Bio Factsheet

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Answering Exam Questions: Mutation

This Factsheet summarises where students commonly go wrong in answering questions about mutation. Candidates frequently confuse **gene mutation** with **chromosome mutation**.

- Gene mutation is a change in the base sequence of DNA or RNA of an organism. In humans common examples are colour blindness, sickle-cell anaemia, cystic fibrosis and haemophilia.
- Chromosome mutation is a change in the structure or number of the chromosomes of organisms. The common chromosome mutations of humans are Down's syndrome, Turner's syndrome and Klinefelter's syndrome.

Always read the complete examination question first, before starting to answer, so that you can assess whether it relates to gene or to chromosome mutation.

*Exam Hint: Candidates frequently confuse the terms 'nucleosides' and 'nucleotides'. A **nucleoside** is a nitrogenous base bonded onto a pentose sugar. A **nucleotide** is a nitrogenous base bonded onto a pentose sugar which is bonded to a phosphate molecule.*
Remember that the pentose sugar is ribose in RNA and deoxyribose in DNA.

The bases are adenine, thymine, guanine and cytosine in DNA and adenine, uracil, guanine and cytosine in RNA. DNA and RNA are polymers of nucleotides.

Question 1

The diagram shows the base sequence on a sense strand from a length of DNA and three possible types of gene mutation.

Normal DNA:	**A C T G A G C T A**
Mutation 1:	**A C T G G A G C T A**
Mutation 2:	**A C T A G C T A**
Mutation 3:	**A C T T A G C T A**

(a) (i) What do the letters A, C, T, G represent? 2

There are two marks available suggesting that more than the four correct base names are needed. One mark would be for the correct base names: A = adenine, C = cytosine, G = guanine and T = thymine. The second mark would be for recognising that the letters actually represent the nucleotides which contain the named bases.

Candidates may give A = adenosine, C = cytidine, G = guanosine and T = thymidine. This is acceptable if it is clear they are nucleoside names and not base names.
Incorrect spelling of a base or nucleoside name would lose the mark. A mixture of base and nucleoside names would also lose the mark.

(ii) Name and describe the type of mutation shown in 1, 2 and 3 6

1. *Addition/insertion. An extra G (nucleotide) has been added/inserted after the 4th locus/nucleotide.*
2. *Deletion. The G (nucleotide) at the fourth locus has been lost.*
3. *Substitution. The G (nucleotide) at the 4th locus has been lost and replaced with a T (nucleotide).*

In each example there will be one mark for naming the mutation and one mark for describing it.

Candidates often make an error by writing, for example, 'an extra guanine/G base has been added….'. Remember – it is a complete nucleotide that has been added, deleted or substituted, not just the base. To score the description mark examiners will look for two facts, first, the actual base/nucleotide change, second, the position of the change on the DNA molecule.

(b) A gene mutation may cause no change in the structure of the polypeptide coded for. Explain why. 2

Note the verb 'explain' used in the question. This means that you must give more than a simple description to score marks. Thus referring to a 'degenerate' code would not suffice, you must explain what it means.

One mark would be for explaining the 'degenerate' nature of the genetic code. The code is referred to as degenerate because it contains more codons than there are amino acids, thus some amino acids have several codons, which can cause their insertion into a polypeptide chain.

The second mark would be for a statement explaining that 'the new codon produced by the mutation coded for the same amino acid as the original codon, so there would be no change in the amino acid sequence of the polypeptide'.

Question 2

The protein 'globin' of haemoglobin contains two types of polypeptide chain. In sufferers of sickle-cell anaemia one type of polypeptide chain contains an amino acid which differs from normal. This is due to a DNA mutation which produces the base sequence CAT instead of CTT.

(a) (i) Name two different types of factor which may increase the frequency of mutation. 2

One mark would be for naming a mutagenic chemical, for example, mustard gas, dioxin, benzene derivatives in tobacco smoke.

One mark would be for naming a radiation, for example, alpha, beta, gamma rays, Y-rays, UV rays.

Candidates who only gave two types of radiation or two types of chemical would only score one mark. Candidates who just answered 'radiation and mutagenic chemicals' would not score – the question asks for the factors to be named.

(ii) What type of gene mutation produced the sickle-cell anaemia allele? 1

The only answer is 'substitution'. You are not asked to state that T was substituted by A – so refrain from doing so, because if you make an error you will lose the mark.

(iii) Explain why the mutation resulted in only one different amino acid in the affected polypeptide chain. 3

One mark would be for stating 'one codon/triplet codes for one specific amino acid'.

The second mark would be for stating that 'the mutation only affected one codon in the codon sequence of the gene so there was no effect on subsequent codons in the gene/no frame shift'.

The third mark would be for stating 'thus only one amino acid altered, amino acids further along the chain were unchanged'.

(b) **Sufferers of sickle-cell anaemia have brittle red cells that carry less oxygen than normal. Explain why changing one amino acid alters the properties of haemoglobin. 3**

One mark would be for stating 'change in the sequence of amino acids alters the shape of the polypeptide/protein/globin'. A second mark would be for stating 'this is because the (ionic and hydrogen) bonding in the polypeptide would be altered'. The third mark would be for a comment that 'the shape of the polypeptide/protein determines its properties/ability to allow oxygen transport (by haem)'.

A common error is for candidates to refer to 'peptide bonds being altered'. The peptide bonds are involved in joining adjacent amino acids together and these bonds are not altered by the substitution.. It is the ionic and hydrogen bonds involved in holding the polypeptide folds together that are altered by the mutation.

Another error is to state 'the shape of the polypeptide affects its ability to carry oxygen'. Remember, it is the 'haem' groups on the polypeptide which carry the oxygen. A good answer would be 'the shape of the polypeptide/globin affects the ability of haem to carry oxygen'.

(c) The table shows some mRNA codons for some amino acids.

mRNA codon	Amino acid
CAU	histidine
CAA	glutamine
GUA	valine
GAA	glutamic acid
CUU	leucine
GAU	aspartic acid

Use the information in the table to determine the change in the amino acid which occurred because of the gene mutation. Explain your reasoning. 4

First mark: CTT mutated to CAT in DNA, but in RNA thymine(T) is replaced by uracil(U).

Second mark: mRNA is complementary to the mutated DNA strand.

Third mark: thus, the codons in mRNA become GAA, which mutates to GUA.

Fourth mark: GAA codes for glutamic acid (normal globin) but GUA codes for valine (in abnormal globin).

The commonest error is to forget that mRNA and the DNA sense strands are complementary. Candidates who made this error would incorrectly suggest that leucine was replaced with histidine. It is important to present the data in this answer in a logical sequence in order for it to make sense.

(d) The beta chains of globin are 146 amino acids long. What would be the minimum number of nucleotide bases on DNA needed to code for this polypeptide? Explain your answer. 2

A chain of 146 amino acids would be coded for by a chain of 146 codons. (1 mark)

Each codon contains 3 adjacent nucleotide bases.

$3 \times 146 = 438$ bases. (1 mark)

Candidates who ignore the instruction 'explain your answer' would lose at least one mark. A frequent error made by candidates in this type of question is to divide the number of amino acids by three rather than multiplying it by three.

Question 3

Malignant melanoma (skin cancer) is associated by excess exposure to ultra-violet light in sunlight.

(a) Explain how UV radiation may cause skin cancer. 4

Mark 1: reference to mutation induced in dividing cells of skin/germinative layer/ Malpighian layer. Some precision is needed here, it is not enough to just state 'mutation in skin cells'. Mark 2: UV radiation raises energy levels of purine/pyrimidine bases which then tend to join in pairs/form dimers/ref to thymine dimers. Candidates are incorrect if they state that the bases become ionised.

Mark 3: this changes base sequences in genes/mutates genes, which control, for example, growth, development, cell division, oncogenes (tumour causing genes), tumour suppressor genes. It would not be necessary to list all these genes to score the mark. Mark 4: cells containing the mutant gene/genes divide and migrate uncontrollably through the skin (and underlying tissues) to produce cancer. To score this point you must refer to uncontrolled cell division and to migration.

(b) Suggest why skin cancer is commonest in people who have pale coloured skin which does not tan easily on exposure to the sun. 2

Mark 1: melanin in skin absorbs UV radiation thus shielding DNA from it.

Mark 2: pale coloured/fair people have less melanin/may lack melanin synthesising genes and so have less protection.

A simple reference to melanin is not enough – you must state what the melanin does. Some candidates may be tempted to give details of the gene mutation albinism – when there is no melanin in the skin. This is not asked for in the question so is irrelevant and will not score marks. It also wastes time, which would be better used scoring other marks.

(c) Suggest why UV radiation does not cause other cancers in humans. 1

UV radiation does not possess enough energy to penetrate beyond the dermis of the skin and so cannot affect deeper organs. This answer would score the mark. Some candidates confuse their answer by referring to the fact that UV radiation has insufficient energy to cause ionisation. This is a separate issue and relates more to deep cancers induced by, for example, X-rays.

The intensity of UV light in solar radiation has increased in recent years due to the destruction of ozone in the upper atmosphere. This may increase the incidence of mutations in plant and animal populations.

(d) Discuss whether an increase in the mutation rate, due to increased UV irradiation, will cause an increase in phenotypic variation of animal and plant populations. 6

Examples of points the examiners would expect candidates to make are:

1. UV light only reaches the surface somatic cells of organisms, not the gonads or gametes;
2. Not all mutations result in observable changes in phenotype;
3. Many mutations are recessive and so are less likely to be expressed;
4. Mutations may be in parts of the DNA/introns which do not code for polypeptide synthesis;
5. Many mutations are disadvantageous/lethal so that organisms possessing them are rapidly eliminated by natural selection;
6. Other mutations are beneficial and so will be selected, increasing phenotypic variation;

Other valid points could be accepted instead of the above. Note that the instruction in the question is 'discuss'. Examiners would therefore expect points to be made supporting both an increase and a decrease in phenotypic variability and would penalise answers which did not include these. Answers which only refer to plants or animals would also be penalised.

Question 4

It is probable that primitive mammals possessed only one type of photosensitive visual pigment in their eyes and so could only had monochromatic vision. Colour-sensitive visual pigments probably developed from the ancestral pigment.

(a) Explain how the colour-sensitive pigments could have been developed. 5

Possible mark points (max 5) would be:

- *The ancestral visual pigment would be a protein coded for by a specific allele;*
- *The ancestral pigment would be sensitive to all wavelengths of light;*
- *Gene mutation could alter the codon sequence of the allele;*
- *By deletion/addition/substitution/inversion of bases/ nucleosides;*
- *Thus the amino acid sequences in the visual pigment protein would be altered;*
- *Thus its shape and properties would alter, reducing its sensitivity to certain wavelengths of light/enhancing its sensitivity to some wavelengths of light;*
- *Several gene mutations would produce several different visual pigments all with different light sensitivities;*

Beware giving irrelevant details about rhodopsin/photopsins/ opsins/red, blue, green cones – stick to the mutation theme.

(b) Explain how alleles for pigments sensitive to a colour could spread in a population of mammals. 4

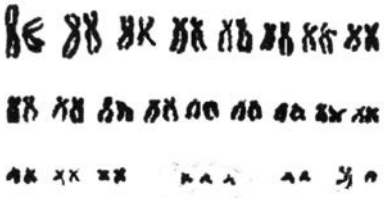
Possible mark points would be:

- *Alleles for colour vision confer a survival advantage to the organism;*
- *Colour vision enables better detection of predators/better foraging/better hunting of prey;*
- *Thus mammals with colour vision alleles are more likely to survive than mammals with no colour vision;*
- *Thus more likely to reproduce/breed and pass the alleles onto their offspring;*

The commonest error candidates make is to give a general answer about natural selection/survival of the fittest. To score marks restrict your answer specifically to the selection of colour vision alleles.

Question 5

The picture shows a human karyotype which shows a specific mutation.



(a) (i) Describe the mutation shown in the karyotype. 2

One mark would be for recognising that this is 'chromosome mutation'. The other mark would be for referring to the fact that 'there are three of one chromosome /chromosome number 21, instead of the usual two'.

Candidates who do not look carefully enough often make the error of stating that 'the last but one chromosome is bigger than its partner'. This is normal – the large chromosome is the X and its small partner is the Y – so this is a male karyotype.

(ii) **Name the condition caused by this mutation. 1**

One mark for 'Down's syndrome' or 'Trisomy 21'. Do not be tempted to describe the symptoms – unless they are asked for.

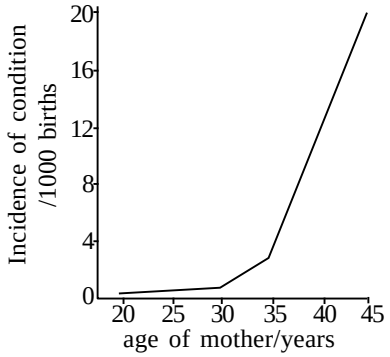
(iii) **Describe how this mutation happens. 4**

Possible marks would be:

- *reference to non-disjunction;*
- *description , for example, in anaphase I of meiosis both of chromosome 21 go to one pole instead of one chromosome 21 to each pole;*
- *this happens more in females giving eggs with two of chromosome 21;*
- *when such an egg fuses with a sperm, with one chromosome 21, the zygote has three of this chromosome;*

Be logical with your description – remember that both meiosis and fertilisation are involved. Weaker candidates tend to omit the meiotic phase when the unequal segregation occurs (anaphase I) or forget to refer to fertilisation.

(b) (i) The graph below shows the incidence of this condition in relation to the age of the mother. Describe the changes shown by the graph from the age of 20 to the age of 45 years. 3



Possible marks would be:

- *from 20 to 30 years the incidence increases slightly but stays below 1 per 1000;*
- *from 30 to 35 years the incidence increases more quickly up to about 3 per 1000;*
- *from 35 to 45 years the incidence increases greatly up to about 20 per 1000;*

Be logical and precise - for each mark both age range and incidence change must be stated. Vague answers with no stated figures will not score. A very common error, in this type of question, is to explain the data. This, unless asked for in the question, wastes time and is poor examination technique.

(ii) Suggest why the incidence of non-disjunction increases with increasedmaternal age. 3

Possible marks would be:

- *in oogenesis meiosis commences in the fetal ovary and remains in the prophase I stage until puberty;*
- *this gives a period of about 13 years during which time some of the bivalent units, (paired homologous chromosomes), could become separated;*
- *this period of possible separation of homologous pairs is extended as the mother grows older so the chances of non-disjunction increase with age;*

(iii) Suggest why non-disjunction rarely affects sperm. 1

The mark would be for 'meiosis does not stop and start/ occurs continuously in spermatogenesis, so there is little time for the bivalent units to break apart;

Questions (ii) and (iii) use the verb 'suggest' and so examiners will give some leeway and accept other valid suggestions. However, to answer the questions well, you need to know the topics of gametogenesis, meiosis and chromosome mutation and to apply your knowledge to explain the data.

Acknowledgements: *This Factsheet was researched and written by Martin Griffin.*