SURFING

WACE HUMAN BIOLOGY

Unit 4 Human Variation and Evolution

• Kerri Humphreys •

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Bag 7023 Marrickville NSW 1475 Australia
Tel: (02) 9516 1122 Fax: (02) 9550 1915
sales@sciencepress.com.au
www.sciencepress.com.au

Contents

Introduction

Each book in the *Surfing* series contains a summary, with occasional more detailed sections, of all the mandatory parts of the syllabus, along with questions and answers.

All types of questions – multiple choice, short response, structured response and free response – are provided. Questions are written in exam style so that you will become familiar with the concepts of the topic and answering questions in the required way.

Answers to all questions are included.

A topic test at the end of the book contains an extensive set of summary questions. These cover every aspect of the topic, and are useful for revision and exam practice.

Words To Watch

account, account for State reasons for, report on, give an account of, narrate a series of events or transactions.

analyse Interpret data to reach conclusions.

annotate Add brief notes to a diagram or graph.

apply Put to use in a particular situation.

assess Make a judgement about the value of something.

calculate Find a numerical answer.

clarify Make clear or plain.

classify Arrange into classes, groups or categories.

comment Give a judgement based on a given statement or result of a calculation.

compare Estimate, measure or note how things are similar or different.

construct Represent or develop in graphical form.

contrast Show how things are different or opposite.

create Originate or bring into existence.

deduce Reach a conclusion from given information.

define Give the precise meaning of a word, phrase or physical quantity.

demonstrate Show by example.

derive Manipulate a mathematical relationship(s) to give a new equation or relationship.

describe Give a detailed account.

design Produce a plan, simulation or model.

determine Find the only possible answer.

discuss Talk or write about a topic, taking into account different issues or ideas.

distinguish Give differences between two or more different items.

draw Represent by means of pencil lines.

estimate Find an approximate value for an unknown quantity.

evaluate Assess the implications and limitations.

examine Inquire into.

explain Make something clear or easy to understand.

extract Choose relevant and/or appropriate details.

extrapolate Infer from what is known.

hypothesise Suggest an explanation for a group of facts or phenomena.

identify Recognise and name.

interpret Draw meaning from.

investigate Plan, inquire into and draw conclusions about.

justify Support an argument or conclusion.

label Add labels to a diagram.

list Give a sequence of names or other brief answers.

measure Find a value for a quantity.

outline Give a brief account or summary.

plan Use strategies to develop a series of steps or processes.

predict Give an expected result.

propose Put forward a plan or suggestion for consideration or action.

recall Present remembered ideas, facts or experiences.

relate Tell or report about happenings, events or circumstances.

represent Use words, images or symbols to convey meaning.

select Choose in preference to another or others.

sequence Arrange in order.

show Give the steps in a calculation or derivation.

sketch Make a quick, rough drawing of something.

solve Work out the answer to a problem.

state Give a specific name, value or other brief answer.

suggest Put forward an idea for consideration.

summarise Give a brief statement of the main points.

synthesise Combine various elements to make a whole.

1 Assumed Knowledge

QUESTIONS

1. The diagram shows a chromosome.

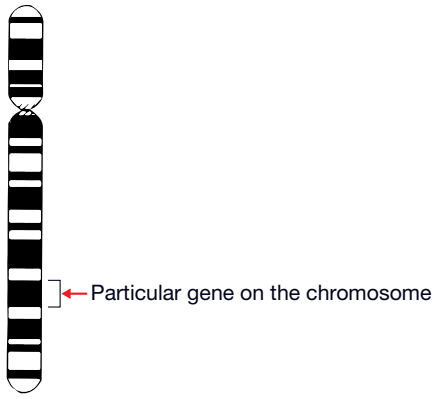


Figure 1.1 Chromosome.

   (a) Define a chromosome.
   (b) What is the relationship between gene and chromosome?
2. Distinguish between a gene and an allele.
3. Distinguish between autosomes and sex chromosomes.
4. The diagram shows the karyogram for person A.

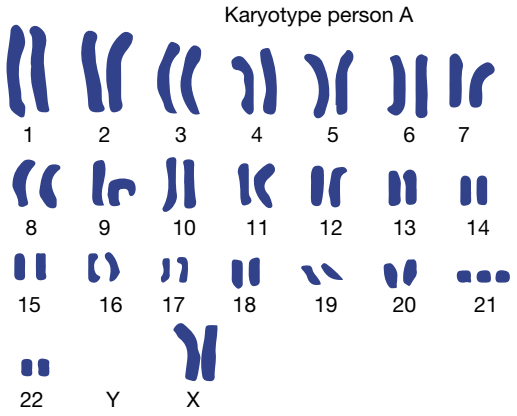


Figure 1.2 Karyogram.

   (a) Is this person male or female?
   (b) Define trisomy.
   (c) Person A has a trisomy disorder. Name this disorder.
5. What is meant by the genome sequence?
6. Define a gene pool.
7. What is meant by allele frequency?
8. Define polyploidy.
9. What is a mutation?
10. Distinguish between genotype and phenotype.
11. What features classify humans as primates?
12. What is comparative genomics?
13. Define biodiversity.
14. What is a fossil?
15. What is an index fossil?
16. Define a species.
17. Where is most DNA in a human (eukaryote) cell?
18. The diagram shows a biological process.

Figure 1.3 Biological process.

    Name this process.
19. Name the four nitrogenous bases in DNA.
20. What is a nucleotide?
21. State the law of superposition.
22. Distinguish between absolute dating and relative dating.
23. List the levels of classification from kingdom to species.
24. (a) What is meant by binomial nomenclature?
    (b) In this system how are humans classified?
25. Humans are classified in the order 'Primates'. Name some other animals that are primates.
26. Define natural selection.
27. When does evolution occur?
28. List the major stages in the evolution of living things from organic molecules to multicellular organisms.
29. The photograph shows a model of the human head and brain.

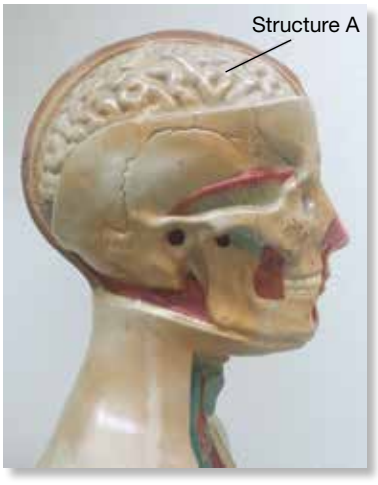


Figure 1.4 Human head and brain.

   (a) Identify structure A.
   (b) Outline the function of structure A.
   (c) Suggest why the size of structure A is important in human evolution.
30. Define biotechnology.

2 Mutation

Mutation is the change in the DNA genetic make-up of a cell. A mutation may be neutral and have no observable effect on the organism, it may be harmful and decrease the lifespan of the organism or it may be beneficial, giving it an evolutionary advantage over other individuals in the population.

Causes of mutation

Mutations can occur spontaneously and randomly, e.g. due to errors in DNA replication or cell division, or they can be induced by mutagens (environmental factors) such as radiation (e.g. X-rays and UV rays) or chemical agents (e.g. benzene, formalin or Agent Orange).

If the mutation is in a gonad cell, it may be inherited with the sperm or ova, while mutations in body cells are not inherited. In the 1920s, Hermann Muller used X-rays to obtain mutant fruit flies, *Drosophila melanogaster*, so he could carry out his experiments on inheritance, showing radiation caused mutation. The atomic bomb on Hiroshima caused many mutations, showing gamma radiation is mutagenic.

Types of mutation

There are two basic types of mutation – point mutation and chromosome mutation.

A **point mutation** changes the base sequences of a single gene and may form a new allele. For example, during DNA replication, sometimes one base is replaced by another nitrogenous base which in turn changes the mRNA. Since the code on the mRNA is translated into amino acids, the activity of the cell and the proteins it produces will be affected, e.g. on mRNA the codon GGG = glycine but if there is a base-pair substitution so that the mRNA reads CGG = arginine, the cell will now make arginine instead of glycine.

There are two types of point mutations – base pair substitutions and base pair insertions or deletions. Insertions and deletions can have a massive impact as they cause a **frameshift** and the triplet code is not read correctly, unless the shift is a multiple of three. To show the impact consider the sentence – *The dog ran up the road*. If you delete the 'e' from 'the', the sentence becomes – *thd ogr anu pth ero ad.* As the new sentence makes no sense, a deletion in a triplet code makes no sense and the polypeptide cannot be synthesised.

A **chromosome mutation** can involve either a change in the number of chromosomes or a rearrangement in the structure of a chromosome. Sometimes there are not 46 chromosomes present; Down syndrome, or trisomy 21, involves the presence of an extra copy of chromosome 21, so that the person has 47 chromosomes rather than 46. People with Klinefelter syndrome have 44 autosomes and the sex chromosomes XXY.

The rearrangement of a chromosome can involve inversion, when chromosome segments are upside down so the genes appear in the reverse order; translocation, when pieces are removed and inserted somewhere else; or deletion, when pieces of chromosome are lost.

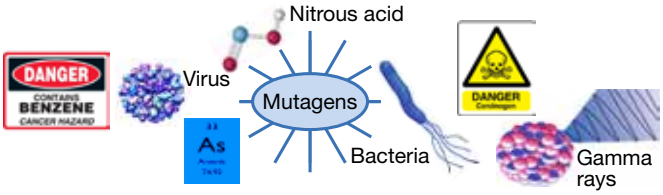


Figure 2.1 Mutagens.

Mutation and variation

The discovery that mutations can be caused by radiation, certain chemicals and so on is most important to Darwin's theory of evolution. When Darwin proposed his theory he did not know how variations arose in populations. Mutation explains one source of variation in a population.

Variation can arise several ways. Variation occurs due to random segregation during meiosis – each chromosome of the homologous pair sorts independently and randomly so that the gametes can have different combinations of chromosomes. Variation occurs due to crossing over during meiosis as new combinations of characteristics arise. Variation occurs due to sexual reproduction when the union of a sperm with an ovum forms a new combination of genes, not identical to the parents. Variation is mainly important when the environment is changing. If one variant has features more suited to the new environment, natural selection will lead to evolution and survival of the population.

QUESTIONS

1. What is a mutation?
2. Describe two 20th century examples of causes of mutation.
3. Use an example to show how changes in DNA sequences can result in changes in proteins and thus in cell activity.
4. What is a mutagen? Give an example.
5. Describe the cause of mutations.
6. Describe the circumstances needed for a mutation to be inherited.
7. Distinguish a point mutation from a chromosome mutation.
8. (a) What are the two types of point mutation?
   (b) Explain why base pair deletions of insertions can have a dramatic effect on polypeptide synthesis.
9. Explain how an understanding of the source of variation in organisms has provided support for Darwin's theory of evolution by natural selection.

10. (a) Describe three ways in which variation can arise in a population.
    (b) Explain why variation in a population is important.
11. The diagram shows the karyotype from a pair of human twins.

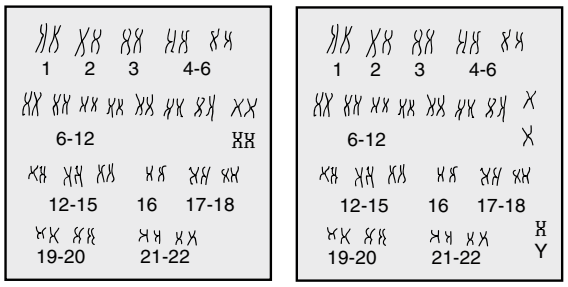


Figure 2.2 Karyotype of twins.

    (a) What is a karyotype?
    (b) Are the twins identical? Explain your reasoning.
    (c) Karyotypes are often used to show genetic malfunctions and mutations. Describe one type of mutation detected by karyotypes and explain its significance.
12. Natural selection requires that there is variation within a population. Which of the following is a source of variation in both sexual reproduction and asexual reproduction?
    (A) Crossing over.
    (B) Mutation.
    (C) Random segregation.
    (D) Union of gametes.
13. The diagram shows the eye colour of three members of one family.

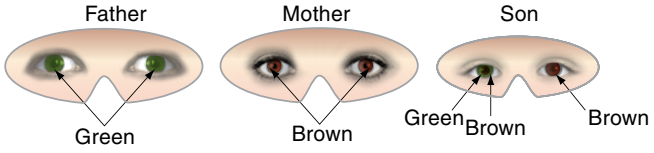


Figure 2.3 Eye colour of three family members.

    The appearance of the son's right eye is probably due to a mutation in which of the following?
    (A) Sperm. (B) Ova.
    (C) Zygote. (D) Embryo.
14. Why are harmful mutations not always eliminated from the gene pool?
    (A) They are needed in case the environment changes.
    (B) They all provide immunity against one disease.
    (C) They are recessive and carried by heterozygous forms.
    (D) They are dominant and prevent their removal.
15. Mutations are a source of new alleles in organisms. What causes mutation?
    (A) Environmental agents such as X-rays, ultraviolet radiation and gamma rays.
    (B) Chemicals such as mustard gas which react with DNA.
    (C) Spontaneous occurrence during cell division.
    (D) All of the above.
16. When insecticides, such as pyrethrum, are first introduced, the recommended concentration kills nearly all of the targeted insect pests. After widespread use and several years, the same concentration is only partially effective. What is the development of resistance in insect pests due to?
    (A) The insects realised they needed to acquire a resistance for survival of their species.
    (B) The insects built up a resistance to the insecticide over several generations.
    (C) Some insects were naturally immune, survived and reproduced.
    (D) The insecticide caused a mutation to make the insect immune.
17. Chromosome 11 consists of 438 bases. If there is a change on this chromosome in the gene coding for β-chain haemoglobin for the sixth amino acid, the haemoglobin produced has different properties, i.e. the haemoglobins cluster together to form fibres to deform the red blood cell into a sickle shape. The person has sickle cell anaemia. Identify this type of mutation.
    (A) Point mutation.
    (B) Chromosome mutation.
    (C) Translocation.
    (D) Deletion.
18. The table shows the mutation rate per million gametes per generation.

Disease	Dominant or recessive gene	Mutation per million gametes per generation
Haemophilia	Sex-linked recessive	25 to 32
Tay-Sachs disease	Recessive	11
Retinoblastoma	Dominant	15 to 23
Albinism	Recessive	28

    From this data, what can you conclude about mutation within the population?
    (A) A high proportion of people have these diseases.
    (B) The incidence of these diseases is low.
    (C) Sex-linked genes have a higher mutation rate than autosomal genes.
    (D) Everyone has a mutation, somewhere.
19. About 10 000 chemicals in common use in industrialised countries have been identified as mutagens. What could be one effect of these chemicals?
    (A) Increased birth rate.
    (B) Increased incidence of cancer.
    (C) Decreased water purity.
    (D) Decreased incidence of melanomas.

3 Mutation and Polypeptide Synthesis

A **mutation** is a permanent change in the genetic information. Mutations can occur in somatic cells or in germ line cells. Most mutations are in somatic cells, usually have a localised influence, e.g. the descendants of that cell and do not affect the next generation. A **somatic cell** is any cell in a multicellular organism except gametes. A mutation in a **germ line cell** occurs in any germ cell, will involve all cells and can be inherited by offspring. A germ cell is any cell that gives rise to the gametes.

Most mutations are recessive and harmful; some are lethal.

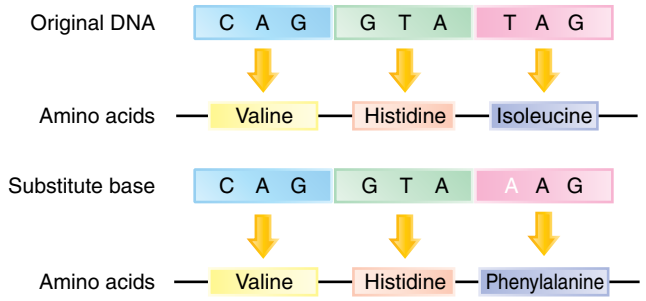


Figure 3.1 A change in code changes the amino acid sequence.

If a mutation causes a change in the DNA code, this will influence the protein produced. The activities of the cell can be disrupted if a particular protein cannot be produced. This can even lead to disease. For example, if a mutation on the β-haemoglobin gene puts thymine instead of guanine at one particular location, the person will suffer from the disease thalassemia major, which results in abnormalities such as severe anaemia and growth retardation.

Spontaneous and induced mutations

Spontaneous mutations occur naturally with about one in every million to one in every billion divisions and the causative agent cannot be identified. Mutations can also be induced. In an **induced mutation** the causative agent can be identified, e.g. exposure to radiation such as X-rays, gamma rays or certain chemical substances.

Missense and nonsense mutation

Sometimes a codon is changed by point mutation and the base pair substitution makes sense and still codes for an amino acid. However, it is not the right amino acid and it is a missense mutation. Sometimes the codon is changed by a point mutation and the code becomes a stop codon. This is a nonsense mutation and stops the polypeptide production at that point making a shorter polypeptide. The short polypeptide usually becomes a non-functional protein and the activities of the cell are interrupted.

QUESTIONS

1. Define mutation.
2. Distinguish between a somatic cell and a germ line cell.
3. What is a spontaneous mutation?
4. What is meant by induced mutation?
5. Give an example to show how a mutation can disrupt the activities of a cell.
6. Distinguish between a missense mutation and a nonsense mutation.
7. The diagram shows polypeptide synthesis in a cell.

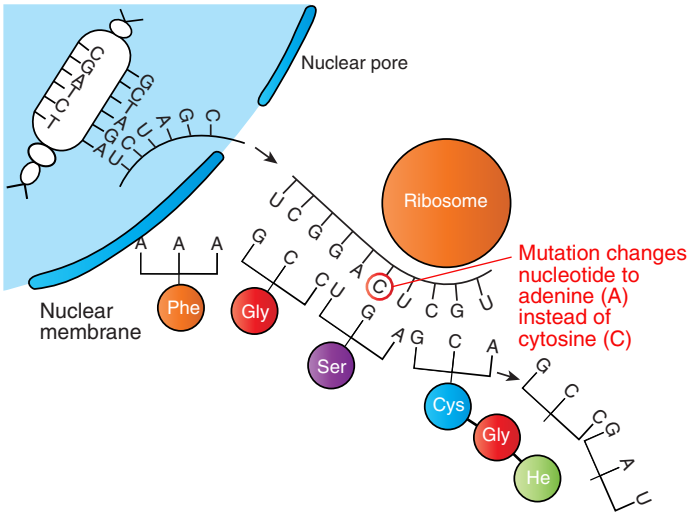


Figure 3.2 Polypeptide synthesis in a cell.

If a mutation occurred at the position marked in the diagram, use the table of the triplet codes to explain how the change would affect the synthesis of the polypeptide and the activities of the cell.

UUU Phe	UGU Cys	GGU Gly	U – uracil (thymine)
UUC Phe	UGC Cys	GGC Gly	C – cytosine
		GGA Gly	A – adenine
UCU Ser	AUU He	GGG Gly	G – guanine
UCC Ser	AUC He		Cys – cysteine
UCA Ser		AGU Ser	Gly – glycine
UCG Ser	ACU Thr	AGC Ser	He – isoleucine
	ACC Thr		Phe – phenylalanine
UAA stop	ACA Thr		Ser – serine
UAG stop	ACG Thr		Thr – threonine
UGA stop			

Figure 3.3 Some of the triplet genetic codes found in mRNA.

8. Which of the following mutations would have the most harmful impact on an organism?
   (A) A substitution mutation near the end of a coding sequence in a somatic cell.
   (B) Deletion of three nucleotides near the end of a coding sequence in a somatic cell.
   (C) Substitution of three nucleotides in a row.
   (D) A deletion of a single nucleotide close to the start of a coding sequence.

4 Point Mutations

A mutation is a permanent change in the genetic information and is a cause in genetic diversity. A gene mutation is a permanent change in the genetic information in a gene. The mutation can involve one or more base pairs and can be anywhere in the gene.

A point mutation is a change in one base in a single nucleotide in a gene. If the point mutation occurs in a gamete or zygote the change will affect every cell in the developing organism and will be passed to future generations. If the point mutation occurs in the developing embryo or foetus the change will affect tissues and cells that descend from this cell and may be passed to future offspring depending on the location of the mutation, e.g. in reproductive organs. If the point mutation occurs in an adult somatic cell the change will not be inherited by future generations and the effect on the person will depend on the specific mutation and how the body detects and responds to the error.

There are four basic types of point mutation – base pair substitution, insertion, deletion and inversion.

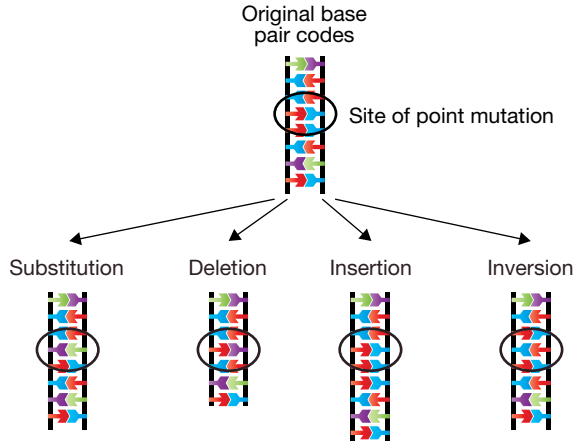


Figure 4.1 Point mutations.

Base pair substitution

In a base pair substitution one nucleotide and its complementary partner replace another pair of nucleotides. Sometimes this change is a **silent mutation** as the change has no effect on the protein being produced. For example, using the mRNA codes from Table 4.1 a base pair substitution from CUU to CUC will be a silent mutation as both code for the amino acid leucine. Other silent mutations may change the amino acid but have little effect on the protein. This can occur when the new amino acid has properties similar to the amino acid it replaced or the substitution has occurred in an area of the protein that is not an important determinant of the shape of the protein and its function.

Silent mutations occur fairly frequently but are hard to detect as they are not easily observed. Occasionally the change can be beneficial and can increase variation.

If the base pair substitution affects the shape of the protein or is at the active site of an enzyme, the change can seriously affect the functioning of the protein. For example, disulfide bridges are formed when two cysteine amino acids are brought close together with their sulfhydryl groups (–SH) on their side chains in close proximity due to the folding of the protein and a change in the code from UGC (cysteine a polar amino) to UUC (phenylalanine a non-polar amino acid) can affect the structure and functioning of the protein. Disulfide bridges are important in maintaining the structure of immunoglobulins (antibodies) and the antigen receptor sites on lymphocytes.

Table 4.1 mRNA codes.

UUU Phe	UCU Ser	UAU Tyr	UGU Cys
UUC Phe	UCC Ser	UAC Tyr	UGC Cys
UUA Leu	UCA Ser	UAA stop	UGA stop
UUG Leu	UCG Ser	UAG stop	UGG Trp
CUU Leu	CCU Pro	CAU His	CGU Arg
CUC Leu	CCC Pro	CAC His	CGC Arg
CUA Leu	CCA Pro	CAA Gln	CGA Arg
CUG Leu	CCG Pro	CAG Gln	CGG Arg
AUU He	ACU Thr	AAU Asn	AGU Ser
AUC He	ACC Thr	AAC Asn	AGC Ser
AUA He	ACA Thr	AAA Lys	AGA Arg
AUG Met	ACG Thr	AAG Lys	AGG Arg
GUU Val	GCU Ala	GAU Asp	GGU Gly
GUC Val	GCC Ala	GAC Asp	GGC Gly
GUA Val	GCA Ala	GAA Glu	GGA Gly
GUG Val	GCG Ala	GAG Glu	GGG Gly

U – uracil (thymine)	Cys – cysteine	Met – methionine
C – cytosine	Gln – glutamine	Phe – phenylalanine
A – adenine	Glu – glutamine	Pro – proline
G – guanine	Gly – glycine	Ser – serine
Ala – alanine	His – histidine	Thr – threonine
Arg – arginine	He – isoleucine	Trp – tryptophan
Asn – asparagine	Leu – leucine	Tyr – tyrosine
Asp – aspartic acid	Lys – lysine	Val – valine

Most base pair substitution mutations cause a missense mutation. A **missense mutation** is a changed codon that codes for an amino acid but does not necessarily make the correct sense. A **nonsense mutation** is a point mutation that changes a codon for an amino acid into a stop codon. The stop codon causes translation to stop shortening the polypeptide chain that is being synthesised. In most cases a nonsense mutation creates a non-functional protein. For example, a change in the code UCA for serine to UAA will create a stop at this point in translation and process of protein synthesis.

Deletion

Deletion is a loss of nucleotide pairs in a gene sequence. This causes a **frameshift mutation**. The nucleotide sequence is read in multiples of three (the code for each amino acid) so the deletion of one nucleotide will change the reading sequence. A frameshift mutation will not occur if the change was an insertion or deletion of three nucleotides. The example in Figure 4.2 shows how the reading frame is changed with a deletion.

The old dog sat on a hot day on a red mat.

As a triplet code this would be read

The/ old/ dog/ sat/ on a/ hot/ day/ on a/ red/ mat/

If the 'e' from 'The' is deleted, the code is read

Th o/ ldd/ ogs/ ato/ nah/ otd/ ayo/ nar/ edm/ at

Figure 4.2 Frameshift mutation due to deletion.

Insertion

Insertion is a point mutation where a nucleotide is added into the code. This will also cause a frameshift mutation. A frameshift mutation can be a nonsense mutation. Depending on the location of the insertion a number of different effects can occur.

Point mutations can occur spontaneously, e.g. during replication or can be induced by mutagens including ionising radiation, e.g. X-rays, cosmic rays, non-ionising radiation, e.g. UV light, various chemicals, e.g. benzene and some biological agents.

Inversion

In an inversion point mutation a nucleotide pair reverse positions with the next pair of nucleotides.

QUESTIONS

1. Define a mutation.
2. What is a gene mutation?
3. Define a point mutation.
4. Name the four basic types of point mutation.
5. What is a silent mutation?
6. Use Table 4.1 with the mRNA codes for amino acids to determine which of the following would be silent mutations.
   (a) GUU to GUG (b) ACG to AAG
   (c) GGU to GAU (d) CGG to UGG
   (e) GCU to GCC
7. Distinguish between a missense mutation and a nonsense mutation.
8. What is a frameshift mutation?
9. Use an example to show how a point mutation can have serious consequences.
10. What are the mRNA stop codes?
11. The diagram shows a section of DNA of a gene which undergoes a point mutation.

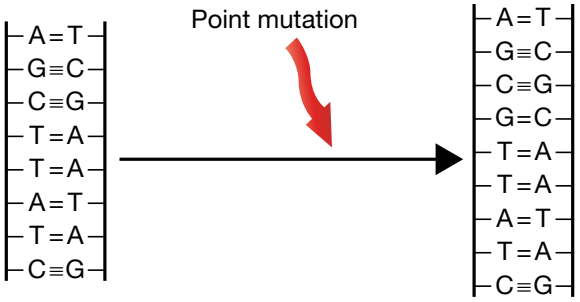


Figure 4.3 Point mutation in a gene.

Copy the diagram and label the location of the point mutation and which type of point mutation has occurred.

Use the diagram which shows a deletion of two nucleotides for the next THREE questions.

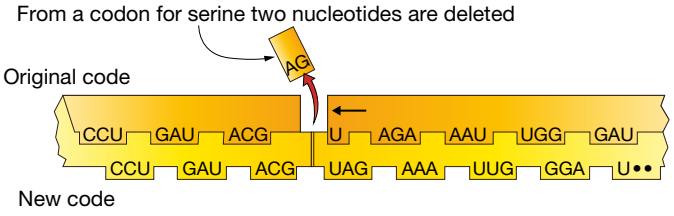


Figure 4.4 Deletion of two nucleotides.

12. What is the best description of this mutation?
    (A) Frameshift.
    (B) Chromosomal.
    (C) Insertion.
    (D) Base pair substitution.
13. Why is this mutation a nonsense mutation?
    (A) The new code does not read correctly.
    (B) The right proteins will not be produced.
    (C) There is no codon with only one nucleotide.
    (D) The new code is UAG which is a stop codon.
14. What was the code for serine that was involved in the mutation?
    (A) AGC (B) AGU
    (C) UGA (D) UAG
15. What is the best definition of a point mutation?
    (A) A permanent change in the genetic information.
    (B) An agent that interacts with DNA to cause a change.
    (C) A change in one base in a single nucleotide in a gene.
    (D) A change in an amino acid that alters protein structure.

5 Block Mutations

A block mutation is a permanent change to a segment of a chromosome that rearranges, deletes or disrupts many loci. Many block mutations are harmful changing the structure of the chromosome, though some are neutral especially if genes remain intact and sometimes the change can be beneficial, e.g. the change links genes that together now produce a positive effect.

Block mutations can be caused by **transposons** (transposable genetic elements) which are DNA segments that can move from one position to another in the chromosome. Transposons are sometimes called 'jumping genes' which is not how they move as they do not 'jump'. When the folding of the DNA molecule brings segments near each other transposons follow a 'cut and paste' mechanism to move to a new location or follow a 'copy and paste' mechanism replicating a section of DNA and adding it to another area. Transposons were discovered by Barbara McClintock when studying corn in the 1940s and she was awarded the Nobel Prize in Physiology or Medicine in 1983 for her discovery of 'mobile genetic elements'. She was the first female to receive this prize unshared. It is estimated that about 44% of the human genome is **repetitive DNA** which is multiple copies of DNA sections.

Types of block mutations include duplications, inversions, deletions, insertions and translocations.

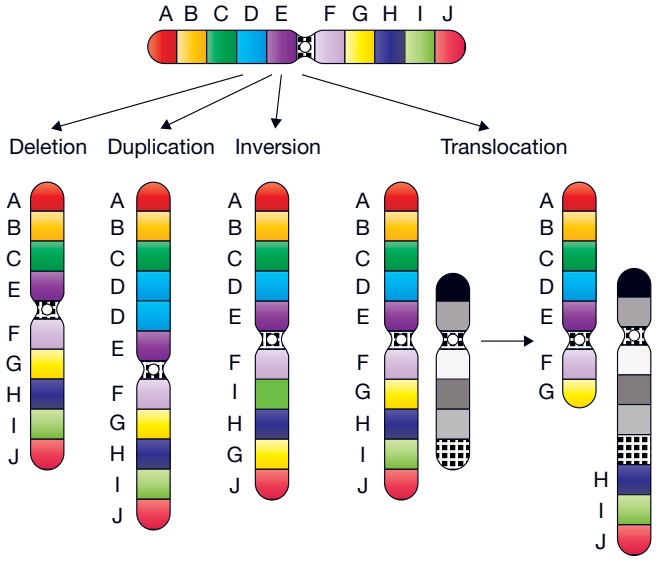


Figure 5.1 Types of block mutations.

Some sections of DNA are called **hotspots** as they are places that are more likely to undergo mutation than other places with an observable higher mutation frequency. Hotspots can be single nucleotides or short stretches of repeated nucleotides that have some basic instability or chemical tendency for nucleotide substitution.

Deletions

Deletions occur when a section of DNA is removed from a chromosome. The effect of a deletion depends on the size and location of the removed block sequence. Large deletions can involve several genes and have greater effect on phenotype and the health of the individual. Cri du chat syndrome is a deletion disorder that is caused by a deletion on the short arm of chromosome 5.

Duplications

Duplications occur when sections of DNA are replicated making the chromosome longer. Repetitive DNA can occur during DNA replication or recombination in crossing over and segregation during mitosis or meiosis. If the copies of a repeat sequence lie adjacent to each other they are called **tandem repeats**. Tandem repeats can vary in length with the large repeat units called satellites. Satellite DNA was first discovered when DNA was centrifuged and the repetitive units appeared as a distinct band in the tube. **Satellite DNA** (also now called simple sequence DNA) is a section of tandem, non-coding DNA that can be thousands of base pairs long. Microsatellite DNA is a short region of repeats that are used as genetic markers in DNA fingerprinting. In humans some microsatellites have 20 or more alleles which provides the variation to assist in identifying particular individuals by their DNA. **Trinucleotide disorders** occur when there are too many trinucleotide repeats in a gene, e.g. Huntington's disease occurs when there are more than 35 CAG repeats on the gene coding for the protein HTT. A genetic disorder due to duplication is Charcot-Marie-Tooth disease type 1 with duplication of 17p12 – a large section on the short arm of chromosome 17.

Inversions

Inversions occur when a section of DNA breaks and is reattached in the reverse orientation and order. This changes chromosome structure. Inversion is a cause for haemophilia A with an inversion in the factor VIII gene on X chromosome. The inversion within this gene stops protein production which means that testing for this disorder often involves measuring protein activity rather than a genetic test for the inversion.

Translocation

In translocation a section of one chromosome moves to a non-homologous chromosome. In a **reciprocal translocation** the non-homologous chromosomes exchange segments. Myeloproliferative syndrome is a genetic disorder caused by translocation of genetic material from chromosome 8 to other chromosomes, e.g. t(8;13)(p11;q12) which involves translocation of chromosomes 8 and 13 in lymphoma cells.

QUESTIONS

1. Define a mutation.
2. What is a transposon?
3. Explain why the term 'jumping gene' is not an accurate description of transposons.
4. What is repetitive DNA?
5. Outline Barbara McClintock's contribution to our understanding of genetics.
6. List the main types of block mutations.
7. Describe hotspots.
8. The diagram shows a type of block mutation.

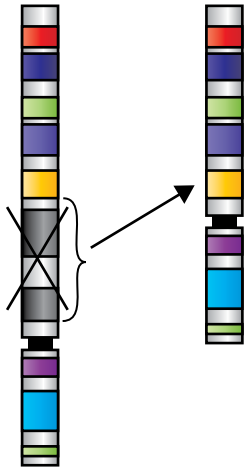


Figure 5.2 Type of block mutation.

Identify this type of block mutation and explain what has happened,

9. Construct a table to summarise the main types of block mutation – deletion, duplication, inversion and translocation explaining what is happening and giving a genetic example.
10. What are tandem repeats?
11. What is satellite DNA and how was it discovered?
12. Outline a use for microsatellite DNA.
13. What is a trinucleotide disorder and give an example.
14. The diagram shows an example of translocation.

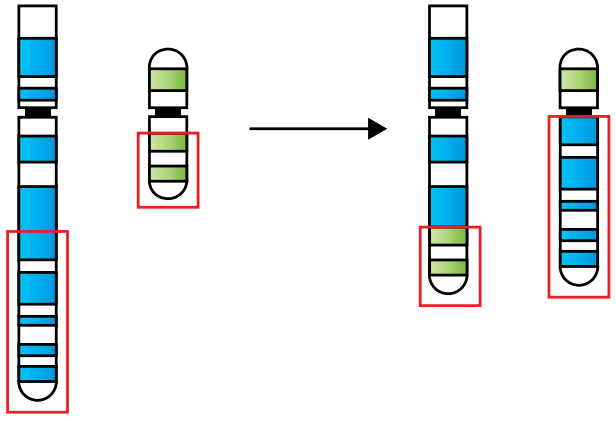


Figure 5.3 Translocation.

Explain why this is an example of reciprocal translocation.

15. If DNA duplications occur that involve one or more genes to make a gene pair and both copies stay in the genome and are inherited by future generations then a multigene family can be created.
    (a) Explain why the genes in a multigene family code for proteins with similar sequences.
    (b) Explain why the genes in a multigene are usually involved in the same body functioning.
    (c) Discuss why comparative genomics is interested in multigene families such as the globin genes for haemoglobin.

Use the following diagram for the next TWO questions.

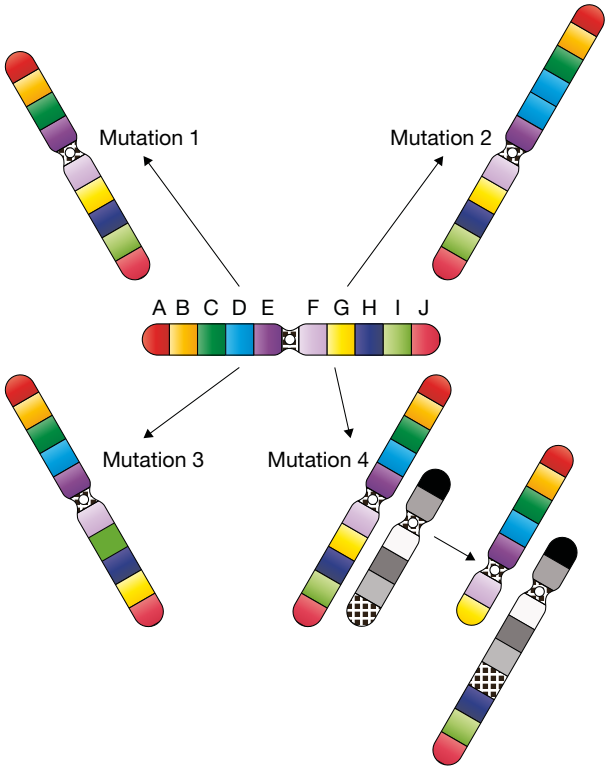


Figure 5.4 Mutation types.

16. Which mutation type shows inversion?
    (A) Mutation 1 (B) Mutation 2
    (C) Mutation 3 (D) Mutation 4
17. Which type of mutation would be involved in the creation of repetitive DNA?
    (A) Mutation 1 (B) Mutation 2
    (C) Mutation 3 (D) Mutation 4
18. The following code shows a section of a simple sequence DNA showing only one strand of the DNA.

    .GCTTAGCTTAGCTTAGCTTAGCTTAGCTTA.

    How many nucleotides are in this repeat unit?
    (A) 3 (B) 5 (C) 15 (D) 30
19. Which disease can be caused by translocation?
    (A) Trisomy 21. (B) Measles.
    (C) Cri du chat. (D) Malaria.

Answers

1 Assumed Knowledge

1. (a) Chromosomes are long strands of hereditary information containing genes. Chromosomes are made up of DNA and histone proteins.
   (b) Each gene is found at a particular locus on a chromosome.
2. A gene is a section of DNA coding for proteins that expresses itself as the phenotype for that trait, e.g. gene for plant height whereas an allele is an alternative for a particular trait, e.g. there are two alleles for height in pea plants – tall (T) or short (t). Alleles are the alternative forms of a gene and occupy a particular locus on a chromosome.
3. Autosomes are chromosomes that are not directly involved in determining sex whereas sex chromosomes are responsible for determining the sex of an individual. In humans there are two sex chromosomes X and Y. Males are XY and females are XX.
4. (a) Person A is female as they have XX.
   (b) Trisomy is the presence of three copies of a homologous chromosome rather than the normal two copies.
   (c) Person A has trisomy 21 with three copies of chromosome 21 – this is Down syndrome.
5. A genome sequence is the order of the As, Ts, Cs and Gs in the DNA code.
6. A gene pool is the total aggregate of genes in a population at any one time.
7. The frequency of an allele in a population refers to the proportion of the population that has that allele.
8. Polyploidy occurs when cells contain more than two haploid (n) sets of chromosomes, e.g. triploid ($3n$), tetraploid ($4n$).
9. A mutation is a permanent change in the genetic information. This causes genetic diversity.
10. The genotype shows the genetic make-up or set of alleles of an organism that controls a characteristic whereas phenotype is the observable physical and physiological traits of an organism and the outward appearance of an organism. A dominant phenotype can have two dominant alleles, e.g. TT or one dominant allele and one recessive allele, e.g. Tt. The recessive phenotype has two recessive alleles, e.g. tt.
11. Humans are classified as a primate as they have – 1. An opposable thumb. 2. Shoulder joint with high rotating ability. 3. Forward facing eyes with stereoscopic vision. 4. Reduced snout and olfactory centre of the brain. 5. Enlarged skull with large cerebrum. 6. Five digits on limbs. 7. Nails (not claws). 8. Bicuspid teeth.
12. Comparative genomics studies compare genomic features of different organisms, e.g. looking for differences and similarities in DNA sequence, genes, gene order and regulatory sequences.
13. Biodiversity refers to the amount of variation within the group.
14. A fossil is a remain or trace of a pre-existing organism.
15. Index fossils are fossils of organisms that lived for a short time and were found over a wide area.
16. A species is a group of organisms that can interbreed to produce fertile offspring. They share a common gene pool.
17. Most DNA in eukaryote cells is in the nucleus. DNA is also found in mitochondria and chloroplasts.
18. Diagram shows DNA replication.
19. Four nitrogenous bases are adenine, thymine, cytosine and guanine.
20. A nucleotide is the basic unit of DNA consisting of a nitrogenous base, sugar and a phosphate group.
21. The law of superposition states that the oldest layers are on the bottom and the youngest layers are on top, unless there has been folding or faulting or another form of dynamic Earth movement.
22. Relative dating uses the law of superposition determining if something is 'older than' or 'younger than' whereas absolute dating gives a date in years with the experimental error of the method used in determining the date.
23. Levels are kingdom, phylum, class, order, family, genus, species.
24. (a) Binomial nomenclature is calling an organism by its genus species name.
    (b) Humans are *Homo sapiens*.
25. Primates include the lemurs, lorises, tarsiers, monkeys, macaques, baboons, gibbons, orangutans, chimpanzees and gorillas.
26. Natural selection is a process that leads to a change in a population over time due to some phenotypes having more success surviving and reproducing in particular environmental conditions.
27. Evolution occurs when natural selection causes changes in relative frequencies of alleles in the gene pool.
28. The order of evolution of living things was organic molecules, membranes, prokaryotic heterotrophic cells, prokaryotic autotrophic cells, eukaryotic cells, colonial organisms and multicellular organisms.
29. (a) Structure A is the cerebrum.
    (b) The cerebrum is concerned with receiving and responding to sensory signals and carrying out mental processes, e.g. memory, abstract thought.
    (c) The size of the cerebrum is an important indicator in human evolution as the cranial capacity relative to body size is related to thought processes, the ability to make complex tools, produce language with symbolic thinking and complex social interactions.
30. Biotechnology is the use of organisms or their parts to make useful products.

2 Mutation

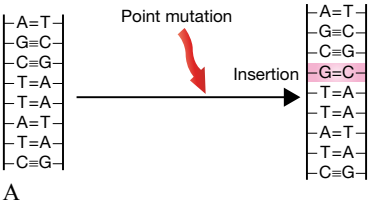
1. Mutation is the change in the DNA genetic make-up of a cell.
2. In the 1920s, Hermann Muller used X-rays to obtain mutant fruit flies, *Drosophila melanogaster*, so he could carry out his experiments on inheritance, showing radiation caused mutation. The atomic bomb on Hiroshima caused many mutations, showing gamma radiation is mutagenic.
3. During DNA replication, sometimes one base is replaced by another which in turn changes the mRNA. Since the code on the mRNA is translated into amino acids, the activity of the cell and the proteins it produces will be affected, e.g. on mRNA the codon GGG = glycine, but if there is a base pair substitution so that the mRNA reads CGG = arginine, the cell will now make arginine instead of glycine.
4. Mutagens are environmental factors such as radiation (e.g. X-rays and UV rays) or chemical agents (e.g. benzene) that cause mutations to occur.
5. Mutations can occur spontaneously and randomly, e.g. due to errors in replication, or they can be induced by mutagens such as radiation or certain chemicals.
6. For a mutation to be inherited it needs to be in a gonad cell, so that the sperm or ova will carry the mutation. Mutations in body cells are not inherited.
7. A point mutation changes the base sequences of a single gene and may form a new allele, while a chromosome mutation can involve either a change in the number of chromosomes or a rearrangement in the structure of a chromosome.
8. (a) Two types of point mutation are base pair substitutions and base pair insertions or deletions.
   (b) Base pair insertions and deletions can have a massive impact as they cause a frameshift and the triplet code is not read correctly, unless the shift is a multiple of three. To show the impact consider the sentence – *The dog ran up the road*. If you delete the 'e' from 'the', the sentence becomes – *thd ogr anu pth ero ad.* As the new sentence makes no sense, a deletion in a triplet code makes no sense and the polypeptide cannot be synthesised.
9. Darwin's theory of evolution states that there is variation within a population and those with favourable characteristics will survive to reproduce by natural selection. When Darwin proposed his theory he did not know how variations arose in populations – the discovery of mutations caused by radiation, certain chemicals etc. explains the source of variation.

10. (a) Variation can arise by random segregation during meiosis – each chromosome of the homologous pair sorts independently and randomly so that the gametes can have different combinations of chromosomes. Crossing over during meiosis can lead to a new combination of characteristics, increasing variation. Sexual reproduction involving the union of a sperm with an ovum means that the offspring have a new combination of genes and are not identical to the parents, thus increasing variation in the population.
    (b) Variation is mainly important when the environment is changing. If one variant has features more suited to the new environment, natural selection will lead to evolution and survival.
11. (a) Karyotype is the pairs of chromosomes obtained while the cell is divided and the chromosomes are sorted according to size from biggest to smallest.
    (b) No, twins are not identical as twin A is female and twin B is male.
    (c) One type of abnormality is having an incorrect number of chromosomes, e.g. some humans have 47 chromosomes instead of 46 chromosomes. These can be counted on the karyotype. For example, trisomy 21, or Down syndrome, is a genetic disease where there are three copies of chromosome 21; this causes specific symptoms in the phenotype of people with the disease.
12. B
13. D
14. C
15. D
16. C
17. A
18. B
19. B

3 Mutation and Polypeptide Synthesis

1. A mutation is a permanent change in the genetic information.
2. A somatic cell is any cell in a multicellular organism except gametes. A germ line cell is any cell that gives rise to the gametes.
3. Spontaneous mutations occur naturally and the causative agent cannot be identified, e.g. they occur in about one in every million to one in every billion divisions.
4. In an induced mutation the causative agent can be identified, e.g. exposure to radiation such as X-rays, gamma rays or certain chemical substances.
5. The activities of the cell can be disrupted if a particular protein cannot be produced, e.g. due to a mutation that causes a change in the DNA code which affects the production of a particular protein. This can even lead to disease. For example, if a mutation on the β-haemoglobin gene puts thymine instead of guanine at one particular location, the person will suffer from the disease thalassemia major, which results in abnormalities such as severe anaemia and growth retardation.
6. Both missense mutations and nonsense mutation are point mutations caused by a base pair substitution in a codon. In a missense mutation the codon still codes for an amino acid and a polypeptide is produced, though it is not the right amino acid in the polypeptide. In a nonsense mutation the substitution makes the stop codon which means the synthesis of the polypeptide stops at that point shortening the length of the polypeptide and usually making a non-functional protein.
7. The diagram shows polypeptide synthesis and the codon affected by the mutation on the mRNA is UCA. This is the codon for the amino acid serine which is shown in the diagram lining up to become part of the polypeptide. If the cytosine (C) is changed to adenine (A) in a substitution mutation the code becomes UAA. This is a stop codon which means the synthesis of the polypeptide will now stop at this point due to the nonsense mutation. This will result in a shortened polypeptide and probably form a non-functional protein. This could have a dramatic affect on cell metabolism and activities as it could interrupt and stop a chain of reactions, e.g. due to the lack of an enzyme to catalyse one of the steps in the metabolic pathway.
8. D

4 Point Mutations

1. A mutation is a permanent change in the genetic information and is a cause in genetic diversity.
2. A gene mutation is a permanent change in the genetic information in a gene. The mutation can involve one or more base pairs and can be anywhere in the gene.
3. A point mutation is a change in one base in a single nucleotide in a gene.
4. There are four basic types of point mutation – base pair substitution, insertion, deletion and inversion.
5. A silent mutation is a change that has no effect on the protein being produced.
6. (a) GUU (valine) to GUG (valine) is a silent mutation.
    (b) ACG (threonine – polar amino acid) to AAG (lysine – electrically charged amino acid) is not likely to be a silent mutation.
    (c) GGU (glycine a non-polar amino acid) to GAU (aspartic acid – electrically charged amino acid) is not likely to be a silent mutation.
    (d) CGG (arginine is an electrically charged amino acid) to UGG (tryptophan a non-polar amino acid) is not likely to be a silent mutation.
    (e) GCU (alanine) to GCC (alanine) is a silent mutation.
7. A missense mutation is a changed codon that codes for an amino acid but does not necessarily make the correct sense whereas a nonsense mutation is a point mutation that changes a codon for an amino acid into a stop codon. The stop codon causes translation to stop shortening the polypeptide chain that is being synthesised.
8. A frameshift mutation occurs when a deletion or insertion causes an incorrect reading of the nucleotide sequence. The sequence is read in multiples of three (the code for each amino acid) so the deletion or insertion of one nucleotide will change the reading sequence but it is not affected if the change was an insertion or deletion of three nucleotides.
9. If the point mutation affects the shape of the protein or is at the active site of an enzyme, the change can seriously affect the functioning of the protein. For example, disulfide bridges are formed when two cysteine amino acids are brought close together with their sulfhydryl groups (–SH) on their side chains in close proximity due to the folding of the protein and a change in the code from UGC (cysteine a polar amino) to UUC (phenylalanine a non-polar amino acid) can affect the structure and functioning of the protein. Disulfide bridges are important in maintaining the structure of immunoglobulins (antibodies) and the antigen receptor sites on lymphocytes. Inability to form functional antibodies will reduce the effectiveness of the immune system.
10. The mRNA stop codes are UAA, UAG and UGA.
11. 

12. A
13. D
14. B
15. C

5 Block Mutations

1. A block mutation is a permanent change to a segment of a chromosome that rearranges, deletes or disrupts many loci.
2. Transposons (transposable genetic elements) are DNA segments that can move from one position to another in the chromosome.
3. The term 'jumping genes' is not accurate as it does not explain how transposons move as they do not 'jump'. When the folding of the DNA molecule brings segments near each other transposons follow a 'cut and paste' mechanism to move to a new location or follow a 'copy and paste' mechanism replicating a section of DNA and adding it to another area.
4. Repetitive DNA is multiple copies of DNA sections which are found in the genome.
5. Barbara McClintock discovered transposons when studying corn in 1940s and she was awarded the Nobel Prize in Physiology or Medicine in 1983 for her discovery of 'mobile genetic elements'.
6. Block mutations can be duplications, inversions, deletions, insertions or translocations.

7. Hotspots are places that are more likely to undergo mutation than other places with an observable higher mutation frequency. Hotspots can be single nucleotides or short stretches of repeated nucleotides that have some basic instability or chemical tendency for nucleotide substitution.
8. The diagram shows a block deletion. In this type of mutation a section of DNA is removed from the sequence in a chromosome and in this case several genes have been removed near the centromere.
9.

Change	What happens	Example
Deletion	A section of DNA is removed altering chromosome structure.	Cri du chat syndrome involves a deletion of the end of the short arm of chromosome 5.
Duplication	A section of DNA is repeated and added to the chromosome.	Charcot-Marie-Tooth disease type 1 with duplication of 17p12 – a large section on the short arm of chromosome 17.
Inversion	A section of DNA breaks and is reattached in the reverse orientation and order.	In factor VIII gene on X chromosome causing haemophilia A.
Translocation	A section of one chromosome moves to a non-homologous chromosome. In a reciprocal translocation the non-homologous chromosomes exchange segments.	Myeloproliferative syndrome caused by translocation of genetic material from chromosome 8 to other chromosomes, e.g. t(8;13)(p11;q12).

10. Tandem repeats are copies of a repeat sequence that lie adjacent to each other
11. Satellite DNA or simple sequence DNA is a section of tandem, non-coding DNA that can be thousands of base pairs long and was discovered when DNA was centrifuged and the repetitive units appeared as a distinct band in the tube.
12. Microsatellite DNA is a short region of repeats that are used as genetic markers in DNA fingerprinting. In humans some microsatellites have 20 or more alleles which provides the variation to assist in identifying particular individuals by their DNA.
13. Trinucleotide disorders occur when there are too many trinucleotide repeats in a gene, e.g. Huntington's disease occurs when there are more than 35 CAG repeats on the gene coding for the protein HTT.
14. The diagram shows reciprocal translocation as the exchange is between non-homologous chromosomes (they are different lengths and have different genes) with blocks of DNA being swapped and two new different chromosomes are formed with different sets of genes.
15. (a) Multigene families arise after duplication of one or more genes to make a gene pair and both copies stay in the genome and are inherited by future generations. This means that the genes in the multigene family started with genes that coded for particular proteins which started the multigene family.
    (b) Sine the original genes that were duplicated and started the multigene family were involved in a particular body function, the future forms of the genes in the multigene family are most likely to be involved in the same process.
    (c) Comparative genomics studies compares genomic features of different organisms, e.g. looking for differences and similarities in DNA sequence, genes, gene order and regulatory sequences. Researchers are interested in multigene families such as the globin genes for haemoglobin as differences and similarities in the DNA sequences found in the genomes of different species can provide information about evolution and the interrelatedness of the species.
16. C
17. B
18. B
19. A

6 Transposable Genetic Elements

1. Transposable genetic elements are DNA segments that can move from one position to another in the chromosome.
2. Transposition is the movement of a transposon.
3. A prokaryote does not have membrane bound organelles, e.g. nucleus, while a eukaryote does have membrane bound organelles, e.g. has a nucleus.
4. Transposons have been found in prokaryotes and eukaryotes, being first found in plants.
5. The work of Barbara McClintock was not recognised until 1983 as the discovery of 'jumping genes' in the 1940s was quite ahead of its time. Watson and Crick did not propose the double helix structure of DNA until 1953 and thus the idea of genes moving location and changing the Mendelian laws of inheritance would have been unexplainable at that stage of genetic understanding. With the advent of genetic engineering her work could be fully recognised.
6. In humans, jumping genes have been linked with antibody production by the immune system and some of the rearrangements caused by jumping genes are believed to be the cause of some forms of cancer.
7. Retrotransposons use a 'cut and paste' method to move genetic information from one location on a chromosome to another but they copy RNA rather than DNA.
8. Transposons have been called 'junk' DNA as there is no clear indication how they benefit the host; and they have been called 'selfish' DNA as they often make multiple copies of themselves.
9. Since transposons have been found in all life forms, transposons may have been present in the last universal common ancestor. Or transposons may have evolved independently several times.
10.

Feature	Transposable genetic element (TE)	Germ line mutation
Location	If the change in position occurs in a germ line cell then the gametes will have the change. If the change occurs in somatic cells then the gametes will not have the change. The gap in the DNA is not usually repaired.	Occurs in any cell that gives rise to the gametes and the gametes will have the mutation.
Inheritance	If the change is in a germ line cell then it will be transmitted to offspring and potentially future generations. If it is in a somatic cell then it will not be transmitted to offspring and future generations. If the move leads to chromosome elongation this can disrupt cell division, e.g. pairing in mitosis and meiosis.	Mutation is transmitted to offspring and potentially future generations.
Phenotype	When TE change their relative position on the genome or are replicated within the genome they change the coding of a functional gene and can disable the gene so that it cannot produce the correct polypeptide and often no polypeptide can be synthesised. This can change the functional protein and hence phenotype.	If the change is part of the coding portion of the genome then phenotype will be affected, e.g. base pair substitution to change an amino acid that changes the structure of a polypeptide. This can change the functional protein and hence phenotype.
Effect on organism	If the change is in a somatic cell and in coding that is not expressed then there will be minimal effect on the organism. If the change is in the gamete and stops the effective expression of a gene then the organism and the functioning of the organism could be highly affected.	If a functional protein can no longer be produced the metabolism of the organism would be dramatically affected with a disabled biochemical pathway and the proper functioning of the organism would be affected.

11. A

7 Chromosome Abnormalities

1. Polyploidy is the possession of more than two sets of chromosomes per nucleus e.g. hexaploid (6*n*), while monoploidy is the loss of an entire set of chromosomes (the haploid number *n*) and aneuploidy is the addition of all or part of a chromosome.
2. Monosomy is the lack of one chromosome from the normal number of chromosomes and trisomy means there are three copies instead of the normal two copies of a particular chromosome.