CHAPTER

07 Inheritance

Throughout history, people have wondered why children resemble their parents. Today we know that many characteristics are inherited, such as the colour of our hair, eyes and skin, as are many conditions such as haemophilia and colour-blindness. Sexual reproduction results in offspring with a set of unique characteristics inherited from their parents.

In this chapter, you will explore the complex interplay between DNA, genes, chromosomes and the traits they control. You will gain an understanding of how genes and their interactions determine the inheritance of characteristics from generation to generation. You will learn how to predict the inheritance patterns of traits using laws developed by Gregor Mendel, as well as learning about the role, structure and types of chromosomes. You will also discover how errors in chromosome replication lead to mutations that may have drastic impacts on the characteristics of an organism.

Syllabus subject matter

Topic 1 • DNA, genes and the continuity of life

MUTATIONS

- identify how mutations in genes* and chromosomes can result from errors in
  - DNA replication (point and frameshift mutation)
  - cell division (non-disjunction)
  - damage by mutagens (physical, including UV radiation, ionising radiation and heat and chemical)
- explain how non-disjunction leads to aneuploidy
- use a human karyotype to identify ploidy changes and predict a genetic disorder from given data
- describe how inherited mutations can alter the variations in the genotype of offspring.

INHERITANCE

- predict frequencies of genotypes and phenotypes using data from probability models (including frequency histograms and Punnett squares) and by taking into consideration patterns of inheritance for the following types of alleles: autosomal dominant, sex-linked and multiple
- define polygenic inheritance and predict frequencies of genotypes and phenotypes for using three of the possible alleles.

* The greyed out sections of this dot point are addressed specifically in Chapter 5.

7.1 Chromosomal abnormality

BY THE END OF THIS MODULE, YOU SHOULD BE ABLE TO:

- understand that different species have different numbers of chromosomes
- differentiate between allosomes and autosomes
- recall the human karyotype and recognise that errors in the karyotype result in genetic abnormalities
- explain non-disjunction and aneuploidy.

Chromosomes are the structures that allow DNA to be maintained in discrete packages. Their structure protects the integrity of the information stored on DNA and reduces the chance of error in replication. All organisms have their genetic material stored in some form of chromosome. An understanding of the structure and function of chromosomes is essential for understanding inheritance. Chromsomes are discussed in detail in Module 5.1.

KARYOTYPES

When examining chromosomes and identifying pairs, look at:

- chromosome length
- centromere position
- banding patterns.

The coiling and supercoiling of DNA found in eukaryotic nuclei produces chromosomes (Module 5.1). Scientists examine eukaryotic chromosomes when they are most visible in the cell—at the metaphase stage of the cell cycle. The chromosomes are stained so that characteristic patterns of light and dark bands (G bands) appear along the arms of the chromosomes. The bands reflect regional differences in the amounts of bases A and T versus G and C.

Homologous chromosomes have the same gene loci, so chromosomal length and the banding patterns of homologous chromosomes are similar. In other words, banding patterns are specific and consistent. They can be used to distinguish between chromosomes and to identify subtle changes in chromosome structure that may be associated with genetic abnormalities (Figure 7.1.1). Specific banding patterns can also be used to identify the same chromosomes or regions of chromosomes across different species.

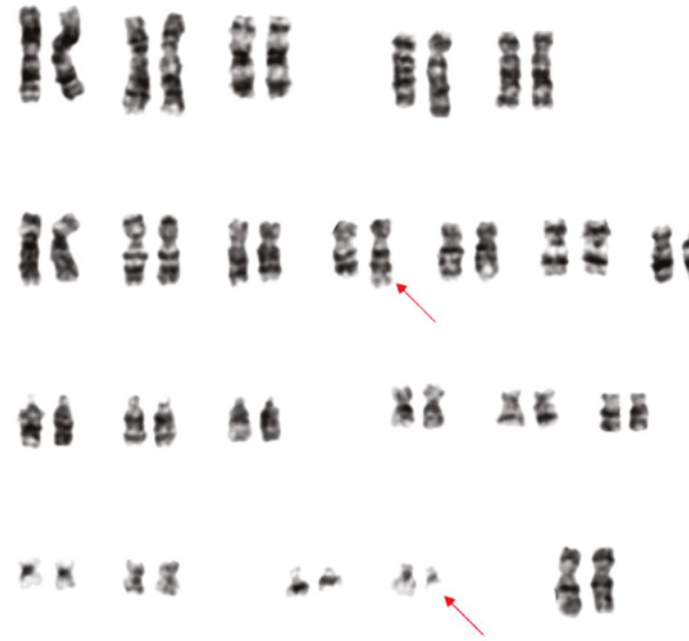


FIGURE 7.1.1 The banding pattern on the chromosomes indicated with the arrow shows researchers where mutations have occurred.

A **karyotype** is the image or picture of the full set of chromosomes from an individual's cell (Figure 7.1.2). A karyotype is represented by photographs or diagrams of the homologous chromosomes arranged in pairs according to their length and the position of the centromere. Karyotypes allow scientists to compare the chromosome sets of related species. Karyotypes also allow scientists to identify changes that may be associated with genetic abnormalities, such as:

- changes in chromosome number (the loss or gain of whole chromosomes)
- changes in structure (such as the duplication, inversion or deletion of part of a chromosome).

The human karyotype

In humans (and some other organisms), sex chromosomes are distinguished from the remaining chromosomes (after the homologous autosomes have been paired). A karyotype for a human male shows that there are 22 pairs of autosomes and two sex chromosomes, X and Y. Sex chromosomes are also referred to as allosomes (Module 5.1). A karyotype for a human female shows 22 pairs of autosomes and two X chromosomes (Figure 7.1.2). The autosomal pairs are numbered 1 to 22 and ordered from largest to smallest. The allosomes are usually shown after the autosomes.

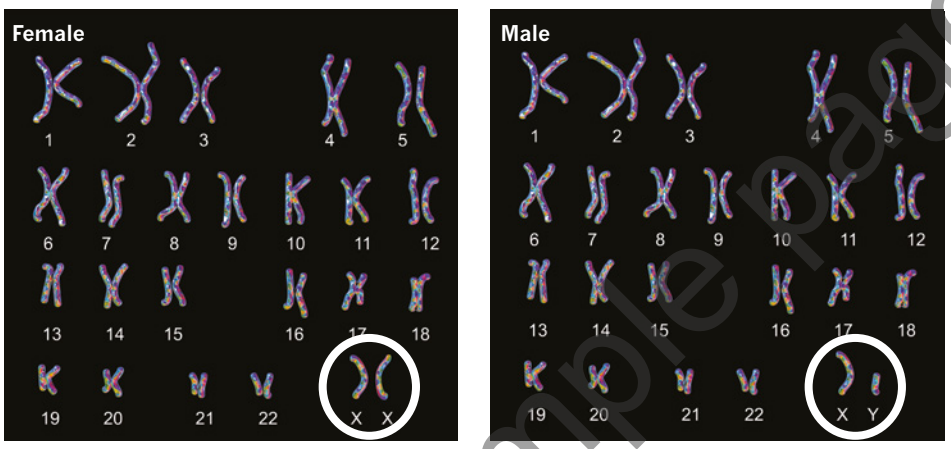


FIGURE 7.1.2 The human karyotype with the sex-determining chromosomes circled.

CHROMOSOMAL ABNORMALITIES

The expected normal karyotype is not always observed in individuals. This is because chromosomal mutations and other abnormalities may occur. The two major forms of chromosomal abnormalities are block mutations and aneuploidy.

Block mutations

As shown in Module 5.4, genetic mutations can occur within an individual gene as a result of altering a single nucleotide or small sequence of nucleotides. However, mutations can also affect genetic material at a chromosomal level. Mutations that affect large sections of a chromosome, typically multiple genes, are called **block mutations** (or chromosomal mutations). These types of mutations usually occur during meiosis in eukaryotic cells. They can also be caused by mutagens such as radiation. When a gene is disrupted by the mutation, the effects are serious, even lethal. There are five main forms of block mutations:

- duplication
- deletion
- inversion
- insertion
- translocation.

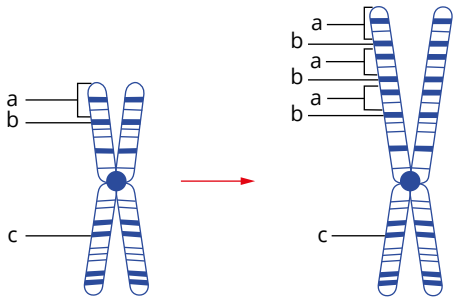


FIGURE 7.1.3 Chromosomal duplication mutations result in multiple repetitions of a sequence of DNA.

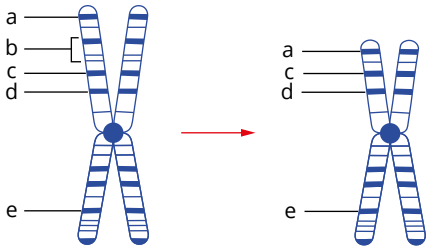


FIGURE 7.1.4 Chromosomal deletion mutations involve the loss of large sequences of DNA from the chromosome (sometimes whole genes).

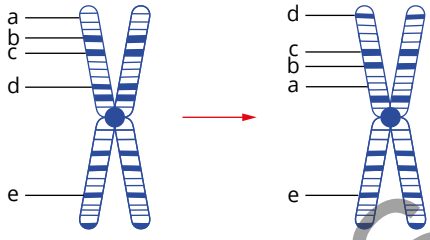


FIGURE 7.1.5 Chromosomal inversion mutations involve a broken section of the sequence rotating 180° before reattaching.

Duplication mutations

Duplication mutations involve the replication of a section of a chromosome that results in multiple copies of the same genes on that chromosome (Figure 7.1.3). There can be thousands of repeats and the repeats can increase gene expression.

One form of a common inherited neurological disorder called Charcot-Marie Tooth (CMT) disease results from the duplication of the gene on chromosome 17. This gene codes for a protein in peripheral nerve myelin. As a result of this duplication mutation, the expression of protein-22 in the peripheral nerve cells is affected, which causes a slow degeneration of the peripheral nerves in the feet, legs, arms and hands. The disease is not life-threatening. Approximately one in 2500 people in Australia have been diagnosed with CMT disease.

Deletion mutations

Deletion mutations remove sections of a chromosome (Figure 7.1.4). Deletions lead to disrupted or missing genes and the resultant change in gene expression can have serious effects on growth and development. Chromosomal deletions are often fatal. Wolf-Hirschorn syndrome is an example of the deletion of the short arm of chromosome 4. Symptoms include epilepsy, facial deformities and delayed bone development. People with this syndrome who survive infancy have severe disability and immune deficiency.

Inversion mutations

During an **inversion mutation**, a section of the double-stranded polynucleotide chains break off the chromosomes, rotates 180° and reattaches to the same chromosome (Figure 7.1.5). Inversions may involve as few as two bases or they may involve several genes. Haemophilia A is one example of an inversion mutation. The mutation occurs in the factor VIII gene on the X chromosome. This particular type of block mutation is found in approximately 43% of haemophilia A patients.

Insertion mutations

An **insertion mutation** occurs when a section of one chromosome breaks off and attaches to a different chromosome (Figure 7.1.6). In eukaryotes, the effects of this type of mutation depend on whether the cell retains two copies of every gene. During meiosis, if the chromosome now containing the insertion is separated from the chromosome in which the material originated, some gametes may have two copies of the genes in the inserted section, while others will be missing them entirely (Figure 7.1.7).

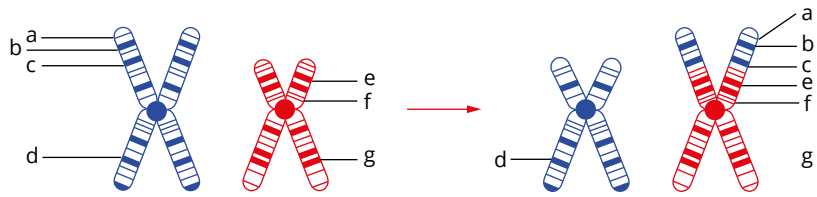


FIGURE 7.1.6 Chromosomal insertion mutations involve a sequence breaking off one chromosome and attaching to another.

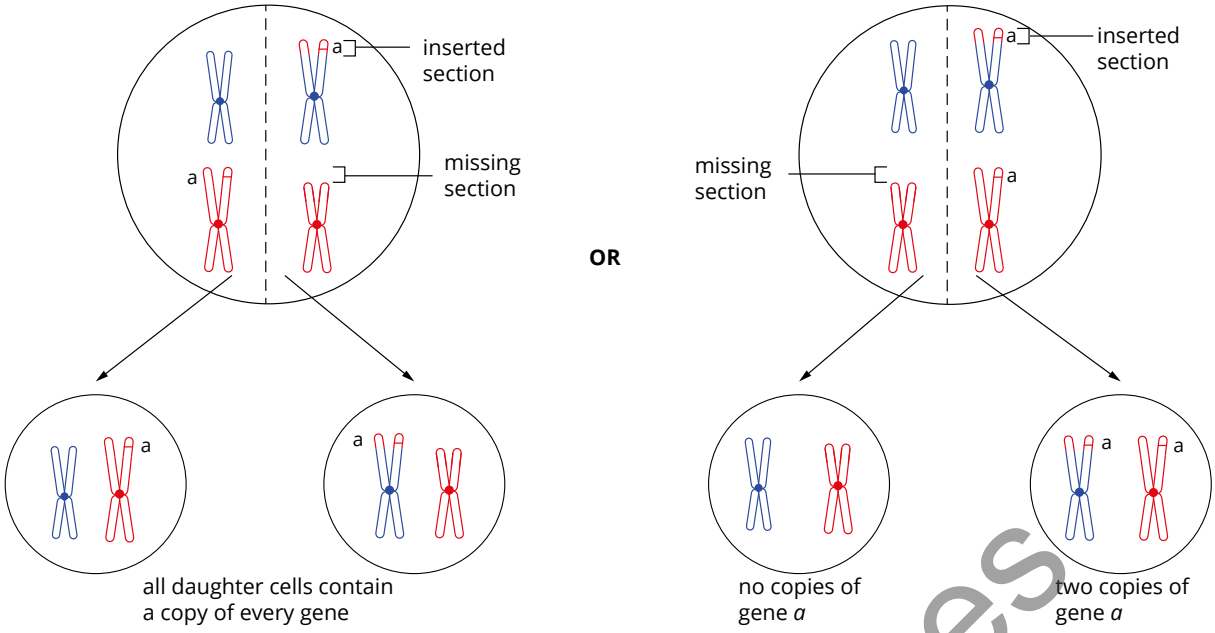


FIGURE 7.1.7 As a result of random assortment in meiosis, a chromosomal insertion mutation may lead to daughter cells with one, two or no copies of the inserted region. This image depicts meiosis I only.

Translocation mutations

In **translocation mutations**, a whole chromosome or a segment of a chromosome becomes attached to or exchanged with another chromosome or segment. For example, sections from two non-homologous chromosomes may break off at the same time. They may reattach to the other chromosome, swapping genetic material (Figure 7.1.8). Translocations typically interrupt normal gene regulation and are the cause of some forms of cancer, such as leukaemia and Ewing's sarcoma.

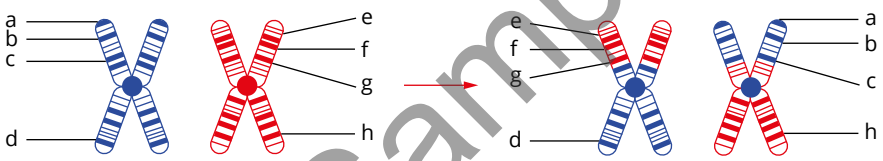


FIGURE 7.1.8 Chromosomal translocation mutations can involve two different chromosomes exchanging segments.

Non-disjunction and aneuploidy

Under certain circumstances during meiosis and mitosis, chromosomes fail to separate correctly. This is referred to as **non-disjunction**. When there is an error in chromosome separation, the result is an abnormal number of chromosomes in the daughter cells. This abnormal number of chromosomes is referred to as **aneuploidy**.

During mitosis, non-disjunction occurs when sister chromatids fail to separate correctly. During meiosis, non-disjunction is the result of homologous chromosomes incorrectly separating. Figure 7.1.9 (page 330) shows non-disjunction in meiosis I and meiosis II.

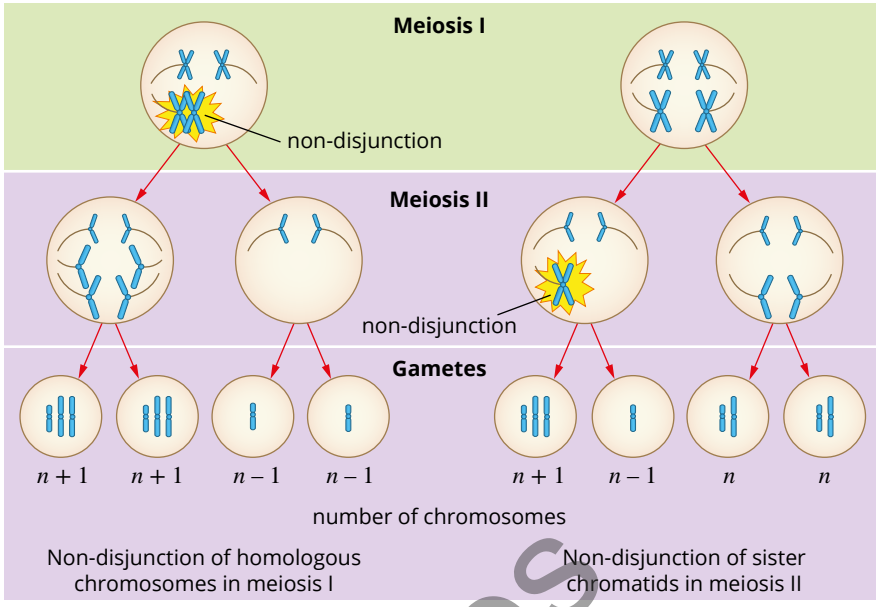


FIGURE 7.1.9 Non-disjunction occurring in meiosis.

Using karyotypes to identify chromosomal number abnormalities

A number of syndromes result from aneuploidy. Down syndrome is a typical example of a syndrome that results from having one extra chromosome. It results from one extra copy of chromosome 21, which can be identified via a karyotype (Figure 7.1.10). This type of abnormality is called a trisomy, because there are three copies of the chromosome.

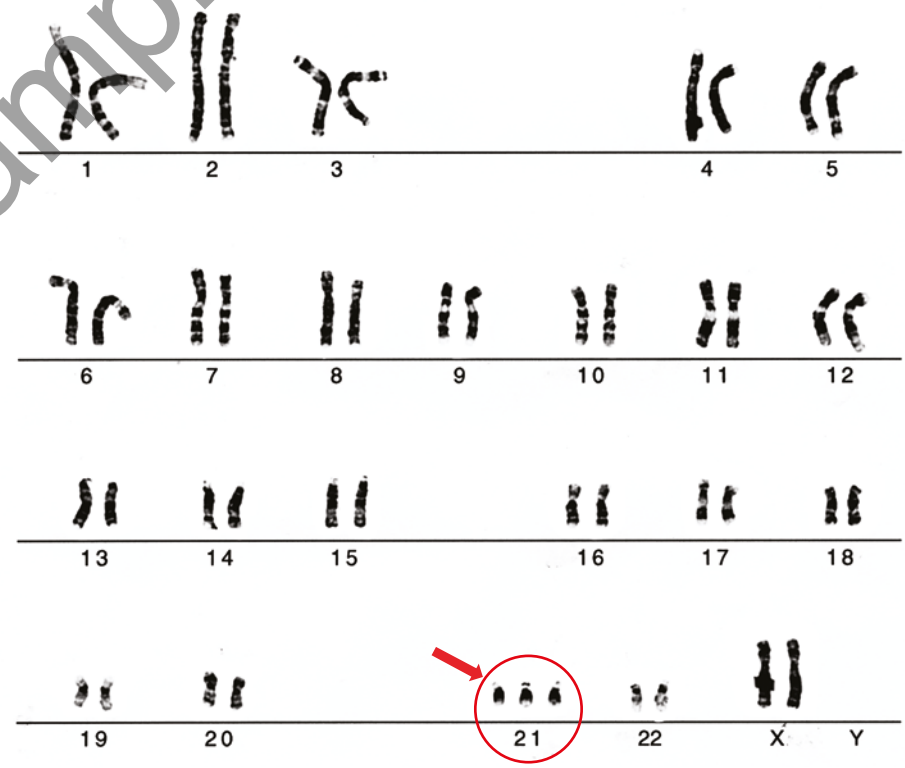


FIGURE 7.1.10 The Down syndrome karyotype, showing an extra copy of chromosome 21.

Two other abnormalities formed as a result of an abnormal chromosome number are Klinefelter syndrome and Turner syndrome. In Klinefelter syndrome (also called XXY syndrome), males have two X chromosomes and one Y chromosome instead of one X and one Y chromosome (Figure 7.1.11). As a result, they have 47 chromosomes. Males with Klinefelter syndrome are infertile and have other characteristics such as breast development and a tall stature.

In Turner syndrome (also called monosomy X), which occurs only in females, there is one X chromosome instead of two (Figure 7.1.12). People with Turner syndrome are infertile and have a short stature.

Table 7.1.1 shows some of the consequences in humans of abnormal chromosome numbers. This is the result of abnormal meiosis in one of the parents of the person with the condition.

TABLE 7.1.1 Conditions in humans that are a result of errors during meiosis and genetic recombination

Condition	Chromosome change	Traits of person with condition
Down syndrome	• three copies of chromosome 21 present (trisomy 21) • 47 chromosomes	• male or female • some intellectual disability • characteristic palm prints and facial features • may be infertile
Klinefelter syndrome	• extra X chromosome (XXY) • 47 chromosomes	• male • sterile • often some intellectual disability • female secondary sex traits (e.g. breast enlargement)
Patau syndrome	• three copies of chromosome 13 present (trisomy 13) • 47 chromosomes	• male or female • small skull • intellectual disability • cleft lip • cleft palate • usually has heart defects • seldom survives more than four months after birth
Turner syndrome	• all or part of one X chromosome is altered or missing (monosomy) • 45 complete chromosomes	• female • short stature • infertile • fluid retention and puffiness in hands and feet • kidney and heart problems • some learning difficulties but usually has normal intelligence

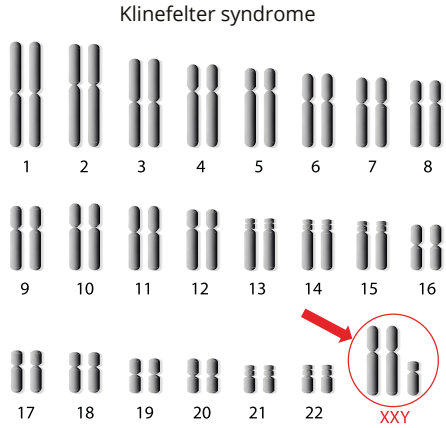


FIGURE 7.1.11 Klinefelter syndrome karyotype, showing an extra copy of the X chromosome.

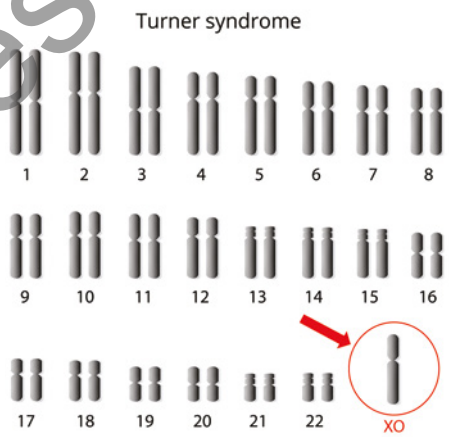


FIGURE 7.1.12 Turner syndrome karyotype, showing only one copy of the X chromosome.

7.1 Review

SUMMARY

- Chromosomes vary in size, banding pattern and centromere position.
- Homologous chromosomes are matching pairs of chromosomes (one set from each parent) that have the same genes.
- Sex chromosomes (allosomes) are chromosomes that are involved in sex determination.
- In humans the sex chromosomes are X and Y.
- Females have two X chromosomes and males have an X and Y.
- Other organisms may have other sex chromosomes, or not at all.
- Autosomes are chromosomes that are not involved in sex determination.
- A karyotype is the number and appearance of a cell's chromosomes.
- A karyotype can identify:
  - the number of chromosomes in a cell
  - the gender of the individual
  - whether an individual has an extra chromosome, such as in Down syndrome and Klinefelter syndrome
  - where an individual is missing a chromosome, such as in Turner syndrome
  - the position of the centromere
  - the size of the chromosome.

KEY QUESTIONS

Retrieval

1 Recall how many homologous pairs of chromosomes you would expect to find in the cells of most:
- **a** human females
- **b** human males

2 Explain aneuploidy.

3 State the chromosomal variations for the aneuploidy syndromes listed below.
- **a** Down syndrome
- **b** Turner syndrome
- **c** Klinefelter syndrome

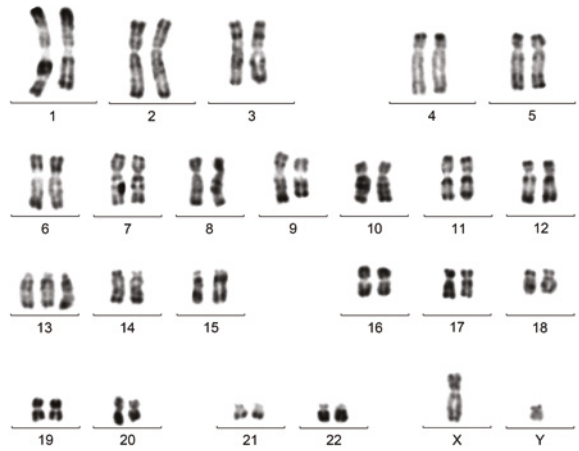
Comprehension

4 Describe how karyotypes can be used by scientists to determine information about chromosomes.

5 Explain the effect duplication mutations have on chromosomes.

Analysis

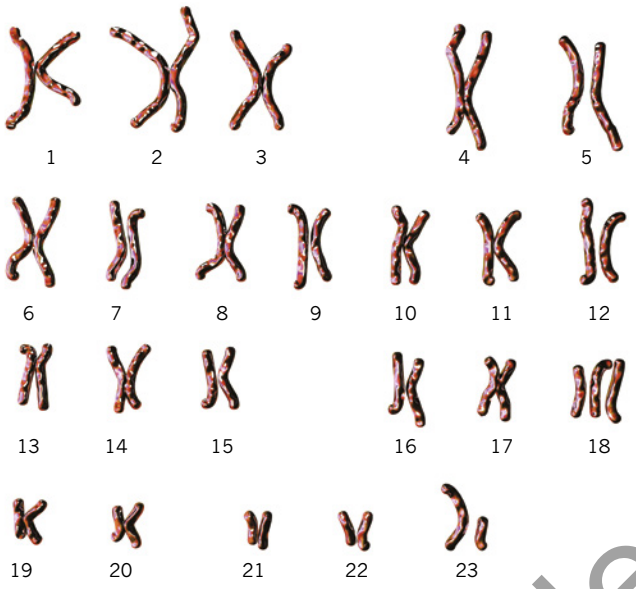
6 The figure below shows a human karyotype.
- **a** Determine the sex of the individual.
- **b** Justify whether or not this is a normal karyotype.



7 Using your knowledge of the human karyotype, examine the image below.

a Determine if this individual has trisomy 21.

b Explain how you made your diagnosis and comment on whether any other diagnoses can be made.



8 The image below shows the homologous pair of chromosome 5 in a person who suffers from cri du chat syndrome. Identify the abnormal chromosome and determine the chromosomal disorder.

9 The karyotype below is from a miscarried fetus.

a Determine the sex of the fetus.

b Identify the chromosomal disorder.

c Explain how the disorder may have occurred.

7.2 Genotypes and phenotypes

BY THE END OF THIS MODULE, YOU SHOULD BE ABLE TO:

- recall the difference between genotype and phenotype
- understand how genes and alleles are named and written
- explain dominance, recessiveness, co-dominance and incomplete dominance
- understand and interpret frequency histograms.

Since the work of Gregor Mendel, the fundamentals of gene expression have been crucial to the understanding of inheritance. This module discusses the key principles of genotype and phenotype, along with monogenic and polygenic traits.

GENOTYPE

A **genotype** is the set of alleles present in the DNA of an individual organism. It is the result of inheritance. In Chapters 5 and 6, you learned that an allele is an alternative form of a gene. Each individual usually only has two alleles for each gene: one inherited from their mother and one inherited from their father. However, one gene may have many alleles, and this is what leads to variation in a population. Characteristics that are determined by a single gene are called **monogenic** traits.

Multiple alleles at a locus

Consider a gene, which we will call gene *A*, which has two alleles. Different alleles are represented by different symbols. One allele can be represented by an upper-case *A*, and the other by a lower-case *a*.

If the locus of gene *A* is on a homologous chromosome, there will be two copies of the gene in a diploid cell (the maternal and paternal copy). If you inherited the allele *A* from both parents, your genotype for gene *A* will be *AA*. If you inherited the allele *A* from one parent and the allele *a* from the other parent, you will have the genotype *Aa*. If you inherited the allele *a* from both parents, you will have the genotype *aa*.

Therefore, there are three different combinations or genotypes of gene *A*: *AA*, *Aa* or *aa* (Figure 7.2.1). Genotypes *AA* and *aa* contain only one type of allele, so the individual is said to be homozygous for that gene and is called a **homozygote**. Genotype *Aa* contains two different alleles, so the individual is said to be heterozygous for that gene and is called a **heterozygote**.

Now consider a gene, which we will call gene *B*, on the X chromosome. Because this gene is on the X chromosome, it is said to be **X-linked**. Gene *B* also has two alleles, *B* and *b*. To show that this gene is on the X chromosome and therefore X-linked, the symbol 'X' is used, with a superscript to represent the gene's allele. So the two alleles are named X^B and X^b (Figure 7.2.2).

Because females have two copies of the X chromosome, they can be homozygous (X^BX^B or X^bX^b) or heterozygous (X^BX^b) for gene *B*.

Males only have one copy of the X chromosome, so they are referred to as being **hemizygous** ('hemi' means 'half'). This term indicates that a male has only half the number of copies of genes on the X chromosome compared with a female. The Y chromosome is used in describing the genotype to emphasise that the individual is a male. As shown in Figure 7.2.2, the two possible genotypes of gene *B* for a male are X^BY and X^bY.

> The names of genes and alleles are always italicised.

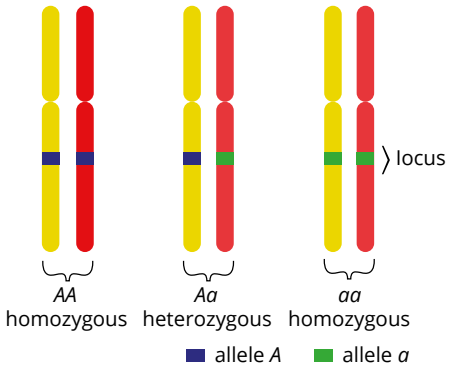


FIGURE 7.2.1 On homologous chromosomes, alleles of a gene occur at the same locus. If a gene has two alleles, there can be three different combinations or genotypes. Two of these combinations are homozygous, and one is heterozygous.

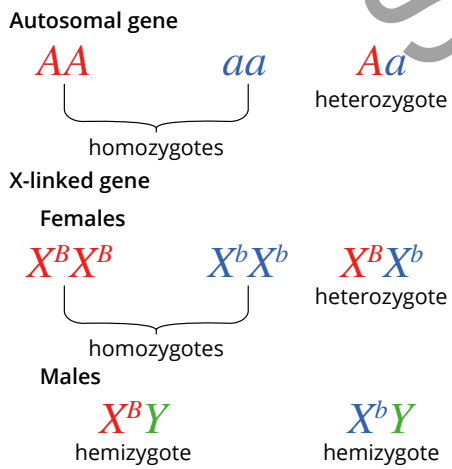


FIGURE 7.2.2 The symbols used to record genotypes of autosomal and X-linked genes.

Naming genes

There are internationally accepted names for genes and their abbreviated forms. For example, the gene that codes for phenylalanine hydroxylase, an enzyme involved in the inherited disorder phenylketonuria, is abbreviated to *PAH*. The gene name is always italicised, to distinguish genes from the proteins they encode. For example, BRCA1 is an enzyme expressed in the cells of breast and other tissue, where it helps repair damaged DNA or destroy cells if DNA cannot be repaired. The gene that codes for this enzyme is known as *BRCA1* (breast cancer gene 1).

PHENOTYPE

An organism's **phenotype** is all of its observable characteristics. It is the result of inheritance such as genotype but also the effects of the organism's environment. When studying inheritance, it is important to know the genotypes of parents and offspring. However, it is equally important to know the specific observable characteristics, or phenotype, that can result from a given genotype. The phenotype includes any distinct property of an organism: physical, chemical, physiological or behavioural. In experimental crosses (matings), such as those carried out by Gregor Mendel, phenotypes are observed to determine the underlying genotypes.

Influences on phenotype

An example of a phenotype is skin colour. Your skin colour depends on how much skin pigment (melanin) you produce, which is determined by your genotype. Your skin colour phenotype also depends on environmental factors such as exposure to sunlight, especially in pale-skinned people, which stimulates the activity of the genotype. The greater the exposure, the more melanin is produced temporarily until the exposure is ceased (Figure 7.2.3).

FIGURE 7.2.3 The effect of sun exposure on skin colour. The darker part of the skin has been exposed and has produced more melanin, causing it to darken (neck and shoulders). Unexposed skin (back) does not produce extra melanin.

The amount of melanin that is able to be produced in response to environmental factors is dependent on inherited regulatory genetics and the genotype. The genotype determines the possible range of phenotypes for a particular characteristic or trait, and the environment influences where in that range the actual phenotype will be.

In Arctic foxes, two fur colour genotypes occur, called 'white morph' and 'blue morph'. The fur of the blue morph remains dark blue-grey throughout the year, but the fur of the white morph varies from dark brown or grey to pure white. In summer the fur is dark, but as winter approaches the fur gradually changes to white in response to the increasing cold and shorter day length (Figure 7.2.4). At the end of winter the fur gradually returns to its summer colour.

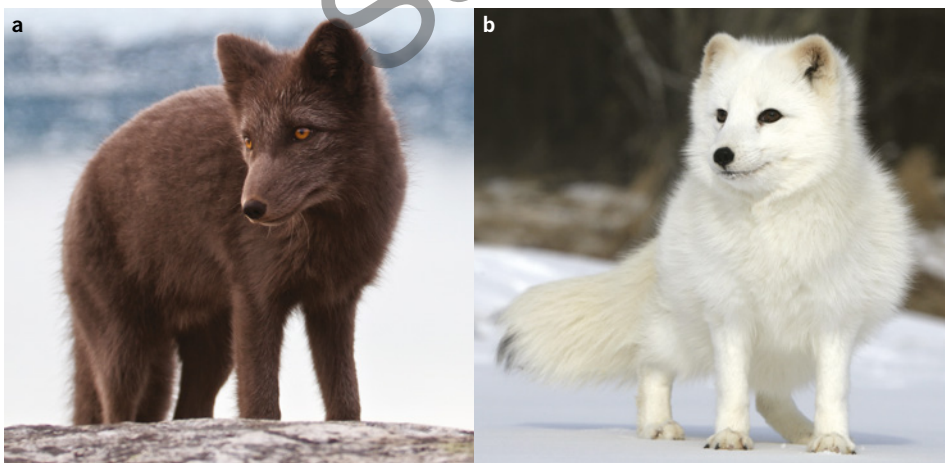


FIGURE 7.2.4 The fur of the white morph genotype of the Arctic fox changes from (a) dark brown or grey to (b) pure white.

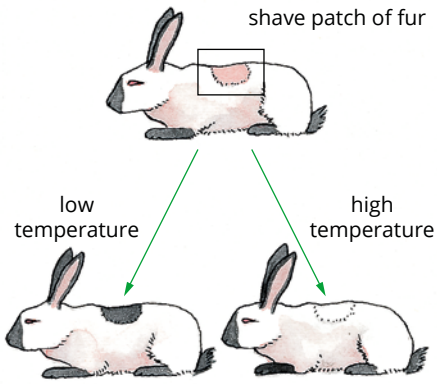


FIGURE 7.2.5 The relationship between temperature and fur colour in Himalayan rabbits.

Phenylketonuria

The inherited disorder phenylketonuria (PKU) is a consequence of the build-up of an amino acid called phenylalanine in the blood. This is toxic to developing neurons, leading to abnormal development of the nervous system and intellectual disability. PKU is caused by a mutation in the *PAH* gene, which codes for an enzyme that converts phenylalanine into another amino acid, tyrosine. If an individual inherits two copies of the mutant allele (that is, they are homozygous for the gene), they will develop PKU. Fortunately, development of the symptoms can be prevented by modifying the diet (environment) of babies that test positive for PKU shortly after birth. If homozygous individuals reduce their intake of dietary phenylalanine, particularly during childhood, they show normal brain development. Newborns in Australia are routinely tested for genetic disorders like PKU.

Fur colour in Himalayan rabbits

The coat colour of Himalayan rabbits provides an example of the effect of environmental temperature on phenotype. The Himalayan rabbit is homozygous for a mutant allele that encodes for a heat-sensitive enzyme called tyrosinase. Tyrosinase catalyses the production of melanin and other pigments. At normal body temperature, tyrosinase is produced but it is inactivated, resulting in no melanin being produced and a white coat. At low temperatures, tyrosinase is activated and results in the formation of melanin, causing black fur to form. When a small section of fur is shaved from a white region on the back, the fur grows back black if the animal is kept at low temperatures, but white if the animal is kept at high temperatures (Figure 7.2.5).

Flower colour in hydrangeas

Hydrangeas are a commonly seen example of environmental effects on phenotype. If cuttings of a single hydrangea plant are grown in very acidic soil (pH 5.5 or less), the flowers produced are blue. If the cuttings are grown in weakly acidic or alkaline soil (pH 6.5 or higher), the flowers are pink (Figure 7.2.6). The cuttings are of identical genotype, so it must be the environment (the pH of the soil) that affects the phenotype of the hydrangea.

FIGURE 7.2.6 Flower colours of cuttings of the same hydrangea plant grown in an acid soil (left) and an alkaline soil (right).

This effect is caused by the relationship between soil pH, a pigment called anthocyanin and the availability of aluminium in the soil for uptake by the plant. At a soil pH of 5.5 or less, aluminium is free to be taken into the plant. Anthocyanin is normally red, but it binds to aluminium in the plant to form a blue pigment called metalloanthocyanin, resulting in blue flowers. At a soil pH of 6 or higher the aluminium binds to soil particles and is less available to the plants. This leaves most of the anthocyanin in the plant in its red form, resulting in pink flowers.

This illustrates that genotypes establish the coded information for traits, and then the environment influences the expression of the alleles in the genotype to physiologically respond to the environment. Some alleles have a wide range of responses, meaning the amount of expression of the gene can vary significantly or alternative splicing can result in numerous variations of the proteins produced (see Chapter 5 and 6), hence the results in varied phenotypes. Other alleles have a limited range in the amount that the gene is expressed and there are few options for alternative splicing.

GENETIC DOMINANCE

The relationship between genotype and phenotype gives an insight into an important property of phenotypes known as **dominance**. For a given gene, the phenotype of the heterozygote compared with the appearances of each homozygote allows us to determine whether a phenotype is completely dominant, co-dominant or recessive. It is important to understand that dominance and recessiveness are properties of alleles, not genes. They are expressed as dominant or recessive phenotypes. Genes are neither dominant nor recessive.

Complete dominance

To understand complete dominance it is useful to consider the white eye gene in blowflies. There are two alleles for the white eye gene, *W* and *w*. Individuals with genotype *WW* have red eyes, while individuals with genotype *ww* have white eyes (Figure 7.2.7). Individuals with genotype *Ww* do not show an in-between trait such as pink eyes, but instead have red eyes, making them indistinguishable from those of the *WW* genotype.

Blowflies with genotype *Ww* display the red eye because the *W* allele makes enough membrane transporter protein to give the eye normal red pigment levels. The red eye colour phenotype is referred to as the **dominant phenotype**, because it only needs one *W* allele for that phenotype to be displayed. The white eye colour phenotype is referred to as the **recessive phenotype** because it is not observed in the heterozygote. It needs two copies of the *w* allele for it to be observed in the phenotype. This example shows that scientists can determine if a phenotype is dominant only by examining the heterozygote.

By convention, the allele associated with a dominant phenotype is represented by an upper-case symbol (e.g. *W*). The allele associated with a recessive phenotype is represented by a lower-case symbol (e.g. *w*). The blowfly's white eye is an example of complete dominance. *Ww* individuals have the same eye colour as *WW* flies.

Co-dominance

In **co-dominance** the full phenotypic expression of both alleles is observed. The classic example is the ABO human blood group system. Figure 7.2.8 shows red blood cells displaying the four possible phenotypes: AB, A, B and O. In the ABO blood group system, there are three allelic forms (I^A, I^B and i) at the same locus and individuals can have A, B, AB or O phenotypes. Those with the less-common AB blood group are heterozygotes carrying one allele (I^A) that produces the A antigen (a polypeptide) and one allele (I^B) that produces a B antigen (a different polypeptide).

Because both the A and B antigens are present on the surface of red blood cells and can be detected using appropriate antibodies, neither phenotype is truly dominant. This is co-dominance. Thus, A and B phenotypes are co-dominant and the O phenotype is recessive.

FIGURE 7.2.7 Blowflies with the *WW* and *Ww* genotypes have a red-eye phenotype (top). Blowflies with the *ww* genotype have a white-eye phenotype (bottom).

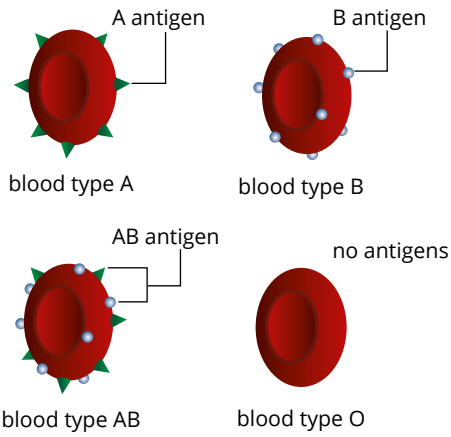


FIGURE 7.2.8 The four possible phenotypes of red blood cells: AB, A, B and O.

Incomplete dominance

Sometimes neither phenotype is completely dominant, and intermediate phenotypes occur. The presence of intermediate phenotypes occurs when one allele for a specific trait is not completely expressed over another allele. This form of dominance is known as **incomplete dominance**.

An example of incomplete dominance is found in snapdragons (Figure 7.2.9). Homozygous snapdragon flowers can have a red flower phenotype (R_1R_1) or a white flower phenotype (R_2R_2). In this case upper-case letters and subscripts are used to distinguish the alleles because neither phenotype is completely dominant. Plants of the R_1R_2 genotype have pink flowers. In R_1R_1 flowers, both copies of the R_1 allele produce an enzyme required to produce red pigment. In R_2R_2 flowers, no pigment is produced because the R_2 allele produces either no enzyme or a defective enzyme.

Since the R_1R_2 flower has one R_1 allele, which produces the active enzyme, and one R_2 allele, which does not, it will produce half the amount of pigment as the R_1R_1 flower. The resulting flower is pink.

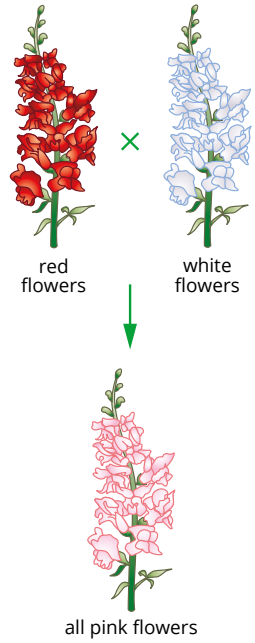


FIGURE 7.2.9 When red (R_1R_1) (left) and white (R_2R_2) (centre) snapdragons are crossed, the resulting heterozygotes are pink (R_1R_2) (right) because only half the amount of red pigment is produced.

MONOGENIC AND POLYGENIC TRAITS

An individual's phenotype is dependent on the alleles present and, depending on the trait, environmental conditions. Some phenotypes are determined by one set of genes. These phenotypes are considered to be monogenic. Phenotypes that are determined by the interaction of multiple genes are said to be **polygenic**.

Monogenic traits

Many traits, such as seed colour and texture in the case of Mendel's pea experiments, are controlled by the expression of single genes, hence the term monogenic. Monogenic traits tend to have very predictable inheritance patterns and a smaller range of phenotypes than polygenic traits.

The human ABO blood group is an example of a monogenic trait. As discussed above, the human ABO blood group system is determined by three alleles, represented as I^A, I^B and i. Allele I^A produces the A antigen, I^B produces the B antigen, and i produces no antigen. Each person carries two copies of these three possible alleles (a maternal and paternal copy). There are therefore six possible genotypes and four phenotypes (Figure 7.2.10).

ABO blood groups				
Blood type	**Type A**	**Type B**	**Type AB**	**Type O**
Possible allele combinations	$I^A I^A$ $I^A i$	$I^B I^B$ $I^B i$	$I^A I^B$	$i\ i$
Antigen (on RBC)	A antigen	B antigen	AB antigens	no antigens

FIGURE 7.2.10 The ABO blood group system is based on three alleles. The production of antigens A and B depends on the combination of alleles present.

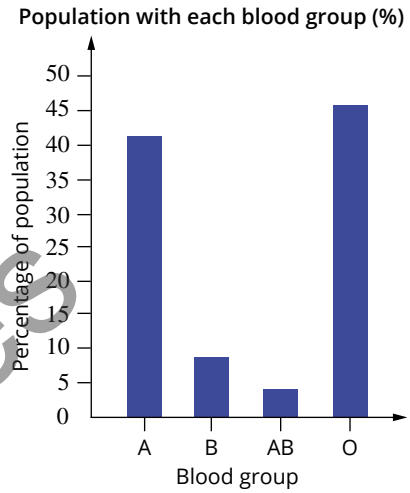


FIGURE 7.2.11 The ABO blood system is an example of discrete variation.

When only one gene with a few alleles controls a trait, and the environment has little effect on the phenotype, **discrete variation** of the phenotypes is observed. Discrete variation (also known as discontinuous variation) is when observed individuals show distinct classes or categories. Discrete variation of phenotypes is a characteristic of monogenic traits. The ABO blood system, described above, is one example of discrete variation of a monogenic trait (Figure 7.2.11).

Polygenic traits

For some traits, such as skin colour and height in humans, more than one gene (and a number of alleles for each gene) contributes to the phenotype of an individual. This is known as **polygenic inheritance** and results in a much greater range of phenotypes. Polygenic traits in non-human animals include wing shape and bristle count in *Drosophila*; birth weight, temperament and milking ability in cattle; and plumage and beak size in birds. When shown on a graph, the result is a bell-shaped curve (typical of **continuous variation**), which is referred to as a normal distribution.

Height in humans

Height in humans is controlled by about 50 genes or regions of the genome (Figure 7.2.12). Some individual characteristics of height are controlled by genes that include the secretion of thyroid gland hormones and human growth hormones. A deficiency in the amount of these hormones during childhood and puberty can result in stunted growth. Too much of them can cause excessive growth resulting in exceptional height. The greater the number of genes that control a characteristic, the more possible gene combinations exist. This results in a greater number of genotypes for a characteristic and more phenotypes.

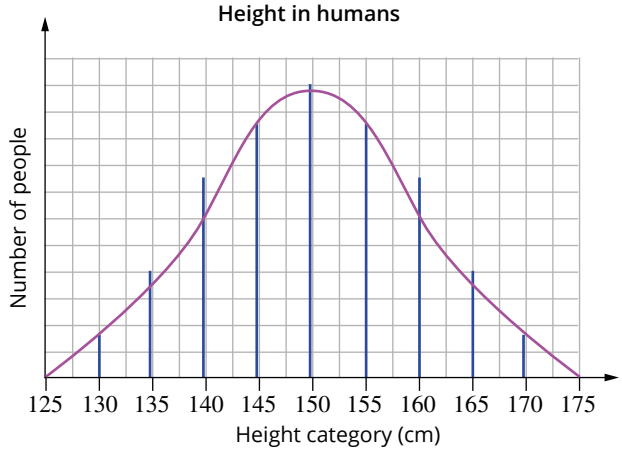


FIGURE 7.2.12 Height in humans is an example of continuous variation resulting from polygenic inheritance.

HISTOGRAMS

Variation in allele frequencies can be represented in the form of a histogram. Figure 7.2.13 shows frequencies for alleles related to a number of conditions in humans. Figures 7.2.11 and 7.2.12 (page 339) show simplified histograms for blood types and height. Frequency histograms like these can represent simplified data where discrete traits are listed on the x-axis and a percentage occurrence in a population is given on the y-axis. For example, Figure 7.2.11 shows that the B blood type occurs in approximately 8% of the sampled population.

Other histograms can be used in industries such as agriculture and biosciences. The histograms presented in Figure 7.2.13 show frequencies for alleles related to the length of maize (corn) ears and the width of maize ear leaves (the leaves that grow around the corn cob). The maize ear leaf is the largest leaf on the plant and is a large photosynthetic region for the plant. Leaf size significantly impacts plant growth and productivity. By studying data such as this histogram, plant scientists can select the best genotypes for crossbreeding or genetic engineering in order to produce superior crops.

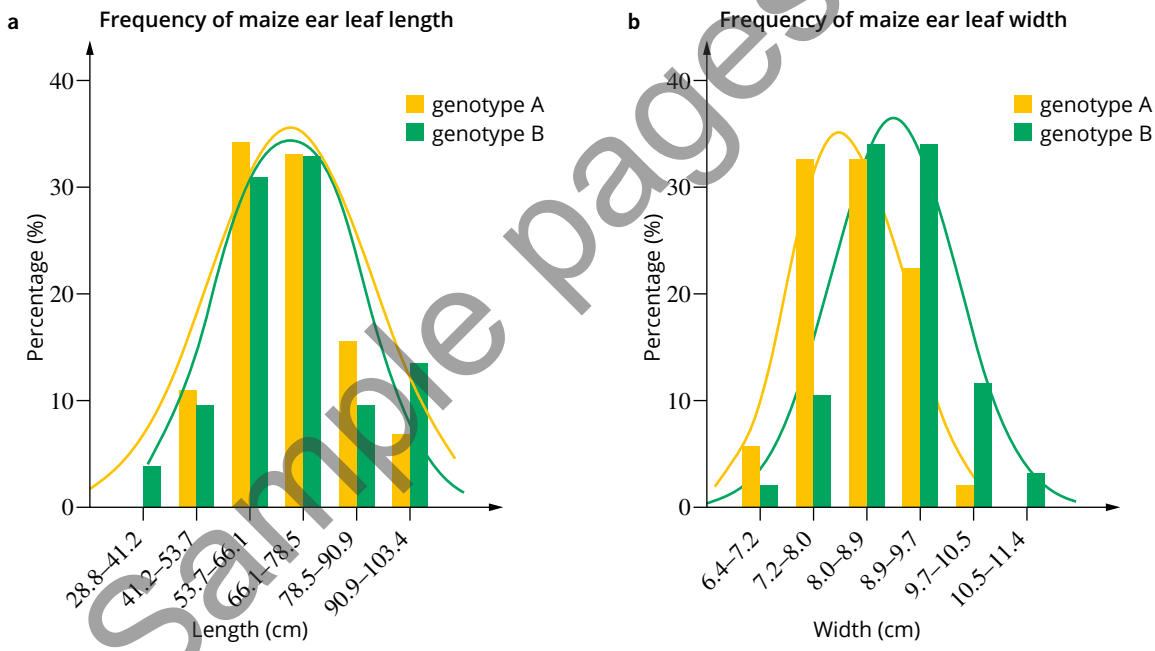


FIGURE 7.2.13 Allele frequency histograms for (a) maize ear length and (b) maize ear leaf width of two genotypes.

7.2 Review

SUMMARY

- Genotype is the combination of alleles at a particular locus.
- An organism that has two copies of the same allele is homozygous for that allele.
- An organism that carries two different alleles is heterozygous.
- Phenotype is an observable characteristic or trait that results from the genotype under the influence of the environment.
- Dominance and recessiveness are properties of alleles and are expressed as dominant or recessive phenotypes.
- A phenotype can be dominant or recessive depending on its appearance in the heterozygote.
  - A dominant phenotype is visible in the heterozygote and one homozygote.
  - A recessive phenotype is only observed in the homozygous condition.
- An italic upper-case letter is used to signify the allele for a dominant phenotype. An italic lower-case letter is used to signify the allele for a recessive phenotype.
- When more than one gene influences a trait, it is called polygenic inheritance.
- Polygenic inheritance causes a wide variety of phenotypes. This is called continuous variation.
- Discontinuous variation occurs when a single gene determines a trait.
- Phenotype is influenced by:
  - genotype
  - interactions between genotype and the environment.
- Fur colour in rabbits, flower colour in hydrangeas and the management of PKU are examples of the way that environment can affect an organism's phenotype.

KEY QUESTIONS

Retrieval

1 Define genotype.

2 Define phenotype.

3 Explain what is meant by a monogenic trait.

4 Recall a polygenic trait in humans.

Comprehension

5 Determine the possible combinations of the alleles *E* and *e* for a particular autosomal gene in an organism with 2*n*. Identify whether each is homozygous or heterozygous.

6 Describe what factors contribute to an individual's phenotype. Give an example.

7 Using an example, explain whether two organisms can have the same phenotype but different genotypes.

8 Explain, using examples, the difference between dominant and recessive phenotypes.

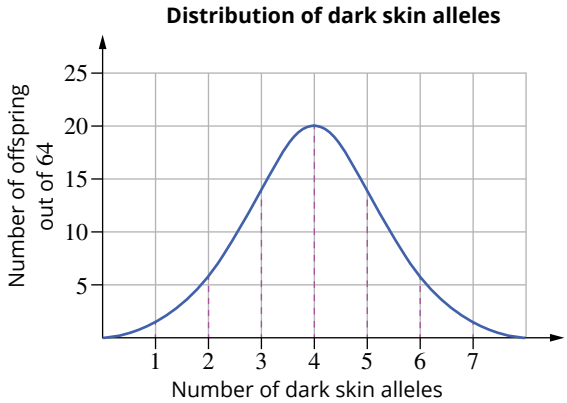
9 Explain why monogenic traits generally show discrete variation.

Analysis

10 From the frequency histogram below:

a Determine the most common allele.

b Calculate the percentage of the sample population that contains the most common allele.



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7.2 Review *continued*

11 Cystic fibrosis (CF) is a genetic disorder that affects the cells that produce mucus, sweat and digestive juices. The gene responsible for causing CF is located on chromosome 7. More than 1500 CF mutations have been identified. For an individual to express CF, they must inherit two mutated CF alleles. The table below shows the frequency of the four most common CF mutations in people living with CF in Australia in 2014.

Frequency of CFTR mutations in people living with CF in Australia, 2014

CFTR mutation	Number of alleles
F508del	4321
G551D	238
R117H	122
G542X	91
other	1298

a Construct a histogram from the table above.
b Determine if CF is a monogenic or polygenic trait.

7.3 Monohybrid crosses

BY THE END OF THIS MODULE, YOU SHOULD BE ABLE TO:

- recall Mendel's principles of inheritance
- choose appropriate symbols for alleles when calculating inheritance patterns
- calculate the outcome of a monohybrid cross
- calculate genotypic and phenotypic ratios
- conduct a test cross
- identify sex-linked patterns of inheritance
- calculate predicted offspring ratios from dihybrid crosses.

Much of what is now understood about natural variation and patterns of inheritance in sexually reproducing organisms was originally gained through the work of Gregor Mendel in the 1860s. Mendel accurately deduced the basic principles of inheritance by studying several inheritable traits in pea plants (Figure 7.3.1), using precise experimentation and careful observations over many years.

In this module, you will learn about the basic principles of inheritance, focusing on autosomal and sex-inked inheritance.

FIGURE 7.3.1 After carefully studying the results of crossing different pea plants in his garden, Gregor Mendel deduced the basic principles of inheritance.

MENDEL'S STUDY OF PATTERNS OF INHERITANCE

Mendel demonstrated that traits are passed from parents to offspring, and that these traits form specific patterns over generations of crossbreeding.

Mendel made several observations in his pea experiments:

- purple flowers were dominant over white flowers
- a round seed shape was dominant over a wrinkled seed shape
- a green pod colour was dominant over a yellow pod colour.

These variant or alternative phenotypes occur because of the various alleles of genes on autosomes. Autosomes are chromosomes that are not involved in sex determination (Module 7.2). One of Mendel's most significant observations was that the offspring of the pea plants did not always have the same phenotype as the parents, and that offspring from the same parents were often different from one another. Mendel hypothesised that hereditary units or 'factors' (now called genes) must have different forms (now called alleles) that separate randomly during the production of gametes. These forms would then unite after fertilisation, with each parent contributing one allele to the offspring. Mendel's hypothesis became known as the Law of Segregation or Mendel's first law.

Dominant phenotypes are expressed if the individual carries at least one allele for the dominant trait. Recessive phenotypes are expressed only if the individual carries two alleles for the recessive trait, or is homozygous recessive.

A **cross** is the intentional breeding of two genetically different organisms that results in offspring that inherit genetic material from each parent. A cross of the traits being studied can be carried out to determine which trait is dominant. A **monohybrid cross** is a cross between two individuals with different alleles at a single locus. Multiple crosses of successive generations can be used to determine allelic dominance.

- The first generation is termed the **parental generation** (P).
- Offspring of the parental generation is termed the first filial generation (**F1 generation**).
- Offspring of F1 generation is called the second filial generation (**F2 generation**).

The phenotypic ratios in the F1 and F2 generations indicate which phenotypes are dominant or recessive. Mendel used monohybrid crosses to discover the dominance relationships of traits in pea plants (Figure 7.3.2).

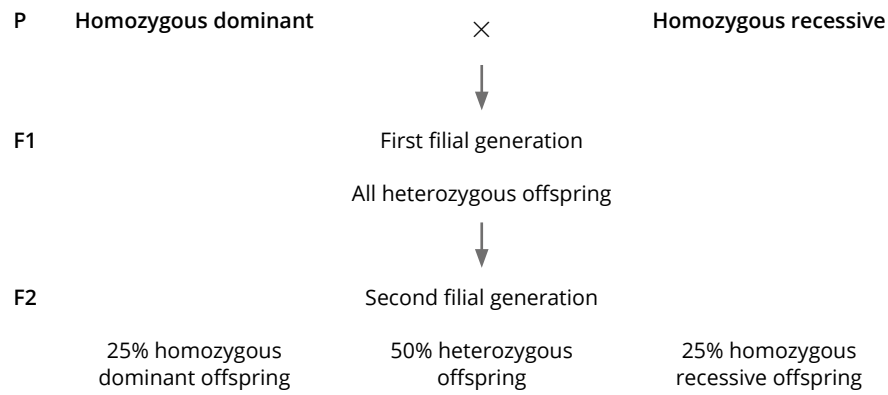


FIGURE 7.3.2 The expected genotypic ratios in the F1 and F2 generations.

AUTOSOMAL DOMINANT INHERITANCE

Autosomal dominant inheritance (complete dominance) refers to a dominant trait that is passed on to offspring via an autosomal gene (Module 7.2). Only one copy of the allele from one parent is needed to express a dominant phenotype.

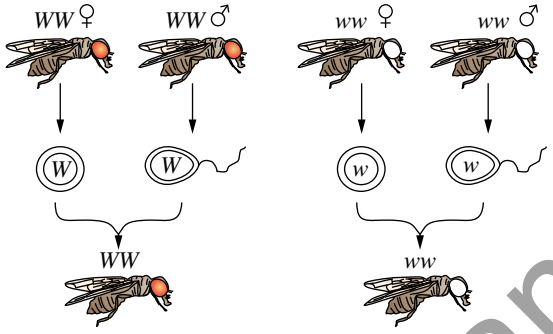


FIGURE 7.3.3 Homozygous genotypes produce only one type of gamete. By crossing homozygotes of the same genotype together, a true-breeding strain can be established.

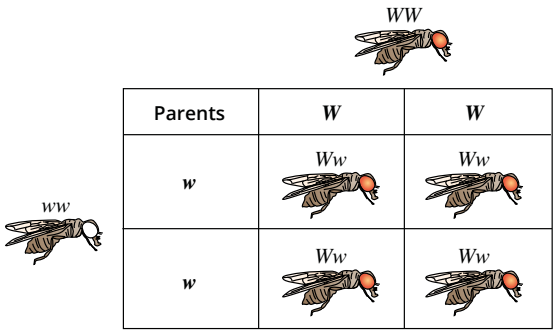


FIGURE 7.3.4 A Punnett square for a cross between two homozygous parents to produce an F1 generation. All F1 individuals are heterozygous.

Parent generation

The inheritance of eye colour in the Australian sheep blowfly is an example of a single gene with two alleles (found on an autosomal chromosome) coding for the trait. In the blowfly, red eye colour is dominant over white eye colour. The homozygous genotypes are *WW* and *ww*. Homozygous genotypes produce only one type of gamete. *WW* individuals produce only *W* gametes and *ww* individuals produce only *w* gametes.

In a cross between two red-eye homozygous (*WW*) individuals, all the offspring would be homozygous *WW* (red eye). As long as *WW* individuals were crossed together, it would be a **true-breeding** red eye strain. Similarly, as you can see on the right side of Figure 7.3.3, crosses between two homozygous white eye (*ww*) individuals would yield a true-breeding white eye (*ww*) strain.

Punnett squares

In 1905, geneticist Reginald Punnett devised a simple method for showing the random combination of gametes and the genotypes of the resulting offspring. In a Punnett square, the alleles of each parent are first written in the top and side cells. By going down each column and across each row, the alleles are combined and written into the remaining cells, showing the expected genotypic ratios of the offspring (Figure 7.3.4)

When choosing symbols for alleles, it is common practice to select one that relates to the dominant phenotype. For example, if the dominant phenotype is grey fur, the dominant allele would be given the symbol *G* and the recessive phenotype would be *g*.

However, the symbols *W* and *w* are traditionally used for eye colour alleles in flies, even though red eye colour is dominant. This is because other genes are involved in eye colour in flies, and the discoverers of this gene named it 'white eye gene'.

Punnett squares make it easy to establish all the possible combinations of alleles carried by the gametes and, therefore, all the possible genotypes of the offspring. This is useful in fields such as animal husbandry and horticulture because it allows breeders to select individuals to cross according to the desired traits of the offspring.

F1 generation

To test the principle of dominance, two true-breeding parents with two different traits can be crossed. This type of cross is known as hybridisation, and the offspring are known as **hybrids**.

In the blowfly example, two true-breeding strains (one with red eyes, *WW*, and one with white eyes, *ww*) can be crossed to produce an F1 generation. The results of the cross can be shown in a Punnett square (Figure 7.3.4).

Each of the offspring in the F1 generation has the heterozygous genotype *Ww*. The phenotype resulting from this genotype is red-eyed. From this, it can be deduced that the red-eye phenotype is dominant over the white-eye phenotype.

F2 generation

The F2 generation is the result of crossing the individuals from the F1 generation. In this example, half of the gametes produced by an F1 individual (*Ww*) will be *W* and half will be *w*. Three different combinations of alleles are possible in the F2 generation: *WW*, *Ww* and *ww* (Figure 7.3.5).

Parents	*W*	*w*
W	*WW*	*Ww*
w	*Ww*	*ww*

FIGURE 7.3.5 A Punnett square of a cross between two F1 individuals to produce an F2 generation.

The Punnett square shows that the F2 genotypic pattern is:

WW : *Ww* : *Ww* : *ww* or 1 *WW* : 2 *Ww* : 1 *ww*

Because red eye colour is dominant over white eye colour, the F2 phenotypic pattern is:

3 red-eyed flies (*WW* : *Ww* : *Ww*) : 1 white-eyed fly (*ww*)

In other words, in the F2 generation, the dominant phenotype is likely to occur in 3 out of 4 crossings, and the recessive phenotype only once.

From this information, it can be determined that the trait that is most common in the natural population is red eyes. The most common trait in the natural population is also known as the **wild type**.

The genotypic pattern 1 : 2 : 1 ratio of the F2 generation resulting from a monohybrid cross occurs for two reasons:

- In meiosis, heterozygous (*Ww*) individuals (both male and female) produce two gametes (a *W* gamete and a *w* gamete). This is because of the separation of pairs of alleles during the formation of reproductive cells.
- Fertilisation occurs at random. A *W* sperm has equal chance of fertilising a *W* egg or a *w* egg, because these eggs are produced in equal frequency. A *w* sperm also has an equal chance of fertilising a *W* egg or a *w* egg. The four equally possible genotypic outcomes are *WW*, *Ww*, *wW*, *ww*.

The Punnett square accounts for both of these factors in demonstrating the possible outcomes of the cross.

Genotypic and phenotypic ratios

Genotypic and phenotypic ratios are used to express the expected frequency of genotypes and phenotypes in the offspring from a genetic cross. Punnett squares are used to calculate the expected outcomes of a cross and the possible genotypes and phenotypes generated in the offspring.

The ratio of genotypes in the offspring is written in the following order:

homozygous dominant : heterozygous : homozygous recessive

The ratio of phenotypes observed in the offspring is written as:

dominant phenotype : recessive phenotype

Genotypic and phenotypic ratios sometimes differ because the dominant or recessive nature of traits means that different genotypes can result in the same phenotype. For example, both *WW* and *Ww* result in red eyes in flies.

Test crosses

It is not immediately obvious whether an individual with a dominant phenotype is homozygous, because it might be either *AA* or *Aa*. Apart from sequencing the gene involved (which is very expensive and time-consuming), the only way to determine this is to do a **test cross**. A test cross involves crossing the individual with another that has the recessive trait and is therefore homozygous. Homozygous individuals produce gametes with one type of allele, whereas heterozygous individuals can produce gametes with two types of alleles.

If the offspring from the test cross all have the dominant phenotype, then both the parents are likely to be homozygous. (It is not possible to be certain because of the random nature of fertilisation.) If the offspring have both dominant and recessive phenotypes, then the parent with the dominant phenotype must also carry a recessive allele and is therefore heterozygous.

Coat colour in guinea pigs

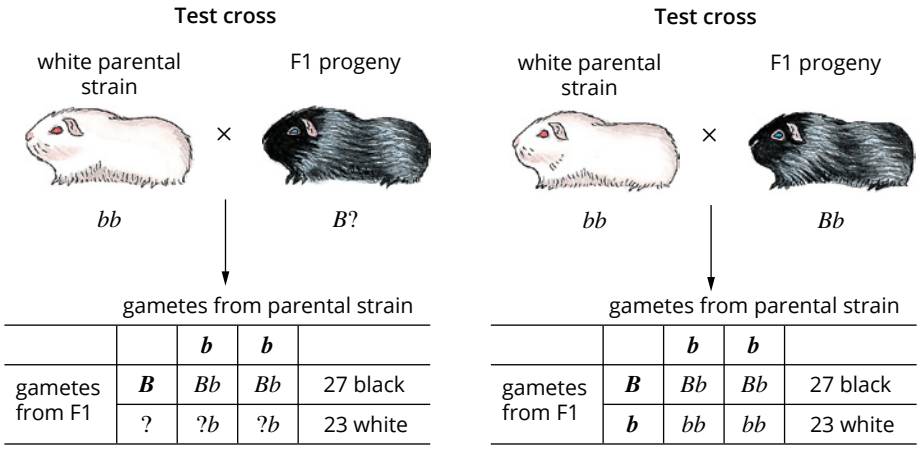
The coat colour of guinea pigs is determined by the alleles of one gene, and black fur is the dominant phenotype. If a true-breeding white guinea pig (*bb*) is crossed with a true-breeding black guinea pig (*BB*), the resulting F1 has black fur (*Bb*). But if the genetic history of a black guinea pig is unknown, its genotype can be determined by crossing the black guinea pig with a white guinea pig, which must be *bb* (homozygous recessive).

Figure 7.3.6 illustrates the test cross that would be carried out. Of the resulting offspring in this example, half are white and half are black. This ratio of 1 : 1 is consistent with the results of a heterozygote crossed with a homozygote if the trait is determined by the alleles of one gene and one trait is dominant. Therefore, the black guinea pig is likely to be heterozygous. If all the offspring of the test cross had black coats (all *Bb*), the black F1 guinea pig would have been shown to be homozygous dominant (*BB*).

The predicted outcome for a cross between heterozygote black guinea pigs is 1 black (*Bb*) : 1 white (*bb*). However, as the diagram shows, the resulting ratio of the test cross was 27 black (*Bb*) : 23 white (*bb*) rather than, for example, 23 : 23 (which is equal to a 1 : 1 ratio). The difference between predicted and observed ratios is due to chance.

Punnett squares provide only the theoretical results of a cross. The actual results from an experiment may be different. Fertilisation can be compared to tossing a coin: for most genes, there are two possible outcomes. If a coin is tossed, there is a 50% chance of getting heads and a 50% chance of getting tails. If the coin is tossed 10 times, you might not get 5 heads and 5 tails, but if it is tossed 1000 times, a heads : tails ratio very close to 1 : 1 would be observed.

Similarly, the more fertilisation events (data) there are in a breeding experiment, the closer the results will be to the theoretical ratio.



		b	b	
gametes from F1	B	Bb	Bb	27 black
	?	?b	?b	23 white

		b	b	
gametes from F1	B	Bb	Bb	27 black
	b	bb	bb	23 white

FIGURE 7.3.6 A test cross between a white guinea pig and a black guinea pig whose genotype is not known.

PA 4.1.3

AUTOSOMAL CO-DOMINANT INHERITANCE

Some traits do not show simple dominance or recessiveness. These are instances in which both alleles are expressed to varying degrees in the phenotype of heterozygous individuals. This is called co-dominance.

Autosomal co-dominance

One example is co-dominance in snapdragons, where in the case of flower colour, neither trait is dominant. In the individual heterozygous for this trait, neither allele is completely expressed and the result is a blending effect of the two phenotypes.

In snapdragon flowers, R_1 represents the red colour allele and R_2 represents the white colour allele. In this case, because neither is completely dominant, upper-case letters and subscripts are used to distinguish the alleles.

Crossing red-flowering snapdragons (R_1R_1 genotype) with white-flowering snapdragons (R_2R_2 genotype) will yield an F1 generation in which all individuals have the genotype R_1R_2 and are pink-flowering (Figure 7.3.7a). If the F1 plants (R_1R_2 × R_1R_2) are crossed, an F2 generation with a 1 : 2 : 1 genotypic ratio (1 R_1R_1 : 2 R_1R_2 : 1 R_2R_2) would be expected (Figure 7.3.7b).

Parents		Red flowers	
		R_1	R_1
White flowers	R_2	R_1R_2	R_1R_2
	R_2	R_1R_2	R_1R_2

Parents		Pink flowers	
		R_1	R_2
Pink flowers	R_1	R_1R_1	R_1R_2
	R_2	R_1R_2	R_2R_2

The heterozygote pink-flowering snapdragon (R_1R_2) can be distinguished from the two homozygotes, red R_1R_1 and white, R_2R_2 due to the co-dominance of both the red and white alleles resulting in a pink-flowering phenotype.

Genotype ratio: 1 R_1R_1 : 2 R_1R_2 : 1 R_2R_2

Phenotype ratio: 1 white : 2 pink : 1 red

This phenotypic ratio of 1 : 2 : 1 (Figure 7.3.7) is different to the 3 : 1 ratio of two phenotypes observed in complete dominance.

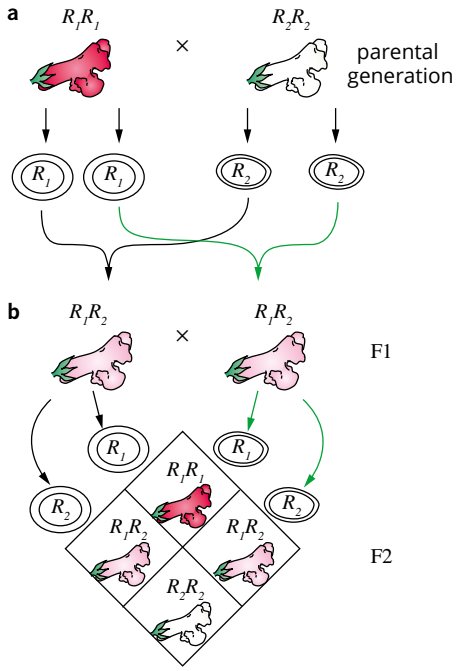
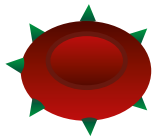
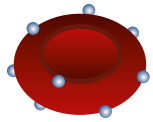
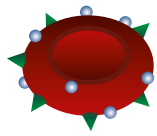
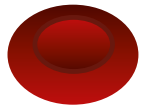


FIGURE 7.3.7 (a) A cross between homozygous red and white snapdragons produces pink-flowering progeny in the F1 generation. (b) If plants from the F1 are then crossed, a phenotypic ratio of 1 red : 2 pink : 1 white would be expected in the F2 generation.

Multiple alleles at a single locus

Blood group systems provide a demonstration of the effects of multiple alleles at the same locus. For example, in the ABO blood grouping system the three alleles are represented as I^A, I^B and i. I^A codes for the A antigen, I^B codes for the B antigen and i does not produce either antigen. The effects of I^A and I^B dominate over i, while the A and B phenotypes co-dominate. Each person carries copies of one or two of these three possible alleles. Table 7.3.1 shows the possible genotypes and phenotypes for the ABO blood group system.

TABLE 7.3.1 Possible genotypes and phenotypes in the ABO blood group system

Genotype	Phenotype (blood group)	Red blood cell
I^AI^A I^Ai	A	
I^BI^B I^Bi	B	
I^AI^B	AB	
ii	O	

From Table 7.3.1 it can be seen that there are six possible genotypes and four phenotypes, with the A and B blood groups both having two possible genotypes.

The possible genotypes and phenotypes of the offspring of a parent with blood type O and a parent with blood type AB can be determined using a Punnett square, as shown below.

Parents		**Blood type AB**	
		I^A	I^B
Blood type O	i	I^Ai	I^Bi
	i	I^Ai	I^Bi

The F1 generation in this example would be either blood type A or B, but all would be heterozygous.

If a heterozygous individual for blood type A and a heterozygous individual for blood type B were to have children, four possible combinations of blood type are possible, as shown in the following Punnett square.

Parents		**Blood type B**	
		I^B	i
Blood type A	I^A	I^AI^B	I^Ai
	i	I^Bi	ii

The F1 generation would show all of the phenotypes possible: AB, A, B and O. The important principle illustrated by this example is that phenotypes are not always dominant or recessive. The dominance of a phenotype is always in relation to another phenotype. Thus, phenotype A is co-dominant with B, but dominant to O.

WS 4.1.9

SEX-LINKED INHERITANCE

So far you have examined the inheritance of genes located on autosomes. However, the patterns of inheritance are not the same for genes located on either of the two sex chromosomes. Phenotypes inherited through genes on sex chromosomes are said to be 'sex-linked' and they show **sex-linked inheritance**. It is important to remember that sex chromosomes also carry other genes that are not related to sex determination.

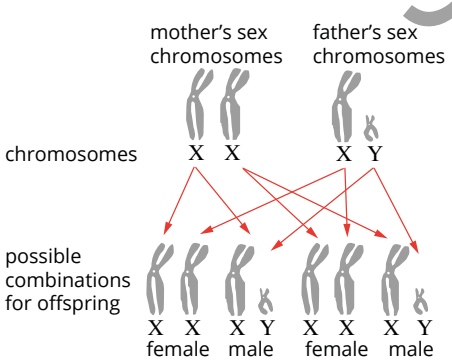


FIGURE 7.3.8 Inheritance of the sex chromosomes in the XY sex-determination system. The outcome of this inheritance is two possible arrangements—XX or XY with half the offspring being female and half being male.

Figure 7.3.8 shows how sex chromosomes are transferred to the offspring, with an equal probability of the offspring being female or male. The XY system determines sex in humans, most other mammals, some insects and some plants. In this system, females are homogametic (XX) and males are heterogametic (XY). The female passes one X chromosome on to her offspring, while the male can pass on either an X or Y chromosome. An X chromosome from the father produces female offspring and a Y chromosome from the father produces male offspring. It is the father's genetic contribution that determines the sex of the offspring. In birds, some fish, some insects and some reptiles, sex is determined by ZW chromosomes. In this system, females are the heterogametic sex (ZW) and males are the homogametic sex (ZZ).

X-linked recessive inheritance

In humans, X-linked recessive traits are predominantly expressed in males, because males carry only one X chromosome. Females carrying an X-linked recessive allele might not express the trait, or show only mild expression. This is because the second X chromosome that females carry could mask the recessive trait. The probability in humans of a female carrying two X-linked recessive alleles is very low.

The pattern of sex-linked inheritance is evident when a **reciprocal cross** is performed. A reciprocal cross is an experiment to investigate the role of parental sex on the inheritance of genotypes. A reciprocal cross involves two crosses: one crossing a male with the trait of interest with a female not expressing the trait (usually homozygous wild type), and another crossing a female with the trait of interest (homozygous) with a male that does not express the trait (usually wild type). If the trait is sex-linked (carried on the X chromosome), the phenotypic ratios of the male and female offspring will be different.

Paralysis in Drosophila

The temperature-sensitive paralytic gene, named after the mutant phenotype, is on the X chromosome of the fruit fly (*Drosophila melanogaster*). A mutant phenotype arises from a genetic mutation that causes phenotypic change from the normal wild type phenotype. Individuals with the mutant allele are paralysed when incubated to a temperature of 29°C, whereas wild type flies show normal behaviour at this temperature. The paralytic phenotype is recessive to the wild type. For this trait, wild type flies move around normally and are not paralysed when the temperature is 29°C.

Alleles are defined differently for sex-linked traits. An *X* is used to indicate that the trait is carried on the X chromosome, and the allele is written in superscript next to the X. In the example of the fruit flies, the alleles can be written as:

X^P = wild type

X^p = paralysis.

As the paralytic phenotype is recessive, females that are homozygous for the mutant allele (X^pX^p) express the mutant paralysis phenotype. Females that are homozygous dominant (X^PX^P) and females that are heterozygous (X^PX^p) both have the wild type phenotype.

As males have only one X chromosome, there are only two male genotypes: X^pY males are paralytic and X^PY males are wild type.

If paralytic females (X^pX^p) are crossed with wild type males (X^PY), all of the F1 male offspring will be paralytic (X^pY) and all of the F1 female offspring will be wild type phenotype (X^PX^p) (Figure 7.3.9a). This pattern of transmission of the mutant phenotype from the female parent to male offspring is characteristic of X-linked recessive inheritance.

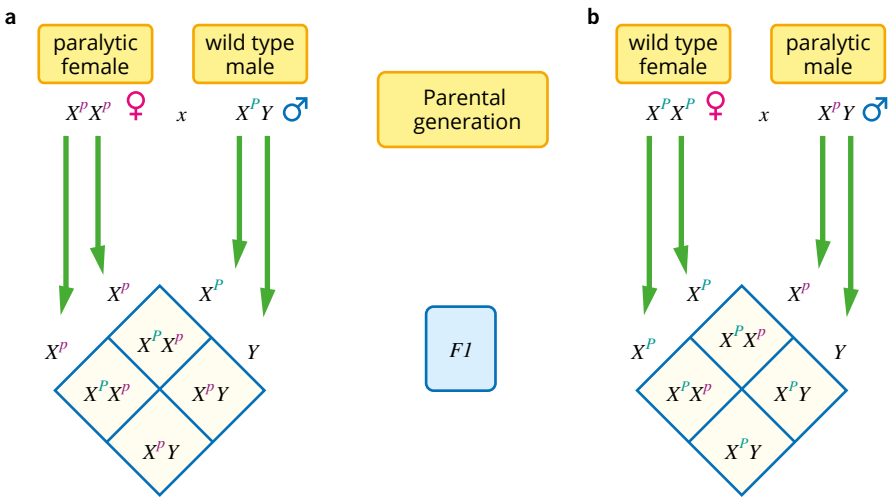


FIGURE 7.3.9 The characteristics of X-linked inheritance are evident in a reciprocal cross. (a) A male receives an X chromosome from the female parent, so males are paralytic (X^pY) and females are wild type (X^PX^p). (b) In the reciprocal cross, both the male and female offspring are wild type.

The reciprocal cross produces a different outcome (Figure 7.3.9b on page 349). If a wild type homozygous female (X^PX^P) is crossed with a paralytic male (X^pY) all of the offspring (male and female) are wild type (X^PX^p and X^PY).

These different outcomes of the reciprocal crosses are characteristic of X-linked recessive inheritance.

Haemophilia in the British royal family

Figure 7.3.10 is a pedigree chart showing part of the family tree of the British royal family (pedigree charts are discussed further in Module 7.4). The chart includes Queen Victoria, whose eighth child, Leopold, was born with haemophilia. Haemophilia is a blood disorder in which blood clotting is slow, resulting in excessive bleeding. It results from a mutation in a gene on the X chromosome that is involved in the production of a blood-clotting protein that controls bleeding.

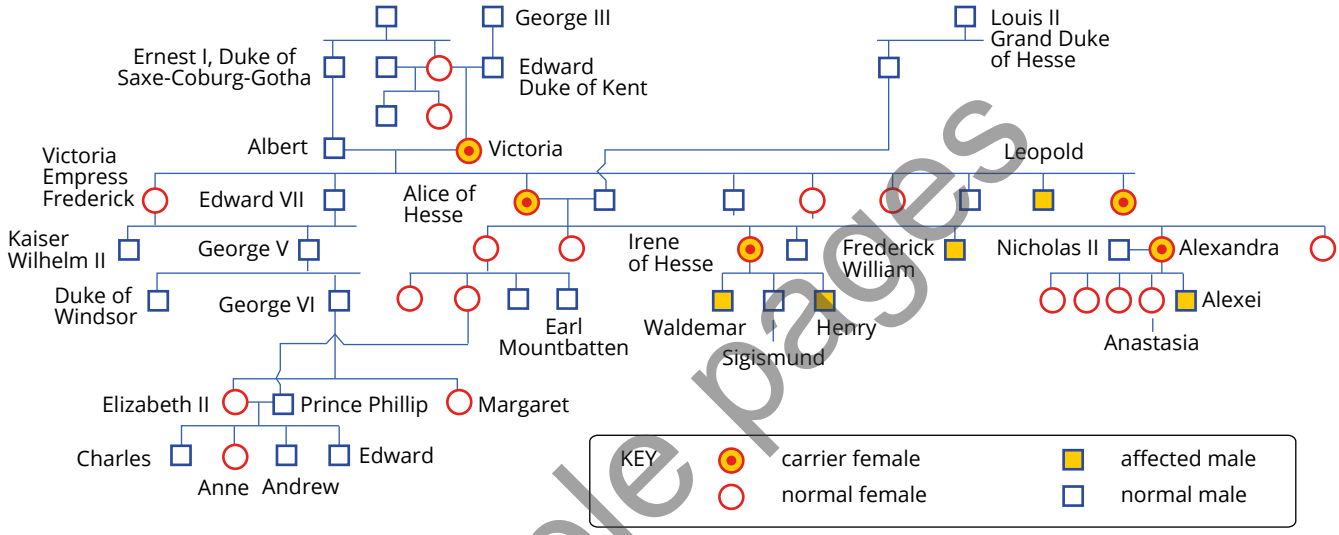


FIGURE 7.3.10 Queen Victoria was a carrier of a mutation that causes haemophilia. The affected gene codes for a blood-clotting protein. She had one copy of the normal allele and one copy of the mutant allele. Some of Queen Victoria's female descendants have been carriers, and some male descendants have had the disease.

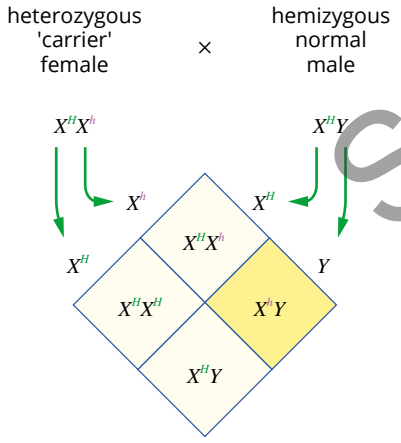


FIGURE 7.3.11 Diagram highlighting the typical situation for the inheritance of X-linked recessive diseases such as haemophilia. A female who is phenotypically normal carries one copy of the allele for the dominant normal phenotype X^H and one for the recessive (mutant) phenotype X^h. All of the female offspring will have a normal phenotype, but there is a 50% chance that each male offspring will inherit the disease.

The incidence of haemophilia in the descendants of Queen Victoria shows the hallmarks of X-linked recessive inheritance. All of the haemophiliacs shown in the tree are male. The female **carriers** of the disease are heterozygous, carrying one haemophiliac allele and one normal allele. Given that the haemophilia phenotype is recessive, carrier females are phenotypically normal. However, because females produce eggs carrying the normal and haemophiliac alleles with equal frequency, and males receive their single X chromosome from the egg, there is a 50% chance that the son of a carrier will have haemophilia.

Through marriage, some of Victoria's phenotypically unaffected daughters who carried this mutation spread haemophilia to other royal families in Europe. For example, Irene of Hesse transmitted the haemophilia allele to her sons Waldemar and Henry, and the normal allele to her other son, Sigismund. This form of haemophilia occurs at a frequency of 1 in 10 000 males and 1 in 100 million females in the general population.

In general, X-linked recessive disorders occur at much higher frequencies in males than females because, in order to be affected, females need to inherit a copy of the allele from both parents (their mother must be a carrier and their father must be affected by the disorder). Males, however, need only inherit one copy of the X-linked allele from their carrier mother (Figure 7.3.11).

X-linked dominant inheritance

X-linked disorders may also display a dominant phenotype. Consider the inheritance of vitamin D–resistant rickets disorder, which causes bone deformities, a pedigree for which is shown in Figure 7.3.12 (pedigree charts are explained in more detail in Module 7.4). The mother of the first generation is heterozygous and affected by the condition. Her children had a 50% chance of having vitamin D–resistant rickets, regardless of whether they were male or female.

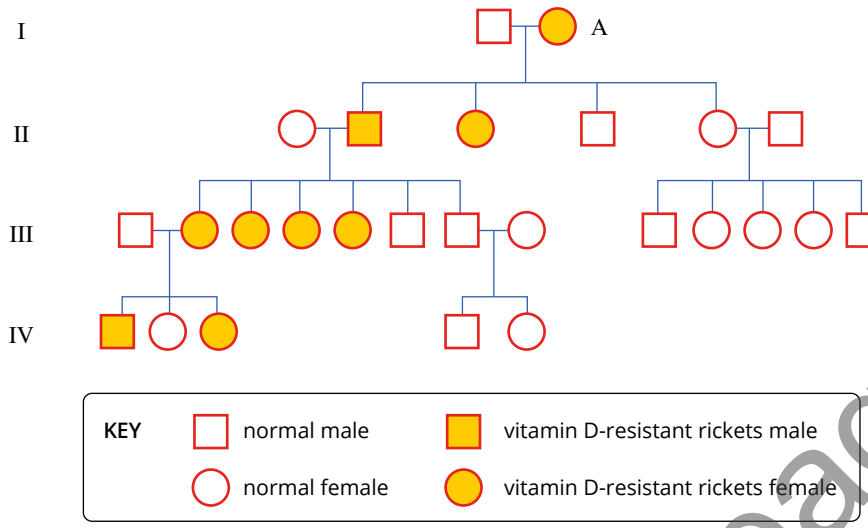


FIGURE 7.3.12 Pedigree chart showing the inheritance of the X-linked dominant condition vitamin D–resistant rickets. The mother (A) of the first generation is heterozygous for the gene that controls the condition.

When a father is affected and a mother is normal (as in the first generation), all female offspring will show the condition, and all male offspring will be normal. This is because female children all receive an X chromosome, which carries the allele for the disease, from their father.

The alleles for this trait could be shown as:

X^D = vitamin D–resistant rickets allele

X^d = normal allele

The following Punnett square shows the pattern of inheritance of offspring of a heterozygous female affected by the vitamin D–resistant rickets allele and a male with the normal allele.

Parents		**Mother**	
		X^D	X^d
Father	X^d	X^DX^d	X^dX^d
	Y	X^DY	X^dY

The possible genotypes of the offspring are:

$X^DX^d : X^dX^d : X^DY : X^dY$

1 : 1 : 1 : 1

The possible phenotypes are therefore:

vitamin D–resistant rickets female : normal female : vitamin D–resistant rickets male : normal male

1 : 1 : 1 : 1

The following Punnett square shows the pattern of inheritance of the offspring of a homozygous unaffected female and a male with the vitamin D–resistant rickets disorder.

Parents		Mother	
		X^d	X^d
Father	X^D	X^DX^d	X^DX^d
	Y	X^dY	X^dY

The possible genotypes of the offspring are:

$X^DX^d : X^dY$

1 : 1

The possible phenotypes are therefore:

all females have vitamin D–resistant rickets : all males are unaffected

Male pattern baldness

It is estimated that 80% of hair loss is genetic, and though the causes are not yet well understood, it is known that several genes are involved. Baldness is therefore a polygenic trait.

Male pattern baldness is the most common type of baldness. It affects around 40% of men by the age of 40 and around 60% by the age of 60. Affected males gradually start losing their hair, until eventually they have hair only on the sides and back of the head (Figure 7.3.13).

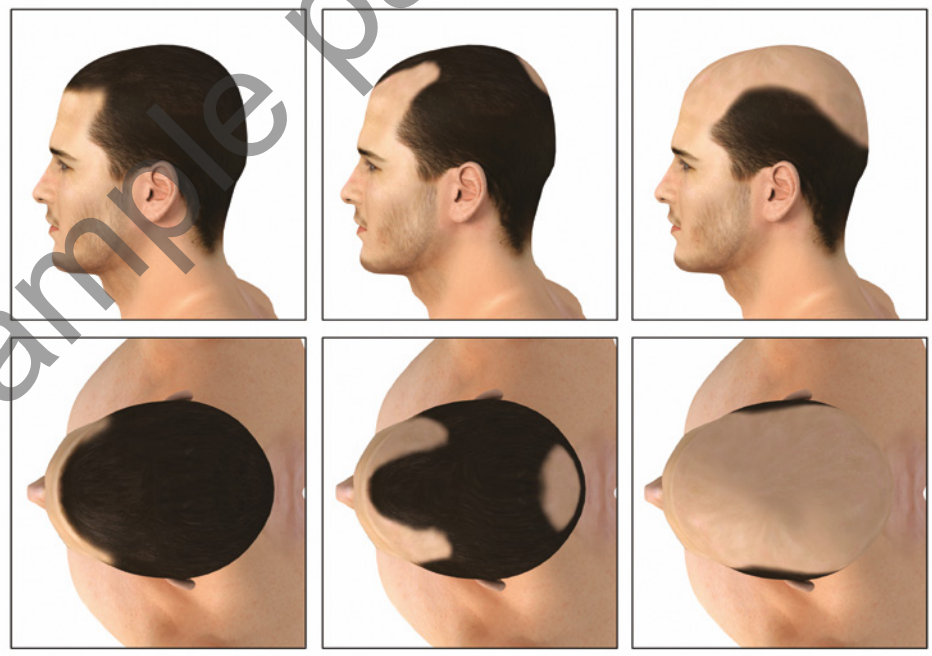


FIGURE 7.3.13 Head of a man showing the change over time of hairline with male pattern baldness. This phenotype can be caused by several genes located on autosomes and the X chromosome.

You may have heard that baldness is inherited from your mother's father. This is because one of the key genes associated with balding is on the X chromosome. If your mother's father has male pattern baldness, then your mother will carry the allele for this characteristic on the X chromosome that she inherited from her father. Because you inherited one of your X chromosomes from your mother, there is a 50% chance that you will inherit the affected X chromosome. However, males are much more likely to express the balding phenotype because females have a second X chromosome to mask the expression of the gene.

Balding can also be passed from fathers to offspring, indicating that autosomal genes must be involved. Two genes on chromosome 20 have been found to contribute to balding. The effects of these genes are neither dominant nor recessive, but have an additive effect—the more copies of the alleles you have, the more likely you are to go bald. Even though these genes are found on autosomes, males are affected more than females. This is because some of the genes are associated with male hormone receptors. This is an example of **sex-limited inheritance**—males and females may have the same genotype but express different phenotypes.

Y-linked inheritance

Compared to the X chromosome, the Y chromosome has few genes. It has only about 72 protein coding genes, compared to 800–900 on the X chromosome. Most of these genes are involved in male sex determination and fertility. Therefore, there are far fewer **Y-linked** traits than X-linked traits.

If a trait is passed from father to son and never observed in females, it is likely to be Y-linked, meaning the gene for that trait is on the Y chromosome. Until recently hairy ears were thought to be controlled by a Y-linked gene, but recent studies suggest there are also autosomal genes involved in the trait.

Sex-limited inheritance

The Y-linked pattern of inheritance is sometimes confused with sex-limited inheritance. Sex-limited traits can only occur in one sex because the feature affected is unique to that sex. Therefore males and females have different phenotypes. For example, complete androgen insensitivity syndrome, in which the fetus is unresponsive to male hormones, can only occur in males, because only males carry the Y chromosome. This means that even if females have the genotype for this syndrome, they cannot express the condition.

7.3 Review

SUMMARY

- The Law of Segregation states that individuals carry pairs of alleles of each gene, which segregate into gametes during meiosis so that each gamete carries one allele of each gene.
- True-breeding strains are homozygous at the locus of interest and produce genetically identical progeny when crossed with each other.
- A phenotypic ratio approaching 3 : 1 will be observed in the F1 generation of a monohybrid cross between two heterozygous individuals for any trait controlled by a single autosomal gene, with two different alleles, controlling a dominant trait.
- A test cross involves crossing an individual displaying the dominant phenotype but unknown genotype with an individual displaying the recessive phenotype(s).
- Test crosses are used to determine whether an individual of dominant phenotype is homozygous or heterozygous.
- A phenotypic ratio approaching 1 : 2 : 1 will be observed in the F2 generation of a monohybrid cross for any trait controlled by a single autosomal gene, with two different alleles, displaying co-dominance.
- Co-dominant inheritance can be seen in ABO blood grouping.
- Phenotypes inherited through the action of genes located on either the X or Y chromosomes show sex-linked inheritance.
- X-linked recessive inheritance shows a pattern of transmission of the mutant phenotype from the female parent to male offspring.
- X-linked dominant inheritance shows a pattern of transmission of the dominant trait from an affected male parent to all female offspring and from an affected heterozygous female parent to 50% of all offspring.
- Y-linked inheritance shows a pattern of transmission of the trait from father to son, and it is never observed in females.

KEY QUESTIONS

Retrieval

1 Explain what an autosomal dominant trait is.

2 Explain the function of a Punnett square in genetics.

3 Define sex-linked inheritance.

4 Recall the term given to the first generation of offspring from a test cross.

Comprehension

5 **a** Define monohybrid cross. Select an example to illustrate your answer.
b In analysing data from a monohybrid cross, explain why you might not expect the results to be exactly the same as the expected ratios.
c Identify what experimental change would increase the probability of the measured data matching the expected ratios.

6 Explain what the following ratios of phenotypes in the F2 generation suggest about inheritance patterns for a particular trait.
a 3 : 1
b 1 : 2 : 1

7 Use the example of eye colour inheritance in the Australian sheep blowfly to answer the following questions.
a Define pure-breeding strain.
b Distinguish between the parental (P), first filial (F1) and second filial (F2) generations.
c Explain why the individuals of the F1 generation are all red-eyed.
d Explain why the phenotypes in the F2 generation occur in the ratio 3 red eye : 1 white eye.

8 Freckles are an inherited trait that result in the formation of spots on fair skin. The gene responsible for freckles is found on chromosome 4 and shows a dominant inheritance pattern.

a Determine the type of inheritance, autosomal or sex-linked.

b Explain how a mother and father who have freckles can have a child that does not have freckles. Determine the probability of this result. Include a Punnett square in your answer.

9 Explain why sex-linked disorders affect males more than females.

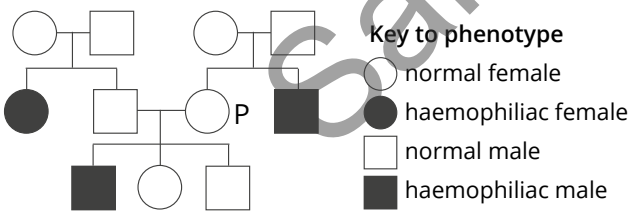
10 Explain why there are fewer Y-linked disorders than X-linked disorders.

11 Determine the probability of the outcome in the following scenario. Blue eyes in humans is a homozygous recessive trait. All other eye colours are dominant to blue. If two non-blue-eyed individuals, who each have one blue-eyed parent, were hoping to have a blue-eyed child together, determine the probability of them having a blue-eyed child.

Analysis

12 Determine the probability of Robert, who has blood type A, and Lee, who has blood type B, having a baby of blood type O. Assume Robert and Lee are heterozygous. Include a Punnett square in your answer.

13 The figure below shows the inheritance of haemophilia in a family. Haemophilia has a recessive X-linked inheritance pattern.



Determine the genotype of individual P. Show your working using a Punnett square and symbolise your answer appropriately.

14 A genetics student undertakes a study of inheritance patterns of feather colour in domestic chickens. The student observes the following:

- Matings between black-feathered adults always result in black-feathered offspring.
- Matings between white-feathered adults always result in white-feathered offspring.
- Matings between black-feathered adults and white-feathered adults produce only blue/grey-feathered offspring.
- Matings between blue/grey-feathered adults result in black, blue/grey and white chickens in a ratio of 1 : 2 : 1.

a Describe the inheritance pattern of this trait. Outline the evidence that leads you to this conclusion.

b Determine how many genes and alleles control this trait. Outline the evidence that leads you to this conclusion.

c Use appropriate notation to set up a model that explains the student's observations.

15 Males of a pure-breeding strain of blowfly with black bodies are crossed to females of a pure-breeding wild type strain. All the offspring are wild type. Male offspring of the reciprocal cross are black-bodied while females are wild type.

a Provide a genetic explanation for these results.

b If offspring of the first cross are mated together, calculate the expected phenotypic ratios of the F2 offspring.
Wild type = X^B and black body = X^b