Genetics 2

Genetic Diagrams and Mendelian Genetics:

Genetic diagrams show the genotype and phenotype of the offspring of two organisms. The different generation are abbreviated like so:

- P – parent generation
- F1 – 1st generation offspring
- F2 – 2nd generation offspring
    - F = filial, meaning 'child'

Mendel experimented on pea plants, analysing characteristics such as height, pod shape and colour and flower colour. He was hoping to establish what happens to different forms of a trait when they are combined to form a hybrid.

He conducted many **monohybrid crosses**, in which only one pair of contrasting traits is considered. He created pure-breeding lines (plants that always produce offspring similar to themselves) for each trait and crossed them with plants with alternative traits, producing F1. He then self-fertilised their offspring to create F2.

An example of a monohybrid cross would be Mendel crossing pure-breeding tall pea plants with pure-breeding short pea plants:

- In the F1 generation, all the plants were tall
- This generation was allowed to self-pollinate, creating the F2 generation
- In this generation, three-quarters were tall and one quarter was short. The ratio of tall plants to short plants was 3:1
- From the disappearance and reappearance of the short phenotype, we can deduce that:
    - When a dominant and a recessive allele are present, only the dominant allele influences phenotype
    - The recessive allele will only express itself when the organism is homozygous for it

An easy to way to represent the cross between two organisms for any number of traits for which both parental genotypes are known is the **Punnett square**. It indicates the probability of the offspring's traits.

- The **alleles** of the female gametes are written **in the top line**
- The **alleles** of the male gametes are written **down the left side**
- The allele of each male gamete is combined with each female gamete, and the genotype and phenotype are written in the box

	T	**t**
T	TT – tall	Tt – tall
t	Tt – tall	Tt – short

Phenotypes: ¾ tall; ¼ short
Ratio – **3 : 1**

Genotypes: ¼ TT; ½ Tt; ¼ tt
Ratio – **1 : 2 : 1**

These ratios are only likely to be achieved when a large number of offspring are produced.

Genetic Diagram to show monohybrid inheritance:

Key: T = tall; t = short

Parental phenotypes: tall pea plant x short pea plant

Parental genotypes: TT tt

F1 – genotype: Tt

F1 – phenotype: all tall

Self-pollination of F1 generation

P2 genotypes: Tt x Tt

F2 – genotype: TT Tt tT tt

F2 – phenotype: tall tall tall short

Phenotypic ratio: 3 : 1

Genotypic ration: 1 homozygous tall : 2 heterozygous tall : 1 homozygous short

From his experiments, Mendel discovered five basic principles:

- The units that determine a characteristic come in different forms. These units are called alleles
- The principle of segregation states that an organism's characteristics are controlled by pairs of alleles, which separate during meiosis
- The principle of independent assortment states that alleles of different genes segregate randomly and independently of one another during meiosis
- If an organism has two identical alleles of a gene, it is homozygous for that characteristic. If they are different, it is heterozygous for that characteristic
- A characteristic that is expressed in a heterozygous organism is the **dominant allele**. The characteristic that is suppressed is the recessive allele.

You will often be presented with a problem such as this following:

"Sally is a Dalmatian breeder. In Dalmatians, the allele for black spots is dominant, while the allele for liver spots (red) is recessive. She has a black-spotted dog (call it Spot) that she wants to breed from, but is not sure if it is homozygous or heterozygous. How would she go about finding out?"

The answer will always be something like this:

The only way to determine the genotype of Spot is to breed him with a Dalmatian that exhibits the recessive trait, in this case liver spots. This is called a ***test cross****. If the offspring all exhibit the dominant characteristic, then Spot was homozygous dominant. If the cross yields any recessive offspring, then Spot was heterozygous.*

Mutations:

A mutation is a sudden change in the genetic makeup of an organism. This may be caused by:

- A chromosome mutation (discussed in the section on meiosis) or a
- Gene mutation

A **gene mutation** is the result of a change in the sequence of nucleotides in a DNA molecule. This changes the information given to the cell by the gene. The codons being altered will result in the production of a faulty protein or no production at all.

This change in nucleotides is brought about by chance. Occasionally, things go wrong, even though DNA is a very stable molecule. One or more nucleotides can be lost or damaged during:

- Crossing over
- Replication of DNA
- Transcription of DNA to RNA

Point mutations are small-scale mutations that affect one or very few nucleotides in a DNA molecule. They include:

- Substitution mutations – one nucleotide is exchanged for another
- Insertions – one or more extra nucleotides are added to the DNA molecule
- Deletions – one or more nucleotides are removed from the DNA molecule

Larger mutations involve more than one nucleotide and can include the rearrangement of nucleotides or duplication of an entire gene.

Mutations occur naturally, but usually at a very slow rate. However, there are some environmental factors that can increase this rate, such as **ionising radiation** (such as UV light or X-rays), **mutagenic chemicals** (such as benzene) as well as **viruses** and **micro-organisms**. These factors are called **mutagens.**

Mistakes in the DNA can be recognised and repaired by a cell. This is a way in which the body protects itself from disease.

Mutations can have a variety of effects on organisms, depending on the type of mutation, the importance of the genetic material affected and whether the affected cells are somatic cells or gametes.

- Somatic mutations occur in somatic cells and are not transferred to the next generation. These can cause cells to become malignant, causing cancer. They may be transmitted in plants by vegetative propagation
- Gametic mutations affect the reproductive organs, and result in changes to the gametes produced. These germ-line mutations can be passed on to offspring and play a role in evolution or causing hereditary diseases

Neutral mutations do not affect the life of the organism.

Beneficial mutations constitute a small percentage of mutations that occur. They have a positive effect on the phenotype of the organism. They may help an organism to adapt to their surroundings, such as the peppered moth in Great Britain adapting a darker form. Some bacteria have become resistant to antibiotics. These superbugs are harmful to humans, but their mutations are beneficial to them.

Harmful mutations constitute the majority of mutations that occur. Many result in the death of the organism. Many genetic disorders are caused by a single gene mutation, such as:

- Albinism
- Sickle cell anaemia

1. Albinism

A brown pigment called melanin protects the body from the harmful effects of ultraviolet rays. Albinism is a rare, inherited condition of humans and other mammals where there is a block in the pathway by which melanin is formed. This results in partial or full absence of melanin in the skin, hair and eyes, causing:

- Pink skin
- Lighter than normal or white hair
- Iris colour that is pale or blue
- Vision defects

Albinism is caused when the gene in skin cells, responsible for making melanin from tyrosine cannot do so, because a **different** gene, which is responsible for the production of tyrosinase (the enzyme which catalyses the synthesis of tyrosine) has mutated. This mutation of one gene resulting in a second gene not functioning properly, resulting in a change to the phenotype, is an example of epistasis.

Albinism exhibits a pattern of recessive monohybrid inheritance. The mutated allele passes from generation to generation, but is only expressed if both parents have the mutated gene, as it is recessive.

2. Sickle cell anaemia

Sickle-cell disease is a blood disorder in which the red blood cells lose their biconcave shape and collapse, forming sickle-shapes. Haemoglobin, the pigment in red blood cells, carries oxygen and carbon dioxide to and from all parts of the body. Every person has two alleles of the haemoglobin gene, which usually code for normal haemoglobin (HbA). A recessive mutation, however, of one of these alleles causes the production of an abnormal haemoglobin protein (HbS).

The disease is caused when the recessive allele coding for HbS is inherited from both parents. A sickle-cell carrier receives one dominant allele coding for HbA and one recessive allele coding for HbS. These people have enough normal haemoglobin to carry oxygen effectively and live healthy lives.

Symptoms include:

- HbS causes RBCs to lose their shape
- Less oxygen can be carried, causing anaemia
- The sickle-shaped cells get stuck in small blood vessels, causing pain, fever and swelling
- The cells are destroyed in the spleen

Children with sickle-cell anaemia often die at an early age.

Gene therapy is available to rectify the genes in the patient's bone marrow cells. Other treatments include frequent blood transfusions or bone marrow transplants.

There is a link between the disease and malaria, with many people in malaria areas carrying the sickle-cell trait. Sickle-cells are rapidly destroyed in the spleen because of their shape. This also kills any malaria parasites living in them, probably before they are able to reproduce and spread. Carriers of sickle-cell disease are therefore more likely to survive a malaria infection. These survivors will pass on the HbS allele to their offspring, spreading malaria resistance.

Sex chromosomes and sex-linked diseases:

Of the 23 pairs of chromosomes in a human cell, 22 pairs have more or less the same shape. They are called autosomes. The two chromosomes of the 23rd pair differ in shape and are called gonosomes. These are the sex chromosomes, and they determine the sex of the offspring.

- The longer sex chromosome is called an X chromosome
- The shorter sex chromosome is a Y chromosome
- Females have two X chromosomes, so they have the genotype XX (homogametic)
- Males have one X chromosome and one Y chromosome, genotype XY (heterogametic)

If the sex chromosomes are XX, the undifferentiated sex organ in a very young embryo will develop into an ovary and the foetus will grow into a female.

If the sex chromosomes are XY, the presence of a gene on the Y chromosome will trigger the development of the gonad tissue into a testis, and the foetus will grow into a male.

In mammals, it is always the male that is heterogametic. In birds and butterflies, it is the female.

Sex-linked alleles:

- The Y chromosome is very short and contains few alleles not responsible for 'maleness'
- The X chromosome is much longer and carries many alleles in addition to those responsible for 'femaleness'
- Only a very small part of the X and Y chromosomes can pair up during meiosis and so no crossing over occurs
- The alleles carried on the non-homologous part of an X chromosome are called x- or sex-linked alleles
- Because men have only one X chromosome, they will have only one of the sex-linked allele on the X chromosome
- Women have two X chromosomes and so have two of the sex-linked alleles
- Alleles on the X chromosome can be inherited by either sex, but the male can only inherit one of the possible alleles. This makes males far more likely to suffer from sex-linked diseases, as they have only one sex-linked allele and if it is mutated, it **will** cause a disease
- The female can be homozygous or heterozygous for the X-linked allele and will only suffer from a sex-linked disease if both X chromosomes have to allele

1. Red-green colour blindness

There is a sex-linked gene on the X chromosome which enables green, yellow, orange and red to be distinguishable. If this gene mutates, all these colours appear to be the same. More men are red-green colour blind than women, as the gene controlling the disease is recessive and occurs only on the X chromosome – therefore if the single male X chromosome has the colour blind allele, the male will be colour blind. A female will only be red-green colour blind if both of her X chromosomes have the allele.

2. Haemophilia

Haemophilia is a rare, genetic condition of frequent and excessive bleeding, as the blood clots very slowly. The dominant allele H allows blood to clot, while the recessive allele h does not allow it to clot normally. These sex-linked alleles are located on the X chromosome.

There are only two possible genotypes for a male:

Genotype	Phenotype
X^HY	normal
X^hY	haemophiliac

There are no known female haemophiliacs as there are no known women who are homozygous for the recessive allele X^hX^h. This is because this causes a miscarriage. Woman can, however, be carriers of the recessive allele. Haemophilia is, therefore, a male disease.

Genetic Counselling:

Genetic counsellors provide information to families who have members with birth defects or genetic disorders, such as Down syndrome, Huntington's disease, deafness, cancers, etc. As these conditions may be passed from parent to children, genetic diseases or disorders tend to run in families. Counsellors study family and medical histories, analysing inheritance patterns to determine the risk of the problem reoccurring.

Gene testing is the examination of the DNA molecule itself to determine whether or not a person is at risk for a genetic disorder. The pros of this are:

- It can clarify a diagnosis, allowing the correct treatment to be administered
- It allows families to avoid having children with devastating diseases
- Identify people at risk for preventable conditions

The cons:

- Possibility for errors
- Uncertainty surrounding results, as they can only provide a probability of the problem developing
- Lack of cures for many diseases
- Anxiety caused by results
- Risk of discrimination