Rewarding Learning

eGUIDE//Biology

Biochemistry, Genetics and Evolutionary Trends

Unit A2 2 5.5 Genes and Patterns of Inheritence

This e-book is designed to complement other support materials and enhance the understanding of this unit for students at GCE level. The topics covered are in accordance with those topics present in the current specification.

Contents

Genes and Patterns of Inheritance

5.5

Learning Outcomes from A2 2 5.5

Students should be able to:

- Demonstrate knowledge and understanding of the terms genotype and phenotype
- Demonstrate knowledge and understanding of the relationship between chromosomes, genes and alleles
- Demonstrate knowledge and understanding of the inheritance of traits showing discontinuous variation
- Demonstrate knowledge and understanding of sex determination and sex linkage
- Demonstrate knowledge and understanding of gene interaction
- Demonstrate knowledge and understanding of the inheritance of traits showing continuous variation (polygenic inheritance).

Genotypes and phenotypes

A gene is a functional unit of DNA which codes for a polypeptide chain. These polypeptide chains may be proteins or form part of a protein which in turn determine the characteristics on an organism. Genes are also the units of heredity and can be passed on from parents to offspring.
Genes coding for specific polypeptides (or proteins), and therefore determining characteristics, are found in specific positions (loci) along the length of chromosomes.

The genotype of an organism is the genetic makeup of an organism responsible for a particular trait.

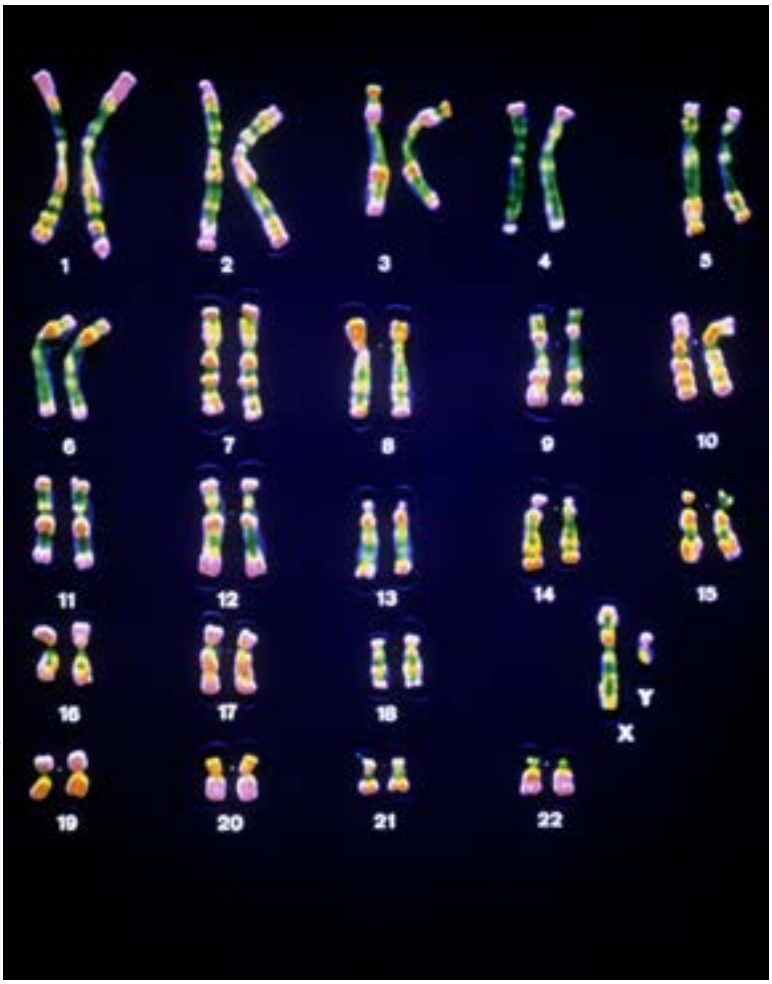
The phenotype of an organism is the outward appearance or observable physical attributes of that trait.

Relationship between chromosomes, genes and allels

In diploid organisms such as humans, there are two of every type of chromosomes, i.e. we have pairs of homologous chromosomes (homo=same). In humans we have 23 pairs of homologous chromosomes; 46 chromosomes in total. Homologous chromosomes appear similar and have the genes coding for the same characteristic in the same position (locus) along their length.

The chromosomes can be photographed during metaphase of cell division and then arranged into homologous pairs as shown below. This type of image showing the pairs of homologous chromosomes in an individual organism is called a karyotype. The particular karyotype shown is from a human male; a female would have two X chromosomes instead of an X and a Y as shown here.

Karyotypes can also be used to indicate genetic mutations where there is an extra chromosome such as in Down's Syndrome, an absent chromosome (Turner's Syndrome) or other chromosomal abnormalities.



False-colour light micrograph of a normal trypsin/leishman banded male karyotype, the full complement of male chromosomes arranged in numbered homologous pairs. The chromosomes are presented in this manner by matching up unpaired chromosomes photographed during the metaphase stage of cell division. Each member of a homologous pair is similar in length & banding pattern. Male & female sets differ only in the sex chromosome (bottom right); a female would be labelled XX instead of XY. The nucleus of each human cell contains a total of 46 chromosomes, 23 of maternal and 23 of paternal origin. Magnification: x1,400 at 35mm size.

For each individual trait (such as hair or eye colour), a cell contains instructions on two alleles, one on each of the homologous chromosomes.

Alleles are alternative forms of the gene, one obtained from each of the mother and the father. An individual's genotype refers to the combination of these two alleles. The genotype is described as either homozygous (the alleles are the same) or heterozygous (the alleles are different). Homo=the same; hetero = different.

Dominant = if this allele is present, it will express its phenotype at the expense of the recessive allele.
Recessive = this allele will only be expressed in the phenotype in the absence of the dominant allele.

If the letters R and r are used to represent the alleles coding for round and wrinkled seed type in a pea plant, where R = round (and is the dominant allele) and r = wrinkled (and is the recessive allele).

In the following combinations of alleles:
RR = homozygous dominant. The resulting seed phenotype will be round.
Rr = heterozygous. The resulting seed phenotype will be round.
rr = homozygous recessive. The resulting seed phenotype will be wrinkled.
Watch Asap Biology – Episode 1 – Genes and Alleles (2mins 56 secs) to help understand the difference between genes and alleles.
https://www.youtube.com/watch?v=udyat7YFdFc
Watch the animation DNA, Chromosomes and Genes by Jeremy LeCornu to revise the relationship between DNA, chromosomes and genes.
https://www.youtube.com/watch?v=z8ojaHrxQR0

Effect of environmental factors

Genes carry the instructions for growth and development. However, the phenotype is influenced throughout your life by environmental factors. These include factors such as nutrition and diet, climate, illness, exercise, toxicity in your surroundings and stress.

'Phenotypic plasticity' is described as the degree to which the phenotype is determined by the genotype's interaction with the environment. If environmental factors have a strong influence, the phenotypic plasticity is high. If genotype can be used to reliably predict phenotype, the phenotypic plasticity is low.

Some genes are better in one environment than another environment, leading to a range of phenotypes for the same gene. There are many studies investigating such genotype by environment interactions. A change in the phenotype due to environmental conditions is most easily studied in plants where you can grow a number of identical plants are grown under differing conditions of for example light, nutrients, in the presence of heavy metals.

The amount of influence that environmental factors have on the phenotype is a hotly debated scientific issue, often referred to as the 'nature (genes) versus nurture (environment)' debate. For example, many different factors are known to contribute to obesity, but how influential are environmental factors over an individual's genotype? Different environmental factors, such as types of food, amount of exercise, type of job may affect different people in different ways. An average figure for research studies estimates that obesity is approximately 40% genetic and 60% environmental, but not all scientists agree on whether genotype or environmental factors play the bigger role.

Identical twin studies are often used to study the impact of environment on phenotype in humans, due to the similarity of their genotype. This is shown in the animation 'Genotype-Environment Interaction and Phenotypic Plasticity' at Study.com (7mins 35secs)
http://study.com/academy/lesson/genotype-environment-interaction-and-phenotypic-plasticity.html

Inheritance of traits – heredity

This link will take you to a page by 'Yourgenome' which covers a number of the basic principles of heredity.
http://www.yourgenome.org/facts/what-is-inheritance

Monohybrid inheritance

Monohybrid inheritance looks at the inheritance of a single trait (a characteristic such as eye colour, round or wrinkled seed type) coded for by a single gene locus on a chromosome.

'Gregor Mendel' by Teacher's pet looks at Mendel's first experiments on pea plants.
https://www.youtube.com/watch?v=cWt1RFnWNzk

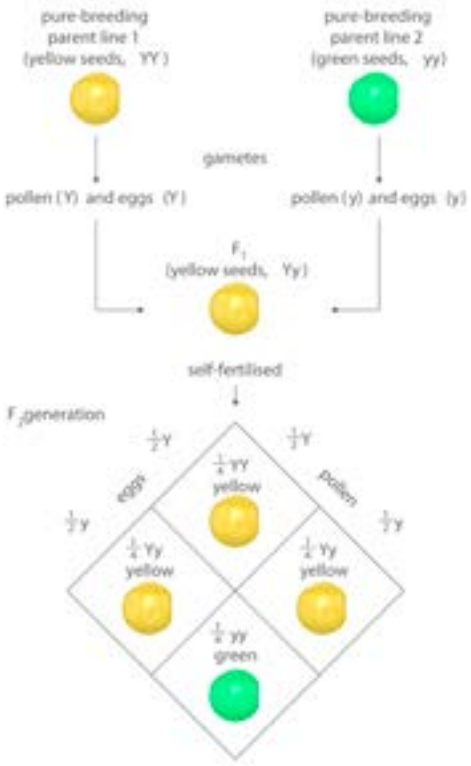
A similar experiment also carried out by Mendel is shown below, where pure breeding parent plants with yellow seeds are crossed with pure breeding parent plants with green seeds.

P_1 = the first parental generation
F_1 = the first filial generation (first generation offspring)
F_2 = the second filial generation (second generation offspring)

Note that:

- Each plant is diploid i.e. contains two alleles of each gene.
- Each gamete produced is haploid i.e. contains one allele of each gene.
- All of the offspring receive one allele from each parent – on a random probability basis
- There is only one possibility for the F_1 offspring as they must contain one 'Y' and one 'y' gene (from each parent)

The Punnett square can be used as shown below to ensure that all possible combinations of gametes in the F_2 offspring have been included. This will also show the probability (or percentages) of producing offspring with the different possible genotypes.
See http://www.dnaftb.org/5/animation.html to learn more about Punnett squares.



Mendelian genetics, Punnett square. Diagram showing the genetics of seed colour in peas, as discovered by Gregor Mendel in the 1850s and 1860s. The genes controlling seed colour are Y and y, with Y dominant over y. The combinations YY and Yy produce yellow seeds. The combination yy produces a green seed. The pure parent lines (top) combine gametes (pollen and eggs) to produce a first generation (F_1) of yellow seeds (Yy). This self-fertilises to produce the second generation (F_2). The colour proportions of the F_2 generation of seeds are shown in the form of a Punnett square, with a quarter of the seeds being green (yy, bottom) and three-quarters yellow.

Questions

1. How would you describe the genotypes of each of the P_1 plants?
2. How would you describe the genotype of the F_1 plants?
3. Why are the F_1 plants yellow?
4. How do you know that gene 'y' has not been lost in the first cross?
5. Write down each of the possible genotypes and give both the ratios and the corresponding percentages of phenotypes you would expect to achieve of each in the F_2 generation.
6. There is no basis for expecting that any one type of allele will combine specifically another other type of allele i.e. the alleles combine randomly. When does this combination take place in a cell, and how do we know there is a random combination of alleles?
7. This type of inheritance can also be described as discontinuous inheritance. Explain why this is so?
8. Give some examples of discontinuous inheritance in humans.

Mendel's First Law – The Law of Segregation

Each gamete produced is haploid i.e. contains one allele of each gene. This is the basis of Mendel's First Law – 'The Law of Segregation' (separation). The two alleles are separated from each other during meiosis. They line up together at the equator of the cell during metaphase and then are pulled to opposite poles, ending up in separate daughter cells; the gametes.

Mendel's ratio for a monohybrid cross

Mendel found that if he crossed two heterozygous plants (P_2 above) looking at one particular trait (a monohybrid cross), he always ended up with a 3:1 ratio of phenotypes in the F_2 generation. In other words approximately 75% of the F_2 offspring exhibited the dominant trait and approximately 25% exhibited the recessive trait.

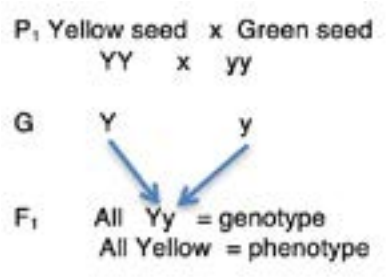
A table showing 'Results from Mendel's Experiments', showing the results of a number of monohybrid crosses looking at seed type, flower colour and height in pea plants.
https://www.ndsu.edu/pubweb/~mcclean/plsc431/mendel/mendel1.htm
These short animations (approx. 1min each) from 'DNA from the beginning', show Professor Robert Olby (University of Pittsburg) discussing the accuracy of Mendel's results.
http://www.dnaftb.org/5/av.html
The Amoeba's Sisters' animation 'Monohybrids and the Punnett square Guinea Pigs' (6mins 27 secs), gives a simple reminder of the vocabulary used in genetics, dominant and recessive alleles, homozygous and heterozygous, genotypic and phenotypic ratios and percentages, probabilities and predictions.
https://www.youtube.com/watch?v=i-0rSv6oxSY
The Amoeba Sisters have a number of straightforward animations on genetics and other topics and with access to free video handouts at their website www.amoebasisters.com

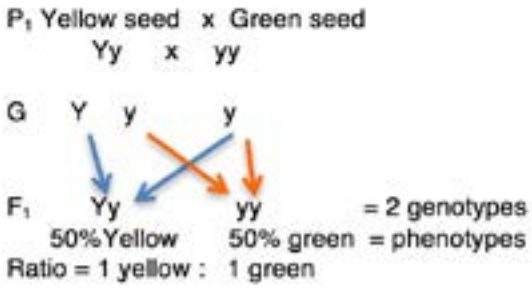
Test cross against a double recessive

All yellow seeds produced in the crosses above look the same, so how can the genotype of a yellow seed can be worked out?
The green seeds are double recessives (genotype rr), so use a test cross or back cross against a double recessive to predict what offspring should be seen for each of the following crosses.

a) Homozygous dominant vs Double recessive
YY X yy

b) Heterozygous dominant vs Double recessive
Yy X yy





From the results of the genetic diagrams above it can be seen if any offspring from the test cross have green seeds, then the yellow parent must be heterozygous.

Dihybrid inheritance

This is the inheritance of two unrelated traits that are not linked i.e. the alleles controlling the two traits are located on different chromosomes.
An example of this could be the inheritance of two traits in the peas – whether the seeds are yellow or green in colour as before, but also whether the seeds are round or wrinkled in shape.

Let Y = yellow and R = round
y = green r = wrinkled

Assume the dominant genes are Y=yellow, and R= round.

The experimental cross is carried out as shown below, a pure-breeding plant with yellow round seeds, against a pure-breeding plant with green, wrinkled seeds. The results in the F_1 generation will confirm these assumptions.

Note

- For each diploid parent the genotypes will have 2 of each type of allele for each of the 2 traits for example YYRR and yyrr.
- The gametes must each contain 1 allele for each trait, for example in the first generation cross they are YR, yr as the alleles are segregated according to Mendel's First Law during meiosis.
- The F_1 plants all have the genotypes YyRr and their seeds are all yellow and round.
- These F_1 plants are then self-pollinated.

List the gametes formed from the self-pollination of the F_1 plants (the P_2 cross) here:

1.
2.
3.
4.

As there are 4 possible types of gamete formed from the self-pollination of F_1 plants, the Punnett square is now 4x4 giving 16 possible combinations.

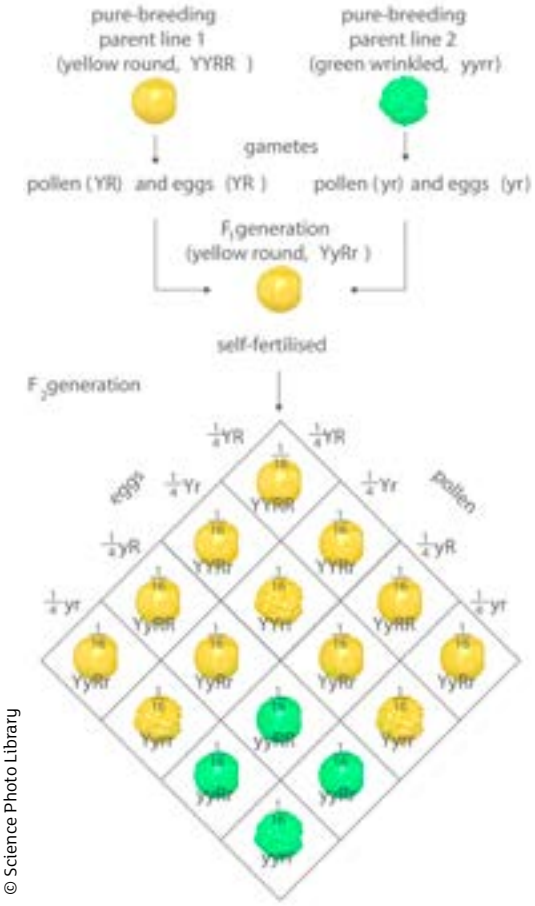


Diagram showing the genetics of seed colour and shape in peas, as discovered by Gregor Mendel in the 1850s and 1860s. The colour genes are Yy (yellow-green) and the shape genes are Rr (round-wrinkled). Yellow (Y) and round (R) are dominant. The pure parent lines (top) combine gametes (pollen and eggs) to produce a first generation (F1) of yellow round seeds (YyRr). This self-fertilises to produce the second generation (F2). The colour and shape ratios in this F2 generation are shown in the form of a Punnett square, with the ratios being 9:3:3:1 of phenotypes (yellow round, yellow wrinkled, green round, and green wrinkled).

This is because the genes controlling the two traits are found on separate chromosomes and they assort independently during meiosis, giving greater potential variation among the offspring. This is Mendels' Second Law – The Law of Independent Assortment.

Mendel's Second Law – the Law of Independent Assortment

Mendel found that the combinations of traits in the offspring did not always match the combinations of traits in the parental organisms. There was variation between parents and offspring, and between the offspring themselves.

To explain this he put forward the principle or Law of Independent Assortment:
The factors (genes) controlling different traits, separate independently during the formation of gametes and so are transmitted to offspring independently of one another. This principle depends on the genes being located on different chromosomes.

During meiosis, when pairs of homologous chromosome are separated to form haploid gametes there is an independent and random assortment of homologous chromosomes along the equator during metaphase. This ensures that all of the maternal chromosomes will not be simply separated into one cell while all paternal chromosomes are separated into another. Instead, after meiosis occurs, each gamete contains a mixture (random assortment) of genes from the organism's male and female parent cells.

Task

Take the 4 types of gamete genotypes from the list from the above example and construct a Punnett square, showing the genotype combinations for each of the offspring.
Use these results to determine the phenotypes, the ratios of each and equivalent percentages in the F_2 generation.

Mendel's ratio for a dihybrid cross

Mendel found that if he crossed two heterozygous plants (P_2 above) looking at two independent traits (a dihybrid cross), he always ended up with a 9:3:3:1 ratio of phenotypes in the F_2 generation.

In the above example this equates to:
9 plants with yellow round seeds
3 plants with yellow wrinkled seeds
3 plants with green round seeds
1 plant with green wrinkled seeds

This 9:3:3:1 ratio is Mendel's Ratio for a dihybrid cross.

The Amoeba's Sisters' animation 'Dihybrid Crosses and a Cat Called "Moo" '(8mins 31 secs) which looks at a dihybrid test cross against a double recessive for two traits. It also explains the FOIL method for combining gametes.
https://www.youtube.com/watch?v=qIGXTJLrLf8&feature=youtu.be

The Amoeba Sisters have a number of straightforward animations on genetics and other topics and you can access free video handouts at their website www.amoebasisters.com

Test Cross against a double recessive (in dihybrid crosses)

As in the case of monohybrid crosses, it is not possible to tell the genotypes of all offspring as some may be homozygous and some heterozygous for the dominant trait. A test or back cross would be carried out against a double recessive and predict what offspring we should see for each of the crosses.

Q. In the example used above, look at the seed type, and decide to find out the genotype of a plant with yellow, round seeds.
   1. What are the possible genotypes of plants with yellow, round seeds?
   2. Which plant phenotype/genotype would you use to test cross against?
   3. Show by means of a genetic diagram (including a Punnett square), the expected results from a test cross if the unknown plant is heterozygous for both traits.

An example of the Punnett square for this cross and the resultant genotypes and phenotypes is shown here. Note that the traits are represented by different letters than have been used, but that the resultant phenotypic ratios are the same.
https://www.ndsu.edu/pubweb/~mcclean/plsc431/mendel/mendel3.htm

The results of the test cross above are, out of 16 potential offspring:
1 plant with yellow, round seeds
1 plant with yellow, wrinkled seeds
1 plant with green round seeds
1 plant with green wrinkled seeds

In all of the Mendelian inheritance crosses above, three principles apply;
1. The principle of segregation
2. The principle of independent assortment
3. The principle of dominance.

However as more work on genetics has been carried out, it is clear that there are some examples of inheritance in which the ratios of offspring do not appear to follow Mendel's

patterns of inheritance. This applies to the following forms:

- Codominance
- Multiple alleles
- Lethal genes
- Sex-linked inheritance
- Gene interaction and epistasis
- Polygenic inheritance

Sometimes we refer to these as non-Mendelian inheritance.

Codominance and incomplete dominance

Not all alleles are dominant and recessive like the ones Mendel studied in his pea plants. There are some situations where the following happens:

Incomplete dominance – both genes are equally strong, neither acts in a dominant way and the resulting phenotype is a blend of the effects of both genes – a third type of intermediate phenotype. An example of this is in the snapdragon flower, where red and white flowered plants are crossed to give pink flowered offspring.

Codominance – neither allele is recessive but in this instance the phenotypes of both alleles are expressed and both are visible in the phenotype. An example of codominance is found in chickens. When white chickens are crossed with black chickens, the resulting offspring has both black and white feathers.

Incomplete dominance and co-dominance are illustrated here, and the main points summarised, in an animation by the Amoeba sisters.
https://www.youtube.com/watch?v=YJHGfbW55l0

Look at the information and genetic diagrams on incomplete dominance and codominance at the following link.
http://www.hobart.k12.in.us/jkousen/Biology/inccodom.htm

Multiple Alleles

In the examples that have been looked at so far, the genes have two alleles. However there are a number of instances where each gene has more than two alleles and is described as having 'multiple alleles'.

An example is the ABO Blood Group gene, where there are three possible alleles, only two of which can occur in the genome of an individual. The alleles code for the presence or absence of protein antigens on the surface of red blood cells. The symbols used are shown in the table to describe the alleles where the letter 'I' stands for 'isohaemogglutinin' (the type of antigen).

Allele	Expressed as
I^A	**Type A antigen** on the surface of red blood cells
I^B	**Type B antigen** on the surface of red blood cells
i	**No antigen**

The antigens can trigger an immune response if they are recognised as foreign by the antibodies in the blood plasma. This will cause clotting or agglutination of the donor blood by the recipient's antibodies in a transfusion, blocking blood vessels and causing haemoglobin to leak from disrupted cells (haemolysis). This can be toxic to the body when outside the red blood cells.

I^A and I^B are codominant forms of the allele, and therefore both expressed in the production of their respective forms of antigen. i is recessive to both I^A and I^B, and therefore only influences the phenotype if it is present on both chromosomes. Knowing this we can represent the ABO Blood Group phenotypes and genotypes as shown in the following table. (Sometimes a simple alternate format of AA, AO is used and this is also shown in brackets). The resultant antigens present on the red cells and antibodies in the plasma are also shown. Remember that an individual will not produce antibodies against it's own antigens, but will recognise 'other' antigens as 'foreign'.

Phenotype (Blood Group)	Genotypes	Antigens present on red blood cells	Antibodies present in plasma
A	I^AI^A (or AA) I^AI^O (or AO)	A	anti-B
B	I^BI^B (or BB) I^BI^O (or BO)	B	anti-A
AB	I^AI^B (or AB)	A and B	None
O	I^OI^O (or OO)	None	anti-A and anti-B

Watch the animation 'Multiple Alleles (ABO Blood Types) and Punnett squares' by the Amoeba sisters
https://www.youtube.com/watch?v=9O5JQqlngFY

Q. In the ABO blood grouping system, a single gene with three alleles (I^A I^B I^O) controls the production of the antigens that determine an individual's blood group. I^A and I^B are co-dominant and each is dominant to I^O.

1. State the possible genotypes for an individual who is:
   Blood Group A
   Blood Group AB
2. In a particular family, the father is blood group A and the mother is blood group B. They have four children, each with a different blood group.
   Draw a genetic diagram to show how it is possible for the parents to have four children all with different blood groups.
3. Using the information provided, explain fully why it is possible for the mother (blood group B), to donate blood safely to only two of her children and not the other two.

This link looks at multiple alleles in terms of blood groups.
http://www.cccoe.net/genetics/blood.html

Lethal Genes

Lethal genes are genes which prevent development or result in the premature death of the organism. There are two types of lethal genes.

- Recessive lethal genes, which will only result in death in the homozygous recessive condition.
- Dominant lethal genes which cause death in the heterozygous condition.

Recessive lethal genes

Lethal genes were discovered in 1905 by Lucien Cuénot while studying the inheritance of coat colour in mice. Mating two yellow mice, he found always produced offspring in a ratio of two yellow mice : one grey (agouti) mouse. He never achieved the Mendelian 3:1 ratio that was expected. From test crosses, Cuénot determined that all his yellow mice were heterozygotes for coat colour. He also knew from the results of his experiments that the yellow coat gene was dominant in the phenotype, but he never produced a homozygous dominant mouse.

The answer was discovered by Castle and Little in 1910, who demonstrated that the gene for yellow coat was lethal in the homozygous condition. They did this by showing that 25 per cent of the offspring of a cross between two heterozygous yellow mice died during embryonic development. Some of the genotypes and phenotypes are as below

Genotype	Phenotype	Description
AA	Agouti	Wild type. Banding of yellow and black pigmentation – looks grey at a distance.
AA^Y	Yellow	Yellow is dominant in the coat colour phenotype
A^YA^Y	Dead	Two copies of the recessive lethal gene result in the death of the mouse during embryonic development

This is shown in the genetic diagram below, using A for agouti and A^Y for yellow coat

P AA^Y AA^Y

G A A^Y A A^Y

Gametes	A	A^Y
A	AA Grey	AA^Y Yellow
A^Y	AA^Y Yellow	A^YA^Y Dead

This is the ratio 2 yellow: 1 grey: 1 dead which explains the 2:1 ratio for lethal recessive genes. So, in effect the gene A^Y is dominant in the expression of coat colour and recessive in its lethality effect.

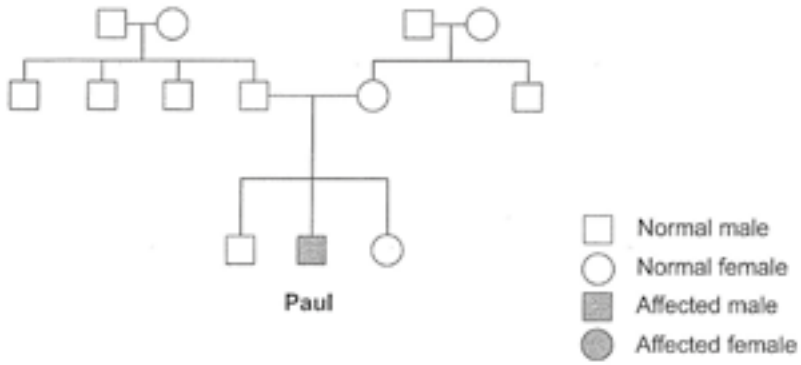
A gene which affects more than one phenotype in this way is called a pleiotropic gene.

Examples of recessive lethal genes in humans include cystic fibrosis, sickle cell anaemia and achondroplasia (dwarfism). Note that not all homozygous combinations of lethal genes cause death in the embryonic stage but, like cystic fibrosis may have a profound effect on the length of life and health of the individual who is homozygous for the lethal allele. Individuals heterozygous for the lethal allele are carriers of the disease and can pass the faulty gene onto their offspring.

Download this pdf by the Genetic Alliance to find out more about cystic fibrosis and how it is inherited. Use the information to help you answer the questions below.
http://www.geneticalliance.org.uk/docs/translations/english/8-cf-t.pdf

Cystic fibrosis sample question from CCEA past paper May/June 2011 Q6.

(a) The pedigree diagram below shows the incidence of cystic fibrosis in a family. Cystic fibrosis is a recessive autosomal condition.



Q. Ignoring the possibility of a recent mutation, explain the genetic basis for Paul having cystic fibrosis.

Dominant lethal genes

As the lethal allele is dominant in this instance, it is expressed in both the homozygous and heterozygous conditions. If this is the case, how is it passed onto future generations and so maintaining a presence in populations?
In many cases, dominant lethal genes are not detected in populations as they are quickly eliminated by the death of individuals carrying the gene.
However, in the case of Huntington's disease, a degenerative neurological condition in humans, the onset of the disease may be slow, and although it significantly reduces life expectancy, individuals may survive long enough to pass the lethal gene onto offspring.

Sex determination and Sex linkage

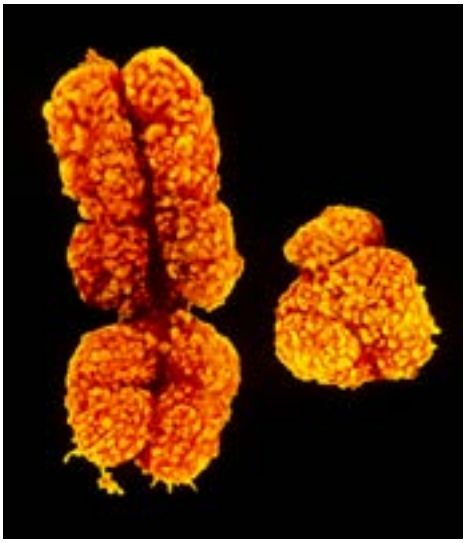
In our cells we have 23 pairs of chromosomes. One pair of chromosomes determines sex (the sex chromosomes) and the other 22 pairs of homologous chromosomes are called autosomes (see page 2).

Sex determination in humans is dependent on the combination of X and Y sex chromosomes; females have two X chromosomes i.e. XX, males have one X and one Y chromosome i.e. XY.

The Y chromosome is the smaller of the two, and X and Y are partially homologous. They pair and segregate into daughter cells during meiosis, so egg cells will possess one X

chromosome, while sperm cells can contain either one X or one Y chromosome.

Computer illustration of human X (left) and Y (right) chromosomes



Coloured Scanning Electron Microscope (SEM) of human X and Y chromosomes, as found in a male. The X chromosome (at left) is roughly X-shaped; the Y chromosome (at right) is Y-shaped. There are 23 pairs of chromosomes found in each human cell, but only the sex chromosomes differ so much in appearance. In a normal female one X chromosome becomes inactive and the other controls female development. In the male, the Y chromosome forms the male genital system.

The inheritance of sex-linked characteristics

X Linked Recessive, a short animation from the National Centre for Medical Genetics at UCD explains what X-linked recessive genetic conditions are and what they mean for an affected person's offspring. This can be used as an introduction to sex-linked traits or as a revision tool.
https://www.youtube.com/watch?v=Vdam8pKhRNo

Sex-linked traits tend to be recessive and carried on the X chromosome. This is important when looking at the inheritance of these traits as males only have one X chromosome but females have two. Having two copies of a gene can be important when one copy is broken or defective, particularly if the defective gene is recessive. Then presence of a normal gene will still be expressed and can mask the effects of the recessive gene.

Examples of sex-linked traits carried on the X chromosome in humans include red-green colour-blindness, haemophilia, Duchenne Muscular Dystrophy and male baldness.
In the case of colour-blindness, you need at least one normal (functional) gene to be able

to see red-green. Since boys have just one X chromosome, which they receive from their mother, inheriting one defective copy of the gene will render them colour-blind. Girls have two X-chromosomes, so in order to be colour-blind they must inherit two defective copies, one from each parent. Consequently, red-green colour-blindness is much more frequent in boys (1 in 12) than in girls (1 in 250).

The diagrams below illustrate how red-green colourblindness is inherited.

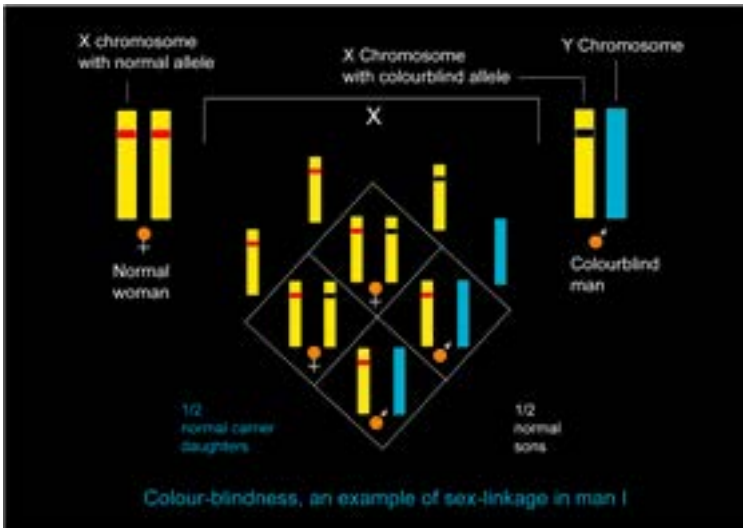
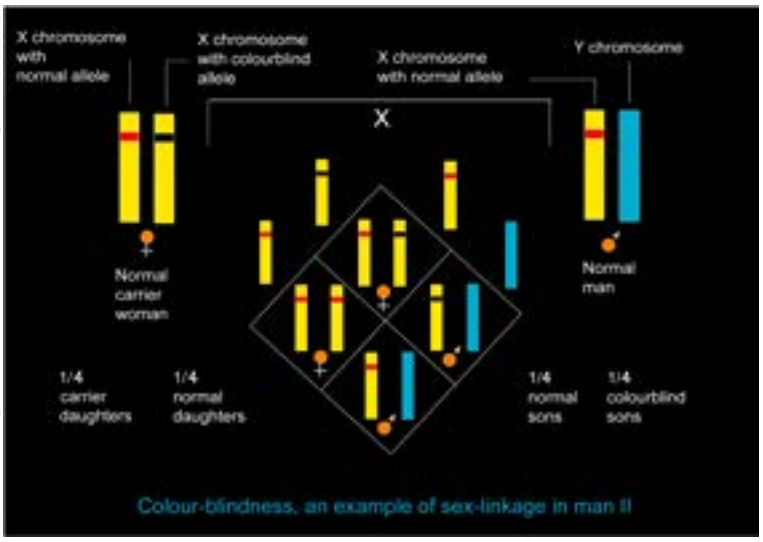


Diagram showing the inheritance of colour-blindness genes. X-chromosomes (yellow) and Y-chromosomes (blue) combine at centre. The normal colour vision allele is a red bar, and the colour-blindness allele is a black bar. The male symbol (arrow) and female symbol (cross) show the male and female parents and the offspring (sons and daughters). The cross-table shows the probability for colour-blindness in the offspring of a normal woman and colour-blind man is half normal sons, and half carrier daughters. This trait is thus classed as X-linked recessive



X-chromosomes (yellow) and Y-chromosomes (blue) combine at centre. The normal colour vision allele is a red bar, and the colour-blindness allele is a black bar. The male symbol (arrow) and female symbol (cross) show the male and female parents and the offspring (sons and daughters). The cross-table shows the probability for colour-blindness in the offspring of a carrier woman and normal man is a quarter each normal sons, colour-blind sons, normal daughters, and carrier daughters.

Watch the Amoeba Sisters' animation Punnett squares and Sex-Linked Traits (6mins 11 secs) which focuses on the inheritance of haemophilia.
https://www.youtube.com/watch?v=h2xufrHWG3E

Haemophilia

Haemophilia is a bleeding disorder that slows the blood clotting process. People with this condition experience prolonged bleeding following an injury, surgery, or having a tooth pulled. In severe cases of haemophilia, continuous bleeding occurs after minor trauma or even in the absence of injury (spontaneous bleeding). Serious complications can result from bleeding into the joints, muscles, brain, or other internal organs.

Haemophilia is the result of a defective gene responsible for blood clotting which is recessive and located on the X chromosome. There are actually two types of haemophilia, called haemophilia A and B. Individuals who have haemophilia A have low factor VIII clotting activity. Individuals who have haemophilia B have low factor IX clotting activity. Both genes, for clotting factors VIII and IX are recessive and carried on the X chromosome, so are inherited in the same way. Haemophilia A is the more common condition.

About one third of new cases of haemophilia are caused by a new mutation of the gene in the mother or the child. In these cases, there is no previous history of haemophilia in the family.

Because it is unlikely that females will have two altered copies of these genes, it is very rare for females to have haemophilia. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons, as they only pass on the Y chromosome to them. However a female with one altered copy of the gene on her X chromosomes is called a carrier, and can pass this altered gene to her son, who as a result would have haemophilia.

In a cross between a carrier female and a normal male, we can work out the probability of having a son who is a haemophiliac. We will use the superscript H on the X chromosome to represent the normal allele, and h to represent the recessive haemophilia allele.

P X^HXh X^HY
G X^H X^h X^H Y

Gametes	X^H	X^h
X^H	X^HX^H Normal female	X^HX^h Carrier female
Y	X^HY Normal male	X^hY Haemophiliac male

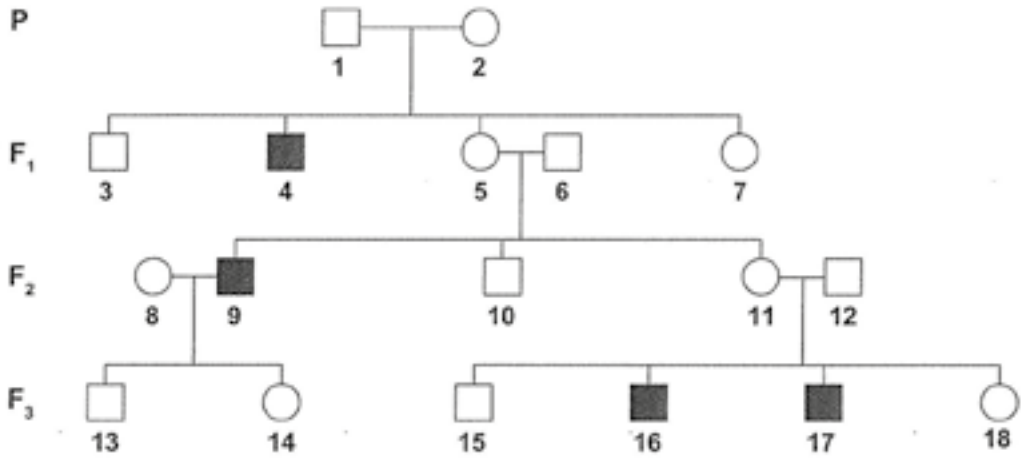
From the above cross we can see that there is a 25% probability of the couple having a child who is a son with the disease haemophilia. We can also say that any son borne to these parents will have a 50% chance of having the disorder.

Questions

1. CCEA past paper May/June 2012 Q6

Haemophiliacs possess a non-functional form of the gene responsible for the production of blood clotting factors.

The pedigree diagram below shows the incidence of haemophilia in an affected family.



Individuals within the pedigree are numbered. Males are represented by squares and females by circles. Those who have haemophilia are represented by solid symbols.

a) On the basis of the information provided, is the inheritance of haemophilia:
   i) Autosomal or sex-linked? Justify your answer.
   ii) Dominant or recessive? Justify your answer.

b) Using the symbols h to represent the allele for haemophilia, and H for the normal allele, state the genotype of each of the following.
   - Individual 2
   - Individual 4

c) Individual 14 carries a recessive allele for albinism (lack of normal body pigment) which is not sex-linked. She marries a man who is also a carrier for albinism but who does not carry the haemophilia allele. The genes exhibit independent inheritance.
   Using the symbol a for albinism and A for normal pigmentation, show, by means of a suitable genetic diagram, the probability of this couple producing a male child who has both haemophilia and albinism.

d) There is no evidence of haemophila in previous generations of this family. State the most likely reason for the condition appearing in the family pedigree.

2. The fruit fly, *Drosophila melanogaster*, is ideally suited for genetic investigations and has been widely used for this purpose for many years.

The fly on the right, with the red compound eye, is the natural, or wild type, known as Oregon R. The fly on the left is a mutant type known as White Miniature Forked. It has white eyes, shorter wings than the normal fly, & the bristles on its face & body are distorted & forked. D. melanogaster has been used for many years in genetic studies because it is easy to raise in large numbers, reproduces rapidly, & many of its mutations are easy to spot under a low-powered light microscope. The adult flies are 2-3mm long

The normal eye colour in *Drosophila* is red but a white-eyed form exists. In the genetics of eye colour, red eye (**R**) is dominant to white eye (**r**) and the inheritance of eye colour is sex linked (in a similar way to sex linked conditions in humans).

(a) State the genotypes of:
- a male with red eyes
- a female with white eyes

(b) In a particular cross, a red-eyed female was crossed with a red-eyed male. The offspring produced are shown in the following table.

	Red eyes	White eyes
Males	48	53
Females	102	0

(ii) As with most genetic crosses, the numbers of offspring in this cross do not fit exactly with the predicted ratio. State the name of the statistical test that can be used to identify if observed offspring numbers are significantly different from expected numbers.

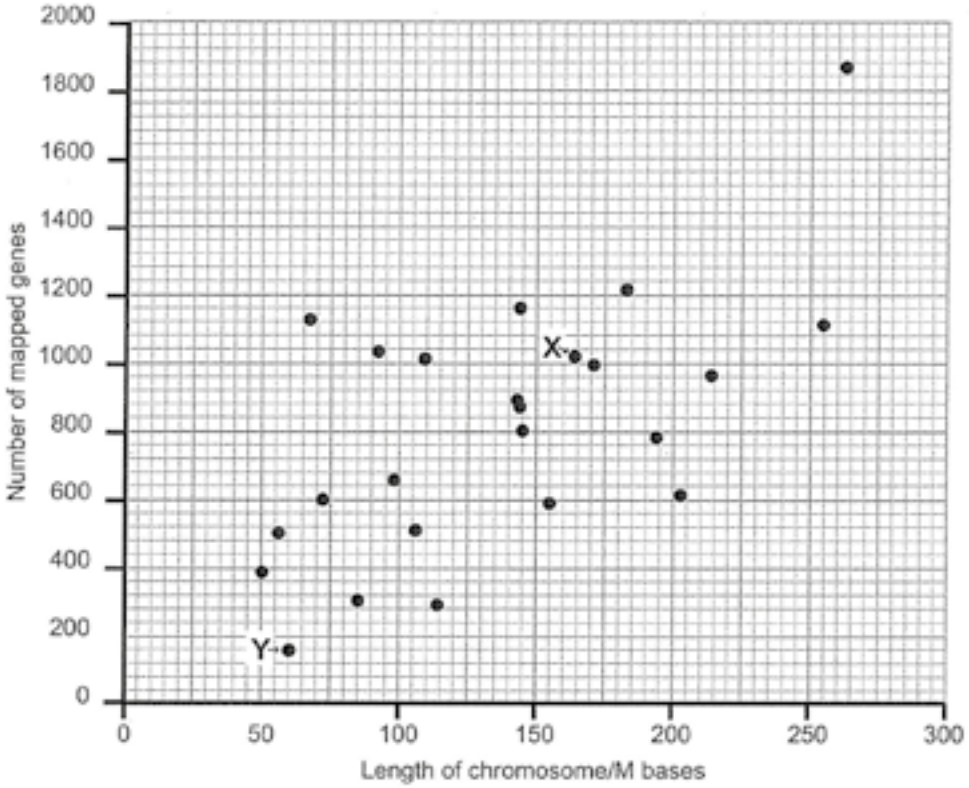
(c) In *Drosophila*, the genes for wing type and body colour are located on separate autosomes and so are independently inherited. Normal wing is dominant to vestigial wing and normal body colour is dominant to ebony body colour.
A cross between a fruit fly with normal wings and normal body colour and one with vestigial wings and ebony body colour produced offspring displaying four different phenotypes.
Using a genetic diagram, explain these results.
(Let A = normal wing and B = normal body colour)

(d) Suggest two reasons why *Drosophila melanogaster* is ideally suited for genetic investigations.

3. Question from CCEA past paper May /June 2010 Q3

The Human Genome Project was organised to sequence all the nucleotides and map the genes present in human DNA.

The graph below shows the number of mapped genes for different sized chromosomes.



a) Describe the trend evident in the graph.
b) The sex chromosomes, X and Y, are identified in the graph. Compare the number of genes in these chromosomes with other similar sized chromosomes.
c) Explain the significance for males of the difference between the number of genes on the X and Y chromosomes.

Gene interaction

While one gene codes for one polypeptide, the genes do not operate in isolation, but interact as demonstrated by Batson and Punnett's experiment on comb type in chickens (1904–1910). This experiment is shown in the link below. Note that the genes interact to produce new phenotypes in the F_1 and F_2 offspring that were not evident in the P_1 generation.

https://www.ndsu.edu/pubweb/~mcclean/plsc431/mendel/mendel6.htm

This experiment, and subsequent test crosses, demonstrated that the comb type is determined by the interaction of two genes, R/r and P/p.

R is dominant over r

P is dominant over p

A walnut comb is due to the interaction of an R with a P

A rose comb occurs when at least one R is present with pp

A pea comb occurs when at least one P is present with rr

A single comb occurs only when the genotype is rrpp.

Look at the table showing the genotypes for the four phenotypes and give possible genotype combinations.
Try crossing different parental genotype combinations (rose x pea, walnut x single etc.) to find the ratios of offspring produced using the table of genotypes/phenotypes.

We can describe gene interactions as interactions between genes located on the same or on different (but not homologous) chromosomes, which control the expression of a single phenotype to produce different outcomes.

Teachers can use and clip this slide show to demonstrate different types of gene interaction.
http://www.slideshare.net/purakichha/interaction-of-genes-for-slide-share

Epistasis
Epistasis is a term which describes how genes interact to affect a phenotype whereby an allele at one locus prevents an allele at another locus from manifesting its effect. One gene is effectively interfering with or masking the effects of another gene. Genes with epistatic relationships tend to code for proteins (mainly enzymes) involved in the same biochemical pathway.
An analogy of genes working together:
http://learn.genetics.utah.edu/content/pigeons/epistasis/

Different types of epistasis have been identified which give variations on the Mendelian ratio of 9:3:3:1 when crossing two dihybrids. Some examples are:
Recessive epistasis – the homozygous recessive state of one gene blocks the expression of another gene. In this instance there is a 9:3:4 ratio in the offspring of a dihybrid cross.
Dominant epistasis – the presence of a dominant allele of one gene blocks the expression of another gene. In this instance there is a 12:3:1 ratio in the offspring of a dihybrid cross.
Duplicate recessive epistasis – the homozygous recessive state of either gene blocks the expression of the dominant allele of the other gene. In this instance there is a 9:7 ratio in the offspring of a dihybrid cross.

The following section on 'Gene Interactions' by Phillip McClean works through some examples of different types of epistasis and the ratios produced.
https://www.ndsu.edu/pubweb/~mcclean/plsc431/mendel/mendel6.htm

Look at the section on 'Gene Interaction' in the following
https://www2.estrellamountain.edu/faculty/farabee/BIOBK/BioBookgeninteract.html

Epistasis is illustrated here, and the main points summarised, in an animation by the Amoeba sisters. (Watch from the beginning to 4mins 35 secs to the end)
https://www.youtube.com/watch?v=YJHGfbW55l0

This video, 'Epistasis! From the Science Club!' Looks at some of the mechanisms of Epistasis.
https://www.youtube.com/watch?v=ctjw-ZijciM

Read about examples of different types of epistasis and their patterns of inheritance here.
http://www.yourarticlelibrary.com/biology/6-most-important-kinds-of-epistasis-biology/6436/

Questions

1. Watch Gene Interaction I (until 3mins 16 seconds) by Crystal Clear Biology and use the information to help you answer the questions on Labrador retrievers below from CCEA past paper May/June 2010 Q 7 .
https://www.youtube.com/watch?v=UCvxZD1dyrw
Labrador retrievers are dogs with black, brown or yellow coats. The coat colour is controlled by two independently inherited genes which are not sex-linked.
The alleles of a pigment gene at the B/b locus determine the amount of black pigment produced. A brown coat is produced by the bb genotype.
A second gene at the E/e locus influences the expression of the alleles at the B/b locus. The presence of the E alleles allows the alleles at the B/b locus to be expressed.
A yellow coat is always produced if the genotype is ee, no matter which alleles are present at the B/b locus.

   a. State the genotype of the pure breeding brown Labrador
   b. State the genetic term which describes the relationship between the B/b and the E/e loci.
   c. Two black dogs known to be heterozygous for both genes (BbEe) were crossed. Determine the expected proportions of the offspring produced with respect to both genotypes and phenotypes. Show your working in a genetic diagram.
   d. A litter of pups, which resulted from a cross between a yellow male and a black female Labrador, consisted of 7 yellow and 3 black pups.
      i) With respect to the alleles at the E/e locus only, state the genotypes for the male and female parents. Give a reason for each of your answers.
      ii) Suggest an explanation for the lack of brown pups in the litter.

2. Try this question from CCEA past paper May /June 2014 (Q6)

   a. Distinguish between the terms ‘dominance’ and ‘epistasis’.
   b. The colour of squash fruit is controlled by two genes that have the alleles A/a and B/b. The B/b gene is suppressed (not expressed) in the presence of the A allele. If the B/b gene is expressed, the presence of the B allele codes for a yellow squash and absence of the B allele codes for green. If the B/b gene is suppressed the squash are white. A cross between two squash plants, each heterozygous for both genes, produced 126 white squash, 26 yellow squash and 8 green squash, approximating to a ratio of 12:3:1.
   Complete a genetic diagram to show the genotypes and phenotypes of the offspring.
   c. The chi squared test can be used to check if the results of the cross statistically fit a ratio of 12:3:1.
   Complete the table below and calculate the chi^2 for these results.

Category	Observed (O)	Expected (E)	(O–E)	$(O–E)^2$	$\frac{(O–E)^2}{E}$
white	126				
yellow	26				
green	8				

Calculated chi^2 value _____

On the basis of your calculated chi^2 value, state the following:
- the degrees of freedom for the test
- the probability value

Explain fully the outcome of your statistical test.

Polygenic inheritance

Poly = many; therefore this term tells us that we are looking at situations in which a single characteristic is controlled by a number of different genes.

Examples of polygenic inheritance include:
- Human skin colour
- Height in humans
- Kernel colour in wheat
- Rhesus blood groups
- Eye colour in humans

Human skin colour

Skin colour in humans is determined by the amount of the pigment melanin it contains. It is thought that at least four different gene loci are involved in the production of melanin. Each gene has two alleles, one allele which contributes to the amount of melanin in the skin, and one which does not.

An example of how polygenic inheritance works could be in the hypothetical situation where three genes code for skin colour.

There are three genes
Gene A with alleles A = add melanin a = don't add melanin
Gene B with alleles B = add melanin b = don't add melanin
Gene C with alleles C = add melanin c = don't add melanin
Each individual will have copies of each gene A, B and C.

A person with a genotype AABBCC will have most melanin, and the darkest skin.
A person with the genotype aabbcc, will have no melanin, and the lightest skin.

If these two genotypes are crossed, we will get offspring with genotypes AaBbCc, and intermediate coloured skin, which we describe as mulatto.

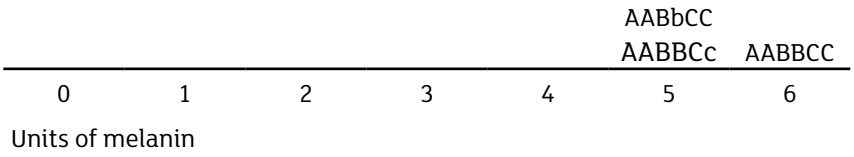
If these heterozygous individuals are crossed there will be eight potential types of gamete produced by each, ABC, ABc, AbC, aBC, Abc, aBc, abC and abc. The Punnett square will look like this.

Gametes	ABC	ABc	AbC	aBC	Abc	aBc	abC	abc
ABC	AABBCC	AABBCc	AABbCC	AaBBCC	AABbCc	AaBBCc	AaBbCC	AaBbCc
ABc	AABBCc	AABBcc	AABbCc					
AbC	AABbCC	AABbCc	AAbbCC					
aBC	AaBBCC	AaBBCc	AaBbCC					
Abc	AABbCc	AABbcc	AAbbCc					
aBc	AaBBCc	AaBBcc	AaBbCc					
abC	AaBbCC	AaBbCc	AabbCC					
abc	AaBbCc	AaBbcc	AabbCc					

Task

- Complete the Punnett square to show all genotype combinations.
- Assuming each capital letter (A, B or C) will contribute one unit of melanin to an individual's skin, complete the graph below by placing each genotype in the correct position.

The first three examples (working through them vertically) are done for you.



The above table demonstrates that polygenic inheritance gives rise to continuous variation in the phenotype and so will, if mapped in a population, produce a normal distribution curve.

In this instance, using three different genes controlling the characteristic, we can see that there are a total of seven different skin colour phenotypes (shades of skin colour) present. By increasing the number of genes controlling the trait, the number of possible phenotypes also increases.

Polygenic characteristics are influenced by the environment for example a person with light skin, may find that it darkens if they spend some time in bright sunshine. A tall plant will not reach its full height if it is lacking in nutrients or growing in the shade.

Teachers can use this slide share entitled 'Polygenic inheritance (IHL)' by Stephen Taylor, IB Bio & MYP Science Teacher, HOD Science, MYP Coordinator at Canadian Academy, Kobe, to look at polygenic inheritance of skin colour in humans, colour of wheat kernals and continuous variation.
http://www.slideshare.net/gurustip/polygenic-inheritance-ahl-7933636

Alternatively this resource from the TES website is a powerpoint on polygenic inheritance. Teachers must register to access TES.
https://www.tes.com/teaching-resource/polygenic-inheritance-6316105

In 'Polygenic inheritance' by Brian Schultz, he looks at how height is determined by polygenetic inheritance.

https://www.youtube.com/watch?v=XNnavVYPM7I

Polygenic Inheritance (IB Biology) by Alex Lee (6 mins 51 secs) looks at the polygenic basis of determination of skin colour and demonstrates how it is an example of continuous variation.
https://www.youtube.com/watch?v=jibL4HvhgQg

Height and skin colour are used to illustrate polygenic traits in this animation by the Amoeba sisters. (Watch from 3mins 25 secs to 4mins 34 secs)
https://www.youtube.com/watch?v=YJHGfbW55l0

In the video 'Genotypes and Phenotypes' by Bozeman Science, Paul Andersen explains how changes in the genotype of an individual can affect the phenotype, and the effect of mutations.
https://www.youtube.com/watch?v=OaovnS7BAoc

These Quizlet flash cards provide a useful tool for revision of genetics terminology.
https://quizlet.com/73375659/chapter-7-extending-mendelian-genetics-flash-cards/

This resource on the TES website by Philip Crudden gives a series of questions on genetics and pedigree charts. Teachers must register to access TES.
https://www.tes.com/teaching-resource/pedigree-charts-6427830

Another quick revision or starter exercise on pedigree charts is 'A2 pedigree diagram analysis activity- genetics' by Sciencefun
https://www.tes.com/teaching-resource/a2-pedigree-diagram-analysis-activity-genetics-6109465

CCEA past examination questions on 'Genes and Patterns if Inheritance'
(all from Assessment Unit 2 2)

May/June 2015	Question 7
May/June 2014	Question 6
May/June 2013	Question 5
May/June 2012	Question 6
May/June 2011	Question 5
May/June 2010	Question 7