Patterns of Single-Gene Inheritance

-Which of the following terms refers to a set of alleles that is inherited together on a chromosome?

Linkage disequilibrium

Chromatid

Haplotype (correct)

Epistatic alleles

Genotype

What degree of relationship to each other are half-siblings?

First

Second (correct)

Third

Fourth

Fifth

What is the term used to describe the patient who first brings a family to a geneticist's attention?

Consultand

Primary case

Proband (correct)

Referral case

Any of the above

Most traits that exhibit an autosomal recessive pattern of inheritance are the result of what type of mutation?

Loss of function (correct)

Dominant negative

Haploinsufficient

Nonpenetrant

Any of the above

Which of the following terms refers to the fact that different people with the same genotype can have variation in phenotype?

Reduced penetrance

Variable expressivity (correct)

Incomplete dominance

Codominance

Allelic heterogeneity

When a set of parents has a child affected by an autosomal recessive disorder, the most likely recurrence risk is:

100%

50%

33%

25% (correct)

12.5%

If an uncle has children with his niece, which of the following genetic terms is used to describe this relationship?

Interrelatedness

Recessivity

Inbreeding loop

Pedigree inversion

Consanguinity (correct)

For an autosomal dominant disease, if two affected parents have a child, what is most likely the risk of passing on the disorder?

100%

25%

50%

75% (correct)

What is the risk for hemophilia A in the grandsons if their paternal grandfather is a hemophiliac?

0 (correct)

1/8

1/4

1/2

100%

A process that can greatly affect the presentation of an X-linked phenotype in carrier females is:

Interfering mutations

X-inactivation (correct)

Mitochondrial expression

Recombination between X homologues

Mutation repair between homologues

Which of the following is a likely explanation that a male could survive an X-linked dominant, male lethal disorder?

He could have a mutation reversion

He could have a compensating mutation

He could be 47, XXY (correct)

There is recombination between the X and Y chromosome

Any of the above is likely

What is the most likely explanation for a set of unaffected parents having two children with a highly-penetrant, autosomal dominant disorder?

Two new mutations occurred in the same gene

Germline mosaicism in one of the parents (correct)

Variable expressivity

Somatic reversion in carrier parent

Inactivation of mutant allele in carrier parent

Anticipation is the finding in a genetic disorder that:

Mutations in the promoter are more severe than those in exons

One is more likely to diagnose genetic disease in additional family members once a family is referred for genetic counseling

The severity of phenotype increases, and age of onset decreases as some genetic disorders are passed through families (correct)

The known variability in a disease phenotype increases once a disorder is described in the literature because of better clinical observation

For many complex traits, the likelihood of having an affected child increases the risk of having a second affected child

In certain proteins, expansion of a tract of which amino acid is associated with various genetic forms of progressive neurodegeneration?

Alanine

Proline

Valine

Methionine

Glutamine (correct)

Trinucleotide repeat alleles that are not associated with the disease phenotype but that can expand during meiosis are known as:

Permutations (correct)

Pseudo-disease alleles

Pre-expansions

Expansion-prone alleles

Unstable alleles

Unstable trinucleotide repeat alleles can be observed to expand in which of the following situations?

During meiosis in a male premutation carrier

During meiosis in a female premutation carrier

During mitosis in an individual with a disease allele

Both A and B

Both B and C (correct)

Genetic anticipation is associated with:

More mutated mitochondria being passed from the mother in later generations

An increased age of onset in later generations

Toxic metabolites being passed to the fetus in an affected mother

Trinucleotide repeat instability (correct)

Threshold of expression of mutations

Heteroplasmy is associated with:

Difficulty in making a prenatal diagnosis (correct)

Random inactivation of the X chromosome

Repeat instability

Increased severity in later generations

All of the above

Which of the following are true about mitochondrial inheritance?

There is heteroplasmy

The mitochondria segregate randomly as cells divide

Mitochondria are maternally inherited

There are approximately 1000 mitochondrial DNA (mtDNA) molecules per cell

All of the above (correct)

What genetic force leads to the variability in the percentage of mutant mtDNA molecules that are present in the children of a mother who exhibits heteroplasmy for the mutation?

Positive selection

Negative selection

Genetic bottleneck (correct)

Reduced fitness

Balancing selection

Which type of mitochondrial mutation is NOT passed from an affected mother to her child when the mother exhibits heteroplasmy for the mutation?

Deletion (correct)

Duplication

Missense mutation

Nonsense mutation

Repeat expansion

Complex Inheritance

Q1: For a certain malformation, the recurrence risk in sibs and offspring of affected persons is 10%, the risk in nieces and nephews is 5%, and the risk in first cousins is 2.5%.

A: Is this more likely to be an autosomal dominant trait with reduced penetrance or a multifactorial trait? Explain.

Autosomal dominant with reduced penetrance. If it were truly multifactorial, the risk for more distantly related relatives would drop by more than 50% with each increase in the degree of relatedness.

B: What other information might support your conclusion?

In dominant disease, a study of multiple families with the condition would reveal the expected 50% ratio of affected to unaffected in the children of an affected individual (after correcting for bias of ascertainment of the families). In multifactorial inheritance, there would be fewer than the expected 50% affected in the children of an affected individual.

Q2: A large sex difference in affected persons is often a clue to X-linked inheritance. How would you establish that pyloric stenosis is multifactorial rather than X-linked?

Male to male transmission can disprove X-linkage; other criteria of multifactorial inheritance can be examined, as in the text.

Q3: A series of children with a particular congenital malformation includes both boys and girls. In all cases, the parents are normal. How would you determine whether the malformation is more likely to be multifactorial than autosomal recessive?

For autosomal recessive but not for multifactorial inheritance, all of the affected individuals in a family tend to be in the same sibship, with unaffected parents, whereas diseases with multifactorial inheritance can present as affected parents with affected children. It is generally rare for a parent of children with an autosomal recessive disorder to be himself or herself affected because it would require a homozygote or compound heterozygote–affected parent to mate with a carrier of a mutant allele at that same locus. There can be an increased incidence of such rare matings, however, when there is assortative mating or if the couple is consanguineous or comes from an inbred population.

High blood pressure can be considered as which type of trait in a genetic study?

Complex

Quantitative

Qualitative

Multifactorial

Any of the above (correct)

Twin studies are used as a way to separate genetic effects from confounding by which of the following factors?

Epigenetics

X inactivation

Heteroplasmy

Environment (correct)

Somatic mutation

The fact that two family members who share a genetic disease phenotype are more likely to participate in a family study than two who are discordant is a form of:

Ascertainment bias (correct)

Experimental selection

Population stratification

Type 1 error

Familial aggregation

For qualitative traits, we use concordance as a measure of heritability. What is the measure we use for the heritability of quantitative traits?

Deviations from the mean in a normal distribution

Coefficient of correlation (correct)

Regression to the mean

Measured trait similarity

Difference in the trait measurements

Variation in which two genes is known to greatly increase the risk of venous thrombosis in women using oral contraceptives?

C-reactive protein and factor V

Factor VIII and factor IX

Factor IX and factor X

C-reactive protein and prothrombin

Factor V and prothrombin (correct)

The factor V Leiden mutation is associated with:

Reduced cleavage of factor V by protein C (correct)

Factor V deficiency

Decreased clotting

Resolution of phenotype during puberty

Delayed presentation caused by fetal hemoglobin expression

The vast majority of people with type 1 diabetes share alleles surrounding which genes?

Insulin receptors

Glucose-transport protein 2 (GLUT-2)

Insulin genes

Major histocompatibility complex (MHC) (correct)

Phospholipase C

Which of the following is the first known powerful, predisposing allele for common, late-onset Alzheimer disease?

Factor V Leiden

Prothrombin 20210 G>A

DQB1 57D

PTPN22 R620W

ApoE ε4 (correct)

In mothers, variation in which gene increases the susceptibility of their offspring to neural tube defects?

Tetrahydrofolate (THF)

Methylene tetrahydrofolate reductase (MTHFR) (correct)

Cystathionine β-synthase

Dihydrofolate (DHF)

Thymidylate synthase

When providing genetic counseling to an individual with a relative who has a complex trait, which of the following types of information is used?

Empirical risk estimates based on averages from similar families (correct)

The mode of inheritance

Hardy-Weinberg law

Estimates of heritability from family studies

All of the above

Cytogenetics & Genome analysis

Q1) You send a blood sample from a dysmorphic infant to the chromosome laboratory for analysis. The laboratory's report states that the child's karyotype is 46,XY,del(18)(q12).

A) What does this karyotype mean?

(a) Forty-six chromosomes, male; one of the chromosome 18s has a shorter long arm than is normal.

B) The laboratory asks for blood samples from the clinically normal parents for analysis. Why?

To determine whether the abnormality is de novo or inherited from a balanced carrier parent.

C)The laboratory reports the mother's karyotype as 46,XX and the father's karyotype as 46,XY,t(7;18)(q35;q12). What does the latter karyotype mean? Referring to the normal chromosome ideograms in Figure 5-2, sketch the translocation chromosome or chromosomes in the father and in his son. Sketch these chromosomes in meiosis in the father. What kinds of gametes can he produce?

Forty-six chromosomes, male, only one normal 7 and one normal 18, plus a reciprocal translocation between chromosomes 7 and 18. This is a balanced karyotype

Q2) A spontaneously aborted fetus is found to have trisomy 18.

A) What proportion of fetuses with trisomy 18 are lost by spontaneous abortion?

Approximately 95%.

B) What is the risk that the parents will have a liveborn child with trisomy 18 in a future pregnancy?

No increased risk, but prenatal diagnosis may be offered.

Q3) A newborn child with Down syndrome, when karyotyped, is found to have two cell lines: 70% of her cells have the typical 47,XX,+21 karyotype, and 30% are normal 46,XX. When did the nondisjunctional event probably occur? What is the prognosis for this child?

Postzygotic nondisjunction, in an early mitotic division. Although the clinical course cannot be predicted with complete accuracy, it is likely that she will be somewhat less severely affected than would a nonmosaic trisomy 21 child.

Q4) Which of the following persons is or is expected to be phenotypically normal?

A) a female with 47 chromosomes, including a small supernumerary chromosome derived from the centromeric region of chromosome 15

Abnormal phenotype, unless the marker is exceptionally small and restricted only to the centromeric sequences themselves. Gametes may be normal or abnormal; prenatal diagnosis indicated.

B) a female with the karyotype 47,XX,+13

Abnormal phenotype (trisomy 13; see Chapter 6); will not reproduce.

C)a male with deletion of a band on chromosome 4

Abnormal phenotype in proband and approximately 50% of offspring.

D) a person with a balanced reciprocal translocation

Normal phenotype, but risk for unbalanced offspring (see text).

E) a person with a pericentric inversion of chromosome 6

Normal phenotype, but risk for unbalanced offspring, depending on the size of the inverted segment

Q5) For each of the following, state whether chromosome analysis is indicated or not. For which family members, if any? For what kind of chromosome abnormality might the family in each case be at risk?

A) a pregnant 29-year-old woman and her 41-year-old husband, with no history of genetic defects

Not indicated.

B) a pregnant 41-year-old woman and her 29-year-old husband, with no history of genetic defects

Fetal karyotyping indicated; at risk for trisomy 21, in particular.

C) a couple whose only child has Down syndrome

Karyotype indicated for child to determine whether it is trisomy 21 or translocation Down syndrome. If it is translocation, parental karyotypes are indicated.

D) a couple whose only child has cystic fibrosis

Not indicated, unless other clinical findings might suggest a contiguous gene syndrome (see Chapter 6).

E) A couple who has two boys with severe intellectual disability

Karyotype indicated for the boys to rule out deletion or other chromosomal abnormality. If clinical findings indicate possibility of fragile X syndrome, a specific DNA diagnostic test would be indicated.

Which of the following is not seen in a normal human karyotype?

Acrocentric chromosome

Metacentric chromosome

Submetacentric chromosomes

Satellite sequences

Telocentric chromosomes (correct)

Cells are arrested at which stage of the cell cycle for use in routine karyotyping?

Interphase

Prophase

Metaphase (correct)

Anaphase

Telophase

This type of chromosome has satellites attached to their short arms by stalks.

Acrocentric (correct)

Metacentric

Submetacentric

Sex chromosomes

Autosomes

To do high resolution banding of chromosomes, what change to the procedure must be made relative to normal G-banding?

Use more cells

Lengthen the staining procedure

Amplify the chromosomes

Use a more sensitive stain

Arrest the cells earlier in mitosis (correct)

Which of the following is the most common cause of chromosomal aneuploidy?

Unbalanced translocation

Nonhomologous recombination

Chromosomal nondisjunction (correct)

Sequence inversion

Meiotic arrest

What is needed in determining to assess whether a nondisjunction event occurred at meiosis I or meiosis II?

The karyotype

Whether the abnormal gamete contributed two copies of the same chromosome or one of each homolog (correct)

The parent of origin of the nondisjunction

Whether or not recombination occurred between the homologs of the nondisjoined chromosome

Cannot be determined

To be stable, a rearranged chromosome must have which of the following?

No inverted segments

A centromere and two telomeres (correct)

A centromere

A balanced composition (no losses or gains of genetic material)

A similarly rearranged homolog in the embryo

From largest to smallest, put these techniques in order in terms of the size of the genetic abnormality each could detect.

I. Comparative genome hybridization

II. G-banding

III. Allele specific oligonucleotide hybridization

IV. Fluorescent in situ hybridization (FISH)

I, II, III, IV

II, IV, III, I

IV, II, III, I

II, IV, I, III (correct)

I, II, IV, III

The inability of one copy of a gene to perform the function of the normal two copies of the gene is known as:

Dominant negativity

Recessivity

Deletion sensitivity

Mutation threshold

Haploinsufficiency (correct)

What is the term used for a chromosome in which one arm is deleted and the other arm is duplicated in a mirror image fashion?

Robertsonian translocation

Balanced translocation

Ring chromosome

Mirrored chromosome

Isochromosome (correct)

What type of chromosomal aberration is indicated by the following cytogenetic abbreviation: 46,XX, t(1;2)(q25;p23)?

Translocation (correct)

Transition

Transversion

Terminal deletion

Loss of telomeres

Without taking into account the likelihood of each type of segregation, what portion of the possible 2:2 segregation products resulting from meiosis in a carrier of a balanced translocation will be normal?

1/2

1/3

1/4

1/6 (correct)

1/12

When two or more chromosome complements can be found within an individual, this is known as:

Heterozygosity

Mosaicism (correct)

Genetic heterogeneity

Genomic duplication

Trisomy

Which term is used to describe differences in gene expression based on the parent of origin of an allele?

Parental determination

Sex-determination

Imprinting (correct)

Sex-linked dominance

Heterodisomy

If a single, 23X sperm fertilizes an ovum that lacks a nucleus, and its chromosomes double to yield a 46XX karyotype, what is the outcome?

A normal female

A partial mole

An ovarian teratoma

A complete mole (correct)

A normal placenta but no fetus

Which of the following are possible causes of Angelman syndrome?

Uniparental disomy for chromosome 15

A maternal deletion on chromosome 15q

Defects in the imprinting center at chromosome 15q

A mutation in the gene for E6-AP ubiquitin protein ligase

All of the above (correct)

Genetic variation in populations

Which of the following is not a chromosome mutation?

Translocation

Aneuploidy (correct)

Partial duplication

Inversion

Partial deletion

Which of the following is a possible consequence of a nonsense mutation?

Dominant negative mutation

Truncated protein

No translation

Protein instability

All of the above (correct)

Why is it believed that transitions are overrepresented among the disease-causing mutations?

Increased susceptibility of guanines to mutagens

Weaker hydrogen bonding between A-T pairs

Spontaneous deamination of 5-methylcytosines (correct)

Overrepresentation of cytosine phosphate guanine (CpG) in the genome

DNA repair mechanisms work less efficiently on these changes

Aberrant recombination between which of the following sequences can lead to a deletion?

Alu elements

Different members of a gene family

Mispaired chromosomes

Repetitive sequences

All of the above (correct)

The age-dependent increase in replication errors in sperm versus oocytes is caused by which of the following?

Oocytes sitting dormant for longer periods of time

Increased number of mitotic divisions in developing sperm compared to oocytes (correct)

Greater chance of exposure to mutagens for sperm

Less efficient DNA repair systems in developing sperm

Natural selection for variability in sperm

A genetic polymorphism is a sequence change that is present in at least what proportion of the general population?

If it is present at all

1% (correct)

5%

10%

25%

This type of genetic variation is detailed in the high-density map of the human genome called the HapMap.

Short tandem repeats (STRs)

Insertion/deletion polymorphisms (Indels)

Single nucleotide polymorphisms (SNPs) (correct)

Variable number of tandem repeats (VNTR)

Copy number polymorphisms (CNPs)

Because of its high level of informativity, the Federal Bureau of Investigation (FBI) uses a set of 13 of this type of marker for identity testing.

STRs

Indels

SNPs

VNTR (correct)

CNPs

Copy number polymorphisms are generally detected using this method.

DNA sequencing

Karyotyping

Fluorescent in situ hybridization (FISH)

Array comparative genomic hybridization (CGH) (correct)

Southern blot

The O blood type is _____ the A and B blood types.

Dominant to

Recessive to (correct)

Codominant with

Inherited separately from

The Hardy-Weinberg law relates genotype frequencies with which of the following?

Disease frequencies

Phenotype frequencies

Allele frequencies (correct)

Mutation frequencies

Either A or B

Which of the following is an assumption that the Hardy-Weinberg law depends on?

Random mating (correct)

There are only two alleles for a gene

Positive natural selection

Constant mutation rates

One allele is dominant to the other in the calculation

The Hardy-Weinberg law is important for genetic counseling of autosomal recessive disorders because it allows us to calculate which of the following?

Recurrence risk in a family

Population frequency of the disorder

Carrier frequency (correct)

Whether an affected is likely to be a homozygote or compound heterozygote

Risk to other branches of a family

When a population has subgroups that tend to remain genetically separate from each other, this is known as:

Population selection

Natural selection

Consanguinity

Population subdivisions

Population stratification (correct)

If two deaf people have children together, this deviation from random mating is known as:

Inbreeding

Population selection

Consanguinity

Population isolation

Assortative mating (correct)

Which of the following terms describes the small, random effects that cause changes to allele frequencies in small populations?

Population stratification

Natural selection

Assortative mating

Genetic drift (correct)

Genetic isolation

Which of the following determines the likelihood that an allele will be passed to the next generation?

Positive selection

Negative selection

Fitness of the allele (correct)

Population frequency of the allele

Assortative mating

An autosomal dominant disorder with near-zero fitness would be seen in a population as a result of which genetic force?

Positive selection

Balancing selection

Inbreeding

New mutation (correct)

Genetic drift

For an autosomal recessive and autosomal dominant disorder, respectively, what would be the effect on allele frequency of improved treatment for the disorder if it originally had low fitness?

Allele frequency would increase in both cases

Allele frequency would decrease in both cases

Allele frequency would increase, allele frequency would decrease

Allele frequency would decrease, allele frequency would stay the same

Allele frequency would stay the same, allele frequency would increase (correct)

For X-linked genetic lethal diseases, in what proportion of cases are mothers at low risk of having a second affected child?

0

25%

33% (correct)

66%

75%

As treatment of hemophilia A improves, the proportion of cases of hemophilia caused by new mutations would be expected to:

Increase

Decrease (correct)

Stay the same

Approach 0

Approach 100%

Which of the following favors the fitness of carriers of deleterious mutations?

Genetic drift

Gene flow

Heterozygote advantage (correct)

Inbreeding

Assortative mating

A relatively rare disease allele can be found at high frequencies in particular isolated subpopulations as a result of which of the following?

Founder effect (correct)

Balancing selection

Heterozygote advantage

Population stratification

Gene flow

Gene structure & function

Translation involves which type of RNA?

Messenger RNA (mRNA)

Ribosomal RNA (rRNA)

Transfer RNA (tRNA)

All of the above (correct)

None of the above

What is the central dogma of molecular biology?

DNA to RNA to protein (correct)

Transcription to splicing to translation

Meiosis, recombination, fertilization

Mitosis, cell division, cell death

DNA synthesis, homologous pairing, recombination

What types of sequences are located in the 5′ region of human genes?

Exons and introns

Start and stop codons

Promoters and enhancers (correct)

Splice signals

Polyadenylation sequences

Which of the following sequences is located in the 3′ region of human genes?

Splice signals

Promoters

Start codons

Locus control regions

Polyadenylation sequences (correct)

Gene families can arise by which of the following mechanisms?

Transcription

Recombination

Gene duplication (correct)

Gene replication

All of the above

DNA sequences that resemble known genes but are nonfunctional are called:

Pseudogenes (correct)

False genes

Dead genes

Faux genes

Noncoding genes

Which of the following are final products of a gene?

Protein

RNA

Exons

Both A and B (correct)

A, B, and C

Which of the following steps must a primary RNA transcript undergo before it becomes a fully processed, mature mRNA?

Capping, polyadenylation, and splicing (correct)

Splicing

Splicing and reverse transcription

Capping and splicing

Splicing and transport

Translation is always initiated at a codon for which amino acid?

Alanine

Glycine

Tryptophan

Methionine (correct)

Phenylalanine

Which of the following describes the system of codons in our DNA?

Each codon encodes a unique amino acid

It is degenerate (correct)

Each codon specifies an amino acid

Codons are overlapping

The molecular link between codons and amino acids is mRNA

This modification of cytosine phosphate guanine (CpG) islands is associated with transcriptional repression:

Phosphorylation

Protein binding

Methylation (correct)

Lipidation

None of the above

In humans, which of the following are mechanisms by which a single gene can produce multiple gene products?

Suppressor codons

Alternative stop codons

RNA splicing (correct)

Recombination

Use of tumor-associated transplantation antigen (TATA) boxes

Mutation & Polymorphism

How did the development of bacterial artificial chromosomes (BACs) facilitate the sequencing of the human genome?

It allowed human DNA to be cloned into bacteria for the first time

It allowed larger pieces of human DNA to be cloned (correct)

It allowed human chromosomes to be grown in bacteria

It allowed recombinants between human and bacteria to be made

It allowed recombination between human and bacterial chromosomes

Which of the following techniques is used to examine proteins?

Northern blot

Southern blot

Western blot (correct)

Microarray

All of the above

The generation of complementary DNA (cDNA) libraries requires which enzyme?

Reverse transcriptase (correct)

DNA polymerase

RNA polymerase

Polyadenylic (poly-A) polymerase

Exonuclease

A Southern blot detects which of the following?

Alternative splicing

Point mutations

Transcriptional start sites

Large deletions (correct)

Frameshift mutations

Allele specific oligonucleotides are most useful for detection of what kind of mutations?

Small insertions

Common point mutations for a specific disease (correct)

Rare mutations

Frameshift mutations

Splice site mutations in a particular exon

This technique allows the amplification of DNA sequences:

Polymerase chain reaction (PCR)

Cloning into bacteria

Incorporation of dideoxynucleotides

A and B (correct)

A and C

Which of the following techniques detects a translocation?

Southern blot

PCR

Spectral karyotyping (correct)

Microarray

Comparative genome hybridization

Comparative genome hybridization detects what type of change in the DNA?

Point mutations

Frameshift mutations

Alternative splicing

Dosage changes (correct)

Recombination

Which of the following techniques is used to measure the relative expression of many transcripts simultaneously?

Microarray (correct)

Northern blot

Reverse transcriptase polymerase chain reaction (RT-PCR)

cDNA cloning

Comparative genome hybridization

What specifies the DNA sequence amplified in a PCR reaction?

The promoter and stop codon

The splice sites

The primers (correct)

DNA polymerase

The physical ends of the DNA

Which of the following techniques allows staining a particular chromosome specifically?

Comparative genome hybridization

Southern blot

G-banding

Fluorescent in situ hybridization (FISH) (correct)

Karyotyping

Restriction enzyme digestion would NOT be used for which of the following techniques?

Restriction fragment length polymorphism (RFLP)

Cloning a PCR fragment

Southern blot

Northern blot (correct)

Construction of a BAC library

A probe is required for which of the following?

FISH

Northern blot

Southern blot

Western blot

All of the above (correct)