4.1.3 Genes and alleles

The study of genetics aims to explain similarities and differences between parents and their offspring. Genes are lengths of DNA that form part of chromosomes and carry the instructions for the production of a particular protein and the development of specific characteristics. Each gene occupies its own specific position known as a locus, on a chromosome, for example the human insulin gene is located on the short arm of chromosome 11. Chromosome 16 contains more than 90 million DNA base pairs, almost 3% of the total DNA in a human cell. It contains 800–900 genes.

In diploid organisms homologous chromosomes carry the same genes at the same loci, but any gene can occur in one of a number of different forms, known as **alleles**. Alleles differ from one another by a few bases or sometimes a more substantial amount. In sexually reproducing organisms, one of each pair of homologous chromosomes passes to the gametes, which are haploid. At fertilisation alleles are passed on and form part of the genotype of new offspring. As alleles interact they contribute to the phenotype of the new organism. Most characteristics are determined by more than one gene, for example human height and skin colour are determined by many genes.

KEY POINTS

genotype refers to the genetic constitution of an individual, the alleles it contains; each allele is represented by a letter; chromosomes come in pairs and so alleles come in pairs, so a genotype is represented by a pair of letters, such as TT or Tt.

locus is the specific position of a gene on a homologous chromosome; a gene locus is fixed for a species, for example, the insulin gene is always found at the same position on chromosome 11 in humans.

phenotype means the characteristics of an organism that may be physical appearance or biochemical features.

4.1.4 Karyotyping

Chromosomes have unique banding patterns that are revealed if they are stained with specific dyes. These patterns enable us to study the structure and type of chromosomes present in an organism. The technique has been used in prenatal diagnosis and in forensic science. Chromosomes are prepared from the nuclei of dividing cells. If human cells are being studied, a sample of cells may be taken from amniotic fluid, in the case of a fetus, or from a blood sample. Division is halted at the end of prophase when chromosomes are condensed and can be seen (Section 6.5). A **karyogram** is a photograph or diagram of the stained chromosomes. Each chromosome is a characteristic length and each one has a homologous partner. The karyogram image is organised so that each chromosome is separated from the others and they are arranged in order of their size, as shown in Figure 4.1.2.

A karyogram shows the **karyotype** of the cell, that is, the number and types of chromosomes present in its nucleus. It indicates the sex of an individual because it shows the **sex chromosomes** and in prenatal diagnosis it is possible to check for chromosome abnormalities.

KEY POINTS

karyogram a diagram of photograph of the chromosomes from an organism.

karyotype the number and type of chromosomes present in the nucleus.

Some chromosome abnormalities result from non-disjunction, the failure of homologous pairs of chromosomes to separate properly during meiosis (Section 6.5). It results in gametes that contain either one too few or one too many chromosomes. Those with too few seldom survive, but in some cases a gamete with an extra chromosome does survive and after fertilisation produces a zygote with three chromosomes of one type. This is called a **trisomy**.

Trisomy in chromosome 21 results in the human condition known as **Down syndrome** (Figure 4.1.3), a condition in which a child is born with an extra copy of chromosome 21 resulting in physical and mental disabilities. A gamete, usually the female one, receives 24 chromosomes instead of 23 and a baby with 47, instead of the usual 46, chromosomes in each cell is born.

Karyotyping is used when there is concern about potential chromosome abnormalities. Cells from an unborn child are collected in one of two ways: chorionic villus sampling (CVS) or amniocentesis (Section 8.4). The cells are grown in the laboratory and a karyogram is prepared. This is checked for extra or missing chromosomes. The procedure is normally used if the mother is over the age of 35 years, because Down syndrome is more common in babies of older mothers and can be detected using this method (Figure 4.1.3).

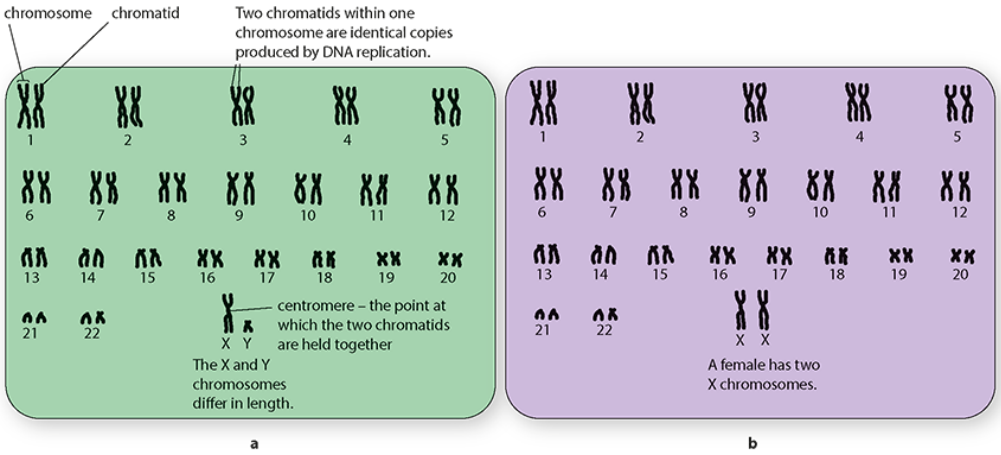


Figure 4.1.2: Karyograms for a human male **a** and a human female **b**.

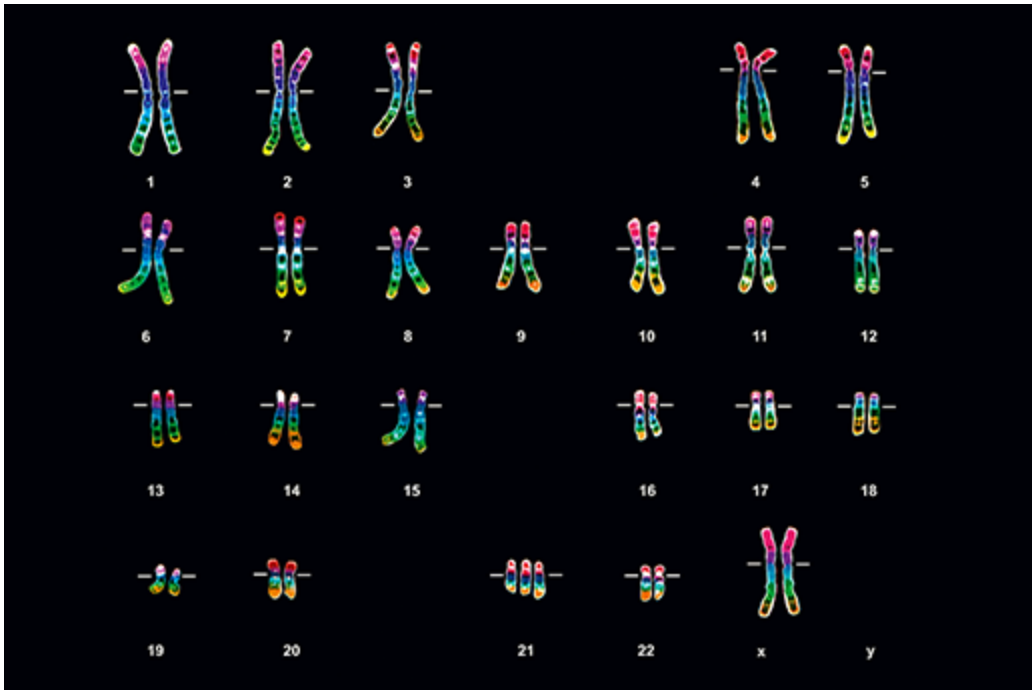


Figure 4.1.3: People with Down syndrome have characteristic physical features. The karyogram, showing chromosomes that are stained and photographed, for a person with Down syndrome shows three copies of chromosome 21 (called trisomy 21).

4.1.5 Determination of sex

Most mammals, including humans, have one pair of chromosomes that determines whether the person or organism is male or female. These sex chromosomes are the last two chromosomes shown in the human karyograms in Figure 4.1.2 (in the centre of the bottom row, in each case). These chromosomes determine the sex of an individual: a human female has two X chromosomes (XX), whereas a male has one X and one Y chromosome (XY). In humans, the X chromosome is longer than the Y and carries more genes (Figure 4.1.4). Sex chromosomes are inherited in the same way as other chromosomes.

The other 44 chromosomes in a human karyotype are known as autosomes and they determine the other characteristics of the individual. (Sometimes, you will see sex chromosomes referred to as the non-autosomal chromosomes.)

THEORY OF KNOWLEDGE

Prenatal screening

Obtaining fetal cells for karyotyping by amniocentesis involves taking a sample of amniotic fluid from the mother between weeks 14 and 16 of her pregnancy. Chorionic villus sampling (CVS) means taking a sample of cells from the chorionic villi, which are the fine projections of the placenta embedded in the lining of the uterus. This can be done at 8–10 weeks into the pregnancy. Both methods carry a small risk of damaging the fetus or even causing a miscarriage. If the results of the test reveal abnormalities, the parents may be offered the option to terminate the pregnancy. The test may

show an abnormality, but it cannot give any indication about the likely severity of the condition.

To consider:

1. Karyotyping is a procedure involving medical and ethical decisions. Who should make the decision to carry out the procedure, the parents or health care staff? How important are legal and religious arguments?
2. Both procedures carry the risk of a miscarriage. How can this potential risk to the unborn child be balanced with the parents' desire for information? What safeguards should be in place when the karyotyping procedure is used?
3. Does the importance of the information that can be obtained from the karyogram outweigh the risk to the unborn child?
4. If the karyogram indicates a genetic abnormality, should the parents be permitted to consider a termination of the pregnancy?

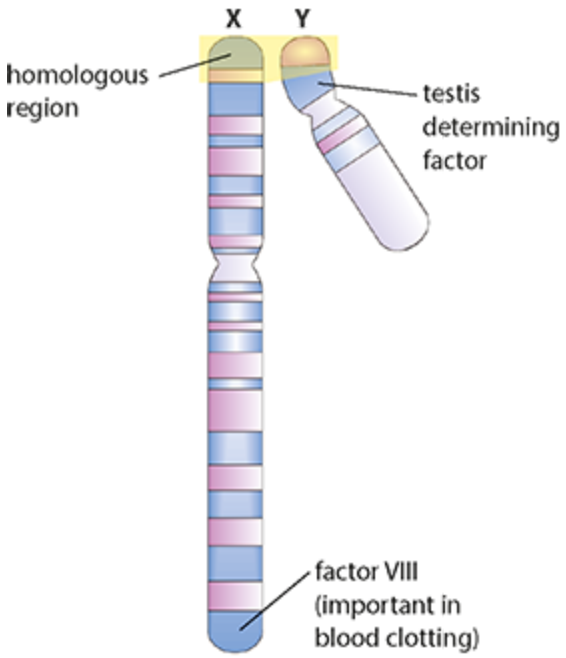


Figure 4.1.4: Human X and Y chromosomes.

In mammals, a process called X inactivation 'switches off' one of the two X chromosomes, which remains as an inactive Barr body. This occurs early in the early development of a female in a random way. A female receives one X chromosome from her male parent and the other from her female parent. If X inactivation occurs at the 100-cell stage of development, 50 cells may have the maternal X chromosome activated while the other 50 have the paternal X chromosome activated.

This pattern of activation will be retained throughout fetal development. Females have a combination of different cells containing either the paternal or maternal X chromosome.

In most cases this does not affect the organism's phenotype, but in tortoiseshell cats it can be clearly seen. A female may have inherited a 'ginger' allele from her mother and a 'non-ginger' allele from her father on her X chromosome. After X inactivation, some of her cells will produce ginger pigment, and

some will produce black. During development all cells specialise and occupy different parts of the cat's body. Some cells will specialise to produce pigment in the skin of the cat. Those carrying the 'ginger' allele will produce orange pigment and those without this allele will produce black pigment. The result is the characteristic appearance of a tortoiseshell cat (Figure 4.1.5).

KEY POINTS

autosome a chromosome that does not determine an organism's sex.

Barr body an inactivated X chromosome found in the cells of human females. Barr bodies appear as darkly stained masses in cells during interphase.

Figure 4.1.5: Tortoiseshell cat fur colour is a result of X chromosome inactivation.

Over evolutionary time non-autosomal chromosomes developed from autosomes to form the sex chromosomes we have today. But different types of non-autosomal chromosomes have evolved in different species. In birds, females are **heteromorphic** and males are **homomorphic**: female birds have ZW and males have ZZ as their sex chromosomes.

KEY POINTS

heteromorphic is a homologous chromosome pair that is not morphologically identical.

homomorphic is a homologous chromosome pair that is morphologically identical.

EXAM TIP

Take time to check you can define similar pairs of terms that appear in the same topic. For example: karyogram and karyotype, heteromorphic and homomorphic, diploid and haploid.

TEST YOUR UNDERSTANDING

1 Define the terms genome, diploid and homologous.

2 Outline the relationship between a locus, a gene and an allele.

3 State two differences between prokaryotic and eukaryotic chromosomes.

4 Suggest how karyograms are useful in prenatal diagnosis.

5 Describe what is meant by X inactivation.

6 Explain the difference between an organism's genotype and its phenotype.

Links

- How does DNA fit into the tiny volume of a nucleus?
- How does chromosome behaviour during cell division lead to variation?
- How does understanding genes help us understand cladistics and classification?

4.2 Genetic inheritance

LEARNING OBJECTIVES

In this section you will:

- learn that the principles of inheritance were first described by Greg Mendel
- recall that gametes are haploid and contain one allele of each gene
- understand that diploid zygotes contain two alleles of each gene
- recognise that alleles represent an organism's genotype; its phenotype is the observable result of the genotype
- learn that dominant alleles mask the effects of recessive alleles. Codominant alleles have combined effects
- recognise that although many genes have multiple alleles but an organism will only inherit one of each from their parents
- learn that polygenic inheritance occurs when two or more genes influence a characteristic. Phenotypes may be continuous or discrete
- understand that due to their location on sex chromosomes, sex-linked genes show different inheritance patterns from autosomal genes. Some sex chromosomes carry genes for genetic disorders

- learn that many human diseases are recessive but some are dominant

  - learn that environment can determine the sex of offspring in some species
  - learn that PKU is a recessive condition caused by a mutation
  - understand that gene loci are linked if they are on the same chromosome
  - learn that unlinked genes segregate independently at meiosis. Linked genes do not.

GUIDING QUESTIONS

- How do recessive conditions contribute to resilience in a population?
- How does a gene pool change over time?

4.2.1 Principles of inheritance

The study of genetics aims to explain similarities and differences between parents and their offspring. Today we discuss genes, chromosomes and DNA but the study of inheritance began in the 19th century with the work of a monk, Gregor Mendel, who lived in what is now Czechia. Mendel knew nothing of DNA or chromosomes, but his studies of plant breeding are crucial to our understanding of inheritance.

Sexual reproduction involves the fusion of two gametes: an egg and a sperm in animals, or pollen and ovule in plants. Each gamete is haploid and contains one allele of each gene of the parent individual. Alleles separate from one another at meiosis (Section 6.5). When two gametes fuse at fertilisation, a diploid zygote with two copies of each allele is produced. The zygote develops to form a new individual, with its own genotype determined by the alleles it has received. The phenotype or appearance of the individual is determined by its genotype.

In the mid-1850s Gregor Mendel began a series of hundreds of painstaking experiments with pea plants, which he grew at his monastery. Mendel chose plants with characteristics he wanted to study – such as those with short or long stems, or with wrinkled or smooth seeds – and he made crosses between them. He pollinated selected plants with characteristics of interest, using pollen from specially chosen plants, and grew new plants from the seeds that were produced. He observed, counted and recorded the different characteristics of all the plants that he grew.

Mendel's early studies involved the inheritance of just one pair of characteristics. He conducted what is now called a **monohybrid cross** using **pure-breeding** plants, which, when

crossed with each other, always produce offspring that resemble their parents. Mendel crossed pure-breeding short pea plants with pure-breeding tall plants and grew seeds that were produced from the crosses (Figure 4.2.1). In the new generation of peas (known as the first filial or **F_1 generation**) he noted that all the plants were tall.

Mendel self-pollinated these tall F_1 plants and grew seeds from the cross to produce a second filial or **F_2 generation**. He discovered that in this generation both tall and short plants were present (Figure 4.2.1). Mendel recorded the results from 1064 plants. He found 787 tall plants and 277 short plants. Approximately three-quarters of the plants were tall or, put another way, the ratio of tall : short plants was 3 : 1.

Mendel carried out other monohybrid crosses with several other characteristics and obtained similar results. These are shown in Table 4.2.1.

The results showed that inheritance did not produce a blending between the characteristics of the parent plants – so, for example, in the first cross there were no plants of medium height – and he described inheritance as being ‘particulate’. We call the inherited particles genes or alleles, but Mendel called them ‘factors’. He understood that factors were transmitted to offspring in gametes.

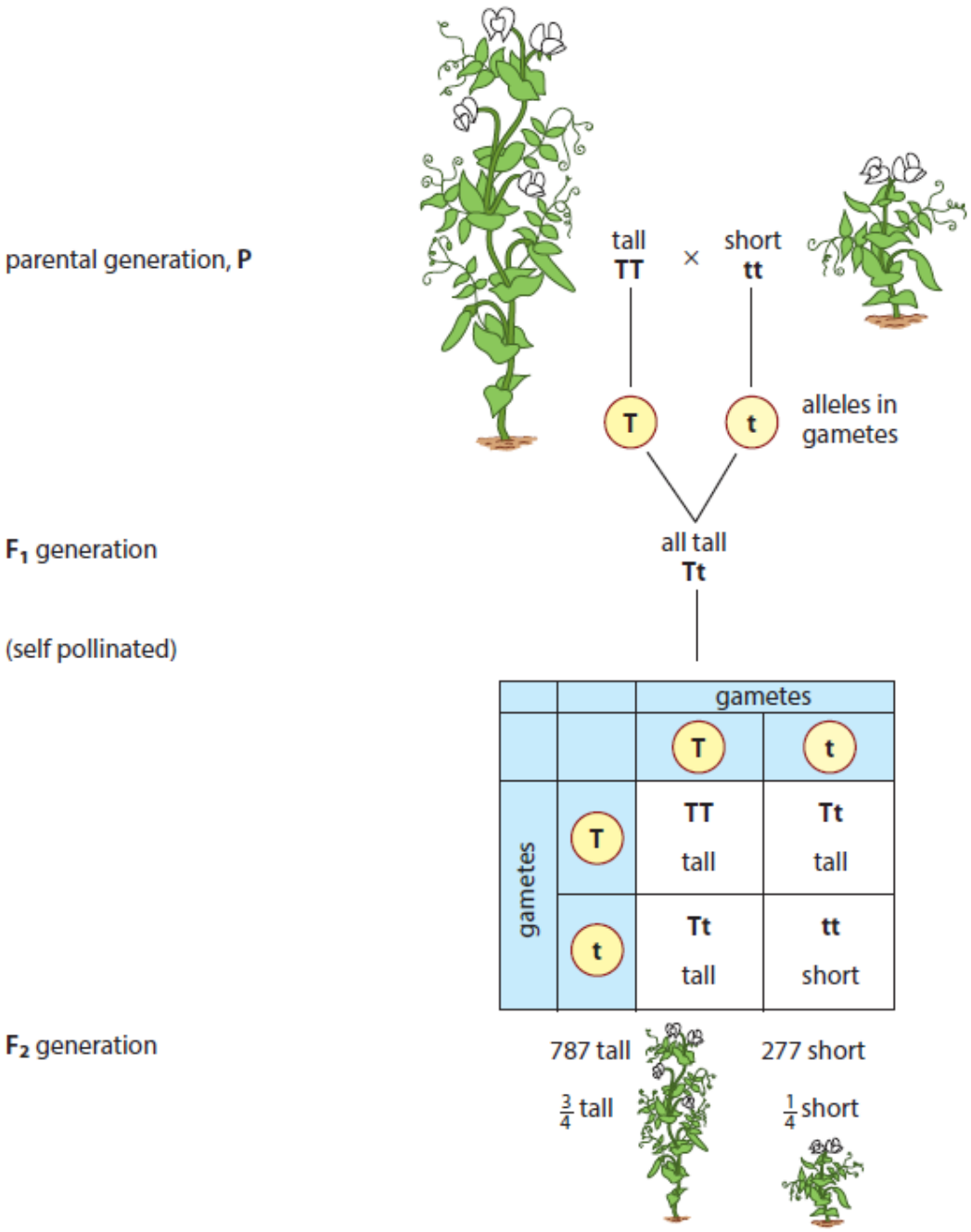


Figure 4.2.1: Diagrams to show Mendel's crosses of tall and short pea plants, with modern knowledge of alleles included.

Characteristic	Cross made	Numbers produced in F_2 generation	Ratio calculated

height of stem	tall × short	787 tall, 277 short	2.84 : 1
petal colour	purple × white	704 purple, 244 white	2.89 : 1
seed shape	smooth × wrinkled	5474 smooth, 1859 wrinkled	2.95 : 1
seed colour	yellow × green	6022 yellow, 2001 green	3.01 : 1

Table 4.2.1: Mendel's experimental results.

Mendel also noted that short plants 'reappeared' in the F_2 generation despite the fact that there were no short plants in the F_1 generation.

Although all the F_1 plants were tall they must contain a 'factor' from their short parent that was 'masked' and did not reappear until the F_2 generation. Today, the factor for tallness is described as being dominant to the factor for shortness, which is said to be recessive. If a dominant and a recessive allele are present together the dominant allele masks the recessive allele.

NATURE OF SCIENCE

Evidence

Mendel used thousands of pea plants in his meticulous experiments. Without this amount of data he would not have been able to establish the ratios he observed with any certainty. If fewer replicates are used in any trial, the degree of uncertainty increases and the results are less reliable. Large numbers of quantitative measurements are more objective

than qualitative observations and today are analysed using statistical methods.

KEY POINTS

dominant an allele that has the same effect on the phenotype when in either the homozygous or heterozygous state; the dominant allele is always given a capital letter, for example, T.

recessive an allele that only has an effect on the phenotype when in the homozygous state; a recessive allele is always given the lower case of the same letter given to the dominant allele, for example, t.

Mendel proposed that factors were transmitted to offspring via gametes and came to the conclusion that gametes contain only one of the factors for height, for example, while the seeds and plants that grow from them contain both. Put another way, we would now say that gametes are haploid and seeds are diploid.

Without knowledge of genes and alleles, Mendel demonstrated that gametes contain one allele of each gene. Nowadays we know that the two alleles of each gene separate into different haploid daughter nuclei during meiosis (Section 6.5). Furthermore, his experiments showed that the fusion of gametes at fertilisation produces diploid zygotes (which in Mendel's experiments developed into seeds) with two alleles of each gene. The reappearance of short plants in the F_2 generation proves that the two alleles may be the same or different. Genetic crosses similar to Mendel's are used by horticulturalists and plant breeders today to develop new varieties of crops and ornamental plants.

4.2.2 Determining allele combinations (genotypes) and characteristics (phenotypes) in genetic crosses

Using a Punnett grid

A genetic diagram called a Punnett grid can be used to work out all the possible combinations of alleles that can be present in the offspring of two parents (the **parental generation**) whose genetic constitutions (genotypes) are known. Punnett grids show the combinations and also help to deduce the probabilities of each one occurring.

When working out a problem, it is helpful to follow a few simple steps.

1 Choose a letter to represent the gene. Choose one that has a distinctly different upper and lower case for the alleles, so for example O, P and W would not be good choices. It is useful to base the letter on the dominant phenotype, so for example R = red could be used for petal colour.

2 Represent the genotype of each parent with a pair of letters. Use a single letter surrounded by a circle to represent the genotype of each gamete.

3 Combine pairs of the letters representing the gametes to give all the possible genotypes of the offspring. A Punnett grid provides a clear way of doing this.

4 From the possible genotypes, work out the possible phenotypes of the offspring.

Worked examples 4.2.1 and 4.2.2 show how to tackle genetics problems using these steps.

Single-nucleotide polymorphisms

Single nucleotide polymorphisms, often called SNPs, are the most common type of human genetic variation. Each SNP represents a difference in a single DNA nucleotide. For example, a SNP may replace the nucleotide cytosine (C) with the nucleotide thymine (T) in a certain stretch of DNA. SNPs are found throughout a person's genome. They occur approximately once in every 1,000 nucleotides, which means there can be 4 to 5 million SNPs in a person's DNA. The variations are very common and to be classified as a SNP, a variant must be found in at least 1 percent of the population, so far scientists have identified more than 600 million SNPs in populations around the world.

WORKED EXAMPLE 4.2.1

Suppose that fur colour in mice is determined by a single gene. Brown fur is dominant to white. A mouse homozygous for brown fur was crossed with a white mouse. Determine the possible genotypes and phenotypes of the offspring.

Step 1 Choose a letter. Brown is dominant, so let B = brown fur and b = white fur.

Step 2 We are told the brown mouse is homozygous, so its genotype must be BB. As white is recessive, the genotype of the white mouse can only be bb. If a B were present, the mouse would have brown fur.

Step 3 Set out the diagram as shown.

Step 4 The Punnett grid shows that all the offspring will be phenotypically brown and their genotype will be Bb.

Answer

parental phenotypes: brown white

parental genotypes: **BB** **bb**

gametes: (B) (B) (b) (b)

Punnett grid for F1:

		gametes from brown parent	
		(B)	(B)
gametes from white parent	(b)	**Bb** brown	**Bb** brown
	(b)	**Bb** brown	**Bb** brown

KEY POINTS

heterozygous having two different alleles at a gene locus, for example, Tt.

homozygous having two identical alleles at a gene locus; the alleles may both be dominant or both recessive, for example, TT or tt.

WORKED EXAMPLE 4.2.2

Seed shape in the pea plant is controlled by a single gene. Smooth shape is dominant to wrinkled shape. A plant that was heterozygous for smooth seeds was crossed with a plant that had wrinkled seeds. Determine the possible genotypes of the offspring and the phenotype ratio.

Step 1 Choose a letter. Smooth is the dominant trait but S and s are hard to distinguish so use another letter, such as **T**.

Step 2 We are told the smooth plant is heterozygous so its genotype must be **Tt**. Since 'wrinkled' is a recessive trait, the genotype of the wrinkled-seed plant must be **tt**.

Step 3 Set out the diagram as shown, in exactly the same way as before. Notice that, in this case, the smooth-seeded parent produces two different types of gamete because it is heterozygous.

Step 4 Here the Punnett grid shows us that half of the offspring will have smooth seeds with the genotype **Tt** and half will have wrinkled seeds with the genotype **tt**.

Answer

parental phenotypes: smooth wrinkled

parental genotypes: **Tt** **tt**

gametes: T t t t

Punnett grid for F_1:

		gametes from smooth-seed parent	
		(T)	(t)
gametes from wrinkled-seed parent	(t)	**Tt** smooth	**tt** wrinkled
	(t)	**Tt** smooth	**tt** wrinkled

TEST YOUR UNDERSTANDING

7 Define each of these terms:

a genotype

b phenotype

c dominant allele

d recessive allele

e homozygous

8 If red R is dominant to yellow r, state the phenotype of each of these genotypes:

a RR

b Rr

c rr

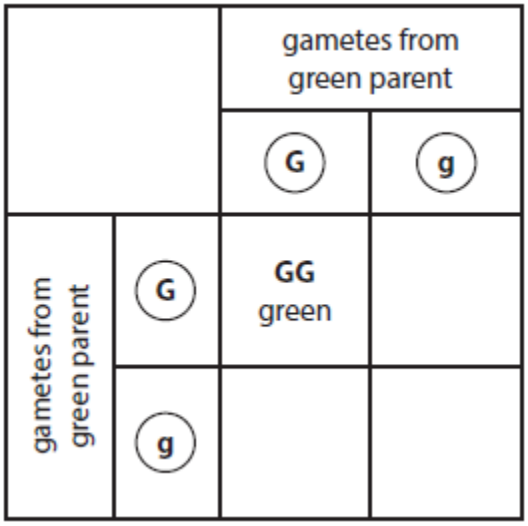
9 State the gametes produced by a parent with each of the following genotypes

a RR

b rr

c Rr

10 Copy and complete this Punnett grid. Green seed colour G is dominant to purple seed colour g. Label the colours of the seeds that are produced.



Most commonly, SNPs are found in between genes. They can act as biological markers, and help scientists to locate genes that are associated with disease. When SNPs occur within a gene or in a regulatory region near a gene, they may affect the gene's function.

The majority of SNPs have no effect on a person's phenotype. But some can help predict an individual's response to certain drugs or the risk of developing diseases. SNPs can also be used to follow the inheritance of some genetic diseases in families.

4.2.3 Codominance and multiple alleles

In Worked examples 4.2.1 and 4.2.2, one of the alleles completely dominates the other, so in a heterozygous genotype the phenotype is determined solely by the dominant allele. In the case of codominance, both alleles from the parents contribute to the phenotype of the offspring. The examples of the mouse coat colour and the smooth and wrinkled peas are both known as monohybrid crosses because they involve just one gene with two alleles: brown **B** and white **b**, or smooth **T** and wrinkled **t**. But in many other cases characteristics are determined by genes which have more than two alleles. Any number of alleles of a gene can be present in the gene pool of a species but any individual can only inherit two of them, one from each parent. One example of this is human blood groups.

The ABO human blood grouping is an example of both **codominance** and multiple alleles. There are three alleles: I^A, I^B and i which determine a person's blood group.

I^A and I^B are both are dominant to i but are codominant to one another. This results in four different phenotypes or blood groups.

KEY POINT

codominance in which a pair of alleles both have an influence on the phenotype when present in the heterozygous state, so that both parental phenotypes are expressed together in their offspring. Codominant alleles are represented in a different way in genetics: a capital letter is chosen to represent the gene and then other (superscript) letters represent the alleles (for

example, in human blood grouping, A and B are codominant alleles and are represented as I^A and I^B).

Genotype	Phenotype or blood group
I^AI^A	A
I^Ai	A
I^BI^B	B
I^Bi	B
I^AI^B	AB
ii	O

Table 4.2.2: Human blood groups and their genotypes.

A person's blood group depends on which combination of alleles they receive. Each person has only two of the three alleles and they are inherited just as though they are alternative alleles of a pair. Table 4.2.2 shows the possible combinations of alleles and the resulting phenotypes.

4.2.4 Incomplete dominance

Incomplete dominance occurs when a dominant allele does not completely mask the effects of a recessive allele and the resulting phenotype is a combination of both alleles. One example is seen in the colour of the flowers of the Marvel of Peru. Flowers with homozygous alleles may be red with alleles RR, or white with the alleles rr. If a red flower is crossed with a white one, neither allele is dominant and the flowers that are produced are pink (Figure 4.2.2).

KEY POINT

incomplete dominance is when the phenotype of heterozygous offspring is a combination of the two homozygous phenotypes, for example, a cross between a red and a white flower producing pink offspring.

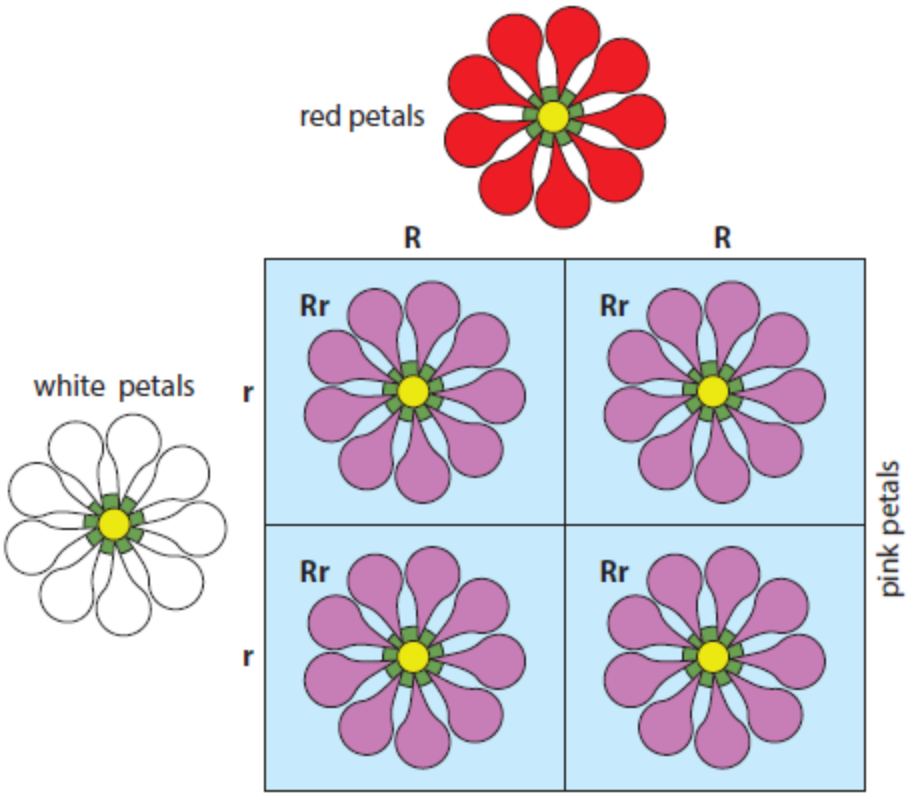


Figure 4.2.2: Red and white petal colour in the Marvel of Peru (*Mirabilis jalapa*) show incomplete dominance so a cross between red and white flowers produces pink offspring.

Genotype or environment?

Sometimes a person's phenotype is determined only by their genotype but in other cases their environment plays a part. For example, a farmer knows the effect that fertiliser, water and pesticides have on the growth of plants even when all the plants have the same genotypes. It is often difficult to assess how much variation is due to genes and how much to environmental factors.

Here are some examples of human variation. Can you identify which are determine by genes, which by the environment and which by a combination of both?

- Blood group

- Eye colour
- Freckles
- Curliness of hair
- Interest in music
- Sense of humour
- Hair colour
- Shape of earlobes
- Mass
- Height

EXAM TIP

Note that incomplete dominance is different from codominance. In incomplete dominance the phenotype is new and somewhere between the two homozygous phenotypes, but in codominance both parent phenotypes are expressed at the same time in offspring.

4.2.5 Sex chromosomes and autosomes

Humans have one pair of chromosomes that determine whether the person is male or female. These chromosomes are called the sex chromosomes. Each person has one pair of sex chromosomes, either XX or XY, along with 22 other pairs known as autosomes. The X chromosome is longer than the Y and carries more genes. Human females have two X chromosomes and males have one X and one Y.

Sex chromosomes are inherited in the same way as other chromosomes.

The ratio of phenotypes female : male is 1 : 1. This means, at fertilisation, there is always a 50% chance that a child will be a boy and 50% that it will be a girl.

Sex chromosomes and genes

The sex chromosomes not only carry the genes that control sex, the X chromosome also carries genes called sex-linked or X-linked genes. These genes occur only on the X chromosome and not on the Y chromosome, which is much shorter. The Y chromosome carries alleles that are mainly concerned with male structures and functions.

Sex linkage has a significant effect on genotypes. Females have two X chromosomes, so they have two alleles for each gene and may be homozygous or heterozygous. In a female, a single recessive allele will be masked by a dominant allele on her other X chromosome. Males only have one allele on their X chromosome with no corresponding allele on the Y chromosome, so a recessive allele will always be expressed in a male.

A female who is heterozygous for a sex-linked recessive characteristic that does not affect her phenotype is called a **carrier**.

KEY POINT

carrier an individual with one copy of a recessive allele that causes a genetic disease in individuals that are homozygous for this allele.

Examples of sex-linked characteristics

Two examples of sex-linked human characteristics are hemophilia and red–green colour blindness.

Hemophilia is a condition in which the blood of an affected person does not clot normally. It is a sex-linked condition because the genes controlling the production of the blood-clotting protein factor VIII are on the X chromosome. A female who is X^HX^h will be a carrier for hemophilia. A male who has the recessive allele X^hY will have hemophilia. Figure 4.2.3 is a pedigree chart showing how a sex-linked condition like hemophilia may be inherited. Notice that hemophilia seldom occurs in females, who would have to be homozygous for the recessive allele X^hX^h. This condition is usually fatal before birth, resulting in a miscarriage. Today, hemophilia is treated by giving the affected person the clotting factor they cannot produce.

EXAM TIP

When you write diagrams for alleles that are on the X chromosome make sure you use the standard format required for your exams. Use a superscript letter on an upper case X, like this: X^BX^b

A person with red–green colour blindness has difficulty distinguishing between red and green. Red–green colour blindness is inherited in a similar way to hemophilia. A female who is X^BX^b is a carrier for colour blindness and a male with just one copy of the recessive allele will be colour blind. Remember that a male cannot be a carrier for a sex-linked gene.

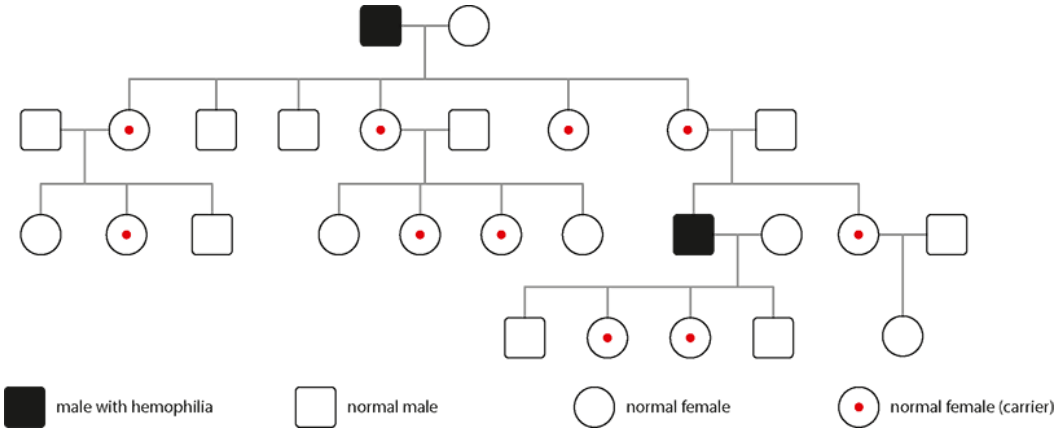


Figure 4.2.3: Pedigree for a sex-linked recessive disease, such as hemophilia.

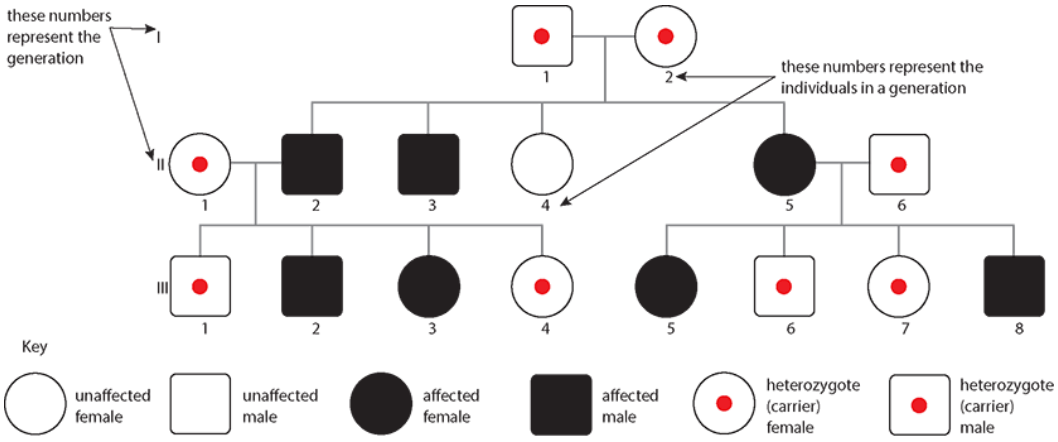


Figure 4.2.4: This pedigree chart shows the occurrence of an autosomal recessive genetic condition cystic fibrosis in a family.

4.2.6 Pedigree charts

Pedigree charts, like the ones shown in Figures 4.2.3 and 4.2.4, are a way of tracing the pattern of inheritance of a genetic condition through a family. Specific symbols are always used, and the chart is set out in a standard way. The horizontal lines linking the male and female in a generation indicate a marriage (or mating) and the vertical lines indicate their offspring. Offspring are shown in the order of their birth. For example, in the family shown in Figure 4.2.4, the oldest individual affected with the genetic condition is II2, who is a male.

4.2.7 Genetic diseases

As well as the inherited genetic conditions that are carried on the sex chromosomes and inherited with the sex of an individual, there are many other inherited disorders that occur due to mutations in single genes on the autosomal chromosomes (numbers 1–22). Most are caused by the presence of two recessive alleles, although some – such as Huntington's disease – are caused by a dominant allele (Table 4.2.3). Genetic 'diseases' are unlike other diseases such as a cold or flu. They cannot be 'caught' from another person but they may be passed through families from parent to child. More than 6000 physiological 'diseases', caused by mutations to single genes, are known. Most are very rare (Table 4.2.3) and there is a wide variation in the occurrence of some genetic disorders between different racial groups and geographic locations of people or their ancestors.

WORKED EXAMPLE 4.2.3

A female who is homozygous for normal vision married a male who is red–green colour blind. Determine the possible types of vision inherited by their two children, one girl and one boy.

Step 1 Standard letters are used for these alleles – normal vision is $\mathbf{X^B}$ and colour blind is $\mathbf{X^b}$. The X is always included.

Step 2 The female is homozygous for normal vision so her genotype must be $\mathbf{X^BX^B}$.

Since the male is colour blind, his genotype must be $\mathbf{X^bY}$.

Step 3 Set out the diagram as shown.

Step 4 The Punnett grid shows that a daughter will have normal vision, but be a carrier for red–green colour blindness. A son will have normal vision.

Answer

parental phenotypes: female male

parental genotypes: X^BX^B X^bY

gametes: X^B X^B X^b Y

Punnett grid for F_1:

		gametes from the male	
		X^b	Y
gametes from female	X^B	X^BX^b girl, normal vision, carrier	X^BY boy, normal vision
	X^B	X^BX^b girl, normal vision, carrier	X^BY boy, normal vision

TEST YOUR UNDERSTANDING

11 A person is blood group A. What are the possible combinations of alleles that this person could have? Use the proper notation for your answer.

12 What is meant by the term ‘sex-linked condition’?

13 Write down the combination of alleles that a female with hemophilia would have.

Phenylketonuria

Phenylketonuria (PKU) is an error in metabolism that leads to decreased metabolism of the amino acid phenylalanine. It is an autosomal recessive condition caused by a mutation in the gene on chromosome 12 that codes for the liver enzyme tyrosine hydroxylase. This enzyme converts phenylalanine into another amino acid, tyrosine. Phenylalanine is essential for normal growth but, if too much builds up the blood, it can cause brain damage and lead to intellectual disability, seizures and other mental disorders. The condition can be treated if it is diagnosed soon after birth. Babies in many parts of the world are given a simple blood test to check for PKU. Babies identified as having the condition must be given a special low-protein diet containing low amounts of phenylalanine. They must avoid many high-protein foods such as milk and dairy products, nuts, fish and meat. PKU only affects children until puberty, after which they can have a non-restricted diet.

Genetic disease or condition	Frequency	Cause	Gene location (chromosome number)
Cystic fibrosis (CF)	Variable. About 1 in 25 people of a white ethnic background are carriers of the disease. In Europe, about 1 in 2000	Autosomal recessive allele; more than 500 different mutations of the CF gene have been found.	7

	babies are born with CF. In the USA, the incidence is 1 in 3500.		
β Thalassemia	Most common in Asia, Middle East and Mediterranean areas where malaria was or is endemic. 1% of people here may be affected. α and β Thalassemias are the world's most common single-gene disorders.	Autosomal recessive allele of the gene that codes for the β chain of hemoglobin.	11
Sickle-cell disease	Most common in people whose ancestors come from sub-Saharan Africa but also in South and Central	Autosomal recessive mutation, which causes substitution of one amino acid in the β chain of hemoglobin.	11

	America, Mediterranean countries and India. In West Africa, 1% of the population are affected.		
Huntington's disease (HD)	Rare disease affecting about 1 in 20 000 people. Males and females are equally affected and the disease occurs in all ethnic and racial groups.	Autosomal dominant mutation of the HD gene, which increases the length of a repeated sequence of CAG.	4
Phenylketonuria (PKU)	Rare condition affecting about 1 in 25,000 people world wide.	Caused by mutation in the gene that codes for the enzyme needed to convert phenylalanine to tyrosine. Phenylalanine can build up in the brain and blood and	12

		lead to brain damage. Can be detected in new born babies by a blood test and treated with special diet.	

Table 4.2.3: Some information on five well documented genetic diseases that affect human metabolism (data from the World Health Organization).

PKU is a recessive condition, which means that a child must inherit a copy of the recessive allele from both parents (Figure 4.2.5).

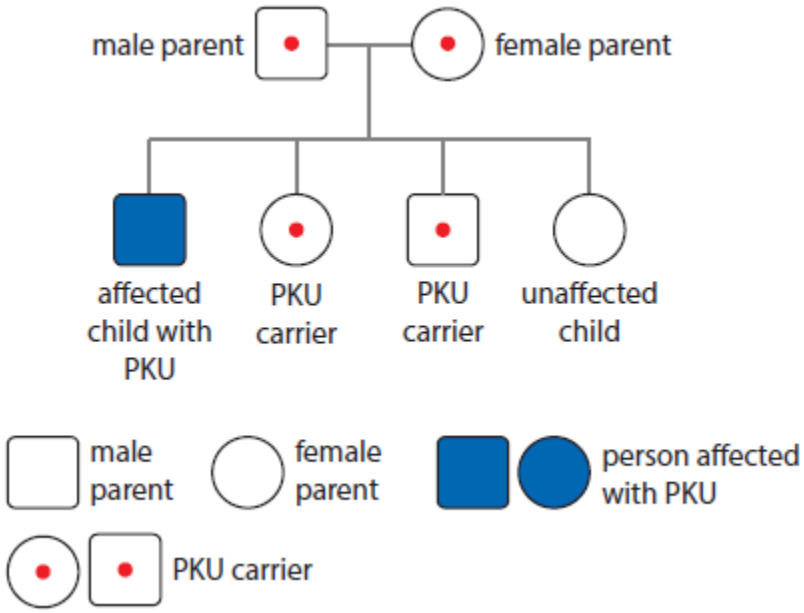


Figure 4.2.5: A person with PKU must inherit a recessive allele from both parents. Their siblings may either be carriers or

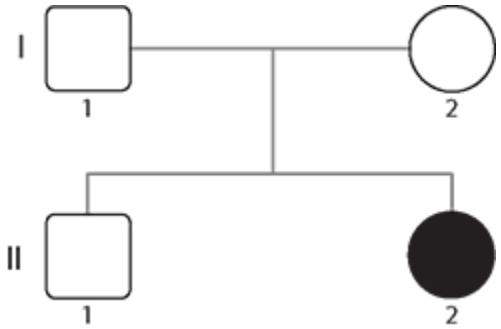
unaffected by the condition.

WORKED EXAMPLE 4.2.4

Cystic fibrosis (CF) is a genetic disorder that causes the excessive production of thick sticky mucus. It is due to a recessive allele that is not sex linked. The pedigree chart shows two generations of a family. A filled-in symbol represents an individual who has cystic fibrosis.

Deduce the genotypes of the parents I1 and I2.

Deduce the probability that II1 is heterozygous.



Step 1 Cystic fibrosis is a recessive disorder. The 'normal' condition, without cystic fibrosis, is dominant. So choose **N** to represent the normal allele.

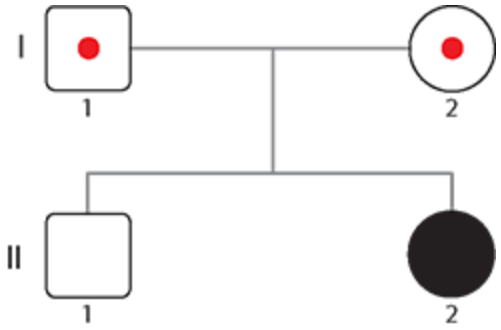
Step 2 Neither of the parents, I1 and I2, have cystic fibrosis so both must have at least one normal allele **N**. As cystic fibrosis is recessive and II2 has the condition, she must have the genotype **nn**.

II2 received one allele from each of her parents so both of them must have passed one n allele to her. Both parents must have one **n** but they do not have cystic fibrosis so their genotype must be heterozygous **Nn**.

The pedigree chart could now be redrawn to show that the parents are heterozygous carriers.

Step 3 Now that both parents are known to be heterozygous, a Punnett grid can be drawn.

Step 4 Person II1 does not have cystic fibrosis and so could have the allele combination shown by any of the shaded boxes in the grid. The probability of person II1 being heterozygous is 2 out of 3, or $\frac{2}{3}$ or 66%.

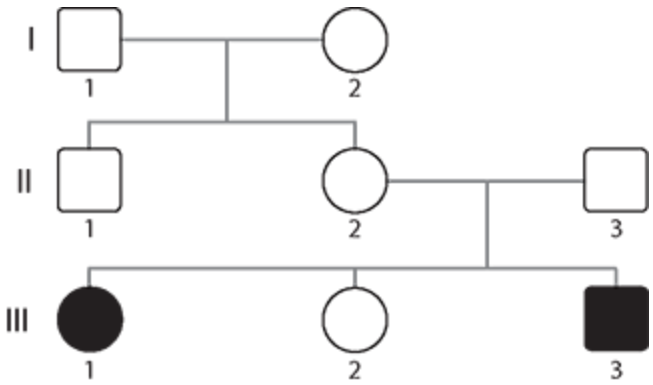


Answer

		gametes from I 1	
		N	n
gametes from I 2	N	**NN** normal	**Nn** normal
	n	**Nn** normal	**nn** II 2 with CF

WORKED EXAMPLE 4.2.5

The pedigree chart shows the family history of a recessive human condition called woolly hair. A filled-in symbol indicates that the person has woolly hair. Deduce whether this condition is sex linked or not.



Step 1 Remember that in a sex-linked condition, the allele occurs only on the X chromosome and males only have one X chromosome.

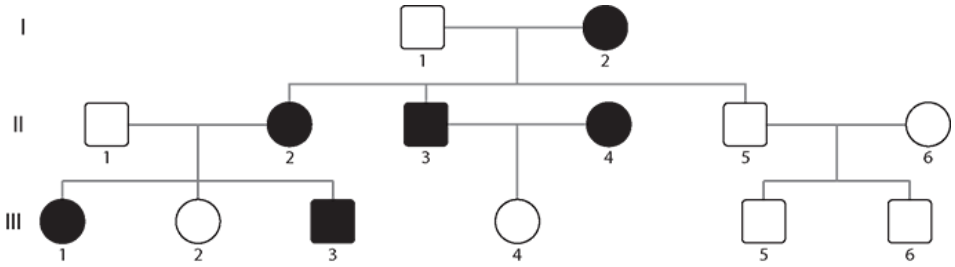
Step 2 Using N to represent the condition, we can see that female III1 must be nn as she has the condition and thus has inherited one n from each parent.

Step 3 If woolly hair is not sex linked, both her parents would be Nn as they have non-woolly hair.

Step 4 If it is sex linked, her mother (II2) would be $\mathbf{X^NX^n}$ and her father (II3) would be $\mathbf{X^nY}$. This would mean he has the recessive allele and no dominant allele. If the condition is sex linked, he would have woolly hair, which he does not. This proves that it is not sex linked.

WORKED EXAMPLE 4.2.6

The pedigree chart in this example shows the inheritance of a particular genetic condition in a family. A filled-in circle or square means that the individual is affected – that is, shows the genetic condition. The condition is not sex linked. Deduce whether the characteristic is dominant or recessive.



We can see that the genetic condition is dominant for the following reasons:

- affected individuals occur in every generation
- every affected individual has at least one affected parent.

THEORY OF KNOWLEDGE

Ethics of genotype identification

Sequencing of the bases of the human genome was completed in 2003 and now the task of identifying all of the genes is on going. As these genes are found, it may be possible for a person to be screened for particular alleles of genes that could affect them, for example, by increasing their susceptibility to cancer or the likelihood that they will develop Alzheimer's disease in later life. Alleles for genetic diseases such as

Huntington's disease, whose onset is typically later in life, can already be identified.

To consider:

1. Does simply knowing the sequence of the 3 billion base pairs of the human chromosomes tell us anything about what it means to be human?
2. Should third parties such as health insurance companies have the right to see genetic test results or demand that a person is screened before offering insurance cover or setting the level of premiums?
3. If treatment is unavailable, is it valuable to inform a person that they carry a genetic condition?
4. Knowledge of an individual's genome has implications for other members of their families. Should their rights be protected?

SCIENCE IN CONTEXT

Why is marriage between close relatives forbidden in many societies?

A marriage between two closely related people, with common grandparents is known as a consanguineous marriage and defined as a union between two individuals who are related as second cousins or closer. Cousin marriages were once common but have declined since the end of the 19th century in Western countries but in other parts of the world many such marriages still take place to preserve family property, cultural values and family structure. If the partners in a marriage are closely related it is more likely that they will carry the same

recessive genes and therefore be more likely to pass them on to their offspring. Even if there is no known genetic disorder in a family, first cousin marriages are generally at double the risk for birth defects in the offspring than the risk in unrelated people.

In some parts of the world including China, North and South Korea and many of the states of the USA cousin marriage is prohibited. Different religions have different rules on marriage; in Roman Catholicism marriages more distant than first-cousins are permitted, whereas protestant churches and Islam permit cousin marriage. Cousin marriage increases the burden of genetic diseases in a society, especially if cousin marriages have taken place over several generations. Genetic education and genetic counselling programmes to make people aware of potential problems are some of the ways in which societies can help to reduce the number of children born with harmful genetic conditions.

To consider:

How does a society balance the freedom of individuals to select their marriage partners with the potential health care needs of their children?

KEY POINTS

continuous variation refers to variation that does not fall into categories, there is a range of measures from one extreme to another. An example is human height.

discrete variation (discontinuous variation) is variation that is clearly distinguishable, categories of a feature can be

identified and for which there are no intermedites. Examples include blood groups.

4.2.8 Polygenes

In the genetic examples considered so far, a particular characteristic is controlled by one gene, which can have different alleles at a specific locus on a pair of chromosomes. There is a clear difference between organisms with different alleles. An organism either has the characteristic or it does not – there are no intermediate forms. These phenotypes are examples of discrete (or discontinuous) variation.

But very few characteristics are controlled by single genes; most are controlled by groups of genes, which together are known as polygenes. The genes that form polygenes are often located on different chromosomes and known as unlinked genes. When two or more genes, each with multiple alleles, are responsible for a characteristic the number of possible phenotypes is greatly increased. Each gene separately may have little impact but their combined effect produces a whole variety of phenotypes. Unlinked polygenes result in a range of degrees of the characteristic from one extreme to another – that is, continuous variation. Human height and skin colour are two examples of continuously varying characteristics. The average heights of males and females will be different in different countries and in different populations but all of them will show continuous variation as shown in Fig 4.2.6.

Human skin colour

Human skin colour is determined by the amount of the pigment melanin that is produced in the skin. Melanin synthesis is controlled by genes. The degree of pigmentation can range from the very dark skin of people originating from regions such as

Namibia in southern Africa, through to the very pale skin of native Scandinavian people.

Melanin protects the skin from the harmful UV rays from the Sun. In parts of the world close to the equator, the Sun's rays are particularly intense so people need more protection from sunburn. Dark-skinned people have a high concentration of melanin, which protects them, while fair-skinned people have much less. Although skin colour is genetically determined, environmental factors also influence it. Fair-skinned people who are exposed to sunlight produce extra melanin and develop a protective suntan. Exposure to sunlight also allows vitamin D to be produced in the skin.

Several genes are involved in determining skin colour and they produce the almost continuous variation that can be seen in the global human population. In Figure 4.2.6 only three genes – A, B and C – are shown. Each gene has two alleles: Aa, Bb and Cc. The Punnett grid shows the possible combinations of skin colour in children from two parents, both heterozygous for all three genes. The parents' phenotype is light brown skin (3).

In this simplified example there are only seven categories of pigmentation but you can see that if the frequencies of the different skin colours in the Punnett grid are plotted on a histogram, as in Figure 4.2.6, it produces a normal distribution. In the case of human skin colour, it is known that more than three genes are involved and the number of categories exceeds seven. The result is a wider distribution curve and more 'continuous' variation.

Other environmental factors can also affect human skin colour. Paler-skinned people will naturally produce more melanin in their skin to protect them from UV rays when they are exposed

to intense sunlight for a period of time. But this is a temporary effect and their skin colour will return to its genetically determined colour when they are no longer exposed to the sun.

Human height and body mass are also examples of polygenic characteristics, but both can be influenced by environmental factors, such as nutrients in a person's diet or the quantity of food that they consume.

4.2.9 Variation in phenotypes without change to genotype

Phenotypic plasticity

Phenotypic plasticity is defined as the ability of individual genotypes to produce different phenotypes when exposed to different environmental conditions. Polyphenism is a type of phenotypic plasticity by which some species adapt to drastic and recurrent changes in the environment such as seasonal alternation in temperate and tropical regions. Polyphenism is the process by which two or more different phenotypes are produced from the same genotype. Seasonal polyphenism in butterflies allows many species can change the colour of their larvae, pupae or adult forms in response to changes in temperature, day length or humidity, for example the squinting bush brown butterfly (*Bicyclus anynana*) of eastern Africa are dull brown in colour during the dry season but in the wet season butterflies with large eyespots develop. The eyespots help to defend the insects from bird predators. Another example is caste polyphenism in social insects which allows species such as ants to develop into either a reproductive queens or a sterile worker ants. In this case females with highly similar genomes look and behave very differently. Many other insect species divide their life stages between larval feeding and growing stages and adults which reproduce and disperse. Among the vertebrates, the sex of offspring in reptiles such as crocodiles is determined by the temperature at which eggs are incubated.

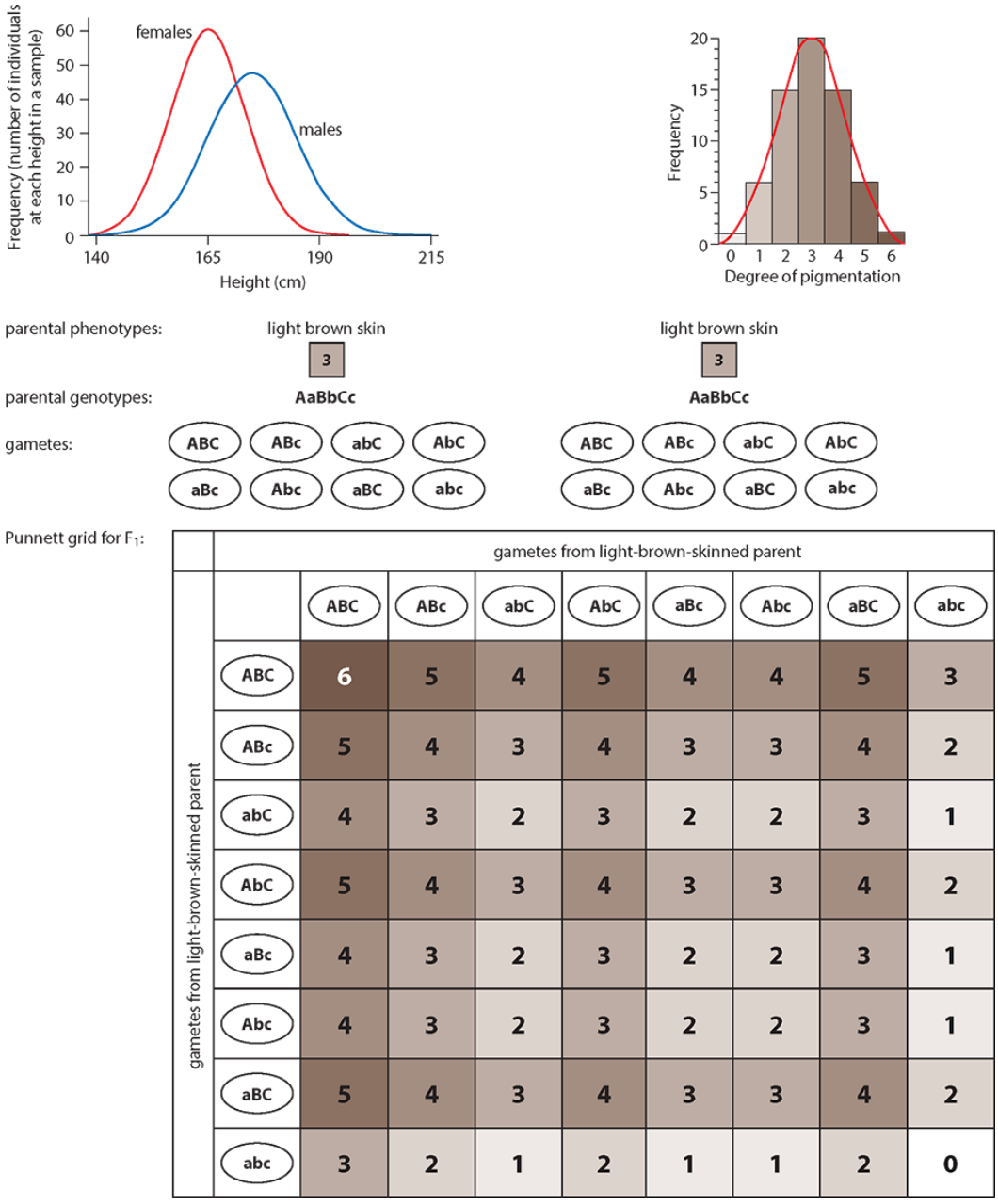


Figure 4.2.6: Top, human height demonstrates continuous variation – when frequency is plotted against height, a normal distribution is obtained. Bottom, frequency of skin variation shown on a bar graph and Punnett grid show the possible combinations of skin colour in children from two heterozygous parents.

Factors affecting sex determination

In some species, sex is influenced not only by genotype at conception but also by the environment that offspring experience during their early development. **Environmental sex determination (ESD)** probably provides a means for the species to adapt when seasonal variations in environmental conditions give one sex an advantage over the other. Temperature, location, nutrient availability and **photoperiodism** are four environmental factors that have been shown to affect the sex of offspring in a number of species.

Temperature

The sex of all crocodiles and most turtle species is determined by the temperature that their eggs experience after fertilisation. The temperature at a critical point in their development is crucial and small changes can cause a dramatic difference in the sex of offspring that hatch. In many species males and females only hatch from the same clutch of eggs over a small range of temperatures. Figure 4.2.7 shows the percentage of male animals produced for three species, the pond slider turtle (*Trachemys scripta*), the freshwater alligator snapping turtle (*Macroclemys temminckii*) and the American alligator (*Alligator mississippiensis*). The alligator snapping turtle produces a higher proportion of males in a clutch up to a temperature of 26 °C but the percentage decreases as the temperature rises beyond this. The American alligator's eggs all develop into male animals when the temperature is 33 °C, whereas the pond slider turtle eggs all hatch as male between 26 and 28 °C.

KEY POINTS

environmental sex determination (ESD) refers to a mechanism by which sex is determined in some species, not only by genotype, but also by the environment that offspring experience in early development.

photoperiodism is the reaction of organisms to changes in day length.

polygenic inheritance is the inheritance of a characteristic controlled by two or more genes.

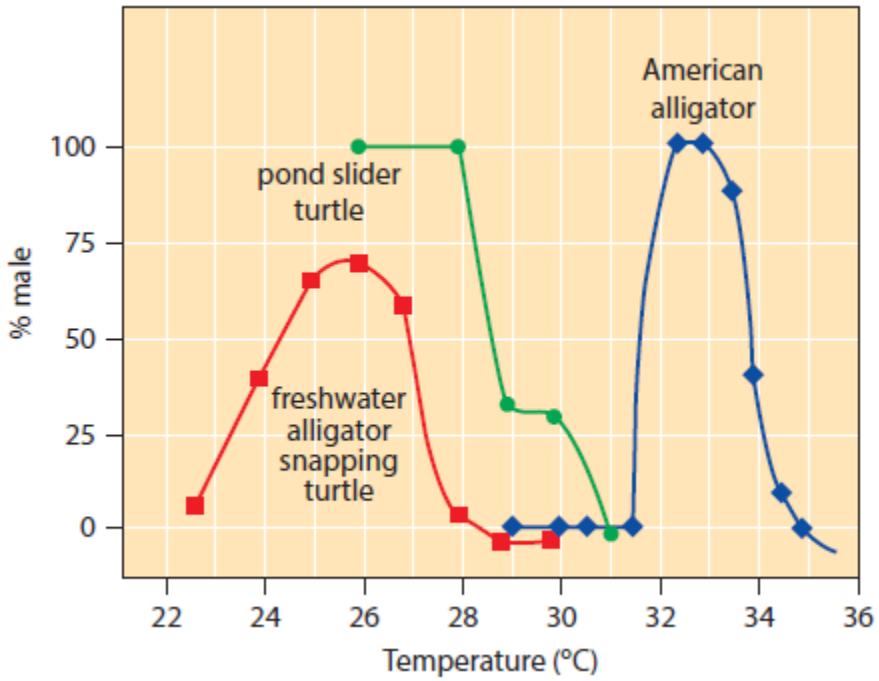


Figure 4.2.7: Temperature-dependent sex determination in three reptile species.

Location

Location is also a factor in determining the sex of the common slipper limpet *Crepidula fornicata*. In this species, individuals pile up on top of one another to form a small tower (Figure

4.2.8). Young individuals are always male but their reproductive systems degenerate after the early stages of their development. In the next phase of their life the individuals can become either male or female, and this will depend on their position in the pile. If the snail is attached to a female, it will become male. But if a snail is removed from its attachment, it will transform into a female. If there are too many males present, some will become females, but once an individual has become female it will not change again.

Figure 4.2.8: Common slipper limpets attach to one another to form piles which determine their sex.

4.2.10 Dihybrid crosses and linked genes

Single genes and monohybrid (single gene) genetic crosses produce variation, while multiple alleles, such as those that control blood groups, increase the possible variety still further. But other dihybrid crosses involve more than one gene. Single genes alone control very few characteristics and, when several genes control a characteristic, the phenotype is determined by their combined effect.

During meiosis (Section 6.5) the two alleles of every gene separate in a process called segregation. Genes found on separate chromosomes segregate independently of the alleles of other genes. Genes found on the same chromosomes are linked genes and so do not segregate independently. In dihybrid crosses the inheritance of two genes is investigated together.

Mendel's law of independent assortment

Gregor Mendel formulated a 'law of independent assortment' that states:

- When gametes are formed, the separation of one pair of alleles into the new cells is independent of the separation of any other pair of alleles.

Or:

- Either of a pair of alleles is equally likely to be inherited with either of another pair.

The dihybrid cross

A **dihybrid cross** involves two pairs of genes on different chromosomes instead of just one pair on one chromosome, but

the principles of setting out a genetic cross diagram to predict the offspring that will be produced are exactly the same as that for the monohybrid crosses. The genetic diagrams should include parental phenotypes, parental genotypes, gametes in circles and a Punnett grid for the F_1 or F_2 generation.

KEY POINTS

dihybrid cross is a cross involving two pairs of genes on different chromosomes.

linked genes genes which have gene loci on the same chromosome.

linkage group in genetics, the genes carried on one chromosome that do not show random or independent assortment.

EXAM TIP

Remind yourself of the correct way of writing dominant, recessive and codominant alleles in genetics problems.

Mendel carried out dihybrid crosses and an example is shown as one of the following Worked examples.

Linkage

The human genome contains between 25 000 and 30 000 genes, but there are only 23 pairs of chromosomes. This means that each chromosome must carry very many genes. Chromosome 1 contains over 3000 genes but the much smaller chromosome 21 contains only around 400 genes.

Any two genes with loci on the same chromosome are said to be linked. Linked genes are usually passed on together. The genes on any chromosome form a linkage group, so a human has 23 linkage groups. The difference between unlinked and linked genes is shown in Figure 4.2.9.

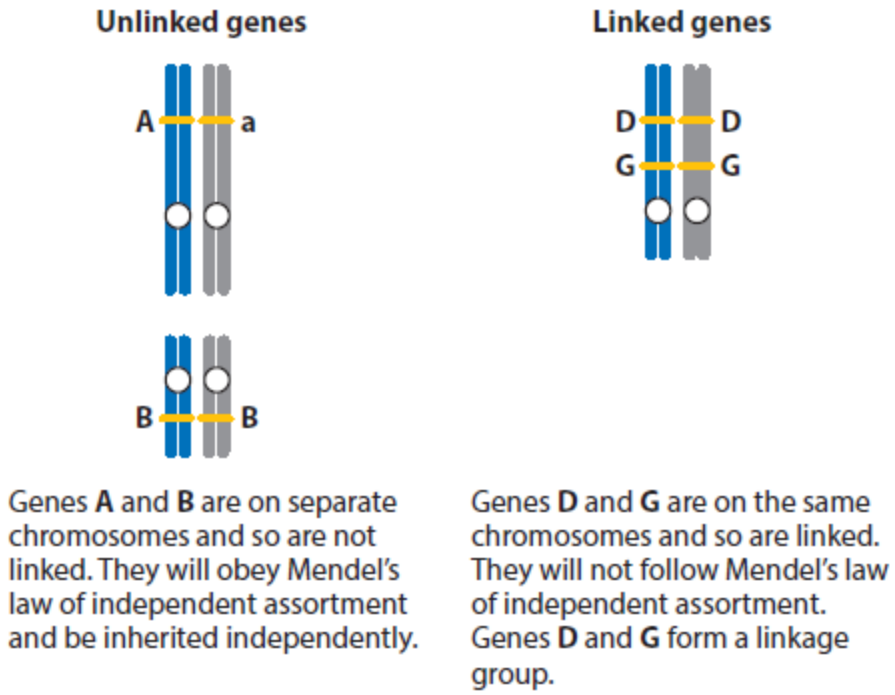


Figure 4.2.9: The difference between unlinked and linked genes.

WORKED EXAMPLE 4.2.7

Fur colour in mice is determined by a single gene. Brown fur is dominant to white. Ear size is also determined by a single gene. Rounded ears are dominant to pointed ears.

A mouse homozygous for brown fur and rounded ears was crossed with a white mouse with pointed ears. Determine the possible phenotypes and genotypes of the offspring.

Step 1 Choose suitable letters to represent the alleles. Brown fur is dominant, so let **B** = brown fur and **b** = white fur. Rounded ears is dominant, so let **R** = rounded ears and **r** = pointed ears.

Step 2 The brown mouse with rounded ears is homozygous so its genotype must be **BBRR**.

As white and pointed are recessive, the genotype of the white mouse with pointed ears must be **bbrr**.

Step 3 Set out the genetic diagram as shown.

Step 4 All the F_1 mice have brown fur and rounded ears.

Answer

parental phenotypes:	brown fur, rounded ears	white fur, pointed ears
parental genotypes:	**BBRR**	**bbrr**
gametes:	all (**BR**)	all (**br**)

Punnett grid for F_1:

	gametes from brown, round-eared parent	
		(**BR**)
gametes from white, pointed-eared parent	(**br**)	**BbRr** brown, rounded ears

WORKED EXAMPLE 4.2.8

Mendel carried out genetic studies with the garden pea. Tall plants are dominant to short, and green seed pods are dominant to yellow. Mendel crossed a homozygous tall plant with yellow seed pods with a short plant homozygous for green seed pods. Determine the possible genotypes and phenotypes in the offspring.

Step 1 Tall is dominant to short, so T = tall and t = short. Green pod is dominant to yellow so G = green and g = yellow.

Step 2 Each parent has one dominant and one recessive characteristic but we are told the dominant characteristic is homozygous. The tall plant with yellow seed pods therefore has genotype TTgg, and the short, green-podded plant is ttGG.

Step 3 Set out the genetic diagram as shown.

Step 4 All the offspring are tall plants with green seed pods.

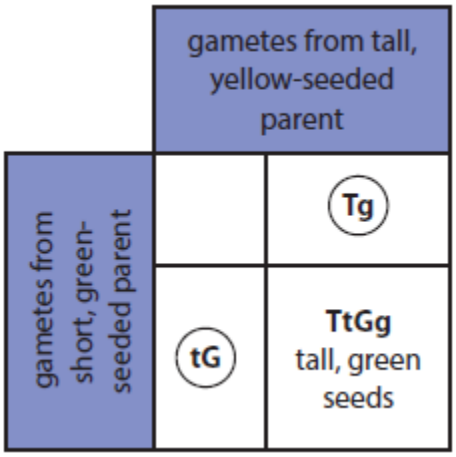
It was fortunate that Mendel chose these two characteristics for his crosses. Seed pod colour and height are unlinked genes on different chromosomes. Had they been on the same chromosome and linked, the results would have been different.

Answer

parental phenotypes:	tall, yellow seed pods	short, green seed pods
parental genotypes:	**TTgg**	**ttGG**
gametes:		

all (Tg) all (tG)

Punnett grid for F_1:



WORKED EXAMPLE 4.2.9

One of the heterozygous F_1 mice with brown fur and rounded ears from the cross in Worked example 4.2.7 was crossed with a mouse with white fur and rounded ears. Some of the offspring had pointed ears. Deduce the genotype of the second mouse and state the phenotype ratio of the offspring.

Step 1 Use the same letters as in Worked example 4.6.7: **B** = brown fur and **b** = white fur, **R** = rounded ears and **r** = pointed ears.

Step 2 The first mouse has the genotype **BbRr**.

We are told the second mouse is white, so it must have the alleles **rr**. It has rounded ears but we are not told if this is homozygous or heterozygous, so the alleles could be **RR** or **Rr**.

Reading on, we find that there are some offspring with pointed ears, so they must have the genotype **rr**. This means that the unknown parent genotype must have been heterozygous, **Rr**. If the parent was **RR**, no recessive allele would have been present so that a homozygous genotype could not occur in the offspring, and none of them would have had pointed ears.

Step 3 Having written down your reasoning, as in Step 2, now set out the usual genetic diagram.

Answer

parental phenotypes:	brown rounded ears	white rounded ears
parental genotypes:	**BbRr**	**bbRr**
gametes:	(BR) (Br) (bR) (br)	(bR) (br)

Punnett grid for F_1:

		gametes from brown, rounded-eared parent			
		(BR)	(Br)	(bR)	(br)
gametes from white, rounded-eared parent	(bR)	**BbRR** brown, rounded ears	**BbRr** brown, rounded ears	**bbRR** white, rounded ears	**bbRr** white, rounded ears
	(br)	**BbRr** brown, rounded ears	**Bbrr** brown, pointed ears	**bbRr** white, rounded ears	**bbrr** white, pointed ears

Step 4 The phenotypes produced are:

3 brown fur, rounded ears

3 white fur, rounded ears

1 brown fur, pointed ears

1 white fur, pointed ears.

This produces a ratio of phenotypes of 3 : 3 : 1 : 1, which is an important Mendelian ratio.

Notice that the individuals with white fur and pointed ears and brown fur and pointed ears are recombinant offspring because they have characteristics that differ from both their parents. Recombinants are always present in lower numbers than non-recombinant individuals.

KEY POINT

recombinant offspring is an offspring with characteristics that are different from both their parents. They are always present in lower numbers than other offspring.

Linkage and inheritance

If alleles are linked together on a chromosome, then it follows that they will be inherited together because during meiosis they will move together as the cell divides. In genetics problems, dihybrid crosses involving linked genes do not produce Mendelian ratios.

Linked genes do not follow Mendel's law of independent assortment, they are not inherited independently and can give a variety of different ratios.

Writing a linkage genotype

In the dihybrid crosses considered so far, genotypes have been written in the form AABB. With linked genes, a different notation has to be used because, although there are still four alleles to be considered, they are found on only one pair of

chromosomes. The genotype is therefore always written as shown in Figure 4.2.12. The horizontal lines signify that the two genes occur on the same chromosome.

EXAM TIP

In monohybrid crosses, two ratios for the offspring of a genetic cross are possible.

The first is 1 : 1 if a heterozygous individual **(Aa)** and a homozygous recessive individual (**aa**) are crossed. The second is 3 : 1 when two heterozygous individuals are crossed (**Aa** × **Aa**). These are called Mendelian ratios.

Mendelian ratios also occur in dihybrid crosses, but with more gametes there are more possibilities. A heterozygous individual (**AaBb**) crossed with a homozygous recessive (**aabb**) produces a 1 : 1 : 1 : 1 ratio and the ratio produced by crossing two double heterozygous (**AaBb**) individuals is 9 : 3 : 3 : 1.

The 3 : 3 : 1 : 1 ratio in Worked example 4.6.9 is another Mendelian ratio. It is helpful to be familiar with these ratios.

NATURE OF SCIENCE

Looking for trends and discrepancies: the work of T.H. Morgan

Thomas Hunt Morgan (1866–1945) was a pioneering geneticist who studied the inheritance of mutations in the fruit fly *Drosophila melanogaster*. After the rediscovery of Mendelian genetics in 1900, Morgan worked to show that genes are carried on chromosomes and provide the basis for inheritance. He induced mutations in his flies using chemicals

and radiation and began cross-breeding experiments to find mutations that were inherited. Despite the difficulty of spotting mutations in the tiny flies, he eventually noticed a white-eyed mutant male among the typical 'wild type' red-eyed flies. He bred white-eyed male flies with red-eyed females and all the offspring were red-eyed. The F_2 (second generation) cross produced white-eyed males so Morgan concluded that the white-eye mutation was a sex-linked recessive trait (Figure 4.2.10). He also discovered a pink-eyed mutant which was not sex linked.

Morgan reported his discoveries of sex linkage and autosomal inheritance in the journal *Science* in 1911. Morgan's team discovered more mutants amongst thousands of flies they studied and also identified flies with multiple mutations. They studied more complex patterns of inheritance, finding more examples of crosses that did not fit the pattern of simple Mendelian ratios. To explain these discrepancies, Morgan went on to suggest that genes could be linked and inherited together.

Morgan proposed the hypothesis of crossing over in his book and the relationship between crossing over and linked genes. He suggested that cross-over frequency gave a measure of the distance separating genes on a chromosome.

His book *The Mechanism of Mendelian Heredity*, published in 1915, was a foundation for modern genetics. (Morgan, Thomas Hunt, *The Mechanism of Mendelian Heredity.* New York: Henry Holt and Company, 1915. Electronic reproduction. New York, N.Y. : Columbia University Libraries, 2007.)

To consider:

1 In what ways do scientists improve the quality and quantity of evidence they collect?

2 *Drosophila* flies are known as 'model' organisms and are used in many genetic experiments. Investigate other model organisms and their importance to science.

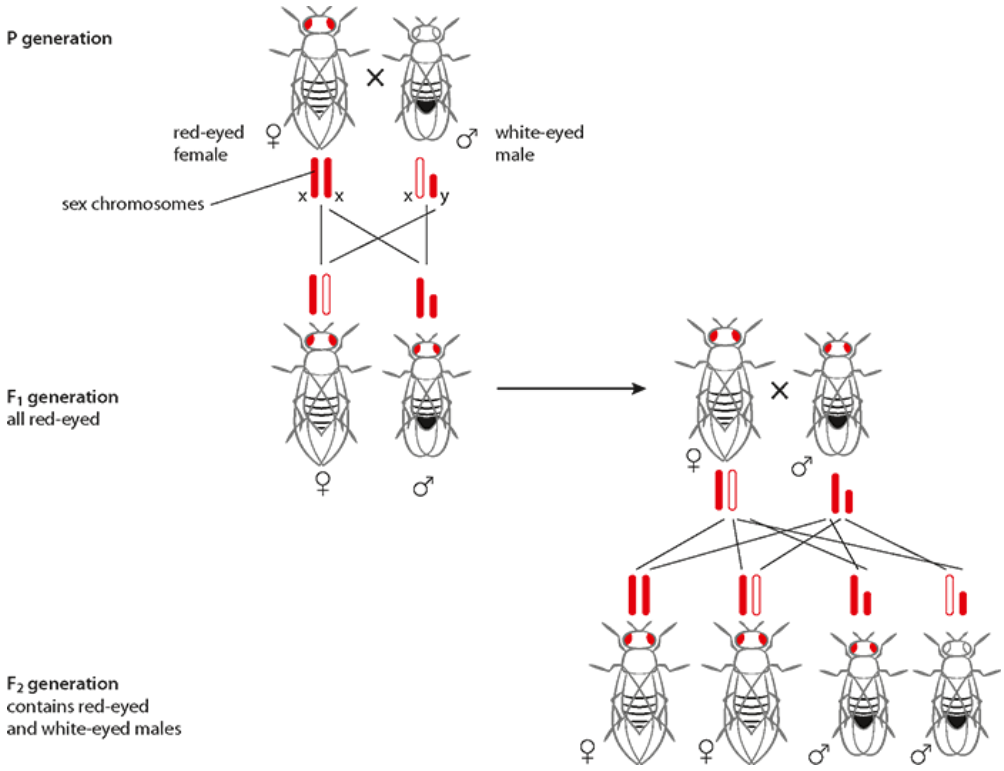


Figure 4.2.10: Inheritance of a sex-linked characteristic in Drosophila.

Linkage and crossing over

In Chapter 6, Figure 6.5.9 you can study how crossing over creates genetic variety by exchanging parts of the maternal and paternal chromosomes during meiosis. Figure 4.2.13 shows what

happens to two closely linked alleles after a cross-over occurs between them.

Look back at the left-hand example in Figure 4.2.11. Without crossing over, the parental gametes formed will be **DG** and **dg**. If a cross-over does take place (as shown by the red cross in Figure 4.2.12) then additional recombinant gametes **Dg** and **dG** will be formed.

Four types of gamete – **DG**, **dg**, **Dg** and **dG** – are possible, but there is a very significant difference in the numbers of each type that are formed. The chance of a chiasma forming between the two loci, which are close together, is very small. So the chance of forming the gametes **Dg** and **dG** is also very small. The majority of gametes therefore carry the alleles **DG** and **dg** and they will form in equal numbers. If a cross-over does takes place, for every **Dg** gamete there will be a **dG** gamete. The numbers of these two gametes will also be equal but very small. The geneticist T.H. Morgan made these observations in his work (see Nature of Science, Looking for trends and discrepancies: the work of T.H. Morgan).

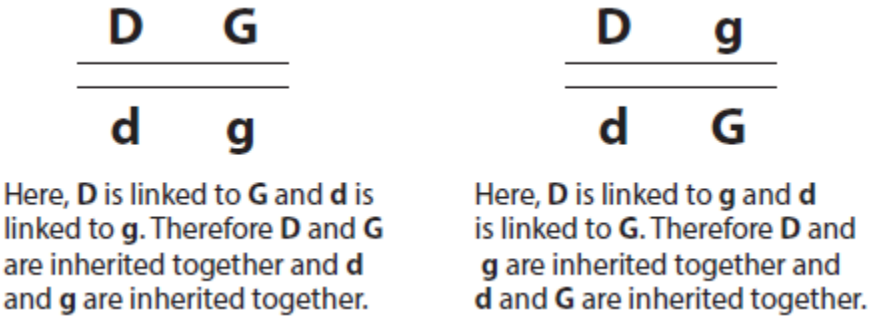


Figure 4.2.11: The two possible linkage patterns for the four alleles. The difference between the two linkage patterns makes a very big difference in the ratios of the phenotypes in the offspring of a cross.

Figure 4.2.12: If a cross over (shown by the red cross) takes place then the recombinant gametes Dg and dG will be formed.

Now look at the right-hand example in Figure 4.2.13. What will be the allele combinations in gametes where crossing over has not taken place? What will be the allele combinations in gametes where crossing over has taken place, and which combinations will be present in greater numbers?

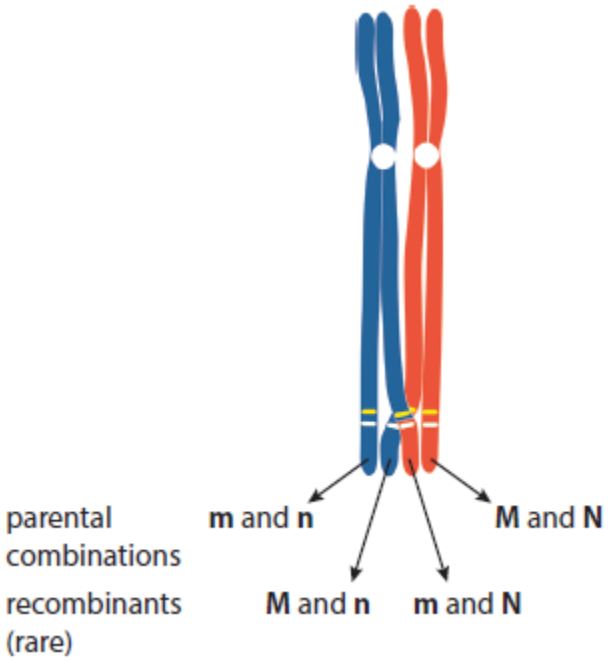


Figure 4.2.13: A single chiasma (point of contact) has formed between two chromatids so crossing over of the alleles can take place to form recombinant gametes. No crossing over has taken place with the other chromatids and so these will retain the parental combination of alleles.

WORKED EXAMPLE 4.2.10

In the fruit fly, *Drosophila*, red eye colour is dominant to purple eyes and long wings is dominant to dumpy wings. These genes are linked on chromosome 2. A fly that was homozygous for red eyes and long wings was crossed with a fly that had purple eyes and dumpy wings. Determine the ratios of genotypes and phenotypes of the F_2 offspring by using a full genetic diagram.

Step 1 Red eye colour is dominant so **R** = red eye and **r** = purple eye. Long wings is dominant so **N** = long wings and **n** = dumpy wings.

Step 2 The fly with the dominant characteristics is homozygous and the other fly shows both recessive characteristics. The parental genotypes are:

$$\frac{RN}{RN} \text{ and } \frac{rn}{rn}$$

Step 3 Set out the genetic diagram as below.

Answer

parental phenotypes:	red eyes, long wings	and	purple eyes, dumpy wings
parental genotypes:	$\frac{R\ N}{R\ N}$	and	$\frac{r\ n}{r\ n}$
gametes:	all (RN)		all (rn)

Punnett grid for F_1:

	gametes from red-eyed, long-winged parent	
gametes from purple-eyed, dumpy-winged parent		RN
	rn	$\frac{R\ N}{r\ n}$ red eyes, long wings

All the F_1 have red eyes and long wings.

Now, the F_2 generation is obtained by crossing two offspring from theF_1 generation.

parental phenotypes: red eyes, long wings and red eyes, long wings

parental genotypes: $\frac{R\ N}{r\ n}$ and $\frac{R\ N}{r\ n}$

gametes: RN rn RN rn

Punnett grid for F_2:

		gametes from red-eyed, long-winged parent	
		RN	rn
gametes from red-eyed, long-winged parent	RN	$\frac{R\ N}{R\ N}$ red eyes, long wings	$\frac{R\ N}{r\ n}$ red eyes, long wings
	rn	$\frac{R\ N}{r\ n}$ red eyes, long wings	$\frac{r\ n}{r\ n}$ purple eyes, dumpy wings

Step 4 In the F_2 generation, the ratio of phenotypes is 3 red eye, long wing : 1 purple eye, dumpy wing. Note that

this 3 : 1 ratio is what you would expect in a monohybrid cross. The reason for this is that the two genes are linked and so there is only one pair of chromosomes involved, as in monohybrid crosses.

WORKED EXAMPLE 4.2.11

Grey body and red eyes are dominant to stripe body and cardinal eye in *Drosophila*. They are autosomal, linked genes on chromosome 3. Homozygous grey flies with red eyes were crossed with stripe flies with cardinal eyes. No crossing over occurred.

Then the F_1 flies were crossed with stripe, cardinal flies.

If no crossing over occurs between the two loci, what phenotypes would be expected in the offspring of this second cross?

If crossing over did occur between the loci, what phenotypes would be expected this time?

Answer

First cross, with no crossing over:

Step 1 Grey body is dominant, so **G** = grey body and **g** = stripe body. Red eye is dominant so **R** = red eye and **r** = cardinal eye.

Step 2 The fly with the dominant characteristics is homozygous and the other fly shows both recessive characteristics. The parental genotypes are:

$\frac{GR}{GR}$ and $\frac{gr}{gr}$.

Step 3 Set out the diagram as shown.

parental phenotypes: grey body, red eyes stripe body, cardinal eyes

parental genotypes: $\frac{G\ R}{G\ R}$ $\frac{g\ r}{g\ r}$.

gametes: all (GR) all (gr)

Punnett grid for F_1:

gametes from stripe-bodied, cardinal-eyed parent	gametes from grey-bodied, red-eyed parent: (GR)	gametes from grey-bodied, red-eyed parent: (gr)
	(GR)	
(gr)		$\frac{G\ R}{g\ r}$ grey body, red eyes

Step 4 All the F_1 flies have a grey body and red eyes.

Second cross, with no crossing over:

parental phenotypes: grey body red eyes stripe body, cardinal eyes

parental genotypes: $\frac{G\ R}{g\ r}$ $\frac{g\ r}{g\ r}$.

gametes: (GR) (gr) all (gr)

Punnett grid for F_1:

		gametes from grey-bodied, red-eyed parent	
		(GR)	(gr)
gametes from stripe-bodied, cardinal-eyed parent	(gr)	$\frac{G\ R}{g\ r}$ grey body, red eyes	$\frac{g\ r}{g\ r}$ stripe body, cardinal eyes

Second cross, with crossing over:

parental phenotypes: grey body red eyes / stripe body cardinal eyes

parental genotypes: $\frac{G\ R}{g\ r}$ / $\frac{g\ r}{g\ r}$

gametes produced by crossing-over: (GR) (gr) (Gr)+ (gR)+ all (gr)

Punnett grid for F_1:

		gametes from grey-bodied, red-eyed parent			
		(GR)	(gr)	(Gr)	(gR)
gametes from stripe-bodied cardinal-eyed parent	(gr)	$\frac{G\ R}{g\ r}$ grey body, red eyes	$\frac{g\ r}{g\ r}$ stripe body, cardinal eyes	$\frac{G\ r}{g\ r}$ grey body, cardinal eyes	$\frac{g\ R}{g\ r}$ stripe body, red eyes

Step 4 The four F_1 phenotypes are:

- grey body and red eyes
- stripe body and cardinal eyes
- grey body and cardinal eyes
- stripe body and red eyes

The 'grey, cardinal' and 'stripe, red' (shown in red type) flies are recombinants as they have a phenotype that is

different from the parental phenotypes. These recombinant phenotypes will occur in approximately equal numbers. The parental phenotypes (shown in black type) will also be in approximately equal numbers among the offspring, but the recombinant phenotypes will be very few in number compared to the parental phenotypes.

NATURE OF SCIENCE

Careful observation: were Mendel's results 'too good to be true'?

In Mendel's time, statistical analyses, such as the chi-squared test, were not routinely used to test the validity of scientific results. Analysis of the ratios that Mendel published in 1866 suggests that they may be too close to the expected 3 : 1 ratio. Some have suggested that Mendel selected the data to present or that, having obtained a 3 : 1 ratio in some experiments, he persisted with counting until he achieved his expectations in subsequent experiments.

Mendel considered seven genes in his monohybrid experimental crosses, and also carried out dihybrid crosses involving pairs of these same genes. Crosses involving a pair of genes on different chromosomes produce the ratios Mendel reported, but he would have obtained unexpected results had he used linked genes, that is, genes that occur on the same chromosome. It is not likely that the seven genes Mendel investigated would each occur on a different chromosome by chance (the pea plant only has seven pairs of chromosomes) so perhaps some of his crosses did involve linked genes. He would not have been able to explain the results from such crosses as he did not know about chromosomes, so it may be

that he only published results from crosses that met his expectations.

Later work by T.H. Morgan involving meticulous observation and record keeping revealed anomalous data in dihybrid crosses similar to those that Mendel had performed. As a result, Morgan developed his ideas of gene linkage to explain the results.

To consider:

1 How do expectations and personal bias affect the results that scientists collect and present?

2 How is our understanding of science improved by reviewing results from experiments conducted a long time ago?

3 How important are statistics to modern science?

THEORY OF KNOWLEDGE

Breaking the law

Mendel's law of independent assortment was found to have exceptions that geneticist T.H. Morgan explained by using the idea of linked genes that occur on the same chromosome

To consider:

1 Is it correct to call Mendel's proposals a 'law'?

2 What is the difference between a law and a theory in science?

4.2.11 The chi-squared test and dihybrid crosses

The chi-squared (χ^2) test is a statistical test used to check if the results of an experiment support a theory. It can be used in cases in which variation is discrete. In genetic or ecological investigations, the chi-squared test is useful to compare your observed results with the results that you would expect if your theory about how the system works is correct. The test tells you whether or not any difference between your observed results and your expected results is significant. If the difference is significant that means the results do not fit well with your theory, so you may need to revise your theory. If the difference is not significant – that is, it is so small that it could have occurred by chance – then you can say that your results do support your theory.

In the case of genetics the test is used to check if the results of genetic crosses (the Observed results) match predictions made from Mendelian ratios (the Expected results). The formula for calculating the chi-squared value is:

$$\chi^2 = \sum \frac{(O - E)^2}{E}$$

where χ^2 is the test statistic, Σ means 'the sum of', O is the observed frequencies and E is the expected frequencies.

The greater the value of chi-squared you calculate, the greater the difference between your observed and expected results. To find out whether the difference is significant or not, you must compare your chi-squared value with a table of 'critical values' like the one in Table 4.2.4. The **null hypothesis** states that there is no significant difference between the observed and expected results, that is, that the results fit the expected pattern and therefore support your theory.

The chi-squared test can be used to test the outcome of monohybrid or dihybrid crosses, to see if the observed ratios fit the expected pattern. The worked examples that follow use data that were produced as a result of dihybrid crosses.

The null hypothesis predicts the ratio of offspring of different types from Mendelian ratios for the cross, assuming that there is no linkage. A

significant difference from the predicted ratio can indicate that alleles are linked.

WORKED EXAMPLE 4.2.12

Theory tells us that wing length in *Drosophila* is controlled by a single pair of genes on their second chromosome. Wings may be normal or vestigial. Flies with vestigial wings have a recessive gene and cannot fly. If two heterozygous parents are crossed, a ratio of 3 : 1 normal to vestigial wings is the expected result. We put forward a null hypothesis that there is no significant difference between the observed and expected results. If the chi-squared test shows that there is no difference between observations and expectations we can accept the null hypothesis that wing length is controlled by monohybrid inheritance.

In a cross between heterozygous parents, 320 offspring were counted.

Answer

Step 1 Set the null hypothesis; this predicts the ratio of offspring of each phenotype according to Mendelian ratios for the cross. For a monohybrid cross, the expected ratio of phenotypes in the F1 generation is 3 : 1. So here, with 320 flies, our expected result is that we should see a ratio of 3 : 1 normal : vestigial wings,

¼ × 320 = 80 flies should have vestigial wings and

¾ × 320 = 240 flies should have normal wings

The actual numbers of offspring were counted and recorded:

Phenotype	Ratio	Expected result	Observed result
Normal wings	3	240	232
Vestigial wings	1	80	88

Step 2 We must now use the chi-squared equation to test whether the observed numbers differ significantly from our expectations. Calculate the value of chi-squared. This is the sum of the differences between

each pair of observed and expected values, squared, and divided by the expected value:

$$\chi^2 = \sum \frac{(O-E)^2}{E}$$

Phenotype	Ratio	Expected result	Observed result	$O-E$	$(O-E)^2$	$\frac{(O-E)^2}{E}$
Normal wings	3	240	232	−8	64	0.266
Vestigial wings	1	80	88	8	64	0.80

Using the formula, $\chi^2 = 0.266 + 0.80 = 0.376$.

Step 3 Select the appropriate row in a table of critical values of chi-squared, like the one in Table 4.6.4.To do this, we must calculate the 'degrees of freedom', which is the number of categories among your results, minus 1. In this case there are two categories (normal wings and vestigial wings) so the degrees of freedom 2 − 1 = 1. Look along the row of the table that corresponds to 1 degree of freedom.

Step 4 Find the critical chi-squared value at the 5% (0.05) significance level. In biology, the 5% significance level is used. This level means that the probability for rejecting the null hypothesis is 5%, that is, there is a 5% probability that the difference between the observed results and the expected values occurred purely by chance, and is not significant. If our calculated chi-squared value is less than the critical value at the 5% level, then the probability of obtaining the difference we observed by chance alone is greater than 5%, so we can accept the null hypothesis and have no reason to think that our results differ significantly from our expected values.

In this case, the chi-squared (0.376) value is lower than the value in the table (3.841) so we accept the null hypothesis that there is no significant difference between the observed and expected results. In other words, our results support the theory on which the expected ratio of 3 : 1 was based. We can accept the theory that wing length in these flies is due to monohybrid inheritance.

Degrees of freedom	*p*									
	0.995	**0.99**	**0.975**	**0.95**	**0.90**	**0.10**	**0.05**	**0.025**	**0.01**	**0.005**
1	---	---	0.001	0.004	0.016	2.706	3.841	5.024	6.635	7.879
2	0.010	0.020	0.051	0.103	0.211	4.605	5.991	7.378	9.210	10.597
3	0.072	0.115	0.216	0.352	0.584	6.251	7.815	9.348	11.345	12.838
4	0.207	0.297	0.484	0.711	1.064	7.779	9.488	11.143	13.277	14.860
5	0.412	0.554	0.831	1.145	1.610	9.236	11.070	12.833	15.086	16.750
6	0.676	0.872	1.237	1.635	2.204	10.645	12.592	14.449	16.812	18.548
7	0.989	1.239	1.690	2.167	2.833	12.017	14.067	16.013	18.475	20.278
8	1.344	1.646	2.180	2.733	3.490	13.362	15.507	17.535	20.090	21.955
9	1.735	2.088	2.700	3.325	4.168	14.684	16.919	19.023	21.666	23.589
10	2.156	2.558	3.247	3.940	4.865	15.987	18.307	20.483	23.209	25.188

Table 4.2.4: A chi-squared table. Critical values of the chi-squared distribution, showing how to read across the appropriate 'degrees of freedom' row to find the critical chi-squared value at the 0.05 level (p).

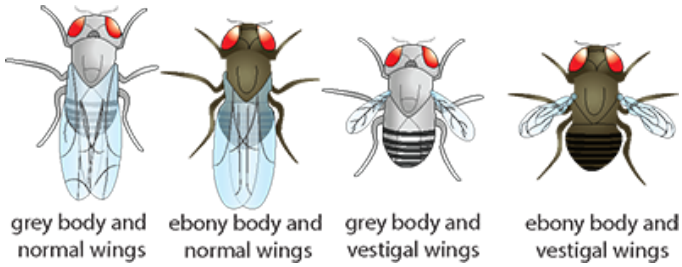


Figure 4.2.14: Diagram to show some inherited characteristics of Drosophila sp.

A cross between *Drosophila* involved four characteristics: ebony body, grey body, long wings and vestigial wings (Figure 4.2.14). Assuming that there is no linkage of alleles our expected result should be a 1 : 1 : 1 : 1 ratio.

After the cross, 800 flies were collected and the numbers of offspring of each type were recorded:

Grey body, normal wings 196	Ebony body, normal wings 204
Grey body, vestigial wings 176	Ebony body, vestigial wings 224

Phenotype	**Ratio**	**Expected result**	**Observed result**	$O-E$	$(O-E)^2$	$\frac{(O-E)^2}{E}$
Grey, normal wings	1	200	196	−4	16	0.08
Grey, vestigial wings	1	200	176	−24	576	2.88
Ebony, normal wings	1	200	204	4	16	0.08
Ebony, vestigial wings	1	200	224	24	576	2.88

Using the formula, $\chi^2 = 0.08 + 2.88 + 0.08 + 2.28 = 6.52$

From Table 4.2.4, the critical value at the 5% (0.05) level, for 3 degrees of freedom = 7.815

Our calculated value is less than the critical value so we can accept the null hypothesis that there is no significant difference between our observations and expectations. We can accept the conclusion that a 1 : 1 : 1 : 1 ratio is the result of this type of dihybrid cross.

TEST YOUR UNDERSTANDING

14 List three environmental factors that can determine the sex of offspring of certain organisms.

15 Define the term linked gene loci.

16 How do we work out the ‘degrees of freedom’ in a chi-squared test?

EXAM TIP

If the expected ratio in a Mendelian cross is 9 : 3 : 3 : 1 the expected values (E) must be calculated accordingly and the totals divided by 16 (9 + 3 + 3 + 1).

Links

- How do variations that are inherited contribute to evolution? (Chapter 11)
- How do genetic conditions caused by dominant alleles remain in the population? (Chapter 11)
- To what extent does sexual reproduction contribute to variation? (Chapter 6 and 8)

SELF-ASSESSMENT CHECKLIST

Think about the topics covered in this chapter. Which parts are you most confident with? Which topics require some extra practice?

I can...	Subsection	Needs more work	Nearly there	Confident to move on
define genome	4.1.1			
summarise the differences between prokaryotic and eukaryotic chromosomes	4.1.2			
differentiate between diploid and haploid nuclei and a chromosome and a chromatid	4.1.2			
recall that genome sizes are different in different species but that size does not relate to	4.1.2			

complexity of the organism				
define a gene and explain how a gene may have different alleles at the same locus	4.1.3			
recall that chromosome number is a characteristic of a species	4.1.4			
summarise the how karyograms are made and their uses, including benefits and disadvantages	4.1.4			
outline the importance of X inactivation and why Barr bodies are produced	4.1.5			
summarise the importance of Mendel's work to genetics	4.2.1			
state that gametes are haploid, and that fusion of	4.2.1			

gametes produces a diploid zygote				
work out genotypes and phenotypes from genetic crosses using Punnett grids	4.2.2			
define the terms genotype, phenotype, homozygous and heterozygous, incomplete dominance and codominance	4.2.3, 4.2.4			
describe the ABO blood system as an example of the inheritance of a characteristic with multiple alleles	4.2.3			
outline how sex chromosomes are inherited and explain how sex-linked disorders such as hemophilia are inherited	4.2.5			
give examples of	4.2.7			

recessive conditions caused by inherited alleles				
explain polygenic inheritance and the difference between discrete and continuous variation	4.2.7			
outline the genetic condition PKU caused by a mutation	4.2.7			
define phenotypic plasticity	4.2.8			
give examples of species in which environmental conditions determine the sex of organisms	4.2.9			
use a Punnett square to demonstrate the inheritance of unlinked dihybrid characteristics	4.2.10			
explain the difference	4.2.10			

between linked and unlinked alleles and identify recombinants in crosses involving two genes				
use the chi-squared test on data from dihybrid crosses to check for the significance of results.	4.2.11			

REFLECTION

Reflect upon the content of this chapter and identify those areas of strength and weakness in your understanding. How can you improve in those topics you have found difficult?

EXAM-STYLE QUESTIONS

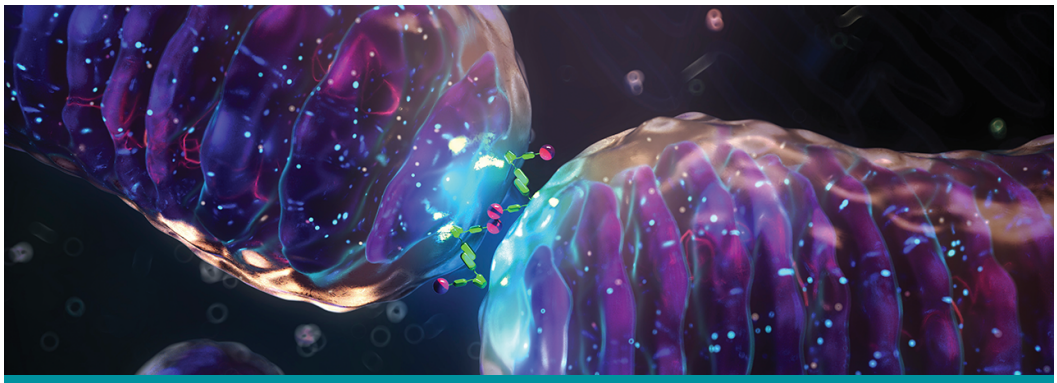
You can find questions in the style of IB exams in the digital coursebook.

Unit 2
Cellular organisation

INTRODUCTION

Cells as we know them today originated millions of years ago. Most scientists agree that life arose from organic molecules that were present on the early Earth. These molecules provided the building blocks of the cells that make up all living organisms. All cells have similarities, but also many differences. Structures such as membranes and mitochondria are organised in the same ways in different cells, but cells can express different genes and develop their own unique properties. Some cells become neurones, while others grow into bone or brain cells. In multicellular organisms cells interact to form tissues and organs to carry out their life processes.

All cells are limited in size and must remain small because substances must enter and leave through their plasma membrane. As cells grow larger they divide to replace parts of the body or to enable an organism to grow larger. Cells communicate with one another by cell signalling. Different parts of multicellular organisms communicate as nerve impulses and chemical signals that pass between their cells.



Chapter 5

Cell structure

A2.1, A2.2, A2.3

INTRODUCTION

In the middle of the 17th century, one of the pioneers of microscopy, Robert Hooke (1635–1703), decided to examine a piece of cork tissue with his home-built microscope. He saw numerous box-shaped structures that he thought resembled monks' cells or rooms in a monastery, so he called them 'cells'. As microscopes became more sophisticated, other scientists observed cells and found that they occurred in every organism. No organism has yet been discovered that does not have at least one cell. Living things may vary in shape and size but scientists agree that they are all composed of cells. The

study of cells has enabled us to learn more about how whole organisms function.

5.1 Origins of life

LEARNING OBJECTIVES

In this section you will:

- recognise how conditions on the early Earth led to the formation of organic molecules and the origins of life
- recognise that boundaries separate cells from their environments
- learn that cell theory states that cells are the smallest functional unit of life
- recognise that all cells arise from pre-existing cells
- discover that the Miller–Urey experiments provided evidence on the origin of organic compounds
- understand that the deep-sea vent hypothesis suggested how energy was provided for primitive life forms
- learn that RNA has properties that make it a likely part of primitive life
- learn that lipids have properties that make them important in protocell growth
- understand that the Last Universal Common Ancestor is proposed as the link between the abiotic and biotic phases of the early Earth

- learn that the evidence for LUCA comes from the genetic code shared across all organisms and fossilised evidence of life from ancient seafloor hydrothermal vents.

GUIDING QUESTIONS

1. What plausible hypothesis could account for the origin of life?
2. What is the evidence that supports the theory that life arose from organic molecules?

5.1.1 Forming organic molecules in the early Earth

Most scientists agree that evidence gathered from many sources indicates that the Earth formed about 4.5 billion years ago. Within the first billion years, the first signs of life appeared in the oceans and Earth's atmosphere began to change. Living organisms emerged, changed and have evolved, but how did the first molecules and organisms arise?

Abiogenesis, the origin of life, was a natural process. Scientists think that life arose from non-living, simple molecules and organic compounds. This probably did not happen all at once but in stages, so that life gradually became more complex and produced molecules that could self-replicate, assemble themselves and eventually produce a cell membrane that separated them from the environment. We say that life is an emergent property that has evolved over a long period of time.

KEY POINTS

abiogenesis the process by which life has arisen from non-living matter.

emergent properties of a complex system that arise from simple interactions of individual component parts. In the case of water, these properties are due to interactions between individual molecules.

In 1952 an experiment was carried out by Stanley Miller and Harold Urey which attempted to show that the conditions that existed on Earth millions of years ago were suitable for the synthesis of complex organic molecules from simple ones. The

experiment used molecules that were present on the early Earth: water, methane, ammonia and hydrogen. In a sealed flask (Figure 5.1.2) the water was heated and electrical sparks used to simulate lightning in the water vapour and mixture of gases. The experiment showed that organic compounds, amino acids, did form from the simple ingredients. The experiment is described in more detail in Section 5.1.3 The Miller–Urey experiments.

The next step in evolution must have been the formation of macromolecules. Monomers of macromolecules can polymerise spontaneously in the conditions that existed billions of years ago. For example, amino acids can polymerise to form polypeptides. But the most important feature of the macromolecules from which life evolved must have been the ability to replicate themselves. Only a macromolecule able to synthesise new copies of itself would have been able to reproduce and evolve.

We can never recreate the conditions that were present at the time, but the first cell is presumed to have developed when self-replicating RNA was enclosed in a membrane of phospholipids. Phospholipids are the main component of biological membranes in both prokaryotic and eukaryotic cells (Section 5.2). Because they are amphipathic molecules they can form a bilayer boundary that separates the interior of a cell from the external environment.

Primitive **protocells** containing RNA and enclosed in a membrane would have been able to evolve further and eventually code for, and produce, their own proteins.

KEY POINT

protocells structures formed from the aggregation of abiotic components but which have some similarities to living cells.

5.1.2 Cell theory

Today, scientists agree that the cell is the fundamental unit of all life forms. **Cell theory** proposes that all organisms are composed of one or more cells and, furthermore, that cells are the smallest units of life. An individual cell can perform all the functions of life – it must have a metabolism and the ability to replicate – and anything that is not made of cells, such as viruses, cannot be considered living (Section 5.3).

KEY POINT

Key principles of cell theory

- Living organisms are composed of cells.
- Cells are the smallest units of life.
- All cells, apart from the first cells, come from pre-existing cells.

As one of the key life processes of all living organisms is reproduction, one of the first principles of cell theory is that cells can only come from pre-existing cells. Louis Pasteur (1822–1895) carried out experiments that provided evidence for this. He showed that bacteria could not grow in a sealed, sterilised container of chicken broth. Only when living bacteria were introduced would more cells appear in the broth. Figure 5.1.1 summarises Pasteur's experiment.

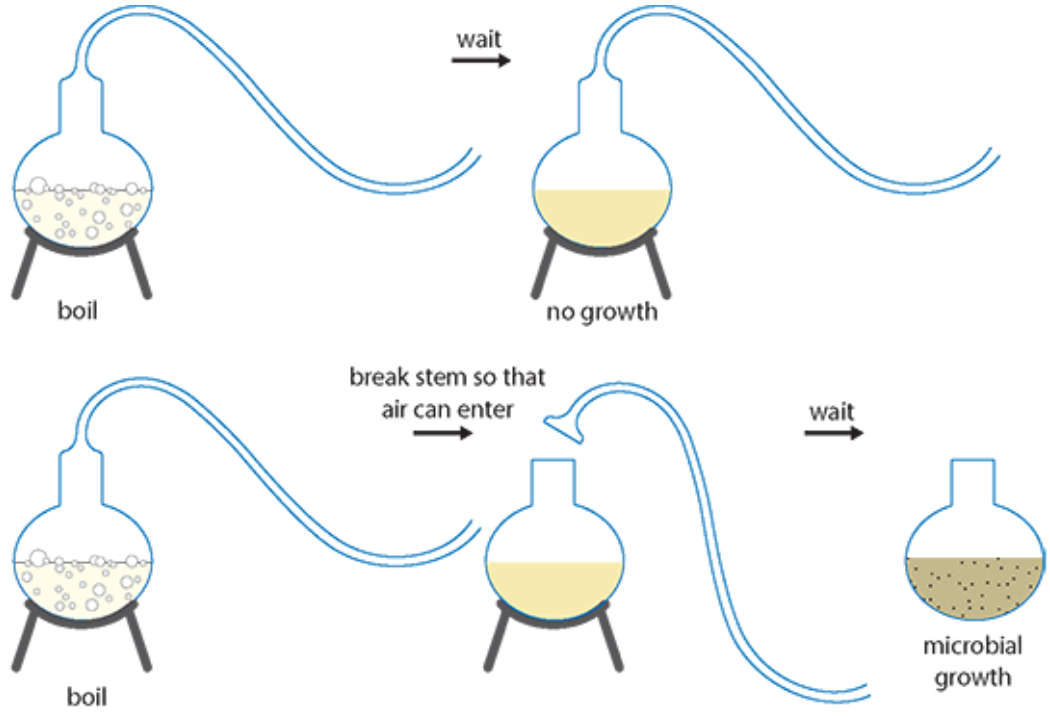


Figure 5.1.1: Pasteur demonstrated that living cells cannot 'spontaneously generate' but must originate from pre-existing cells.

TEST YOUR UNDERSTANDING

1 Name two substances present on the early Earth that may have contributed to the formation of the first organic molecules

2 Define emergent property.

3 List the fundamental features of a living cell.

5.1.3 The Miller-Urey experiments

In 1952 Stanley Miller and Harold Urey, working at the University of Chicago, simulated the conditions that they thought existed on Earth at the time life originated. The gases they used were enclosed in a sealed glass flask connected to a source of water vapour (Figure 5.1.2). Water vapour evaporated into the larger flask and electrical sparks were used to imitate lightning. Liquid from the flask was cooled and flowed down to the trap at the bottom of the apparatus. After a week the solution in the trap was removed and tested. It was found to contain at least five amino acids.

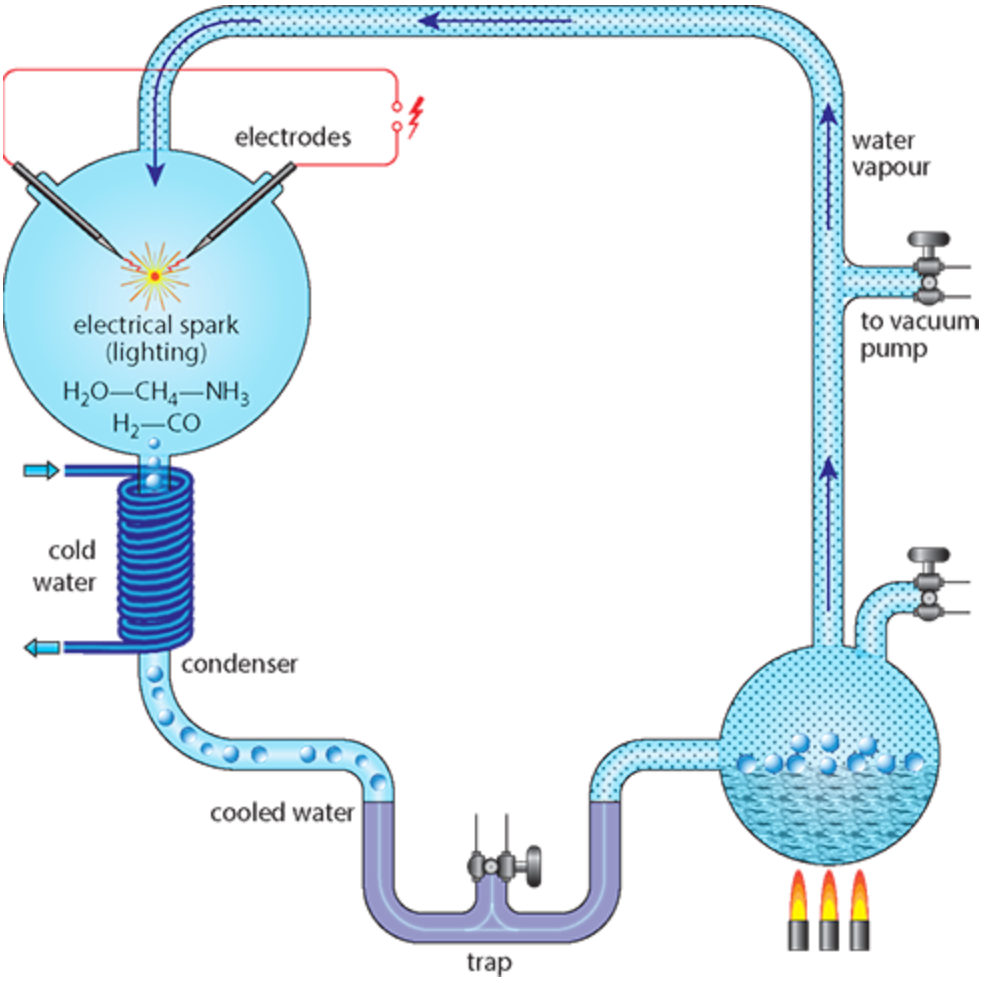


Figure 5.1.2: Diagram of the apparatus used in the Miller–Urey experiment.

In the early 21st century sealed flasks that had been kept from the original experiment were reopened and found to contain more than 20 amino acids. These results provide strong evidence that it is possible to create complex molecules from simple substances that were present on the prebiotic Earth.

More recent evidence has been gathered about the atmosphere on the early Earth and it suggests that the gas mixture Miller and Urey used was not exactly right. Nevertheless, similar experiments using different proportions of gases have been able to convert simple substances to complex compounds.

Today there are several different hypotheses about how life might have arisen on Earth.

5.1.4 The deep-sea vent hypothesis and a source of energy for primitive life

We do not know where life on Earth started and we cannot be sure what the environmental conditions were like 3–4 billion years ago. However, since their discovery in 1977, deep-sea hydrothermal vents under the oceans have been investigated as a possible place where life started.

The first vents to be discovered were ‘black smokers’, which give out plumes of hot water at temperatures of up to 400 °C. This water contains high levels of sulfides that produce the black smoke that is seen as they come into contact with the cold ocean water. In 2000, a new type of alkaline hydrothermal vent was discovered, the first one, located on the seabed in an area of the mid-Atlantic is known as the Lost City.

In 1993, an American geochemist, Michael Russell, first suggested a theoretical mechanism to explain how alkaline vents might have been important to the development of early life. He suggested that the energy gradients that exist when alkaline vent water mixes with more acidic seawater could fuel the formation of organic molecules.

In some ways this is similar to the way in which cells harness energy. Cells maintain a proton gradient by pumping protons across their membranes to create a charge difference from inside to outside (Chapter 3). When protons are allowed to pass back through the membrane they phosphorylate adenosine diphosphate (ADP) and make ATP, an energy source that can be used by the cell. Russell’s theory suggests that pores in the hydrothermal vent chimneys worked in a similar way and provided energy that fuelled the reduction of carbon dioxide and

the production of organic molecules. In time, this could have led to self-replicating molecules, and eventually true cells with their own membranes.

Scientists are working on this theory in laboratories in the USA and the UK. They use small-scale models of hydrothermal vents (Figure 5.1.3) and seed them with chemicals that are present around them in the deep oceans in an attempt to produce organic molecules. One way that RNA might have first formed is with the help of minerals, such as iron and sulfur, that are found at alkaline hydrothermal vents on the seabed. These minerals act as catalysts and help to build organic compounds from inorganic molecules.

Figure 5.1.3: Hydrothermal volcanic vents deep under the ocean. Minerals dissolve in their hot waters and concentrations of molecules may have played a role in the origin of life.