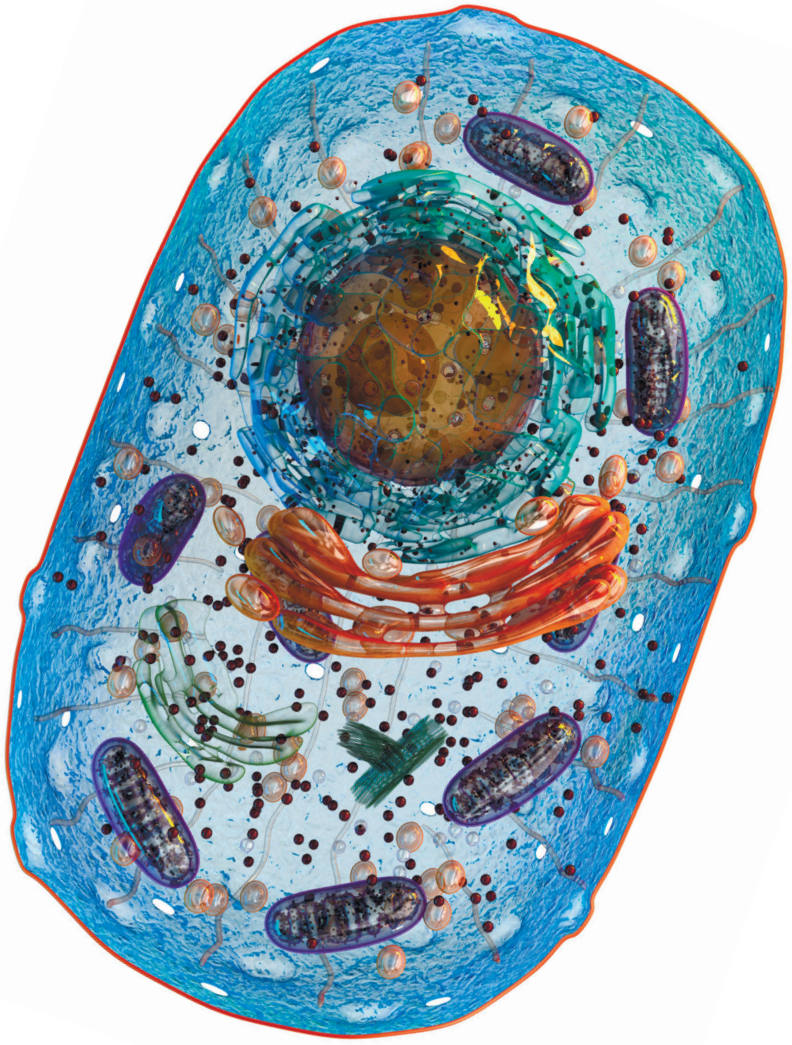
MINISTRY OF HEALTH OF THE RUSSIAN FEDERATION
PIROGOV RUSSIAN NATIONAL RESEARCH MEDICAL UNIVERSITY

Department of Biology. Pediatrics Faculty

INTRODUCTION TO CELL BIOLOGY

STUDENT WORKBOOK

Edited by prof. A.G.Mustafin



Moscow

2021

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O.N. Khrushchova, E.A. Bogdanova, A.V. Nesterova, E.I. Romashevskaya, A.G. Ermolaev, Y.I. Voldgorn, A.G. Mustafin

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Recommended by the Central Coordination Board of Federal State Autonomous Educational Institution of Higher Education «Pirogov Russian National Research Medical University» of the Ministry of Health of the Russian Federation

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The workbook is intended for students of medical universities enrolled in the educational program “General Medicine” to master the discipline “Biology”. It includes basic information and practical tasks that help to better understand structure and functioning of cells.

The workbook is prepared in accordance with the requirements of the Federal state educational standard of higher professional education in the areas of training 31.05.01 “ General medicine”.

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TABLE OF CONTENT

TOPIC 1. CELL AS A UNIT OF LIFE

Cell is a basic unit of life. The term **cell** was coined by Robert Hooke after observing a thin piece of cork under a microscope in which he saw walled compartments that reminded him of the cells a monk might live in.

The cell theory is a fundamental conception of biology. It was developed in XIX century by Matthias Schleiden, Theodor Schwann, and Rudolf Virchow.

Cell theory (modern interpretation):

1. The cell is the fundamental unit of structure and function in living things.
2. All cells come from pre-existing cells by division.
3. All cells are basically the same in chemical composition.
4. The activity of an organism depends on the total activity of independent cells.

Task 1.1. Cells are fundamental units of life. Explain what it means:

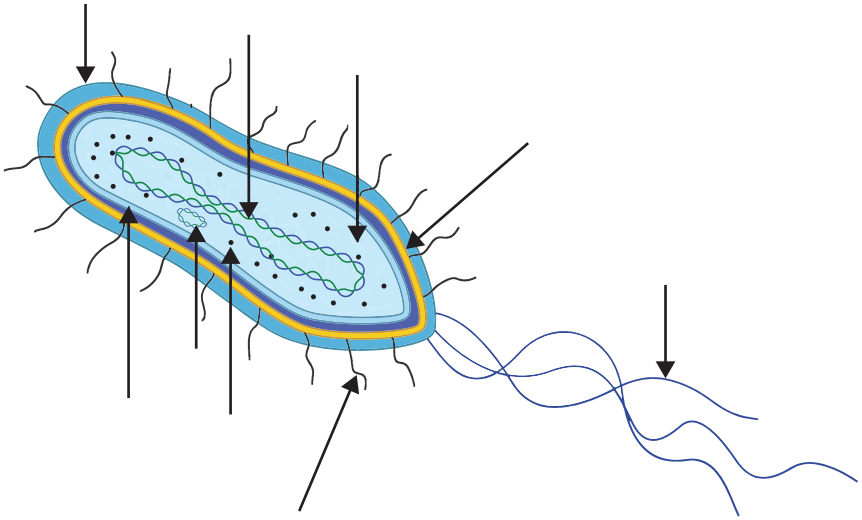
Task 1.2. Fill in the table "Comparison of features of prokaryotic and eukaryotic cells":

Characteristics	Prokaryotes	Eukaryotes
Typical organisms (kingdoms)		
Typical size		
Cell wall		
Form of DNA (linear or cilcular) and its location in a cell		
Where does the RNA synthesis (transcription) take place		
Where does the protein synthesis (translation) take place		
Ribosomes (size and location)		
Cell movement devices		
Mitochondria		
Chloroplasts		
Cell division (types)		
Time of origin		

Prokaryotic cell

A typical prokaryotic cell has cytoplasm with ribosomes and a circular DNA (prokaryotic chromosome) and is surrounded by plasma membrane. Cell wall is attached to plasma membrane outside. The cell may also have small circular extrachromosomal DNA molecules — plasmids (usually containing antibiotic resistance genes), pili, flagellae, and capsule.

Task 1.3. Label the parts of a typical prokaryotic cell using the following list of terms: 1 – cell wall, 2 – ribosome, 3 – plasma membrane, 4 – pilus, 5 – flagellae, 6 – chromosomal DNA (nucleoid), 7 – plasmid DNA, 8 – cytoplasm, 9 – capsule.



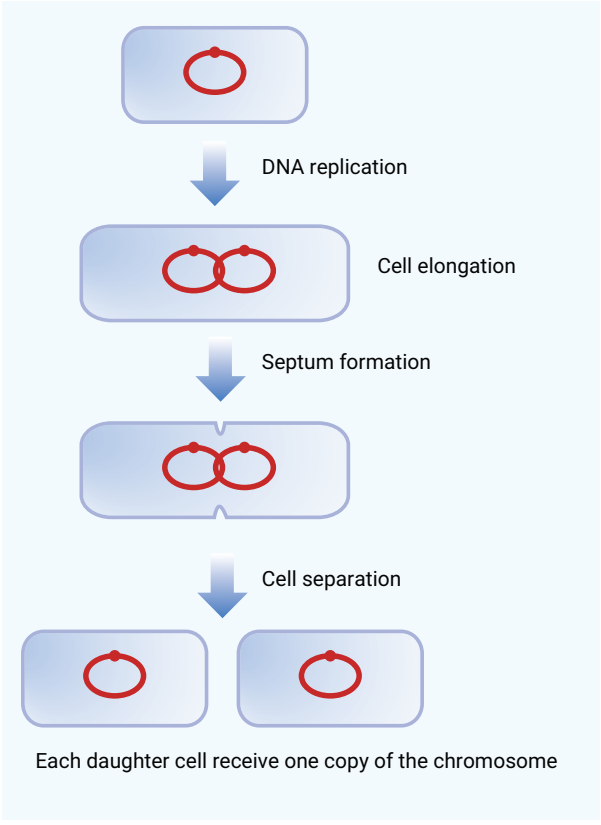


Fig. 1. Binary Fission in Prokaryotes.

Procaryotic cells divide by **binary fission**. It is division of the parent body into two fairly equal parts to produce two identical cells (Fig.1). It is a form of asexual reproduction carried out by most prokaryotes. Time required for a bacterial cell to divide is called the **generation time**.

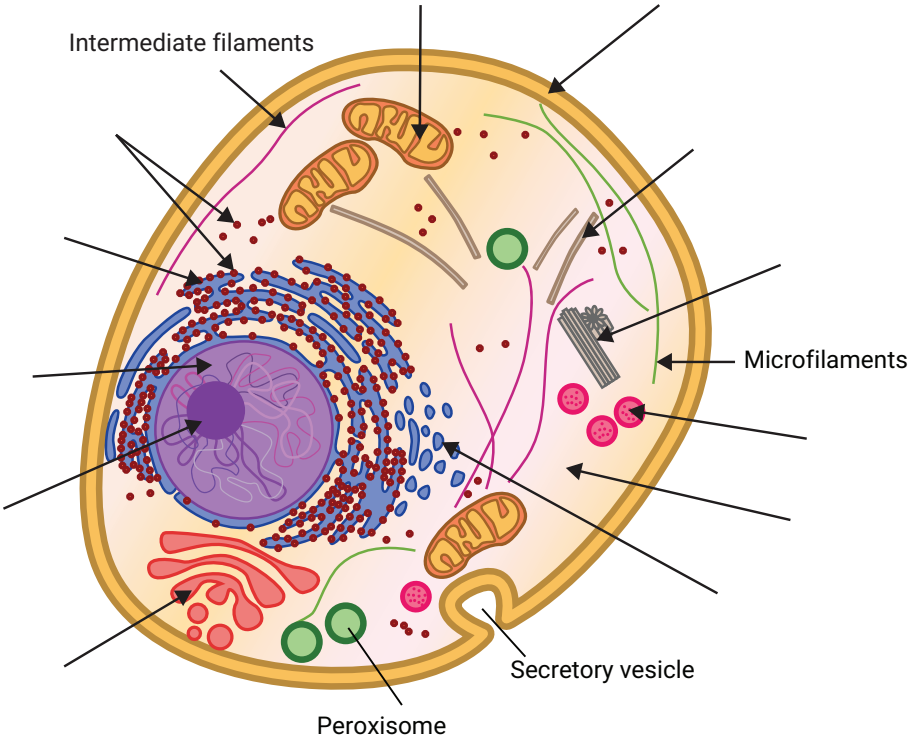
Task 1.4. Complete the table by calculating the number of bacteria present at 20 minutes intervals.

Generation time (min)	Population size
0	1
20	2
40	4
60	
120	
160	
180	

Eukaryotic cell

A typical eukaryotic cell has a cell membrane, cell nucleus and cytoplasm with organelles and inclusions. Organelles are specialized subunits within a cell that have specific structures and functions. Cell inclusions are a nonliving material in the protoplasm of a cell, such as pigment granules, fat droplets, or nutritive substances.

Task 1.5. Identify and label structures in the animal cell below using the following list of terms: 1 – cytoplasm, 2 – plasma membrane, 3 – rough endoplasmic reticulum, 4 – smooth endoplasmic reticulum, 5 – ribosomes, 6 – nucleus, 7 – nucleolus, 8 – Golgi apparatus, 9 – centriole, 10 – lysosome, 11 – microtubule, 12 – mitochondrion, 13 – centriole.



What features of the cell above identify it as eukaryotic?

Task 1.6 Fill in the table "Organelles of eukaryotic (animal) cell":

Organelles	Structure(Draw schematically)	Function
Mitochondria		

Rough endoplasmic reticulum		
Smooth endoplasmic reticulum		
Golgi complex		
Lysosomes		
Ribosome		
Centrioles		

Cytoskeleton		
Ciliae and flagellae		

Task 1.7 Match each of the key terms (column A) with its corresponding definition (column B)

COLUMN A

(1) Nucleolus

(2) Nucleus

(3) Ribosome

(4) Centrioles

(5) Rough endoplasmic reticulum

(6) Golgi apparatus

(7) Cytoskeleton

(8) Smooth endoplasmic reticulum

(9) Mitochondria

(10) Vacuole

(11) Cytoplasm

(12) Lysosome

(13) Chloroplasts

(14) Cell membrane

COLUMN B

(a) Built of protein and RNA, has two subunits; in them protein synthesis takes place

(b) Double-membrane semiautonomous organelle capable of ATP production

(c) System of microtubules and microfilaments

(d) Single-membrane organelle for cellular digestion

(e) The main double-membrane organelle of eukaryotic cell where chromosomes are situated

(f) Small dense region inside nucleus where rRNA is produced

(g) Membranous vesicle often storing important chemical or food substances

(h) Membranous canals and cisterns where synthesis of lipids and polysaccharides takes place

(i) Built of microtubules arranged in two cylinders of 9 triplets each; in animal cell organize mitotic spindle

(j) Membranous canals and cisterns where synthesis of protein takes place thus possess ribosomes

(k) Inner content of a cell where organelles and inclusions are

(l) Chlorophyll-containing double-membrane organelles of plant cell

(m) System of flat membranes and vesicles where products for cell "export" and lysosomes are synthesized

(n) Built of phospholipids and protein; is found both in pro- and eukaryotic cells

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

Plasma membrane

The **plasma membrane**, also called the cell membrane, separates the interior of the cell from the outside environment. The plasma membrane defines the borders of the cell as well as allows the cell to interact with its environment in a controlled way.

Plasma membrane is found in all cells. In prokaryotic and plant cells, plasma membrane is attached on its outside surface to a cell wall. Animal cells do not have cell wall.

The principal components of the plasma membrane are lipids (phospholipids and cholesterol), proteins, and carbohydrate groups.

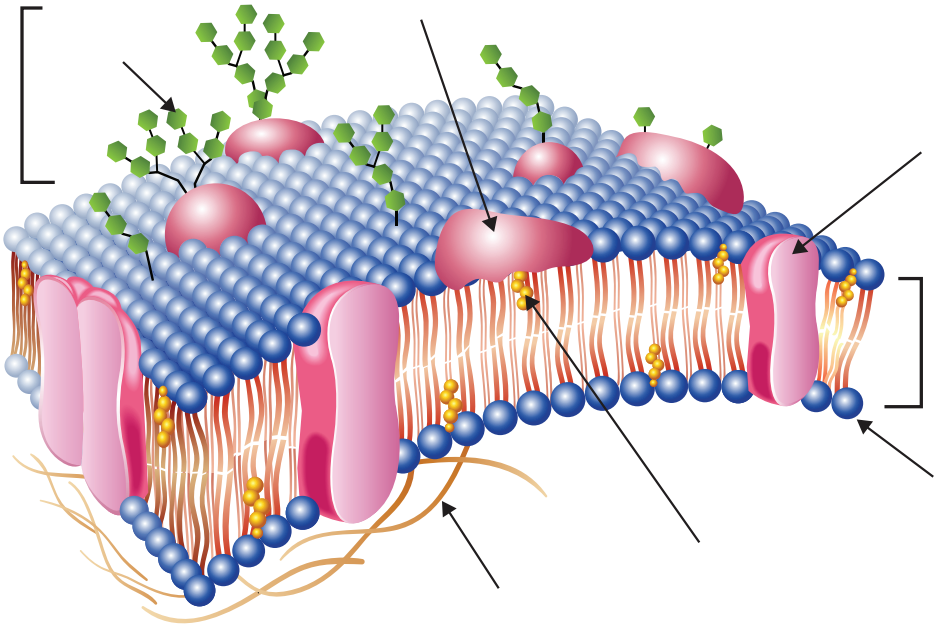
Lipids are organized in lipid bilayer, which make a semi-permeable barrier between the cell and its environment.

Proteins are involved in cross-membrane transport and cell communications.

Carbohydrate groups (sugars and sugar chains) are attached to proteins, forming glycoproteins, or lipids, forming glycolipids and are present only on the outer surface of the plasma membrane. The layer of carbohydrate groups is called **glycocalyx** (or "sugar coat"). Carbohydrates help cells to recognize each other.

The inside part of plasma membrane is often found attached to major cytoskeletal elements of the cell. They provide changes of cell form and cell movement.

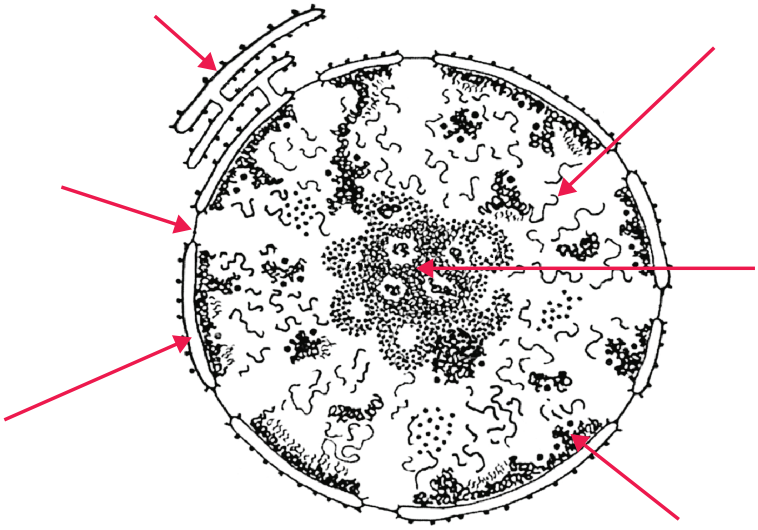
Task 1.8. Label parts of the plasma membrane of animal cell using the following list of terms: 1 – lipid bilayer, 2 – phospholipid, 3 – cholesterol, 4 – transmembrane protein, 5 – peripheral membrane protein, 6 – carbohydrate group, 7 – glycocalyx, 8 – cytoskeleton.



Cell nucleus

The nucleus is the most important part of a eukaryotic cell. It is isolated from the cytoplasm by a **double membrane** with **pores** in it and contains inside most of cellular DNA. DNA in the nucleus exists as a loosely packed structure called **chromatin** and is represented multiple long linear double stranded molecules in a complex with proteins, such as **histones**.

Task 1.9. Label the parts of a cell nucleus using the following list of terms: 1 – nuclear envelope (double membrane), 2 – nuclear pore, 3 – rough endoplasmic reticulum, 4 – euchromatin, 5 – heterochromatin, 6 – nucleolus.



Home Work

Answer the questions using information from textbook «ESSENTIAL MEDICAL BIOLOGY», Chapter 1.1, pp 4–17.

1. Compare typical plant and animal cell.

Characteristics	Plant cell	Animal cell
Cell wall		
Chloroplasts		
Central vacuole		
Centrioles		

2. What are functions of cell envelope?

3. Which organelles including nucleus of a eukaryotic cell have a membrane structure?

Single membrane	Double membrane
1)	1)
2)	2)
3)	3)
4)	

4. What is phagocytosis? What cells (animal, plant, fungal) is it inherent?

5. Indicate three main differences between pro- and eukaryotic cell:

1)

2)

3)

6. What are the main parts of a cell nucleus?

7. Where is DNA located in a eukaryotic cell?

8. What are the differences between organelles and inclusions?

9. What do we call 'a nucleoid'?

10. Which organelles of a eukaryotic cell are referred to as semiautonomous and why?

1)

2)

11. What does the endosymbiotic theory propose?

TOPIC 2. NUCLEIC ACIDS. DNA REPLICATION

Structure of the nucleic acids

Biological information in cells is encoded in the DNA molecules. Biological function emerges primarily from protein molecules. RNAs play a major role in the implementation of genetic information. So proteins and nucleic acids are the most important biopolymers of life.

Nucleic acids (DNA and RNA) are long molecules composed of nucleotide monomers. Every nucleotide consists of three parts: **nitrogenous base**, **pentose sugar** (ribose in RNA and deoxyribose in DNA) and **phosphate** residue (Fig. 2). The purine bases **adenine** and **guanine** and pyrimidine base **cytosine** occur in both DNA and RNA, while the pyrimidine bases **thymine** (in DNA) and **uracil** (in RNA) occur in just one. The bases are often abbreviated A, G, C, T, and U, respectively.

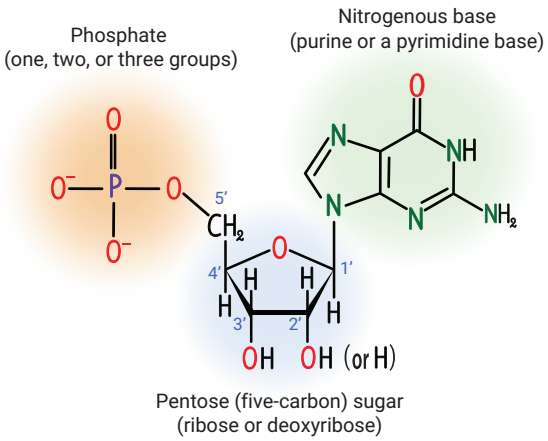
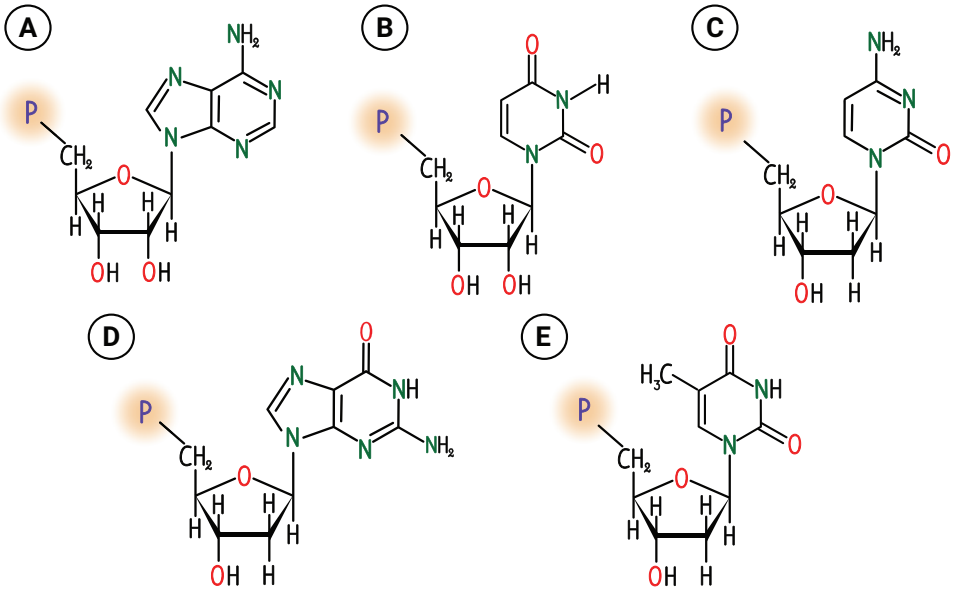


Fig. 2. Scheme of a nucleotide (on example of guanosine phosphate).

Task 2.1. Learn the nucleotide chemical formulas below. Fill in the table for each nucleotide, indicating the sugar and type of base (purine or pyrimidines), the names of the nucleotides and which nucleotides are the DNA monomer and which are the RNA monomer.



	Pentose	Base type	Nucleotide name	Monomer of
A				
B				
C	Deoxyribose	Citosine (C)	Deoxycytosine monophosphate	DNA
D				
E				

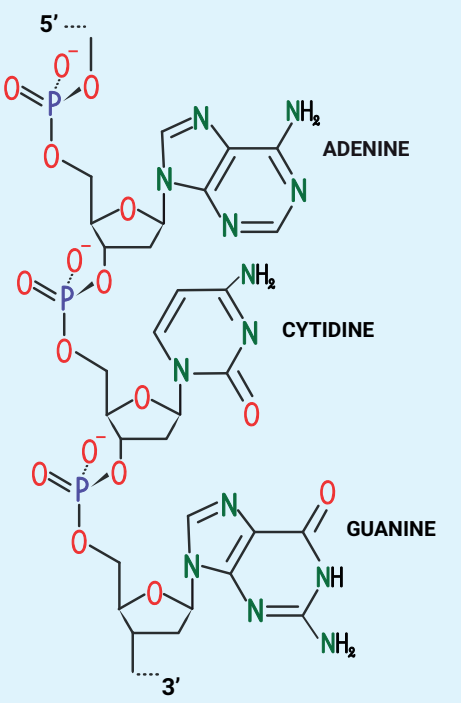


Fig. 3. Primary structure of nucleic acids.

Although the primary structures of DNA and RNA are generally similar, their conformations are very different. Unlike RNA, which usually exists as a single polynucleotide strand, DNA contains two polynucleotide strands that form a double helix structure. The strands are in antiparallel orientation; that is, their directions 5'→3' are opposite and are held by hydrogen bonds between complementary bases (Fig. 4).

The bonds joining one nucleotide to another are covalent **phosphodiester bonds** (Fig. 3). The linear sequence of nucleotides linked by phosphodiester bonds constitutes the primary structure of nucleic acids. A polynucleotide chain has **5′-end** and **3′-ends** (determined by the number of the carbon group in pentose). New nucleotides are added to the 3′-end.

Hydrogen bonds can join nitrogenous bases. Between A and T (U in RNA) there are two hydrogen bonds and between C and G — three hydrogen bonds (complementary base pairing).

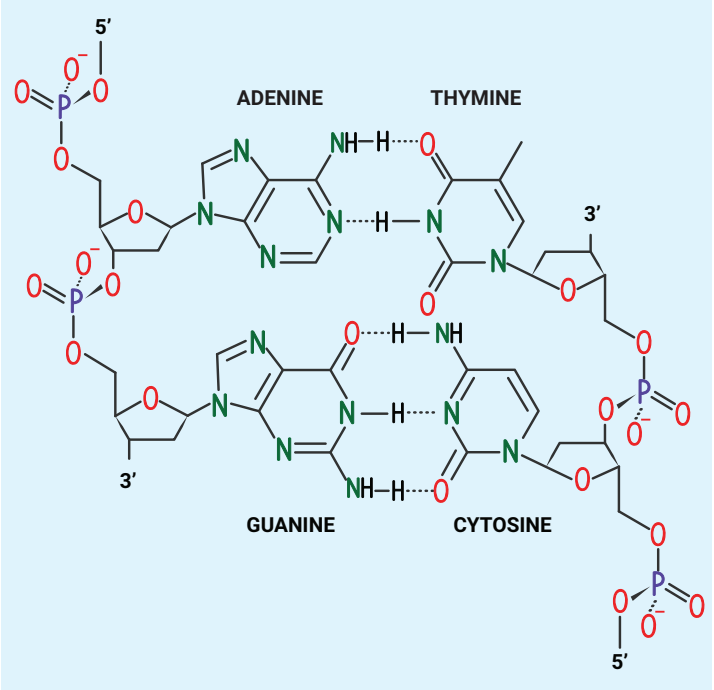
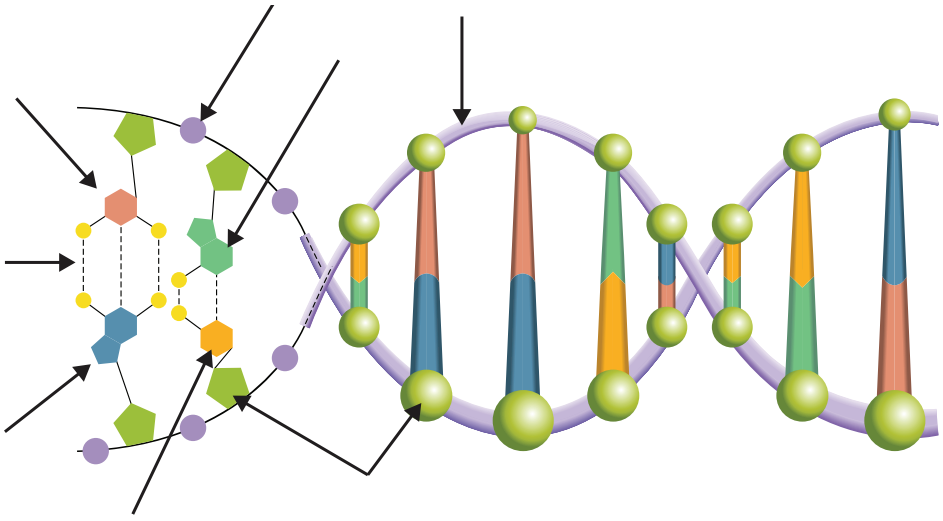


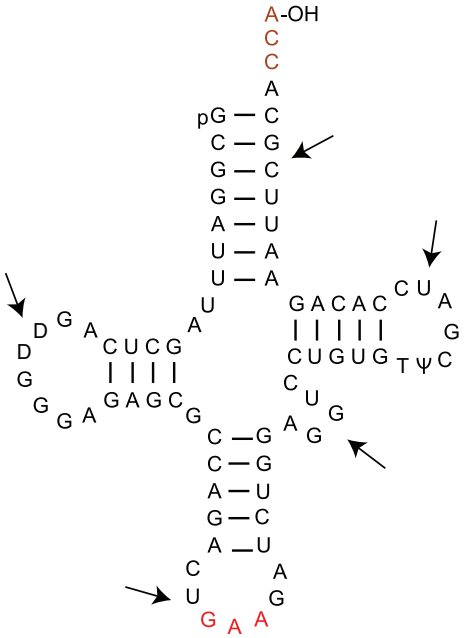
Fig. 4. Secondary structure of nucleic acids.
Dots indicate hydrogen bonds.

Task 2.2. Label parts of the DNA double helix model below using the following list of terms: 1 – deoxyribose, 2 – nitrogenous bases (A, T, G, and C), 3 – phosphate residue, 4 – phosphodiester bond, 5 – hydrogen bond. Label 5′- and 3′-ends of DNA strands.



Different types of RNA exhibit different conformations, usually due to formation of hairpins by pairing complementary bases in one molecule. For example, due to hydrogen bonds, the molecules of transfer RNA (tRNA) have a characteristic folded structure with three loops, which are often called the “three-leaf clover”.

Task 2.3. Learn structure of tRNA molecule. Designate 1 – T-loop, 2 – D-loop, 3 – anticodon loop, 4 – acceptor stem where amino acid is attached, 5 – additional loop. Label 5′- and 3′-ends of RNA molecule.



Task 2.4. Compare DNA and RNA and fill in the table

Feature	Deoxyribonucleic acid (DNA)	Ribonucleic acid (RNA)
Nitrogenous bases		
Pentose sugar		
Double/ single-stranded		
Location in the cell		
Function		mRNA
		tRNA
		rRNA

Nucleic acids in a cell undergo **replication, transcription, reverse transcription, repair, recombination, and mutagenesis.**

- **Replication** is the process of duplicating DNA (occures before cell division).
- **Recombination** means an exchange of portions between different DNA molecules. Example of such a process is **crossing over** between homologous chromosomes in prophase-1 of meiosis or integration of a virus into host cell chromosome.
- **Repair** of DNA is a process of identification and correction damage or mistakes in DNA structure. Many enzymes are involved in the process and different kinds of repair are known. Examples are: **photo reactivation, excision repair, post-replicational repair** (daughter strand gap repair) and others.
- **Mutation** is a result of mistakes in "**three R**" – replication, repair or recombination that lead to change in nucleotide sequences of DNA. Mutation involves both strands of DNA and the smallest unit of mutation (muton) is a pair of complementary nucleotides.
- **Transcription** is synthesis of RNA on DNA as a template. Transcription is an important part of protein synthesis.
- **Reverse transcription** is the synthesis of DNA on RNA as a template. Examples of reverse transcription are observed during RNA viruses replication and under activation of telomerase enzyme in eukaryotes.

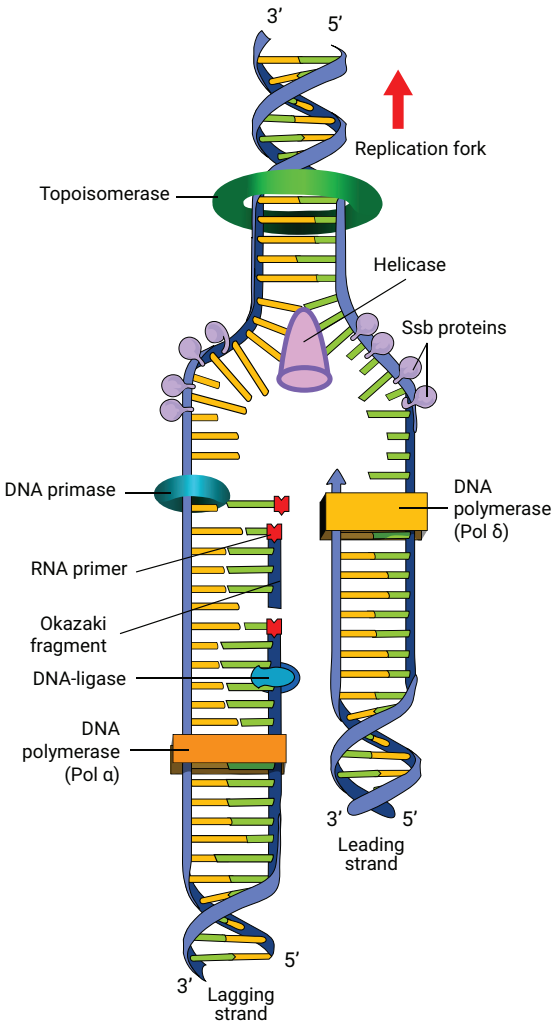


Fig. 5. Schematic outline of DNA replication.

Credit: Mariana Ruiz. Located at: https://commons.wikimedia.org/wiki. File: DNA_replication_en.svg.

DNA replication

Replication is a process of copying DNA. Chromosomes duplicate during S-period of interphase of cell cycle. Human DNA has about 6 000 000 000 pairs of nucleotides so it needs lots of time to copy itself. This is why replication in eukaryotes begins at many ori (origin) points and is referred to as **polyrepliconic**. In prokaryotes circular DNA replicates as a single replicon (**monorepliconic** replication, Fig. 1).

Once begins, replication progresses in both directions forming two replication forks. New strand of DNA growths at the 3′-end so one strand is **leading** and the other — **lagging**. Short DNA fragments (called **Okazaki fragments**) are produced during synthesis of the lagging strand, they are then joined together to produce whole DNA strand. Okazaki fragments are ususally 100—1000 bases in length.

Many proteins are involved in the replication process (Fig. 5). **Helicase** unzips DNA into two single strands. **Topoisomerase** (**gyrase**) helps DNA not to supercoil during replication. **SSBP** (**single-stranded binding proteins**) prevent single-stranded DNA from contact with the other strand. **DNA primase** synthesizes a short — usually 10–12 bases in length — fragments of RNA (primers), which serve as a starting points for DNA synthesis because DNA polymerase is only capable of adding nucleotides to the 3′-end of an existing strand. **DNA polymerase** adds free nucleotides to the 3′-end of the newly forming strand; **DNA ligase** form phosphodiester bonds between DNA fragments (e.g. Okazaki fragments).

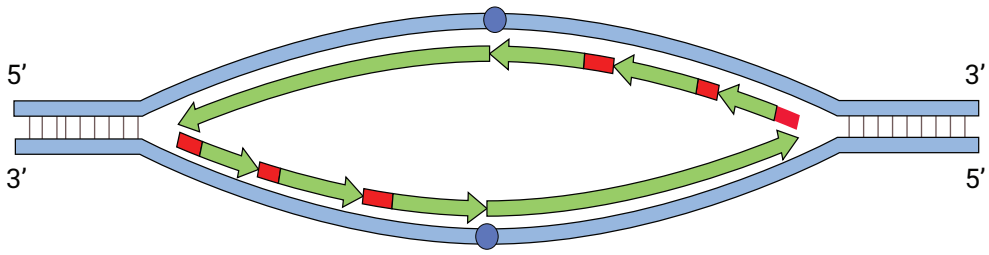
Task 2.5. Choose the phrase from the column B that best fits the term in the column A:

COLUMN A	COLUMN B
(1) Replication	(a) DNA is constructed from an RNA strand as a template
(2) Transcription	(b) The enzyme facilitates joining of DNA fragments
(3) Recombination	(c) Synthesis of RNA from a DNA template

(4) Repair	(d) Alterations of the genetic material
(5) Mutation	(e) Exchange of parts between DNA molecules
(6) Reverse transcription	(f) Self-copying of DNA, typically takes place in the S-period of interphase
(7) Translation	(g) Correction of mistakes in DNA structure
(8) Helicase	(h) Synthesis of a polypeptide from an RNA template
(9) Ligase	(i) Enzyme that unwinds DNA double helix by breaking hydrogen bonds between bases

A	1	2	3	4	5	6	7	8	9
B									

Task 2.6. Indicate leading and lagging strands on both replication forks. Add labels: 1 – Okazaki fragments, 2 – primers, and 3 – origin of replication.



Task 2.7. Write down a complementary strand to the following fragment of DNA. Label the 3′ and 5′ terminuses of the new-synthesized DNA molecule.

3'– T – A – C – G – T – A – G – G – T – A – T – T –5'

Task 2.8. Fill in the table using information from textbook «ESSENTIAL MEDICAL BIOLOGY» pp 20–22:

Protein involved in DNA replication	Protein function
Topoisomerase (gyrase)	
Helicase	
SSB proteins	
Primase	
DNA polymerase	
DNA ligase	

Task 2.9. Match the statements in the columns A and B to form complete sentences, and arrange sentences in the order to make a coherent paragraph about DNA replication and its role:

COLUMN A	COLUMN B
(I) The enzymes also proofread the DNA during replication…	(a) …is required before mitosis can occur.
(II) DNA replication is the process by which the DNA molecule…	(b) …by enzymes.
(III) Replication is tightly controlled…	(c) …to correct any mistakes.
(IV) The chromatids separate…	(d) …and half new DNA.
(V) DNA replication…	(e) …during mitosis.
(VI) Each chromatid contains half original…	(f) …is copied to produce two identical DNA strands.
(VII) After replication, the chromosome…	(g) ...is made up of two chromatids.

Sentence #	1	2	3	4	5	6	7
Column A							
Column B							

Home Work

Answer the questions using information from textbook «ESSENTIAL MEDICAL BIOLOGY», Chapter 1.2 pp. 17–22, Chapter 5 pp. 37–39.

1. What are the building units of nucleic acids? _____

2. List components that make up a nucleotide: _____

_____

3. What do 5′ and 3′ ends of a polynucleotide strand mean?

_____

_____

_____

_____

4. What bonds are between nucleotides on a polynucleotide chain? _____

5. What bonds are between nitrogenous bases in DNA? _____

6. List the main differences between DNA and RNA:

1) _____

2) _____

3) _____

7. What is the role of tRNA in translation? _____

_____

8. What base in RNA is complementary to thymine in DNA? _____

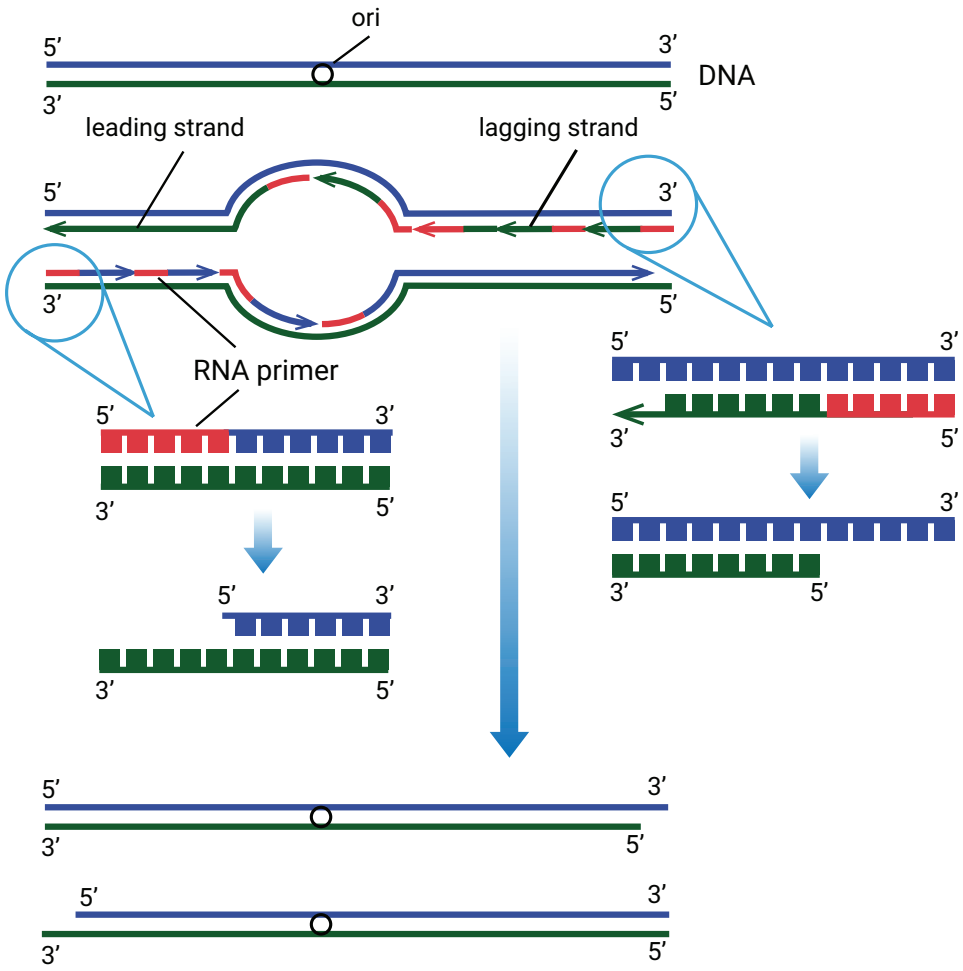
9. What base is RNA complementary to adenine in DNA? _____

10. Define transcription of DNA: _____

11. Define recombination of DNA: _____

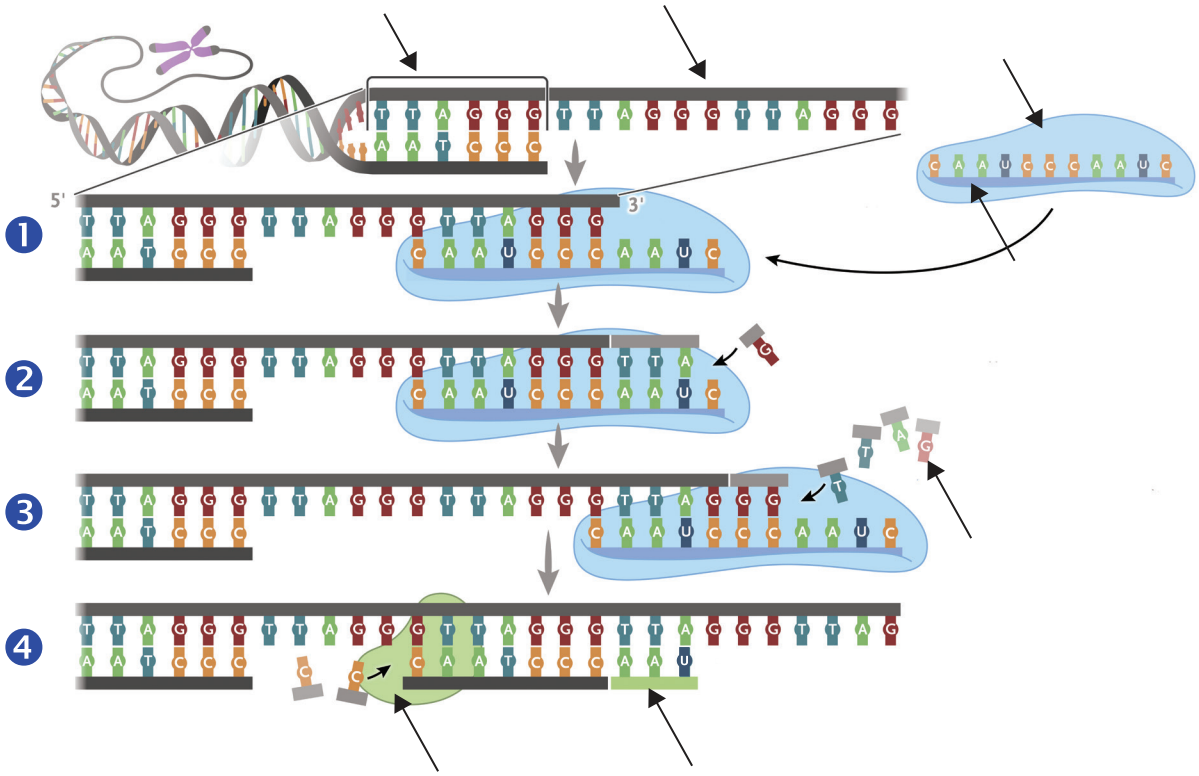
12. Indicate what damage the DNA had got and mark the sequence to be cut off during excision repair in the diagram below:

13. During replication, the linear DNA is shortened, as shown in the scheme below. Why is this happening?



14. Learn the reverse transcription reaction by the example of telomerase action. (A) Label elements on the illustration below* using the following list of terms: 1 – DNA, 2 – telomere repeat, 3 – telomerase, 4 – non-coding template RNA, 5 – primer, 6 – DNA polymerase, 7 – dNTPs. (B) Match the process descriptions with the step numbers in the illustration:

Process description	Step number
Template snRNA is hybridized with the overhanging 3' end of DNA, the telomerase uses the unhybridized portion of snRNA as a template to restore DNA	
DNA polymerase and primase synthetise the completely strand	
Telomerase binds to the 3'-overhang	
Telomerase moves forvard and repeat reverse transcription	



* Source: New England Journal of Medicine (NEJM) Illustrated Glossary.

TOPIC 3. GENE EXPRESSION AND REGULATION

Proteins

Proteins are important organic molecules of the living organisms. Proteins, or polypeptides, are polymeric molecules built of **amino acids**. Cells use mainly 20 different amino acids for protein building. Every amino acid can be designated by a short symbol. For example Gly or G stands for glycine, Phe or F for phenylalanine and so on.

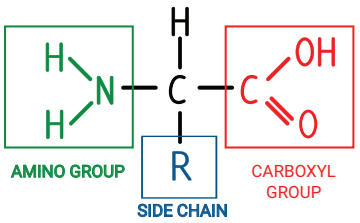


Fig. 6. Chemical formula of an amino acid.

A general formula for amino acid is shown in Fig. 6. "R" is a radical, a side chain that distinguish each of the 20 amino acids. R group can be as simple as a hydrogen atom (in amino acid glycine) or as complex as benzene ring (in phenylalanine). Some radicals are chemically neutral and nonreactive; others are acidic or basic.

Amino acids are categorized as essential, conditionally essential or nonessential depending on several factors. Unlike nonessential amino acids, **essential amino acids** can't be synthtized by organism and must be obtained from food. **Conditionally essential amino acids** are considered to be essential only under specific circumstances such as illness or stress.

Task 3.1. Write the full names of amino acids in the table:

Essential	Conditionally essential	Non-essential
(His, H)	(Arg, R)	(Ala, A)
(Ile, I)	(Cys, C)	(Asp, D)
(Leu, L)	(Gln, Q)	(Asn, N)
(Lys, K)	(Gly, G)	(Glu, E)
(Met, M)	(Pro, P)	
(Phe, F)	(Ser, S)	
(Trp, W)	(Tyr, Y)	
(Val, V)		

A pair of amino acids connected by a peptide bond (Fig. 7) is a **dipeptide**; several amino acids constitute an **oligopeptide**; hundreds to thousands amino acids are known as **polypeptides**.

Like the chain of nucleotides in DNA or RNA, polypeptides have a chemical polarity. On end of a polypeptide is called the **N-terminus**, and another — **C-terminus**.

The sequence of amino acids is known as primary structure of a polypeptide and it determines a protein's three-dimensional shape and thus its function (Fig. 8).

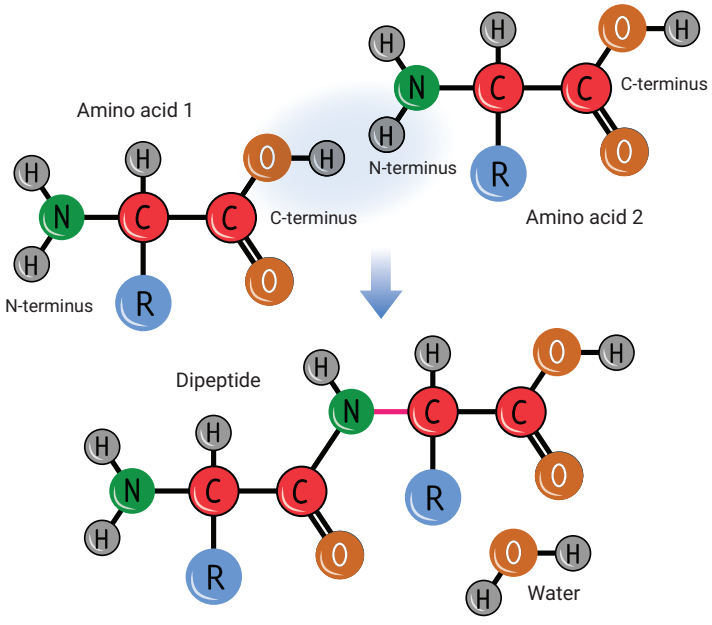


Fig. 7. Peptide bonds formation.

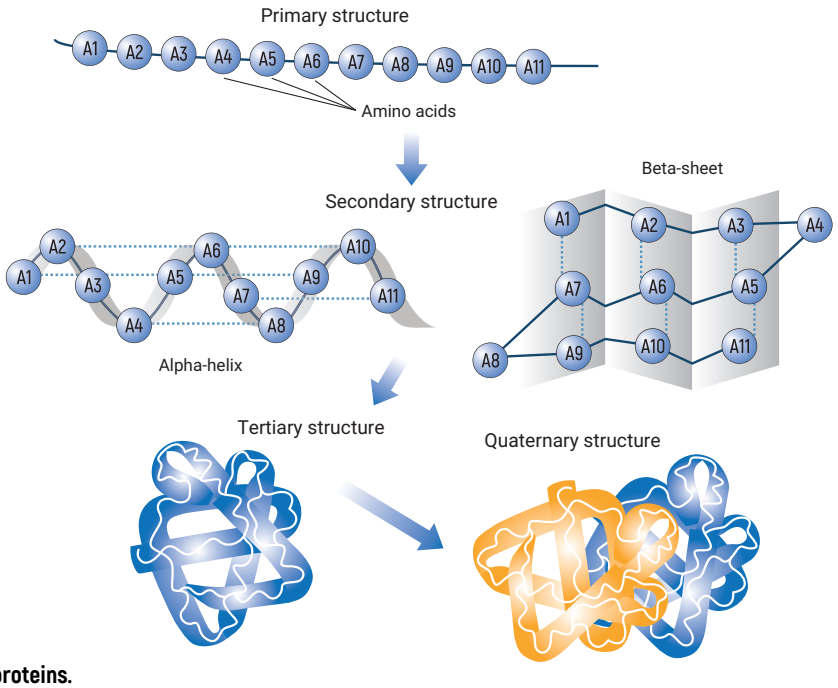


Fig. 8. The shape of proteins.

Denaturation of protein is a process that involves breaking the secondary, tertiary, quaternary structures of the molecule under the influence of various factors, such as pH, temperature, ionic strength and so on.

Task 3.2. Explain why the beginning of a polypeptide is called N-terminus and the end is called C-terminus.

Task 3.3. Why does denaturation often result in the loss of protein functionality?

Task 3.4. What chemical bonds are involved in making primary, secondary, tertiary and quaternary structure of a protein?

Primary structure:

Secondary structure:

Tertiary and quaternary structures:

Task 3.5. Fill in the table "Main functions of proteins" by giving examples.

Function	Example
Structural (building blocks)	Collagen is the main protein of connective tissue.
Catalytic (enzymes)	

Motility	
Transport	
Regulative	
Energetic (source of energy)	
Protection	

From genes to proteins

Proteins are synthesized in ribosomes. Amino acid sequence of a protein is encoded by the specific DNA sequence (called a **gene**). Genes expression involves gene transcription into messenger RNA (mRNA) and it's translation into a protein. mRNA is a small molecule that can squeeze through pores in the nuclear membrane. It transfers information from nuclear DNA to ribosomes in the cytoplasm and thus helps to assemble protein. This path is summarized in the central dogma of molecular biology:

DNA → mRNA → Protein

The discovery of this sequence of events was an important milestone in molecular biology.

Genetic code

Genetic code is the set of rules by which information encoded in genetic material (DNA or mRNA sequences) is translated into proteins (amino acid sequences) by living cells (Table 1).

Table 1. Genetic code

1st nucleotide	2nd nucleotide				3rd nucleotide
	U	**C**	**A**	**G**	
U	Phe (F)	Ser (S)	Tyr (Y)	Cys (C)	**U**
	Phe (F)	Ser (S)	Tyr (Y)	Cys (C)	**C**
	Leu (L)	Ser (S)	stop	stop	**A**
	Leu (L)	Ser (S)	stop	Trp (W)	**G**
C	Leu (L)	Pro (P)	His (H)	Arg (R)	**U**
	Leu (L)	Pro (P)	His (H)	Arg (R)	**C**
	Leu (L)	Pro (P)	Gln (Q)	Arg (R)	**A**
	Leu (L)	Pro (P)	Gln (Q)	Arg (R)	**G**
A	Ile (I)	Thr (T)	Asn (N)	Ser (R)	**U**
	Ile (I)	Thr (T)	Asn (N)	Ser (R)	**C**
	Ile (I)	Thr (T)	Lys (K)	Arg (R)	**A**
	Met (M)	Thr (T)	Lys (K)	Arg (R)	**G**
G	Val (V)	Ala (A)	Asp (D)	Gly (G)	**U**
	Val (V)	Ala (A)	Asp (D)	Gly (G)	**C**
	Val (V)	Ala (A)	Glu (E)	Gly (G)	**A**
	Val (V)	Ala (A)	Glu (E)	Gly (G)	**G**

How to use the table: codons in mRNA are given. First nucleotide is on the left, second on the top and the third in the right column.

The features of the genetic code are:

1. The code consists of **triplet codons** (total 64 codons)
2. The codons are **non-overlapping**, it means that each nucleotide is part of only one triplet.
3. The code includes **three stop or nonsense codons:** UAA (ocher), UAG (amber) and UGA (opal). These codons do not encode an amino acid and thus terminate translation.
4. The code is **degenerate**, which means that in many cases more than one codon specifies the same amino acid.
5. Translation of mRNA starts from a fixed starting point that establishes a reading frame. Open reading frame starts at the **initiation codon** (AUG).
6. Genetic code is **collinear**, that means the parallel between the sequence of nucleotides in DNA and the order of amino acids in a polypeptide.
7. The code is **universal** — the same in different living organisms (with very few exceptions).

Task 3.6. Give an example to illustrate the degeneracy of the genetic code

Task 3.7. How the universality of genetic code is used in genetic engineering?

Task 3.8. What amino acids are encoded by unique triplets?

Task. 3.9. Does the initiation codon encode any amino acid? What about the stop codons?

Task 3.10. Choose the phrase from the column B that best fits the term in the column A:

COLUMN A	COLUMN B
(1) Initiation codon	(a) Addition or deletion of a number of nucleotides other than three into the coding sequence
(2) Nonsense codons	(b) AUG in a particular content
(3) Reading frame	(c) The linear sequence of amino acids in the polypeptide corresponds to the linear sequence of nucleotides in DNA
(4) Degeneracy of the genetic code	(d) Most amino acids are specified by more than one codon
(5) Frameshift mutation	(e) UAA, UGA or UAG.
(6) Transcription	(f) Group of three mRNA bases signifying one amino acid
(7) Codon	(g) Grouping of mRNA bases in threes to be read as codons
(8) Translation	(h) Change a codon for one amino acid to a codon for another amino acid
(9) Nonsense mutation	(i) The change a codon for an amino acid to a stop codon
(10) Missense mutation	(j) Synthesis of RNA from DNA template
(11) Collinearity of the genetic code	(k) Synthesis of a polypeptide on a ribosome

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

Gene expression and gene regulation

Gene is a segment of DNA representing a functional unit of heredity. Most researchers define a gene as "the complete sequence region necessary for generating a functional product". This encompasses promoters and control regions necessary for the transcription, processing and, if applicable, translation of a gene. Many genes encode proteins, while many encode tRNA, rRNA and various non-coding RNAs (ncRNAs).

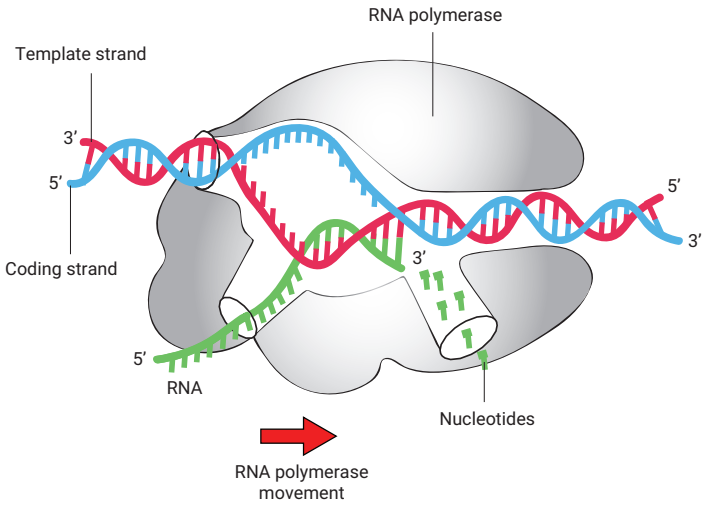


Fig. 9. Transcription of DNA.

Both prokaryotes and eukaryotes express genes to produce proteins. There are basic similarities in gene transcription between them: in both cases, RNA polymerase binds on gene promoter to initiate the process of gene transcription and synthetises mRNA from 5′ to 3′-end using DNA template, until will reach the terminator sequence (Fig. 9). However, the processes they use for gene expression and expression regulation are different.

Task 3.11. Compare gene expression in pro and eukaryotes and fill in the empty cells of the table:

Prokaryotes	Eukaryotes
Circular DNA is located in cytoplasm. It is non-condensed and is not associated with histones	
	Much of DNA does not code for proteins (~98% is non-coding in humans). DNA contains large regions of repetitive DNA
The genes typically have no introns	
	Genes have individual promoters and transcription terminators (as parts of gene)
Transcription and translation can take place simultaneously off the same piece of DNA	
	mRNA is monocistronic
Prokaryotes use the same type of RNA polymerase to transcribe all genes	

	Gene expression is controlled at the levels of transcription, post-transcription, translation, and post-translation

Gene expression in prokaryotes

Process and regulation of gene expression in prokaryotes can be illustrated on the example of the lac-operon of *E.coli* (Fig. 10). **Operon** is a functioning unit of DNA containing a cluster of genes under the control of a single promoter. The genes are transcribed together into a **polycistronic mRNA** and translated together on ribosome to produce proteins.

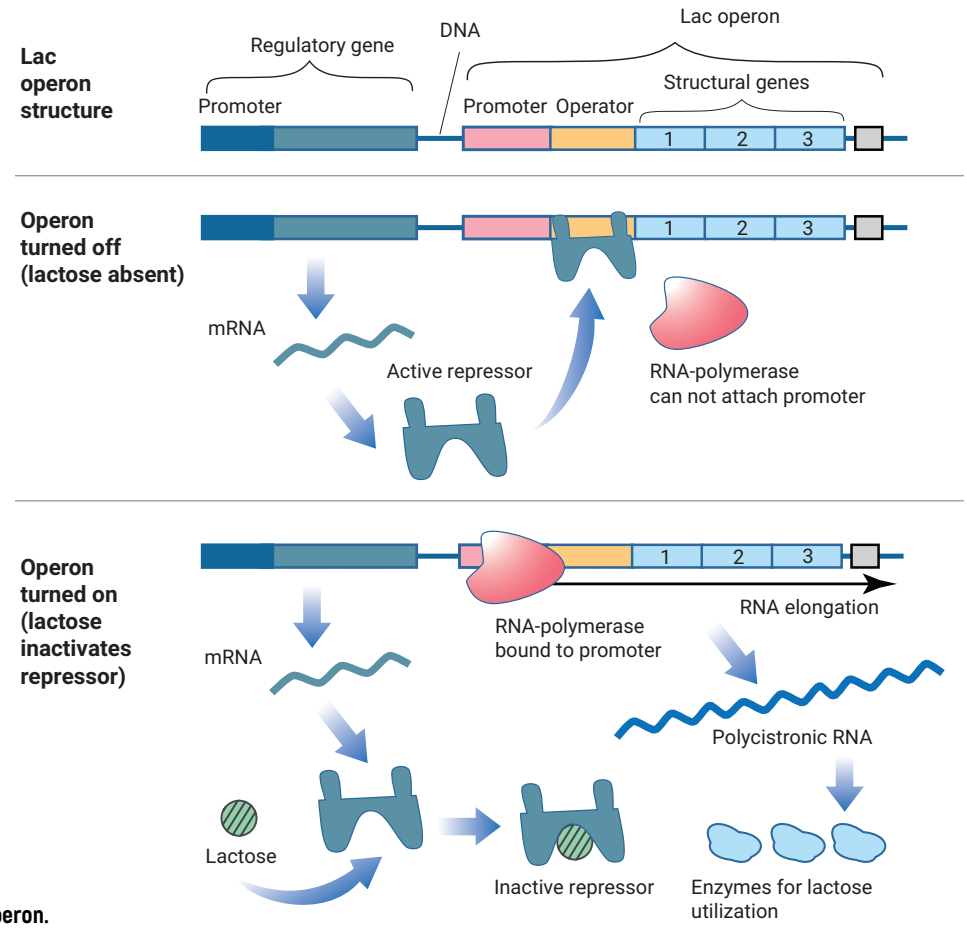


Fig. 10. Lac operon.

Task 3.12. Choose the phrase from the column B that best fits the term in the column A:

COLUMN A	COLUMN B
(1) Operon	(a) The enzyme for RNA synthesis
(2) Induction	(b) Group of genes under the control of one promotor
(3) Repressor	(c) Stimulation of protein synthesis by a specific molecule (lactose in lac operon)
(4) Operator	(d) Site to which repressor binds
(5) Polycistronic mRNA	(e) A sequence of DNA to which RNA polymerase binds
(6) RNA polymerase	(f) Negative regulator
(7) Promoter	(g) mRNA that encodes for more than one protein

A	1	2	3	4	5	6	7
B							

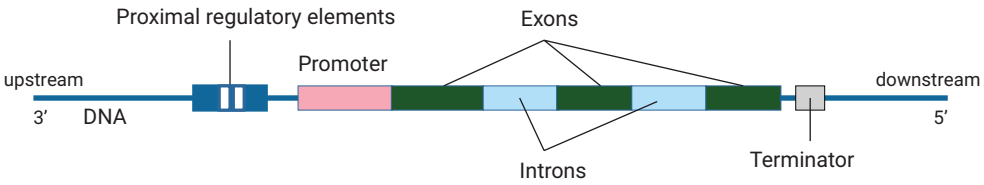


Fig. 11. Typical eukaryotic gene (DNA template strand).

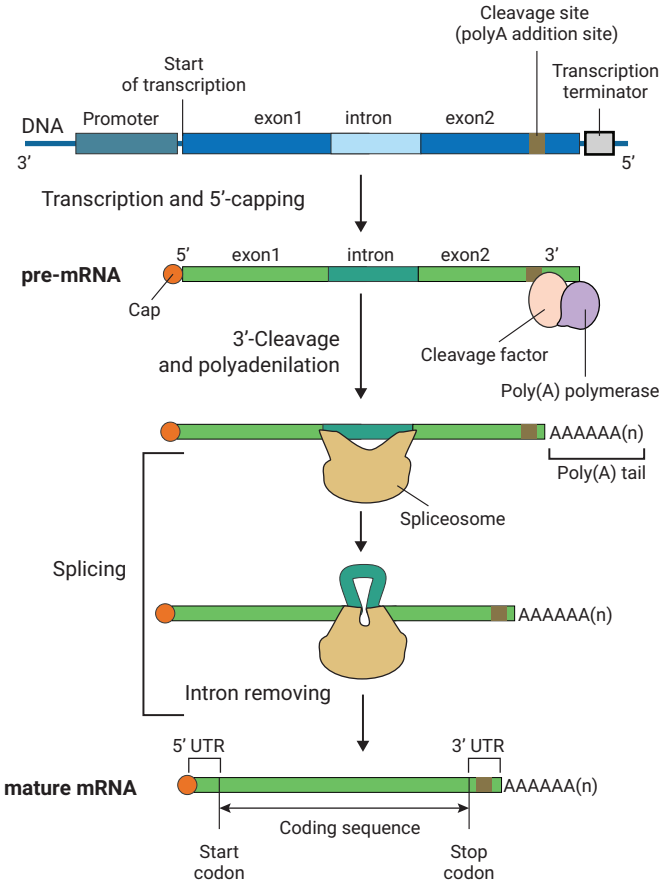


Fig. 12. Transcription and processing of mRNA.

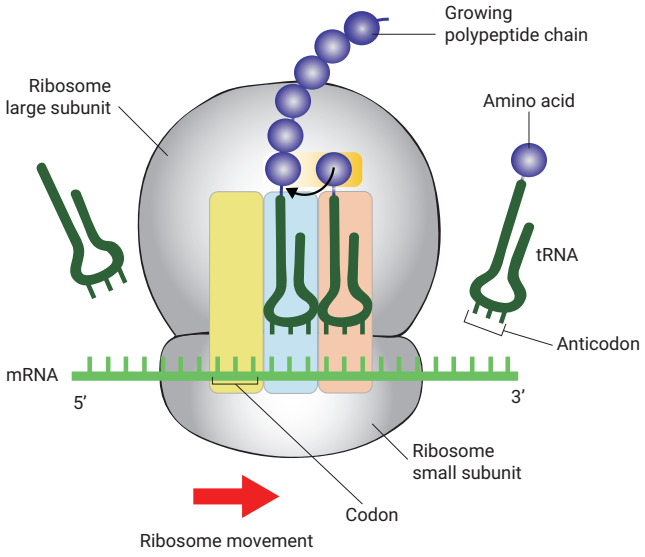


Fig. 13. Translation of mRNA.

Gene expression in eukaryotes

Typical eukaryotic gene is shown in Fig. 11. It consists of exons and introns as well as different regulatory elements including promoter and terminator regions. Usually only one strand of DNA serves as a template for transcription. Exons and introns are transcribed together, but then the introns are excised.

Gene expression in eukaryotes includes four steps (for protein-coding genes). Transcription and processing of mRNA occurs in the cell nucleus; translation and processing of protein — in the cytoplasm.

Transcription (synthesis of RNA on DNA template) occurs in the cell nucleus. The result of transcription is known as a **primary transcript** (pre-mRNA). Most eukaryotic genes contain non-coding sequences — introns, and pre-mRNAs are processed to remove them and converted into mature mRNAs. **Processing of RNA** includes **removing of introns** and **splicing** of exons as well as adding a **"cap"** to 5'-end (happens during transcrition) and a **polyA "tail"** to the 3'-end of mRNA (Fig. 12). In processing of mRNA, snRNA (small nuclear RNAs) and special proteins are involved. They form a structure called **spliceosomes** that recognize specific sequences of the intron-exon junction, catalyze the removal of the intron and **splicing** of exons. Typical eukaryotic mature mRNA comprises coding sequence of the gene product, 5'- and 3'-untranslated regions (UTRs), cap at 5'-end and poly(A) sequence at 3'-end. After processing, the mature mRNA leaves the cell nucleus and directs itself to ribosomes.

Translation is schematically drawn in Fig. 13. **Ribosomes** facilitate polypeptide synthesis. They recognize mRNA "cap" to start the translation. First codon to be translated is the **initiation codon** AUG at the 5'-end of mRNA. During translation, ribosomes stabilize interaction between **mRNA codons** and **tRNA anticodons** and supply enzymatic activity that links amino acids into a growing polypeptide chain. In the process of translation there are two distinct areas in a ribosome known as peptidyl (or P) site and aminoacyl (or A) site, which simultaneously bind to two different tRNA molecules. E-site is a place where tRNA exits from the ribosome. Translation terminates when the ribosome reaches UAA, UAG or UGA **nonsense codons** at the 3'end of mRNA and dissociates from both mRNA and polypeptide product.

Task 3.13. Fill in the following table:

Sequence	Function
Exon	
Intron	
Promoter	
Terminator	
Poly(A) tail	
5′-Cap	

Task 3.14. Transcribe the following sequence of DNA (use the strand 3′ → 5′ as a template), then wright an amino acid sequence of the polypeptide part. Label terminuses of the synthesized RNA molecule.

Coding strand 5′–T–T–A–A–A–C–C–C–G–T–G–C–3′

Template strand 3′–A–A–T–T–T–G–G–G–C–A–C–G–5′

mRNA _____

Polypeptide _____

Task 3.15. Fill in the gaps and indicate 3′- and 5′- terminuses in polynucleotide and N- and C- terminuses in polypeptide chains:

	Terminus	Sequence															Terminus
Coding strand of DNA	5′						G	G						T	A	A	
Template strand of DNA					T	A											
mRNA codon									G	C							
tRNA anticodon																	
Polypeptide	N	Met									Trp						

Task 3.16. Determine which color indicates which site (P, A, and E-sites) in the ribosome in Fig. 13. Give their full names and explain the role in translation.

Color	Site
Blue	
Yellow	
Pink	

Processing of a polypeptide: Translation completes the flow of genetic information from the DNA sequence to the sequence of amino acids in a polypeptide. However, to obtain functional protein, folding into distinct

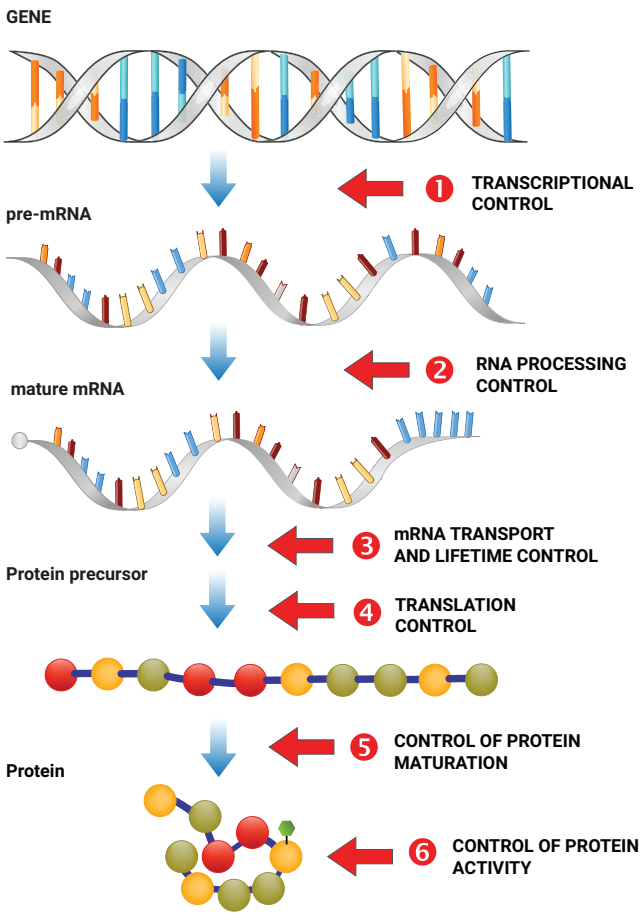


Fig. 14. Gene regulation levels in eukaryotes.

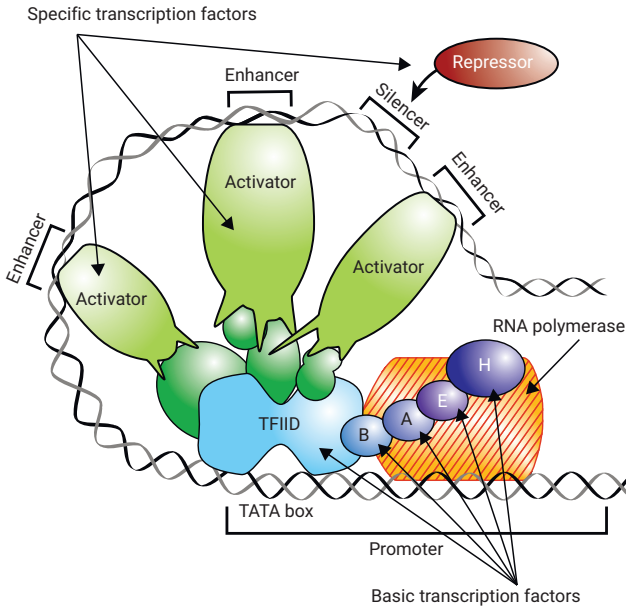


Fig. 15. Transcription regulation in eukaryotes.

three-dimensional conformation is required. Proteins that facilitate the folding of other proteins are called **molecular chaperones**. Chaperones do not convey additional information required for the polypeptide folding, rather, they assiste the self-assembly process by binding to and stabilizing unfolded or partially folded intermediates polypeptides.

In many cases, proteins also undergo further post-translational modifications, such as covalent modifications of amino acids (phosphorylation, methylation, acetylation, etc.) and cleavage of the **protein precursor** to produce a smaller active protein. A simple example of protein cleavage is removal of the initiator methionine from the amino terminus of many polypeptides, which occurs soon after the amino terminus of the growing polypeptide chain emerges from the ribosome.

Gene regulation in eukaryotes

In eukaryotes, regulation of gene expression is much more complex than in prokaryotes. Different sets of genes are expressed in different cells of a multicellular organism, even though they contain the same DNA. Regulation of gene expression can take place at all the stages of DNA → RNA → protein pathway. Stages of eukaryotic gene expression are shown on Fig. 14.

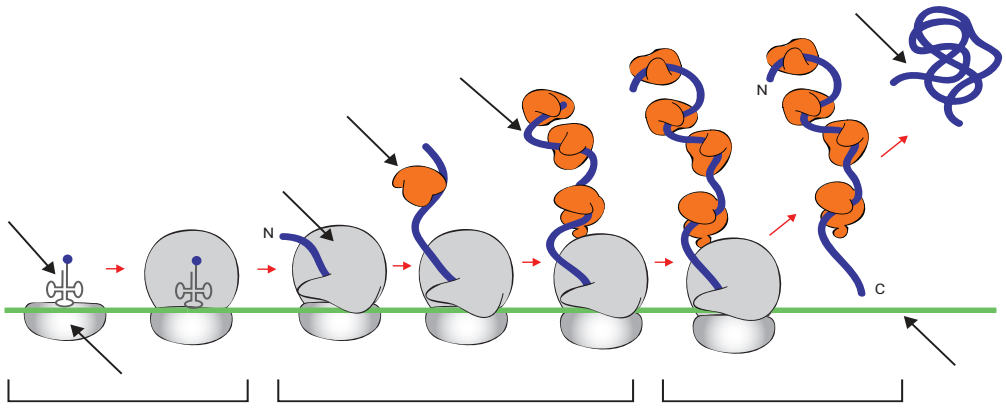
Transcription is a key regulatory point for many genes. Regulation include chromatin remodeling, nucleosome positioning, histone modifications, DNA binding with regulatory proteins such as transcription factors and noncoding RNAs.

Sets of **transcription factor proteins** bind to specific DNA sequences and promote or repress its transcription. **Binding sites** for transcription factors are often close to a gene promoters. Within promoter region, just upstream of the transcriptional start site, resides the TATA box. To initiate transcription, a **basic transcription factor** (TFIID) is the first to bind to the TATA box. Binding of TFIID recruits other basic transcription factors to the TATA box. Once this **transcription initiation complex** is assembled, RNA polymerase can bind to promoter.

Further, regulatory sequences can also be found in other parts of DNA, sometimes very far away from the promoter: a gene may have several **enhancers** (far-away clusters of binding sites for activators) or **silencers** (the same thing, but for repressors). DNA-bending proteins bring the enhancers in contact with **specific transcription factors** and **mediator proteins** (Fig. 15).

Task 3.17. What is the difference between basic and specific transcription factors?

Task 3.18. Learn processes of translation and folding in the figure below. Designate I – initiation of translation, II – elongation of polypeptide, III – termination of translation; 1 – small ribosome subunit, 2 – large ribosome subunit, 3 – mRNA, 4 – tRNA, 5 – growing polypeptide chain, 6 – chaperone, 7 – folded protein. Label 5′- and 3′-ends of mRNA.



Task 3.19. Correlate regulatory factors (column A) with their effect on gene expression (column B).

COLUMN A	COLUMN B
(1) Long poly-A tail of mRNA	(a) Facilitation of protein folding
(2) Silencers	(b) Activation of transcription
(3) Enhancers	(c) Suppresion of transcription
(4) DNA methylation	(d) Increasing of RNA life span
(5) Histone acetylation	(e) Alternative splicing
(6) Protein precursor cleavage	(f) Protein activation
(7) Repressor transcription factors	
(8) Transcription factors (activators and coactivators)	
(9) Chaperones	
(10) Spliceosome	

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

Home Work

Answer the questions using information from textbook «ESSENTIAL MEDICAL BIOLOGY», Chapter 3, pp.22–33; Chapter 4, pp.33–37; Chapter 6, pp.39–44.

1. What are the building units of proteins? _____

2. How many amino acids are found in proteins? _____

3. What bonds are between amino acid residues in a protein? _____

4. Describe primary, secondary and tertiary structure of a protein.

5. Define the following terms:

Transcription

Translation

Splicing

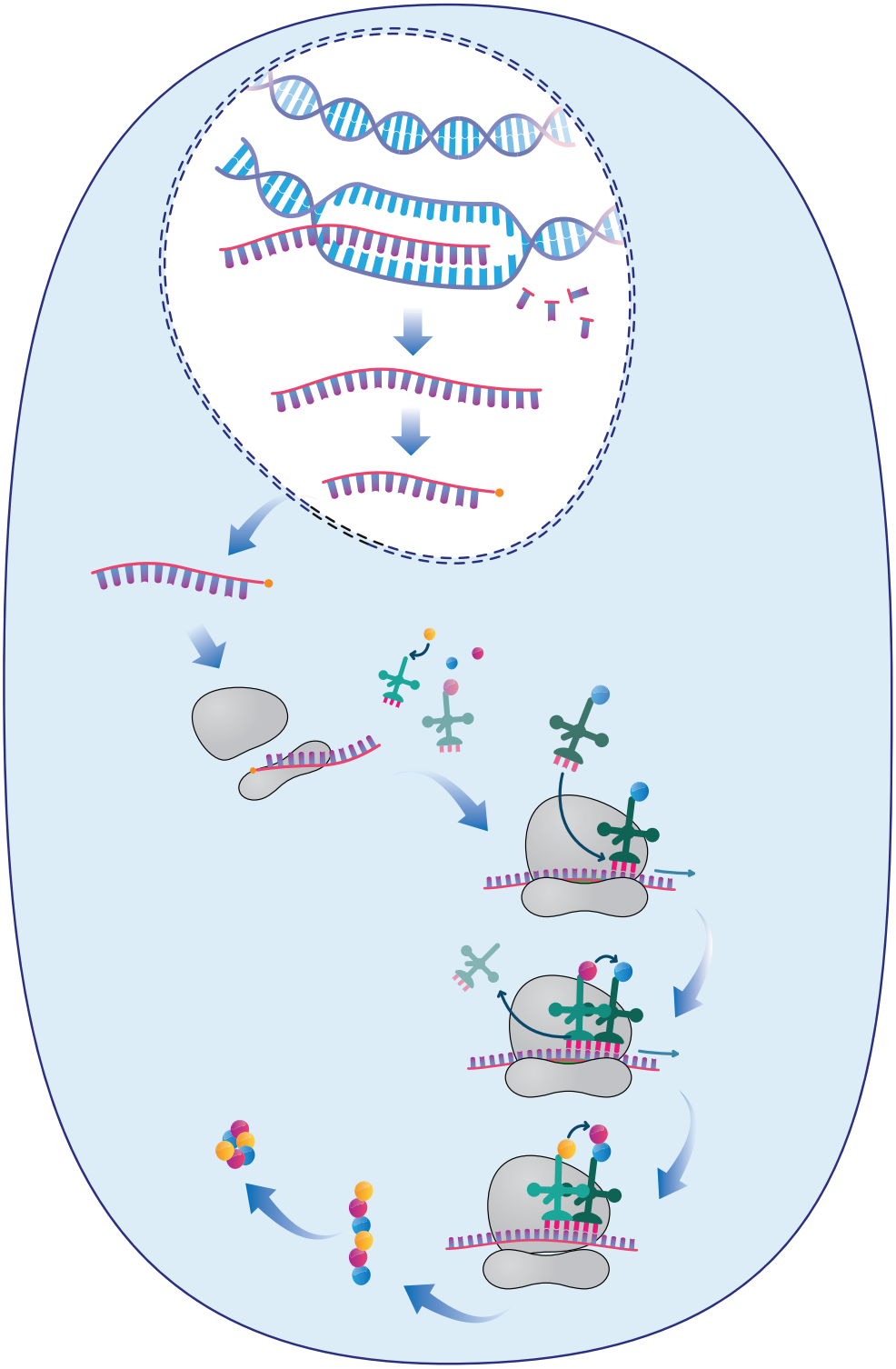
6. What do terms 'codon' and 'anticodon' mean?

7. What is the role of tRNA in translation?

8. What is the role of nonsense triplets?

9. What is the difference between introns and exons?

10. The diagram on the page 31 shows an overview of the process of protein synthesis. Identify and label the structures in this diagram using the following list of terms: 1 – transcription, 2 – translation, 3 – nucleus, 4 - cytoplasm, 5 – nucleotides, 6 – mRNA, 7 – DNA, 8 – ribosome, 9 – codon, 10 – anticodon, 11 – post-transcription modification of pre mRNA, 12 – tRNA, 13 – growing polypeptide chain, 14 – amino acid, 15 – folding, 16 – folded protein.



TOPIC 4. CHROMOSOME. KARYOTYPE. CYTOGENETIC METHOD

Chromosome

Eukaryotic chromosome is a linear nucleoprotein complex. The nucleoprotein material of the eukaryotic chromosome is referred to as **chromatin**. The degree of condensation of chromatin varies during cell cycle. In interphase, most of DNA is non-condensed and can be transcribed or replicated. During mitosis or meiosis DNA is highly condensed and form **chromosomes**.

Diameter of DNA molecule helix is about 2 nm. A **nucleosome** is the basic unit of DNA packaging in eukaryotes and consists of a segment of DNA wound around a protein core of 8 histone molecules (Fig. 16). Repeating nucleosomes with intervening "linker" DNA form a 11 nm fiber, described as "beads on a string". A chain of nucleosomes can be arranged in a 30 nm fiber, a compacted structure whose formation is dependent on the presence of the **H1 histone**. The 30 nm fiber is arranged into loops along a central protein **scaffold**. By metaphase, the loops gather and give rise to highly condensed, rod-like shapes referred to as mitotic chromosomes (Fig. 16).

Task 4.1. The average length of DNA molecule composing a human chromosome is about 4 cm. The average length of a metaphase chromosome is 6 mkm. Calculate how many times the linear size of DNA decreased as a result of condensation?

Task 4.2. How many molecules of histones make up the core of a nucleosome?

Task 4.3. There are about 6200000000 bp (base pairs) of DNA in human cell. How many nucleosomes are there if every nucleosome contains about 142 bp and about 70 bp is a linker (a fragment of DNA between two nucleosomes)?

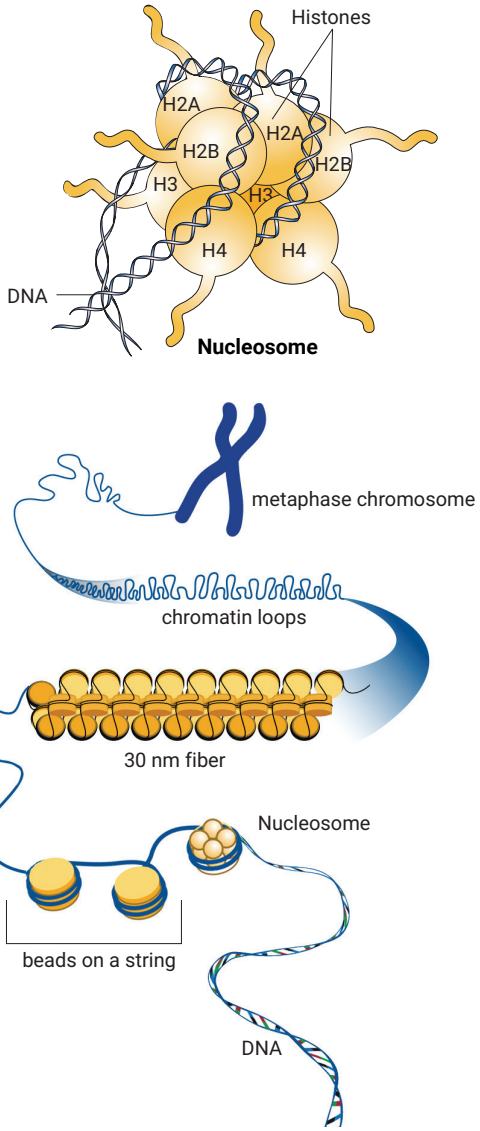


Fig. 16. Levels of chromosome condensation.

Credit: National Human Genome Research Institute https://www.genome.gov/genetics-glossary/Chromatin (with changes).

The cell cycle (mitotic cycle) consists of two parts: interphase (during which the cell performs special functions and prepares for division) and mitosis (division itself). The degree of chromosome condensation changes significantly during cell cycle.

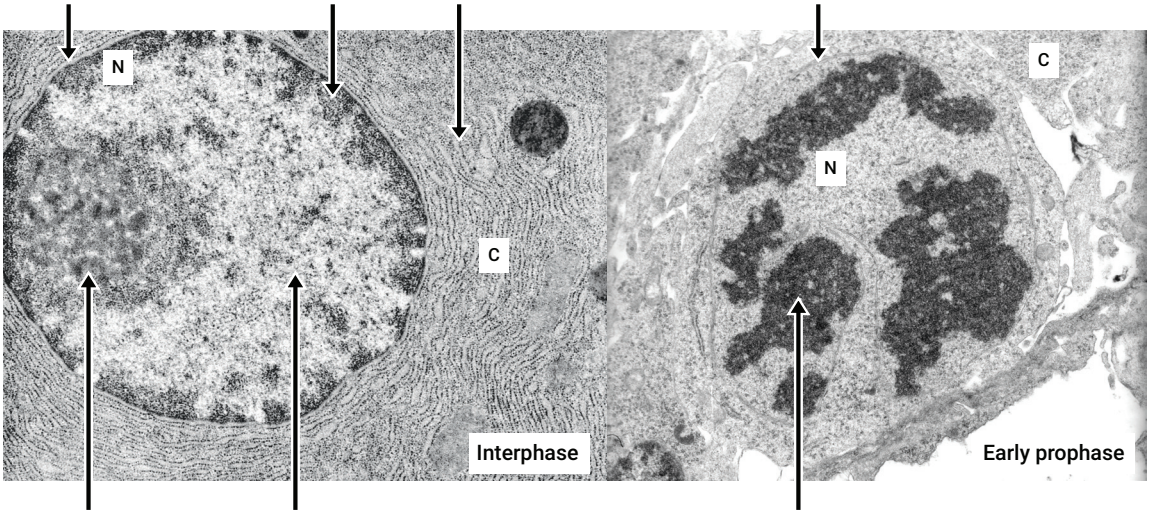
In the interphase nucleus, chromosomes are unpacked and active. They are difficult to distinguish from each other. Lighter stained **euchromatin** and the patches of darker **heterochromatin** are, on the other hand, easy to visualize under a microscope.

During the cell division, chromosome territories transform into highly condensed chromosomes, which then can be clearly distinguished from one another.

Task 4.4. Complete the following table:

Chromatin	Degree of condensation	Presence of genes	Presence of active transcription
Euchromatin			
Constitutive heterochromatin			
Facultative heterochromatin			

Task 4.5. Learn chromosome changes in the cell cycle in transmission electron microscope micrographs (credit: Jlcalvo | Dreamstime.com). Check the following items: 1 – nucleolus, 2 – euchromatin, 3 – heterochromatin, 4 – nuclear envelope, 5 – rough endoplasmic reticulum, 6 – condensing chromosome. N – nucleus, C – cytoplasm.



Model of facultative heterochromatin formation is X-chromosome inactivation in mammalian females. During early development, one of the two X chromosomes is transcriptionally silenced in every cell of a female embryo. The X inactivation process is dependent on the action of a special noncoding RNA, Xist, which coats the X chromosome and induces its inactivation (Fig. 17). Silencing on the inactive X chromosome coincides

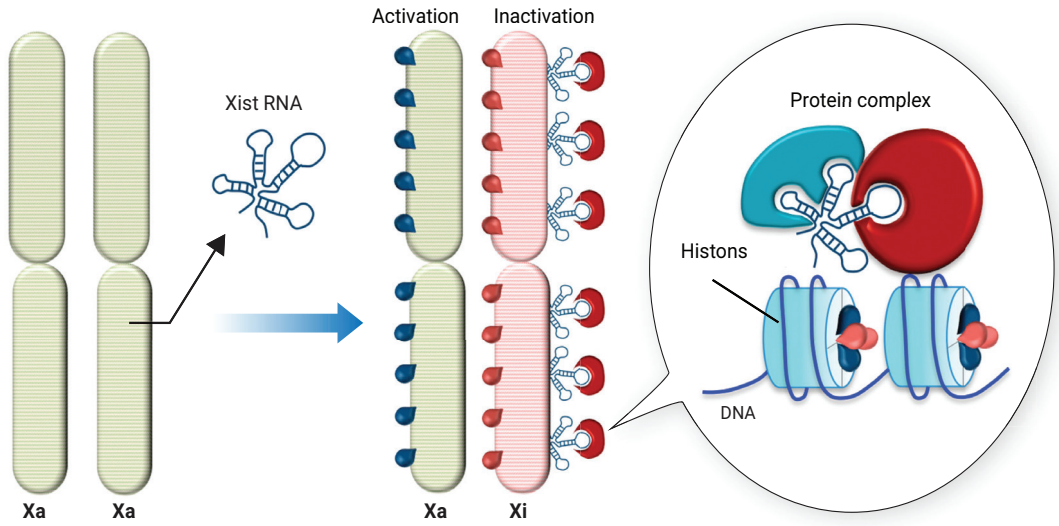


Fig. 17. Mechanism of X cromosome inactivation.

Source: Fiorenzano A, Pascale E, Patriarca EJ, Minchiotti G, Fico A. Epigenomes. 2019; 3(3):14.

with the acquisition of a multitude of chromatin modifications, resulting in the formation of extraordinarily stable facultative heterochromatin that is saved in subsequent cell divisions. The inactive state of the X chromosome is only reversed in the female germ line. As a result, every female is a mosaic of cells, each expressing exclusively her mother's or father's X-chromosome genes.

A classic example of a mosaic caused by X-inactivation is seen in cats. In female cats, heterozygous for alleles of black and yellow color, X chromosomes are accidentally inactivated in different cells during development. The result is a tortoise shell pattern consisting of alternating spots of black and yellow fur. Black spots come from groups of cells in which X^B with the black allele is active, and orange spots come from cells in which X^Y with the orange allele is active (Fig. 18). The calico cat has the same black and orange colors as the tortoise shell, plus white.

Fig. 18. Kitten with a tortoise shell pattern of coloration.

The inactive X forms a discrete body within the nucleus called a **Barr body** (named after discoverer Murray Barr). The number of Barr bodies in somatic cells of a mammal female is the number of X-chromosomes in karyotype minus one.

Task 4.6. In Figure 18, mark the spots where the X^Y allele is active with arrows.

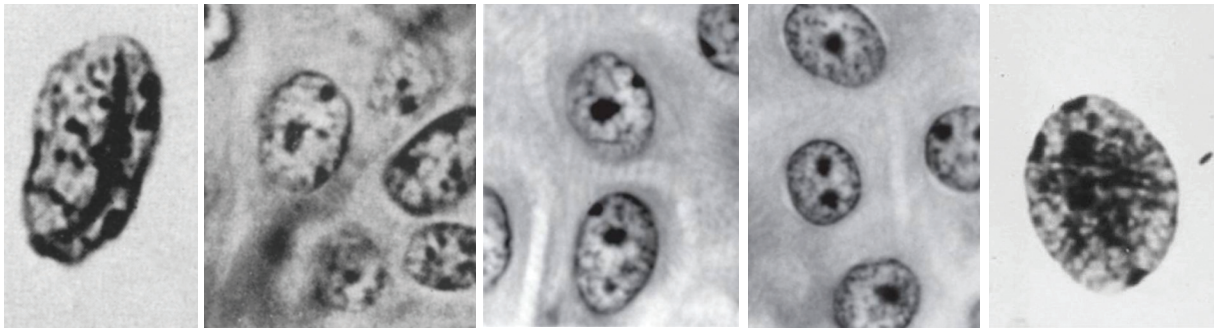
Task 4.7. Fill in the empty cells in the tables below, indicating how many Barr bodies are present in people with the indicated karyotypes.

Karyotype	Number of Barr bodies
46, XX female	
46, XY male	
47, XXY male	

Karyotype	Number of Barr bodies
48, XXXX female	
45, X0 female	
47, XYY, male	

Task 4.8. If you meet a tortoise shell cat on the street, can you determine its gender from a distance?

Task 4.9. Using micrographs of cell nuclei, determine the number of X chromosomes in human karyotypes. Do not confuse Barr's bodies and nucleolus.



A	B	C	D	E

Mitotic chromosomes

During cell division all the chromosomes are highly condensed to move successfully to different poles of the cell. Mitotic chromosomes can be studied under the light microscope using a procedure called karyotyping (cytogenetic study or chromosome analysis). In human, karyotyping can be performed on a samples of blood, bone marrow, amniotic fluid, or placental tissue.

Chromosomal analysis in human includes the following stages:

1. Blood cells are stimulated to divide. For example, human lymphocytes start to divide if a substance called phytohemagglutinin is added to the medium. Cells are cultivated at 37°C for 3 days.
2. Colcemide (or colchicine) is then added to arrest cell division in metaphase by blockage of microtubules of mitotic spindle.
3. Hypotonic solution is added to swell the cells and separate chromosomes from each other.
4. After histological fixation the swollen cells are dropped onto a glass slide so that the cell membranes are broken and the chromosomes are spread around (so called metaphase plate is formed). After staining, every particular chromosome can be identified.

Chromosome staining techniques:

1. Routine staining was used in 1950s. Only size and shape of chromosome can be characterized by this method. The method was used to ctreate Denver nomenclature, which divides all human chromosomes in 7 groups, from A to G, according to their size and position of a centromere (Fig. 19 A).
2. Banding was developed in 1960s. There are methods of G, R, Q and C banding (Fig. 19 B). This technique allows every chromosome identifying by its specific banding pattern. Paris nomenclature is based on this staining technique.
3. FISH method (fluorescence in situ hybridization technique, Fig. 20) was developed in 1990s. This method uses fluorescent tags to detect hybridization of sequence-specific probes with metaphase or interphase chromosomes.
4. Spectral karyotyping (SKY) is a novel FISH-based technique for chromosome analysis, in which all the chromosome pairs are simultaneously visualized in different colors in a single hybridization. A set of probes labeled with combination of different fluorescent tags is used for hybridization (Fig. 21).

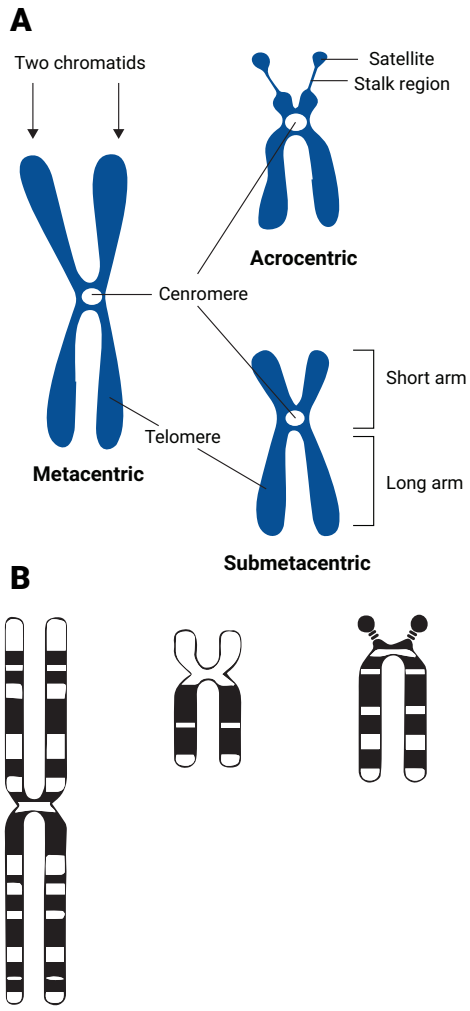


Fig. 19. Types of chromosomes: A – routine staining; B – banding pattern (Giemsa).

Task 4.10. Try to suppose when the bone marrow and when the amniotic fluid are used as a material for karyotyping.

Karyotype. Chromosome nomenclature

The chromosomal complex of a somatic cell is referred to as a **karyotype**. Chromosomes are divided into two parts with a constriction point in the in the middle which is known as the centromere. Three types of chromosomes in human cells are classified by the position of the centromere (Fig. 19).

The first **chromosome nomenclature** was decided in **Denver, 1966** and based on chromosomal size and shape. Chromosomes were divided into 7 groups (A–G). The basic terminology for banded chromosomes was decided at a meeting in Paris in 1971, and is often referred to as the Paris nomenclature (Fig. 22). Short arm locations are labeled **p (petit)** and long arms **q (queue)**. Each chromosome arm is divided into regions labeled p1, p2, p3 etc., and q1, q2, q3, etc., counting outwards from the centromere. Regions are delimited by specific

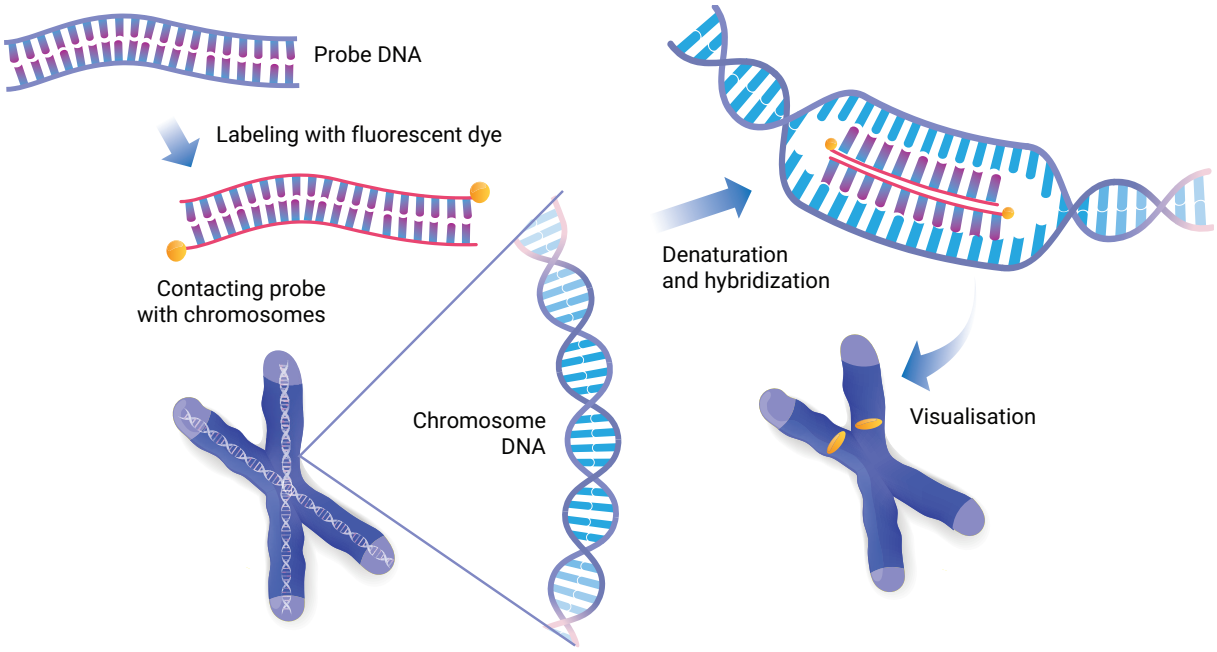


Fig. 20. FISH technique.

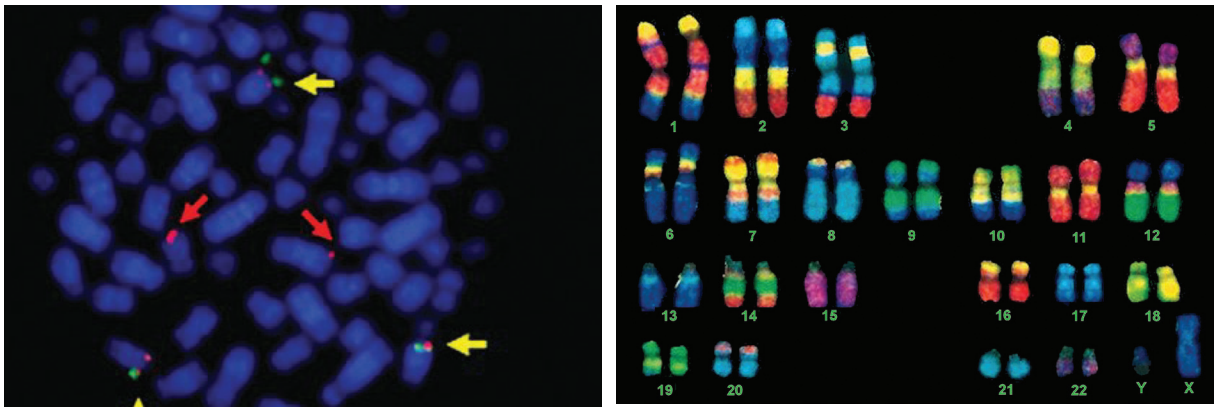


Fig. 21. Results of FISH and SKY.

Left – FISH. Source: H. Nagoshi et al., Cancer Res. 2012 (72) (19) 4954–4962; DOI: 10.1158/0008-5472.CAN-12-0213. Right – SKY. Source: Memorial University of Newfoundland collection.

landmarks, which are consistent and distinct morphological features, such as the ends of the chromosome arms, the centromere and certain bands. Regions are divided into bands labeled p11 (one-one, not eleven!), p12, p13, etc., sub-bands labeled p11.1, p11.2, etc., and sub-sub-bands e.g. p11.21, p11.22, etc., in each case counting outwards from the centromere. The centromere is designated '**cen**' and the telomere '**tel**'.

Task 4.11. Fill in the table using the Fig. 22. What pairs of human autosomes in a human karyotype are metacentric? Acrocentric? Submetacentric?

Group of chromosomes	Characteristics of the group	Numbers of chromosome pairs
A	Big meta- or submetacentric	1–3
B		
C		
D		

E		
F		
G		

Task 4.12. In human, rRNA genes are situated at stalk regions of acrocentric chromosomes. How many clusters of rRNA genes are there in human karyotype?

Chromosome map is a graphic representation of the positions of genes on chromosomes. There are different types of chromosome maps (Fig. 23):

1. Linkage (or genetic) maps show the arrangement of genes and genetic markers along the chromosomes as calculated by the frequency with which they are inherited together. The unit of this map is cM (centi-Morgan) which is 1% of crossing over frequency between particular genes. Cluster of tightly linked genes on a chromosome that are inherited together from a single parent are referred to as haplotype.
2. **Cytogenetic map** indicates banding pattern of a chromosome.
3. **Physical maps** provide physical distances between chromosomal landmarks ideally measured in nucleotide bases, for example 1 Mb means 1000000 pairs of nitrogenous bases (nucleotides).

The development of easy-to-use genetic maps, coupled with the successful sequencing of the entire human genome, has greatly advanced genetics research. The improved quality of genetic data has reduced the time

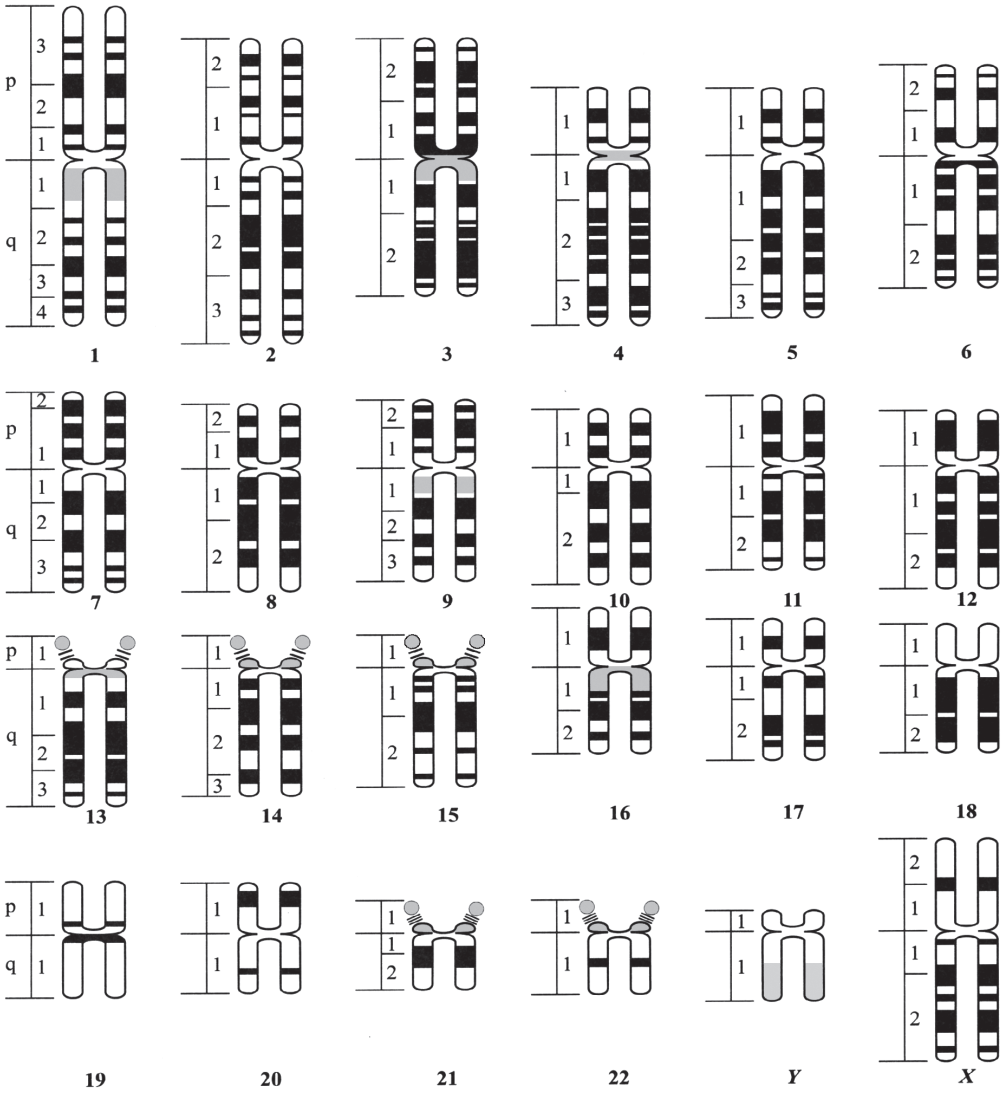


Fig. 22. Schematic representation of human chromosomes and their banding.

required to identify a gene from a period of years to weeks.

Task 4.13. Below are cytogenetic maps of human X and Y chromosomes (credit: National Institutes of Health). Localize genes for 1 – hemophilia B (Xq27.1); 2 – Duchenne muscular dystrophy (Xp21.2); 3 – SRY gene (Yp11.3); 4 – SHOX gene (Xp22.33; Yp11.3); 5 – fragile X syndrome (Xq27.3) gene; 6 – vitamin D-resistant rickets gene (Xp22.2). Which of them are X-linked, which Y-linked and which are in pseudo-autosomal regions of these chromosomes?

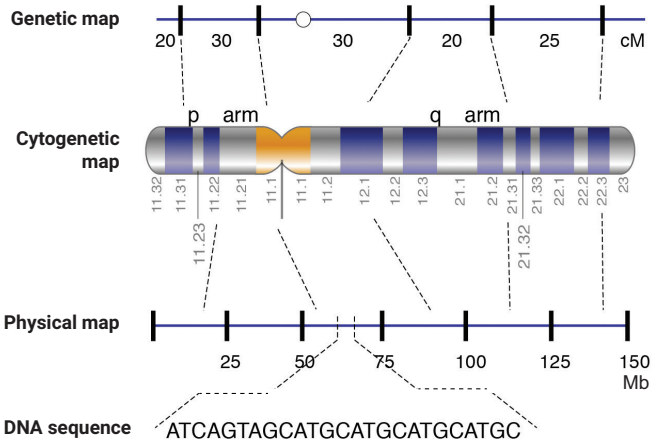
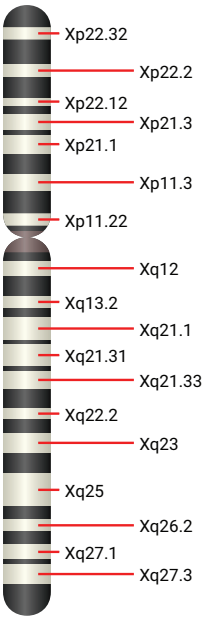
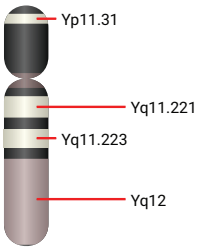


Fig. 23. Chromosome maps.





Home Work

Answer the questions using information from textbook «ESSENTIAL MEDICAL BIOLOGY», Chapter 8, pp. 49–53.

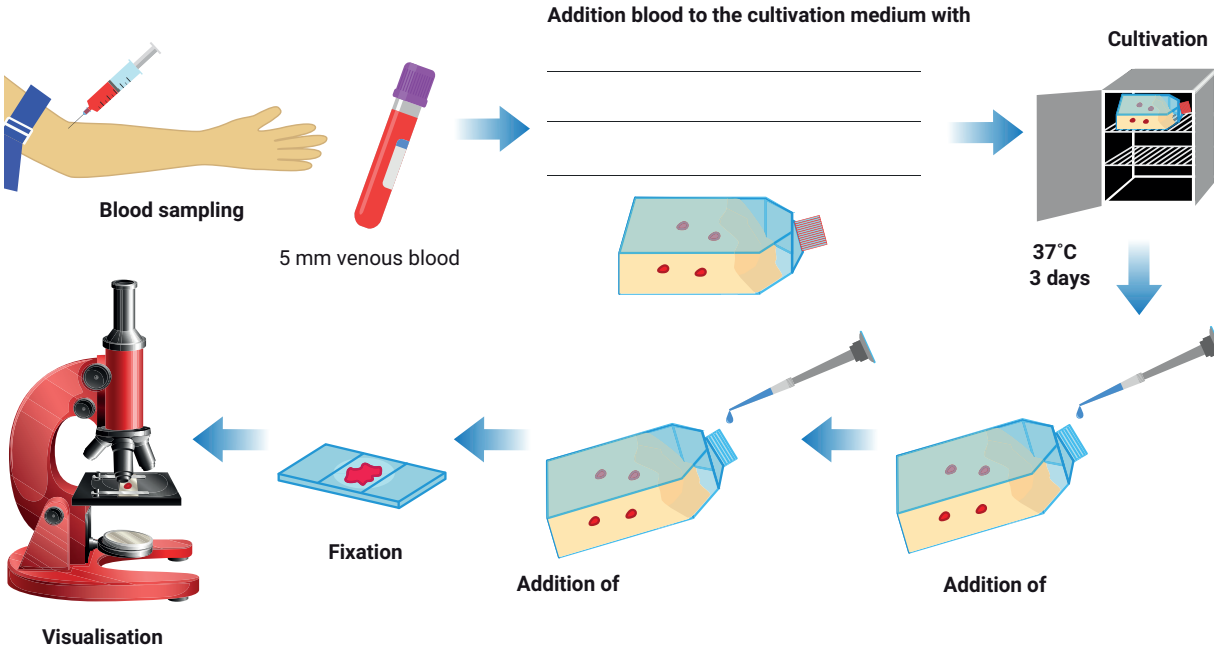
1. What difference is there in the compaction of chromosomes during interphase and metaphase?

2. What's a nucleosome?

3. What's karyotype?

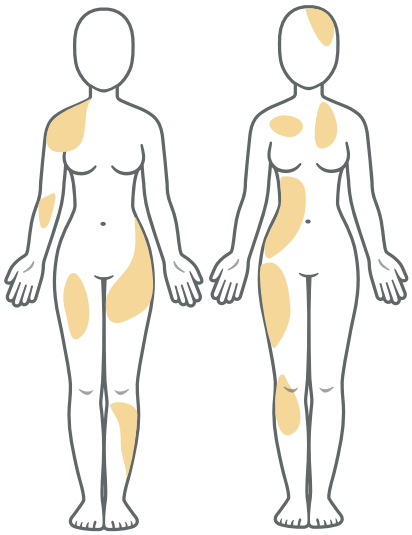
4. What do you know about Barr's body?

5. Indicate what important reagents are added at each stage of karyotiping and what is their role:



6. Define 'p' and 'q' arm, centromere, telomere, chromatid.

7. Identical twins develop from one zygote (monozygous twins) and share the same genotype. Gene mutation "ectodermal dysplasia", responsible for sweat glands is X-linked. Explain why two identical twins heterozygous for this mutation have different pattern of sweat glands distribution on their skin (lack of sweat glands is shown in yellow in diagram).



8. What chromosome staining techniques do you know?

9. What does the abbreviation 'FISH' mean?

TOPIC 5. CELL CYCLE. MITOSIS. ABNORMALITIES OF MITOSIS

Cell Cycle

Cell cycle refers to a set of events, through which a cell grows, replicates its genome, and ultimately divides into two daughter cells. Thus, cell cycle includes **interphase** and **mitosis**. Interphase lasts about 20 hours and has pre-synthetic (G_1), synthetic (**S**) and post-synthetic (G_2) periods. Mitosis has four phases (prophase, metaphase, anaphase and telophase). G_0 is a period when a cell stops its division and begins differentiation.

There are a number of **checkpoints** — moments at which the cell evaluates the results of previous stage, which allow the precise coordination of cell-cycle events. Perturbation of cell cycle control and unlimited cell proliferation are hallmark features of neoplasia. Cell progression the cell cycle involves a complex of events regulated by specific proteins: **cyclins**, **cyclin-dependent kinases** (CDKs) and their **inhibitors**.

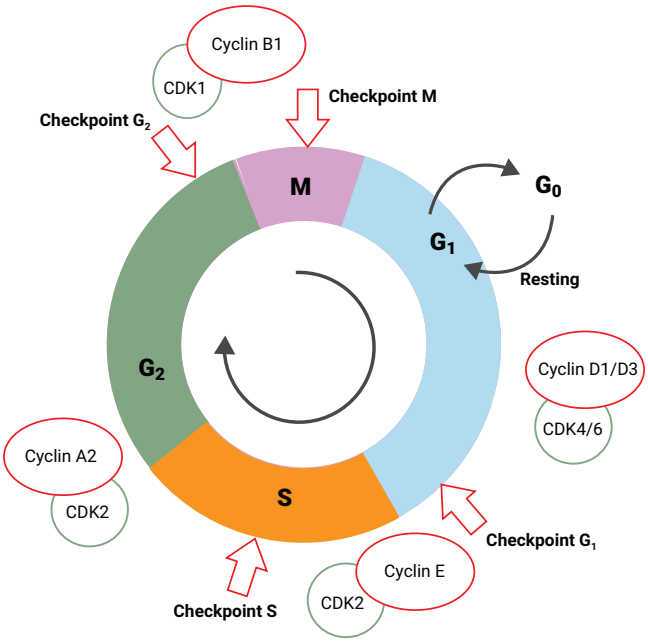
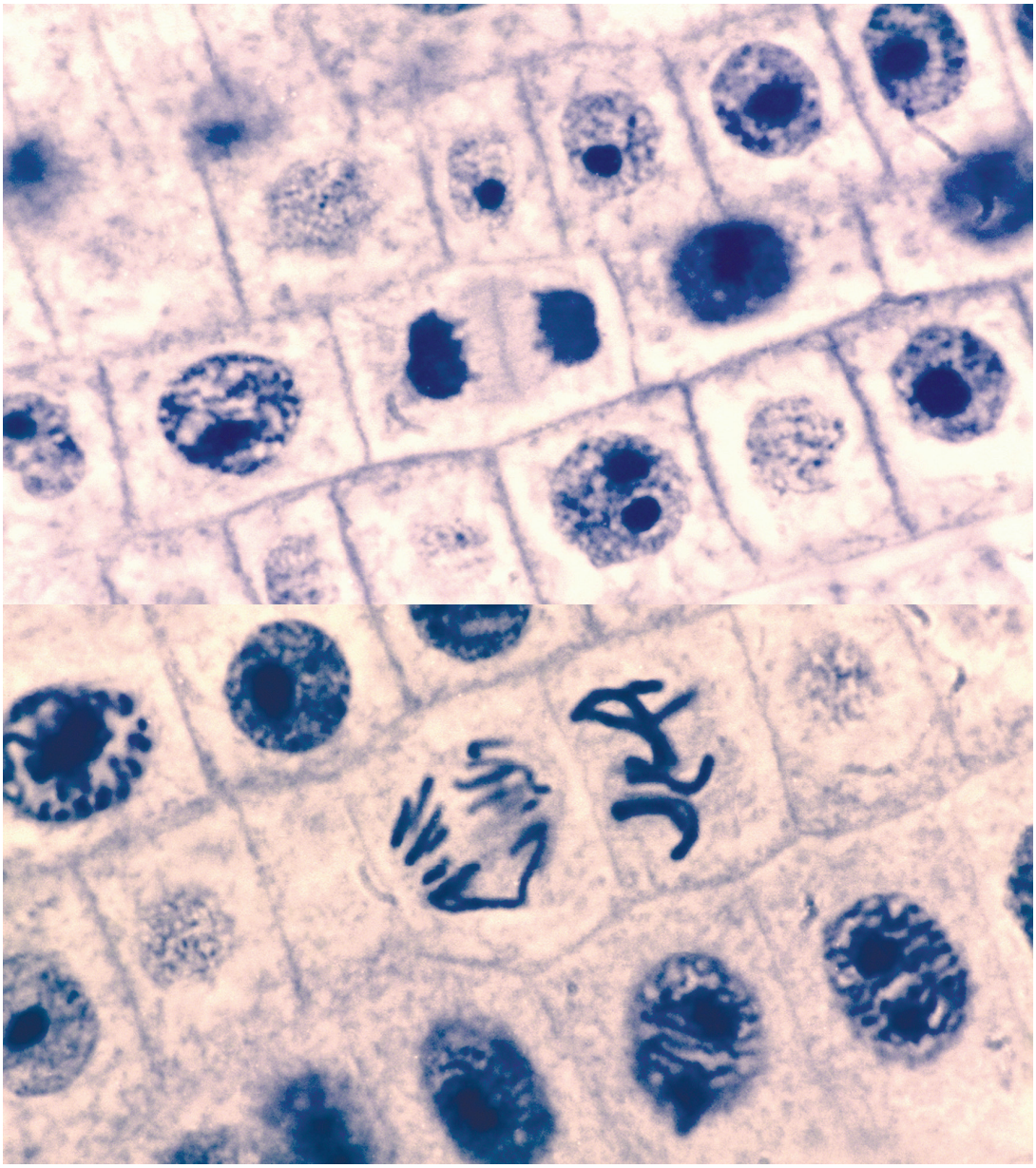


Fig. 24. Cell cycle regulation.

Task 5.1. Fill in the table:

Stages of cell cycle	What happens to chromosomes and cell	Amount of chromosomes (n) and DNA (c)
G1 period	Growth of cell, protein synthesis	2n2c
S period		
G2 period		
Prophase		
Metaphase		
Anaphase		
Telophase		

Task 5.2. Indicate which cell of onion root shown below matches each of the following stages of mitotic cycle: A – interphase; B – prophase; C – metaphase; D – anaphase; E – telophase.



Task 5.3. Draw cells in interphase and in all the stages of mitosis (use image of the onion root cell division).

INTERPHASE **PROPHASE** **METAPHASE**

ANAPHASE **TELOPHASE**

Task 5.4. Fill in the table:

Checkpoint	Signal(s) for cell to start next stage
G1 checkpoint	
S checkpoint	
G2 checkpoint	
Metaphase/ anaphase checkpoint	

Labile, stabile and permanent cells

All somatic cells could be put into three groups: labile, stabile or permanent cells.

Labile cells (or stem cells) are cells that multiply constantly. They have very short or absent G_0 phase. Examples include cells of early embryo, hematopoietic cells of bone marrow, and cells of sexual glands.

Stabile cells are cells that multiply only when needed. They spend most of the time in G_0 phase of the cell cycle, but can be stimulated to enter the cell cycle. Examples include liver cells, epithelium of endocrine glands, lymphocytes of peripheral blood.

Permanent cells are terminally differentiated and incapable to proliferate. They are called post-mitotic and are in G_0 phase for the rest of the life. Examples are brain cells, heart cells, skeletal muscles and red blood cells.

Task 5.5. In the myth about Prometheus an eagle every day pecked at his liver, but at night the organ regrew. To which type of cells do liver cells belong?

Task 5.6. Why the RBCs in mammals are incapable to divide?

Task 5.7. At what stage of cell cycle does colchicine stop cell division? _____

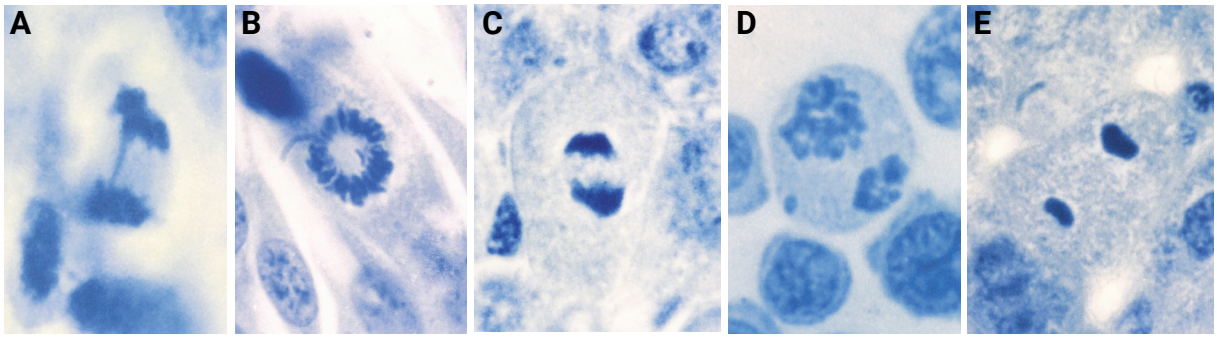
Task 5.8. It is known that phytohemagglutinin stimulates division of lymphocytes in peripheral blood samples (so called blast transformation). What can you say about the stage of the lymphocyte's cell cycle before and after adding of phytohemagglutinin:

Abnormalities of mitosis

Breakdown of the mitotic machinery can produce division mistakes. Improper chromosome segregation can lead to **numerical chromosomal abnormalities** in daughter cells thus causing serious malfunction or even the death of daughter cells. Some chemicals such as colchicine can disrupt mitotic spindle, kinetochores or centrosomes. If in cells normal control of division has broken down, these cells begin to divide uncontrollably giving rise to a tumor. Physical agents, such as temperature, radiations and chemicals like narcotics and enzyme inhibitors, can easily produce mitotic deformities. Examples of mitotic abnormalities are:

- Multipolar mitosis: Mitotic division with several spindles. Multipolarity is usually caused by uneven division of centrosome as well as irregular distribution of chromatids on different spindles. It results in the formation of cells with aneuploidy (uneven chromosome number).
- C-mitosis (abnormal spindle formation): Colchicine inhibits mitosis by disorganizing spindle formation. The results are the formation of polyploid cells, and reduplication of chromosomes.

Task 5.9. Decide which photos demonstrate normal and which abnormal mitosis?



NORMAL	
ABNORMAL	

Task 5.10. Compare the cell cycle step (column A) and the best match term in column B.

COLUMN A	COLUMN B
(1) Synthetic period (S)	(a) The gap between DNA synthesis and mitosis, the cell will continue to grow. The G2 checkpoint control mechanism ensures that everything is ready to enter the M (mitosis) phase and divide.
(2) Mitosis (M)	(b) Cell growth stops at this stage and cellular energy is focused on the orderly division into two daughter cells. A checkpoint in the middle of mitosis (Metaphase Checkpoint) ensures that the cell is ready to complete cell division.
(3) Postsynthetic period (G2)	(c) A phase where the cell has left the cycle and has stopped dividing.
(4) Resting phase (G0)	(d) DNA (and centrosome) replication occurs.
(5) Postmitotic period (G1)	(e) Cells increase in size. The G1 checkpoint control mechanism ensures that everything is ready for DNA synthesis.
(6) Cell cycle checkpoint	(f) Times during the cell cycle in which the cell checks to see whether it is ready to proceed with mitosis

A	1	2	3	4	5	6
B						

Home Work

Answer the questions using information from textbook «ESSENTIAL MEDICAL BIOLOGY», Chapter 10, pp.59—66.

1. Which stages are included in interphase? _____

_____

2. In which phase of the cell cycle is DNA replicated? _____

3. What types of cells – somatic or sex are formed as a result of mitosis? _____

4. What is cytokinesis? How does it happen in plant and animal cells?

_____

_____

_____

_____

5. What is C-mitosis?

_____

_____

6. How many chromosomes (n) and chromatids (c) does have a diploid cell with n=23 in metaphase and anaphase of mitosis?

_____

_____

TOPIC 6. SEXUAL REPRODUCTION. MEIOSIS. GAMETOGENESIS

Reproduction is a process by which new individual organisms – "offspring" – are produced from their "parents". There are two forms of reproduction: asexual and sexual. Sexual reproduction requires production of gametes.

Task 6.1. Compare asexual and sexual reproduction (in animals). Fill in the table:

	Asexual reproduction	Sexual reproduction
How many parents take part in reproduction?		
What is the mechanism of cell division		
Are gametes produced?		
Are all offspring genetically identical?		

Gametogenesis

Gametogenesis is the process of producing gametes whereby haploid cells (n) are formed from a diploid cell (2n) through **meiosis** and cell differentiation (Fig. 25). Producing of ova is called **ovogenesis** and producing of sperm is called **spermatogenesis**. In females ovogenesis takes place in **female gonads** — **ovaries**; in males — in **male gonads — testes**.

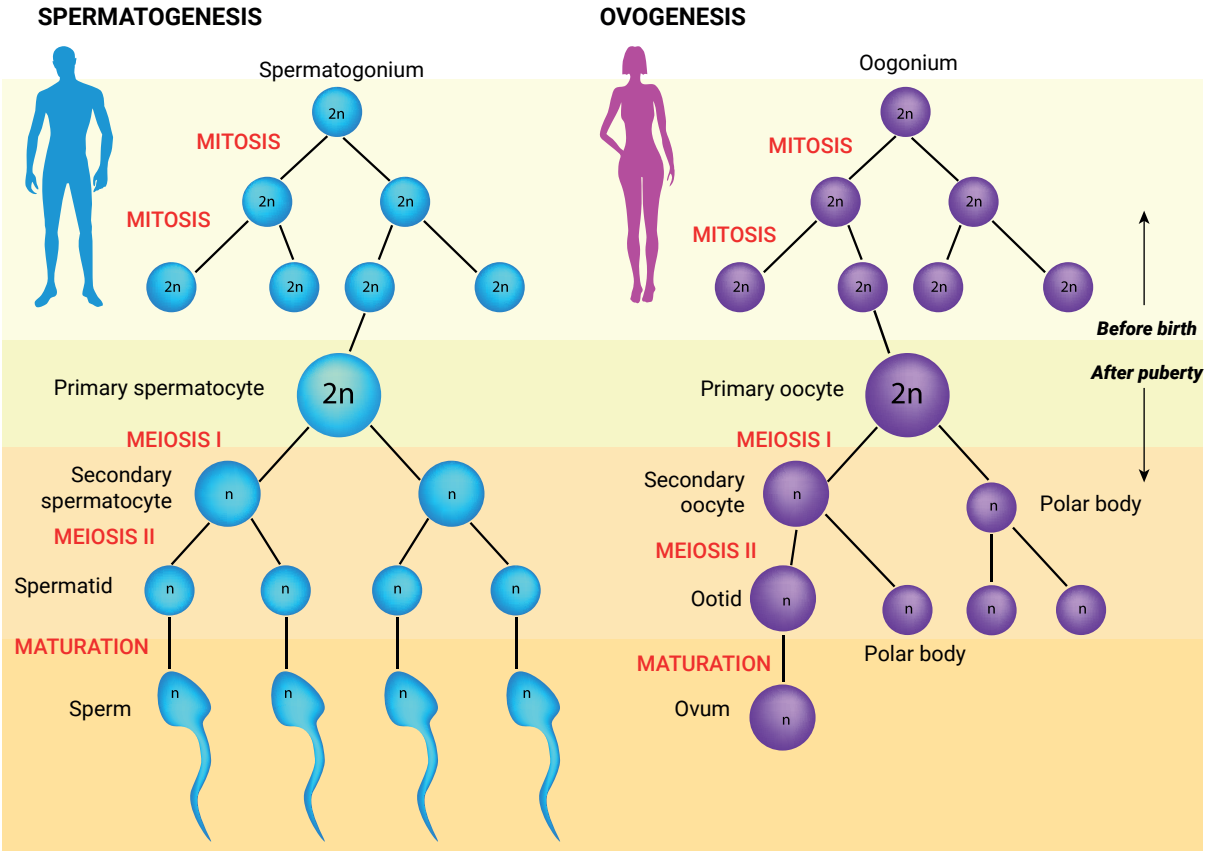


Fig. 25. Gametogenesis in human.

Task 6.2. Indicate periods of life when does periods of gametogenesis occur. Compare ovo- and spermatogenesis and fill in the table:

Period of gametogenesis	Ovogenesis	Spermatogenesis	Amount "n" and "c"
Mitotic division (spermatogony or ovogony)			
Growth of primary spermatocytes or ovocytes			
Meiosis 1 (secondary spermatocytes or ovocytes formation)			
Meiosis 2 (spermatids or ovotids formation)			
Differentiation (maturation)			

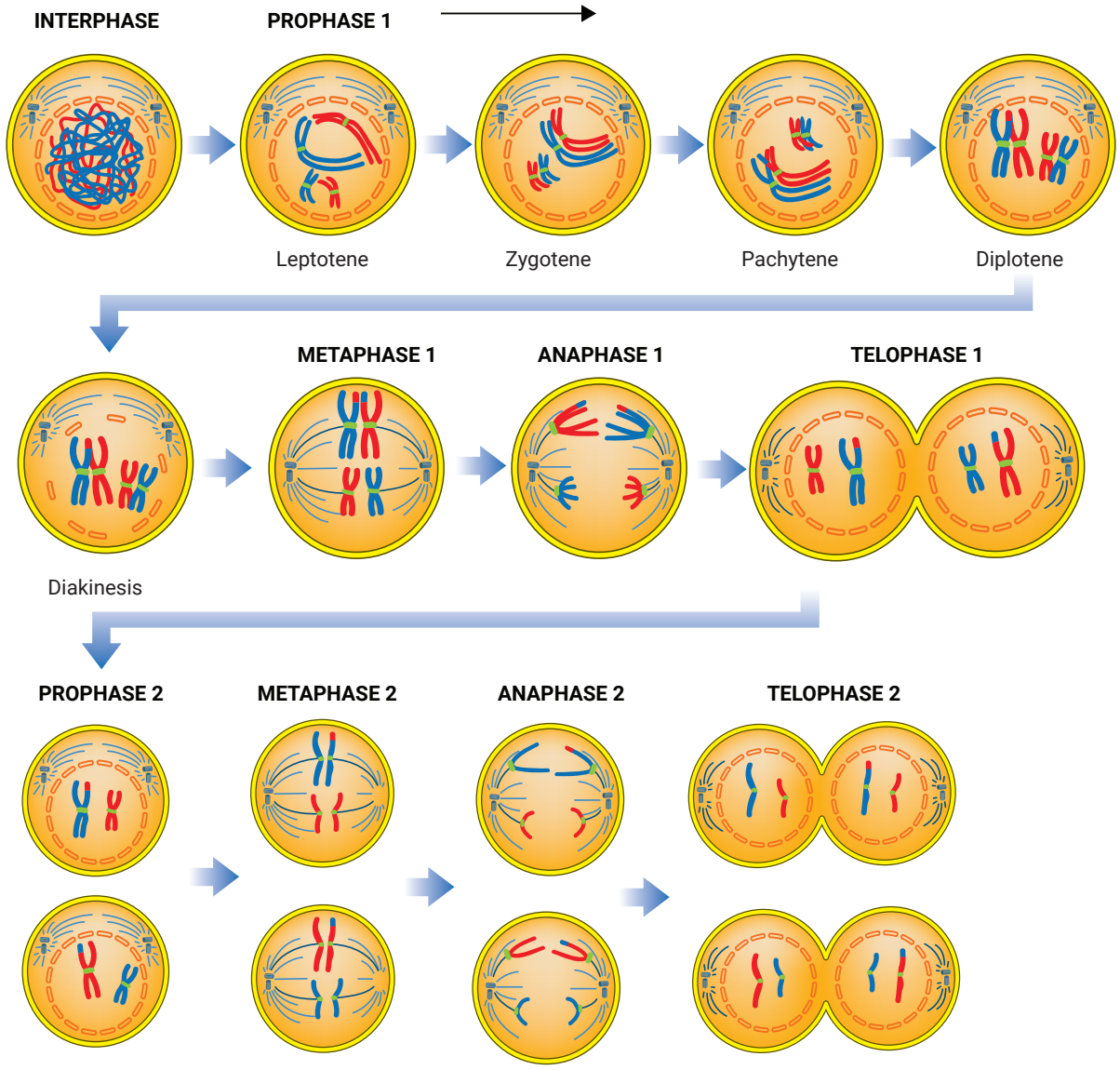


Fig. 26. Meiosis.

Meiosis

Meiosis consists of two rounds of cell divisions with no interphase between them. They are named meiosis-1 and meiosis-2 respectively, and include prophase, metaphase, anaphase and telophase each (Fig. 26). First meiotic division takes about 90% of the whole time of meiosis and can last for weeks or years (in case of oogenesis).

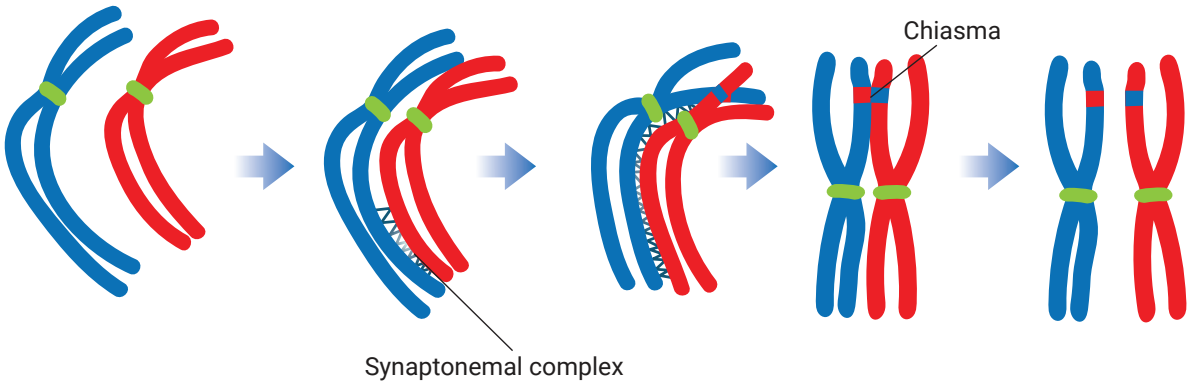
Prophase 1 of meiosis 1 is defined by five different phases: **leptotene**, **zygotene**, **pachytene**, **diplotene** and **diakinesis**. The most important even during prophase 1 is the **crossing over** and recombination of genetic material between non sister chromatids resulting in the genetically unidentical, haploid daughter chromatid cells.

Crossing over is the exchange of genetic material between non-sister chromatids of homologous chromosomes during meiosis, which results in new allelic combinations in the daughter cells.

Prophase 1 during oogenesis also includes **dictyotene** (meiotic resting phase between diplotene and diakinesis). The chromosomes that have already undergone crossing over may remain in this stage for months or even years.

Task 6.3. Explain the difference between homologous chromosomes and sister chromatids.

Task 6.4. Identify the stages of meiosis at which the events depicted below occur:

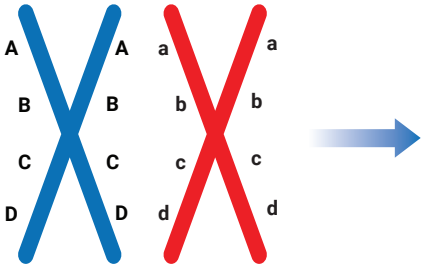


Task 6.5. Indicate main differences between mitosis, meiosis 1, and meiosis 2:

Phase	Mitosis	Meiosis 1	Meiosis 2
Prophase			
Meta-phase			

Anaphase			
Telophase			

Task 6.6. Draw schematically crossing over between two homologous chromosomes during prophase 1. Let's assume that the break happened between the centromere and loci C/c.



Two events in meiosis contribute to **genetic diversity** in the offspring. First, in prophase 1 due to **crossing over** between homologous chromosomes new combinations of paternally and maternally derived genes appear. Second, during anaphase 1 by **independent assortment of paternal and maternal chromosomes** from each bivalent, the gametes acquire different mix of chromosomes. The amount of potential variations increases with the number of chromosomes.

In *Ascaris*, for example, where n=2, the random assortment of homologs could produce only n^2, or 4 types of gametes. In humans, where n=23, the same mechanism alone could generate 2^{23}, or more than 8 billion genetically different kinds of gametes.

Task 6.7. How many genetically different kinds of gametes could produce following species (do not take crossing over into account):

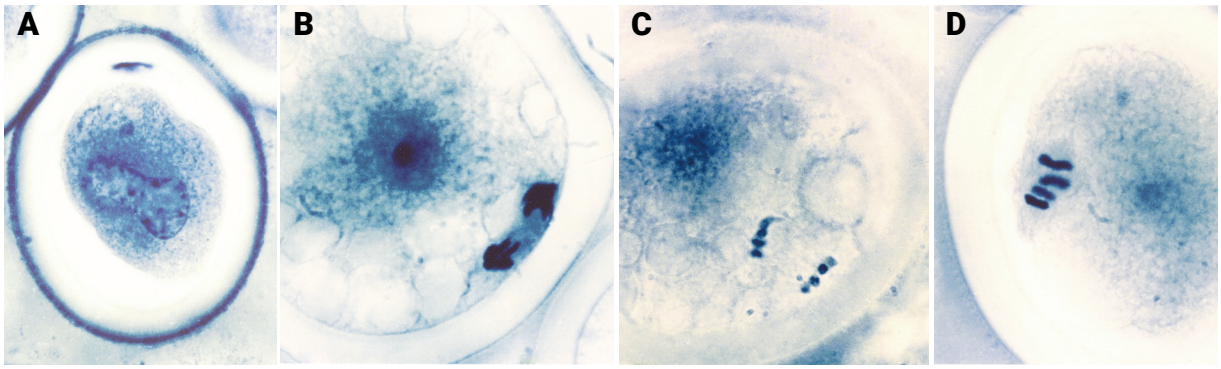
Species	2n = 6	2n = 10	2n = 46
Number of kinds			

Task 6.8. Choose the phrase from the column B that best fits the term in the column A:

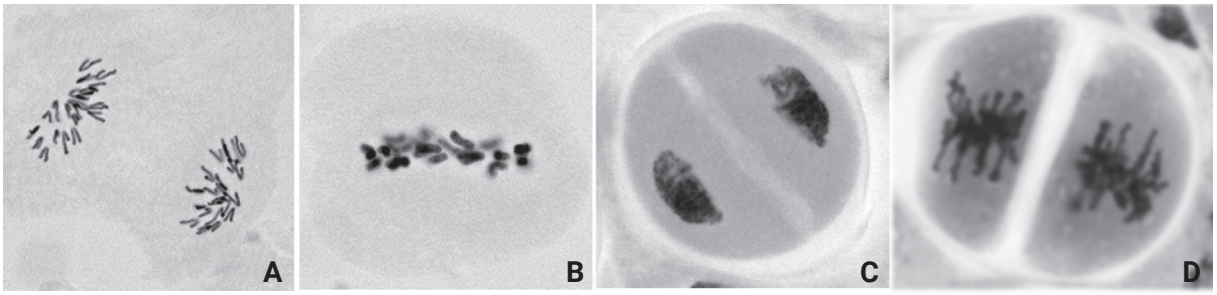
COLUMN A	COLUMN B
(1) Meiosis	(a) Chromosomes do not differ between the sexes
(2) Gametes	(b) One of the two identical halves of a duplicated chromosome
(3) Synapsis	(c) The time when sister chromatids separate
(4) Chromatid	(d) One diploid cell gives rise to four haploid cells
(5) Anaphase	(e) Division of the cytoplasm
(6) Autosomes	(f) Haploid cells specialized for reproduction
(7) Karyotype	(g) Pairing of homologous chromosomes
(8) Interphase	(h) One diploid cell gives rise to two diploid cells
(9) Mitosis	(i) The set of chromosomes of a somatic cell or of a biological species
(10) Cytokinesis	(j) The part of a cell cycle when chromosomes are not visible

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

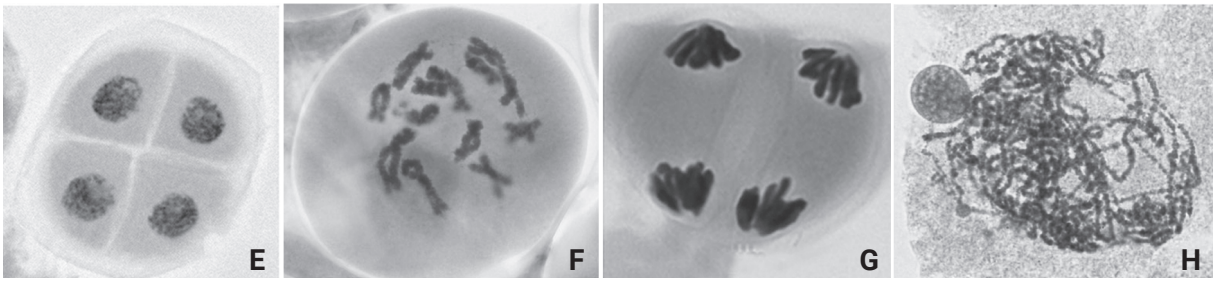
Task 6.9. Decide which stages of meiosis and fertilization in askaris are at the photos below. Label following structures: 1 – genetic material of a spermatozoa, 2 – tetrads, 3 – dyads, 4 – male pronucleus, 5 – female pronucleus, 6 – fertilization envelope, 7 – polar body.



Task 6.10. Decide which stages of meiosis in plant are at the photos* below. Label following structures: 1 – cytoplasm, 2 – nucleus, 3 – nucleolus, 4 – chromosomes, 5 – chiasmata, 6 – tetrads.



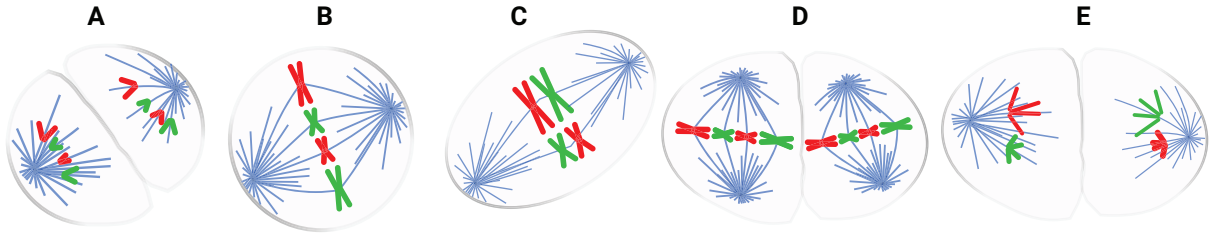
wheat *wheat* *wheat* *lily*



wheat *lily* *barley* *lily*

* Photos of wheat are from Matsuoka Y. et al., PLoS One. 2013, 8;8(8): e68310, doi: 10.1371/journal.pone.0068310; rice – Wu J. et al., Plant Physiology 2015, 169 (4) 2700–2717; DOI: 10.1104/pp.15.00791; barley – Szurman-Zubrzycka M. et al., Frontiers in Plant Science 2019, 10, 761, DOI=10.3389/fpls.2019.00761.

Task 6.11. Cells at different phases of mitosis and meiosis are shown. Identify the process and the stage of cell division. How many "n" and "c" are there?



Images credit: domdomegg with modifications. URL: https://commons.wikimedia.org/wiki/File:Three_cell_growth_types.svg

A	
B	
C	
D	
E	

Home Work

Answer the questions using information from textbook «ESSENTIAL MEDICAL BIOLOGY», Chapter 11, pp.66–71.

1. Compare meiosis 1 and meiosis 2 and fill in the table:

Phases of meiosis	nc	What happens to chromosomes
Prophase 1. Leptotene		The chromosomes begin to condense and are attached to the nuclear membrane via their telomeres
Prophase 1, Zygotene		
Prophase 1, Pachytene		
Prophase 1, Diplotene		
Prophase 1, Diakinesis		
Prophase 1, Dictyotene (in oogenesis)		

Metaphase 1		
Anaphase 1		
Telophase 1		
Prophase 2		
Metaphase 2		
Anaphase 2		
Telophase 2		

2. During what phase of meiosis are homologs pulled to opposite poles of the cell? _____

3. During what phase of meiosis are chromosomes split into chromatids? _____

4. During what phase of meiosis do tetrads line up at the center of the cell? _____

5. In human 2n = 46. How many chromosomes would you find in:

brain cell	
red blood cell	
polar body	

sperm	
secondary oocyte	
zygote	

6. Define the following terms:

Dyads –

Tetrads (bivalents) –

Dictyotene –

Polar body –

Crossing over –

7. How many tetrads are there in a species with 2n=4; 2n=8; 2n=46?

2n = 4	2n = 8	2n=46

8. A 40-year-old woman becomes pregnant. For approximately how long was the primary oocyte that formed the ovum arrested in prophase of meiosis 1?

9. What may happen if separation of chromatids during anaphase does not work properly?

10. How many spermatozoa come from ten primary spermatocytes? _____

11. How many ova come from ten primary oocytes? _____

12. Why parthenogenesis is an example of sexual reproduction? _____

TOPIC 7. GENETIC VARIATIONS. MUTATIONS

Mutations are heritable alterations in genetic material. Genes and chromosomes can mutate in either somatic or germinal tissue, and these changes are called **somatic mutations** and **germinal mutations**, respectively. Somatic mutations may lead to mosaicism. A mosaic, or mosaicism, is the presence of two or more populations of cells with different genotypes in one individual, who has developed from a single fertilized egg.

Mutations are divided into **gene mutations**, **chromosomal structural** and **chromosomal numerical** mutations (aberrations).

Gene mutations

Gene mutations are the result of change in the nucleotide sequence of a gene. Gene mutations may happen during DNA replication, repair or recombination. Frequency of gene mutations is 1:10000 – 1:100000 for a locus per a generation. The smallest unit of mutation in DNA is referred to as **muton** – a pair of complementary nucleotides. Gene mutations may give rise to new allelic forms of a gene. If a particular gene has more than two allelic forms it is referred to as **multiple allelism**. Exact mechanism of gene mutation can be:

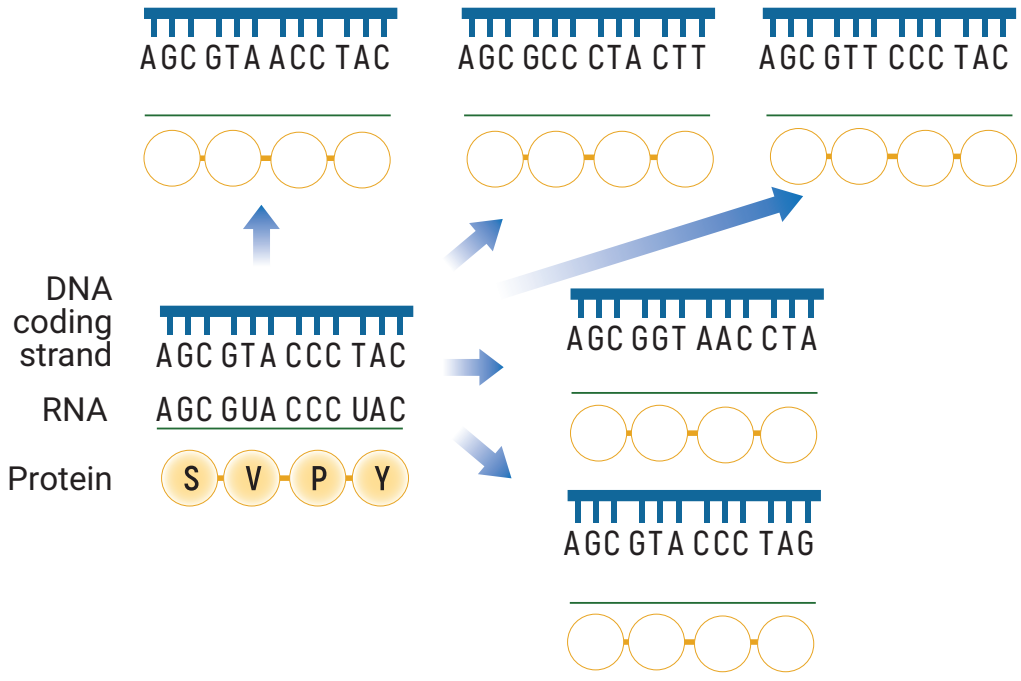
1. substitution of a nucleotide pair (most common),
2. deletion or insertion of nucleotide pairs,
3. inversion of nucleotide pairs (rare).

Substitution of a purine for a purine (A → G, or G → A) or a pyrimidine for a pyrimidine (C → T or T → C) is referred to as **transitions** (2/3 of all substitutions). Substitution of a purine for a pyrimidine, or vice versa, is known as a **transversions** (1/3 of all substitutions).

The consequences of substitution of nucleotides in DNA may have no effect due to degeneracy of the genetic code (**silent mutations**); may lead to a change of amino acid (**missense mutation**) or result in the production of shorter proteins than normal polypeptide (**nonsense mutations**).

Deletions or insertions may be "**in frame**" when the number of extra or missing nucleotides are multiples of three. It may results in a deletion/insertion of 1 or more amino acids in the protein. Mutation is "**frameshift**" if the number of nucleotides is not divisible by three. In this case deletion or insertion will skew the reading frame downstream of the mutation.

Task 7.1. Using the genetic code table (Table 1, page 22), restore the structure of mutated mRNA and peptides and indicate the type of mutation in the figure below. DNA coding strand is shown. Label 5′ and 3′-ends of DNA; N and C-ends of polypeptide.



Mutations in a gene outside the coding region also can alter gene expression. For example, mutations in promoter sequence of a gene make it difficult for RNA polymerase to recognize the site. As a result transcription is diminished or prevented. Mutations in splicing sites can obstruct normal splicing and so on.

Nomenclature of mutations specifies the type of mutation and base or amino acid changes.

- In DNA. **Nucleotide substitution** (e.g. A36T) means that adenine is substituted by thymine. The number indicates the nucleotide position from 5' end. A — adenine, T — thymine, C — cytosine, G — guanine.
- In the polypeptide. **Amino acid substitution** (e.g. D151E) — the first letter is the one letter code for amino acid, the number is the position of the amino acid from the N-terminus and the second letter is the one letter code of the amino acid present in the mutation, X stands for nonsense triplet.

  Amino acid deletion (e.g. ΔF508) — the Greek symbol Δ or 'delta' indicates a deletion. The letter refers to the amino acid and the number is the position from the N-terminus of the polypeptide.

Task 7.2. In human HbS allele (sickle-cell anemia) the sixth animo acid in the beta-globin chain is changed from glutamic acid to valine. In HbC the sixth amino acid is changed from glutamic acid to lysine. What type of gene mutations are they? Use the genetic code table (Table 1, page 22).

Type of hemoglobin	Normal hemoglobin HbA	HbS	HbC
Amino acid	Glutamic acid	Valine	Lysine
Codons of mRNA			
Codons in DNA			

Task 7.3. Do you think each of the following types of mutations would have very severe effects, mild effects or no effect at all?

Nonsense mutation occurring in the sequences encoding amino acids near the N terminus of the protein		Frameshift mutation occurring in the sequences encoding amino acids near the C terminus of the protein	
Nonsense mutation occurring in the sequences encoding amino acids near the C terminus of the protein		Silent mutation	
Frameshift mutation occurring in the sequences encoding amino acids near the N terminus of the protein		Missense mutation in the middle of the second intron	
Deletion of the dinucleotide AT in the middle of the first intron		Missense mutation affecting the active site of a protein	

Examples of gene mutations in human (monogenic, or Mendelian diseases):

- Autosomal dominant (Marfan's syndrome, achondroplasia)
- Autosomal recessive (phenilketonuria, albinism)
- X-linked dominant (vitamin D-resistant rickets)
- X-linked recessive (hemophilia, color blindness)

Chromosomal aberrations

Chromosomal abnormalities can be numerical or structural. **Structural chromosomal abnormalities** may appear as a result of mistakes during DNA recombination (unequal crossing over) or replication and repair of

DNA. Usually, they are causes of diseases and genetic syndromes

Structural chromosomal rearrangements may involve one or more chromosomes. Rearrangements of one or a pair of homologous chromosomes include the following types (note that the letters are not individual genes, but chromosome segments):

- **Deletions (del):** A portion of the chromosome is deleted. For example, Cru di Chat ("cat cry") syndrome is due to deletion of a short arm of chromosome 5 (Fig.27). Affected infants cry like a kitten due to affected larynx and nervous system. Other symptoms are severe cognitive, speech and motor delays.
- **Duplications (dup):** A portion of the chromosome is duplicated, resulting in extra genetic material. Deletions and duplications can lead to departure from normal gene dosage and be harmful to the organism.
- **Isochromosome (i)** is a result of deletion of one arm of a chromosome and duplication of another. Thus, isochromosome has two p or two q arms.
- **Inversions (inv):** A portion of the chromosome has broken off, turned upside down and reattached, therefore the genetic material is inverted. Inversions alter the order, but not the number of genes on a chromosome and do not affect gene dosage balance.

  Paracentric inversions does not include centromere, while **pericentric** — includes centromere.
- **Ring chromosome (r)** appears when telomeres of a chromosome are missed and so called "sticky ends" join to form a circle or ring (Fig. 28). This can happen with or without loss of genetic material.
- **Translocations (t)** are rearrangements that involve two or more non-homologous chromosomes: A portion of one chromosome is transferred to another. There are several types of translocations:

  — Reciprocal translocation: Segments from two different chromosomes have been exchanged. Myeloid leukemia is due to a reciprocal translocation between chromosomes 9 and 22 (Philadelphia chromosome, Fig. 29).

  — Non-reciprocal translocation means that a part of one chromosome is placed to some other non-homologous chromosome.

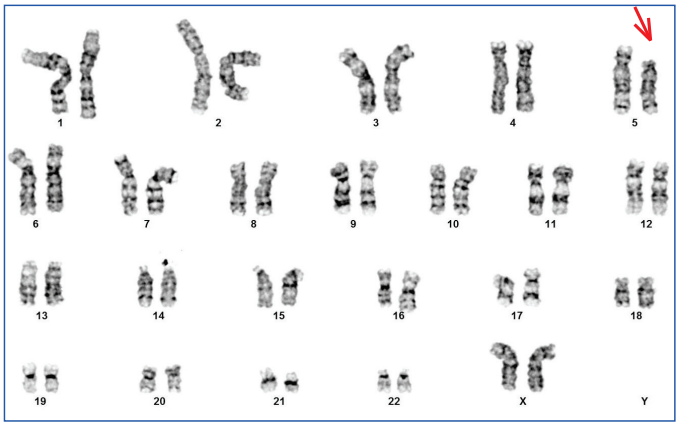


Fig. 27. Karyotype of a female patient with cri du chat syndrome.

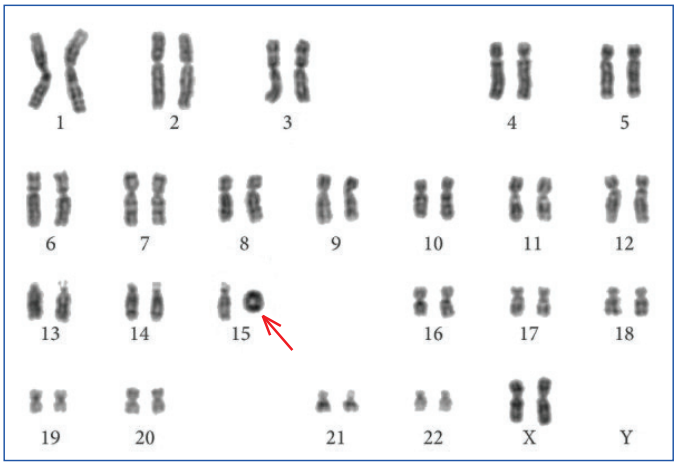


Fig. 28. Karyotype of a patient with a ring chromosome 15: 46, XX, r(15).

From: Britto I.S. et al., Case Rep Obstet Gynecol. 2014 – 2014: 495702; doi: 10.1155/2014/495702.

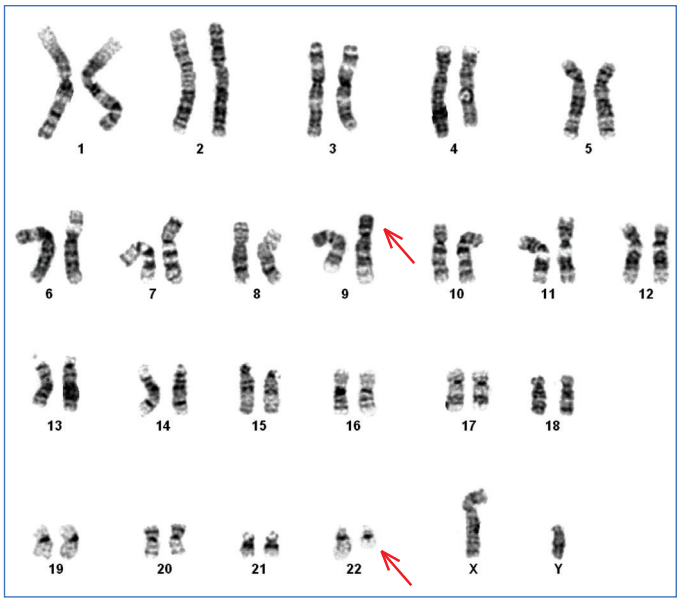
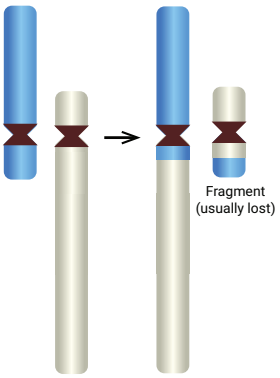


Fig. 29. Karyotype of a patient with a balanced reciprocal translocation: 46,XY,t(9;22) (q11; p11).

This type of translocation (Philadelfia chromosome) may lead to myeloid leukemia.

– **Robertsonian translocation (rob)**, or centric fusion (Fig. 30): an entire chromosome has attached to another at the centromere. Is named after W.R.B. Robertson who suggested that during evolution, metacentric chromosomes may arise from the fusion of two acrocentrics.



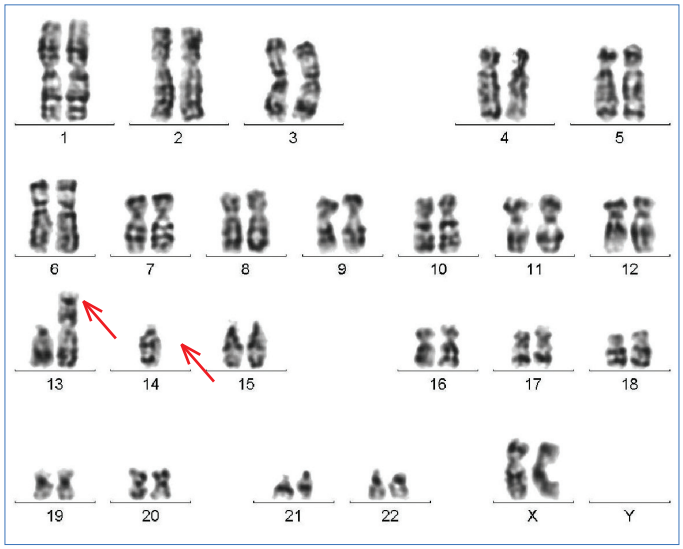
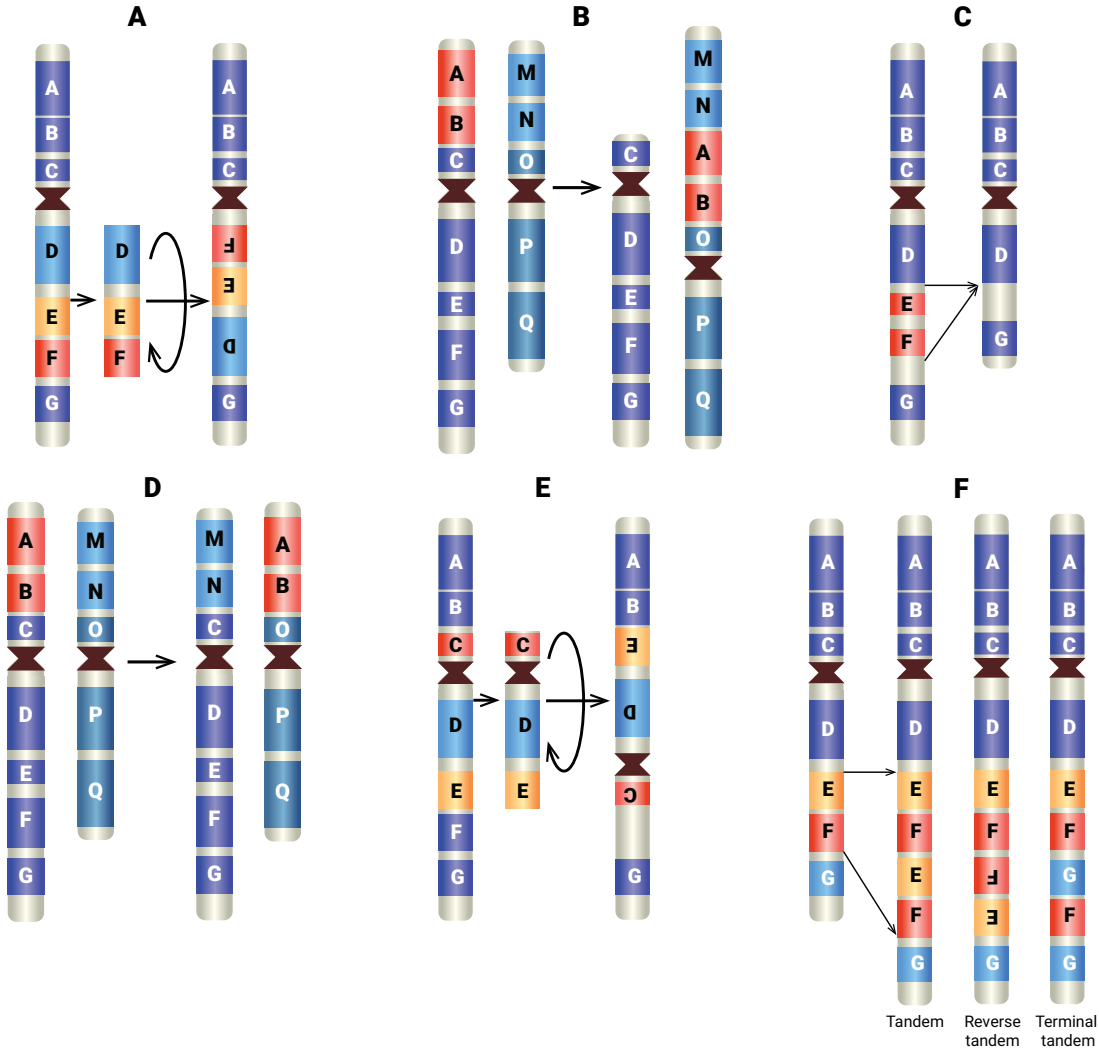


Fig. 30. Scheme of Robertsonian translocation and karyotype of a patient with Robertsonian translocation: 45, XX, t(13;14)(q10;q10).

Task 7.4. Identify the types of chromosomal rearrangements in the diagrams below:



A	
B	
C	

D	
E	
F	

If a chromosome as a result of translocation has got a fragment with centromere it may become **dicentric (dic)**. Part of a chromosome without a centromere is referred to as **acentric fragment (f)**.

In a standard metaphase chromosome spread, the replicated chromosomes appear as a single chromosome with two centromeres (Fig. 31). At mitosis or meiosis, the two centromeres may segregate together to the same pole so as to produce a product a more or less complete gene set. Alternatively, they may segregate to alternate poles, in which case the region between the two centromeres will be broken at random, and produce segmental aneuploidy in the daughter cells.

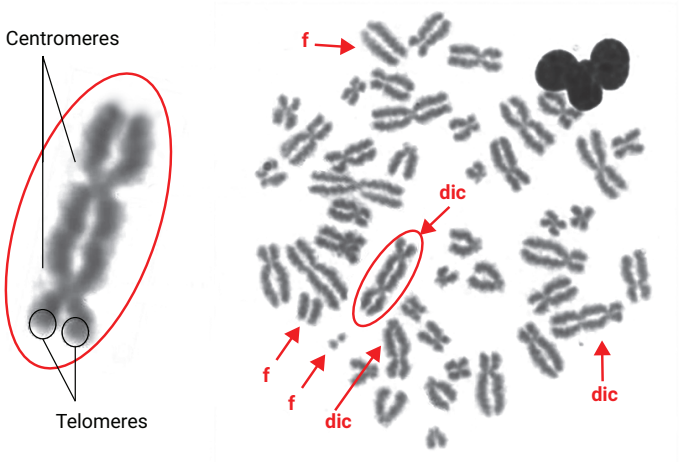


Fig. 31. Dicentric chromosomes and acentric fragments.
From: Shen X. et al. Scientific Reports 2019 – 9, 10.1038/s41598-019-38614-7.

Task 7.5. Explain what type of chromosomal structural aberration are described in the following diagnoses:

Diagnosis	Chromosomal structural aberration
46, XX, t(9;22)	
46, XY, del 5p	
46,X, i(Xq)	
46,XY, r(18)	
45, XX, rob(13;14)	

Task 7.6. Draw chromosome aberrations and explain how they could happen:

Aberration	A sketch of aberrant chromosome	Mechanism of the aberration
Dicentric chromosome and acentric fragment		

Ring chromosome		

Numerical chromosomal abnormalities (genomic mutations)

There are two types of numerical chromosomal aberrations:

Euploid organisms contain complete sets of chromosomes. Organisms with three or more sets of chromosomes are **polyploids** (**triploidy** with 3 sets and **tetraploidy** or 4 sets).

Aneuploidy, the loss or gain of one or more chromosomes (a missing chromosome is referred to as monosomy, an extra chromosome(s) are referred to as **trisomy**, **double trisomy**, **tetrasomy**) creates a genetic imbalance. Autosomal aneuploidy is usually lethal to the organism. Only 13, 18 and 21 trisomic babies can survive up to birth, because these chromosomes contain less genes than big chromosomes. Aneuploidy for sex chromosomes is better tolerated because of dosage compensation mechanisms (Barr body formation).

The five major aneuploidy syndromes in human are shown in Table 2.

Mosaic forms of syndromes lead to milder clinic manifestations. An example of this is one of the milder forms of Klinefelter syndrome, called 46/47 XY/XXY mosaic wherein some of the patient's cells contain XY chromosomes, and some contain XXY chromosomes.

All types of mutations are an important instrument of evolution – they are material for natural selection. In humans, different mutations very often result in genetic disorders.

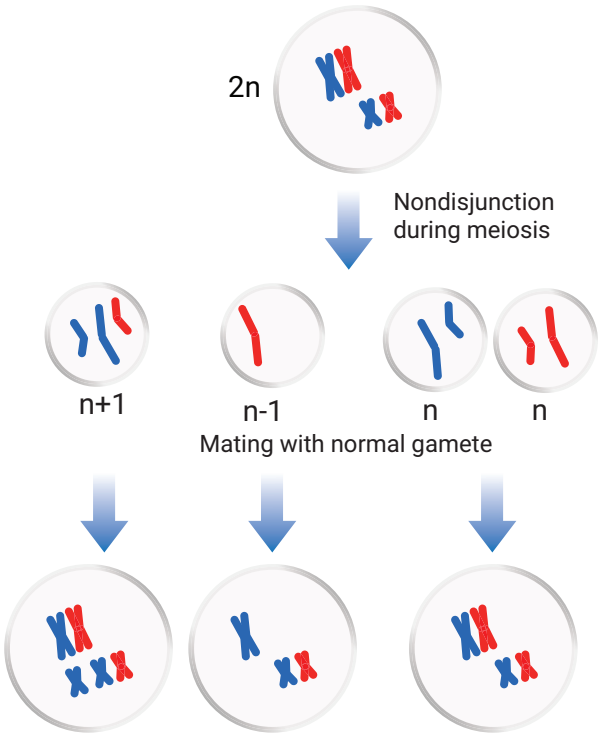


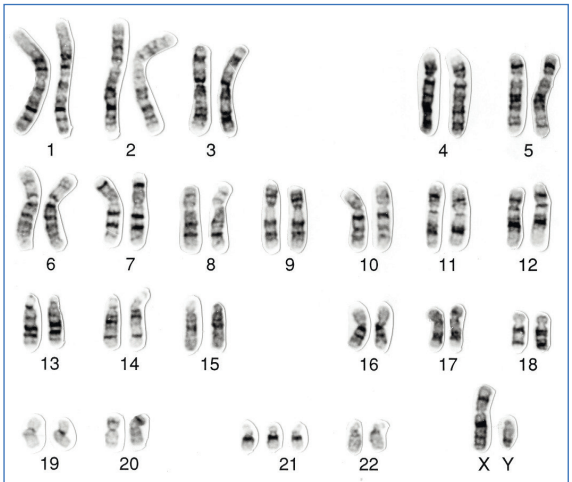
Fig. 32. Changes in chromosomal number (aneuploidy) can result from mistakes in meiosis or mitosis (germ cell or somatic mutations respectively).

Table 2. Major aneuploidy syndromes in human

	Down's syndrome	Edwards' syndrome	Patau's syndrome	Turner's syndrome	Klinefelter's syndrome
Chromosome formula	47, XX or XY, 21+	47, XX or XY, 18+	47, XX or XY, 13+	45, XO	47, XXY or 48, XXXY
Frequency	1:700	1:7000	1:8000	1:1000 females	1:1000 males

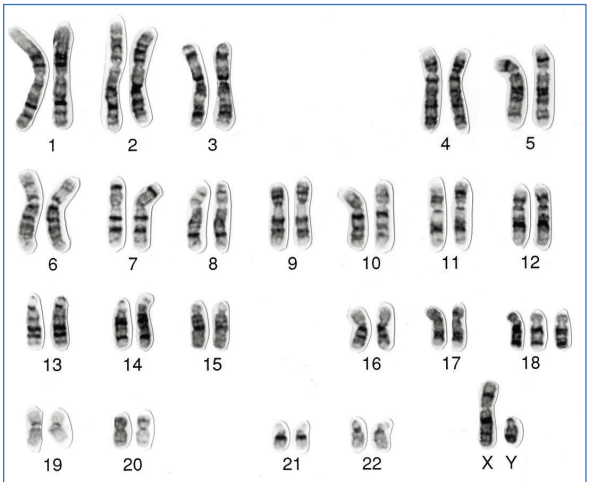
Task 7.7. Decide which types of numerical chromosomal abnormalities are at the pictures bellow (image source: Ross.Wessex Reg. Genetics Centre) and fill in the table.

A



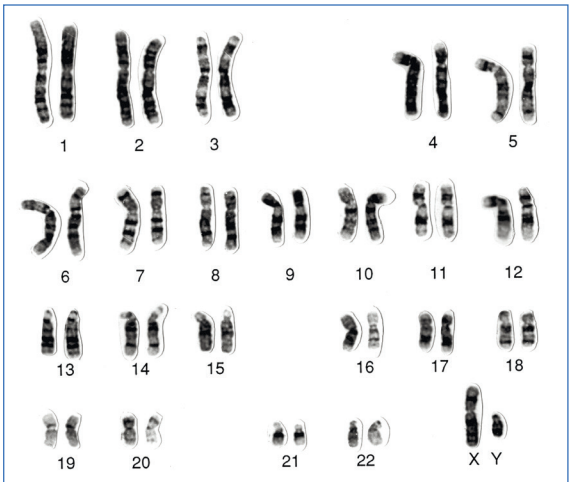
Number of chromosomes	47
Sex of the individual	male
Polyploidy, aneuploidy or normal	aneuploidy
Abnormality type	trisomy 21
Chromosome formula	47,XY,21+
Syndrome name	Down's syndrome

B



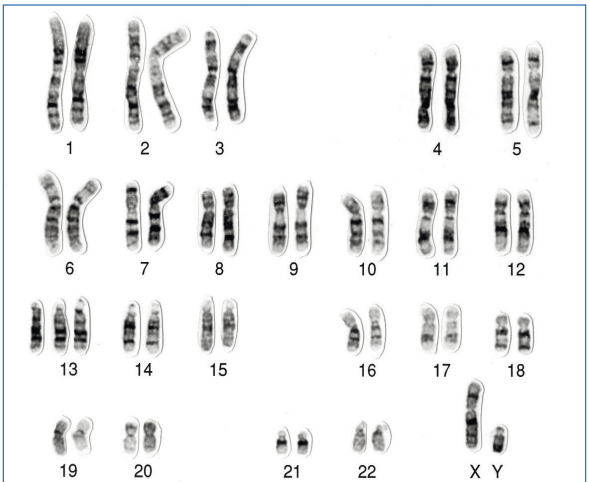
Number of chromosomes	
Sex of the individual	
Polyploidy, aneuploidy or normal	
Abnormality type	
Chromosome formula	
Syndrome name	

C



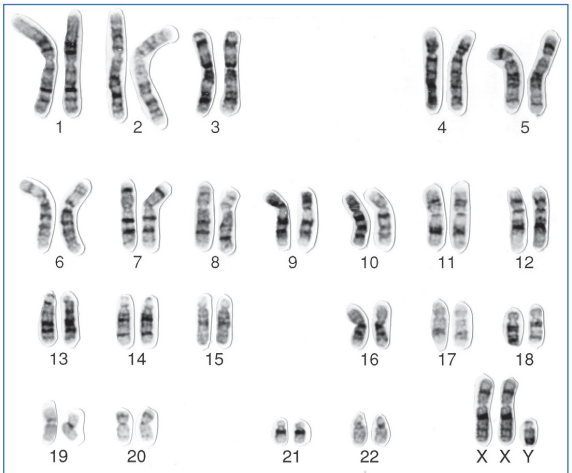
Number of chromosomes	
Sex of the individual	
Polyploidy, aneuploidy or normal	
Abnormality type	
Chromosome formula	
Syndrome name	

D



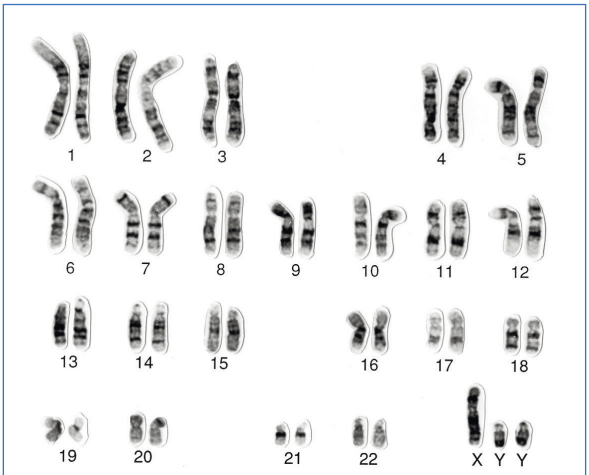
Number of chromosomes	
Sex of the individual	
Polyploidy, aneuploidy or normal	
Abnormality type	
Chromosome formula	
Syndrome name	

E



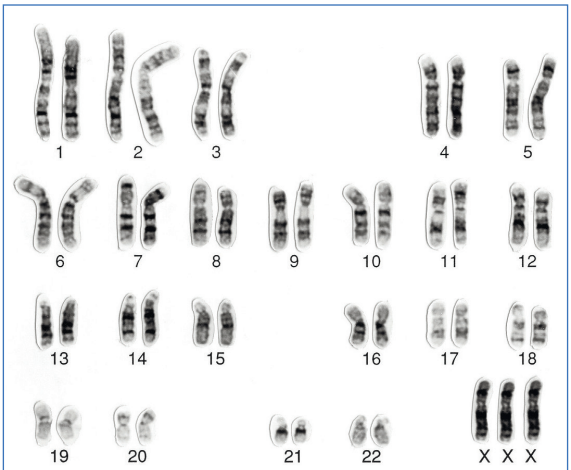
Number of chromosomes	
Sex of the individual	
Polyploidy, aneuploidy or normal	
Abnormality type	
Chromosome formula	
Syndrome name	

F



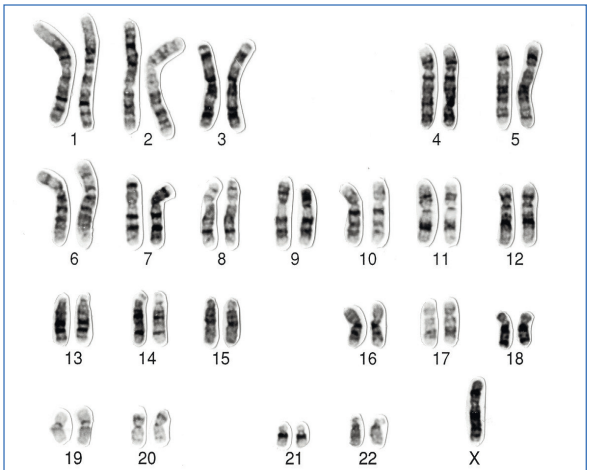
Number of chromosomes	
Sex of the individual	
Polyploidy, aneuploidy or normal	
Abnormality type	
Chromosome formula	
Syndrome name	

G



Number of chromosomes	
Sex of the individual	
Polyploidy, aneuploidy or normal	
Abnormality type	
Chromosome formula	
Syndrome name	

H



Number of chromosomes	
Sex of the individual	
Polyploidy, aneuploidy or normal	
Abnormality type	
Chromosome formula	
Syndrome name	

Task 7.8. Explain the type of mutation and what exactly happened:

Example	Type of mutation	What happened
ΔF508 in CFTR protein	Gene mutation	Deletion of a triplet in DNA leads to absence of phenylalanine at position 508
t(9;22)(q34;q11)	Chromosome structural mutation	
47, XX, 13+		
E6V in β-globin polypeptide		
R261X in enzyme phenylalanine hydroxylase		
46,XY, 5p—		
48, XXXY		

Home Work

Answer the questions using information from textbook «ESSENTIAL MEDICAL BIOLOGY», Chapter 11, pp.66–71.

1. What is a missense mutation? _____

2. What is nonsense mutation? _____

3. What is silent mutation? _____

4. What is an "in-frame" mutation? _____

5. What is a frame-shift mutation? _____

6. Decide which type of gene mutation is shown below. Here are the changes in mRNA. DNA is not shown. Indicate mutated position(s), 5'-and 3'-ends of RNA and N- and C-ends of polypeptide (see genetic code in the Table 1, page 22). Complete the table:

Normal (wildtype) mRNA	5' - GCU GGA GCA CCA GGA CAA GAU GGA - 3'
Normal polypeptide	N - Ala Gly Ala Pro Gly Gln Asp Gly - C

Silent mutation (A→C)	GCU GGA GCC CCA GGA CAA GAU GGA
Normal polypeptide	Ala Gly Ala Pro Gly Gln Asp Gly

	GCU GGA GCA CCA AGA CAA GAU GGA
	Ala Gly Ala Pro Arg Gln Asp Gly

	GCU GGA GCA CCA GGA UAA GAU GGA
	Ala Gly Ala Pro Gly stop

	GCU GGA GCC ACC AGG ACA AGA UGG
	Ala Gly Ala Thr Arg Thr Arg Trp

7. What do we call an absence of a segment of a chromosome? _____

8. What is the difference between terms 'trisomy' and 'triploidy'.

_____

_____

_____

9. What autosomal aneuploidy syndromes in human do you know?

_____

_____

10. Exchange of parts between non-homologous chromosomes is named _____

11. Organisms with cells containing three sets of chromosomes are called _____

12. What sex-chromosome aneuploidy syndromes in human do you know? How many Barr bodies do these patients have in their somatic cells?

_____

_____

_____

_____

13. Among adults with Turner syndrome, it has been found that a very high proportion of them are genetic mosaics. These are of two types: in some individuals the karyotype was 46, XX / 45, XO. In other Turner individuals, the karyotype was 46, XY / 45, XO. Explain how these somatic mosaics could arise.

QUESTIONS TO THE COLLOQUIUM 1

1. Cell theory. Pro-and eukaryotic cells. Comparison characteristics of pro- and eukaryotic cells.
2. Cell organelles. Structure and function of non-membrane organelles.
3. Cell organelles. Structure and function of membrane organelles.
4. Plant and animal cell differences.
5. Nucleic acids. DNA and RNA chemical composition and function.
6. Levels of protein structure. Chemical composition and function in cell.
7. DNA replication. Repair of DNA chain.
8. Gene expression. Regulation of gene activity in pro- and eukaryotes.
9. Ribonucleic acids. Function of different types of RNA .
10. Gene expression. Structure of eukaryotic gene. Transcription and RNA processing.
11. Genetic code. Translation and post-translational processes.
12. Control of gene expression in bacteria by induction and repression.
13. Structure of chromosomes. Karyotype. Karyotyping.
14. Chromosome maps. Types of chromosome maps.
15. Normal human karyotype. Denver and Paris nomenclature.
16. Structure of chromosomes. Eu- and heterochromatin.
17. Cell cycle. Mitosis. Abnormalities of mitosis.
18. Meiosis. Abnormalities of meiosis.
19. Gametogenesis: spermatogenesis and oogenesis.
20. Comparison characteristics of spermatogenesis and oogenesis.
21. Chromosomal numerical and structural aberrations.
22. Gene mutations. Classification. Clinical examples.

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