Genetics and Genomics in Medicine Chapter 5 Questions

Multiple Choice Questions

Question 5.1

The term phenotype can be applied to a wide range of manifestations. Which of the following properties, if any, do not constitute a phenotypic manifestation?

a) The number of digits a person has.
b) The transcriptome of a single T cell.
c) The sequence of a person's beta globin gene.
d) autistic behavior

Question 5.2

Which, if any, of the following is incorrect? When used in genetics, the term *character*

a) may apply to an anatomical, morphological, or physiological feature.
b) may apply to a type of behaviour.
c) may apply to any intracellular property, such as the sodium ion concentration of a cell or the mitochondrial DNA sequence.
d) implies a phenotypic feature that is not disease-associated.

Question 5.3

Which, if any, of the following is incorrect? When used in human genetics, the term *allele*

a) describes any individual gene variant.
b) refers to a nuclear gene at a locus on a single chromosome
c) primarily means an individual DNA sequence copy at a locus that is common to two homologous chromosomes.
d) is often used loosely at the protein level to describe a protein made by a single copy of a nuclear gene.

Question 5.4

Which, if any, of the following is incorrect? When used in human genetics, the term *heterozygote*

a) applies even if a person possesses two alleles that differ by just one nucleotide out of a million
b) consistently applies to Y-specific loci because men must be heterozygotes at these loci, having a very different sequence on the X chromosome.

c) may apply to a person with a recessive disease when the two mutant alleles are not identical.
d) does not apply to loci on the X chromosome in women because in each of a woman's cells one X chromosome is inactivated.

Question 5.5

Which, if any, of the following is incorrect? When used in human genetics, the term *hemizygous* is a property that

a) applies to all loci on the X chromosome in males.
b) applies to Y-specific DNA because loci here are exclusively paternally inherited
c) applies to loci on mitochondrial DNA because they are exclusively maternally inherited.
d) does not apply to loci in the pseudoautosomal regions.

Question 5.6

Which, if any, of the following is incorrect? When used in human genetics,

a) the terms *dominant* and *recessive* apply equally to alleles and phenotypes.
b) *dominant* describes a phenotype that is manifested in the heterozygote, that is, the phenotype is attributable to just a single allele.
c) *recessive* describes a phenotype that is manifest as a result of the combined effects of both alleles at a locus.
d) the AB blood group is an example of a co-dominant phenotype.

Question 5.7

With respect to autosomal dominant inheritance in human genetics, which, if any, of the following statements is incorrect?

a) One of the parents of an affected person will be affected.
b) Both parents of an affected person may be unaffected, but one of them at least will carry the mutant allele in all of their nucleated cells.
c) A child born to an affected parent and a normal parent has a 50% chance of inheriting the mutant allele.
d) The term *dominant* applies equally to the phenotype of affected individuals with one mutant allele (heterozygotes) and individuals with two mutant alleles because in practice the phenotypes are essentially identical.

Question 5.8

With respect to autosomal recessive inheritance, which, if any, of the following statements is incorrect?

a) Affected individuals normally have unaffected parents.
b) For unaffected parents who have a previously affected child, there is a 1 in 4 risk of having an affected child on each occasion that they produce a new child.
c) Heterozygotes are always asymptomatic carriers.
d) Some affected individuals have alleles with identical pathogenic mutations but many have two different mutant alleles and are described as compound heterozygotes.

Question 5.9

With respect to X-chromosome inactivation in females, which, if any, of the following statements is incorrect?

a) X-inactivation first occurs in the preimplantation female mammalian embryo.
b) One of the two X chromosomes in each diploid cell of a normal woman is randomly selected to undergo X-inactivation and becomes highly condensed.
c) The process involves epigenetic silencing of each gene on one of the two X chromosomes, either the maternal X chromosome or the paternal X chromosome.
d) Once the decision is made to inactivate a paternal X or the maternal X in a cell, all descendant cells will continue with that pattern of X-inactivation.

Question 5.10

With respect to X-linked recessive inheritance, which, if any, of the following statements is false?

a) Males with just one mutant allele are affected because, lacking a second X chromosome, they do not have a normal allele.
b) Women are always asymptomatic.
c) The disorder is not transmitted from fathers to sons.
d) Each child born to a normal man and a carrier woman has a risk of 1in 4 of being affected.

Question 5.11

With respect to X-linked dominant inheritance, which, if any, of the following statements is false?

a) There are significantly more affected females than males.
b) Each child born to an affected mother has a risk of 1 in 2 of being affected.
c) Each daughter born to an affected father has a risk of 1 in 2 of being affected.

d) Each boy born to an affected father has a negligible risk of being affected.

Question 5.12

With respect to mitochondrial inheritance, which, if any, of the following statements is false?

a) Affected individuals can be of either sex.
b) Mitochondrial disorders are transmitted virtually exclusively through the maternal line.
c) Both the sperm and the egg contribute mitochondrial DNA to the zygote.
d) Clinical variability is a common feature of mitochondrial DNA disorders.

Question 5.13

With respect to mosaicism, which, if any, of the following statements, is false?

a) Any person who has two or more cells that have a different genetic constitution is a mosaic
b) All women are genetic mosaics
c) Every person is a genetic mosaic.
d) Mosaicism is the inevitable consequence of germline mutations.

Question 5.14

An individual single gene disorder can show different levels of genetic heterogeneity, and different mutations in a single gene can sometimes result in a very wide range of different phenotypes. Which, if any, of the following statements, is false?

a) Allelic heterogeneity describes a situation where any of a range of different mutations in one gene can result in the same disorder
b) Sickle cell anemia is an outstanding example of allelic heterogeneity.
c) Locus heterogeneity means that a disease phenotype is manifest only as a result of the additive contributions of genetic variants at multiple loci.
d) The situation where different mutations in a single gene result in quite different diseases can be described as phenotype heterogeneity.

Question 5.15

Purifying selection removes harmful alleles from the population because a proportion, at least, of people who carry the harmful alleles have reduced biological fitness (manifesting by reduced reproductive success rates). For any inherited disorder, the frequency of mutant alleles in the population is usually stable: mutant alleles that are eliminated from the population (because the people that have them do not reproduce, or reproduce less efficiently), and new mutant alleles

are created by *de novo* mutation. Link individual types of single gene disorder a) to e) to one of the values i) to iv) for the percentage of mutant alleles that arise by de novo mutation.

Disorder (*f* = biological fitness of affected person)

a) A severe autosomal dominant disorder (affected individuals do not have children; $f = 0$)
b) Achondroplasia (autosomal dominant; $f = 0.2$)
c) Huntington disease (a late onset autosomal dominant disorder)
d) A severe X-linked recessive disorder, ($f = 0$)
e) A severe autosomal recessive disorder ($f = 0$)

Percentage of mutant alleles arising by de novo mutation

i) very low
ii) 33.3%
iii) 80%
iv) 100%

Essay and List Questions

Question 5.16
The human X and Y chromosomes are thought to have evolved from what used to be a pair of autosomes. Unlike homologous pairs of autosomes, the current X and Y chromosomes are very different in many ways, including their DNA composition, DNA sequence classes, and gene content. Comment on the degree of DNA sequence sharing between these two chromosomes, and the consequences of having very different sex chromosomes in males.

Question 5.17
List three examples of a single gene disorder where there is extremely limited mutational heterogeneity and one example where different mutations in one gene result in a wide range of different diseases.

Question 5.18
For some single gene disorders, some members of a family who have the same genetic variants at the disease locus as strongly affected family members either show a much milder phenotype or no disease symptoms. List five explanations for why there can be a lack of penetrance or variable expressivity of a single gene disorder.

Question 5.19
What is meant by a selfish mutation? Illustrate your answer with reference to achondroplasia.

Question 5.20
The Hardy-Weinberg law is an important law of population genetics that relates the frequencies of genotypes to allele frequencies. Summarize in one short sentence what it states about the relationship of genotype frequencies to allele frequencies.

Question 5.21
What is the chief application of the Hardy-Weinberg law in clinical genetics?

Question 5.22

The Hardy-Weinberg law assumes an idealized population in which mating is random and allele frequencies are constant. Allele frequencies can change in human populations over time but because the changes are often slow and occur in small increments, they often have minor effects. However, certain types of non-random mating can have a major effect on the accuracy of the Hardy-Weinberg predictions. What types of non-random mating occur that can threaten the applicability of the Hardy-Weinberg Law?

Question 5.23

A locus, *A* has two alleles, a major one, *A*01*, with a frequency of 0.7, and a minor one, *A*02*, with a frequency of 0.3. In a suitably ideal population, match the individual genotypes given in a) to c) with one of the expected values for genotype frequency that are located within the possible values given in i) to v).

Genotypes	**Possible values for genotype frequency**
a) *A*01-A*01*	i) 0.21
b) *A*01-A*02*	ii) 0.09
c) *A*02-A*02*	iii) 0.18
	iv) 0.42
	v) 0.98
	vi) 0.49

Question 5.24

Allele frequencies can change from one generation to the next in different ways. Often changes in allele frequency are quite slow, but occasionally the composition of populations can change quickly, producing major shifts in allele frequency. Describe four factors that can cause comparatively rapid changes in allele frequency.

Question 5.25

What is meant by biological fitness?

Question 5.26

What is a founder effect? List three examples where a disorder is extremely frequent in a population as a result of a founder effect.

Question 5.27

Certain recessive disorders appear to be common in the population as a result of balancing selection. What is meant by this? Illustrate your answer with specific examples of disorders to which this applies.