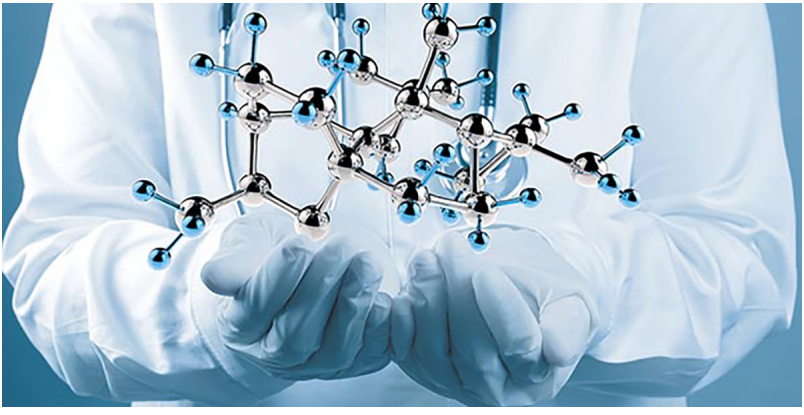
FEDERAL STATE BUDGET EDUCATIONAL INSTITUTION
OF HIGHER EDUCATION «BASHKIR STATE MEDICAL UNIVERSITY»
OF MINISTRY OF HEALTH CARE RUSSIAN FEDERATION
(FSBEI HE BSMU MOH Russia)

MEDICAL GENETICS AND BIOLOGY

Book of situational problems



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M 23 **Medical genetics and biology:** book of situational problems / T.V. Viktorova, S.M. Izmailova, K.V. Danilko, D.N. Kuvatova, G.I. Lucmanova, N.D. Ryabceva. — Ufa: FSBEI HE BSMU MOH Russiaa, 2018. — 80 p.

The training manual was prepared on the basis of the work program, the current curriculum of the Bashkir State Medical University of the Ministry of Health of the Russian Federation in accordance with the requirements of federal state educational standard of higher education when studying the discipline "Biology".

The manual contains up-to-date information on the main sections of general and molecular genetics. The content includes a summary of the theoretical material for each section, examples of problem solving, situational PROBLEMS with reference standards.

The manual is recommended for independent out-of-class work for the 1-st year medical students, who study in the specialty 31.05.01 General Medicine using the language of the intermediary (English).

Recommended for publication by the Coordinating scientific and methodological council and approved by the decision of the Editorial and publishing council of the BSMU of the Ministry of health of Russia.

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CONTENT

INTRODUCTION

According to biologists of different profiles, the 21st century is the age of genetics – the science of heredity and variability. Great importance of genetics for the progressive development of modern medicine. Numerous epidemiological studies in recent years indicate that not only hereditary, but almost all widespread, so-called multifactorial diseases are largely due to genetic predisposition. Without knowledge of the basic patterns of heredity and variability, it is impossible to understand the genetic preconditions for the development of pathological processes and, consequently, to learn how to manage these processes at the stages of diagnosis, treatment, and, most importantly, effective prevention. Already today, a qualified physician should understand the key mechanisms for the transfer of genetic information, its implementation as a sign. To form the basis of medical thinking, it is necessary to develop the ability to solve situational problems.

This training manual is aimed at the formation of the following general cultural (GC) and general professional (GPC) competence:

GC-1 – Ability to abstract thinking, analysis, synthesis;

GC-5 – Readiness for self-development, self-realization, self-education, use of creative potential;

GPC-1 – Readiness to solve standard problems of professional activity using information, bibliographic resources, medical and biological terminology, information and communication technologies and taking into account the basic information security requirements;

GPC-7 – Readiness to use basic physical, chemical, mathematical and other natural science concepts and methods in solving professional problems.

The contents of the collection include the following sections:

1. Molecular Genetics.
2. Cytogenetics.
3. Laws of Heredity.
4. Variability.

5. Methods of human genetics study.

6. Medical-genetic counseling.

Each section is preceded by a brief summary of the theoretical material, examples of problem solving, model and situational PROBLEMS are given. In the compilation and classification of the collection, step-by-step mastering of the material from simple to complex was taken into account, in order to form students' skills of systematization, logical thinking, and decision-making. The manual is intended for independent students' classroom work while studying the training section "General and Medical Genetics". The appendix contains reference materials necessary for solving problems, a brief dictionary with a general characteristic of a number of hereditary syndromes is given.

The manual is recommended for independent out-of-class work for the 1-st year medical students, who study in the specialty 31.05.01 General Medicine.

SECTION I.
MOLECULAR GENETICS

Molecular genetics examines the processes associated with heredity and variability at the molecular level. A gene is a region of a DNA molecule that includes regulatory sequences and corresponds to one transcription unit that contains information about the structure of a single polypeptide chain or RNA molecule. This is a region of DNA responsible for the formation of a certain trait. However, the gene does not become a sign, and from the gene to the trait there is a series of intermediate reactions. It determines only the primary structure of the protein, i.e. the sequence of the location of amino acids in it, on which its function largely depends. Proteins-enzymes control biochemical reactions in the body. For each reaction, there is a specific protein-enzyme. The course of biochemical reactions causes the manifestation of one or another characteristic. Thus, the function of the gene can be represented by the following scheme: gene → protein → biochemical reaction → trait.

At the molecular level, the gene is a fragment of the molecule of deoxyribonucleic acid (DNA), the famous double helix discovered in 1953 by James Watson and Francis Crick. A DNA molecule is a polymer whose monomer is a nucleotide. The nucleotide consists of a monosaccharide, deoxyribose, a phosphoric acid residue and a nitrogenous base. The DNA composition includes four types of nitrogenous bases: purines (adenine (A) and guanine (G)), and pyrimidines (thymine (T) and cytosine (C)). Nucleotides are connected to the polynucleotide chain by phosphodiester bonds through a phosphoric acid residue that is attached to the 3'-position of one deoxyribose and to the 5'-position is another. Chains are connected to each other due to hydrogen bonds between nitrogen bases on the principle of complementarity so that adenine is located opposite thymine, guanine – opposite to cytosine. It is in the alternation of nitrogenous bases that the sequence of amino acids in the protein molecule and the specificity of the protein itself are encoded.

The location of each amino acid in the protein chain is predetermined by triplet nucleotides, i. e. three adjacent nitrogenous bases in one of the strands of DNA. The code is deciphered using ribonucleic acids (RNA).

"Central dogma of molecular biology": DNA – (transcription) – mRNA – (translation) – protein.

The decryption process begins with the synthesis of information or matrix RNA (mRNA). Matrix RNA is a polymer consisting of a single nucleotide chain. Its nucleotides also contain a monosaccharide (ribose), a phosphoric acid residue and one of the nitrogen bases: adenine, guanine, cytosine or uracil (U).

Synthesis of RNA occurs through the template chain of DNA. The construction of the molecule is carried out in such a way that the complementary nitrogenous bases of RNA are constructed in opposition to the corresponding nitrogenous bases of DNA: C-G, A-U, T-A, G-C. The process of reading information on mRNA is called transcription. Naturally, eukaryotic mRNA copies not only coding regions (exons), but also noncoding regions (introns) cut later. The primary transcriptional product (prim-mRNA) synthesized in the nucleus undergoes processing: 5 'end capping, 3' end polyadenylation, intron excision and exon splicing (splicing).

The next stage of decoding takes place in the cytoplasm on the ribosomes, where the polypeptide chain is assembled from amino acids, i.e. process of protein synthesis. In this process, transport RNAs (tRNAs) are involved, the function of which is the transfer of amino acids to the ribosome and the location in the polypeptide chain of the site provided by the mRNA code for each amino acid. All amino acids are recognized by their own tRNA. A complex of tRNA with an amino acid is called aminoacyl-tRNA.

The assembly of the polypeptide chain proceeds according to the following scheme. The place of contact of the mRNA with the ribosome begins counting of triplets. The aminoacyl-tRNA is suitable for the ribosome. Since, in eukaryotes the starting codon in the mRNA is AUG, in the anticodon the first aminoacyl-tRNA that transports the amino acid methionine will be a triplet of the UAC. At the same time, two triplets in the aminoacyl (A) and peptidyl (P) centers and, corresponding-

ly, two aminoacyl-tRNAs are located in the ribosome. Between the two amino acids, a peptide bond is formed, and the ribosome for the mRNA is promoted by one triplet. The combination of amino acids in the peptidyl center collinearly with triplets is called translation.

The proposed PROBLEMS are mainly designed to decipher the structure of the protein from known data on the structure of DNA and reverse analysis using the amino acid coding table (Appendix 1).

Example of problem solving

Problem: The polypeptide consists of the following amino acids: valine-alanine-glycine-lysine-tryptophan-valine-serine. Determine the structure of the DNA region encoding this polypeptide.

Decision. The sequence of amino acids sets the order of nucleotides of mRNA (according to the genetic code table, see Appendix 1):

Step N1: mRNA: 5 'GUU GCU GGU AAA UGG GUU UCU 3'

Through the chain of mRNA, it is possible to reconstruct a cording strand of the DNA (by replace U on T only):

Step N2: The coding strand of DNA: 5’ 'GTT GCT GGT AAA TGG GTT TCT 3'.

In accordance with the principle of complementarity, now construct a second matrix, non-coding strand of DNA:

Step N3: The matrix DNA strand: 3' CAA CGA CCA TTT ACC CAA AGA 5 '

Thus, the complete structure of the DNA molecule:

5’ 'GTT GCT GGT AAA TGG GTT TCT 3 – it is a coding strand.

3 ' CAA CGA CCA TTT ACC CAA AGA 5' – matrix strand.

SITUATIONAL PROBLEMS

1. The portion of the template chain of the DNA molecule that encodes a part of the polypeptide has the following structure:3'CCA TAG TCC AAG GAC5'.

Determine the sequence of amino acids in the polypeptide.

2. The region of the gene coding for the protein consists of sequentially located nucleotides 5 'of AAC GAC TAT CAC TAT ACC GAA 3'.

Determine the composition and sequence of amino acids in the polypeptide chain encoded in this region of the gene.

3. Determine the amino acid composition of the polypeptide, which is encoded by the following sequence of mRNA: 5 'CCA CCU GGU UUU GGC 3'.

4. The polypeptide consists of the following amino acids: val-ala-gly-lys-try-val-ser. Determine one of the variants of the structure of the DNA portion encoding the polypeptide.

5. The polypeptide consists of the following amino acids: ala-cys-leu-met-tyr. Determine one of the options for the structure of the DNA portion encoding this polypeptide chain.

6. The first 10 amino acids in the β-chain of insulin: phe-val-asp-gln-gys-leu-cys-gly. Identify one of the options for the structure of the DNA portion encoding this part of the insulin chain.

7. Anti-codons of tRNA arrive at the ribosomes in the next sequence of nucleotides UCG, CGA, AAU, CCC. Determine the sequence of nucleotides on the mRNA, then on the DNA encoding the specific protein and the sequence of amino acids in the fragment of the molecule of the synthesized protein that are carried by this tRNA.

8. It is known that all types of RNA are synthesized on a DNA matrix. The fragment of the DNA molecule on which the tRNA site is synthesized has the following sequence of nucleotides: TTGAAAAAACCGGAC . Establish the nucleotide sequence of the tRNA site, which is synthesized on this fragment. Which amino acid will this tRNA be transported if the third anticodon corresponds to the mRNA codon?

9. During the translation 30 molecules of tRNA participated. Determine the number of amino acids that make up the synthesized protein, as well as the number of triplets and nucleotides in the gene that encodes the protein.

10. It is known that 34% of the total number of nucleotides of this mRNA is in guanine, 18% in uracil, 28% in cytosine, and 20% in adenine. Determine the per-

centage composition of the nitrogenous bases of double-stranded DNA, the impression of which is the indicated mRNA.

11. It is known that the distance between two adjacent nucleotides in a spiraled DNA molecule measured along the helix axis is 0.34 nm. How long does the coding region of the gene that determines the molecule of normal hemoglobin, including 287 amino acids, have?

12. What is the length of a part of the DNA molecule encoding the bull's insulin if it is known that the bull insulin molecule has 51 amino acids and the distance between two adjacent nucleotides in the DNA is 0.34 nm?

13. The protein consists of 200 amino acids. What is the length of the gene determining it, if the distance between two adjacent nucleotides in a spiraled DNA molecule (measured along the axis of the helix) is 0.34 nm?

14. In the DNA molecule, the proportion of cytosine nucleotides accounts for 18%. Determine the percentage of other nucleotides that make up the DNA molecule.

15. How much adenyl, thymidyl, guanylyl and cytidyl nucleotides are contained in a fragment of the DNA molecule if 950 cytidyl nucleotides are found in it, representing 20% of the total number of nucleotides in this DNA fragment?

Answers

1. Polypeptide: glycine-isoleucine-arginine-phenylalanine-leucine

2. Polypeptide: asparagine-aspartic acid- tyrosine- histidine- tyrosine- threonine- glutamic acid.

3. Polypeptide: proline-proline-glycine-phenylalanine-glycine.

4. DNA:

5'GTTGCTGGTAAATGGGTTTCA3'

3' CAACGACCATTTACCCAAAGT5'

5. DNA:

5' GCTTGTCTTATGTAT3'

3' CGAACAGAATACATA5'

6. DNA:

5′ TTTGTTGATCAACATCTTTGTGAT3′

3′ AAACAACTAGTTGTAGAAACACTA5′

7. иРНК:

5′ AGCGCUUUAGGG3′

ДНК:

5′TCGCGAAATCCC3′

3′ AGCGCTTTAGGG5′

Polypeptide: serine-alanine-leucine-glycine

8. tRNA of the AAC, UUU, UUU, GGC, CUG;

codon of mRNA-AAA; amino acid – lysine.

9. The protein consists of 30 amino acids, they are encoded by 30 triplets, the number of nucleotides in the gene is 90.

10. G = C = 31%; A = T = 19%.

11. The length of the gene is 292.4 nm.

12. The length of the gene is 51.68 nm.

13. The length of the gene is 203.66 nm.

14. G = 18%; A = T = 32%.

15. G = 950 nucleotides, A = T = 1425 nucleotides.

SECTION II.
CYTOGENETICS

The life of a cell from its inception to its own division or death is called the life (cellular) cycle. In order for a number of cell generations to retain and strictly maintain a certain amount of DNA, division necessarily precedes the doubling of chromosomes. If the number of chromosomes in the haploid set is denoted by n and the DNA content is c, then in the diploid set, before replication, there will be 2n2c, and after replication, 2n4c.

Mitosis

Mitosis – indirect division of somatic cells, accompanied by spiralization of chromosomes. Mitosis is preceded by replication (doubling) of DNA, as a result of which a set of genetic material in the cell becomes 2n4c (a diploid set of two-chromatin chromosomes – double-stranded chromosomes).

In mitosis, four phases are distinguished:

1. Prophase (2n4c). There is a spiralization of the chromatin filaments, the formation of the mitotic apparatus, the disappearance of the nucleoli, the dissolution of the nuclear envelope.

2. Metaphase (2n4c). Chromosomes are maximally condensed, located in the equatorial plane of the spindle of cell division, forming a metaphase plate.

3. Anaphase (4n4c). Microtubules begin to shorten, in the kinetochores of chromosomes there is a separation into chromatids, which are sent to the poles of the cell. Two daughter stars (astrosphere) are formed on the poles of the cell (one identical set of (2n2c) chromosomes).

4. The telophase (2n2c). Separated groups of chromosomes approach the poles, lose chromosomal microtubules, loosen, decondensize, transforming into chromatin. By the end of the telophase, the nuclear envelope is restored, nucleoli are formed. Mitosis ends with the division of the cytoplasm – cytokinesis and two daughter cells are formed. Both daughter cells are diploid (2n2c).

As a result of mitosis, daughter cells receive exactly the same set of chromosomes that was in the mother cell, so mitosis underlies the development and growth of the body (in all cells of the body a constant number of chromosomes is maintained).

Meiosis

Meiosis is a type of cell division in which four haploid cells (gametes) are formed from one diploid cell. Meiosis occurs in the stage of maturation of gametogenesis. As a result of meiosis, the number of chromosomes is reduced by half (gametes become haploid).

Meiosis includes two consecutive divisions: a reduction and an equational one.

Interphase I. Cells enter the first meiotic division with unfinished DNA synthesis (from 0.3 to 2%) and histone proteins (from 7 to 25%), which is a prerequisite for conjugation of homologous chromosomes in the zygotene phase of prophase I.

Reduction division:

Prophase I. Genetic material set 2n4c. Prophase I consists of 5 stages:

1. Leptotena (stage of thin filaments). Single strands of slightly helical and long chromosomes are clearly seen. Chromosomes at this time consist of two chromatids, connected by a centromere.

2. Zygotena (the stage of conjugating strands). Chromosomes are the same in size and morphology, i.e. homologous, attracted to each other – conjugated. The synaptonemic complex provides a close contact between the homologous segments of the chromatids. A bivalent is formed. Each chromosome from one bivalent occurs either from the father or from the mother. The number of bivalents is equal to the haploid set of chromosomes.

3. Pakhitena (the stage of thick filaments). Chromosomes somewhat shorten and thicken. Between chromatids of maternal and paternal origin in several places there are compounds – chiasms. In the region of each chiasma, crossing-over occurs-the exchange of the corresponding sections of homologous chromosomes-from

the paternal to the maternal chromosomes and vice versa. Crossingover provides a new combination of genes in chromosomes (recombination of genes in chromosomes).

4. Diplotena (stage of double filaments). The spiralization of chromosomes continues: the chiasis is terminated, as a result of mutual repulsion of homologous chromosomes. This allows chromosomes to move to the poles in anaphase.

5. Diakinesis (stage of divergence of filaments). Bivalents, which fill the entire volume of the nucleus, begin to move closer to the nuclear envelope. By the end of the diakinesis, the contact between the chromatids is maintained at one or both ends. The disappearance of the shell of the nucleus and the nucleoli, as well as the final formation of the fission spindle, complete the prophase I.

Metaphase I. A set of genetic material 2n4c. The chromosome is located in the equatorial plane, forming a metaphase plate. Bivalents – tetrads are aligned along the equator so that both members of each homologous pair are directed by their centromeres to opposite poles.

Anaphase I. A set of genetic material in a 2n4c cell (over n2c at opposite cell poles). To the poles of the cell homologous chromosomes diverge from each bivalent, but centromeres do not divide. As a result of the discrepancy of chromosomes, an independent combination of paternal and maternal chromosomes occurs at the poles of the cell, at each pole the number of chromosomes decreases by half, i.e. there is a reduction in the number of chromosomes (n2c). In this reduced haploid set, there is necessarily one homologous chromosome from each bivalent.

Telophase I. Chromosomes reach the poles, each pole has a haploid number of chromosomes (true reduction of chromosomes). Complete despiralization of chromosomes on occurs. A nuclear envelope and a nucleolus are formed, a fissure of division is formed and deepened, cytokinesis occurs. As a result of cytokinesis, 23 chromosomes are concentrated in each daughter cell.

Interkinesis (interphase II) differs from interphase I in that it does not replicate DNA. Therefore, in the second meiotic division, cells with a haploid set of

chromosomes enter, but with a doubled number of DNA, the chromosome formula in the cell n2c.

Equation division occurs by the type of mitosis:

Prophase II – n2s;

Metaphase II – n2s;

Anaphase II – 2n2c;

Telophase II – nc (in each nucleus there is a haploid number of single-stranded chromosomes).

After the end of meiosis, cytokinesis occurs, as a result of which from each cell with a set of n2c, two haploid cells (four in total) are formed with a set of nc in each.

Gametogenesis

Gametogenesis – the process of formation of sex cells: male – spermatogenesis, female – oogenesis.

Spermatogenesis – the formation of spermatozoa, occurs in the convoluted tubules of the testes (sex glands) in four periods:

1. Reproduction – the original cells – spermatogonia are divided by mitosis (set 2n2c).

2. Growth – increase in cell size, reduplication of DNA and formation of spermatocytes of the first order. A set of chromosomes and DNA 2n4c.

3. Maturation – spermatocytes of the first order undergo two meiotic division. After the first, spermatocytes of the second order are formed with a set of n2c, after the second – spermatids (set nc).

4. Formation-spermatids are transformed into mature spermatozoa.

Ovogenesis – occurs in the ovaries (sex glands) in three periods:

1. Reproduction – primary cells of ovonia are divided by mitosis (set 2n2c).

2. Growth-increase in cell size, DNA replication and the formation of oocytes of the first order. A set of chromosomes and DNA 2n4c.

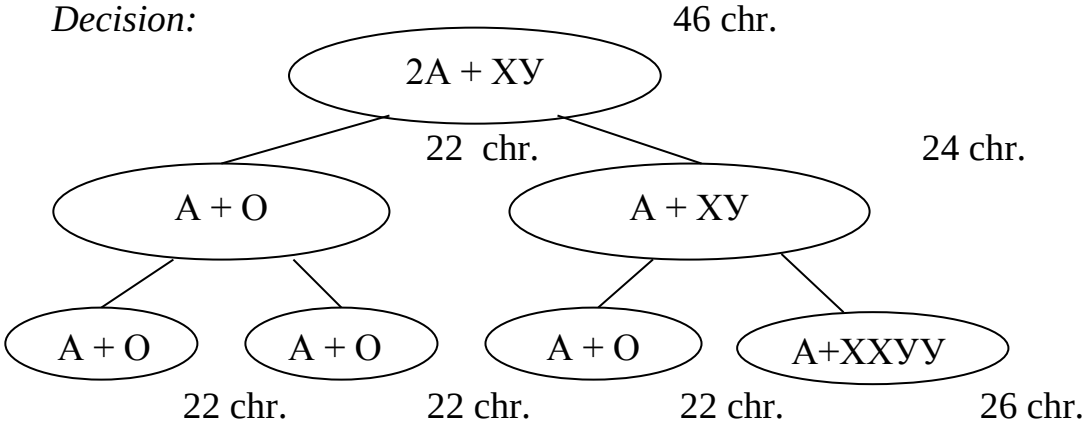
3. Maturation – as a result of meiosis from the first-order oocytes, the second order oocyte with a set of n2c and a directing body is first formed, followed by the ovotid or ovum (set nc) and three directing corpuscles.

Reproduction and growth occur in embryogenesis, meiosis to metaphase II – during puberty, the second meiotic division is completed after fertilization.

Example of problem solving

Problem: what gametes and in what ratio are formed from the first order spermatocyte with the set 2A + XY with non-divergence of the sex chromosomes in two meiotic divisions.

Decision:



A – autosomal set (22 chromosomes)

XY – sex chromosomes

When the sex chromosomes did not dissociate in the first meiotic division from the first order spermatocyte with the set of chromosomes 2A + XY, two second order spermatocytes were formed with a set of A + XY – 24 chromosomes and A + O – 22 chromosomes. According to the condition of the problem, there was a nondisjunction of the chromatids of the sex chromosomes and in the second division of meiosis; therefore, from the spermatocyte of the second order with the A + XY set, two spermatids with a set of A + XXY – 26 chromosomes and A + O – 22 chromosomes are formed. From the second order spermatocyte with a set of A + O, two identical spermatids are formed with a set of A + O – 22 chromosomes. As a result, two types of gametes are formed: A + XXYY with a probability of 25% and a set of A + O with a probability of 75%.

Answer: from the spermatocyte of the first order with the chromosome set 2A + XY, with the non-divergence of the sex chromosomes in the anaphase of two meiosis divisions, two types of gametes are formed: A + XXUU (26 chromosomes) with a probability of 25% and A + O (22 chromosomes) with a probability of 75%.

SITUATIONAL PROBLEMS

1. What gametes and in what ratio are formed in a human from the first order oocyte with a set of chromosomes 2A + XX with non-separation of the sex chromosomes in the first meiotic division? Indicate the number of chromosomes in them.

2. What gametes and in what ratio are formed in man from the oocyte of the first order with a set of chromosomes 2A + XX with non-separation of autosomes in the second division of meiosis? Specify the number of chromosomes in gametes.

3. What gametes and in what ratio are formed in a man from the oocyte of the first order with a set of 2A + XX with non-separation of the sex chromosomes in two divisions of meiosis? Indicate the number of chromosomes in them.

4. What gametes and in what ratio are formed in a person from the first order spermatocyte with a set of chromosomes 2A + XY when the sex chromosomes do not dissociate in the first meiotic division? Indicate the number of chromosomes in them.

5. What gametes and in what ratio are formed in a person from the first order spermatocyte with a set of chromosomes 2A + XY with non-separation of autosomes in the first, and sex chromosomes in the second division of meiosis? Specify the number of chromosomes in the cells.

6. What gametes and in what ratio are formed from the oocyte of the first order with a set of DDEEXX when the sex chromosomes do not divide into the anaphase of the first, and the first pair of autosomes into the anaphase of the second division of meiosis? Specify the number of chromosomes in the cells.

7. What gametes and in what ratio are formed from the first order spermatocyte with the CCEEXY set when the second pair of autosomes does not divide into

the anaphase of the first, and the first pair of autosomes into the anaphase of the second division of meiosis? Specify the number of chromosomes in the cells.

8. What gametes and in what ratio are formed from the first order oocyte with a set of BBEEXX with non-divergence of the sex chromosomes in two meiotic divisions? Specify the number of chromosomes in the cells.

9. What gametes and in what ratio are formed from the first order oocyte with a set of MMNNXX with non-dissociation of autosomes in two meiotic divisions? Specify the number of chromosomes in the cells.

10. What gametes and in what ratio are formed from the first order oocyte with the set of BBXX when the autosomes do not divide into the anaphase of the first, and the sex chromosomes into the anaphase of the second division of meiosis? Specify the number of chromosomes in the cells.

11. What gametes and in what ratio are formed from the first order oocyte with a set of CCEEDDXX when the sex chromosomes do not divide into the anaphase of the first, and the third pair of autosomes into the anaphase of the second division of meiosis? Specify the number of chromosomes in the cells.

Answers

1. Two types of gametes are formed: A + XX (24 chromosomes) with a probability of 50% and A (22 chromosomes) with a probability of 50%.

2. Two types of gametes are formed: 2A + X (45 chromosomes) with a probability of 50% and X (1 chromosome) with a probability of 50%.

3. Two types of gametes are formed: A + XXXX (26 chromosomes) with a probability of 25% and A (22 chromosomes) with a probability of 75%.

4. Two types of gametes are formed: A + XY (24 chromosomes) with a probability of 50% and A (22 chromosomes) with a probability of 50%.

5. Four types of gametes are formed: 2A + XX (46 chromosomes) with a probability of 25%, 2A (44 chromosomes) with a probability of 25%, YY (2 chromosomes) with a probability of 25% and 0 (0 chromosomes) with a probability of 25%.

6. Four types of gametes are formed: DDEXX (25 chromosomes) with a probability of 25%, EXX (23 chromosomes) with a probability of 25%, DDE (23 chromosomes) with a probability of 25% and E (21 chromosomes) with a probability of 25%.

7. Four types of gametes are formed: CCEEX (25 chromosomes) with a probability of 25%, CCX (23 chromosomes) with a probability of 25%, EEY (23 chromosomes) with a probability of 25% and Y (21 chromosomes) with a probability of 25%.

8. Two types of gametes are formed: BEXXXX (26 chromosomes) with a probability of 25% and BE (22 chromosomes) with a probability of 75%.

9. Two types of gametes are formed: MMMMNNNNX (29 chromosomes) with a probability of 25% and X (21 chromosomes) with a probability of 75%.

10. Four types of gametes are formed: BBXX (25 chromosomes) with a 25% probability, BB (23 chromosomes) with a probability of 25%, XX (23 chromosomes) with a probability of 25% and 0 (21 chromosomes) with a probability of 25%.

11. Four types of gametes are formed: CEDDXX (25 chromosomes) with a probability of 25%, CEXX (23 chromosomes) with a probability of 25%, CEDD (23 chromosomes) with a probability of 25% and CE (21 chromosomes) with a probability of 25%.

SECTION III.
LAWS OF HEREDITY

Some general methodical techniques that can be used to solve problems. The majority of mistakes made by students are due to the failure to follow simple rules that they must learn from the course of genetics. These rules include the following:

1. Each gamete (sperm and egg) receives a haploid set of chromosomes.

2. Each gamete contains only one homologous chromosome from each pair, hence only one allele from each gene.

3. The number of possible gamete variants is 2^n, where n is the number of chromosomes containing alleles in the heterozygous state.

4. One homologous chromosome (one gene allele) from each pair receives a child from the father, and the other (the other allele of the gene) from the mother.

5. Heterozygous organisms with complete dominance always show a dominant feature. Organisms with a recessive trait are always homozygous.

6. The solution of the problem of dihybrid interbreeding with independent inheritance usually reduces to a sequential solution of two problems for a monohybrid (this follows from the law of independent inheritance).

In addition, to successfully solve problems in genetics should be able to perform some simple operations and use the methodical techniques that are given below.

First of all, it is necessary to carefully study the condition of the problem. The next step is to determine the type of PROBLEM. To do this, it is necessary to find out how many pairs of attributes are considered in the problem, how many pairs of genes these attributes are coded, and also the number of classes of phenotypes present in the offspring from crossing heterozygotes or in analyzing the crossing, and the quantitative ratio of these classes. In addition, it is necessary to consider whether the inheritance of the trait is related to sex chromosomes, and a pair of characteristics is linked or independently linked. Concerning the latter there can be

direct instructions in the condition. Also, the ratio of classes with different phenotypes in offspring can testify to linked inheritance.

To facilitate the solution, it is possible to write out the scheme of marriage (crossing) on a draft, noting the phenotypes and genotypes of individuals known by the condition of the problem, and then start performing operations to clarify unknown genotypes. For convenience, the unknown alleles on the draft can be denoted by «?».

Clarification of the genotypes of individuals unknown by condition is the main methodical operation necessary for solving genetic problems. In this case, the decision should always begin with individuals bearing a recessive trait, since they are homozygous and their genotype is unambiguous by this sign – aa.

Clarifying the genotype of an organism carrying a dominant trait is a more complex problem, because it can be homozygous (AA) or heterozygous (Aa).

Example of problem solving

Problem: in humans, albinism is an autosomal recessive trait. A male albino married a woman with normal pigmentation. They had two children – a normal and an albino. Identify the genotypes of all of these family members.

Description:

A – normal pigmentation;

a – albinism.

Decision:

I. Record of the scheme of marriage by phenotypes:

P: ♀ Aa – ♂ aa

normal pigmentation — albinism

G: (A) (a) — (a)

F_1: Aa normal pigmentation 50% — Aa Albinism 50%

Answer: the genotype of the husband – aa, the wife – Aa, the child with normal pigmentation – Aa, the albino child – aa.

3.1. MONOHYBRID CROSSING

Monohybrid crossing involves the analysis of inheritance characteristics, determined only by a pair of alleles of one gene. Mendel determined that when crossing individuals, analyzed by one pair of alternative characters, all the offspring are phenotypically monotonous on this basis. For example, when a homozygous yellow pea (AA) is crossed with a homozygous green (aa), all the offspring will be yellow, but heterozygous (Aa). Crossed individuals are not necessarily homozygous. For cases where both individuals are heterozygous, Mendel established that the phenotype splitting would be 3: 1, that is, ¾ of the offspring will appear with dominant traits, ¼ with signs of a recessive type. Exact splitting can be obtained by analyzing an infinitely large number of descendants. In cases of a small number of offspring, one can speak only of the probability of the appearance of individuals with one or another sign.

In genetics, there are also recurrent and analyzing crosses. The return is a hybrid of a hybrid with a homozygous individual of the parent type.

Analyzing – crossing the analyzed individual with a dominant trait (AA or Aa) with a recessive homozygous specimen (aa).

3.1.1. Types of interaction of allelic genes

There are the following types of interaction of allelic genes:

1) complete dominance;
2) incomplete dominance;
3) co-dominance.

Complete dominance

Complete dominance: the dominant allele completely inhibits the action of the recessive allele. The dominant allele has the same phenotypic manifestation in homozygous and heterozygous organisms (G. Mendel's laws are fulfilled). For example, when the color of pea seeds is inherited, the same sign (yellow color) also

appears in heterozygotes with the genotype Aa, and in homozygotes with the AA genotype.

Incomplete dominance

With incomplete dominance, the dominant allele does not completely inhibit the action of the recessive allele. Both heterozygotes function both alleles, so in the phenotype the sign is expressed as an intermediate form. But in the second generation, the offspring are split phenotypically as well as genotypically in a ratio of 1:2:1.

Co-dominance. Multiple alleles

Sometimes in the population there are not two (one pair) of the allele of the gene, but three, four and more: A, a1, a2, etc. They arise as a result of mutations in the locus of chromosomes. Each individual of allelic genes can have no more than two, but in the population their number is almost unlimited. The more allelic variants of the gene, the more opportunities to combine them in pairs. The genes of multiple alleles interact with each other in various ways. Often they form successive series of dominance: A dominates over a1, a2, but at the same time, a1 dominates a2. But there are also more complex combinations.

In humans, the type of multiple alleles inherits blood groups according to the ABO system. In humans, blood groups are determined by three alleles of the same gene. In different combinations, four blood groups are formed: I (0), II (A), III (B), IV (AB). The alleles of the gene are designated by the letters: I^0, I^A, I^B. Genes A and B with respect to the gene 0 behave dominantly. Allelic genes A and B in individuals with IV blood group behave independently of each other: allele A determines antigen A, and allele B – antigen B. The manifestation in the heterozygous state of characters determined by both alleles is called codomination. So the fourth blood group is inherited.

SITUATIONAL PROBLEMS

Complete dominance:

1. Polydactili in humans is inherited as a dominant trait. Determine the probability of birth of healthy children in the family, where both parents are heterozygous.

2. The absence of small molars is inherited as a dominant autosomal trait. What is the probability of the birth of children with an anomaly in the family, where both parents are heterozygous for the analyzed trait?

3. Myoplegia is inherited as the dominant autosomal trait. Determine the likelihood of having children with abnormalities in the family, where the father is heterozygous, and the mother does not suffer from myoplegia.

4. Phenylketonuria is inherited as an autosomal recessive trait. What kind of children can be in the family, where the parents are heterozygous for this reason?

5. The shoulder-lobe-facial form of myopathy is inherited as a dominant autosomal trait. What is the probability of the disease of children in the family, where both parents suffer from this anomaly, but one of them is homozygous, and the other is heterozygous?

Incomplete dominance:

1. Sickle-cell anemia is inherited as an autosomal recessive trait. Homozygous individuals die usually before puberty, heterozygous are viable, their anemia most often manifests subclinically. The malarial plasmodium can’t use for its nutrition S-hemoglobin. Therefore, people who have this form of hemoglobin do not have malaria.

2. What is the probability of producing children resistant to malaria in a family where one parent is heterozygous for sickle-cell anemia and the other is normal with respect to this symptom?

3. What is the probability of birth of children unstable to malaria in a family where both parents are resistant to this parasite?

4. Acatalysis is caused by a rare autosomal recessive allele. In heterozygotes, the activity of catalase is somewhat lowered. In both parents and the only son in the

family, catalase activity was below normal.

5. Determine the probability of birth in the family of the next child without anomaly.

6. Identify the likely phenotypes of children in the family, where one of the spouses suffers from acatalysis, and the other has only a decreased catalase activity.

7. Family hypercholesterolemia is inherited autosomally dominant. In heterozygotes, this disease is expressed in a high content of cholesterol in the blood, in homozygotes, in addition, xanthomas (benign tumor) develop skin and tendons, atherosclerosis. Determine the probability of the birth of children with an anomaly and the degree of its development in the family, where one of the parents, in addition to a high content of cholesterol in the blood, has developed xanthomas and atherosclerosis, and the other is normal with respect to the trait under analysis.

8. One form of cystinuria is inherited as an autosomal recessive trait. But in heterozygotes there is only an elevated cystine content in the urine, in homozygotes– the formation of cystine stones in the kidneys.

9. Identify possible forms of manifestation of cystinuria in children in the family, where one of the spouses suffered from this disease, and the other had only an elevated cystine content in the urine.

10. Identify possible forms of manifestation of cystinuria in children in the family, where one of the spouses suffered from kidney stone disease, and the other was normal with respect to the trait being analyzed.

Co-dominance. Multiple alleles:

1. In the maternity hospital four babies were born in one night, having blood groups I, II, III and IV. Blood groups of four parental pairs were: 1st pair – I and I; The 2 nd pair – IV and I; 3rd pair – II and III; The 4th pair is III and III. Four babies can be completely reliably distributed to parents. How to do it? What are the genotypes of all parents and children?

2. In the maternity house, two boys were accidentally confused. Parents of one of them have II and I blood groups, the parents of the other II and IV, boys

have II and I blood groups. Determine who is whose son and genotypes of parents and children.

3. A woman with group III blood has a child with group I blood. What are their genotypes, and what can not be the father's genotype?

4. A woman has blood group IV, her father has the same blood type. The woman's husband has the I blood group, his mother's second group. Identify the genotypes of all these individuals. What blood groups can a man and woman have in children?

5. If the first child has I blood group in the family, where the father has blood group II, and his mother has III, then what is the probability of the next child with the same blood group? What kind of blood group can there be in children from this marriage?

Answers

Complete dominance:

1. The probability of birth of healthy children in the family is 75%.

2. The probability of having children with an anomaly is 75%.

3. The probability of having children with an anomaly is 50%.

4. 75% of children will be healthy, 25% will suffer from phenylketonuria.

5. The probability of the disease of children in the family is 100%.

Incomplete dominance:

1. The probability of the birth of children resistant to malaria is 50%; 2) the probability of producing malaria-resistant children is 25%.

2. Probability of birth in the family of the next child without an anomaly of 25%; 2) 50% of children will suffer from acatalysis, 50% will have a decreased catalase activity.

3. All children will have a high cholesterol content in the blood.

4. 50% of children will have an elevated cystine content in the urine, 50% will be cystine kidney stones.

6. All children will have an elevated cystine content in the urine.

Co-dominance. Multiple alleles.

1. The first parent pair is 00 and 00, therefore, the child can have only I blood group; The 2 nd parent couple – AB and 00 from this marriage the child can be born with either II group; 3rd pair – AA and BB or AO and BO (in the first case the child has IV group, in the second – all options are possible); The 4th pair is BB and BB or BO and BO (in the first case the child is only with the III blood group, and in the second case, with III or I. A child with group I from the first parent pair, a child with group II from the second pair, a child with group III from the fourth pair, and a child with group IV from the third pair.

2. Parents with II (A0) and I (00) blood group have a son with I (00) blood group; parents with II (AA) and IV (AB) son with II (AA) blood group.

3. The genotype of a woman is B0, the child is 00. The father's genotype can not be: AB, BB, AA.

4. The genotype of a woman and her father is AB; the husband's genotype is 00, his mother has A0. Children can have AO and BO blood groups.

5. The probability of the next child with the same group of 25%. The genotype of the parents AO and BO, therefore, all variants of the blood group are possible.

3.2. DIHYBRID AND POLIHYBRID CROSSING

Having studied the inheritance by one criterion, G.Mendel decided to analyze the character of the inheritance of two characteristics simultaneously. For this, he used homozygous pea plants and analyzed two pairs of alternative attributes: color (yellow and green) and shape (smooth and wrinkled). When crossing clean lines, analyzed for two pairs of alternative characters (yellow smooth and green wrinkled) in the first generation, all individuals were uniform (yellow smooth seeds), and in the second generation a phenotype-splitting in the ratio 9 (yellow, smooth): 3 (yellow, wrinkled): 3 (green smooth): 1 (green wrinkled):

9 – yellow smooth (genotype A_B_);

3 – yellow wrinkled (genotype A_вв);

3 – green smooth (genotype aa B_);

1 – green wrinkled (genotype AAVB).

In the above notation, the bar means the possibility of the presence of any allele – dominant or recessive. Hence follows the third law of Mendel – the law of independent inheritance and combination of features:

When crossing homozygous organisms, analyzed for two (or more) pairs of alternative characteristics, in the second generation, independent inheritance and combination of traits are observed.

Accurate quantitative recording of features allowed G. Mendel to reveal certain statistical patterns in polyhybrid interbreeding: тhe number of possible gamete types is 2^n, where n is the number of heterozygous genotypes in the organism. For example, the genotype AABbcC is heterozygous for 2 genes: B and C (Bb and Cc), since n = 2, the number of different gamete types is:

$2^2 = 4$: ABC, ABc, AbC, Abc.

SITUATIONAL PROBLEMS

1. Albinism is a recessive sign. Thalassemia is a hereditary blood disease caused by the action of one gene. In the homozygote causes the most severe form of the disease – a large thalassemia, usually fatal in childhood (tt). In the heterozygote, the less severe form is manifested – small thalassemia (Tt). The child-albino suffers from a small thalassemia. What are the most likely genotypes of his parents?

2. Parents have II and III blood groups. They had a child with group I blood and sick sickle cell anemia (autosomal recessive inheritance with incomplete dominance, not linked to blood groups). Determine the likelihood of having sick children with IV blood group.

3. A blue-eyed short-sighted man whose mother had normal vision, married a brown-eyed woman with normal vision. The first child from this marriage is brown-eyed, short-sighted, the second – blue-eyed myopic. Establish genotypes of parents and children.

4. Phenylketonuria and one of the rare forms of agammaglobulinemia of the Swiss type (usually leading to death up to six months of age) are inherited as autosomal recessive traits. Advances in modern medicine make it possible to avoid the severe consequences of impaired phenylalanine metabolism. Determine the probability of the birth of patients with phenylketonuria of newborns without signs of agammaglobulinemia in the family, where both parents are heterozygous for both pairs of symptoms.

5. Fructosuria has two forms. One occurs without clinically expressed symptoms, the second leads to inhibition of physical and mental development. Both are inherited as recessive uncoupled between themselves (ie, located in different pairs of chromosomes) signs. One of the spouses has an elevated fructose content in the urine, hence, homozygous for fructosuria, not clinically manifested, but heterozygous for the second form of the disease. The second husband at one time was successfully treated for the second form of fructosuria, but heterozygous for its asymptomatic form. What is the probability of birth in this family of children suffering from a clinically pronounced form of fructosuria?

Answers

1. Both parents are heterozygous for albinism and one of the parents is heterozygous for thalassemia, another is homozygous, or both are heterozygous for thalassemia.

2. The probability of the birth of a sick child with IV blood group 6.25%.

3. The genotype of a woman Aabb, men – aaBb; genotype of the first child AaBb, the second – aaBb.

4. 18.75%.

5. 50%.

3.2.1. Types of interaction of non-allelic genes

In the body simultaneously operates a lot of alleles of different genes, including those located in different pairs of chromosomes. Obviously, in the chain of gene realization, many of them can influence each other at the level of enzymes, or

at the level of biochemical reactions. This can't but affect the formation of the phenotype. There are three types of interaction of non-allelic genes:

1) complementarity;

2) epistasis;

3) polymery.

Complementarity is a kind of interaction of non-allelic genes, when a new attribute is formed in the presence of the dominant alleles of different genes in the genotype at the same time.

Variants of splitting bb phenotype in the second generation with complementary interaction of non-allelic genes.

1. The splitting variant is 9: 3: 3: 1. Each dominant allele has its manifestation, whereas the two dominant alleles in combination form a new sign. An example is the formation of different forms of ridges in chickens and cocks. Allele A monitors the development of the pea-ridge in cocks (A_bb genotype), the allele of B-pink (genotype aaB_), in the absence of dominant alleles a simple (leaf-like) ridge (genotype aabb) develops, in the presence of both dominant alleles, a nutlike crest (genotype A_B_) is formed.

2. The splitting variant is 9: 3: 4. An example is the inheritance of coat color in mice (gray, black, white). The dominant allele (C) controls the synthesis of the black pigment, the recessive allele of this gene (c) does not synthesize the pigment, so the mice are white. The dominant allele (B) of another gene causes the zonal distribution of the black pigment over the hair (at the tip and at the base of the hair), therefore, in the C_B_ mouse genotype, the gray, recessive allele of this gene (b) causes a uniform distribution of the pigment over the hair, hence, in the mouse genotype C_bb will be black. The genotypes of ccB_ and ccbb mice are white.

3. The splitting variant is 9: 6: 1. Dominant alleles of different genes have the same phenotypic manifestation, in the joint presence in the individual another trait is formed. An example is the formation of the shape of the pumpkin fruit (discoid, spherical, elongated shape). In the presence of dominant alleles of different genes in the genotype of the pumpkin, the shape of the pumpkin disc type (genotype

A_B_), in the presence of the dominant allele of one of the genes, a spherical pumpkin shape is formed (genotype A_bb or aaB_), with a recessive homozygous genotype (aabb) – an elongated pumpkin shape.

4. The splitting variant is 9: 7. The symptom is formed only in the presence of two different dominant alleles (genotype A_B_). For example, the formation of hearing in humans is due to the presence in the genotype of the dominant alleles of different genes (D is the development of the cochlea and E is the development of the auditory nerve), and in the absence of one of these dominant alleles (genotypes D_e and ddE_) and the recessive homozygous genotype (ddee) deaf-mute is observed.

Epistasis is a kind of interaction of non-allelic genes. Distinguish between a dominant and a recessive epistasis. With dominant epistasis, the dominant allele of one gene (epistatic) inhibits the manifestation of the dominant allele of another gene (hypostatic). With recessive epistasis, the recessive alleles of one gene, being in a homozygous state, suppress the dominant allele of another gene.

Variants of splitting by phenotype in the second generation with a ***dominant epistasis***.

1. The splitting variant is 13: 3. An example is the inheritance of coloring plumage in chickens. The dominant allele (C) of the gene determines pigmentation of plumage in chickens, recessive (c) does not give pigmentation. The dominant allele (I) of another non-allelic gene is a suppressor, i.e. Suppresses the action of allele C, recessive allele (i) – neutral. Therefore, chickens with genotypes C_I_, ccI_ and ccii will be white, pigmentation of plumage is observed in genotypes C_ii.

2. The splitting variant is 12: 3: 1. As a dominant epistasis, you can consider the inheritance of the suits of horses. If C is a gray suit (suppressor), B is black, then horses with C_B_ and C_bb genotypes will be gray, a black suit will be formed in the genotypes of ccB_, with a recessive homozygous genotype (ccbb), the horses will be red.

An example of ***recessive epistasis*** in humans can be the so-called Bombay phenomenon, when an individual with a dominant allele of the blood group of the

ABO system (A or B) is identified as a person with group OO. This is due to the epistatic effect of the recessive alleles of the hh autosomal suppressor gene, which inhibit the development of blood group antigens. In this case, for example, individuals with the A0hh genotype will have the OO blood group.

Polymeria is a kind of interaction of non-allelic genes, in which the dominant alleles of different genes are responsible for manifestations of the same trait. The splitting for a polymer is expressed as 15: 1, where 15 parts of individuals have a characteristic (genotypes A_B_, A_bb, aaB_) and 1 part of individuals does not have a characteristic (genotype aabb). Polymer interaction can be qualitative – non-cumulative polymer (the presence of at least one dominant allele leads to the formation of a characteristic), or quantitative – cumulative polymorphism (the degree of manifestation depends on the number of dominant alleles).

An example of a quantitative polymer interaction in humans is the inheritance of the intensity of skin pigmentation: the degree of pigmentation is directly proportional to the amount of melanin and the number of dominant alleles (for example, four dominant alleles, the A1A1A2A2A3A3A4A4 genotype, cause black skin, four dominant alleles are dark brown, three dominant alleles are brown two and one dominant allele – swarthy, the absence of dominant alleles – light color of the skin).

SITUATIONAL PROBLEMS

Complementarity:

1. Deafness can be caused by two recessive alleles d and e, lying in different chromosomes. A deaf man with a ddEE genotype marries a deaf woman with the DDee genotype. What rumor can their children have? What can be caused by the birth of a normal child from deaf parents?

2. Normal hearing in humans is caused by two dominant alleles of different genes D and E, one of which determines the development of the cochlea, the other is the auditory nerve. Dominant homozygotes and heterozygotes for both genes have normal hearing, recessive homozygotes for one of these genes are deaf. In one family, where the mother and father are deaf, seven children with normal hearing

were born; in the other – also deaf parents were born four deaf children. Identify the genotypes of parents in two families. What kind of gene interaction is manifested in this case?

Epistasis

Dominant epistasis

A person has several forms of hereditary myopia. Moderate form (from – 2.0 to – 4.0) and high (above 4.0) are transmitted as autosomal dominant uncoupled signs. In a family where the mother was shortsighted, and the father had normal vision, two children were born: a daughter and a son. My daughter had a moderate form of nearsightedness, and her son was tall. What is the probability of the birth of the next child in the family without an anomaly, if it is known that only one of the parents suffered from myopia? It should be borne in mind that in people who have genes of both forms of myopia, only one high appears.

Recessive epistasis

The so-called Bombay phenomenon is that in a family where the father had I blood group, and mother III, a girl with I blood group was born. She married a man with a second blood group, and they had two girls: the first with IV, the second with the I blood group. The appearance in the third generation of a girl with an IV blood group from a mother with a blood group I caused bewilderment. However, several other cases have been described in the literature. According to V. McKusick, some geneticists tend to explain this phenomenon by the action of a rare recessive epistatic allele that can suppress the action of alleles that determine blood groups A and B. Identify the genotypes and phenotypes of parents and children in the first and second generations.

Polymery

The growth of a person is controlled by three pairs of unconnected genes that interact like a polymer. The shortest people have all the recessive alleles and growth of 150 cm, the highest all the dominant alleles and the growth of 180 cm:

a) Determine the growth of people heterozygous for all three genes.

b) A short-grown woman married a man of medium height. They had four children who had a height of 165 cm, 160 cm. 155 cm and 150 cm. Identify the parents' genotypes and their growth.

Answers

Complementarity:

1. Children have the genotype DdEe, they will all have hearing. D – causes the development of the cochlea, E – development of the auditory nerve.

2. In the first family, the parents' genotype: DDee and DdEe, in the second family either the same alleles dominant, or parents have recessive alleys for both genes. Complementary interaction of alleles.

Epistasis

1. 25%

2. In the first generation the genotype of the mother B0Hh, the father – 00Hh, in the second generation the genotype of the mother *B0hh (recessive epistasis)*, the father – A0Hh or AAHh.

Polymery

a) $A_la_1A_2a_2A_3a_3$;

b) The genotype of a woman: $a_la_1a_2a_2a_3a_3$ – 150 cm, male: $A_1a_lA_2a_2A_3a_3$–165cm.

3.3. SEX-LINKED INHERITANCE

In humans, the two sex chromosomes are X and Y (XX in women and XY in men). The study of the structure of sex chromosomes made it possible to distinguish the following areas in them:

A – areas with allelic genes – pseudo-autosomal regions 1 and 2, present in the X- and Y-chromosome. Due to pseudo-autosomal regions, conjugation of sex chromosomes is possible at the heterogametic sex during meiosis.

B – genes linked to the X chromosome, including genes that determine the development of female gender characteristics, genes of hemophilia, color blindness, muscular dystrophy, etc. – more than 200 genes.

C – genes linked to the Y-chromosome. In the Y chromosome, about 100

genes and genetic markers are currently mapped. In the Y chromosome, the region SRY (from the English sex region of Y-chromosome) is localized, which determines the development of testes and differentiation in the male type.

In addition, the Y chromosome maps the genes that determine the hair flow of the auricle (hypertrichosis), the middle phalanges of the fingers, controlling the intensity of growth, the formation of the membrane between the toes and some other signs.

Genes localized in sections A, B and C are called linked to sex chromosomes.

The signs that are inherited through the Y chromosome are called holandric. They appear only in males and are transmitted only through the male line. The signs that are inherited through the X chromosome are called linked to the X chromosome. They are found in both women and men. In this case, women can be both homozygous and heterozygous for genes localized in the X chromosome.

Recessive alleles in women are manifested only in the homozygous state, but in men recessive alleles are always present, are in the hemizygous state, i.e. do not have an allelic pair in the homologous chromosome.

A classic example of such inheritance is hemophilia A – a disease characterized by a violation of blood clotting and bleeding. In this case, mothers – heterozygous carriers of the mutant recessive allele – transmit the disease to their sons with a probability of 50%. It should be borne in mind that, for example, in birds, some insects heterogametic sex – female, homogametic – male.

SITUATIONAL PROBLEMS

1. Classical hemophilia is transmitted as a recessive trait linked to the X chromosome. A man with hemophilia marries a normal woman, whose father suffered from hemophilia. Determine the probability of birth in this family of healthy children?

2. In humans, an allele that causes one form of color blindness, or color blindness, is localized in the X chromosome. The condition of the disease is caused by a recessive allele, the health state is dominant. A girl with normal vision, whose

father had color blindness, marries a normal man whose father also suffered from color blindness. What vision will the children have from this marriage?

3. Hypertrichosis is inherited as a trait linked to the Y-chromosome, which manifests itself only to 17 years of life. One form of ichthyosis is inherited as a recessive trait linked to the X chromosome. In a family where the woman is normal for both signs, and the husband is the owner of only hypertrichosis, a boy with signs of ichthyosis was born. Determine the probability of birth in this family of children without both anomalies, and what they will be sex.

4. A woman right-handed with brown eyes and normal eyesight marries a right-handed man, blue-eyed and color-blind. They had a blue-eyed daughter left-handed and color-blind. What is the likelihood that the next child in this family will be left-handed and suffer color-blindness if it is known that the brown eye color and the ability to own mainly the right hand are dominant autosomal unrelated attributes, and color blindness is a recessive, X-linked trait?

5. In a family where the wife has the I blood group, and the husband – IV, the son of the color-blind man with the III blood group was born. Both parents distinguish colors normally. Determine the likelihood of a healthy son and its possible blood group. Color blindness is inherited as a recessive trait linked to the X chromosome.

Answers

1. The probability of birth in this family of healthy children is 50%.

2. Ratio of phenotypes 75% healthy: 25% patients.

3. The probability of the birth of children without an anomaly is 50% girls.

4. The probability that the next child will be left-handed and color-blind is 12.5%.

5. The probability of a healthy son's birth is 25%, the possible blood groups are II and III.

3.4. LINKED INHERITANCE (MORGAN'S LOWS). CROSSING-OVER

The genes and signs in the body are much larger than the number of chromosomes. So, a person has 23 pairs of chromosomes, but about 22 thousand genes. Consequently, in each chromosome there are many different genes. These genes form one clutch group and are inherited linked.

The patterns of linked inheritance of genes were established in the 1920s. studies of T. Morgan and his followers in experiments on fruit flies – Drosophila. Drosophila has 8 chromosomes (6 autosomes and 2 sex chromosomes: XY – in males, XX – in females).

T. Morgan conducted a dihybrid crossing and studied the following signs: body color and length of the wings. To identify alleles and signs, the following notations were used: allele B – gray body color; b – black body color; V – long wings; v – short wings.

When a homozygous dominant was crossed with a homozygous recessive specimen in the first generation, all flies were gray with long wings, which corresponded to the law of uniformity of hybrids of the first generation of G. Mendel. However, when two heterozygous individuals crossed, T. Morgan observed a significant deviation from the expected cleavage of 9: 3: 3: 1, characteristic of dihybrid crosses. To determine the cause of this phenomenon, T. Morgan conducted an analysis of the crossing of a heterozygous individual showing dominant characters with a recessive homozygous individual. According to the laws of G. Mendel, in this case, with the independent inheritance of the characters, four types of individuals with an equal frequency of 25% each were expected to be obtained (1: 1: 1: 1 splitting).

However, contrary to expectation, when the heterozygous male Drosophila was crossed with recessive females, the cleavage was found to be 1: 1, i.e. There were only 2 variants with an equal frequency (50% and 50%). The reason for this could only be the absolute linkage of the genes, when they are inherited as a single

feature in the pair. Indeed, in Drosophila males, the adhesion of genes is always complete, because crossing-over (exchange of homologous sites) does not occur.

When a heterozygous female was crossed with a recessive male, all four expected variants were obtained in the offspring, but the parental forms significantly prevailed in frequency. The predominance of the original parental forms (83%) indicates that the genes of the body color and the length of the wings are really linked. On the other hand, the appearance in 17% of cases of new forms (gray body and short wings, black body and long wings) testifies to the occurred recombination of the corresponding alleles. This is the result of the conjugation of homologous chromosomes during the prophase of meiosis I and crossing-over.

Thus, with the linked inheritance of genes in the process of meiosis, two variants of gametes are formed: non-crossover (identical to parent) and crossover (combining alleles of both parents due to the crossover that occurred). In the example considered above, the share of non-crossover gametes was 83%, crossover gametes were detected with a frequency of 17%.

The results of the experiments of T. Morgan and his students became the basis of the chromosome theory of heredity.

The main principles of the chromosome theory of heredity:

1. Genes are found in chromosomes. Each chromosome is a clutch of genes.

2. Each gene in the chromosome occupies a certain place – the locus. The genes in the chromosomes are arranged linearly.

3. Between the homologous chromosomes, there may be an exchange of allelic regions between non-sister chromatids (crossing-over).

4. The distance between the genes in the chromosome is proportional to the frequency of crossing-over between them.

According to the provisions of the chromosome theory of heredity, genes localized in one chromosome form a clutch group and are inherited linked. The number of clutch groups is equal to the haploid number of autosomes plus the number of clusters of sex chromosomes and the clutch of mitochondrial DNA. Thus, 25

clutch groups have been identified in human: 22 – autosomal, 2 – the clutch of sex chromosomes (X and Y) and the clutch of mitochondrial DNA.

Thus, according to modern ideas, in any pair of homologous chromosomes, there are always several alleles. The signs whose genes are on the same chromosome are called linked. Naturally, the linked characteristics in the majority are transmitted together. But together the linked characteristics are not always transmitted.

The fact is that in the prophase of the first division of meiosis homologous chromosomes closely approximate each other (conjugate). Sometimes, at the time of conjugation, there may be a cross between homologous chromosomes. In the future, if they are divergent at the intersection site, chromosome rupture is possible, and then the reunion of the lost sites due to the chromosome of the partner. As a result, the paired chromosomes exchange homologous sites. The genes of one chromosome seem to pass into another, homologous to it. This phenomenon is called crossing-over.

In the exchange of homologous regions, the linked genes divide into different gametes. The frequency of the divergence of the characteristics in crossing-over is directly proportional to the distance between the genes, i.e. the farther apart are the genes in the chromosome, the more often there is an exchange, the closer they are to each other, the less the divergence of symptoms.

When the genes are linked, the number of these or those gametes depends on the distance between the genes. This distance is calculated in the Morganids (M). One morganide corresponds to one percent of gamete formation, in which homologous chromosomes exchanged their sites. Patterns of inheritance of linked features of genetics are used to compile chromosome maps. The frequency of the discrepancy of certain features is established experimentally, i.e. distance between genes. Then the chromosome is drawn, and the relative locations of loci are noted on it.

Example of problem solving

Problem 1: in humans, cataracts and polydactyly are determined by autosomal dominant closely linked alleles of different genes. A woman, normal on both

grounds, married a man with two anomalies. It is known that he inherited cataract from his mother, and polydactyly from his father. What is the progeny progeny in this family?

Decision. Denote the alleles of genes:

A – cataract

a is normal vision

B – polydactyly

b – normal number of fingers

We will establish the genotypes of parents: since a woman is phenotypically normal by two features, her genotype is: aab. A man has both anomalies, so his genotype must have dominant A and B alleles. A man inherited one anomaly from his mother, so from his father, by this feature, he inherited a normal allele, i.e. a man is heterozygous for the first sign (genotype Aa). The second anomaly (polydactyly) he received from his father, and from his mother on this basis he received an allele of the norm, i.e. he is heterozygous for the second gene: Bb. Thus, his genotype: AaBb. Since the genes of the two signs are linked, the scheme of the location of alleles in

$$\frac{A \qquad b}{a \qquad B}$$

In the chromosome, which he received from his mother, there are alleles of cataract – A and allele of normal number of fingers – b. In the paternal chromosome there is an allele of normal vision – a and the allele of polydactyly – B. Since the genes of the two characters are completely linked, two types of gametes are formed in the digest heterozygous male with the AaBb genotype: Ab and aB. We will write down the scheme of crossing, write out gametes of parents and all possible genotypes in F1:

P: ♀ aább – ♂ AaBb

G: (ab) (Ab) (aB)

F1 Aabb: aaBb

It turned out that in F1 two genotypes are possible: Aabb – corresponds to the phenotype of cataract and the normal number of fingers, and aaBb corresponds

to normal vision and polydactyly. The probability of each of these genotypes is ½ or 50%.

Answer: In this family, only one anomaly can be born: 50% chance of having children with cataracts and normal number of fingers and 50% having normal vision and polydactyly.

Problem 2: What types of gametes and in what ratio does the individual form the genotype AaBbDd? The distance between the alleles A and b is 20 morganids, the allele D is on the other chromosome.

Decision: We will write down a schematic drawing of the genotype:

A b D

a B d

G: → Non-crossover AbD Abd aBD aBd

→ Crossover abD abd ABD ABd

To calculate the ratio of crossover and non-crossover gametes, we take into account that the number of crossover gametes is equal to the distance between alleles. Hence: 20% of crossover, 80% of non-crossover gametes.

Answer: 20% – crossover, 80% of non-crocodile gametes.

SITUATIONAL PROBLEMS

1. What types of gametes and in what ratio does it form an individual with the AaBbCC genotype:

a) with complete linkage of genes;

b) when the genes are located in different pairs of homologous chromosomes? The answer is explained by the figure.

2. What types of gametes and in what ratio does it form an individual with the AaBbCc genotype:

a) in the absence of gene adhesion;

b) with complete cohesion of the genes A, b and c. The answer is explained by the figure.

3. What types of gametes and in what ratio does the individual form the genotype AaBbDd? The distance between the alleles A and b is 20 morganids, the allele D is on the other chromosome.

4. What types of gametes and in what ratio does the individual form the genotype AaBBCc, if the gene alleles are not linked?

5. What types of gametes and in what ratio does the individual form the genotype NnCcPpDd? Alleles N and c on the other and the distance between them is equal to 10 morganides, alleles P and D are completely adhered, and chromosome there are.

6. Alleles of the genes of color blindness and night blindness, are inherited through the X chromosome and are located at a distance of 50 morganids from each other. Both signs are recessive. Determine the probability of having children simultaneously with both anomalies in the family, where the wife is heterozygous for both signs and both anomalies are inherited from her father, and the husband has both forms of blindness.

7. Classical hemophilia and color blindness are inherited as recessive traits linked to the X chromosome. The distance between the genes is determined in 9.8 morganides. The girl, whose father suffers both hemophilia and color blindness, and the mother is healthy and comes from a happy family for these diseases, marries a healthy man. Identify the likely phenotypes of children of this marriage.

8. Cataract and polydactyly in humans are caused by dominant autosomal closely linked (ie, not detecting crossover) alleles. What offspring can be expected in the family of parents heterozygous for both reasons, if it is known that the mothers of both spouses suffered only cataracts, and fathers only polydactyly?

9. In humans, the Rhesus factor locus is linked to a locus that determines the shape of red blood cells, and is located at a distance of 3 morganides from it. Rhesus positivity and elliptocytosis are determined by dominant autosomal alleles. One of the spouses is heterozygous for both symptoms. At the same time he inherited Rh-positivity from his father, elliptocytosis – from his mother. The second spouse

is Rh-negative and has normal red blood cells. Determine the percentage of probable genotypes and phenotypes of children in

Answers

1. a) ABC (50%), abc (50%); b) ABC, ABc, AbC, Abc, aBC, aBc, abC, abc – 12.5% per each.

2. a) 8 types of gametes: ABC, ABc, AвC, Авс, aBC, aBc, авC, авс – 12.5% per each; b) Abc (50%), aBC (50%).

3. Noncrossover gametes (80%): AbD, Abd, aBd, aBD.

Cross-over gametes (20%): ABD, ABd, авD, авd.

4. 4 types of gametes in equal proportions: ABC, aBC, ABc, aBc

5. 8 types of gametes. Crossover – 10%, non-crossover – 90%.

6. Probability of the birth of a child with both anomalies 25%.

7. Probability of having children: healthy – 72.55%; hemophilia – 2.45%, colorblind – 2.45%, with both anomalies – 22.55%.

8. The probability of the birth of children with: cataracts – 25%, polydactyly– 25%, both anomalies – 50%.

9. 1.5% AaBb – Rh «+», Elliptocytosis;

1.5% aabb – Rh «-», normal red blood cells;

48.5% of Aabb-Rh «+», normal erythrocytes;

48.5% aaBb – Rh«-», Elliptocytosis.

SECTION IV
VARIABILITY

Variability is a common property of living organisms to acquire new signs. Variability happens:

1. Phenotypic, or Modificative (non-hereditary).

2. Genotypic (hereditary): a) combinative; b) mutational.

4.1. PHENOTYPICAL VARIABILITY. PENETRANCE

Modification (Phenotypic) variability occurs under the influence of environmental factors without changing the genotype. Due to the modification variability, organisms adapt to changing environmental conditions.

In the process of ontogeny, not all genes are realized as a sign. Some of them are blocked by other non-allelic genes, the appearance of other signs is not conducive to external conditions. One and the same mutant sign may appear in some and not manifest in other individuals of a related group. This phenomenon is called penetrance of the gene expression. Penetence (P) is expressed as a percentage and is calculated as the ratio of the number of individuals in which this feature is manifested (practical probability, PP) to the total number of individuals having a genotype (theoretical probability, TP) responsible for the possibility of manifesting this attribute:

$$P = PP/TP \times 100\%$$

SITUATIONAL PROBLEMS

1. Otosclerosis is inherited as a dominant autosomal trait with a penetrance of 30%. The absence of lateral upper incisors is inherited as a recessive trait linked to the X chromosome with full penetrance. Determine the likelihood of manifestation in children of both anomalies at the same time in a family where the mother is heterozygous for both signs, and the father is normal for both pairs of gene alleles.

2. The brown eye color dominates over the blue and is determined by the au-

tosomal allele of the gene. Retinoblastoma is determined by another dominant autosomal allele of the gene. Penetration of retinoblastoma is 60%. What is the likelihood that brown-eyed children will be healthy heterozygous for marriage on both grounds?

3. Arachnodactyly is inherited as a dominant autosomal trait with a penetrance of 30%. Left-handedness is a recessive trait with full penetrance. Determine the likelihood of manifestation of both anomalies at the same time in children in the family, where both parents are heterozygous for both pairs of genes.

4. Craniofacial dysostosis (premature overgrowth of the cranial suture and the absence of a large fontanel) is inherited as an autosomal dominant trait with a penetrance of 50%. Determine the probability of the birth of a sick child if one of the parents is heterozygous for this disease, and the other is healthy.

5. Angiomatosis is inherited as a dominant autosomal trait with a penetrance of 50%. Determine the likelihood of children in the family, where both parents are heterozygous carriers of angiomatosis.

Answers

1. The probability of manifestation in children of both anomalies in this family is 12.5%.

2. The probability that children from this marriage will be healthy brown-eyed, is 41.25%.

3. The probability of simultaneous occurrence of both anomalies in a given family is 5.625%.

4. The probability of producing a sick child in a given family is 25%.

5. The probability of the disease of children in this family is 37.5%.

4.2. GENOTYPIC VARIABILITY

Combinative variability is a variability in which the combination of the parents' genes leads to the appearance of new signs in individuals. It is provided by a crossover in the prophase of meiosis I, an independent divergence of chromosomes

in the anaphase of meiosis I and a random combination of gametes with a different set of chromosomes during fertilization.

Mutational variability is caused by mutations – a change in genetic material. Mutations occur under the influence of external or internal factors. The process of mutation formation is called mutagenesis, and the factors causing mutations are mutagenic. By the nature of the change in the genetic material, the mutations are divided into three groups:

1. Gene mutations are changes within a single gene. There are mutations by type:

a) replacement of nitrogenous bases: transitions -A↔G, C↔T and transversions -A↔C, G↔T;

b) frame reading shift mutations: insertion (insertion), reduplication and proliferation (deletion) of nucleotides;

c) inversion of the DNA site.

2. Chromosome mutations (aberrations) are mutations caused by a change in the structure of chromosomes. They can be intrachromosomal (deletions, duplications, inversions), as well as interchromosomal (translocations).

3. Genomic mutations are mutations caused by a change in the number of chromosomes: polyploidy and heteroploidy (aneuploidy). Polyploidy is a multiple of the haploid increase in the number of chromosomes. Polyploidy in humans is a lethal mutation. Heteroploidy is an increase or decrease in the number of individual chromosomes. A person has studied several diseases, the cause of which is the change in the number of chromosomes (Down's syndrome, Klinefelter's syndrome, etc.).

4.2.1. Gene mutations

Example of problem solving

Problem: How will the structure of the protein change if from the DNA coding region 5' TTATGTAAATTTCAG 3 'remove the 5th and 13th from the left nucleotides?

Decision: we construct the mRNA molecule according to the complementa-

rity principle, and then we determine the sequence of amino acids in the polypeptide chain before the changes:

DNA: 5’; TTATGTAAATTTCAG 3’; – coding chain

3’ AATACATTTAAAGTC 5' – matrix chain

mRNA: 5 'UUAUGUAAAUUACAG 3'

am. ac.: leu-cis-lys-phe-gln.

We make these changes in the structure of DNA and again determine the sequence of amino acids:

mRNA: 5 'UUAUUAAAUUUA 3'

am. ac.: leu-leu-asp-leu.

SITUATIONAL PROBLEMS

1. The fragment of the protein chain of the tobacco mosaic virus consists of the following amino acids: ser-gly-ser-ile-thr-pro-ser. As a result of the effect on mRNA of nitrous acid, cytosine RNA is converted into guanine. Determine changes in the structure of the protein of the virus after exposure to mRNA with nitrous acid.

2. The fragment of the coding chain of DNA normally has the following order of nucleotides: AAAACCAAAATACTTATACAA. During replication, the fourth adenine and the fifth cytosine disappeared from the left. What is the name of this type of mutation. Determine the structure of the polypeptide chain encoded by this region of DNA, normal and after nucleotide deposition.

3. The DNA portion encoding the polypeptide has, in the norm, the following order of nucleotides: 5'AAAACCAAAATACTTATACAA3 '. During replication, the triplet ATSTS fell out of the chain. Determine how the structure of the polypeptide chain encoded by this region of DNA will change. What is the name of this type of mutation?

4. What changes will occur in the structure of the protein, if in the coding region of DNA: 5'AAACAAAGAACAAAA3 ', between 10 and 11 nucleotides include cytosine, between the 13th and 14th thymine, and at the end add one more adenine?

5. In patients with sickle-cell anemia in the 6th position of the β-chain of the hemoglobin molecule, glutamic acid is replaced by valine. What is the difference between the DNA of a person sick with sickle cell anemia, from a healthy person?

Answers

1. After exposure to mRNA with nitrous acid, the following changes in the structure of the virus protein occur: in the first, third and seventh positions, serine is replaced by cysteine; in the fifth position, threonine is replaced by serine, and in the sixth position by glycine.(пролин на глицин в 6 положение).

2. The structure of the polypeptide is normal: lys-tre-lys-ile-leu-ile-gln; after nucleotide precipitation: lys-gln-asn-thr-tyr-thr. Mutation is a deletion.

3. The amino acid threonine is released from the polypeptide. Mutation is a deletion.

4. There will be an elongation of the polypeptide chain, an amino acid asparagine is added between threonine and lysine.

5. The DNA of a patient sickle-cell anemia from the DNA of a healthy person is distinguished by the substitution of the thymine nucleotide for adenine at the 6th position.(кодон CTT на CAA).

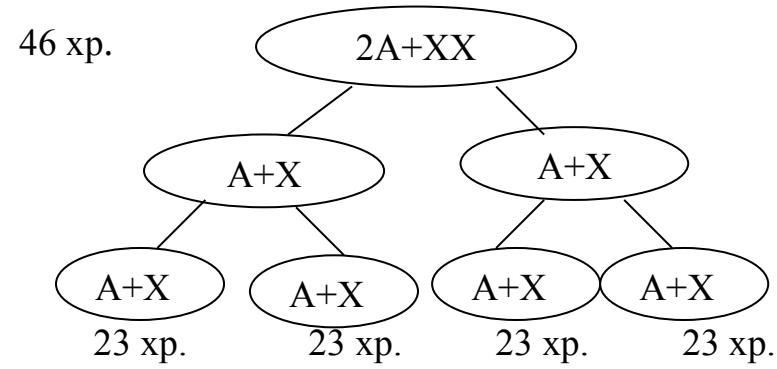
4.2.2. Genomic mutations

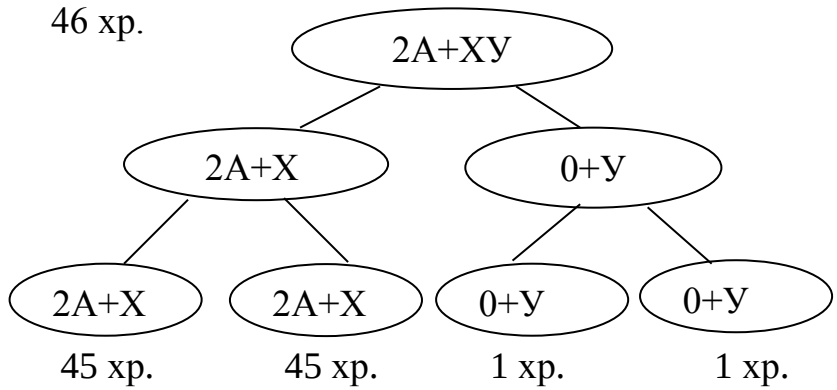
Example of problem solving

When solving such problems, it is necessary to indicate, when merging which gametes a zygote with a given karyotype is formed, then to show the mechanism of the appearance of these gametes in the process of meiosis.

Problem 1: in cells of human embryo fibroblasts, a karyotype 3A + XX. Explain the mechanism of occurrence of such karyotype.

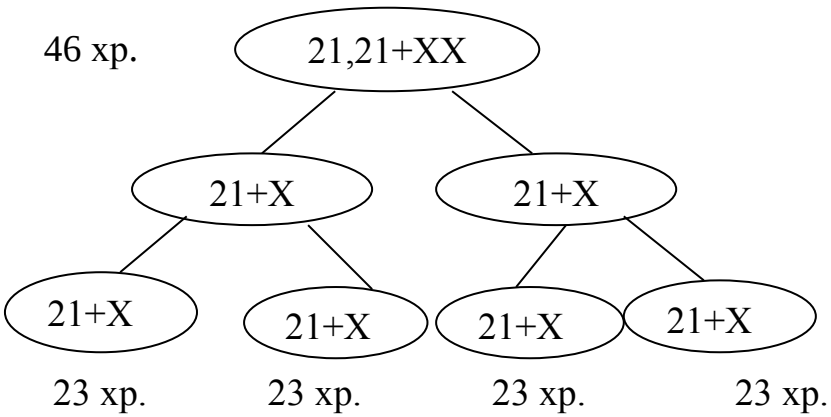
Decisionю. the total number of chromosomes in the karyotype of 3A + XX is 22 × 3 + 2 = 68 chromosomes. A zygote with a karyotype of 3A + XX could have occurred when a normal egg (A + X) merges with an abnormal spermatozoon (2A + X).

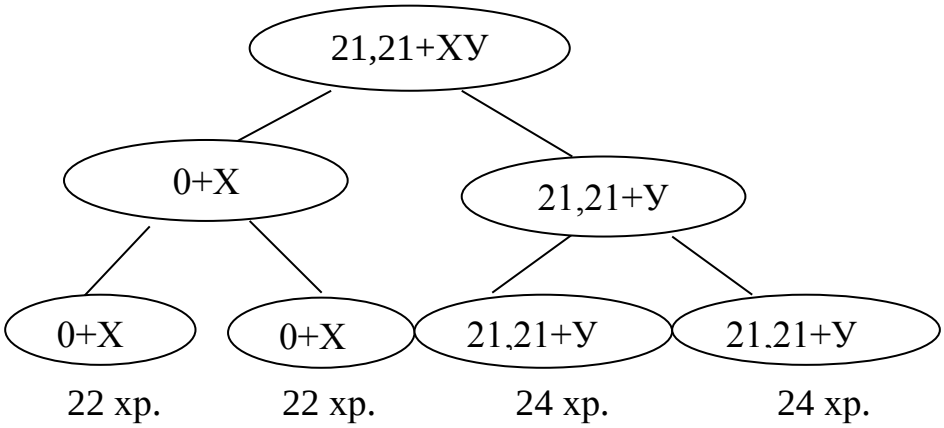




Answer: 3A+XX = (A+X) + (2A+X)

Problem 2*:* explain the mechanism of the occurrence of Down syndrome in a boy (47, XY, 21+).





Answer: (21,21+Y)+(21+X) = (21,21,21+XY) =(47, XY, 21+)

SITUATIONAL PROBLEMS

1. Explain the mechanism of the origin of karyotype 2A + XXYY in men. Determine the number of chromosomes in this karyotype and gametes.

2. Explain the mechanism of formation karyotype 2A + XXXXX in a woman. Specify the number of chromosomes in this karyotype and gametes.

3. Explain the mechanism of the origin of karyotype 2A + XXXX in a woman. Indicate the total number of chromosomes and the number of chromosomes in gametes. What kind of mutation?

4. What is the maximum amount of X-sex chromosomes possible in a karyotype in a woman with non-dissociation of sex chromosomes in the process of gametogenesis in both sexes? Answer the explanation with the diagram.

5. In the fibroblast cells of the human embryo, the following karyotype is 4A + XXXY. What are the consequences of this mutation? Determine the form of mutational variability?

6. Explain the mechanism of karyotypic disorder in a man with a set of chromosomes 2A + XXXXXXYY. Determine the total number of chromosomes.

7. Explain the mechanism of the origin of karyotype 47,XY (+15). Determine the number of chromosomes in gametes. Name the syndrome and explain the mechanism of its occurrence.

Answers

1. The total number of chromosomes in the karyotype of 2A + XXYY = 48 chromosomes. Zygote 2A + XXYY can occur with the fusion of an abnormal egg

(A + XX) – 24 chromosomes with an abnormal spermatozoon (A + YY) – 24 chromosomes. There was a genomic mutation – polysomy of sex chromosomes. Klinefelter's syndrome.

2. The total number of chromosomes in the karyotype of 2A + XXXXX = 49 chromosomes. Zygote 2A + XXXXX may occur when the abnormal egg is fused (A + XXXX) – 26 chromosomes with normal spermatozoon (A + X) – 23 chromosomes. There was a genomic mutation – polysomy of sex chromosomes. Trisomy-X syndrome.

3. Total number of chromosomes in the karyotype of 2A + XXXX = 48 chromosomes. Zygote 2A + XXXX can occur when fusion of an abnormal egg (A + XX) – 24 chromosomes with an abnormal spermatozoon (A + XX) – 24 chromosomes. There was a genomic mutation – polysomy of sex chromosomes. Trisomy-X syndrome.

4. The maximum number of sex chromosomes in a karyotype in women is 6.

5. The total number of chromosomes in the karyotype of 4A + XXXY = 92 chromosomes. Zygote 4A + XXXY can occur when an abnormal egg (2A + XX) merges with an abnormal sperm (2A + XY). There was a genomic mutation – polyploidy. This mutation is not compatible with life.

6. The total number of chromosomes in a karyotype of 2A + XXXXXXYY = 52 chromosomes. Zygote 2A + XXXXXXYY can occur when an abnormal egg (A + XXXX) merges with an abnormal spermatozoon (A + XXYY). Violation of the karyotype occurs when the sex chromosomes do not divide in 2 divisions of meiosis, during oogenesis and spermatogenesis.

7. Patau syndrome, can occur when the chromosomes of the D-group do not divide in one of the meiotic divisions.

SECTION V.
METHODS OF HUMAN GENETICS STUDY

Not all methods of genetics are applicable to the analysis of inheritance of certain features in humans. However, to study the phenotypes of several generations of relatives, it is possible to establish the nature of inheritance of the trait and the genotypes of individual family members, determine the likelihood of occurrence and the degree of risk to the offspring for a particular disease. The method of constructing and analyzing genealogies was named genealogical. It serves as the basis for conducting medical genetic counseling.

5.1. GENEALOGICAL METHOD

The compilation of pedigrees has its own rules. A person, in relation to whom it is made up, is called a proband. Each generation of investigators is placed in one line and numbered in Roman numerals. Members of the same generation are numbered in Arabic numerals. After drawing up the scheme, an analysis is carried out, consisting of several stages:

1. Determining whether a given attribute is inherited.
2. Determining the type of inheritance.
3. Determination of genotypes of members of the pedigree.
4. Determining the likelihood of manifestation of a feature in offspring.

Consider the main features of pedigree schemes for determining the type of inheritance:

1. An autosomal dominant type of inheritance:

• vertical inheritance;

• transmission of the disease from sick parents to children;

• healthy family members have healthy children;

• the symptom is the same in both sexes.

2. Autosomal recessive:

• sick children are born from phenotypically healthy parents;

• inheritance horizontally;

• the symptom is the same in both sexes.

3. X-linked recessive:

• mostly male patients;

• sick children are born from phenotypically healthy parents, but the mother is the carrier of the gene;

• disease of women is possible if the father is sick and the mother is the carrier.

4. X-linked dominant:

• disease is traced in every generation;

• a sick father has all his daughters sick;

• both men and women are sick;

• healthy parents have all children healthy.

5. The *inheritance associated with the Y-chromosome* is characterized by the fact that the symptom is found in men in all generations.

SITUATIONAL PROBLEMS

1. According to the legend, compile a pedigree and determine the type of inheritance. The proband has a "white curl" in his forehead. The brother of the proband without a lock. On the line of the father, a proband of anomalies was not observed. Mother proband with a white lock. She has three sisters. Two sisters with a lock, one without a curl. The third aunt of the proband from the side of her mother without a curl has two sons and one daughter without a curl. The grandfather of the proband on the mother's line and his two brothers had white curls, and two more were without curls. Great-grandfather and great-great-grandfather also had a white curl with a forehead.

2. According to the legend, compile a pedigree and determine the type of inheritance. Newlyweds normally have a right hand. In the family of the woman there were two sisters, normally owning the right hand, and three brothers – left-handed. The mother of the woman is right handed, father is left-handed. The father has a sister and brother left-handed, a sister and two right-handed brothers. Grandfather

on the father's line right-hander, grandmother – left-handed. A mother's mother has two brothers and a sister – all righties. Mother of the husband – right-hander, father – left-handed. Grandmothers and grandfathers on the part of the mother and father of the husband normally own the right hand. Determine the probability of birth in this family of children who own the left hand.

3. According to the legend, compile a pedigree and determine the type of inheritance. The proband suffers from Marfan syndrome. His sister is also sick, and two brothers are healthy. The father of the proband is sick, and his sister is healthy. The mother of the proband is healthy and has a sick sister and a healthy brother. Grandmother and grandfather from the mother of the proband are sick. The great-grandmother (mother of the grandfather on the part of the father of the proband) is healthy, and the great-grandfather is sick and has two healthy brothers and a sick sister. The great-grandfather and great-great-grandmother suffer from Marfan syndrome. The grandmother from the father of the proband is sick, and the grandfather is healthy and has a sick sister and three healthy brothers. Determine the probability of a healthy baby if the proband marries a healthy woman.

4. According to the legend, compile a pedigree and determine the type of inheritance. The proband is colorblind, his sister and brother are healthy, and two brothers are sick. The father of the proband is sick, and his two brothers are healthy. The mother of the proband is healthy and has a sister and brother, too, are healthy. The grandmother of the proband from the mother's side is well, grandfather suffered color blindness. My grandfather's brother and sister are healthy. The grandmother and grandfather on the part of the father of the proband are healthy, but the grandfather has a sick brother and two identical twin sisters. Great-grandfather (from father of probanda) is sick, and great-grandmother is healthy.

5. According to the legend, compile a pedigree and determine the type of inheritance. The proband suffers from mild sickle-cell anemia, his spouse is healthy. He has a daughter also with mild form of anemia. The mother and grandmother of the proband suffered the same form of sickle-cell anemia, the rest of the sibs of the mother and her father are healthy. The wife of the proband has a sister who has a

mild form of anemia, the second sister has died of anemia. The mother and father of the wife of the proband suffered from anemia, in addition, it is known that his father had two brothers and a sister with a mild form of anemia. Determine the likelihood of having children with severe anemia in the family of a proband daughter if she marries the same man as her father.

Answers

1. The presence of a "white curl" in the hair is inherited by an autosomal dominant type.

2. Right-handedness is inherited by an autosomal dominant type. The probability of birth in this family of children owning the left hand will be 25%.

3. The symptom is inherited as autosomal dominant. The probability of the birth of a healthy child, if the proband marries a healthy woman, is 50%.

4. The trait is inherited as linked to X recessive.

5. Sickle cell anemia is inherited as an incompletely dominant trait. The probability of the birth of children with severe anemia in the family of a proband daughter is 25%.

5.2. TWINTH STUDY

The twin study allows one to assess the relative role of genetic and environmental factors in the development of a particular trait or disease. Twins are monozygotic (MZ) and dizygotic (DZ).

Monozygotic twins develop from a single fertilized ovum (zygote) as a result of its division into two with the formation of two embryos. Monozygotic twins have the same genotypes and the difference in their phenotypes is due only to environmental factors. Dizygotic twins are born when two eggs are produced simultaneously, fertilized by two spermatozoa. Dizygotic twins have different genotypes. But thanks to the simultaneous birth and joint education on them will act common environmental factors.

To determine the role of heredity in the development of the trait, it is necessary to compare the proportion (%) of concordant pairs (identical for a particular feature) in the groups of mono- and dizygotic twins. The concordance of monozygotic twins is designated CMZ, dizygotic – CDZ.

CMZ = number of similar pairs of monozygotic twins / total number of pairs of monozygotic twins × 100%;

CDZ = number of similar pairs of dizygotic twins / total number of pairs of dizygotic twins × 100%.

To calculate the role of heredity (H), Holzinger's formula is used:

$$H = \frac{CMZ - CDZ}{100\% - CDZ} \times 100\%$$

To determine the role of the environment (E) in the development of the sign, the formula is used:

$$E = 100\% - H$$

Example of problem solving

Problem: in one of the populations, the heritability of bronchial asthma was studied. 46 pairs of monozygotes and 120 pairs of dizygotic twins were studied. In all these pairs, at least one of the twins suffered from bronchial asthma. Moreover, in 36 pairs of monozygotic twins and in 6 pairs of dizygotic twins, the second twin also suffered from bronchial asthma. Determine the coefficient of heritability and the role of environmental on manifestation of bronchial asthma.

Decision: in order for us to take advantage of the Holzinger formula, we need to calculate the concordance coefficients for bronchial asthma:

a) for monozygotic twins and;

b) for dizygotic twins.

1. First, calculate the concordance coefficient for bronchial asthma for monozygotic twins.

$$CMZ = 36/46 \times 100\% = 78\%$$

2. Then calculate the concordance coefficient for bronchial asthma for dizygotic twins.

$$CDZ = 6/120 \times 100\% = 5\%$$

4. We will write the formula of Holzinger, which allows us to estimate the degree of heredity involvement in the formation of bronchial asthma.

$$H = \frac{CMZ - CDZ}{100\% - CDZ} \times 100\%$$

5. Now, substituting the previously found numerical values of the coefficients of concordance, we calculate the coefficient of heritability of bronchial asthma.

$$H = \frac{78\% - 5\%}{100\% - 5\%} \times 100\% = 77\%;$$

6. Determine the role of the environment (E):

E=100%-77%=23%

Answer: The coefficient of heritability of bronchial asthma is 77%. This means that the development of this disease is significantly influenced by the human genotype.

SITUATIONAL PROBLEMS

1. Determine the coefficients of heritability and the influence of the environment in the development of mental retardation, if the concordance for this characteristic for monozygotic twins is 97%, for dysygotic twins – 37%.

2. Determine the coefficient of heritability in the pathology of the cleft of the upper lip, if the concordance of monozygotic twins is 33%, dysygotic – 5%.

3. 18 pairs of monozygotic twins and 15 pairs of dizygotic twins were registered. It was established that in 12 pairs of monozygotic pairs and in 8 pairs of dizygotic twins, both stomach ulcers suffered. What influences the development of the disease?

4. Twenty pairs of monozygotic twins and 20 pairs of dizygotic twins were registered. The survey found that in 15 pairs of monozygotic twins, both suffered from bronchial asthma, and in the group of dizygotic twins, both suffered from asthma in seven families. Calculate concordance on this trait and determine the role of heredity and environment in the development of this disease.

5. 65 pairs of monozygotes and 87 pairs of dizygotic twins were examined. The survey found that in 63 pairs of monozygotic twins, both were ill with measles and among the dizygotic twins, measles were both sick in 82 pairs. Calculate the concordance (%) separately for each group of twins. Based on this, decide whether there is a genetic predisposition to this disease?

Answers

1. In the development of mental retardation, the heritability factor is 95.2%, and the environment – 4.8%.

2. In the development of the pathology of the cleft of the upper lip, the heritability factor is 29.4%.

3. The development of gastric ulcer is mainly influenced by the environment (E = 71.3%). CMZ = 66.7%; CDZ = 53.3%.

4. In the development of bronchial asthma, the coefficient of heritability is 61.5%, and the environment – 38.5%.

5. Equally, the heredity and the environment are also responsible for the development of a predisposition to measles (H = 45.6%, E = 54.4%).

5.3. POPULATION-STATISTICAL METHOD

Population genetics examines the patterns of distribution of gene alleles in populations. In medical practice, there is often a need to establish quantitative ratios of people with different genotypes by some pathological allele, or the frequency of occurrence of this allele among the population. Calculations are conducted in accordance with the provisions of the Hardy-Weinberg law. The Hardy-Weinberg law is applicable to the analysis of large populations that meet the following requirements: 1) free interbreeding of individuals is possible; 2) there is no outflow and inflow of genes due to migration of individuals; 3) homozygotes and heterozygotes are equally fertile, 4) natural selection.

The first position of the Hardy-Weinberg law is that the sum of allele frequencies of one gene in a population is constant: $p + q = 1$, where p is the frequency of the dominant allele (A), q is the frequency of the recessive allele of the same gene (a). Both values are usually expressed in fractions of one or in percent (then $p + q = 100\%$). The frequency of the allele of each gene depends on the adaptive significance of that characteristic that it determines. Consequently, the frequencies of certain alleles of genes are established by natural selection in a number of previous generations.

The second position of the Hardy-Weinberg law: the sum of genotype frequencies for one gene in a given population is a constant value. The formula for calculating the frequencies of genotypes: $p^2 + 2pq + q^2 = 1$, where p^2 is the fre-

quency of homozygous individuals by the dominant allele (genotype AA), 2pq is the frequency of heterozygotes (genotype Aa), q^2 is the frequency of homozygotes from the recessive allele (genotype aa).

The established relationships can change only if the population loses its equilibrium.

The Hardy-Weinberg law provisions apply to multiple alleles. Then, in the case of three allelic genes, allele frequencies can be determined as p + q + r = 1.

Example of problem solving

Problem 1: albinism is inherited as a recessive autosomal trait. The disease occurs at a frequency of 1: 20,000. Calculate the number of heterozygotes in the population.

Decision:

A – allele, responsible for the normal content of melanin in tissues.

a is the allele responsible for albinism.

1. The allele frequency is a = q; the allele frequency is A = p. Let us calculate the allele frequency a (q). By the condition q^2 = 1/20000 (according to the Hardy-Weinberg law). Hence = 1/141.

2. Frequency of the allele A = p = 1 – q = 141/141 – 1/141 = 140/141.

3. The frequency of heterozygotes in the population is 2pq.

2 × 140/141 × 1/141 = 1/70

4. Consequently, the number of heterozygotes in a population of 20,000 is: 1/70 × 20,000 = 280 people.

Answer: the number of heterozygotes in the population is 280 people.

SITUATIONAL PROBLEMS

1. Determine the genetic structure of the population if it is known that recessive homozygous individuals (aa) constitute 1% in the population.

2. Cystic fibrosis is inherited as an autosomal recessive trait. In Russia, the disease occurs at a frequency of 1: 2.000 (Mutovich, 1997). Determine the frequency of occurrence of heterozygous carriers.

3. Deaf mute is associated with congenital deafness, which prevents the normal assimilation of speech. The inheritance is autosomal recessive. The average incidence of the disease for European countries is approximately 2:10 000. Determine

the possible number of heterozygous for deaf-mute people in a population of 600.000 inhabitants.

4. The low growth of the human body is inherited as an autosomal dominant trait. In the survey of one African population of pygmies, 64 people had normal body growth, and 836 people had low growth. Determine the frequency of occurrence of heterozygotes in this population.

5. In a population of 100 thousand people, 4 thousand have blue eyes, the rest – brown. Calculate the number of heterozygous for coloring the eyes of people.

6. The ability of a person to distinguish the taste of phenylthiourea is controlled by a dominant autosomal gene. In one population, the frequency of people who do not taste the phenylthiourea is 25%. Determine the genetic structure of this population.

7. Aniridia is inherited as a dominant autosomal trait and occurs at a frequency of 1:10.000. Describe the genetic structure of the population.

Answers

1. Genetic structure of the population: AA-81% genotypes, Aa-18% genotypes and aa-1% genotypes.

2. The incidence of heterozygous carriers of cystic fibrosis is 4.4%.

3. The number of heterozygous for deaf-mute people in a population of 600,000 is 16,566 people.

4. The incidence of heterozygotes was 39.4%.

5. The number of heterozygous for coloring the eyes of people in this population will be 32,000 people.

6. Genetic structure of the population by the ability to distinguish the taste of phenylthiourea: 25% of homozygotes by dominant trait, 50% of heterozygotes and 25% of homozygotes by recessive trait.

7. Genetic structure of the population by aniridia: 0.0001% homozygous by dominant trait, 0.198% heterozygotes and 99% homozygotes by recessive trait.

SECTION VI.
MEDICAL-GENETIC CONSELING

The purpose of the genetic consultation is to establish the degree of genetic risk in the family being surveyed and to explain to the spouses in an accessible form the medical genetic conclusion.

Problems of medical genetic counseling:

1) pro and retrospective (before and after birth) counseling of families and patients with hereditary or congenital pathology;

2) prenatal diagnosis of congenital and hereditary diseases;

3) assistance to doctors of various specialties in the diagnosis of the disease, if special genetic methods of investigation are required for this;

4) explaining in an accessible form to the patient and his family the risk of having sick children and helping them to make a decision;

5) maintenance of the territorial register of families and patients with hereditary and congenital pathology and their dispensary observation;

6) propagation of medical and genetic knowledge among the population.

Perspective of the use and effectiveness of prenatal diagnostic methods. Achievements in this area allow planning of childbearing in families with a high risk of inheriting severe pathology (Down's disease, hemophilia, cystic fibrosis, etc.), since these diseases can be reliably detected by prenatal diagnostic methods.

Indications for sending a family to a medical and genetic consultation:

1) the presence of similar diseases among several family members;

2) primary infertility of spouses;

3) primary miscarriage;

4) the child's retardation in mental and physical development;

5) the birth of a child with developmental defects;

6) primary amenorrhea (absence of menstruation), especially with underdevelopment of secondary sexual characteristics;

7) the presence of blood relationship between spouses.

The main indications for cytogenetic analysis:

1) prenatal diagnosis of sex in families burdened with recessive diseases linked to the sex;

2) undifferentiated oligophrenia (dementia);

3) habitual miscarriages and stillbirths;

4) multiple congenital malformations in the child;

5) infertility in men;

6) the mother's age is over 35 years.

The main indications for conducting biochemical or molecular-genetical analyzes:

1) mental retardation of the child;

2) violation of mental status;

3) violation of physical development;

4) convulsions, muscle hypo- or hypertension, impaired gait and coordination of movements, jaundice, hypo- or hyperpigmentation;

5) intolerance of certain foods and medicines, digestive disorders.

The accuracy of the forecast depends on the following factors:

1) the accuracy of the clinical-genetic diagnosis,

2) the thoroughness and objectivity of genealogical research,

3) knowledge of the latest data of genetics.

Precisely put the clinico-genetic diagnosis is currently difficult due to the fact that 75% of the families surveyed there is a single manifestation of the anomaly. Thanks to the popularization of medical knowledge among the population and the quality of training general practitioners, parents turn to medical genetic counseling at the time of the birth of the first child with anomalies. The correct diagnosis is provided by the application of the above methods of human genetics.

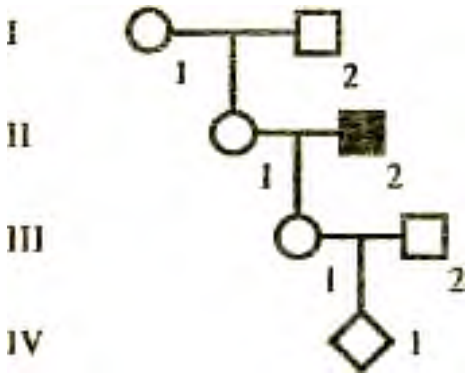
Genealogical analysis is still widely used in the practice of genetic counseling. It is necessary that the genetic history be complete and supported by medical documentation regarding the proband and all his relatives, which is very difficult to do.

Acquaintance with the newest data of medical genetics is necessary both for diagnostics (hundreds of new hereditary anomalies are annually described), and for a choice of the most modern and rational directions of preventive maintenance and methods of prenatal diagnostics.

Example of problem solving

Problem: according to the history of the mother, the mother is healthy and comes from a family that is free from a form of ichthyosis (a recessive type of inheritance linked to the X chromosome), and the father is sick with this form of ichthyosis. The daughter of these parents marries a healthy young man. Determine the degree of genetic risk of the patient's birth by this form of ichthyosis of the child in this young family. What methods of prenatal diagnosis can be used to detect this disease in the fetus? What recommendations should the geneticist give?

Decision: based on the history of the patient, we build a pedigree.



P: ♀ X^AX^A — ♂ X^aY

G: X^A X^a Y

F_1: X^AX^a: X^aY

P: ♀ X^AX^a — ♂ X^AY

G: X^A X^a X^A Y

F_2: X^AX^A: $\underline{X^aY}$: X^AX^a: X^AY

A woman who is going to have a baby is heterozygous for the ichthyosis gene. The probability of the birth of a sick child in marriage with a healthy man is 25% of all children, 50% if a boy is born, 0% if the girl is.

To clarify the possibility of producing a sick child, chorion biopsy (8-12

weeks of pregnancy) and amniocentesis (15-17 weeks of gestation) are shown. Methods allow to determine the presence of X-sex chromatin in the fetal cells for establishing the sex.

If it is determined that the sex of the future child is male (genetic risk is 50%), then the geneticist should explain the severity of the medical consequences of the disease. When a female is identified in a fetus, the risk of having a sick child is 0%.

SITUATIONAL PROBLEMS

1. An anomaly is described in a person – the presence of a membrane between the toes. From marriage between a woman with normal toes and a man who had an eardrum, three children were born: the daughter was normal, and the sons had this anomaly. One of the sons in marriage with a normal woman had 6 daughters with normal fingers and 4 sons with an anomaly. Compile a pedigree and determine:

a) type of inheritance;

b) probability of a child with an anomaly, if the grandson marries a woman with normal toes;

c) what are the methods of prenatal diagnosis of this defect?

2. A proband is a patient with Duchenne myopathy (skeletal musculature atrophy) a boy. According to the history of the parents, the parents themselves and the two sisters of the proband are healthy. On the paternal side, two uncles, aunt, grandfather and grandmother of the probanda – are healthy. Two cousins from his uncle and cousin from aunt probanda – are healthy. On the mother of the proband, one of the two uncles (the elder) was sick with myopathy. The second uncle (healthy) had two healthy sons and a healthy daughter. Auntie proband on the mother's line had a sick son. Grandfather and grandmother are healthy. Compile a pedigree. Define:

a) type of inheritance and genotypes of persons of the pedigree;

b) probability of the birth of a sick child in the family if the proband marries a healthy woman whose father is ill with Duchenne's myopathy;

c) what are the methods of prenatal diagnosis of this disease?

d) what recommendations should the geneticist give?

3. One form of rickets is not cured by usual doses of vitamin D. A proband is a young man suffering from this form of rickets. His sister is healthy. The mother of the proband is sick with rickets, his father is healthy. The mother of the proband had three brothers-all healthy. The grandfather of the proband on the mother's line is sick, the grandmother is healthy. The grandfather had two healthy brothers and one patient. In healthy grandfather's brothers from healthy wives, there were 5 healthy sons (one has 4 sons, the other has 1 son). At the sick brother of the grandfather the wife was healthy, they had three sick daughters and two healthy sons. Two sick daughters of his grandfather's brother had healthy mothers from one healthy daughter. One more sick daughter of the brother of the grandfather of the proband, married to a healthy man, had a daughter and one of two sons. At healthy sons of the brother of the grandfather the proband of the wife and their children are healthy. Compile a pedigree. Define:

a) type of inheritance;

b) probability of the birth of sick children with rickets in the proband family if he marries his sick second cousin;

c) what recommendations should the geneticist give?

4. The son of the American banker Twister suffered simultaneously three diseases: hemophilia, color blindness and total absence of teeth. These diseases are caused by genes present in the X chromosome. Twister Jr. lived for many years away from his parents, in Paris, where he died in 1944. After his death, a Frenchwoman with a 15-year-old boy came to Twister to the eldest, who also had hemophilia, color blindness and lack of teeth. The woman reported that this boy is the son of the late Twister Jr. and his legal heir, but the supporting documents were lost during the occupation of France. Despite the lack of documents, Twister recognized the boy as his grandson. The family doctor convinced him that such a coincidence of a rare combination of three hereditary diseases proves that this boy is his grandson. Do you agree with the opinion of the doctor?

5. A pregnant woman of 50 years, whose father was a hemophilic, performed an amniocentesis in order to determine the sex of the fetus, as well as to identify possible chromosomal abnormalities. But it was not possible to grow a culture of fetal cells for karyotyping, these cells died. Therefore, cytogenetic studies had to be limited to determination of sexual chromatin. It is established that the fetal cells do not contain sexual chromatin. Should you recommend abortion on this basis?

6. The family has a child of 5 years with mental retardation, microcephaly, a "mouse" odor, increased muscle tone, convulsive epileptiform seizures, weak pigmentation of the skin and hair:

a) what disease can be assumed?

b) how to make a diagnosis?

c) what is the probability of the appearance in this family of the next child with the same pathology?

d) what methods of prenatal diagnosis can be used to establish this hereditary pathology?

7. In the family of healthy parents a full-term baby with a body weight of 2400 grams was born. In the medical genetic consultation, the child was diagnosed with microcephaly, low beveled forehead, narrowed eye cracks, microphthalmia, corneal opacity, sunken nose, broad nose base, deformed ears, bilateral clefts of upper lip and palate, finger tip syndactyly, short neck, four-finger groove on the palms, defects of the interventricular septum of the heart, delay in mental development.

a) what disease can be assumed?

b) what method of research can you put an accurate genetic diagnosis?

c) what methods of prenatal diagnosis can be used to detect this disease?

8. In elderly parents (wife – 47 years old, husband – 49 years) a full-term child was born. When contacting a medical genetic consultation, the child found a flat face, a low beveled forehead, a large head, an oblique incision of the eyes, bright spots on the iris, thick lips, thick tongue protruding from the mouth, deformed low-lying ears, high sky, teeth, atrial septal defect, on the palms of the four-

finger groove, the main palm angle 69 °, radial loops on the 4th and 5th fingers of the hands, delay in mental development.

a) what disease can be assumed?

b) what methods should I use to make an accurate diagnosis?

c) what is the prognosis of the future viability of this child?

d) what methods of prenatal diagnosis should be used to detect this disease?

9. A young child was born in a young family whose crying resembles a cat's meow. When contacting a medical genetic consultation, the child was found a moon-shaped face, muscle hypotension, microcephaly, an antimonyholoid cut of the eyes, strabismus, low-lying deformed ears, a delay in mental development:

a) what disease can be assumed?

b) what methods should I use to make a diagnosis?

c) what is the prognosis of the future viability of this child?

d) what methods of prenatal diagnosis should be used to detect the disease?

10. Which of the following symptoms are diagnostic signs of the Marfan syndrome:

a) mental retardation, enlarged liver and spleen, general dystrophy, cataract;

b) microcephaly, microphthalmia, bilateral clefts of the upper lip and palate, syndactyly of the toes, defects of the interventricular septum of the heart, retardation of mental development;

c) subluxation of the lens, heart defects, high growth, long thin fingers, funnel-shaped depression of the sternum;

d) blue color sclera, congenital deafness, brittle bones;

e) flat face, low beveled forehead, light spots on the iris, thick tongue protruding from the mouth, deformed low-lying ears, atrial septal defect, mental retardation?

11. Which of the following symptoms are diagnostic signs of phenylketonuria:

a) mental retardation, enlarged liver and spleen, general dystrophy, cataract;

b) mental retardation, microcephaly, "mouse" odor, convulsive epileptiform

seizures, weak pigmentation of the skin and hair;

c) subluxation of the lens, heart defects, high growth, long thin fingers, funnel-shaped depression of the sternum;

d) blue color sclera, congenital deafness, brittle bones;

e) flat face, low beveled forehead, light spots on the iris, thick tongue protruding from the mouth, deformed low-lying ears, atrial septal defect, mental retardation?

12. Which of the following symptoms are diagnostic signs of the Patau syndrome:

a) microcephaly, microphthalmia, bilateral clefts of the upper lip and palate, syndactyly of the toes, defects of the interventricular septum of the heart, delay in mental development;

b) mental retardation, microcephaly, "mouse" odor, convulsive epileptiform seizures, weak pigmentation of the skin and hair;

c) subluxation of the lens, heart defects, high growth, long thin fingers, funnel-shaped depression of the sternum;

d) blue color sclera, congenital deafness, brittle bones;

e) flat face, low beveled forehead, light spots on the iris, thick tongue protruding from the mouth, deformed low-lying ears, atrial septal defect, mental retardation?

13. Which of the following symptoms are diagnostic features of Down's syndrome:

a) mental retardation, enlarged liver and spleen, general dystrophy, cataract;

b) microcephaly, microphthalmia, bilateral clefts of the upper lip and palate, syndactyly of the toes, defects of the interventricular septum of the heart, retardation of mental development;

c) subluxation of the lens, heart defects, high growth, long thin fingers, funnel-shaped depression of the sternum;

d) blue color sclera, congenital deafness, brittle bones;

e) flat face, low beveled forehead, light spots on the iris, thick tongue pro-

truding from the mouth, deformed low-lying ears, atrial septal defect, mental retardation?

14. Indicate possible variations in the structure of the genetic material that underlie the onset of chromosomal diseases:

a) trisomy, nonsense mutations, deletions;

b) nonsense mutations, missense mutations, shift of reading frames;

c) inversion, monosomy, shift of the reading frame of the genetic code;

d) duplication, translocation, deletion;

e) polyploidy, missense mutation, inversion.

15. Indicate possible variations in the structure of genetic material that underlie metabolic diseases:

a) trisomy, nonsense mutations, deletions;

b) nonsense mutations, missense mutations, shift of reading frames;

c) inversion, monosomy, shift of the reading frame of the genetic code;

d) duplication, translocation, deletion;

e) polyploidy, missense mutation, inversion

16. Specify the formula of a karyotype of a man with a syndrome:

a) Edwards;

b) Patau;

c) Down;

d) "Cat's scream".

17. Which of the following signs are an indication for the cytogenetic study:

a) cutaneous cervical fold, low growth, underdevelopment of primary and secondary sexual characteristics;

b) delayed psychomotor development, hypopigmentation of the skin, unusual odor of urine;

c) Edwards syndrome;

d) cat cricket syndrome;

e) mental retardation, enlarged liver and spleen, general dystrophy, cataracts?

18. Which of the following characteristics is an indication for biochemical

research:

a) cutaneous cervical fold, low growth, underdevelopment of primary and secondary sexual characteristics;

b) delayed psychomotor development, hypopigmentation of the skin, unusual odor of urine;

c) Edwards syndrome;

d) cat cricket syndrome;

e) mental retardation, enlarged liver and spleen, general dystrophy, cataracts?

Answers

1. a) the holland; b) among boys, 100%, among girls 0%; c) Invasive methods, depending on the timing of pregnancy.

2. a) the recessive type of inheritance linked to the X-chromosome. The patients are all male and have the XaY genotype; their mothers bear the gene – HA-HA; sisters have a homo- or heterozygous genotype; b) The probability of having a sick child among boys and girls is 50 per cent; c) Invasive methods depending on the timing of pregnancy; d) The geneticist must explain the severity of the medical consequences of the disease.

3. a) the dominant type of inheritance linked to the X-chromosome; b) 50% chance of having a sick child among boys and 100% of girls; c) The geneticist should explain the severity of the medical consequences of the disease.

4. Do not agree, tk. boys receive from the father of the Y-chromosome, and here all diseases are linked to the X-chromosome.

5. Cells do not have sexual chromatin, therefore, a male fetus develops. The geneticist should explain the severity of the medical consequences of the disease.

6. a) phenylketonuria; b) Molecular genetic and biochemical methods; c) 25 per cent; d) Invasive methods depending on the timing of pregnancy.

7. a) the Patau syndrome; b) cytogenetic method; c) non-invasive and invasive methods depending on the timing of pregnancy.

8. a) Down syndrome; b) cytogenetic method; c) Mental retardation will be observed, the degree of development will depend on the quality of care for the child

and on the presence of concomitant anomalies. In the absence of severe anomalies in the development of the heart and the gastrointestinal tract, life expectancy can reach 40-55 years; d) non-invasive and invasive methods depending on the timing of pregnancy.

9. a) "Cat's Scream" syndrome; b) cytogenetic method; c) life expectancy is greatly reduced, because patients die from concomitant complications (eg, heart or kidney failure). Most children do not survive to a year due to severe accompanying anomalies. Up to adolescence, approximately 10% of patients survive; d) non-invasive and invasive methods depending on the timing of pregnancy.

10. c

11. b

12. a

13. e

14. d

15. b

16. a) 47, XY, 18+; b) 47, XY, 13+; c) 47, XY, 21+; d) 46, XY, 5p-.

17. a, c, d.

18. b, e.

RECOMMENDED LITERATURE

Basic literature:

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2. Medical Parasitology: учеб. пособие / сост.: Ф. Ф. Мусыргалина, О. А. Майорова. – Уфа: ФГБОУ ВО БГМУ Минздрава России, 2017. – 214 с.– on-line.– Режим доступа: http://library.bashgmu.ru/elibdoc/elib665.pdf.

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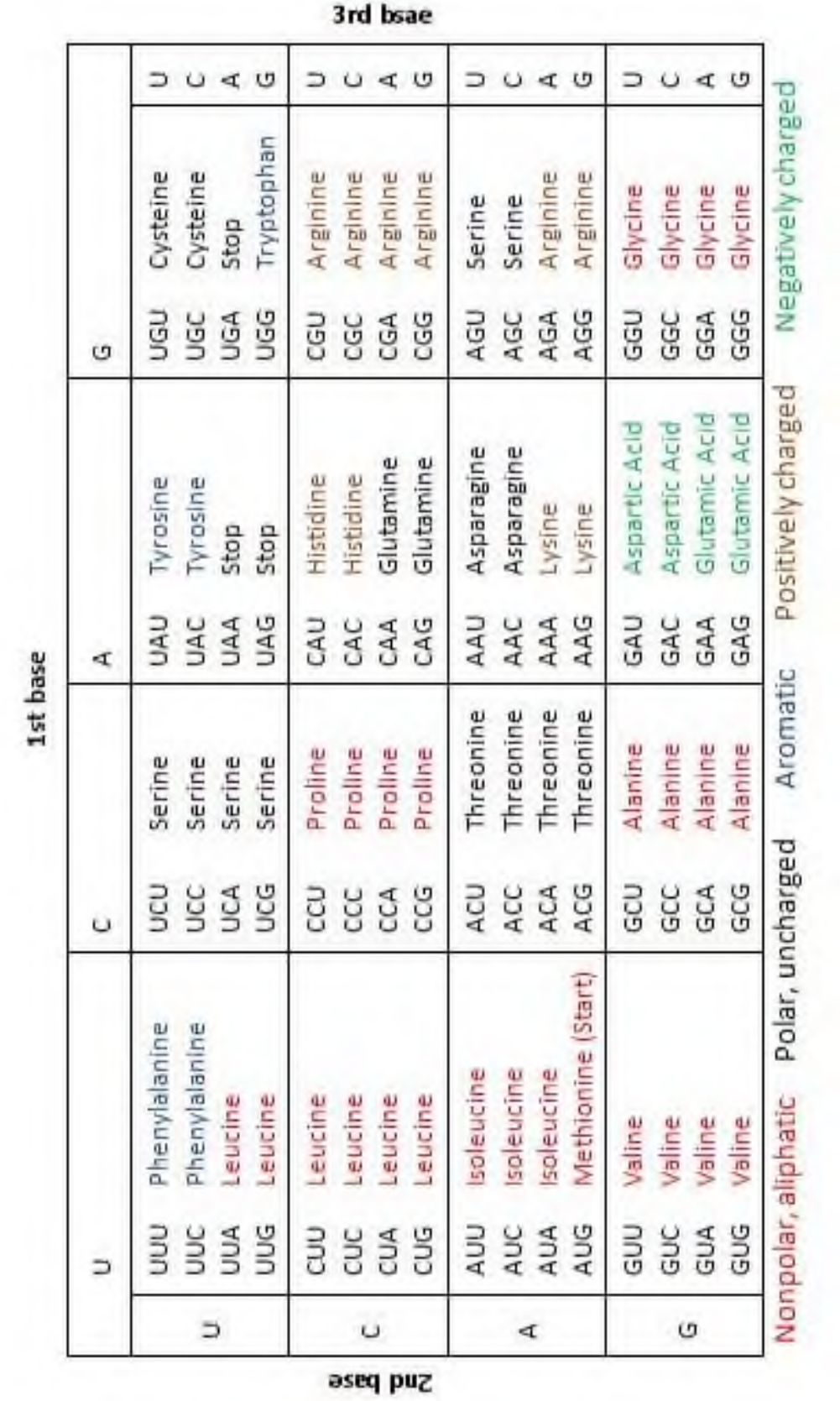
ANNEXES

Annex 1

GENE CODE TABLE



Annex 2

Concordance rates between MZ and

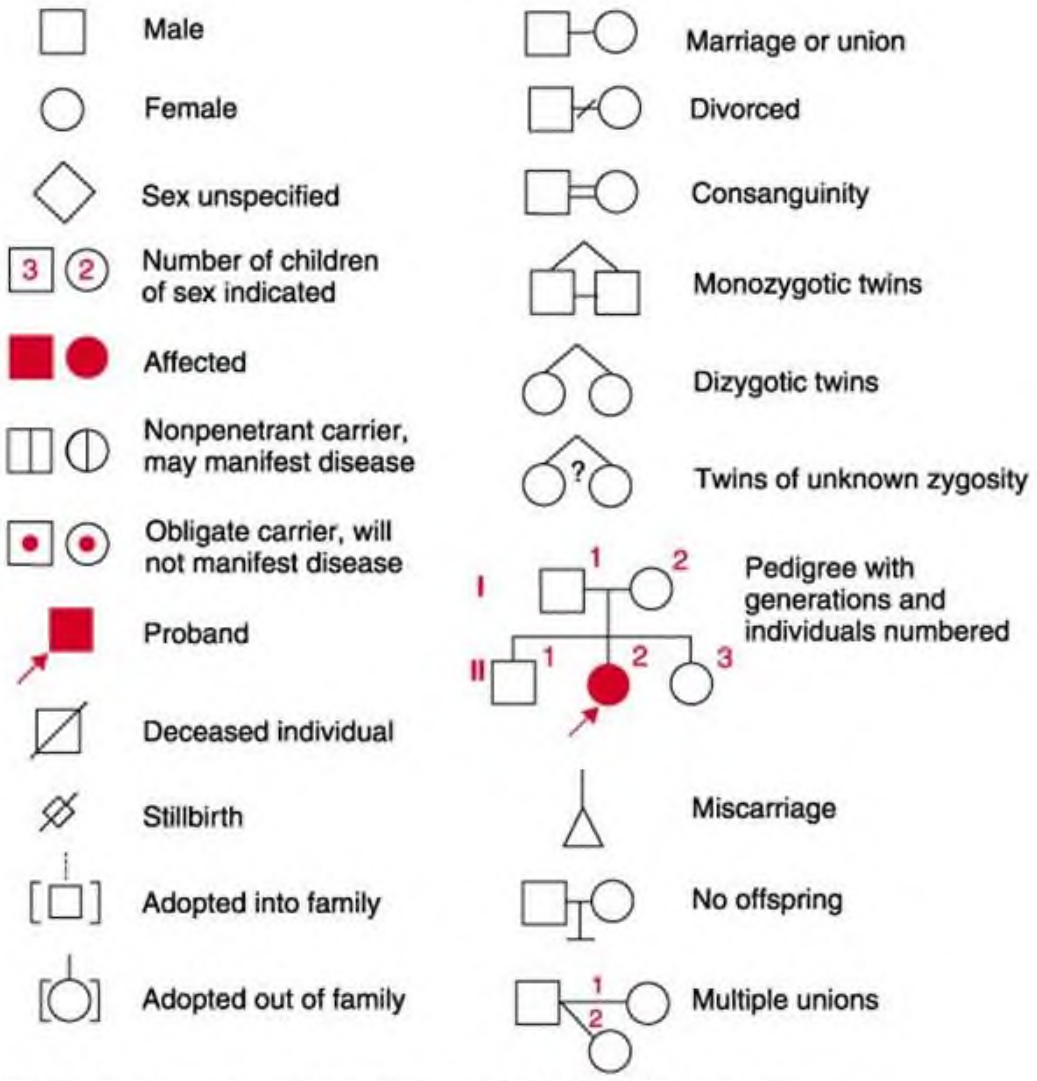
Trait	Concordance %	
	MZ	DZ
Blood types	100	66
Eye colour	99	28
Mental retardation	97	37
Measles	95	87
Idiopathic epilepsy	72	15
Schizophrenia	69	10
Diabetes	65	18
Identical allergy	59	5
Tuberculosis	57	23

Source: Klug, W.S. and Cummings, M.R., *Concepts of Genetics* (2nd edition). Glenview, IL: Scott, Foresman, 1986.

TYPE OF INHERITANCE	CHARACTERISTICS	EXAMPLES
Autosomal dominant	▪ Both sexes equally affected ▪ Vertical transmission ▪ Father-to-son transmission ▪ Affected individuals transmit trait to ~50% offspring	▪ Huntington disease ▪ Achondroplasia ▪ NF type 1 ▪ Marfan syndrome ▪ Familial hypercholesterolemia
Autosomal recessive	▪ Both sexes equally affected ▪ Usually no prior family history ▪ Consanguinity ▪ Mating between two carriers transmits trait to ~25% offspring	▪ Hurler syndrome ▪ Hereditary hemochromatosis ▪ Cystic fibrosis ▪ Sickle-cell anemia ▪ Phenylketonuria (PKU) ▪ β-thalassemia ▪ Tay-Sachs

Annex 4

MOST COMMON SIGNS AND SYMBOLS USED IN PEDIGREE ANALISIS



Annex 5

HEREDITARY DISEASES AND ANOMALIES

(SHORT CHARACTERISTIC)

Acatalysis is the absence of catalase in organs and tissues.

Achondroplasia is a congenital disease with an autosomal dominant type of inheritance, in which the development of cartilage does not lead to insufficient growth of the limbs.

Afibrinogenemia – complete absence in the plasma of one of its proteins – fibrinogen.

Agammoglobulinemia is the absence or sharp decrease in the levels of immunoglobulins of the main classes in the blood.

Albinism is common – congenital absence of normal pigmentation.

Alcaptonuria – excretion in the urine of homogentisinic acid, urine quickly darkens.

Amavrotic family idiocy is a disease of accumulation, characterized by a progressive decrease in intelligence and vision due to changes in the nerve cells of the cortex of the cerebral hemispheres.

Angiokeratoma – a skin disease characterized by the appearance of benign dark red vascular nodules, accompanied by renal failure, opacity of the cornea

Angiomatosis of the reticulum is one of the pathologies in the systemic disease of the eyes and brain. Expressed a sharp expansion and neoplasm of retinal vessels.

Anhidroznaya ectodermal dysplasia – manifested by the absence of sweating, part of the teeth, lean hair, a violation of thermoregulation.

Aniridia is the absence of the iris. It is accompanied by a decrease in vision, opacity of the cornea and lens.

Arachnodactyly – excessively long and thin fingers.

Brahidactyly – shortening of fingers.

Cataract – clouding of the lens.

Cerebellar ataxia – atrophy of the cerebellum and pyramidal pathways of the spinal cord. It begins after 20 years and is characterized by a progressive decline in intelligence.

Color blindness is a partial color blindness.

Cranial-facial dysostosis is a group of skeletal anomalies: cranial sutures grow early, a large fontanel does not grow long.

Cystic fibrosis – characterized by the defeat of the glands of external secretion, severe impairment of respiratory functions.

Cystinuria – an autosomal recessive disease characterized by an elevated urinary content of cystine and some other amino acids.

Deaf-mute is a congenital or acquired deafness that interferes with the assimilation of speech.

Degeneration of the cornea – changes in various areas of the corneal tissue that lead to loss of vision.

Elliptocytosis – erythrocytes acquire an oval form. In the homozygous state, severe hemolytic anemia develops.

Fructozuria – has two forms. One is associated with a deficiency of the enzyme fructokinase liver and is accompanied by increased release of fructose in the urine in the absence of clinically pronounced symptoms. The other is caused by deficiency of liver enzymes, kidneys and intestinal mucosa. As a result, fructose and its metabolic products accumulate in the blood and tissues, which leads to inhibition of physical and mental development.

Galactosemia is a hereditary disease with an autosomal recessive type of inheritance, due to the absence of an enzyme that converts galactose to glucose. The disease is detected during breastfeeding, expressed by a complex of symptoms: jaundice, emaciation, cirrhosis, cataracts, dementia.

Glaucoma – increased intraocular pressure associated with a violation of the outflow of intraocular fluid through the angle of the anterior chamber, leading eventually to loss of vision.

Gout is a chronic disease caused by impaired metabolism and the accumulation of uric acid and its salts in various tissues.

Hemeralopia – sharp deterioration of vision in low light, night blindness.

Hemophilia – blood coagulability, there are no various factors of blood coagulation involved in the formation of thromboplastin.

Hypercholesterolemia – increased cholesterol in the blood in atherosclerosis, hypothyroidism, diabetes, cholestasis, obesity and other diseases. Developed xanthoma – benign tumors, as well as early angina and myocardial infarction.

Hypertrichosis – excess hair growth.

Hypophosphatemia – a reduced content of phosphorus compounds in the blood serum. It is observed with hyperparathyroidism, rickets and other pathologies.

Hypoplasia of the enamel is a sharp thinning of the enamel, accompanied by a change in the color of the teeth.

Ichthyosis is a hereditary disease characterized by a diffuse violation of keratinization of the skin as a type of hyperkeratosis.

Myopathy is a progressive degeneration of skeletal musculature.

Myopia is a visual impairment, in which the subjects under consideration are clearly visible only at close range.

Myoplegia – recurrent paralyzes associated with loss of muscle cells of potassium.

Neurofibromatosis is a common name for two different hereditary diseases that cause the development of tumors associated with nerve trunks, predominantly the trunk.

Otosclerosis is a disease of the bony labyrinth of the inner ear. The degree of hearing loss depends on the location of lesions.

Paragemophilia is one of the forms of blood clotting, caused by a lack of proaccelerin. Characterized by severe bleeding with minor injuries.

Pentozuria is an esential one, characterized by the release of pentose-L-xylulose in the urine. Clinically not manifested.

Phenylketonuria is the absence of an enzyme that converts phenylalanine to tyrosine. As a result, the level of phenylalanine in the blood sharply increases and tyrosine decreases. Developing dementia, as a consequence of the defeat of the central nervous system.

Pigmented retinitis is characterized by a progressive narrowing of the field of vision, which leads to an intensifying night blindness, and then to loss of vision.

Polydactyly – an increase in the number of fingers on the hands or feet.

Retinoblastoma is a malignant retina of the eye. Begins at the age of up to 3 years and leads to loss of vision.

Rickets, resistant to vitamin D – treatment with vitamin D is ineffective. Characteristic is the curvature of long tubular bones, deformation of the joints.

Schizophrenia is a group of mental illnesses that differ in the nature of manifestation and course.

Splenomegaly – an increase in the spleen, due to various causes.

Syndactyly – the full or partial fusion of the adjacent fingers of the hand or foot.

Thalassemia is a blood disease caused by a decrease in the synthesis of polypeptide chains that make up the structure of normal hemoglobin.

Van der Heve Syndrome – increased brittleness of bone, blue sclera and deafness.

Wilson-Konovalov's disease is a violation of the synthesis of the ceruloplasmin protein transporting copper, which is deposited in the liver, brain, and kidneys. There are degenerative changes in these organs. The disease manifests itself at the age of 10-15 years.

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