Medical Genetics 5th edition Jorde Test Bank

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Jorde: Medical Genetics, 5th Edition

Chapter 2: Basic Cell Biology: Structure and Function of Genes and Chromosomes

Sample Problems & Essay Questions

Question 1: In some African populations, the prevalence of sickle cell disease, an autosomal recessive condition, is 1/100. Based on this value, what proportion of the population would be heterozygous carriers of the sickle cell disease gene?

Answer: q = 0.1 p = 0.9 2pq = 0.18

Question 2: If an X-linked dominant disorder affects 1/100 males in a population, what is the gene frequency for the disorder in the population?

Answer: 0.01

Question 3: In the population in question 2 (an X-linked dominant disorder affects 1/100 males in a population), what proportion of females would be affected with the X-linked dominant disorder?

Answer: q^2 + 2pq = ~2q = 0.02 = 1/50

Question 4: A man who is affected with hemophilia A (X-linked recessive) mates with a woman who is a heterozygous carrier of this disorder. What proportion of this couple's daughters will be affected, and what proportion of the daughters will be carriers?

Answer: 0.50; 0.50

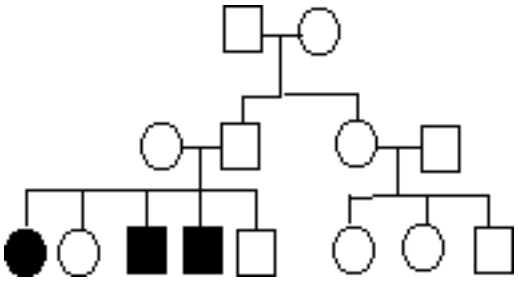
Question 5: A man who has Neurofibromatosis type 1 (autosomal dominant) marries a phenotypically normal woman. If they have five children, what is the probability that none of the children will be affected with this disorder? What is the probability that all of the children will be affected?

Answer: (1/2)^5 = 1/32
1/32; 1/32

Question 6: You have ascertained a fully penetrant autosomal dominant disease condition in three offspring of a couple with no family history of the disorder. What is the most likely explanation for the pedigree shown here?

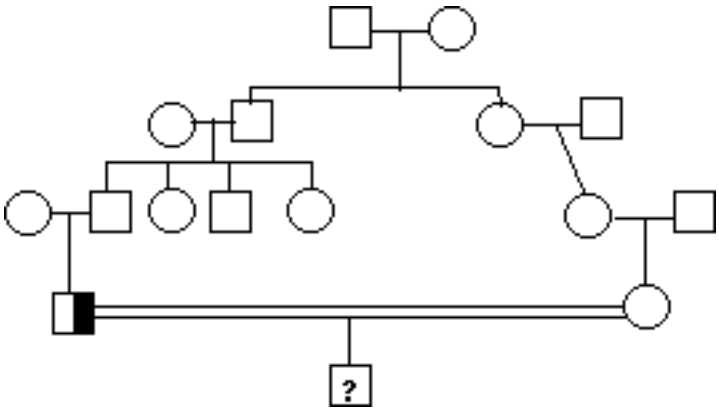
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Answer: Germline mosaicism

Question 7: In the accompanying pedigree, a man is a known heterozygous carrier for an autosomal recessive disease gene that has 60% penetrance in affected homozygotes. If he marries his second cousin, what is the probability that their offspring will be affected with the disorder (i.e., that they will manifest the disease phenotype)?



Answer: 1/32 x 1/4 x 0.6 = 1/128 x 0.6 = 0.0046875

Question 8: Name at least two features you would use to distinguish an autosomal dominant pedigree from an X-linked recessive pedigree.

Answer: Autosomal dominant: Father-son transmission, approximately equal proportions of males and females, skipped generations rare under full penetrance
X-linked recessive: No father-son transmission, males are more often affected than females, skipped generations through unaffected females is common

Question 9: It has been observed that missense mutations in the fibrillin-1 gene on chromosome 15 often produce more severe presentations of Marfan syndrome than do nonsense mutations in the same gene. Explain this (4-5 sentences should suffice).

Answer: The fibrillin-1 gene product forms a subunit of a multimeric protein. An individual with Marfan syndrome is usually a heterozygote and thus has one normal copy of fibrillin-1 and one mutated copy. A nonsense mutation results in premature truncation of the translated fibrillin subunit. Typically this subunit cannot bind with other subunits, so the abnormal fibrillin produced by the mutated gene does not affect the normal fibrillin produced by the normal gene copy. as a result, the individual has about 50% of the

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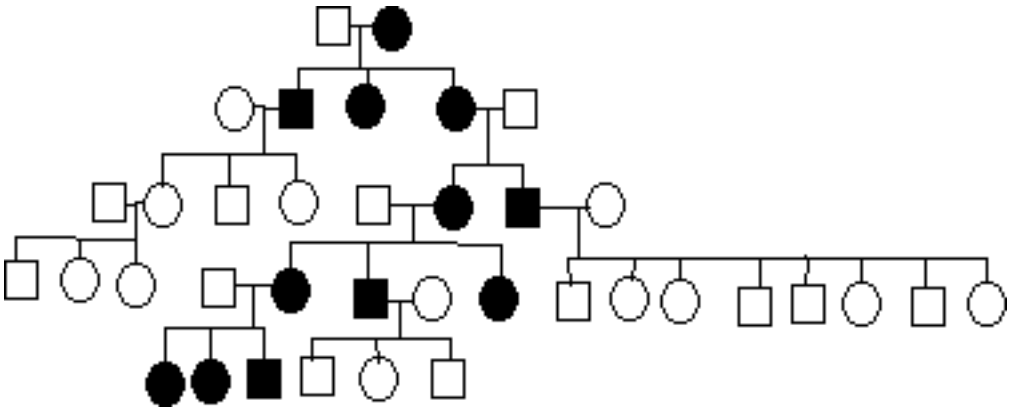
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normal level of fibrillin-1. The abnormal fibrillin-1 resulting from a missense mutation may bind with the normal fibrillin gene product, damaging it as well. This "dominant negative" effect results in a more severe expression of the disease phenotype.

Question 10: Explain the relationship between trinucleotide repeats and anticipation. Use at least two disease examples to illustrate your points.

Answer: Anticipation describes earlier age of onset and more severe expression of a disease phenotype in more recent generations of a pedigree. In some cases, such as Fragile X syndrome, Huntington disease, myotonic dystrophy, and spinocerebellar ataxia type 1, anticipation can be explained by the tendency of trinucleotide repeat units to expand from generation to generation. Sometimes this expansion may be influenced by the parent's gender (e.g., expansion of the Huntington disease trinucleotide repeat is more likely if the transmitting parent is male, while expansion of the myotonic dystrophy and Fragile X repeats are more likely if the transmitting parent is female).

Question 11: Match the pedigree with the most likely mode of inheritance. Note that complicating factors, such as reduced penetrance, may be present. Assume that the gene frequency of the disorder in the general population is very low. These answers may be used more than once.



a. autosomal dominant
b. autosomal recessive
c. X-linked recessive
d. X-linked dominant
e. mitochondrial

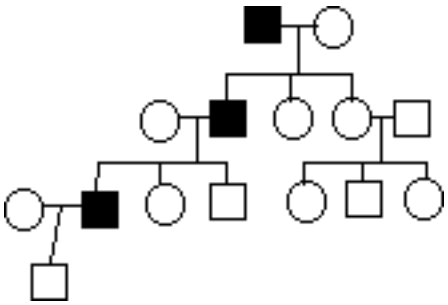
Answer: e

Feedback: (all children of affected females have the disease)

Question 12: Match the pedigree with the most likely mode of inheritance. Note that complicating factors, such as reduced penetrance, may be present. Assume that the gene frequency of the disorder in the general population is very low. These answers may be used more than once.

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a. autosomal dominant
b. autosomal recessive
c. X-linked recessive
d. X-linked dominant
e. mitochondrial

Answer: a

Feedback: (no skipped generations, passed from father to son)

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Chapter 2: Basic Cell Biology: Structure and Function of Genes and Chromosomes

Multiple Choice

1. Mutation in fibroblast growth factor receptor 3 (FGFR3)
a. Retinoblastoma
b. Achondroplasia
c. Neurofibromatosis type 1
d. Huntington disease
e. Marfan syndrome

Answer: b

Correct Feedback: b. Mutations in the fibroblast growth factor receptor 3 do cause achondroplasia.

Incorrect Feedback: a. Retinoblastoma is caused by mutations in a tumor suppressor on chromosome 13.
c. Neurofibromatosis type one is caused by a mutation of the neurofibromin gene (which may act as a tumor suppressor) on chromosome 17q
d. Huntington disease is caused by a CAG expanded repeat on the distal tip of chromosome 4p.
e. Marfan patients have mutations of the chromosome 15 gene encoding fibrillin, a connective tissue protein.

2. Abnormal binding of gene product to GAPDH (enzyme involved in glycolysis)
a. Retinoblastoma
b. Achondroplasia
c. Neurofibromatosis type 1
d. Huntington disease
e. Marfan syndrome

Answer: d

Correct Feedback: d. This is a characteristic of Huntington disease.

Incorrect Feedback: a. Retinoblastoma is caused by mutations in a tumor suppressor on chromosome 13.
b. Mutations in the fibroblast growth factor receptor 3 cause achondroplasia.
c. Neurofibromatosis type one is caused by a mutation of the neurofibromin gene (which may act as a tumor suppressor) on chromosome 17q
e. Marfan patients have mutations of the chromosome 15 gene encoding fibrillin, a connective tissue protein.

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3. phosphorylation of gene product by cyclin-dependent kinases (CDK); binding of gene product to transcription factors such as E2F
a. Retinoblastoma
b. Achondroplasia
c. Neurofibromatosis type 1
d. Huntington disease
e. Marfan syndrome

Answer: a
Correct Feedback: a. The retinoblastoma gene product is phosphorylated by a CDK and then binds to transcription factors.

Incorrect Feedback: b. Mutations in the fibroblast growth factor receptor 3 cause achondroplasia.
c. Neurofibromatosis type one is caused by a mutation of the neurofibromin gene (which may act as a tumor suppressor) on chromosome 17q
d. Huntington disease involves abnormal binding of gene product to GAPDH (enzyme involved in glycolysis)
e. Marfan patients have mutations of the chromosome 15 gene encoding fibrillin, a connective tissue protein.

4. Mutations in fibrillin gene
a. Retinoblastoma
b. Achondroplasia
c. Neurofibromatosis type 1
d. Huntington disease
e. Marfan syndrome

Answer: e

Correct Feedback: e. Marfan patients have mutations of the chromosome 15 gene encoding fibrillin, a connective tissue protein.

Incorrect Feedback: a. The retinoblastoma gene product is phosphorylated by a CDK and then binds to transcription factors.
b. Mutations in the fibroblast growth factor receptor 3 cause achondroplasia.
c. Neurofibromatosis type one is caused by a mutation of the neurofibromin gene (which may act as a tumor suppressor) on chromosome 17q
d. Huntington disease involves abnormal binding of gene product to GAPDH (enzyme involved in glycolysis)

5. Which of the following could produce an XY female?
a. Deletion of the Sry gene
b. Point mutation in the Sry gene
c. Translocation of the Sry gene to the X chromosome during meiosis in the father
d. None of the above

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e. All of the above

Answer: e

Correct Feedback: e. All of the above could produce an XY female.

Incorrect Feedback: a. This is true, but it is not the only true answer.
b. This is true, but it is not the only true answer.
c. This is true, but it is not the only true answer.
d. There are true answers.

6. Which of the following is **not** a characteristic of cystic fibrosis?
a. Chloride channel defect
b. Hyperabsorption of intracellular sodium
c. Elevated sweat chloride
d. Fibrous ovarian cysts
e. Pancreatic insufficiency

Answer: d

Correct Feedback: This is not a characteristic of cystic fibrosis.

Incorrect Feedback: This is a characteristic of cystic fibrosis.

7. Each of the following chromosome abnormalities involves a 20 megabase region of the long arm of chromosome 5 (5q). Which abnormality is **most** likely to cause severe disease?
a. Deletion of the region
b. Duplication of the region
c. A balanced translocation involving the region (i.e., in the translocation carrier)
d. Pericentric inversion
e. Paracentric inversion

Answer: a

Correct Feedback: This is the most likely to cause severe disease.

Incorrect Feedback: This can cause problems, but they are not as likely to be as severe as a deletion of the entire gene.

8. Which of the following diseases is a good example of locus heterogeneity?
a. Prader-Willi syndrome
b. Myotonic dystrophy
c. Osteogenesis imperfecta
d. Duchenne muscular dystrophy
e. Hemophilia A

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Answer: c

Correct Feedback: c. Locus heterogeneity is where genes have more than on discernible effect. OI effects bones, teeth, and sclera.

Incorrect Feedback: a. Prader-Willi syndrome is a good example of genomic imprinting.
b. Myotonic dystrophy is a good example of anticipation.
d. Duchenne muscular dystrophy is an X-linked disease.
e. Hemophilia A is an X-linked disease.

9. Why are some autosomal dominant disorders (e.g., Marfan syndrome) seen more commonly in the offspring of older fathers?
a. Replication errors accumulate as sperm-producing stem cells continue to divide
b. Rate of nondisjunction increases in older males
c. Recombination rates increase in older males
d. All spermatocytes are produced during male embryonic development, so older males produce older sperm cells
e. None of the above

Answer: a

Correct Feedback: a. This is why some autosomal dominant disorders are seen more commonly in the offspring of older fathers.

Incorrect Feedback: b. This is seen in older mothers.
c. This is not true.
d. This is not true.
e. There is a correct answer

10. A woman with phenotypically normal parents has two brothers with Duchenne muscular dystrophy. She experiences mild muscle weakness in her legs. Which of the following mechanisms is **most likely** to be directly involved?
a. Germline mosaicism
b. Skewed X inactivation
c. Mutation near the pseudoautosomal region of the Y chromosome
d. New mutation in this woman
e. Nondisjunction of her mother's X chromosomes

Answer: b

Correct Feedback: b. This is most likely to be directly involved.

Incorrect Feedback: a. This wouldn't explain why a heterotroph would manifest the disease.

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c. A female would not have a Y chromosome.
d. If this were the case it would be unlikely that her brothers had the disease.
e. Duchenne muscular dystrophy is not a chromosomal disease.

11. Consider a fetus affected with one of the following conditions. For which condition is spontaneous loss during pregnancy most likely?
a. Down syndrome
b. Neurofibromatosis type 1
c. Retinoblastoma
d. Huntington disease
e. Trisomy 18

Answer: e

Correct Feedback: e. Chromosomal abnormalities are the number one cause of fetal loss, and trisomy 18 is less compatable with survival than trisomy 21.

Incorrect Feedback: a. Chromosomal abnormalities are the number one cause of fetal loss, but trisomy 18 is less compatable with survival than trisomy 21
b. Chromosomal abnormalities are the number one cause of fetal loss.
c. Chromosomal abnormalities are the number one cause of fetal loss.
d. Chromosomal abnormalities are the number one cause of fetal loss.

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