GENETIC DISORDERS

(CHAPTER 2)

QUESTION 1

List the four types of genetic traits.

Genetic traits can be described as either **autosomal** (meaning that they appear on an **autosome** or "normal" chromosome,) or **sex-linked** (meaning that they appear on a **sex chromosome**.)

In addition, they can display **dominant** or **recessive** inheritance according to the principles of Mendelian inheritance.

In effect, this means that genetic traits fall into four general categories:

autosomal dominant

autosomal recessive

sex-linked dominant

sex-linked recessive

QUESTION 2

What does polygenic inheritance mean?

Polygenic inheritance occurs when multiple genes contribute to the final outcome (or **phenotype**) of the inherited trait.

Many of these traits can be seen as a continuous spectrum rather than a single "on/off" switch: e.g. skin, hair, or eye color.

It also includes many multifactoral disorders, such as diabetes, where family history is a significant risk factor but does not determine presence of the disease outright.

QUESTION 3

How can genes be damaged?

Genetic damage occurs when there is a physical alteration to the structure of DNA due to environmental factors.

(Note that this is **different** from **mutation**, which is an alteration in the DNA **sequence** itself!)

This can occur due to **oxidative stress** from free radicals, **ionizing radiation** including UV, and some **chemicals**.

QUESTION 4

How can DNA be repaired?

Cells contain natural protection mechanisms against **somatic mutation**, which is random mutation that occurs **within the body** rather than during conception.

These typically take the form of **enzymes** which "monitor" for random mutations and work to **restore** the original sequence or **delete** the mutated area entirely.

Failing that, cells can trigger **apoptosis** to destroy the entire mutated cell before the mutation can spread to new cells through mitosis.

QUESTION 5

Is somatic mutation heritable?

Somatic mutation, because it occurs after conception and only affects part of the body, is **not** typically heritable.

While many cells within the body may contain the modified DNA (such as a neoplasia,) the gametes will normally be unaffected and thus the mutation cannot be passed on.

QUESTION 6

Define penetrance.

Penetrance is a measure of the likelihood that a **disease-causing allele** will result in the associated disease actually being expressed.

In other words, if half of the people with a particular allele will develop a disease, and the other half will not, the trait is said to have **50% penetrance**.

Some diseases have **100% penetrance**, meaning that everyone with the particular allele will be **guaranteed** to develop the disease.

However, in some cases, the presence of an allele might only be partially associated with the disease; these traits are said to have a **lower** penetrance.

QUESTION 7

Which sex is most likely to be affected by a sex-linked disorder?

Because they only have **one copy** of each sex chromosome, those who are **genetically male** (XY) are **much more likely** to be affected by sex-linked disorders.

(Remember **hemophilia** from the hemostasis unit?)

Essentially, **all** sex-linked disorders behave as if they were **dominant** in XY individuals, because there's no "backup" copy of the X chromosome to override the recessive allele.

QUESTION 8

Describe chromosome mutations at a site.

deletion – GA**TC**GA → GAGA

(Segment is left out of the sequence)

insertion – GATCGA → GATC**T**GA

(Extra segment is added erroneously)

duplication – GA**TC**GA → GA**TCTC**CGA

(Segment is included too many times)

inversion – G**ATC**GA → G**CTA**GA

(Segment is reversed from normal)

translocation – G**ATC**GA → GG**ATC**A

(Segment is included in the wrong place)

QUESTION 9

List some examples of dominant phenotype disease inheritance.

Autosomal dominant disorders can be expressed if **either** of the inherited genes are of the dominant allele.

This means that only **one** parent needs to have (or carry) the disorder for it to be passed on to offspring.

Examples include:

Huntington disease – neuromuscular degeneration characterized by involuntary movements

Marfan syndrome – connective tissue disorder associated with large stature but weaker tissues

osteogenesis imperfecta – "brittle bone disease"

achondroplasia – most common cause of dwarfism

QUESTION 10

List some autosomal recessive disorders.

Autosomal recessive disorders can be expressed only if **both** of the inherited genes are of the recessive allele.

This means that **both** parents need to have (or carry) the disorder for it to be expressed by offspring.

However, offspring can still become a dormant **carrier** of the disorder if they are passed the recessive allele by **only one** parent.

Examples include:

cystic fibrosis – disease affecting lung secretions and other tissues

Tay-Sachs disease – destroys tissue in the CNS, resulting in juvenile death

thalassemia – congenital anemia due to decreased Hgb production

sickle-cell disease – painful blood disorder characterized by malformed RBCs

phenylketonuria (PKU) – metabolic disorder in which the body cannot break down phenylalanine

albinism – inability of the body to produce melanin, resulting in hypopigmentation

QUESTION 11

List some polygenic disorders.

Polygenic disorders are the result of multiple abnormal genes, often in conjunction with specific environmental factors.

This category includes many **birth defects** which can be triggered by deficits in maternal nutrition during pregnancy, as well as **adult diseases** which may onset later in life.

Examples include:

cleft lip/cleft palate – birth defect in which the upper lip is malformed during fetal development

clubfoot – birth defect of the leg muscles resulting in adduction at the ankle

anencephaly – severe birth defect in which the fetal head fails to completely develop

spina bifida – a category of birth defects in which the spinal cord develops improperly

Others include **hypertension**, **diabetes mellitus**, **coronary artery disease**, and some forms of **cancer**.

QUESTION 12

What is mosaicism?

Somatic mosaicism occurs when some cells in the body mutate and thus contain different DNA from the rest of the organism.

Often, this involves **aneuploidy**: the deletion (**monosomy**) or addition (**trisomy**, **tetrasomy**, etc.) of entire chromosomes from the cells.

QUESTION 13

Describe trisomy 21.

Trisomy 21, also referred to as **Down syndrome**, is a developmental disorder caused by an individual possessing **three copies** of chromosome 21, rather than two.

It results in abnormal fetal and childhood development, causing short stature, characteristic facial features, and almost always some degree of cognitive impairment.

QUESTION 14

What is epigenetic modification?

Epigenetic modification refers to random mutations that alter the **structure and function** of the DNA **without** altering the actual allele sequence.

Although the DNA sequence itself is unaffected, structural changes can affect the way DNA is **used** and **interpreted**.

QUESTION 15

Describe Huntington's disease.

Huntington's disease is an **autosomal dominant** neurodegenerative disease that results in **dyskinesias** (abnormal involuntary muscle movement) and eventually affecting the heart and diaphragm.

Life expectancy once symptoms begin is typically around 20 years.

(We talked about this in the unit on neurologic dysfunction, if you want to go back and review.)

QUESTION 16

Describe sickle cell disease.

Sickle cell disease is an **autosomal recessive** form of hemolytic anemia in which the RBCs become malformed or "sickled," causing them to die prematurely and forming painful obstructions in the blood vessels.

(We talked about this in the unit on hemostasis, as it also results in increased coagulation.)

QUESTION 17

Describe cystic fibrosis.

Cystic fibrosis is an **autosomal recessive** disorder which causes abnormalities in various tissues throughout the body, perhaps most notably the **lungs**.

It interferes with the proper functioning of the Na^+/K^+ exchange pump, impairing the lungs' ability to dilute the lung secretions and thus compromising the airways.

(We talked about this in the unit on pulmonary disorders.)

QUESTION 18

Describe Tay-Sachs disease.

Tay-Sachs disease is an **autosomal recessive** disorder which primarily affects **infants** of **Ashkenazi Jewish** ancestry.

It results in **rapid neurodegeneration** of the CNS, causing seizures and paralysis, and typically results in death by the age of five.