA from the environment;
6. Microinjection of DNA molecules into animal cells;

Using liposomes for incorporation DNA into animal cells. Liposomes are vesicles surrounded by one or several layers of lipids.

5. Using methods of genetic engineering in medicine.

Southern blot hybridization. The method elaborated in 1975 allows to identify restricted DNA fragments (fig. 21).

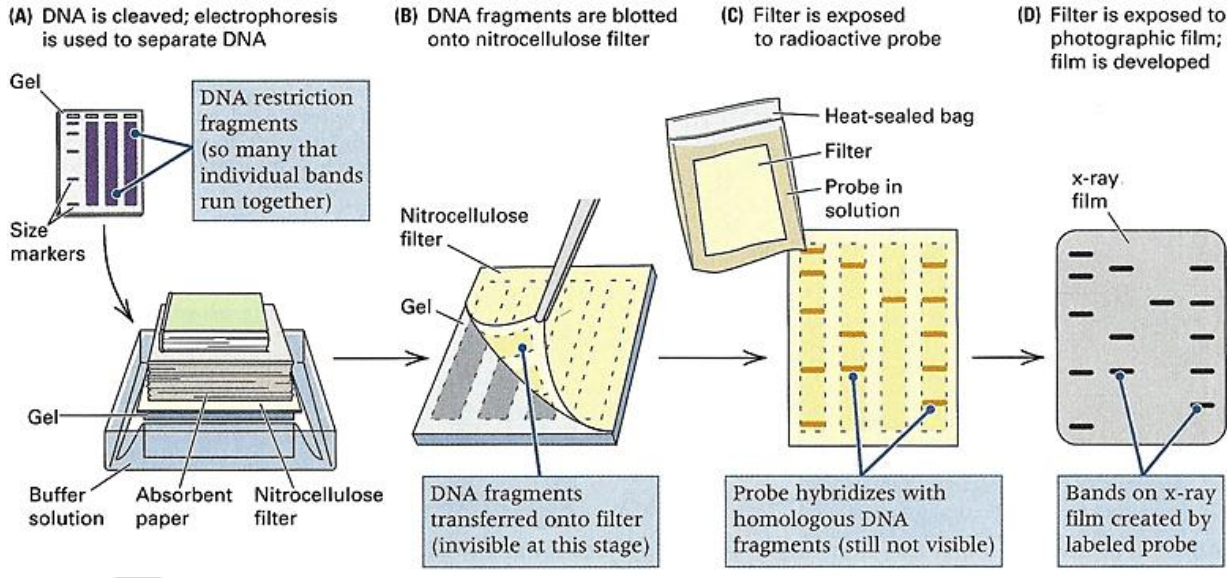


Fig. 21. Southern blot hybridization

A DNA treated with restrictases is placed on agar jelly in a special chamber for electrophoresis where an electric field acts. Under its influence DNA frag-

ments start moving. Short fragments move faster. After electrophoresis the DNA fragments forms some fractions located at some distance from each other. Each fraction corresponds to a certain DNA fragment. DNA fragments separated in the agar jelly **are denaturated to single-sequenced molecules**, and then the whole electrophoresic DNA specter **is printed (blotted**) on a nitrocellulose **filter** applied to the jelly and is fixed by high temperature. Then the filter is placed into the medium containing a **radioactively marked DNA-probe**. The probe can hybridize only with complementary DNA fragment. After interaction with the DNA-probe the film is applied to the nitrocellulose filter containing all obtained DNA fragments. After exposition, lighted spots corresponding to the arrangement of marked DNA fractions appear in the film (autoradiogram).

The method is used for revealing DNA sequences characteristic of mutated genes. It allows diagnosing gene mutations.

Genome dactyloscopy. There are a minisatellite DNA in the human genome, that consist of short (9–64 nucleotide pairs) variable tandem repeating DNA sequences. A tandem repeat is two or more identical DNA sequences located close to each other. The human has many different tandem DNA repeats in different chromosomes, which form in totally a unique complement of minisatellite DNA for each human individual. The method analyzing these fragments got the name of **gene dactyloscopy (fingerprint of DNA)**.

The technique of fingerprint of DNA: a DNA is obtained from cells and cut into fragments of various length with the help of restrictases. Then the Southern-blott analysis is made. *Fractions containing a minisatellite DNA*, are revealed with a probe, which is complementary to 13 repeated nucleotides. The probe is radioactive, it lights the film only in definite places, giving a picture of some alternating dark fractions corresponding to different minisatellites.

Basic terms and concepts:

1. Autoradiogram — film, where lighted spots corresponding to the marked DNA fractions are revealed.

2. Vector — a small autonomously replicated DNA molecule, which provides multiplication and work of a gene incorporated in it.

3. Genome dactyloscopy — a method analyzing fractions of a minisatellite DNA.

4. Hybridization of primers — a second stage of the polymerase chain reaction resulting in linkage of DNA chains with primers.

5. DNA-probe — a radioactively marked short specific DNA sequence.

6. Cosmids — artificial constructions made on the basis of plasmids and phage λ.

7. Sticky ends — single-thread complementary DNA ends which are formed by restrictases.

8. Liposomes — vesicles surrounded by one or several layers of lipids.

9. Plasmids — small autonomously replicated circular DNA molecules of bacterial cells.

10. Restrtictases — enzymes causing DNA hydrolysis with formation of «sticky ends».

11. Restriction sites — sites recognized by restrictases (there are usually recognized parts of 4–6 pairs of nucleotides in length, strictly specific for every enzyme).

12. Phasmids — hybrid vectors which can develop both as a phage and a plasmid.

Topic 11. GENETICS OF POPULATIONS

1. Characteristic of human populations. Types of marriages.

A **Population** is a group of individuals of one species who have an overall genetic fund, capable of free crossing, inhabit same territory for a long time and are relatively isolated from other individuals of the species.

Populations can be large and small. *Large* human populations contain over 4000 individuals. Demes and isolates are *small populations.* The number of individuals in demes is 1500–4000 people. Intergroup marriages between them comprise 80–90 % and the inflow of genes from other groups is 1–2 %. *Isolates* contain up to 1500 people, intergroup marriages are over 90 %, the inflow of genes from other groups is less than 1 %. Marriages among relatives —*inbreeding (incest marriages)* are observed in demes and isolates. Probability of heterozygosity on same pathologic gene is high in relatives and manifestation of hereditary pathology is possible. Outbreeding — non-consanguineous marriages. They sustain a high level of heterozygosity, and hereditary pathology occurs there far more rarely.

Human populations are characterized by demographic factors: the number, birthrate, mortality rate, age and sex structure, occupation, ecologic state of the environment. The action of evolutionary selection is decreased there and destruction of isolates takes place.

2. Genetic processes of large populations. Hardy–Weinberg law.

Large populations are called *panmixed,* as the choice of a partner for marriage is not limited there. Vast populations tends to an *ideal* ones which are characterized by a great number of individuals, isolation from other populations of the species, complete panmixia, absence of mutations and abcence of the natural selection.

Hardy-Weinberg law: In an ideal population frequencies of genes and genotypes are in equilibrium and do not change over generations.

Large populations are characterized by genetic polymorphism (AA, Aa, aa on a definite character) and panmixia. Nine variants of marriages are possible under such conditions (taking into account genotypes):

Genetic records of marriages and offspring:

1. AA x AA → AA.
2. AA x Aa → AA + Aa.
3. AA x aa → Aa.

4. Aa x AA → AA + Aa.
5. Aa x Aa → AA + 2Aa + aa.
6. Aa x aa → Aa + aa.
7. aa x AA → Aa.
8. aa x Aa → Aa + aa.
9. aa x aa → aa.

m \ f	AA	Aa	aa
AA	1	4	7
Aa	2	5	8
aa	3	6	9

Summary: 4AA + 8Aa + 4aa or AA + 2Aa + aa

If one denotes genes frequencies as A — **p**, a — **q**, of genotypes as AA — $\mathbf{p}^2$, 2Aa — **2pq**, aa — $\mathbf{q}^2$, we'll get the following record: $\mathbf{p + q = 1}$ and $\mathbf{p^2 + 2pq + q2 = 1}$.

3. Genetic processes in small populations.

In small populations, **genetic drift** occur. It means incidental fluctuations of genes' frequencies. It is the accumulation of homozygotes, or homozygotization. In the first generation (AA + 2Aa + aa) heterozygotes comprise 50 %, in F_2 their number will be 25 %, in F_3 — 12.5 %, etc. When lethal genes are present, the population comes to extinction due to homozygotization. Evolution in small populations is impossible, there is no genetic diversity.

MuMutation process is an incidental and undirected process. It sustains a high degree of heterogeneity of populations. Mutations can be neutral, negative or positive for the organism. When the environmental conditions change, neutral mutations can become positive or negative. Mutation frequency of a gene is 10^{-5}–10^{-7} per generation. Dominant mutations are revealed in the first generation and are immediately exposed to evolutionary selection while recessive mutations accumulate in the population first and are revealed phenotypically only after the appearance of recessive homozygotes, then evolutionary selection affects them. Mutations are an *elementary evolutionary material*.

Population waves, or life waves are periodical fluctuations of the number of natural populations due to fluctuations of environmental factors. Population waves change the genetic structure of populations removing the least adapted individuals from them.

Isolation is a restriction of free crossing. It leads to separation of the population into groups and changing the genotype frequency. Types of isolation:

1. Geographic or territorial (mountain ridges, rivers).
2. Biological:
   - genetic, or hybrids sterility;
   - ecologo-etological (reducing the probability of meeting partners);
   - morpho-physiological or impossibility to cross due to morphological differences of sex organs.

Migration of the population may increase heterozygosity in human populations. *Immigration* introduces new alleles or new genotype combinations into the population. *Emigration* changes the ratio of different genotypes in the population due to the «outflow» of genes.

Natural selection is the most important evolutionary factor. It removes less favorable combinations of genes from the population and selectively preserves

more favorable genotypes changing genes frequency in populations. Three forms of natural selection are distinguished (stabilizing, directional and disruptive).

4. Genetic load and its biological nature.

5. Saturation of populations with recessive mutations reducing adaptability of individuals to the environment is called a *genetic load* of the population. A part of genetic load is passed from generation to generation (heterozygous carriage of pathologic recessive genes), other mutations arise in every new generation under the effect of mutagenic factors. The amount of genetic load is proportional to the degree of the environmental pollution (5 %).

Basic terms and concepts:

1. Demes — are human populations where the number of individuals is 1500–4000.

2. Genetic drift — incidental fluctuations of genes' frequencies in small populations.

3. Panmixia — absence of limitations in choosing of a partner for marriage.

4. Population —a group of individuals of one species who have an overall genetic fund, capable of free crossing, inhabit one territory for a long time and are relatively isolated from other individuals of the species.

Topic 12. REPRODUCTION OF ORGANISMS

1. Types of reproduction and their characteristic.

Reproduction is a universal organism property of all living things, which provides reproduction of their own selves and is based on transmission of genetic information from generation to generation.

Reproduction on the *molecular level* is DNA replication, on the *subcellular level* — doubling of some organelles, on the *cellular one* — amitosis, mitosis. *Cell division is the basis of organisms' reproduction*.

Forms of organisms' reproduction. The characteristic of asexual reproduction: 1 parental individual takes part in reproduction; somatic cells are a source of genetic information; genotypes of daughter cells are identical to parental ones; the number of individuals increases fast; it provides the existence of a species in constant environmental conditions (fig. 22).

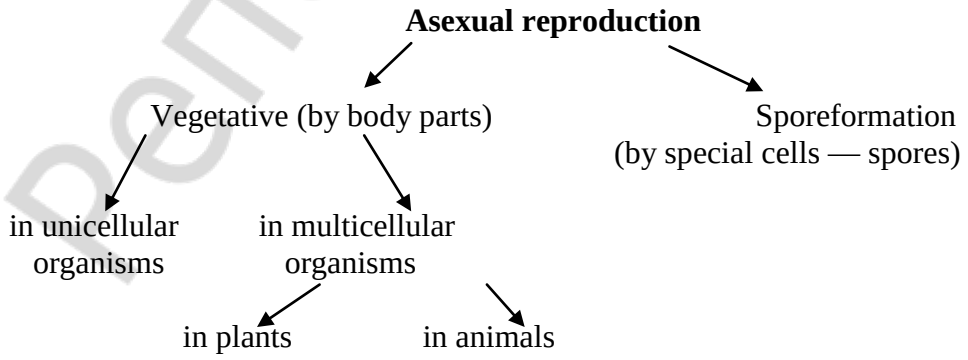


Fig. 22. Asexual reproduction

***Vegetative reproduction of unicellular organisms*:**

a) *division (fission) in two* longitudinal fission (euglenas) transverse fission (infusoria);

b) *schizogony* is a multiple fission. At first, the nucleus divide into several parts, then the cytoplasm do (malaria parasite);

c) *budding* — a bud forms on the mother cell, it grows and then separates from the mother individual (yeast, suctorians).

***Vegetative reproduction in multicellular organisms*:**

A. *In plants* — by vegetative organs: the root, stem, leaves.

B. *Animals*:

a) *budding* (hydra);

b) *fragmentation* — division of the body by constrictions into several parts (ciliates and ringworms);

c) *polyembryony* — division of the zygote into several parts, each form a separate organism (flukes).

***Sporogenesis*:** in special organs (sporogonia) spores are formed, they give rise to a new organism (water-plants, mushrooms, mosses, lycopodia, horsetails, ferns).

Characteristic of sexual reproduction: 2 parental individuals take part in reproduction; parental sex cells are a source of genetic information; genotypes of daughter cells differ from the parental ones due to combinative variation; it promotes the adaptability of organisms to changing environmental conditions (fig. 23).

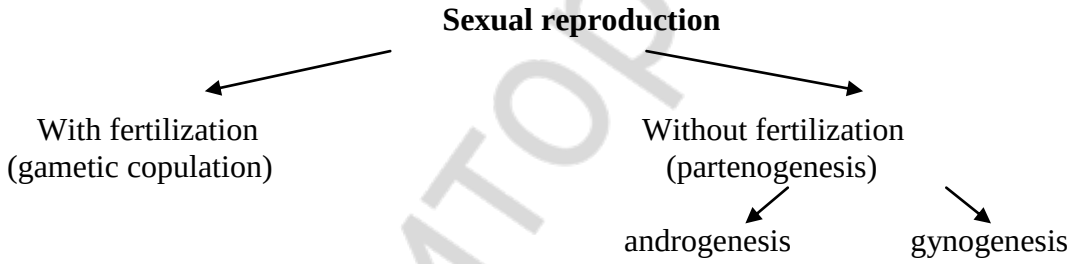


Fig. 23. Sexual reproduction

2. Evolution of the sexual process.

A sexual process is the basis of sexual reproduction.

Conjugation is exchange of genetic information between unicellular organisms. *Copulation* is joining the genetic information of two cells. The number of individuals do not increase in sexual process. *Conjugation* is characteristic of infusoria and many bacteria. During the conjugation infusoria are linked with a cytoplasmic bridge and exchange parts of micronucleus. Then they diverge and multiply by asexual way. The organisms of protozoans perform the function of gametes during some periods of their life cycle. They fuse (the copulation occurs) and then multiply by division.

The copulation during the sexual reproduction is *gametic* copulation.

3. Structure of gametes.

Ova have a round or oval shape from 60μm to several cm in diameter. (human ovum - about 130 μm). They are immovable, have haploid nuclei contain organelles (exept for a centrosome) and store nutrients (yolk). Their cytoplasm is species-specific. The peripheral cytoplasm layer of the human ovum contains *cortical granules* with proteolytic enzymes, polysaccharides and proteins. These substances inetract with another proteins to form the *fertilization membrane* which prevents polyspermia during the fertilization. Ovum is covered with primary membrane wihich is produced by the ovum itself. The secondary membrane is made by follicular cells. It is called *zona pellucida*. Follicular cells form the radiate crown.

Types of ova:

– *isolecithal* — there is a small amount of yolk, it is uniformly distributed (the Lancelet, mammals);

– *heavily telolecithal* — there is a lot of yolk, it is concentrated at the vegetative pole, and both the cytoplasm and the nucleus are on the animal pole (reptiles, birds);

– *moderately telolecithal* — in fish and amphibians;

– *centrolecithal* — there is little amount of yolk, it is in the center (insects).

A **spermatozoon** consists of a head, midpiece (neck) and tail. The sizes of a human spermatozoon are 52–70 μm. There is an *acrosome* (modified Golgi complex) in the tip of the head. It provides the entry of a spermatozoon into the ovum. The most of space in the head is occupied by the nucleus surrounded by a thin layer of cytoplasm. In the midpiece, there is a centrosome and a spiral thread of mitochondria producing energy for movements of the tail. The tail has the cytoskeleton elements (microtubules) covered with membrane. Microtubules slide relative to one another to make wave-like motion of the tail. This provides spermatozoon's movement.

4. Gametogenesis (oogenesis and spermatogenesis).

According to the presence and functioning of sex glands, organisms are classified into hermaphrodites and dioecious organisms (with separate sexes).

The hermaphrodite is an organism with both male and female gonads forming both spermatozoa and ova. Such hermaphroditism occurs in flatworms and ringworms. It is a *true* hermaphroditism. In case of *false* hermaphroditism, one individual has sex organs and secondary sex characters of both sexes, but gonads of only one sex (male or female). The human may have false hermaphroditism.

Dioecious species have only female or only male gonads. Males and females are characterized by the characters of **sexual dimorphism**: differences in body sizes, coloration, structure, voice specificities, behavior and other characters. *The characters of sexual dimorphism in the human are*: peculiarities of the bony-muscular system, distribution of subcutaneous adipose tissue, the degree of hair covering, voice timbre, peculiarities of behavior, etc.

The process of ova formation is oogenesis, that of spermatozoa is *spermatogenesis*. In gametogenesis, haploid gametes are formed from diploid somatic cells of sex glands (fig. 24).

Peculiarities of human gametogenesis:

1. Mitotic division of oogonies is finished before the birth of the organism. Mitosis of spermatogonies starts with puberty.

2. A growth period is clearly marked during oogenesis.

3. In oogenesis, the 1st meiotic division is stoped at the stage diakinesis of prophase untill puberty. The 2nd division of meiosis stops at the metaphase and resumes after fertilization.

4. There is no period of transformation in oogenesis.

5. A newborn girl has about 30 000 oocytes in the ovaries; only 300–400 of them reach their maturity (about 13 cells a year).

6. A male organism produces up to 500 billion spermatozoa during the period of sexual life.

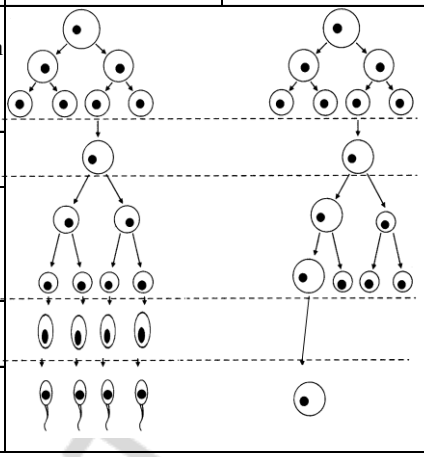
Genetic information	Cells names	Spermatogenesis	Ovogenesis	Cells names	Periods
2n2chr4c	Spermatogonia			Ovogonia	Proliferation (mitosis)
2n2chr4c	Primary spermatocytes			Primary ovocytes	Growth
1n2chr2c 1n1chr1c	Secondary spermatocytes			Secondary ovocytes	Maturation (meiosis)
1n1chr1c	Spermatides				Transformation
1n1chr1c	Spermatozoa			Ovum	

Fig. 24. Gametogenesis

5. Insemination, its forms. Fertilization and its stages

Processes that provide contact of female and male gametes is **insemination**. Water animals have an *external insemination*: gametes are excreted into the water where their fusion occurs.

In an *internal insemination* (terrestrial animals), male gametes are brought into the reproductive tracts of a female during the sexual intercourse.

The insemination is followed by *fertilization*: fusion of gametes with zygote formation. A contact of gametes is provided by:

– opposite charges of gametes;

– movement of spermatozoa and contraction of wall of female reproductive tracts;

– ovum excretie gamones to which spermatozoa have positive chemotaxis.

An external stage of fertilization is entrance of a spermatozoon into the ovum. During the contact with the ovum, the membrane of spermatozoon's acrosome is destroyed and the enzyme *hyaluronidase* is excreted.

The enzyme dissolves the ovum membrane, an acrosomal process stretch from the acrosome; it penetrates membranes of the ovum and fuses with its membrane. A *receptive spot* is formed in this area of the ovum. It encloses the head and centriole of the spermatozoon and takes them into the ovum's cytoplasm. The ovum can be fertilized by one spermatozoon (in mammals) then it is *monospermy*. *Fertilization membrane* is formed on the surfase of the ovum and the rest spermatozoa can not pass through it. If several spermatozoa enter the ovum (insects, fishes, birds), it is *polyspermy.*

Syncaryogamia is associated with an **internal stage** of fertilization. Haploid nuclei of gametes fuse to form a diploid nucleus of a zygote.

A *male pronucleus* (nucleus of the spermatozoon) enlarges to the sizes of a *female pronucleus* (nucleus of the ovum), turns through 180° and moves (together with the centrosome at its front end) to the female pronucleus. The pronuclei fuse to restore the diploid chromosome complement and the zygote is now formed.

A special form of reproduction is **parthenogenesis**, the development of organisms from unfertilized ova. A *natural partenogenesis* occurs in lower cancroids, bees, butterflies, rock lizards. Nuclei of somatic cells in such individuals can be haploid. Diploid complement can be restored by fusion of the ovum's nucleus with the nucleus of a directing body.

6. Biological peculiarities of human reproduction.

1. The human is not only biological but also a social being.

2. The ability for reproduction appears with puberty. Its signs are first periods in girls (on an average from 12–15 years) and pollutions in boys (from 13–16 years).

3. The duration of the reproductive period in women is to 40–45 years, in men — to an old age (gamete production by the testes occurs during the whole life).

4. During one intercourse about 200 million of spermatozoa are excreted with the semen fluid.

5. Since puberty one secondary oocyte is formed once a moon month.

6. Fertilization occurs in upper parts of the uterine tubes, usually within 12 hours after ovulation.

7. Spermatozoa are able for fertilization during 1–2 days after getting into the female reproductive tracts.

8. Human reproduction, unlike that of animals, is not seasonal. It depends on a number of social-economic factors.

9. The human can regulate birthrate.

Basic terms and concepts:

1. Acrosome — modified Golgi complex of a spermatozoon.

2. Conjugation — sexual process, when exchange of genetic information between two cells occurs.

3. Copulation —sexual process, when joining of genetic information of two individuals occurs.

4. Dioecious species — species with distint males and females.

5. Oogamy — form of copulation with a strict differentiation of gametes: a large and immovable ovum and a small and movable spermatozoon.

6. Oogenesis — process of development of maturation of ova.

7. Insemination — are processes providing gametes contact.

8. Hermaphrodite — organism having bothmale and frmale sex organs.

9. Fertilization — fusion of an ovum and a spermatozoon with further formation of a zygote.

10. Parthenogenesis — sexual reproduction without fertilization.

11. Sexual process — exchange of genetic information between two cells or joining the genetic information of two cells; increase of the number of individuals is not observed.

12. Syncaryon — nucleus of a zygote formed as a result of fusion of gametic nuclei.

13. Spermatogenesis — process of spermatozoa development.

Topic 13. FUNDAMENTALS OF ONTOGENESIS (EMBRYONIC DEVELOPMENT)

1. Ontogenesis, its types, division into periods.

Ontogenesis is individual development of an organism from formation of a zygote to death.

Division of ontogenesis into periods (fig. 25).

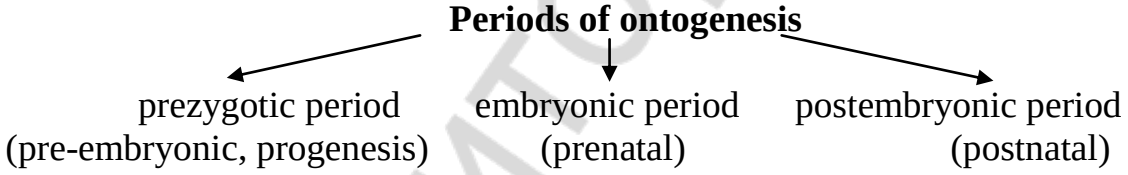


Fig. 25. Periods of ontogenesis

The zygotic period is a period of formation and maturation of those parental sex cells that will form the zygote in future.

Embryonic (or prenatal period) starts at the moment of a zygote formation and ends with birth of a new organism or its leaving egg membranes.

Post-embryonic (or post-natal period) — lasts from birth of the organism or its leaving egg membranes and till death.

2. Division of the human embryonic development into periods.

Embryogenesis of the human includes:

1. Germinative (initial) period — the 1^{st} week after fertilization, a zygote is being split.

2. Embryonic period — the 2^{nd}-3^{rd} weeks after fertilization, a blastula and a gastrula are formed, germinal layers and anlages of axial organs are formed.

3. Pre-fetal period — the 4–8th weeks, formation of anlagen of all organ systems and the placenta.

4. Fetal period — from the 9th week an embryo is called a fetus; it grows, its organs and organ systems are formed.

3. Characteristic of embryogenesis stages. Provisional organs.

Zygote is a unicellular development stage of a multicellular organism; it is formed after fusion of a male and female gametes.

The **cleavage** type of a zygote depends on the type of the ovum. The type of the ovum depends on amount of nutrients (yolk) that it contains and their distribution. Daughter cells of the zygote that are formed during the cleavage are *blastomeres*. Some animals have the development stage when the cleaving zygote resembles a raspberry — **morula**. Eventually only one layer of blastomeres are situated at the periphery and form a **blastula** — a one-layer germ with a cavity inside. This layer of cells is called *blastoderm*. The cavity of the blastula is a *blastocoel*.

The blastula stage is followed by **gastrullation** — formation of a *gastrula*, a two-layer germ. The cell layers of the gastrula got the name of *germinal layers*. There are 4 types of gastrulation (fig. 26).

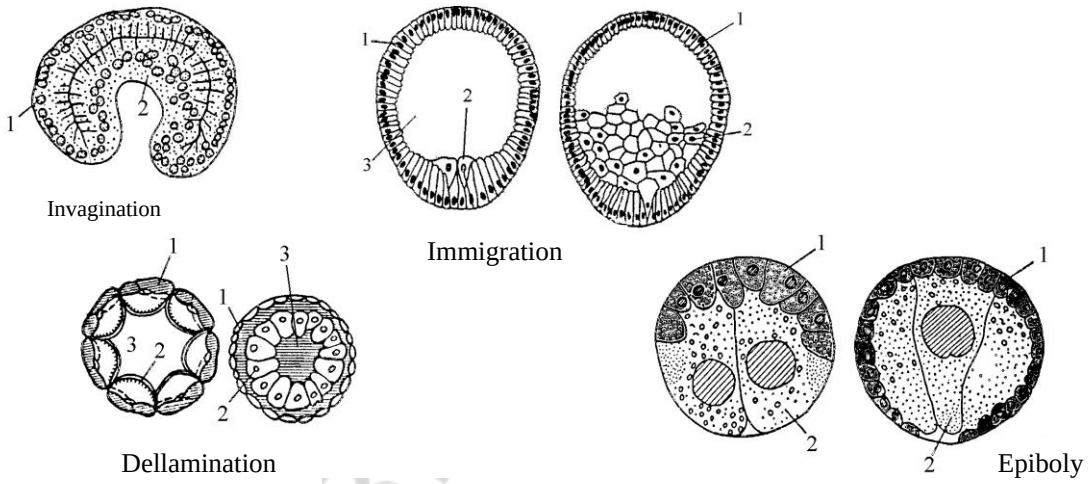


Fig. 26. Types of gastrulation:
1 — ectoderm; *2* — entoderm; *3* — gastrocele

Invagination is migration of some cells inside the cavity and formation of a second cell layer there — entoderm.

Epiboly is over-growing: the cells of the animal pole multiply faster and eventually cover the cells of the vegetative pole that divides slower. The cells of the animal pole form the ectoderm and those of the vegetative pole form the entoderm.

Delamination is division: all cells of the one-layer germ divide parallel to its surface and form two layers — the ectoderm and endoderm.

Gastrulation in mammals and human goes by mixed type — initially by delamination, then by ingression.

All animals (except for sponges and coelenterate) have three germ layers. Anlage of the 3rd germinal layer, **mesoderm**, forms in two ways: *teloblastic* and *enterocoelous*. The *teloblastic way* is characteristic of invertebrates. On two sides of the blastopore per one large cell are formed (*teloblasts*). They start dividing; small cells take place between the ectoderm and entoderm and form the mesoderm. The *enterocoelous way* is characteristic for chordates. Ingrowths (coelomic sacs) form on two sides of the primary intestine. They separate from the primary intestine, grow between the ectoderm and entoderm and give start to the mesoderm. After the formation of germinal layers, anlages of axial organs are formed. It is *hystogenesis* — a process of tissue formation and *organogenesis* — a process of organ formation.

Derivatives of germinal layers. The ectoderm gives start to the epidermis and its derivatives, nervous system, sense organs, initial and ending segments of the alimentary tube.

The notochord, middle part of the alimentary tube, liver, pancreas and respiratory system are formed from by **entoderm**.

The following organs and systems are formed from the **mesoderm:** the connective and muscular tissues, skeletal muscles, skeleton, dermis, dentin, urogenital system, smooth muscles, heart, blood vessels, blood and lymphatic system.

Provisional (temporary) organs of the germ:

1. *Amnion* — is a sac filled with the fluid that forms water environment, protects the germ from drying out and injuries.

2. *Chorion* (a serous membrane) is an external membrane adjacent to shell or mother's tissues. It serves for exchanging substances with the environment.

3. *Yolk sac* takes part in feeding of the germ and is also the first blood making organ.

Allantois is a process of the endgut, a receptacle for urea and the uric acid. In mammals it participates in forming the placenta together with the chorion.

4. Mechanisms of embryogenesis. Morphogenesis.

Mechanisms providing embryogenesis:

1. **Differential activity of genes** — various complexes of genes have a strictly definite order of repression and depression during the embryonic development.

2. **Determination** — cells obtain the ability to develop in a definite way and become limited in their future development. At the beginning of embryogenesis blastomeres are *totypotential* (can give start to a whole organism) and their development depends on external inductors and adjacent cells. At later stages of embryogenesis cells become determined (their development is predestined) and they develop according to a certain plan.

3. **Differentiation** — is a biochemical, functional and morphological specialization of cells; modification of a developing structure, when relatively homogenous formations become more and more different.

Phases of differentiation:

– *dependent* (till the stage of an early gastrula);

– *independent* (at the stage of a late gastrula).

Genetic basis of differentiation. Genetic differentiation is associated with universality of an ovum and inhomogeneity of its cytoplasm — different parts of the cytoplasm contain *different chemical substances* and have different development possibilities. Stages of differentiation (fig. 27).

Chemical heterogeneity of the ovum's cytoplasm (increases after fertilization)

↓

Chemical heterogeneity of the blastomeres' cytoplasm

↓

Different blastomeres have different inductors

↓

Different inductors «switch on» different transcriptones

↓

Different enzymes are synthesized; they catalyze different types of biochemical reactions

↓

Synthesis of different typo- and tissue-specific proteins in different blastomeres

↓

Different types of cells are formed, morphological heterogeneity is made

↓

Different types of cells form different tissues

↓

Different tissues form different organs

Fig. 27. Stages of differentiation

Morphogenesis is a process of creation of new structures and modification of their form during ontogenesis.

Mechanisms of morphogenesis:

1. **Embryonic induction** is influence of a group of embryonic cells on adjacent cells (G. Shpeman, G. Mangold). The primary inductor (*an upper lip of the blastopore*) determines the formation of nerve tube, then of the notochord, and then that of the alimentary tube.

2. **Morphogenetic fields** (A. G. Gurvich) are distant cellular interactions of the electric or gravitational nature.

3. **Gradient of physiological activity** (Ch. Child) — the intensity of substances exchange in the head part of the germ is higher than that in the caudal one.

4. **Positional information of the cell** — due to intercellular interactions, every cell estimates its own position in the anlage of an organ and then differentiates according to this position.

7. Critical periods of the prenatal ontogenesis. Teratogenesis.

Periods of the maximal sensitivity of the embryo or fetus to environmental factors are called **critical periods.**

The human has 3 basic critical periods in embryogenesis:

1) *implantation* of an embryo in the mucous membrane of the uterus (6–7th day after fertilization);

2) *placentation* — the beginning of the placenta formation (14–15th day after fertilization);

3) *delivery* — coming out of the mother's organism, reconfiguration of all organ systems, modification of the way of feeding (39–40th week).

Critical periods coincide with transitions from one development period to the other and modified existence conditions of the germ.

The impairment of the course of embryogenesis under environmental factors is called **teratogenesis** (Greek *teras* — monster).

Factors causing teratogenesis are *teratogens*. They are drugs (antibiotics, quinine, chloride, anti-depressants, etc.), alcohol, nicotine, waste products of parasites, ionizing radiation.

Causes and development mechanisms of development defects are studied by teratology. Incidence frequency of development defects in human populations is 1–2 %.

Variants of congenital development defects: aplasia (hypoplasia), hypo- or hypertrophy, heterotopy, atresia, stenosis, etc.

Basic terms and concepts:

1. Aplasia — absence of an organ.

2. Atresia — imperforation of natural openings and canals.

3. Balstula — a one-layer multicellular germ with a cavity inside.

4. Gradient of physiologic activity — intensity of exchange processes in the head part of the germ are higher then in the caudal one.

5. Critical periods — are periods of the greatest sensitivity of the germ to environmental factors.

6. Morphogenetic fields — distant cellular interactions of the electric or gravitational nature.

7. Ontogenesis — an individual development of the organism from a zygote to death.

8. Progenesis — the period of formation and maturation of parental gametes that will form a zygote.

9. Stenosis — narrowing of a hollow organ canal.

10. Teratogenesis — the impairment of the course of embryogenesis caused by environmental factors.

11. Embryonic induction — the effect of a group of embryonic cells on the adjacent cells.

Topic 14. FUNDAMENTALS OF ONTOGENESIS (POSTEMBRYONIC DEVELOPMENT)

1. Postnatal ontogenesis. Types of development. Metamorphosis.

Post-embryonic (postnatal) period is a period from the moment of birth or coming out of egg membranes and to death. In this period, morphogenesis is finishd, sexual maturation and reproduction occur. The final stage of ontogenesis is aging and death.

Types of development (tab. 3).

Table 3

Types of ontogenesis

Direct development (without metamorphosis)	Indirect development (with metamorphosis)
Laying eggs with a lot of yolk (birds)	Stages of incomplete metamorphosis: egg – larva – mature individual (intestinal helminthes)
Intrauterine development (mammals)	Stages of complete metamorphosis: egg – larva – pupa – mature individual (butterflies, Diptera)

2. Division of the postnatal human ontogenesis into periods.

Neonatal period (1–10 days) is a complex period when reconfiguration of the whole organism occurs in order to adaptat to new existence conditions.

Infancy, or breastfeeding period (11 days – 12 months). A child is feed with mother's milk. The baby grows rapidly.

Early childhood (1–3 years). The child learns to walk and speak, gets acquainted with the world arround.

The 1st period of childhood (4–6 years). The child is interested in everything and tries to understand everything, get hang of basic game skills.

The 2nd *period of childhood* (7–11 years in girls, 7–12 years in boys). The growth slows, intensive development of the muscular system occurs. In this period children go to school.

Puberty, or adolescence (12–15 years in girls, 13–16 years in boys) Sexual maturation starts and growth speed intensity increases.

Juvenilty (16–20 years in girls, 17–21 years in young men) Sexual maturation, growth and physical development have completed.

1st period of middle age (21–35 years in women, 22–35 years in men) an optimal period for childbirth; mastering professional skills.

2nd *period of middle age* (36–55 years in women, 36–60 years in men) is a period of the most active professional activity. The first signs of ageing appear after 35 years).

Advanced age (56–75 years in women, 61–75 years in men). The processes of aging are going on; this is the age of retirement.

Senile age (76–90 years) Senile changes are marked; some people still can work creatively at this age.

Longevity (over 90 years).

3. Critical periods of postnatal ontogenesis.

There are **critical periods** in the postnatal human ontogenesis:

1. *Neonatal period* (the first days after birth) — reconfiguration of all organ systems for a new environment.

2. *Puberty period* (12–16 years) — a hormonal readjastment, formation of secondary *sex characters.*

3. *Period of sexual involution.* (about 50 years in women, 60–70 years in men). Reproductive function fades functional depression of gonads and endocrine glands occur.

4. Growth. Growth types of human tissues and organs. Acceleration.

Growth is enlargement of sizes and body mass. The growth can be **unlimited** (indefinite) and **limited** (definite). Unlimited growth lasts all the life (crawfishes, fish and reptiles) while limited one stops at the certain age (insects, birds, mammals).

The growth of the body in nonuniform: it is most intensive in the first year of life: body length increases by 25 cm. In the 2nd year it increases approximately by 10–11 cm, in the 3rd by 8 cm, from 4 to 7 years by 5–7 cm per year, during 2nd period of childhood it increases by 4–5 cm per year. During puberty the growth speed increases to 7–8 cm a year and then slows down and is 1–2 cm per year till the 20–25 years.

Basic growth types for tissues and organs:

– *general* type. The whole body, muscles, skeleton, respiratory organs, liver grow intensively during the 1st year of life puberty;

– *lymphoid* type. The thymus, lymp nodes and the lymphoid tissue of the intestine, spleen, tonsils grow maximally till the age of 11–12 years and then their involution occurs;

– *cerebral* type. The brain, spinal cord, eyes, head develop earlier than other parts of the body and reach sizes typical for adults by 10–12 years;

– *reproductive* type. Organs of the reproductive system grow fast during puberty.

Growth of the body is regulated by:

1. Somatotropin (a hormone of hypophysis), thyroxine (a hormone of the thyroid gland).

2. Environmental factors such as light, nutrition, vitamins (A, B, D), microelements, social-economic factors.

The somatotropic hormone is produced since the moment of birth till 13–16 years. If the function of hypophysis is lowered, pituitary dwarfism is observed; if it is increased, gigantism is observed — the human height reaches 2 meters and more. Releasing the hormone in an adult person results in acromegaly — enlargement of the hand, foot and face bones. *Thyroxine* enhance energy exchange in the organism. Decrease of the gland's function leads to the slowdown in the growth, disturbance of body proportions, arrest of sexual maturation, mental disorders. *Sex hormones* have an effect on all metabolic processes.

Environmental factors also have a great effect on growth. Balanced meal is necessary for normal growth of the child. It should include vitamins and microelements. The sun light plays an important role in synthesis of vitamin D (calciferol).

In recent decades, the **acceleration** of physical and mental development of children and adolescents is observed. It manifested already on the stage of intrauterine development — body length of newborns increased by 0.5–1.0 cm, body mass by 50–100 g, the terms of teeth cutting out changed. The human height has increased on an average by 8 cm over the recent 100 years. The following factors are supposed to cause acceleration: mixed marriages (increase the heterozygosity), urbanization, increased background radiation, a number of social factors and even changes in the Earth magnet field.

Human age.

1. *Biological age* — the age one looks.
2. *Chronological age* — the number of years a person has lived.

Criteria for determination of a biological age:

− skeletal maturity: ossification of various parts of the skeleton occurs at different ages;

− teeth maturity: appearance of milk teeth and their replacement with permanent ones occurs at a definite age;

− the time when secondary sex characters appear and their development degree.

5. Human constitution and habitus.

Constitution of the human are genetically conditioned peculiarities of human morphology, physiology and behavior. In 1927 M. V. Chernorutsky proposed the classification including three types of constitution.

Ectomorphic type (asthenics): a narrow chest, low position of the diaphragm, elongated lungs, short intestine with low absorption, thin bones and long extremities, a thin layer of subcutaneous fat. Asthenics are characterized by high excitability, tendencies to neuroses, hypotonia, ulcers, sencitivity to tuberculosis.

Mesomorphic type (sthenics): balanced constitution, moderate development of the subcutaneous fat tissue. They are people of action; have tendencies to neuralgias, atherosclerosis and diseases of the upper airways.

Endomorphic type (hypersthenics): a broad chest, voluminous stomach and long intestine, a considerable fat tissue. The amounts of cholesterol, uric acid, erythrocytes and hemoglobin in the blood are higher than in other constitution types. Assimilation processes predominate. Hyperstenics have tendencies to obesity, diabetes mellitus, hyper-tension, diseases of kidneys and galbladder.

Habitus includes peculiarities of morphology, physiology and behavior in a definite period. Habitus shows overall condition of a person and his health at a given moment. It includes: peculiarities of the constitution, pose, bearing, gait, skin color, facial expression, concordance of a biological and chronological age.

6. Ageing of the organism. Basic theories of ageing.

Ageing is a common biological regularity characteristic of all living organisms. Old age is a final stage of ontogenesis. The science about ageing and old age is called **gerontology**. It studies regularities of ageing of various organ systems and tissues. **Geriatrics** is a science about diseases of old people. It studies peculiarities of their development, course, treatment and prophylaxis.

Gerontology supposed more than 300 hypotheses of ageing. The most known of them are:

1. *Energetic theory* (M. Rubner, 1908): the organism of each species has a definite energetic fund. It is being spent during the life and then the organism dies.

2. *Intoxicating theory* (I. Mechnikov, 1903): self-poisoning of the organism due to accumulation of products of nitrogenous exchange and putrefaction in the intestine.

3. *Theory associated with the connective tissue* (A. Bogomolets, 1922): the connective tissue is a nutrition regulator of cells and tissues; its changes impair the inter-tissue interactions and result in ageing.

4. *Overstrain of the central nervous system* (I. Pavlov, 1912. G. Celie, 1936): stress and long nervous strain cause ageing.

5. *Changes of colloidal properties of the cell cytoplasm* (V. Ruzhichka, M. Marinesku, 1922): cytoplasm modifies and does not retain water properly, hydrophilic colloids transform into hydrophobic ones, colloidal particles become bigger and their biological properties change.

6. *Predetermined number of cells' mitoses* (A. Heiflick, 1965): different species have different numbers of possible cell divisions: human fibroblasts of embryos can form about 50 generations (those of mice and hen has about 15 generations).

7. *Genetic theory* is associated with accumulation of mutations, decreasing of its intensity and impairment of DNA transcription, translation and repair; impairment of self-renewal of proteins.

Social factors: living conditions, lifestyle and various diseases have a considerable impact on ageing. Ageing and the life span depend also on the ecological situation.

The science that studies a healthy lifestyle and conditions increasing human life span is called **valeology**. A theoretically possible human age is 150–200 years; a maximum registered one is 115–120 years. An average life span of men in Belarus is 62–70 years, that of women — 72–79 years.

7. Clinical and biological death. Reanimation. Problems of euthanasia.

Ageing of the organism is terminated by **death**. Death provides alternation of generations. Causes of death can be different. *Physiological death*, or natural death, occurs due to ageing. *Pathological death*, or untimely death, is the result of a disease or an accident.

A clinical death occurs as a result of termination of vital functions (heart or respiration failure), but processes of substances exchange in the cells and organs are retained.

A biological death is termination of processes of self-renewal in cells and tissues, impairment of chemical processes, autolysis and decay of cells. In the most sensitive cells of the brain cortex, necrotic changes are revealed already in 5–6 minutes after clinical death. Prolongation of the period of clinical death is possible by using general hypothermia of the organism that slows down metabolic processes and increases the resistance to anoxia.

Reanimation is complex of actions designed to return a person to life from the state of a clinical death (when vital organs are not impaired) within 5–6 minutes while cells of the brain are still alive. Reanimation methods are used in medicine in any threatening conditions.

Euthanasia — is a medical assistance to pass from life for a terminally ill patient at his will or request of his relatives. Euthanasia is allowed by law only in some countries.

Basic terms and concepts:

1. Acceleration — speeding-up of physical and mental development of new generations of children and adolescents .

2. Valeology — a science that studies a healthy lifestyle and conditions for increasing the life span.

3. Biological age — the number of years a person looks.

4. Chronological age — age confirmed by documents.

5. Habitus of the human — peculiarities of morphology, physiology, behavior in a definite time moment.

6. Geriatrics — a science studies diseases of old people, peculiarities of their development, course, treatment and prophylaxis.

7. Gerontology — a science about aging and old age.

8. Human constitution — genetically conditioned peculiarities of human morphology, physiology and behavior.

9. Metamorphosis — transformation of larval organs into organs of an adult organism.

10. Reanimation — complex of actions designed to return a person to life from the state of a clinical death.

11. Euthanasia — medical assistance for passing from life to a terminally ill patient at his will or request of his relatives.

Topic 15. INTRODUCTION TO PARASYTOLOGY

1. Origin of parasitism. Criteria of parasitism.

According to Yevgeny Pavlovsky, «parasites are animals that live at the expense of individuals of other species; they are closely associated with these speces biologically and ecologically during long or short period of their life cycle».

Criteria of parasitism:

1) spacial relations with the host;

2) feeding at the expense of the host;
3) pathogenic action on the host.

The host of the parasite is an organism that provides it with inhabitation and food and is harmed by it.

A specific habitation is characteristic of the parasite. Primary habitation is the host's organism. It actively reacts to the presence of a parasite. The secondary habitation is external environment. The host is a link between the parasite and the environment.

Parasitism is a most common form of symbiosis: all viruses, many bacteria, some kinds of fungi and higher plants are parasites. Parasites are 10 000 species of protozoans, 7000 species of arthropods, 20 000 species of helminthes. Some classes includes only parasites — Sporozoa, Flukes and Tapeworms.

Diseases caused by viruses and bacteria are called infections (flue, hepatitis, tuberculosis, etc.). Protozoans and helminthes cause invasions (ascariasis, teniasis, enterobiasis, etc.). Diseases caused by arthropods (ticks, insects) are infestations (pediculosis, myiasis, scabies, etc.).

Age of parasitism. Theoretically, parasites presumably appeared together with protists - parasitizing bacteria were revealed in the amoebae. Multicellular parasites existed in the paleozoic era: ichnolites of the stems of sea lilies (Echinodermata) had gall-like growths caused by nematodes.

Origin of parasitism:

1. **Predator → ectoparasite**. Medicinal leeches are temporary ectoparasites for the human; the leech can be predators for small animals as it sucks out a great amount of blood and the animal dies.

2. **Free-living organism → attached mode of life → ectoparasitism.** Free-living cirripedia may pass to an attached mode of life. They attach to underwater parts of wooden buildings or bottoms of ships. They pass to ectoparasitism if they attach to living objects —shells of mollusks or fish bodies.

3. **Commensalism → ectoparasitism. Commensalism → endoparasitism.** If a commensal settles on body coverings of the animal, it may become an ectoparasite. It becomes an endoparasite when gets inside the organism (in body cavities connected with the environment). Entamoeba coli is an endocommensal in the human organism.

4. **Transit through the digestive tract → endoparasitism** (larvae of a domestic fly).

Parasitism is an ecological phenomenon. **Ecological Parasitology** studies interrelations of parasites and their populations with each other, with the host's organism and the environment.

2. The «parasite–host» system. This system includes one host individual and a parasite or an entire group of parasites of one species.

Conditions necessary for the formation of this system:

a) a contact between the parasite and the host;
b) the host must have conditions for the development of the parasite;
c) the parasite must resist host's reactions.

Evolution of the system tend to improving its stability, reaching equilibrium, lessing antagonism between the parasite and the host.

Lessen of the antagonism is achieved due to co-adaptation:

– in the parasite — morphologic and biologic adaptations;

– in the host — complication of defense mechanisms.

Directions of evolution are also different (co-evolution):

– in the parasite — complication of adaptation mechanisms to the host;

– in the host — improving all defensive reactions (to kill the parasite).

Parasitic disease (parasitosis) is called *protozoasis* if its causative agents are protozoans; *helminthosis* if causative agents are helminthes; *acariasis* if causative agents are ticks and mites; *insectosis* if causative agents are insects.

Vector-borne diseases are diseases that are transmitted by the bite of infected arthropods — vectors (ticks and insects).

3. Classification of parasites and their hosts.

Classification of parasites:

1. According to relation with the host:

– *obligate parasite* — a parasitic way of life is a species character (ascarids, lice);

– *facultative parasite* — free living, but when they get into a living organism, they may become parasites (larvae of the domestic fly);

– *hyperparasites* or *superparasites* are parasites of parasites (bacteria in parasitizing protozoans).

2. According to location in the host:

– ectoparasites inhabit body coverings of the host (lice, fleas);

– endoparasites live inside the host's organism:

a) intracellular parasites (toxoplasma);

b) cavity parasites (ascaris);

c) tissue parasites (liver fluke);

d) intradermal parasites (itch mite).

3. According to duration of the relation with the host:

– *permanent parasite* — all life cycle proceeds in the host (an ascarids);

– *temporary parasite* — part of their life cycle proceeds in the host: larval parasitism (larvae of a botfly); immaginal parasitism — parasitizm of sexually mature individuals (mosquitoes, fleas).

Classification of hosts:

1. According the parasite's life stage:

a) *principal (definitive) host* — in this host, the parasite reaches its sexual maturity and reproduce sexually (the human for Taenia solium);

b) *intermediate host* — in this host, larvae of the parasite live and reproduce asexually (the human for malaria parasite);

c) *supplementary or accessory host* — additional intermadiate host (fish for a cat liver fluke).

d) *reservoir host* — in this host invasive stage of the parasite accumulates (predatory fish for larvae of Diphyllobothrium latum).

2. According to conditions of parasite's development:

a) *obligate (or natural) host* — provides optimal conditions for parasite's development and there is biocenotic contact (natural ways of invasion) — the human for the Ascaris lumbricoides;

b) *optional (or permissive, accidental) host* — there are biocenotic contact, but no normal biochemical conditions for the parasite's development (the human for the Ascaris suum - affects swines);

c) *potential host* — can provide normal biochemical conditions for the development of the parasite, but there are no biocenotic contact - no ways for invasion (guiney pig for trichinella).

4. Morphological and physiological adaptations of parasites. arasites are highly specialized organisms, maximally adapted to their inhabitation:

a) **progressive adaptations**:

– *enlargement of the body* (up to 20 m in tapeworms);

– *the reproductive system it most developed* as compared to other systems;

– *hermaphroditism*;

– *various fixation organs* (adhesive discs of Giardia lamblia, suckers of flukes, botria or hooks of tape worms, claws of lice, etc);

– *integument* — tegument or cuticle protect the patasite from host's enzymes;

– *molecular mimicry* — similarity of proteins of the parasite and the host;

– *excretion of anti-enzymes, histolysines.*

b) **regressive adaptations**:

– *simplification of sense organs* — endoparasites have only tactile and chemical sense organ;

– *simplification of the organ systems* — absence of the alimentary tract in tape worms.

Biological adaptations are associated with structural peculiarities of the reproductive system, reproduction and life cycles of parasites:

a. *high fertility* (Taenia solium excretes 100 thousand eggs with every mature segment, an ascaris — 250 thousand eggs per day);

b. *various forms of asexual reproduction* (schizogony in malaria parasite, polyembryony in flukes);

c. *migrations within the host's organism* (larvae of Taenia solium and Ascaris lumbricoides);

d. *complex life cycles* with alternation of hosts.

The results of interactions of the parasite and the host on the level organism may be different: *death of the parasite, death of the host and carriage of the parasite*.

5. Transmission rotes of parasites.

1) *alimentary* — orally with food and water (eggs of helminthes, cysts of protozoans);

2) *droplet (respiratory)* — through the respiratory tract (cysts of some Amoebae, some viruses and bacteria);

3) *vertical* — intrauterally from mother to fetus (toxoplasma, malaria parasite);

4) *iatrogenic* — due to medical procedures, for example transfusion of infected blood (trypanosomes, malaria parasite);

5) *indirect contact* — contact with a sick person or animal through household goods (itch mite);

6) *vector-borne* — with participation of an arthropod (trypanosomes, malaria parasite);

7) *sexual* — in sexual contacts (Trichomonas vaginalis).

6. Pathogenic action and specificity of parasites.

Pathogenicity is the ability to cause a disease. It depends on:

– *genotype of the parasite, its species;*

– *host's age* (children and old people are more susceptible to invasion);

– *diet regimen* (improper diet contributes to increasing the number of parasites in the organism and their sizes, reduces the terms of their development);

– *dose and degree of invasion* (the more eggs or larva get to the host's organism, the more severe is the course of the disease);

– *resistance of the host;*

– *presence of other parasites and diseases.*

Specificity of the parasite is degree of a historically formed adaptation of the parasite to the host.

Specificity has the following types:

a) *hostal specificity*: *monohostal* parasites have one species of the host (Ascaris lumbricoides), *polyhostal* parasites have hosts of several species (trichinella);

b) *topical specificity* (a site of parasitizing): Ascaris lumbricoides live in intestine and etc.;

c) *age specificity*: enterobiasis in more common for children;

d) *seasonal specificity*: outbreaks of amebic dysentery are more typical for the end of spring and summer).

Pathogenic action of parasites:

1. *Mechanical*: parasites harm tissues by their body mass (ball of Ascaris lumbricoides in the intestine, a cyst of echinococcus in the brain), by fixation organs (injury of the intestinal mucous membrane by suckers), impairment of skin, etc. This action is revealed due to a pain syndrome.

2. *Toxicoallergic action* is produced by metabolites of parasites that are antigens; histolyzins and decay products of dead parasites. Manifestations of this action: skin eruptions, dermatitis, eosinophilia, allergic reactions.

3. *Absorption of nutrients and vitamins* results in avitaminosis (mainly A and C), loss of weight, exhaustion.

4. *Impairment of the metabolic process* reduces host's resistance and increases sensitivity to pathogens of other diseases.

5. Biologically active substances of some parasites have *immune-depressive effect* on the host.

6. Some parasites *stimulate oncogenesis*: schistosomes may cause cancer of the bladder and rectum.

7. Parasites produce an *unfavorable effect on the course of pregnancy and development of a fetus* (malaria parasite, toxoplasma, cat liver fluke, etc.).

7. Host's response to parasitic invasion.

The basis of all reactions is the host's immune response. Allergy is a kind of immune reactivity. *The first reaction to a parasite* is an attempt to kill it with enzymes, then — to neutralize factors of its «aggression» by proteases, inhibitors of enzymes.

Reactions at cellular level show as hypertrophy and modification of the shape of affected cells (erythrocytes in malaria).

At tissue level: isolation of the parasite from a healthy tissue (formation of a capsule in trichinellosis, formation of pseudocysts in toxoplasmas).

At organism level: humoral reactions (production of anti-bodies) and various forms of immunity: complete — relative, active — passive, inborn — acquired.

Basic terms and concepts:

8. Anthroponoses — diseases in which causing agents are transmitted from a human to human.

9. Invasive diseases — diseases caused by protozoans and helminthes.

10. Infectious diseases — diseases caused by viruses and bacteria.

11. Hyperparasitism — relations between parasites of different species when one parasite parasitize the other parasite.

12. Obligate parasites — parasites that can complete their life cycle only in the host.

13. Criteria of parasitism — characteristics which differ parasites from non-parsites.

14. Pathogenicity — capability of the parasite to cause a disease.

15. Parasitism — antagonistic symbiosis, when the parasite use the host as a habitat and source of food and harm it.

16. Specificity of the parasite — historically formed adaptation degree of the parasite to its host.

17. Vector — organism that carries and transmits a pathogen of a disease into another organism.

18. Invasive stage — parasite's life stage that gets into a host to continue its life cycle and causes a disease.

Topic 16. PARASYTes AS pathogens of the diseases

1. Trichomonas vaginalis is a pathogen of trichomoniasis. The disease is common everywhere.

Morphological peculiarities (fig. 28): The cell is oval, has 5 flagella. An axostyle is in the middle of the body, it form sharpened long spike at the end of

the cell. Size is up to 30 μm. One flagellum follows along the undulating membrane. There is a nucleus and digestive vacuoles in the cytoplasm.

Life cycle: infection occurs in sexual contacts, through unsterile gynecological tools. Trichomonas affects genitourinary tracts; does not form cysts.

Pathogenic action.

1. *Mechanical* (destruction of the urinary mucous membranes).
2. *Toxicoallergic* (poisoning by waste products).

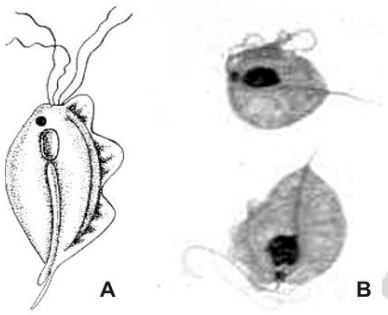


Fig. 28. Morphology of a Trichomonas:
A — scheme; *B* — microphotograph

Clinical manifestations. In acute form: itching, a burning sensation in genitourinary tracts, local inflammation, profuse greenish discharge with unpleasant smell.

Laboratory diagnostics: revealing trophozoites in direct smears from genitourinary tracts.

Prophylaxis: revealing and treating sick people, avoiding accidental sexual relationships, sterility of gynecological tools, personal and social health education.

2. Cat liver fluke. Opisthorchis felineus is a biohelminth, pathogen of opisthorchiasis (opistorchosis). The disease is common in Siberia along the bads of large rivers. Some foci can appear in Belarus and other countries.

Morphological peculiarities: the body length is 10 mm. There are a uterus in its middle, a rounded ovarium and bean-shaped seminal receptacle behind it. There are 2 rosette-shaped testes in the hind part of the body, and S-shaped canal of the excretory system between them. The canals of midgut do not branch. Viteline glands are situated on both sides of the body (fig. 29).

Life cycle: principal hosts are human, cats, dogs and other fish-eating animals. The 1st intermediate host is freshwater mollusks (Bithynia leachi), the 2nd intermediate host is freshwater fish. Life cycle stages: *marita – egg – miracidium – sporocyst – redia – cercaria – metacercaria*. Infection of a human occurs while eating undercooked fish which contains a metacercaria. Marita are located in the liver and pancreas of a principal host.

Pathogenic action:

1. *Mechanical* (injury of the walls of bile ducts by suckers and their obstruction; damaging the liver and pancreas).
2. *Toxicoallergic* (poisoning by waste products).
3. *Feeding at the expense of the host and impairment of metabolic processes.*
4. *Mutagenic* (primary liver cancer is more often in case of the disease).

Fig. 29. Morphological peculiarities of O. felineus:
A — schematic layout of marita; *B* — view of marita (×20); *C* — scheme of the egg;
D — egg (7×40)

Clinical manifestations: pains in the right hypochondrium, loss of appetite, nausea, vomiting, indigestion, weakness, headache. The liver is enlarged.

Laboratory diagnostics: revealing eggs of the parasite in feces or duodenal content. Eggs are 26–30 × 10–15 μm in size, of yellowish-brown color, oval, there is a lid on one pole. Revealing antibodies in the blood serum (immunoassay).

Prophylaxis: proper boiling, frying and salting fish (observing the rules of salting), revealing and treating sick people; prevention of contaminating water reservoirs with feces of sick animals and people; personal and social health education.

3. Taenia solium (pork tapeworm) is a biohelminth. Its sexually mature life tage causes teniasis in the human and its larvae cause cysticercosis

Morphological peculiarities: the length of the tapeworm is 2–3 m, the scolex is equipped with 4 suckers and a rostellum with 2 rows of hooks (fig. 30).

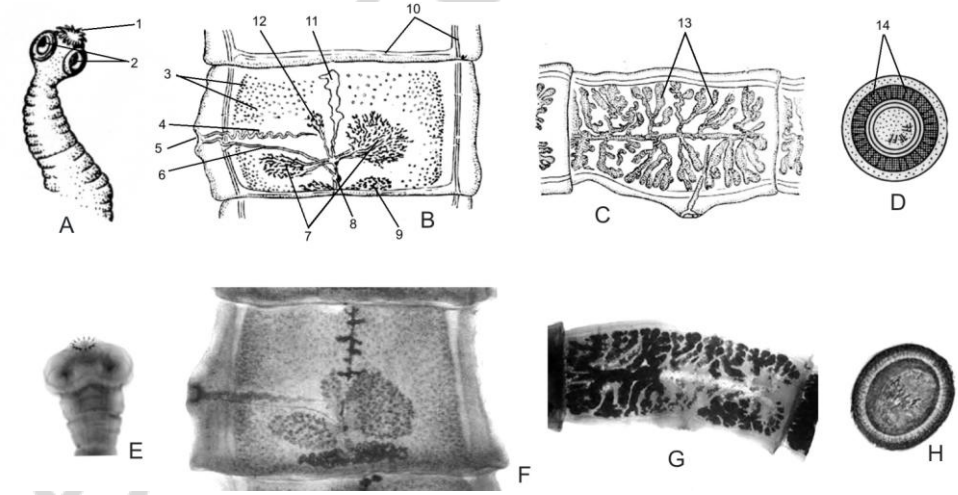


Fig. 30. Morphology peculiarities of Taenia solium:
A–D — sketches, *E–H* — microphotographs: *A*, *E* — scolexes, *B*, *F* — hermaphroditic proglottids, *C*, *G* — mature proglottids, *D*, *H* — eggs: *1* — hooks; *2* — suckers; *3* — testes;
4 — semen duct; *5* — genital atrium; *6* — vagina; *7* — ovarium; *8* — ootype; *9* — viteline glan;
10 — excretory canals; *11*, *13* — uterus; *12* — additional lobe of the pvary;
14 — radial striation

A hermaphroditic proglottid contains a thrilobed ovarium. A mature proglottid contains a uterus with 7–12 branches. Mature segments are immobile.

Life cycle: a principal host is human; an intermediate ones are domestic pigs or wild boars, sometimes human. Getting infected by teniasis occurs while eating undercooked pork with cysticerci. In the intestine a scolex screws out from the cysticercus by action of digestive juices. It attaches to the intestinal wall and begin forming proglottids. In 2–3 months a helminth reaches its sexual maturity. The life span of a tenia is several years.

Pathogenic action:

1. *Mechanical* (by irritation of the intestinal mucous membrane by suckers).
2. *Toxicoallergic* (poisoning by waste products).
3. *Feeding ate the expen the host's organism and impairment of metabolic processes.*

Clinical manifestations: pains in the abdomen, nausea, vomiting, indigestion, headache, dizziness.

Laboratory diagnostics: revealing proglottids or eggs in feces.

Prophylaxis. Personal prophylaxis consists in not eating untested pork. **Social** examination of pig and boar corpses, revealing and treating sick people, prevention of contaminating pastures with feces, sanitary improvements of settlements (closed toilets in rural areas), personal and social health education.

Cystircosis. The pathogen of cystercosis is cysticercus of a Taenia solium. **The human gets infected with cystercosis**:

1) because of noncompliance with rules of personal hygiene and swallowing eggs which can be on hands and food;

2) in autoinvasion: if a person is sick with teniasis, proglottids may get into the stomach during vomiting, then oncospheres are released from eggs, get to various organs (subcutaneous fat tissue, muscles, eyes, brain) and transform into measles;

3) in treating teniasis with drugs that dissolve proglottids.

Pathogenic action:

1. *Mechanical* (pressure on tissues).
2. *Toxicoallergic* (poisoning by waste products).

Clinical manifestations depend on intensity of invasion and location of cysticerci. Their presence in CNS may cause headaches, convulsions, paralysis of extremities and may end up with death. Intraocular cystercosis may cause a tolal loss of vision.

Laboratory diagnostics: immunoassay.

Personal prophylaxis is observing rules of hygiene, **social** measures are health education, revealing and treating sick people.

4. Human ascarides.

Ascaris lumbricoides is a geohelminth, pathogen of ascariasis. The disease is antroponosis. It is common everywhere exept arctic areas, deserts and semi-deserts.

Morphological peculiarities: the length of a female is up to 40 cm, that of a male — 25 cm. The body is cylindrical, sharpened at the ends. There are are cuticular lips on the anterior end of the body (fig. 31).

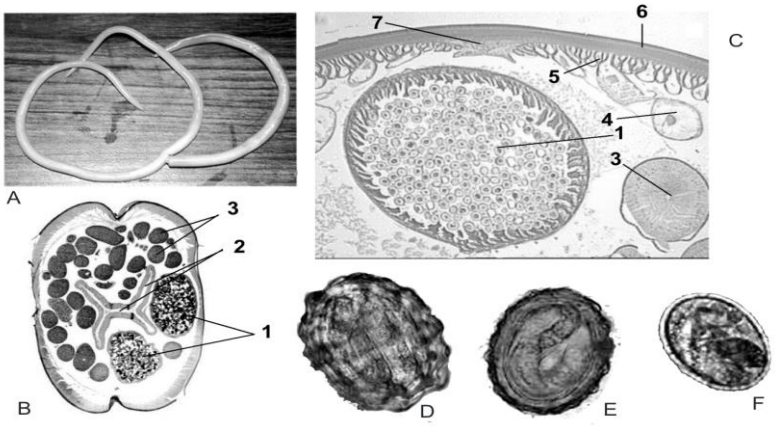


Fig. 31. Morphology of Ascaris lumbricoides:
A — sexually mature helminthes (photograph), *B* — a transverse section (7×8), *C* — a fragment of the transverse section in the area of the uterus (7×40): *1* — the uterus filled with eggs; *2* — midgut; *3, 4* — ovarium; *5* — muscular fibers; *6* — cuticle; *7* — cylinder of hypodermis; *D, E* — fertilized eggs with a larva (7×40); *F* —unfertilized egg (7×40)

Life cycle: a sexually mature ascaris is located in a small intestine. A fertilized female lays up to 240 000 eggs per day, they are excreted into the environment with feces. Eggs develop in soil in proper temperature (20–25 °C), humidity and oxygen. This takes 21–24 days. Such eggs get into the human organism with unwashed vegetables, fruit and water. In the small intestine larvae come out of eggs, perforate its wall, get into blood vessels and *migrate.* Blood carries them through the liver, right atrium, right ventricle, pulmonary trunk and alveolar capillaries. Through the capillary walls larvae get into alveoli, ascend to bronchioles, bronchi, trachea and get into the pharynx to be swallowed. In 2.5–3 months they transform into sexually mature worms in a small intestine. Larval migration lasts about 2 weeks. The life span of mature ascaris is about 1 year

Larvae of another ascaris species (ascaris of pigs, dogs, etc.) may also migrate in the human organism but cannot complete the life cycle. The syndrome they cause is called Larva migrans.

Pathogenic action of larvae of ascaris:

1. *Toxicoallergic* (poisoning by waste products).
2. *Mechanical* (injury of the liver, rupture of capillaries, injury of alveoli).
3. *Feeding at the expense of the host's organism and impairment of metabolic processes (absorption of nutrients and vitamins).*
4. *Mutagenic.*

Clinical manifestations of larval migration stage of ascariasis: persistent spastic cough especially at night, skin rash and itching, weakness, fever, headache, perspiration, oedema of lids and face.

Clinical manifestations of intestinal stage of ascariasis: pains in the abdomen, nausea, vomiting, diarrhea, worsening of appetite, weakness, irritancy, worsening of memory, loss of weight.

Complications of intestinal ascariasis: obstructive jaundice, purulent pancreatitis, purulent cholangitis, appendicitis, peritonitis, spastic and mechanic intestinal obstruction. Sometimes ascarides are found in frontal sinuses, cranial cavity, middle ear and ovaries.

Personal prophylaxis involves observing rules of hygiene, washing vegetables, fruits and berries with hot water. It is necessary to protect food from flies and cockroaches as they are mechanical vectors for eggs of ascaris. **Social prophylaxis** is revealing and treating sick people, protection of the environment from contamination with ascaris eggs, health education.

5. Sarcoptes scabiei (itch mite).

Morphology: the mites have wide, oval, slightly-yellow colored body, covered with bristles. The body sizes are from 0.3–0.4 mm, legs are conical-shaped and shortened, eyes are absent (fig. 32.). They breathe with the whole body surface.

Fig. 32. Morphology of Sarcoptes scabiei:

Life cycle: Sarcoptes scabiei is permanent parasite of the human and animals that burrows into skin and causes *scabies*. Fertilized female burrows into the stratum corneum of the skin per 2 mm a day and lays about 50 eggs in the burrow. Males do not burrow the skin. The mites feed on the host's tissues. The development from an egg to an imago takes about 1–2 weeks. Adult mites live up to 2 months.

Medical significance: the most common symptom is severe itchiness becoming worse at night. These symptoms can be present across most of the body or just certain areas such as the wrists, between fingers, or along the waistline. Scabies is spread during a direct skin contact with a sick person or their clothes. Secondary infection may get in scratches and cause suppuration.

Prophylaxis of scabies: following basic hygiene rules in comminicating with animals and sick people; maintaining the purity of the body; revealing and treating sick persons; sanitary inspection of hostels and bathhouses.

6. Lice (order Anoplura).

Taxonomy: trere are two genera in order Anoplura: genus **Pediculus** and **Phthirus**. Genus Pediculus is represented by one species. **Pediculus humanus** includes 2 subspecies — the **head louse** and the **body louse** which freely cross and

give fertile offspring, but they have some morphological and biological differences.

Head louse (Pediculus humanus capitis).

Morphology: the length of a male is about 2–3 mm, female — 3–4 mm. The posterior end of male's body is rounded, the female body is forked. Mouthparts are piercing-sucking (fig. 33).

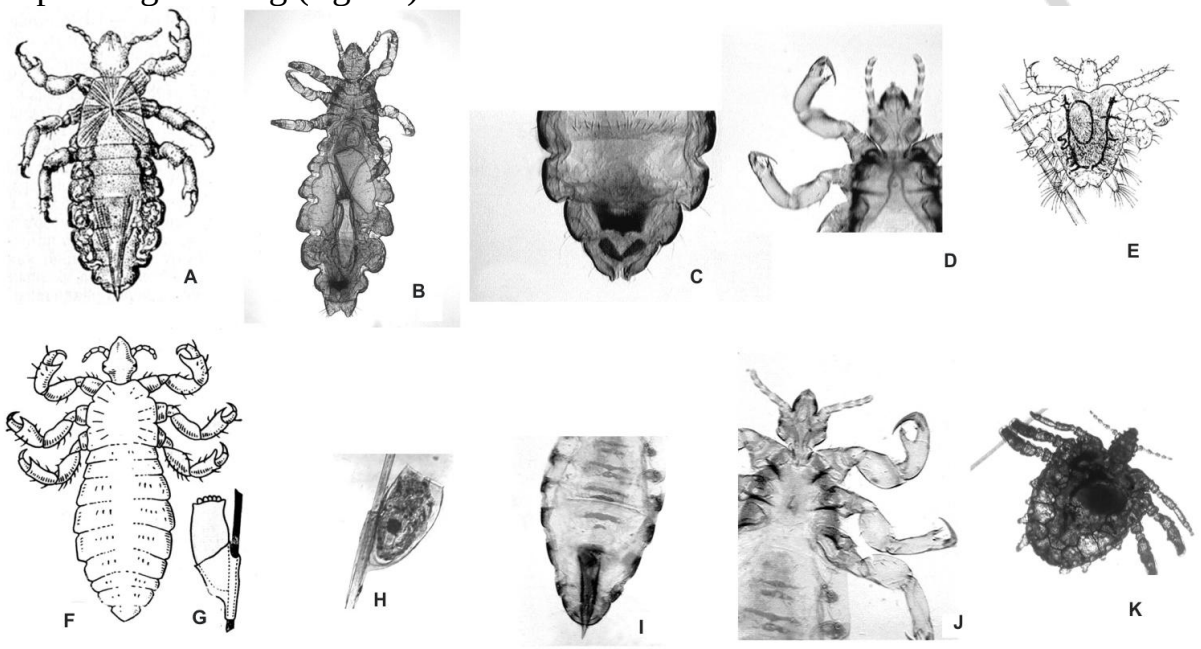


Fig. 33. Representatives of the order Anoplura:

A — Pediculus humanus capitis (scheme); *B*, *C*, *D* — Pediculus humanus capitis (7×8); *F* — Pediculus humanus humanus (scheme); *G*, *H* — nits; *I*, *J* — Pediculus humanus humanus (7×8); *E* — Phthirus pubis (scheme); *K* — Phthirus pubis (7×8)

Life cycle: lice live in the hairy area of the head. They feed on human blood 2–3 times a day, may starve for several days. The life cycle of the body louse consists of three stages: egg (**nit**), nymph, and adult. **Nits** are attached to hair with a sticky secretion. During the whole life (about 38 days) a female lays about 300 eggs. A larva comes from an egg and in several days transforms into imago (a mature form).

Body louse (Pediculus humanus humanus).

Morphology: body louse has larger body sizes than the head louse (to 4.7 mm), carvings along the body edge are not so deep and pigmentation is slightly marked.

Life cycle: body lice live on underwear and clothes, but feed on the skin. Nits are sticked to the clothes or to the hair on human body. The life span is up to 48 days, the development lasts not less than 16 days. By the end of its life female can have about 4000 offspring.

Medical significance: lice of genus Pediculus cause *pediculosis* (or *Vagabond's disease*). During blood feeding lice introduce saliva into the wound. This causes itching. Pediculosis is characterized by pigmentation and scraching on the skin. Lice are specific vectors of *epidemic typhus* (caused by bacterium *Rickettsia*

prowazekii) and a *louse-borne relapsing fever* (caused by bacterium *Borrelia recurrentis*).

Infection of epidemic typhus occurs by a **specific contamination** - rubbing louse intestine content into wounds or into scratches on the skin, and by **contamination** in rubbing lice feces into the skin during scratching. Human can also get louse-borne relapsing fever by a specific contamination - smashing louse and rubbing its hemolymph into the skin during scratching.

Pubic louse (Phthirus pubis) is an ectoparasite of humans; feeds on blood.

Morphology: sizes up to 1.5 mm. The body is short, almost round.

Life cycle: parasitizes usually in the human pubic hair but can also live in other body areas covered with coarse hair, such as armpits, eye-lashes, beard. The female lays about 50 eggs during its life. The life cycle from an egg to a mature form lasts 22–27 days.

Medical significance: pubic lice cause *phthiriasis* (severe itching usually in the pubic-hair area). Human can get phthiriasis by sexual contacts, rarely — through underwear and clothes.

Protective measures against lice: extermination them in the environment, on the human body and on clothes.

Basic terms and concepts:

1. **Prglottid** — a body segment of tapeworms.
2. **Biohelminthes** — worms that require several different host to complete their life cycle.
3. **Cisticercus** — a measle of a Taenia solium.
4. **Dehelmithization** — a complex of measures to eliminate helminthes in the human organism.
5. **Geohelminthes** — worms that have life stages requiring development in soil.
6. **Marita** — a sexually mature life stage of flukers.
7. **Metacercaria** — an invasive stage for a principal host in the life cycle cycle of flukes.
8. **Migration of larvae** — changing the site of parasitizing by a larval stage of roundworms in the human organism.
9. **Migration ascariasis** — a stage of ascariasis associated with migration of ascasis larvae within the body.
10. **Miracidium** — the 1st larval stage in the fluke development cycle.
11. **Pediculosis** — a disease caused by lice of g. Pediculus.
12. **Phthiriasis** — a disease caused by a pubic louse.
13. **Scolex** — a head of tape worms.
14. **Strobila** — a body of tape worms consisting of segments.

Topic 17. VENOMOUS AND POISONOUS ANIMALS

1. Classification of venomous and poisonous animals.

Animals are venomous or poisonous if their organism produces or accumulates substances that can cause death or impairment of vital functions for another organism. There are about 5 000 species of such animals: protozoans — 21, coelenterates — 93, parasitic worms — 16, ringworms — 50, arthropods — about 4000, mollusks — 91, echinodermates — 26, fishes — 500, amphibians — 40, reptiles — 250, mammals — 1 species. According to the presence or absence of special venomous glands animals are primarily-toxic and secondarily-toxic. According to the presence of specific apparatus for injecting venom into the victim («armed»), animals are divided into venomous and poisonous.

Primarily-toxic animals have special glands to produce toxine or specific toxic metabolites. As a rule, toxixity of these animals is a character of the species (jellyfish, scorpions, snakes, fishes).

Secondarily-toxic animals accumulate exogenous toxines from the environment. Such animals are *poisonous* if they are eaten by other organisms (fish adsorb industrial toxins from water).

The primarily-toxic animals are divided according to the ways of producing and using their toxines.

Actively-toxic venomous («armed») animals have a specialized apparatus such as thread cells on tentacles of jellyfishes, a stinger in hymenoptera and fangs in snakes. Venom is injected into the body of the victim parenterally (avoiding the digestive tract).

Actively-toxic poisonous («unarmed») animals have no such apparatus. Secretions of their glands are poisonous in case of direct contact with integuments of the victim (skin glands of amphibians, anal glands of insects).

Passively-toxic poisonous animals (fishes, caudate amphibians, mollusks) can have toxic metabolites that are accumulated in various organs and tissues. They are dangerous only when eaten by a victim.

2. Physiological characteristic of toxins of invertebrates (jellyfish, arachnids, hymenopterans), their effect on the human body; the first aid and prophylaxis of bites and poisonings.

Characteristic of animal toxines. Animal toxines (zootoxins) are biologically active substances that actively interact with biological structures of the body. Zootoxins are diverse by their chemical structure (alkaloids, histamine, various enzymes and their inhibitors).

According to the physiological effect on living systems, zootoxins are subdivided into:

1) neurotoxins affecting predominantly the nervous system;
2) cytotoxins causing damage of cells and tissues;
3) hemorrhagins impairing normal permeability of blood vessels;
4) hemolysins destroying erythrocytes.

A clinical presentation of toxication of human depends on composition of the toxine, the site of affection, the season of the year and the time of the day as well as a overall condition of the person.

Coelenterates (orange-striped jellyfish and physalia) refers to *actively-venomous* animals. Thread cells excrete a neurotropic venom that blocks synapses.

Clinical presentation. In sites of sting by tentacles of the orange-striped jellyfish appears sharp pain, erythema, rash. Symptoms temperature rise, rapid decrease of muscle tone, pains in extremities and lumber area, impairment of consciousness, hallucinations, delirium, respiratory and cardiac affection, in severe cases — death.

First aid. It is required to remove parts of tentacles and striking threads from the skin, treat the affected sites with alcohol or solution of soda.

Prophylaxis. Not to bathe in the thicket of water plants and in places of jellyfish gatherings.

Phylum Arthropoda, class Arachnida, order Scorpions (yellow, Italian, black). They are actively-venomous, have venomous glands located in the last segment of the abdomen. They excrete neurotropic venom that blocks neuromuscular synapses.

Clinical presentation. At the site of a bite appears a severe pain, edema, erythema, vesicles. Symptoms: headache, weakness, impairment of consciousness, and respiration, tachycardia in children. Lethal outcomes are possible.

First aid. Sucking off the venom, applying cold to the site of a bite, taking pain-killers. Injection of specific antiserum.

Prophylaxis. Protection from bites: examination of dwellings, bedding, clothes, shoes.

Order Arachnida. Spiders are actively-venomous. Ducts of their venomous glands open on chelicerae.

Karakurt has neurotropic venom that blocks neuromuscular synapses.

Clinical presentation. At a bite site appears pain, numbness of extremities. Symptoms: pain quickly spreading throughout the body, headaches, breathlessness, heartbeat, bronchial spasms, vomiting and impairment of consciousness. Lethal outcomes are possible.

First aid. Sucking off the venom, slight of the bite site, injection of an anti-karakurt serum can be used. *Prophylaxis.* Prevention from getting caracurts to the places of human lodging for the night.

Tarantulas*'s* venom contains cytotoxins and hemorrhagins and impair permeability of capillary walls.

Clinical presentation. At a bite site appear pain, reddening, edema, skin necrosis. Symptoms: malaise, sleepiness, chills, pulse acceleration, perspiration.

First aid. To treat the site with disinfectants, ensure rest, abundant drinking, pain-killers for the patient. *Prophylaxis:* protection from bites.

Class Insecta, order Hymenoptera (bees, wasps). These insects are actively-venomous, have toxic glands and a sting at the end of the abdomen. The venom has a neurotropic and cytotoxic action and is a strong allergen.

Clinical presentation. After a bite — pain, edema, erythema. Possible symptoms: allergic reactions.

3. Physiological characteristic of toxins of vertebrate animals (fishes, amphibians, reptiles), their effect on the human; the first aid and prophylacxis of bites and poisoning.

Toxic fishes are divided into 2 groups:

1. Venomous species having toxic glands; the secretion of these glands is injected into the wound made by fin rays, teeth or thorns of branchial covers. Representatives: sting ray, sea dragons, ruffs and perches, moray eels, devilfish, firefish. They are spread predominantly in tropic latitudes of the Pacific and Atlantic Oceans.

Pathogenic action and clinical presentation. Toxins pass into the organism through a wound on the skin. At the moment of a prick victim feels pain that quickly spreads to the whole extremity. Then appear fear, breathlessness, heart pain, vomiting and sometimes loss of consciousness. Inflammation, sometimes ulcers and tissue necrosis develop at the bite site. A severe poisoning ends with death within a day.

Treatment: sucking off the venom from the wound, applying a rope, symptomatic treatment. Prophylaxis includes putting on special clothes if deal with the fishes.

2. Fishes that are poisonous when eaten (moray eels, thons, perciformes, pufferfish). When these fishes are used as food, poisoning develops in 20–30 minutes. There appears numbness of the tongue and fingers, nausea, vomiting, breathlessness, respiratory and speech affection. The treatment is symptomatic. As prophylaxis, the mentioned fishes should be excluded from the diet.

Amphibians. There are some toxic substances in the skin of some amphibians. The most virulent poison is produced by African tree-frogs and tree-toads. Toxine of the Columbian cocoa frog (the length of 2–3 cm, the weight is a bit more than 1 g) is 50 times stronger than a tetanus toxin. Other toxic amphibians are not dangerous for the human (they have no mechanism for injecting the toxin into tissues). When their poison gets on the skin or mucous membranes, erythema and inflammation are observed. These symptoms are relieved by washing with water. It is necessary to take care lest amphibians' poison gets to the eyes.

Class Reptila. Families elapids and sea serpents (king cobra and Indian cobra, long-glanded coral snakes, sea kraits). These are primarily-toxic actively-venomous animals. They have toxic immobile fangs with canals for the venom on the anterior part of the maxilla.

Pathogenic action and clinical presentation. The venom contains neurotoxins, cytotoxins, hemolysins. At a bite site develops pain, edema, inflammation. Symptoms: excitation and then depression of CNS; swallowing, speech and breathing are impaired. Lethal outcomes are possible.

Family Viperidae (blunt-nosed viper, phoorsa, Orsini's viper, copperhead snake, rattlesnakes). They are primarily-toxic actively-venomous animals. They have toxic glands and fangs with canals.

Pathogenic action and clinical presentation. The venom contains neurotoxins, cytotoxins, hemolysins, they stimulate blood coagulation. At a bite site develops pain, edema, tissue necrosis. Symptoms: weakness, nausea, dizziness, impairment of blood coagulation. Lethal outcomes are possible.

First aid. The bite site should be treated with an antiseptic and a compressing bandage should be applied. The patient should be transported in a lying position. Injection of snakes' antitoxins should be done.

Prophylaxis: in places of snakes' inhabitance one should not touch them and wear high boots.

Basic terms and concepts:

1. **Primarily-toxic animals** —animals having special glands for production of toxic secretion or some toxic metabolites**Mechanical vector** — vector that transmits pathogens on body surface or on mouthparts.

2. **Secondary-toxic animals** — animals that accumulate exogenous poisons and are toxic when eaten.

3. **Actively- toxic poisonous animals** — have venomous glands but no specialized apparatus for injection of their venom.

4. **Actively-toxic venomous animals** — have venomous glands and a specialized apparatus for injection of their venom.

5. **Passively- toxic poisonous animals** — animals that have toxic metabolites accumulated in various organs and tissues.

GAP-FILLING TESTS

BIOLOGY OF THE CELL. THE FLOW OF SUBSTANCE AND ENERGY IN THE CELL

1. Division of the cell cytoplasm into sections by plasma membranes is called ... .

2. The receptor apparatus located on the outer surface of plasmalemma is called ... .

3. ER (endoplasmic reticulum) and ... form the transport system of the cell.

4. The destruction of cell organelles by its own lysosomes is called ... .

5. Integral proteins in the outer mitochondrion membrane forming pores and providing permeability of membranes are called … .

6. The large subunit of ribosomes contains 40–50 molecules of proteins and … molecules of rRNA.

7. The efficiency of the anaerobic stage of energy exchange is ... %.

THE FLOW OF GENETIC INFORMATION IN THE CELL

8. The nuclear lamina consists mostly of proteins that are called…

9. A protein complex at the site of primary constriction of a chromosome which provide attachment of division spindle fibers is called ... .

10. A chromosome site of a secondary constriction is ... .

11. The content of genetic material in a cell during the G_2 period is … .

12. The content of genetic material in a cell during the diplotene is … .

13. The content of genetic material in a cell during the diakinesis is … .

14. The content of genetic material in a cell during the pachitene is … .

15. Bivalents are bound together only by sites called ... during the diplotene.

16. ... are situated in the equatorial plate during the metaphase of meiosis I.

17. The content of genetic material in a cell during the metaphase of meiosis II is … .

ORGANIZATION OF HERIDITARY MATERIAL

18. The autosynthetic function of the DNA molecula is its … .

19. The DNA-polymerase can move along the matrix strand from the … end to the … end.

20. The direction of the genetic information reading from the 5′ to the 3′-end is the property of the genetic code called ….

21. Identification of an amino acid by a corresponding tRNA is called … .

22. There is the mRNA triplet … in the peptidyl site of a ribosome during initiation of translation.

23. The process which begins with formation of the first peptide bond and ends up with addition of the last amino acid to the polypeptide molecule is called ….

24. Antibiotics are the … of protein biosynthesis.

INHERITANCE REGULARITIES. INTERACTION OF GENES

25. Characters with different qualitative states are called … .

26. The second and third Mendel's laws require the gene penetrance … %.

27. Bombay phenomenon is an example of the genetic interaction which is called … .

28. Phenotypic segregation in ratio 9:7 in crossing diheterozygotes results from interallelic gene interaction called … .

29. Independent combination of two pairs of allelic genes during an analyzing cross result in phenotypic segregation ... in the first generation of offspring.

30. Alleles presented in the populations more than in two states are called ….

GENETIC LINKAGE

31. Conditions limitting Mendel's 3rd law are: incomplete penetrance of genes, lethal and semi-lethal genes, unequal formation of different types of gametes and zygoteges, pleyotropy, various interactions of genes apart from complete dominance and ... .

32. If a diheterozygous organism forms only 2 types of gametes, then genetic linkage is... .

33. If a diheterozygous organism forms 4 types of gametes, then genetic linkage is... .

34. If crossing-over occur between the genes of a pair of homologous chromosomes, then genetic linkage is... .

35. Biological phenomenon breaking the genetic linkage is … .

36. The distance between genes measured in morganids is equal to % of … .

37. The maximal probability of crossing-over for linked genes is ... %.

38. Individuals formed from crossover gametes are called … .

39. The number of human's autosomal linkage groups is ….

VARIATION

40. Enzymes capable of cutting out the damaged part of the DNA during the repair are … .

41. Transgenation when one purine base is replaced with another purine base is called ... .

42. … of the terminal parts of chromosomes leads to formation of ring chromosomes.

43. Mutation of … genes leads to the impairment of alternation of repression and induction of genes.

44. Non-disjunction of chromosomes during the mitosis or meiosis leads to … mutations.

45. Aneuploidy when only one chromosome of a pair is present in the karyotype is called … .

46. Genome mutation when somatic cells have single chromosome set is called … . .

BIOLOGY AND GENETICS OF SEX

47. Two Barr bodies in the nucleus of a female somatic cell are typical for the … syndrome.

48. Female phenotype, low position of ears, short neck with a skin fold are typical for the … syndrome.

49. Men with female constitution, gynecomastia and impairment of spermatogenesis suffer from … syndrome.

50. Phenomenon when sexual excitement and satisfaction are reached while wearing clothes of the opposite sex is called … .

51. Human chromosomal diseases of sex result from the impairmnt of the process called ….

52. Charactrs determined by genes located in the non-homologous region of theY-chromosome are called … .

53. Persistent discordance of person's sexual self-conscious and his real genetic and gonad sex is called … .

FUNDAMENTALS OF HUMAN GENETICS

54. Person from whom medical-genetic examination of family and compiling genealogy start is called … .

55. If parents are heterozygous (complete dominance, type of inheritance is autosomal-dominant and gene penetrance 25%), then the probability of giving birth to a sick baby is ... %.

56. If a mother is heterozygous and a father is healthy (X-linked dominant inheritance, gene penetrance is 40%), then the probability of giving birth to a sick baby is ... %.

57. Determining the order of nucleotides and finding a pathologic gene is possible by the method of nucleic acids' … .

58. Type of inheritance when the father transmits his character to all daughters, but neither to sons is called ... .

59. Method of human genetic that allows to reveal the role of heredity and environment in the formation of a character is called … .

60. Genetic method that allows to reveal genome and chromosome mutations is called … .

61. Chorion biopsy is performed within … weeks of pregnancy.

62. Each pregnant woman compulsory undergoes … — a direct non-invasive method of prenatal diagnostics.

63. Mother's age of over 37 years, spontaneous abortions and stillbirth in the anamnesis, children with congenital malformations are indications for carrying out ... methods of prenatal diagnostics.

64. Y-sexual chromatin is determined at staining of buccal epithelium cells by … .

GENETIC ENGINEERING

65. Enzymes called … are used in the genetic engineering for obtaining genes.

66. Enzymes capable of cutting the DNA molecule in certain sites and form «sticky ends» are called … .

67. The method allowing synthesis of genes by reverse transcription is called … .

68. Bacterial plasmids, phage and viral genome, phasmids and … can be used as vector molecules in genetic engineering.

69. Hybrid vectors capable of developing both as a phage and as a plasmid are called … .

70. The plasmids containing cos-sites (sticky ends) of phage λ DNA are called … .

71. Restrictase Eco R I forms … when cuts the DNA.

72. Restrictase Hind II forms … when cuts both DNA strands in same places.

GENETICS OF POPULATIONS

73. Human populations with the number not exceeding 1500 people where intragroup marriages surpass 90 % are called ….

74. Genetic load has no phenotypic manifestation when … of a pathological gene is observed.

REPRODUCTION OF ORGANISMS

75. Exchange of genetic information between individuals of one species is called ... .

76. Confluence of female and male pronuclei during fertilization is called ... .

77. Sexual reproduction without fertilisation is called ... .

78. Ovum containing a lot of yolk concentrated at one of the poles is called ... .

79. Complete equal cleavage is typical for ... ova.

80. During the period of proliferation of gametogenesis, cells divide by ... .

81. During the period of maturation of gametogenesis, cells divide by ... .

82. Asexual reproduction of a germ that was made by sexual reproduction is called … .

83. Gamones contributing to spermatozoon's fixation on the ovum's membrane are called … .

84. Spermatozoons possess the ability of fertilization within … .

FUNDAMENTALS OF ONTOGENESIS (EMBRYONIC DEVELOPMENT)

85. Mitotic divisions of a zygote and blastomeres during the initial stage of embyogenesis is called ... .

86. Period of human embryonic development from the 4th week to the end of the 8th week is called ... .

87. Type of gastrulation when some cells of blastoderm move into the blastocoel to multiply there and form the second layer of cells is called... .

88. Organisms, in which blastopore transforms into the anal opening and the mouth forms on the opposite side of the body, are called ... .

89. Amnion, chorion, allantois, yolk sac and placenta are ... organs of chordates.

90. The primal cause of cells differentiation in the of embryogenesis is... of the ovum cytoplasm.

91. Impact of a group of embryonic cells on the nearly located ones by specific substances is called ... .

92. Gradual decrease of metabolism intensity in fetus from its head to the caudal part is called ... of physiological activity.

FUNDAMENTALS OF ONTOGENESIS (POSTEMBRYONIC DEVELOPMENT)

93. Thymus and spleen are characterized by … type of growth.

94. The hormone of hypophysis ... play the main role in regulation of human growth.

95. The phenomenon of speeding-up growth, sexual maturity, physical and mental development of children and adolescents is called ... .

96. Stable, genetically determined peculiarities of morphology, physiology and behaviour of a person make his ... .

97. People of … constitutional type are predisposed to neuroses, ulcerous disease, tuberculosis.

98. Peculiarities of development, course, treatment and prevention of diseases of old people are studyed by the science called ... .

99. Science which studies healthy lifestyle is called ... .

100. The state of an organism characterized by cardiac and respiratory arrest, loss of consciousness but without impairments of metabolism, is called … death.

101. Medical assistance to pass from life for a terminally ill patient according to his will or request of his relatives is called ....

INTRODUCTION TO PARASITOLOGY

102. Free-living organisms, which can be parasites in case of invading the organism of other species, are called ...

103. Hosts providing optimal biochemical conditions for the development of the parasite and which have biocoenotic relations with it, are called ...

104. Hosts providing biochemical conditions for the development of the parasite, but which don't have biocoenotic relations with it, are called ...

105. Hosts characterized by the presence of biocoenotic relations with parasites, but have no optimal biochemical conditions for their development, are called ...

106. Way of parasite invasion in to the host organism with water and food-stuffs is called ...

107. Way of parasite invasion in to the host organism through mucous membranes of respiratory tract is called ...

108. Way of parasite invasion in to the host organism by immediate contact with a sick person or animal and with household objects is called...

109. Way of parasite invasion in to the host organism when transfusing unsterile donor blood is called ...

PARASYTES — PATHOGENS OF THE DISEASES

110. Vegetative form of protozoans is called... .

111. Supporting axis of some Zoomastigotes is called ... .

112. Trichomonas vaginalis has ... flagella.

113. Fluke which has 2 rosette-like testes and S-like canal of the excretory system between them is called ... .

114. Life cycle of the cat liver fluke: marita → egg → miracidium → sporocyst → redia → ... → metacercaria.

115. Measle of a Taenia solium is called ….

116. Hermaphroditic progottids of Taenia solium have an ovarium consisting of ... lobes s.

117. Mature proglottid of Taenia solium have... branches of the uterus.

118. Life span of mature Ascaris in the human body is about ... .

119. Pediculus humanus capitis and Pediculus humanus humanus cause ...

120. Phthirus pubis causes ….

121. Eggs of lice are called ... .

122. Lice of the genus Pediculus are specific vectors of … and … .

123. Patogens of relapsing feverare ... .

VENOMOUS ANIMALS

124. Animals having glands producing toxins and specialized apparatus for its injection are called … .

125. According to physiological effect on the body zootoxins are divided into neurotoxins, cytotoxins, hemorrhagins and … .

126. Physalia's stinging organs are … .

127. Toxin of a scorpion belongs to … .

128. Toxin of a karakurt belongs to … .

129. Toxins of a Brazilian spider belong to cytotoxins and … .

130. Toxins of hymenopterans belong to cytotoxins and … .

131. Toxin of Colombian cocoa frog is … times stronger than tetanus toxine.

132. Viper snakes are primarily-toxic … animals.

MULTICHOICE TESTS

BIOLOGY OF THE CELL. THE FLOW OF SUBSTANCE AND ENERGY IN THE CELL

1. erties of plasma membrane are: a) plasticity; b) impermeability and fluidity; c) semi-permeability; d) elasticity; e) self-locking.

2. Transport of substances into the cell that require ATP energy is: a) transport of ions into the cell according to the concentration gradient; b) phagocytosis; c) pinocytosis and diffusion; d) osmosis and endocytosis; e) transport of substances into the cells against the concentration gradient.

3. Organelles of the cell anabolic system are: a) mitochondria and endoplasmic reticulum; b) ribosomes and Golgi complex; c) endoplasmic reticulum; d) lysosomes and peroxisomes; e) glyoxysomes and ribosomes.

4. Organelles of the cell catabolic system are: a) mitochondria; b) ribosomes, glyoxysomes and endoplasmic reticulum; c) endoplasmic reticulum and mitochondria; d) Golgi complex and peroxisomes; e) peroxisomes and lysosomes.

5. Ribosomes are located: a) on membranes of endoplasmic reticulum and in hyaloplasm; b) in hyaloplasm and karyoplasm; c) on internal nuclear membrane and in chloroplasts; d) on external nuclear membrane and in the mitochondria; e) in mitochondrial matrix and lysosomes.

6. Functions of the endoplasmic reticulum are: a) synthesis of proteins; b) DNA synthesis and compartmentalization; c) synthesis of fats and carbohydrates; d) compartmentalization and transport of substances; e) formation of peroxisomes and RNA synthesis.

7. Functions of Golgi complex are: a) sorting, packing and secretion of substances; b) formation of lysosomes and complex organic compounds; c) synthesis of ATP, proteins and glyoxysomes; d) synthesis of cell membranes; e) protein synthesis and substance secretion.

8. Functions of mitochondria are: a) synthesis of specific proteins; b) splitting of proteins into amino acids; c) synthesis of monosaccharides and ATP; d) synthesis of AMP (adenylic acid); e) splitting of organic substances into H_2O and CO_2.

9. Anaerobic stage of energy exchange occurs in: a) intestine; b) cytoplasm and mitochondria; c) cytoplasm and endoplasmic reticulum; d) cytoplasm; e) Golgi complex and cell nucleus.

THE FLOW OF GENETIC INFORMATION IN THE CELL

10. IProcesses that take place in the cell during the pre-synthetic period of interphase are: a) synthesis of RNA, proteins and enzymes; b) synthesis of DNA, RNA, proteins and ATP; c) ATP synthesis and cell growth; d) accumulation of DNA nucleotides, synthesis of proteins of a division spindle; e) synthesis of DNA, RNA and proteins of a division spindle.

11. Processes that take place in the cell during the post-synthetic period of interphase are: a) synthesis of DNA and enzymes; b) synthesis of DNA, rRNA, cell growth; c) ATP synthesis; d) accumulation of DNA nucleotides; e) synthesis of proteins of a division spindle.

12. The content of genetic material in the cell at the end of synthetic period of interphase is: a**)** 1n 1chr 1c; b) 1n 2chr 2c; c) 2n 1chr 2c; d) 2n 2chr 4c; e) 1n 4chr 4c.

13. Causes of mitosis are: a) increase of nuclear-cytoplasmic ratio; b) decrease of nuclear-cytoplasmic ratio; c) replication of DNA and «wound hormones»; d) «wound hormones» and mitogenetic rays; e) impairment of karyolemma's integrity.

14. The content of genetic material in the cell during the telophase of mitosis is: a) 1n 1chr 1c; b) 1n 2chr 2c; c) 2n 1chr 2c; d) 2n 2chr 4c; e) 1n 4chr 4c.

15. Cells that divide by mitosis are: a) somatic cells; b) cells of gonads; c) gametogoniums; d) tumor cell; e) cells of regenerating tissues.

16. Cells that divide by amitosis are: a) somatic and old cells; b) cells of gonads and embryo; c) gametogoniums; d) tumor cells; e) cells of regenerating tissues.

17. Cells that divide by meiosis are: a) somatic and old; b) cells of gonads and embryo; c) gametocytes; d) tumor cells; e) cells of regenerating tissues.

18. Content of cell genetic material in meiosis I prophase is: a) 1n 1chr 1c; b) 1n 2chr 2c; c) 2n 1chr 2c; d) 2n 2chr 4c; e) $1n_{biv}$ 2chr 2c.

19. Processes that take place in the cell during the telophase of meiosis I are: a) condensation of chromatin and dissolution of nucleolus; b) decondensation of chromosomes and formation of nucleolus; c) formation of karyolemma; d) synspsis of chromosomes and crossing-over; e) cytokinesis.

ORGANIZATION OF HERIDITARY MATERIAL

20. Amount of A+G is equal to amount of: a) A + T; b) C + T; c) G + T; d) A + C; e) G +C.

21. Bonds between complementary nucleotides in a two-strand DNA are: a) hydrogen; b) covalent; c) phosphodiester; d) peptide; e) disulfide.

22. DNA functions are: a) storage and reproduction of genetic information; b) transport of amino acids to ribosomes; c) transmission of genetic information to daughter DNA molecules; d) transport of amino acids; e) determination of rRNA synthesis.

23. Functions of tRNA are: a) storage of genetic information; b) transport of amino acids to ribosomes; c) transmission of the genetic information to daughter tRNA molecules; d) direct participation in assembling of polypeptides; e) transfer of the genetic information from DNA to the ribosome.

24. Gene properties are: a**)** stability and lability; b) integrity and pleiotropy; c) integrity, specificity and unambiguity; d) discretion and absence of specificity; e) specificity, tripletness and universality.

25. Specificity is the gene property to: a) mutate; b) determine synthesis of the certain polypeptide; c) be responsible for exhibiting several characters; d) vary the degree of its phenotypic manifestation; e) have different frequency of phenotypic manifestations.

26. Pleiotropy is the gene property to: a) mutate; b) determine synthesis of the certain polypeptide; c) be responsible for exhibiting several characters; d) vary the degree of its phenotypic manifestation; e) have different frequency of phenotypic manifestations.

27. Elementary structural unit of a gene is: a) nitrogenous base; b) pair of complementary nucleotides; c) codon; d) one nucleotide; e) triplet of nucleotides.

28. Elementary functional unit of a gene is: a) one nucleotide; b) pair of complementary nucleotides; c) codon; d) transcripton; e) triplet of nucleotides.

29. Heterosynthetic function of a gene is: a**)** transcription and replication; b) translation and transcription; c) DNA replication and reparation; d) transformation and translation; e) only translation.

30. The genes are classified into: a) structural, modifiers and repressors; b) introns, exons and inhibitors; c) functional and structural; d) co-repressors and operators; e) regulators and intensifiers.

INHERITANCE REGULARITIES. INTERACTION OF GENES

31. The main features of G. Mendel's hybridological method are: a) one or of two pairs of alternative alleles are analyzed; b) many alternative alleles are analyzed; c) analysis starts with cross of homozygous organisms; d) several generations are analyzed; e) one generation is analyzed.

32. Concepts of the hypothesis of purity of gametes: a) genes of one allelic pair of a hybrid organism are hybridized; b) genes of one allelic pair of a hybrid organism are not hybridized; c) genes of different allelic pairs can be hybridized; d) both allelic genes get in one gamete; e) from each pair of allelic genes one gene gets into gamete.

33. The conditions necessary for actuality of Mendel's laws: a) codominance; b) semidominance; c) presence of lethal genes; d) equiprobable formation of gametes and zygotes of different types; e) genes of different allelic pairs are in one chromosome.

34. Analyzing cross is performed to reveal: a) mutations; b) a phenotype of the individual; c) a genotype of the individual with a recessive character; d) a genotype of the individual with dominant character; e) lethal genes.

35. Features of incomplete dominance are: a) a dominant gene does not completely suppress the action of a recessive gene; b) the dominant gene completely suppress the action of a recessive one; c) homo-and heterozygotes are identical phenotypicly; d) homo-and heterozygotes are not identical phenotypicly; e) the dominant gene in a heterozygous state express stronger, than in homozygous.

36. Features of co-dominance are: a) the dominant gene does not completely suppress the action of recessive gene; b) it is a type of interaction of allelic genes,

genes are equivalent; c) homo- and heterozygotes are identical phenotypicly; d) it is a type of interaction of non-allelic genes; e) the dominant gene in a heterozygous state express stronger, than in homozygous.

37. Features of polymeria are: a) mutual influence of different alleles that occupy adjacent loci of one chromosome; b) 2 dominant genes of different allelic pairs are responsible for a new character; c) 2 recessive genes of different allelic pairs are responsible for a new character; d) one gene is responsible for different characters; e) genes from different allelic pairs have an effect on a manifestation degree of one character.

GENETIC LINKAGE

38. The phenomenon of genetic linkage is observed when genes of different allelic pairs are situated: a) in the same chromosome; b) in the different chromosomes; c) only in the autosomes; d) only in the X-chromosome; e) only in the Y-chromosome.

39. Complete genetic linkage is observed: a) in a female Drosophila and a male silkworm; b) if non-allelic gnes are located in different chromosomes; c) if crossing-over occurs; d) if crossing-over does not occur; e) in a male Drosophila and a female silkworm.

40. Partial genetic linkage is observed: a) if genes of different allelic pairs are located in one chromosome; b) if non-allelic gnes are located in different chromosomes; c) if crossing-over occurs; d) if crossing-over does not occur; e) in a male Drosophila and a female silkworm.

41. The main concepts of the chromosome theory of inheritance are: a) allelic genes are located in the linear order in identical locus's of homologous chromosomes; b) allelic genes occupy different locus's of homologous chromosomes; c) the number of linkage groups is equal to monoploid set of chromosomes; d) the number of linkage groups is equal to diploid set of chromosomes; e) between homologous chromosomes of Drosophila male the crossing-over is possible.

42. Phenotypic segregation ratio for monohybrid cross of homozygotes at complete dominance: a) is absent; b) 3:1; c) 1:2:1; d) 9:3:3:1; e) 1:1.

43. Phenotypic segregation ratio for partial genetic linkage in Morgan's experiences: a) 3:1; b) 1:2:1; c) 9:3:3:1; d) 1:1; e) 41.5:8.5:8.5:41.5.

44. Phenotypic segregation ratio for complete genetic linkage in Morgan's experiences: a) 41.5:8.5:8.5:41.5; b) 3:1; c) 1:2:1; d) 9:3:3:1; e) 1:1.

VARIATION

45. Properties of modifications: a) have adaptive character; b) are inherited; c) are not inherited; d) are the matter for natural selection; e) are the matter for artificial selection.

46. Biological mutagens cause: a) structural defects of genes and chromosomes; b) polyploidy; c) formation of thymine dimers; d) haploidy; e) embedding of its DNA in DNA of the host cells.

47. Characteristic features of gametic mutations are: a) occur in sex cells; b) occur in somatic cells; c) manifest in the individual; d) pass to offsprings by sexual reproduction; e) pass to offsprings by asexual reproduction.

48. Types of functional genes mutations: a) a transposition; b) impairment of the alternation of recognition and terminations; c) impairment of the alternation of initiation and elongation; d) impairment of the alternation of induction and repression; e) transitions.

49. Polyploidy is: a) not multiple of a haploid complement increase of the chromosome number; b) multiple of a haploid complement increase of the chromosome number; c) not multiple of a haploid complement decrease of the chromosome number; d) multiple of a haploid complement decrease of the chromosome number; e) haploid set of chromosomes.

50. Haploidy is: a) a positive mutation; b) nullsomy; c) monosomy; d) absence of one chromosome; e) a haploid set of chromosomes.

51. Kinds of structural genes mutations: a) transductions; b) a transpositions; c) translocations; d) reading frame shift; e) transitions.

52. Stages' order of excision repair of a DNA: 1) synthesis of a new DNA strand fragment; 2) ligation of the synthesized strand with the main strand; 3) recognition the damaged DNA strand; 4) cutting out of the damaged DNA fragment; 5) replication of a DNA molecule: a) 1–5–2–3; b) 5–1–3–2; c) 3–4–5–2; d) 3–4–2–1; e) 3–4–1–2.

53. According to the oncogene concept, the basis of carcinogenesis is: a) protooncogenes received from parents or introduced into the genome of the cell by viruses; b) chromosome mutations of somatic cells; c) presence of protooncogenes in somatic cells of an organism; d) genome mutations of somatic cells; e) incorporations of viral DNA in the genome of somatic cells.

BIOLOGY AND GENETICS OF SEX

54. Formation of gonad primordium proceeds untill the week of embryogenesis: a) 1^{st}; b) 2^{nd}; c) 3^{rd}; d) $4t^{h}$; e) 5^{th}.

55. The differentiation of donads' primordia into the gonads occurs during the weeks of embryogenesis: a) from 1^{st} to 4^{th}; b) from 4^{th} to 6^{th}; c) from 4^{th} to 8^{th}; d) from 4^{th} to 12^{th}; e) from 10^{th} to 15^{th}.

56. Till 4^{th} week of an embryogenesis, formation of gonad primordiua goes under the control of genes of: a) autosomes; b) one X-chromosome; c) two X-chromosomes; d) Y-chromosomes; e) X-and Y-chromosomes.

57. The differentiation of donads' primordia into the gonads occurs under the control of genes of: a) autosomes; b) one X-chromosome; c) the second X-chromosome; d) Y-chromosomes; e) cytogene.

58. In case of absence of the second gonosome in karyotype, gonads: a) are differentiated; b) are not differentiated; c) connective tissues are formed on their place; d) partially atrophy; e) completely atrophy.

59. Physical abnormality of sex the determination in humans: a) a genetic gender; b) homosexuality; c) transvestism; d) gametic gender; e) hermaphroditism.

60. Transvestism is a phenomenon, when the person: a) chooses the sexual partner of the other gender; b) chooses the sexual partner of the same gender; c) the sexual satisfaction is reached by wearing clothes of the opposite gender; d) wishes to change his/her gender; e) infertile.

61. The karyotype at Shereshevsky-Turner syndrome is :a) 46, XY, 5p-; b) 45, X0; c) 47, XXY; d) 47, XX, 21 +; e) 46, XX, 9p +.

62. The karyotype at Klinefelter syndrome is :a) 47, XXY; b) 45, X0; c) 47, XXX; d) 46, XY; e) 46, XY, 9p +.

FUNDAMENTALS OF HUMAN GENETICS

63. Difficulties of studying human genetics are: a) simple karyotype; b) early puberty; c) small amount of offsprings; d) a plenty of offsprings; e) an experimentation opportunity.

64. The stages of genealogic analysis: a) the taking the anamnesis; b) definition of frequencies of genes and genotypes in a population; c) making genetic maps of chromosomes; d) studying the role of the environment in exhibiting character; e) analysis of a family tree.

65. Order of stages of the cytogenetic method: 1) processing of the cells by hypotonic solution NaCl; 2) staining of chromosomes; 3) stopping mitosis (with colchicine) at the stage of metaphase; 4) cultivation of cells on artificial nutrient mediums; 5) stimulation of mitosis by PHA: a) 1–5–3–4–2; b) 4–5–3–1–2; c) 4–1–5–3–2; d) 5–3–4–1–2; e) 4–5–1–3–2.

66. Holzinger's formula is used for calculation: a) frequencies of genes and genotypes in a population; b) quotient of inheritance; c) roles of environment in exhibiting the character; d) probabilities of inheritance; e) degree of genetic risk.

67. What is studied by biochemical methods of human genetics? a) general blood analysis; b) activity of enzymes of a blood plasma; c) activity of enzymes of a gastric juice; d) structure of primary urine; e) regional frame of enzymes.

68. Methods of recombinant DNA are based on: a) use of mathematical expression of the law of Hardy-Weinberg; b) extracting DNA fragments and determining nucleotide sequenceces in them; c) analysis of family trees; d) analysis of enzyme systems activity; e) microscopic karyotype studying.

69. Methods recombinant DNA allow: a) to isolate definite genes and their parts; b) to reveal genomic mutations; c) to create unlimited amount of copies of genes; d) to reveal chromosome mutations; e) to reveal type of inheritance.

70. Microbiologic tests allow to: a) build genetical maps of human chromosomes; b) determine the number of X-chromosomes; c) determine the number of Y-chromosomes; d) reveal some chromosome mutations; e) reveal some metabolism defects.

71. Direct noninvasive methods of prenatal diagnostics are: a) definition of alpha-fetoprotein; b) ultrasonography; c) chorionbiopcy; d) aminoicenthesis; e) fetoscopy.

72. Optimal terms for carrying out direct noninvasive methods of prenatal diagnostics are: a) 6–8 weeks; b) 8–10 weeks; c) 12–20 weeks; d) 23–30 weeks; e) 30–35 weeks.

GENETIC ENGINEERING

73. Purposes of genetic engineering are: a) designing of genetic structures according to a plan; b) decoding of the nucleotide orders of DNA; c) creation of organisms with the new genetic program; d) revealing of linkage groups; sequenation of genes; e) construction of a chromosome genetic map.

74. Main stages of genetic engineering are: a) obtaining genetic material; b) construction of a chromosome genetic map; c) decoding of the nucleotide order of a DNA site and building of recombinant DNA; d) selection of the transformed cells; e) incorporation of a recombinant DNA molecules in a chromosome.

75. Ways of obtaining genes for transplantation: a) synthesis of simple genes by chemical reactions; b) synthesis of genes on the base of a protein molecule; c) synthesis of complex genes by reverse transcription; d) making of a genetic map of a chromosome; e) cutting out of genes by restrictases.

76. Recombinant DNA molecules can be received by embedding the gene in: a) protein; b) bacteria plasmid; c) virus genome; d) lipid; e) a bacteriophage genome.

77. The enzymes used in gene engineering are: a) DNA-polymerase; b) lipase and restrictase; c) revertase and restrictase; d) restrictase and amylase; e) ligase.

78. Genetic engineering allowed us to receive: a) the strains of Escherichia coli, capable to synthesize inulin; b) the strain of Escherichia coli, capable to synthesize somatotropinum; c) plants, capable to acquire atmosphere nitrogen; d) microorganisms, capable to synthesize carbohydrates of oil from alimentary proteins; e) antiviral serums.

79. The future of gene engineering is based on the following achievements of molecular biology: a) ability to transmit genetic information by sexual way in eukaryotes; b) receiving of modifications with help of chemical mutagens; c) sequenation of genes; d) substitution of defective genes; e) including artificially synthesized genes in the human genome.

80. The chemical basis of plasmids is: a) RNA; b) DNA; c) proteins; d) lipids; e) polysaccharides.

GENETICS OF POPULATIONS

81. Characteristic features of an ideal population are: a) great number; b) small number; c) complete panmixia; d) absence of mutations; e) presence of mutations.

82. In mathematical expression of the Hardy–Weinberg law, p denotes the frequency of: a) dominant gene; b) recessive gene; c) dominant homozygotes; d) recessive homozygotes; e) heterozygotes.

83. In mathematical expression of the Hardy–Weinberg law, q denotes frequency of: a) dominant gene; b) recessive gene; c) dominant homozygotes; d) recessive homozygotes; e) heterozygotes.

84. In mathematical expression of the Hardy–Weinberg law, 2pq denotes frequency of: a) dominant gene; b) recessive gene; c) dominant homozygotes; d) recessive homozygotes; e) heterozygotes.

85. The genetic load is: a) saturation of the population by positive mutations; b) saturation of the population by mutations, reducing adaptability of individuals; c) saturation of the population by neutral mutations; d) saturation of the population by negative mutations; e) absence of mutations in populations.

REPRODUCTION OF ORGANISMS

86. Characteristics of asexual reproduction is: a) two individuals participate in reproduction; b) only one individual participates in reproduction; c) the genotype of daughter individual differs from parental ones; d) genotype of daughter individuals are identical to parental ones; e) the number of daughter individuals increases slowly.

87. Forms of asexual reproduction of multicellular organisms are: a) reproduction via vegetative organs; b) conjugation; c) copulation; d) polyembryony; e) fragmentation.

88. Characteristics of sexual reproduction is: a) two individuals participate in reproduction; b) only one individual participates in reproduction; c) genotypes of daughter individual differs from parental ones; d) genotypes of daughter individuals are identical to parental ones; e) the number of daughter individuals increases quickly.

89. Sexual process is: a) reproduction; b) fusion of two gametes; c) formation of gametes; d) genetic information exchange between individuals of same species; e) coupling the genetic information of individuals of same species.

90. Characteristics of isolecithal ova: a) contains a lot of yolk; b) contains a little of yolk; c) the yolk is uniformly distributed; d) the yolk is concentrated on the vegetative pole; e) the yolk is located at the animal pole.

91. Movement forward of spermatozoons in the female reproductive tracts is provided by: a) mobility of spermatozoons; b) ovum's immobility; c) contraction of uterine muscles; d) excretion of gynogamones; e) contraction of abdominal muscles.

92. Fertilization stages are: a**)** destruction of the ova by spermatozoons' hyaluronidase; b) acrosome reaction; c) splitting of the ovum; d) entrance of head, neck and tail of the spermatozoon into the ovum's cytoplasm; e) maturation of pronuclei.

93. Features of human reproduction are: a) women are capable for reproduction since the puberty till advanced age; b) men are capable for reproduction since the puberty up to 50 years; c) one oocyte of the second order is formed ones a moon month in women; d) spermatozoons are formed periodically in men; e) the older is the man, the longer is the time between the gamete's meiosis I and meiosis II

FUNDAMENTALS OF ONTOGENESIS (EMBRYONIC DEVELOPMENT)

94. TThe type of zygote cleavage depends on: a) sizes of the ovum; b) shape of the ovum; c) volume of yolk; d) distribution of yolk in the cytoplasm; e) potentialities of ovum's cytoplasm.

95. Derivatives of the dermatome are: a) epithelium of the gut; b) nervous system; c) respiratory system; d) urinogenital system; e) dermis.

96. First causes of cells differentiation during embryogenesis are: a) chemical homogeneity of the ovum's cytoplasm; b) chemical heterogeneity of the ovum's cytoplasm; c) chemical homogeneity of spermatozoon's cytoplasm; d) chemical heterogeneity of spermatozoon's cytoplasm; e) different potencials of animal and vegetative poles of the ovum.

97. Realization sequence of genes' action during the ontogenesis is: a) DNA → enzyme → mRNA → biochemical reaction → character; b) DNA → mRNA → enzyme → biochemical reaction → character; c) other genes have an impact on manifestation of the character; d) other genes do not influence the manifestation of the character; e) environmental factors do not influence the manifestation of the character.

98. The main mechanisms of cell differentiation are: a) blocking of different transcriptones at the certain development stage; b) turning on all genes at the certain development stage; c) blocking of all genes at the certain development stage; d) unblocking of different transcriptones at the certain development stage; e) blocking of one gene at the certain development stage.

99. Characteristics of totypotential cells are: a) their development is preprogrammed; b) their development is not preprogrammed; c) each of them can give rise to any type of cells; d) each of them can give rise to only one certain type of cells; e) the majority of transcriptons are blocked.

100. Characteristics of determined cells are: a) their development is finally preprogrammed; b) their development is not preprogrammed c) each of them can give rise to any type of cells; d) each of them can give rise to only one certain type of cells; e) the majority of genes can join the work.

101. The causes of critical periods of embryogenesis are: a) changes in conditions of embryo existence and feeding; b) transition from one development period to another one; c) appearance of new inductors; d) active dedifferentiation of cells; e) poor nutrition of the pregnant woman.

FUNDAMENTALS OF ONTOGENESIS (POSTEMBRYONIC DEVELOPMENT)

102. Critical periods of a postnatal ontogenesis: a) delivery; b) infancy; c) puberty; d) fading of reproductive function; e) senile age.

103. Characteristics of cerebral growth type of organs: a) intensive growth since birth and till 10–12 years; b) uniform growth during the whole period; c) intensive growth during the first year of life and puberty; d) intensive growth of tissue till 11–12 years, then gradual decrease of its volume up to the level of an adult; e) a rapid growth during puberty.

104. Criteria of biological age: a) a degree of development of a hair coat; b) the size of genitals; c) skeleton maturity ;d) body height; e) dental maturity.

105. The constitution of the person is: a) hereditary features of morphology, physiology and behaviour; b) state of the person at the given moment; c) persistent genetically caused disturbances of morphology, physiology and behaviour; d) a reactivity; e) resistibility to the agents of diseases.

106. Hypersthenic are predisposed to: a) to neurosises; b) hypertension; c) stomach ulcer; d) atherosclerosis; e) obesity.

107. The essence of the intoxicating hypothesis of aging: a) changes of cytoplasm colloidal properties; b) decrease in production of sexual hormones; c) accumulation of waste products in the large intestine and their adsorption to the blood; d) disturbance of adaptation and regulation processes; e) accumulation of mutations.

108. The essence of the genetic hypothesis of aging: a) changes of colloidal properties of a cell cytoplasm; b) decrease in production of sexual hormones; c) impairment of reparation and DNA replication processes; d) impairment of adaptation and regulation processes; e) genetically programmed number of cell's mitosis.

109. Proofs of genetically programmed number of cell's mitoses is: a) fibroblasts of man's embryos in culture give about 50 generations; b) at each DNA replication some nucleotides of telomeres are lost; at each DNA replication some nucleotides of telomeres are added; c) after every mitosis the length of telomeres decreases; d) after every mitosis the length of telomeres increases.

INTRODUCTION TO PARASITOLOGY

110. Characteristic of parasitism: a) both organisms receive benefit; b) the individual of one species uses the individual of another species only as habitation; c) the individual of one species uses the individual of another species as habitation and the source of nutrition, not causing any harm; d) the individual of one species uses the individual of other species as habitation and the source of nutrition and harms it; e) none of the organisms receive any benefit.

111. Examples progressive morpho-physiological adaptations of parasites: a) the presence of attachment organs and specialized body integument; b) simplification of the nervous system and sense organs; c) molecular mimicry

and secretion of anti-enzymes; d) reduction of the alimentary system; e) high fertility and complex life cycles.

112. Examples of biological adaptations of parasites: a) presence of attachment organs and anti-enzymes; b) simplification of the nervous system and sense organs; c) various forms of asexual reproduction and high fertility; d) complex life cycles, alternation of hosts and migration of larvae over the organism of the host; e) immunosuppressive action.

113. Pathogenic action of the parasite: a) mechanical injury of tissues, toxicoallergic; b) supplying the host with vitamins; c) supplying the host with nutrients; d) absorption of nutrients and vitamins from the host; e) weakening the organism and increasing probability of secondary infection.

114. Pathogenicity of a parasite does not depend on: a) host's genotype and environmental factors; b) parasite's genotype and virulence ; c) host's age and diet; d) body height and a sex of the host; e) presence of other parasites in the host.

115. Protective reactions of the host's organism occur at levels: a) subcellular and cellular; b) cellular and organism; c) specific and tissue; d) cellular and tissue; e) population-specific.

116. Adaptation of parasites at the population level: a) presence of cysts and active searching for hosts; b) simplification of nervous system and reduction of alimentary system in tapeworms; c) molecular mimicry and anti-enzymes; d) involving of intermediate and reservoir hosts ino the life cycle; e) synchronization of parasite's life cycle and hosts behavior.

PARASYTES — PATHOGENS OF THE DISEASES

117. Techniques used for laboratory diagnostics of opistorchosis: a) Fulleborn and Kalantaryan techniques; b) Gorachev technique; c) Schulman technique; d) direct smear and thick-blood film; e) adhesive tape technique.

118. Invasion of a person with teniasis occurs during: a) personal hygiene breaches; b) contacts with sick persons; c) eating undercooked beef; d) eating undercooked pork; e) eating undercooked fish, shrimps and crabs.

119. Invasion of a person with cysticercosis occurs during: a) swallowing eggs of park tapeworm; b) eating undercooked pork and beef; c) eating undercooked shrimps and crabs; d) contact with domestic pigs; e) autoinvasion in teniasis.

120. Migration way of ascaris larvae in the body is: a) intestine → right heart → lungs → blood vessels → liver → bronchi → trachea → pharynx → intestine; b) intestine → liver → bronchi → right heart → lungs → blood vessels → trachea → pharynx → intestine; c) liver → bronchi → right heart → lungs→ blood vessels → trachea → pharynx → intestine; d) intestine → blood vessels → liver → right heart → lungs → bronchi → trachea → pharynx → intestine; e) intestine → blood vessels → right heart → lungs → liver → bronchi → trachea → pharynx → intestine.

121. Diagnostic signs of migration stage of ascariasis are: a) intestinal obstruction; b) fever and an asthmatic bronchitis; c) non-constant eosinophilic infiltrations in lungs; d) occlusion of choledoch duct; e) appendicitis.

122. Surgical implications of ascariasis are: a) obstructive jaundice and obstruction of the intestine; b) affection of an eyeball by an adult worm; c) perforation of the intestinal wall; d) pneumonia and bronchitis; e) pancreatitis and appendicitis.

123. Medical significance of Sarcoptes scabiei: a) it is a specific vector of tick-borne relapsing fever; b) it is a specific vector of tularemia and brucellosis; c) it causes inflammation of the intestine; d) it causes asthmatic symptoms; e) it causes scabies.

124. Scabies is spread: a) by vector-bone route; b) during a direct skin contact with a sick person; c) by eating of uncooked fish; d) by bedclothes of sick persons; e) by drinking water from the open sources.

125. Prophylaxis of scabies is: a) revealing and treating sick persons; b) elimination of vectors; c) maintaining the purity of the body; d) washing vegetables and fruits before eating; e) sanitary inspection of hostels, bathhouses and heath education.

126. Morphology of the head louse: a) the body length is 1–4 mm, has no wings; b) the body length is 1–4 mm, one pair of wings; c) mouthparts are chewing; d) the body length is 2–4 mm, wings are absent; e) mouthparts are piercing-sucking.

127. Life cycle features of order Anoplura are: a) lay eggs in dry dust and on food products; b) nits stick to hair; c) development is direct; d) development with incomplete metamorphosis; e) duration of the life cycle is 48 days.

128. Medical significance of order Anoplura is: a) mechanic vectors of helminthes' eggs and protozoans' cysts; b) specific vectors of the louse-borne relapsing fever; c) specific vectors of epidemic typhus; d) lice of genus Pediculus cause pediculosis; e) pubic lice cause phthiriasis.

129. Morphology of pubic louse: a) sizes up to 1.5 mm; b) sizes up to 1.5 cm; c) the body is short, almost round; d) piercing-sucking mouthparts; e) the body is short, almost square.

130. Medical significance of pubic louse: a) mechanic vectors of helminthes' eggs and protozoans' cysts; b) specific vectors of the louse-borne relapsing fever; c) specific vectors of epidemic typhus; d) cause pediculosis; e) cause phthiriasis.

VENOMOUS ANIMALS

131. Actively-venomous and poisonous animals: a) jellyfish and snails; b) cobra and tarantula; c) python and tarantula; d) tarantula and pufferfish; e) pufferfish and snails.

132. Passively-poisonous animals: a) jellyfishes and a tarantula; b) cobra and a boa; c) python and a pufferfish; d) tarantula and snails; e) pufferfish and snails.

133. Actively-venomous animals: a) snakes and sting ray; b) pufferfish and wasps; c) bees and amphibiand; d) snails and bees; e) snakes and amphibians.

134. Actively-poisonous animals: a) both snakes and amphibious; b) pufferfish and sting ray; c) bees and sting ray; d) snails and amphibious; e) sting ray and snails.

135. Toads and frogs are: a) primary-toxic; b) secondary-toxic; c) actively-poisonous; d) passively-poisonous; e) secondary-venomous.

136. Bees and wasps are: a) primary-toxic; b) secondary-toxic; c) actively-venomous; d) passively-venomous; e) passively-poisonous.

137. Factors determining clinical presentation of toxication with zootoxins are: a) composition and the volume of the venom; b) site of biting; c) sex of the affected person; d) habitus of the affected person; e) time of a day.

138. Symptoms of toxication with scorpion venom: a) a sharp pain, hyperemia and edema of the affected area; b) hyperemia and edema of the injured area, fear; c) neither hyperemia nor edema of the injured place, but nausea and vomiting; d) sharp pain, fear; e) fear, nausea and vomiting.

139. Symptoms of toxication with tarantula venom: a) sharp pain and drowsiness; b) hyperemia and a edema of the affected area, necrosis of skin; c) neither hyperemia nor edema of the affected area; d) hyperemia and edema of the affected area, drowsiness; e) drowsiness, necrosis of skin.

140. Symptoms of toxication with bee or wasps venom: a) sharp pain, fear; b) hyperemia and edema of the affected area, allergic reactions; c) neither hyperemia nor edema of the injured area; d) allergic reactions, of fear; e) sharp pain.

141. Symptoms of toxication with cobra venom: a) sharp pain, inflammation of lymphatic vessels; b) inflammation of lymphatic vessels, a necrosis of tissues; c) sharp pain, necrosis of tissues; d) excitation and then depression of CNS, necrosis of tissues; e) excitation and then depression of CNS, impairment of respiration are observed.

142. Symptoms of toxication with Viper snakes venom: a) sharp pain and impairment of blood clotting; b) extremities numbness and hemorrhagic edema; c) hemorrhagic edema; d) numbness of extremities and impairment of respiration; e) impairment of blood clotting and respiration.

143. First aid in a toxication with hymenopterian venom: a) to suck off the venom, to treat the area of stinging with disinfectants; b) to remove a sting, to treat the place of stinging with disinfectants; c) to treat the place of stinging with disinfectants, to apply heat to a place of stinging; d) to apply a warm compressive bandage to the place of stinging; e) to leave a sting, to treat the place of stinging with disinfectants.

144. First aid in a toxication with snake venom is: a) to suck away venom and to treat the place of a biting with disinfectants; b) to scorch the place of biting and to put a victim in a shade; c) to scorch and to treat the place of a biting with disinfectants; d) to transport a victim in lying position; e) to apply a hard bandage to a place of a biting and to transport a victim in any position.

ANSWERS TO THE GAP-FILLING TESTS

BIOLOGY OF THE CELL. THE FLOW OF SUBSTANCE AND ENERGY IN THE CELL

1. Compartmentalization. **2.** Glycocalyx. 3**.** Golgi complex.
4. Autophagy. **5.** Porin. **6.** 3.
7. 40 %.

THE FLOW OF GENETIC INFORMATION IN THE CELL

8. Lamins. **9.** Kinetochore. **10.** Nucleolar organizer.
11. 2n 2chr 4c. **12.** $1n_{biv}$ 4chr 4c. **13.** $1n_{biv}$ 4chr 4c.
14. $1n_{biv}$ 4chr 4c. **15.** Chiasmas. **16.** Bivalents.
17. 1n 2chr 2c.

ORGANIZATION OF THE HEREDITARY MATERIAL

18. Replication. **19.** $3^{/}$–$5^{/}$. **20.** Unidirectionality.
21. Recognition. **22.** AUG. **23.** Elongation.
24. Inhibitor.

INHERITANCE REGULARITIES. INTERACTION OF GENES

25. Alternative. **26.** 100. **27.** Recessive epistasis.
28. Complementation. **29.** 1:1:1:1. **30.** Multiple.

GENETIC LINKAGE

31. Genetic linkage . **32.** Complete. **33.** Partial.
34. Partial. **35.** Crossingover. **36.** Crossingover.
37. 50. **38.** Recombinant. **39.** 22.

VARIATION

40. Exonuclease. **41.** Transition. **42.** Deletions.
43. Functional. **44.** Genome. **45.** Monosomy.
46. Haploidy.

BIOLOGY AND GENETICS OF SEX

47. Trisomy. **48.** Shereshevsky-Turner syndrome.
49. Klinefelter's syndrome. **50.** Transvestism. **51.** Meiosis.
52. Holandric. **53.** Transsexualism.

FUNDAMENTALS OF HUMAN GENETICS

54. Proband. **55.** 18.75 %. **56.** 20 %.
57. Hybridization. **58.** X-linked dominant. **59**. Twin.
60. Cytogenetic. **61.** 8–12. **62.** Ultrasonography
63. Direct invasive. **64.** Acrichine-yperite.

GENETIC ENGINEERING

65. Restrictase. **66.** Restrictase. **67.** Fermentative synthesis.
68. Liposomes. **69.** Phasmids. **70.** Cosmids.
71. Sticky ends. **72.** Blunt ends

GENETICS OF POPULATIONS

73. Isolate. **74.** Heterozygous.

REPRODUCTION OF ORGANISMS

75. Conjugation. **76.** Syncaryogamy. **77.** Partenogenesis
78. Heavily telolecithal. **79.** Isolecithal. **80.** Mitosis.
81. Meiosis. **82.** Polyembryony. **83.** Fertilizin (gynogamone II).
84. 24–48 h.

FUNDAMENTALS OF ONTOGENESIS (EMBRYONIC DEVELOPMENT)

85. splitting **86.** Pre-fetal. **87.** Immigration.
88. Deuterostomes. **89.** Provisional. **90.** Chemical heterogeneity.
91. Embryonic induction. **92.** Gradient.

FUNDAMENTALS OF ONTOGENESIS (POSTEMBRYONIC DEVELOPMENT)

93. Lymphoid. **94.** Somatotropin. **95.** Acceleration.
96. Constitution. **97.** Ectomorphic (asthenics). **98.** Geriatrics.
99. Valeology. **100.** Clinical. **101.** Euthanasia.

INTRODUCTION TO PARASITOLOGY

102. Facultative parasites. **103.** Natural (obligate). **104.** Potential.
105. Optional. **106** Alimentary. **107.** Respirtory
108. Direct contact. **109.** Iatrogenic.

PARASYTES — PATHOGENS OF THE DISEASES

110. Trophozoite. **111.** Axostyle. **112.** 5.
113. |Cat liver fluke. **114.** Cercaria. **115.** Cisticercus
116. 3. **117.** 7-12 **118.** 1 year.
119. Pediculosis. **120.** Phtiriasis. **121.** Nits.
122. Relapsing fever and typhus **123.** Borellia recurrensis.

VENOMOUS ANIMALS

124. Venomous («Armed»). **125.** Hemolyzins. **126.** Thread cells.
127. Neurotoxin. **128.** Neurotoxin **129.** Hemorrhagins.
130. Neurotoxins. **131.** 50. **132.** Venomous («armed»).

ANSWERS TO THE MULTICHOICE TESTS

BIOLOGY OF THE CELL. THE FLOW OF SUBSTANCE AND ENERGY IN THE CELL

1. a, c, e. **2.** b, e. **3.** b, c. **4.** a, e.
5. a, d. **6.** a, c, d. **7.** a, b, d. **8.** a, e. **9.** d.

THE FLOW OF GENETIC INFORMATION IN THE CELL

10. a, c. **11.** c, e. **12.** d. **13.** b, d. **14.** c.
15. a, c. **16.** a, d, e. **17.** c. **18.** d. **19.** c, e.

ORGANIZATION OF THE HEREDITARY MATERIAL

20. b. **21.** a. **22.** a, c, e. **23.** b. **24.** a, b. **25.** b.
26. c. **27.** b. **28.** c, e. **29.** b. **30.** c, e.

INHERITANCE REGULARITIES. INTERACTION OF GENES

31. a, c, d. **32.** b, e. **33.** d. **34.** d. **35.** a, d. **36.** b. **37.** e.

GENETIC LINKAGE

38. a. **39.** d, e. **40.** a, c. **41.** a, c. **42.** b. **43.** e. **44.** e.

VARIATION

45. a, c. **46.** a, e. **47.** a, d. **48.** d. **49.** b.
50. e. **51.** d, e. **52.** e. **53.** a, c

BIOLOGY AND GENETICS OF SEX

54. d. **55.** d. **56.** b. **57.** c. **58.** b, c.
59. e. **60.** c. **61.** b. **62.** a.

FUNDAMENTALS OF HUMAN GENETICS

63. c. **64.** a, e. **65.** b. **66.** b. **67.** b.
68. b. **69.** a, c. **70.** e. **71.** b. **72.** c.

GENETIC ENGINEERING

73. a, c. **74.** a, d, e. **75.** a, c, e. **76.** b, c, e.
77. a, c, e. **78.** b, c, e. **79.** d, e. **80.** b.

GENETICS OF POPULATIONS

81. a, c, d. **82.** a. **83.** b. **84.** e. **85.** b, d.

REPRODUCTION OF ORGANISMS

86. b, d. **87.** b, c. **88.** a, c. **89.** d, e.
90. b, c. **91.** a, d. **92.** b. **93.** c.

FUNDAMENTALS OF ONTOGENESIS (EMBRYONIC DEVELOPMENT)

94. c, d. **95.** e. **96.** b, e. **97.** b, c.

98. a, d. **99.** b, c. **100.** a, d. **101.** a, c.

FUNDAMENTALS OF ONTOGENESIS (POSTEMBRYONIC DEVELOPMENT)

102. b, c, d. **103.** a. **104.** c, e. **105.** a.
106. b, d, e. **107.** c. **108.** c, e. **109.** a.

INTRODUCTION TO PARASITOLOGY

110. d. **111.** a, c. **112.** c, d. **113.** a, d, e.
114. d. **115.** b, d. **116.** a, d, e.

PARASYTES — PATHOGENS OF THE DISEASES

117. b. **118.** d. **119.** a. **120.** d. **121.** b, c.
122. a, c, e. **123.** e. **124.** b, d. **125.** a, c. **126.** d, e.
127. b, d. **128.** b, c, d. 1**29.** b, d. **130.** c, e.

VENOMOUS ANIMALS

131. b. **132.** e. **133.** a. **134.** d. **135.** a, d.
136. a, c. **137.** a, b. **138.** a. **139.** b. **140.** b, e.
141. a, e. **142.** a, c. **143.** b. **144.** a, d.

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