H

Anglo-Chinese Junior College

JC2 Biology Preliminary Examination
Higher 2

Anglo-Chinese Junior College
A Methodist Institution
(Founded 1886)

CANDIDATE NAME		FORM CLASS	
TUTORIAL CLASS		INDEX NUMBER	

BIOLOGY **9744/03**

Paper 3 Long Structured and Free-response Questions 28 August 2024
2 hours

Additional Materials: Free-response Question Answer Booklet

READ THESE INSTRUCTIONS FIRST

Write your Name, Class and Index number in the spaces at the top of this page.
Write in dark blue or black pen.
You may use an HB pencil for any diagrams or graphs.
Do not use staples, paper clips, glue or correction fluid.

Section A
Answer **all** questions in the spaces provided on the Question Paper.

Section B
Answer any **one** question in the spaces provided on the separate Free-response Question Answer Booklet.

The use of an approved scientific calculator is expected, where appropriate.
You may lose marks if you do not show your working or if you do not use appropriate units.

The number of marks is given in brackets [ ] at the end of each question or part question.

For Examiners' use only	
1	/ 30
2	/ 10
3	/ 10
4 / 5	/ 25
Total	/ 75

Section A

Answer **all** the questions in this section.

1 Lactose is the main carbohydrate found in mammalian milk and is important for meeting the nutritional needs of an infant. Lactose is a disaccharide of glucose and galactose, and has been considered healthier than other disaccharides such as sucrose and maltose.

Table 1.1 shows the glycaemic index of lactose, sucrose, maltose and glucose. The glycaemic index measures the rise in blood glucose levels two hours after ingestion of the measured substance.

Table 1.1

carbohydrate	glycaemic index
lactose	46
sucrose	65
maltose	105
glucose	100

(a) Suggest explanations for the following two observations:

(i) the glycaemic index of lactose is lower than glucose

Time is needed for the hydrolysis of lactose after it is ingested;

……..... [1]

(ii) the glycaemic index of lactose is lower than sucrose.

1. **There are fewer types of enzymes / lower concentration of enzymes in the gastrointestinal tract able to hydrolyse lactose compared to sucrose;**
2. **More time / metabolic steps are needed to convert galactose to glucose compared to fructose to glucose;**
   OR
   More time / metabolic steps are needed to hydrolyse lactose compared to sucrose;

……..... [2]

Lactose intolerance is a condition which occurs due to the lack of the enzyme lactase in the small intestines. In humans, lactase is encoded by the *LCT* gene on chromosome 2.

In most of the human population, lactose intolerance occurs as the expression of the *LCT* gene declines past the infant stage due to a reduced reliance on milk. Adults with lactose intolerance will present with gastrointestinal symptoms when milk is consumed, and the condition worsens with age.

It is hypothesised that methylation of the promoter of the *LCT* gene is involved in the age-related decrease in gene expression.

(b) Explain how methylation of the promoter may lead to a decrease in *LCT* gene expression.

1. **Methyl groups may be added to cytosine / CpG sites in the promoter;**
2. **Catalysed by the enzyme DNA methyltransferase;**
3. **Methylation changes the 3D conformation of DNA at the promoter;**
4. **Methylated DNA also attracts other proteins (methyl-CpG-binding proteins) which recruit histone deacetylase enzymes that remove acetyl groups from histones, increasing the affinity of positively-charged histone tails for the negatively-charged DNA and making the chromatin more compact;**
5. **Transcription is inhibited by preventing the binding of the transcription factors and RNA polymerase to form the transcription initiation complex;**

Max 3m

…….. [3]

The extent of methylation of the *LCT* gene was analysed in 48 individuals between the ages of 8 to 23 and of a largely European descent. Fig. 1.1 records the percentage methylation of the *LCT* gene and the lactase activity measured in each individual.

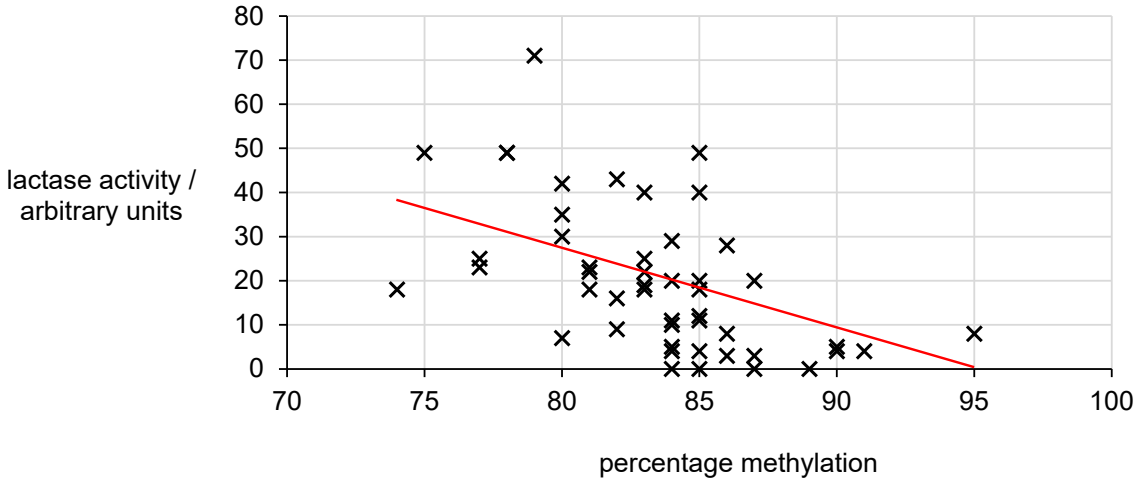

Fig. 1.1

(c) (i) Draw a line of best fit on Fig. 1.1. [1]

Straight or curved line +
extending from 74% to 95% on x-axis, without extrapolation beyond this range +
good distribution of number of data points above and below the best fit line
(A! between 20 to 40 au at starting point, and between 0 to 8 au at ending point);

(ii) Discuss whether the results in Fig. 1.1 support the hypothesis that methylation is involved in the age-related decline in *LCT* gene expression.

Yes

1. **As percentage methylation of the LCT gene increases, there is a general decreasing trend in the lactase activity;**
2. **Quote data based on best fit line drawn e.g. when percentage methylation increases from 74 to 95, lactase activity decreases from 39au to 0au;**

No

3. **Data does not show whether increased percentage methylation is correlated with age;**
4. **Youngest individual is 8 years old, which is long past the infant stage (as the expression of the gene declines past the infant stage);**
5. **Data taken from individuals of largely European descent, hence may not be representative of other human populations/is biased;**
6. **Individual with low percentage methylation may still have low lactase activity;**
7. **Quote data point to support MP6: one individual with low percentage methylation of 74% has a relatively low lactase activity of 18au (A! 17 to 19au);**

At least 1 MP for both 'supporting' and 'not supporting' for full marks, max 4m

..... [4]

In some individuals, *LCT* gene expression continues throughout adulthood, allowing the digestion of lactose in milk. These adult individuals are said to be lactase persistent and can tolerate the consumption of milk.

Genomic studies have identified the *MCM6* gene to be involved in the regulation of the expression of the *LCT* gene. Scientists made these observations of the two genes, represented in Fig. 1.2:

- *MCM6* gene is located upstream of the *LCT* gene on the same chromosome
- *MCM6* gene contains 15 introns
- mutations in specific DNA sequences within two of the introns have been found in individuals who are lactase persistent
- regulatory proteins can bind to these specific DNA sequences that have undergone mutations
- these regulatory proteins control the transcription of the *LCT* gene.

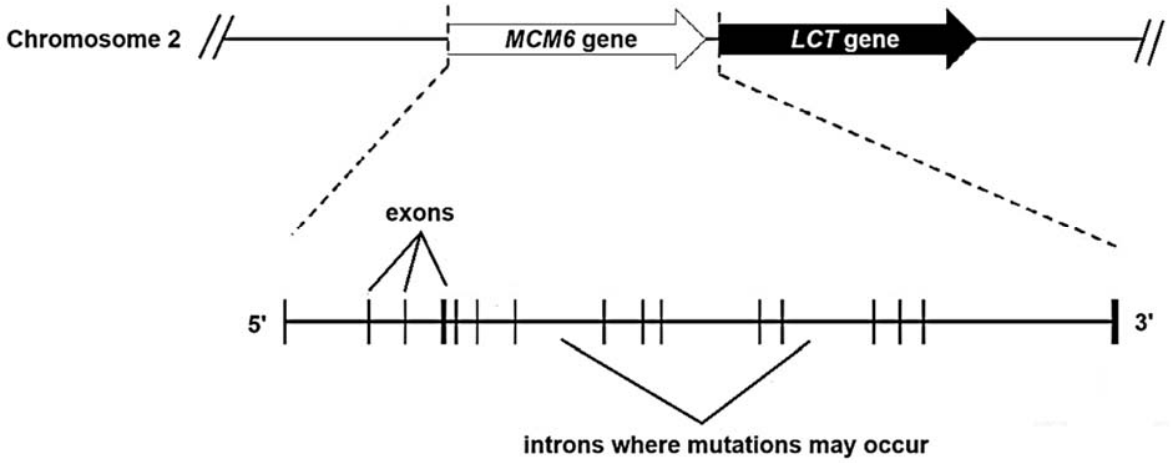

Fig. 1.2

(d) (i) Suggest how mutations to specific DNA sequences in the introns of the *MCM6* gene may result in the lactase persistent condition.

1. ***Mutation results in specific DNA sequences in introns acting as enhancers which allow activator proteins to bind;**

2. **A DNA-bending protein causes DNA bending, which brings the bound activators closer to the promoter;**
3. **Mediator proteins, RNA polymerase, and other transcription factors are also recruited to the promoter;**

OR

4. **The activator recruits a histone acetyltransferase, which adds acetyl groups to histone tails;**
5. **This loosens the packing of the nucleosomes/chromatin/DNA;**

OR

6. **The activator recruits a chromatin remodelling complex;**
7. **which alters the structure of nucleosomes/chromatin around the promoter, rendering it accessible to transcription factors and RNA polymerase;**

8. **increasing the rate of formation of the transcription initiation complex at the *LCT* gene and hence increasing the rate of transcription;**

*** MP1 compulsory**
MP2+3, MP4+5, MP6+7 are alternatives

..... [4]

[Turn over

(ii) Describe one other mechanism by which introns may play a role in the regulation of gene expression.

1. **Alternative splicing;**
2. **where different combinations of exons may be joined by spliceosomes;**
3. **Allowing production of different mRNAs from the same primary RNA transcript / more than one type of polypeptide to be coded for by a single gene;**

Max 2m

……..... [2]

Lactose in milk cannot be directly absorbed at the small intestines. It needs to be hydrolysed by intestinal enzymes before the resulting monosaccharides can be taken up.

When a person with lactose intolerance consumes milk, the unhydrolysed lactose passes into the large intestines, where it is metabolised by bacteria in the large intestines using a mechanism similar to that in yeast under low oxygen conditions. Gas produced through bacteria metabolism of lactose results in bloating and abdominal discomfort. Other metabolic products and any unabsorbed sugars in the lumen of the large intestines also stimulate a watery diarrhoea.

A summary of these effects is shown in Fig. 1.3.

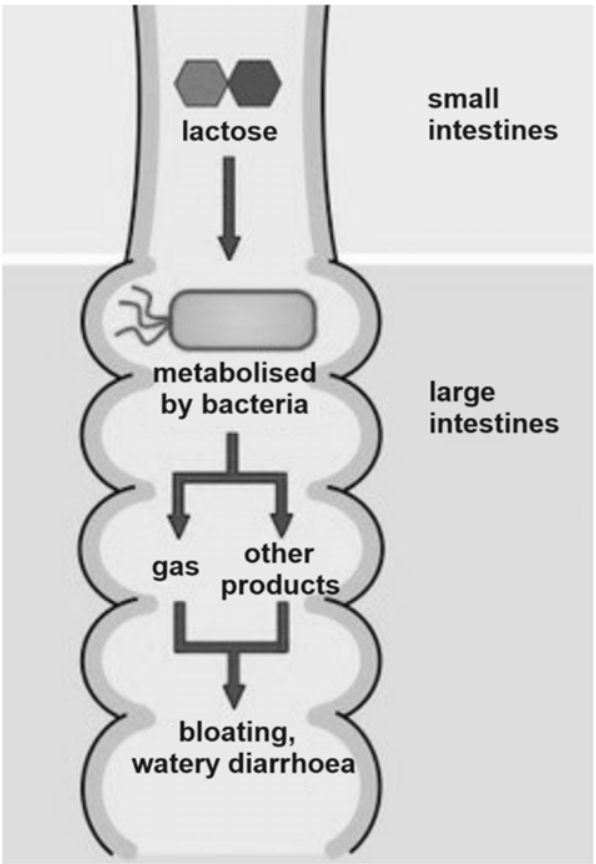

Fig. 1.3

(e) (i) Suggest how unhydrolysed lactose may be metabolised by bacteria in the large intestines to produce gas.

1. **These bacteria may contain the *lac* operon;**
2. **which codes for β-galactosidase that can hydrolyse lactose into glucose and galactose;**
3. **Alcohol / ethanol fermentation of glucose occurs under anaerobic conditions in the large intestines;**
4. **Where pyruvate (formed from glycolysis) undergoes a decarboxylation reaction to form acetaldehyde / ethanal and carbon dioxide, and acetaldehyde / ethanal is then reduced to form ethanol;**

Max 3m

……..... [3]

(ii) Explain how the presence of metabolic products and unabsorbed sugars in the lumen of the large intestines may lead to water diarrhoea.

1. **These substances lower the water potential within the lumen of the large intestines;**
2. **Net movement of water occurs by osmosis;**
3. **Along a water potential gradient from the intestinal cells to the lumen of the large intestines;**

……..... [3]

Glucose taken up by cells will undergo glycolysis in the first phase of respiration. Glycolysis is a multi-step process which converts glucose into pyruvate.

Aldolase is one of the enzymes involved in glycolysis which catalyses the splitting of respiratory substrates into three-carbon molecules. It is encoded by the *ALDOA* gene on chromosome 16. A loss-of-function mutation in both copies of this gene results in a condition characterised by haemolytic anaemia, or the lysis of red blood cells.

Pyruvate kinase is another enzyme in glycolysis which catalyses the transfer of phosphate from a triose phosphate to ADP, forming pyruvate and ATP. The *PKM* gene on chromosome 1 codes for this enzyme, and a loss-of-function mutation in both copies of this gene similarly results in haemolytic anaemia.

(f) **(i)** Suggest why the lack of membrane-bound organelles in mature red blood cells make them more susceptible to the effects of either mutation.

1. *** Mature red blood cells do not have mitochondria;**
2. **Pyruvate cannot be oxidised further to produce the bulk of ATP yield in aerobic respiration; OR cannot carry out oxidative phosphorylation/chemiosmosis to synthesis large amounts of ATP;**
3. **Red blood cells depend on glycolysis for all the energy needs of cellular processes;**

*** MP1 compulsory**

……..... [2]

For Examiner Use

(ii) A man who is a carrier for the mutant alleles of both the *ALDOA* and *PKM* genes is married to a woman who is also a carrier for the mutant alleles of both genes. Both individuals do not suffer from haemolytic anaemia.

Using a genetic diagram, show the probability that their offspring will suffer from haemolytic anaemia.

Let A be the dominant allele for functional aldolase, a be the recessive allele for non-functional aldolase.
Let B be the dominant allele for functional pyruvate kinase, b be the recessive allele for non-functional pyruvate kinase. **1m**

Parental phenotype **normal** **x** **normal**
Parental genotype **AaBb** **x** **AaBb**

1m for both geno+pheno

Gametes **AB** **Ab** **aB** **ab** **AB** **Ab** **aB** **ab** **1m**

F_1 genotype **1m**

Gametes	AB	Ab	aB	ab
AB	AABB normal	AABb normal	AaBB normal	AaBb normal
Ab	AABb normal	AAbb haemolytic anaemia	AaBb normal	Aabb haemolytic anaemia
aB	AaBB normal	AaBb normal	aaBB haemolytic anaemia	aaBb haemolytic anaemia
ab	AaBb normal	Aabb haemolytic anaemia	aaBb haemolytic anaemia	aabb (severe) haemolytic anaemia

F_1 phenotypic ratio **9 healthy : 7 haemolytic anaemia (OR 9 : 6 : 1)** **1m**

Probability of offspring with anaemia = 0.44 / 44% / 7 in 16 **1m**

Max 5m

[5]
[Total: 30]

[Turn over

2 *Mycobacterium tuberculosis* is the organism which causes tuberculosis, a lung infection that is difficult to treat.

Fig. 2.1 shows the structure of a tubercle, a mass of cells found in an infected lung, from which the name of the disease is derived. Each tubercle is surrounded by fibroblasts, which are cells responsible for forming connective tissue that makes up the boundary of the tubercle.

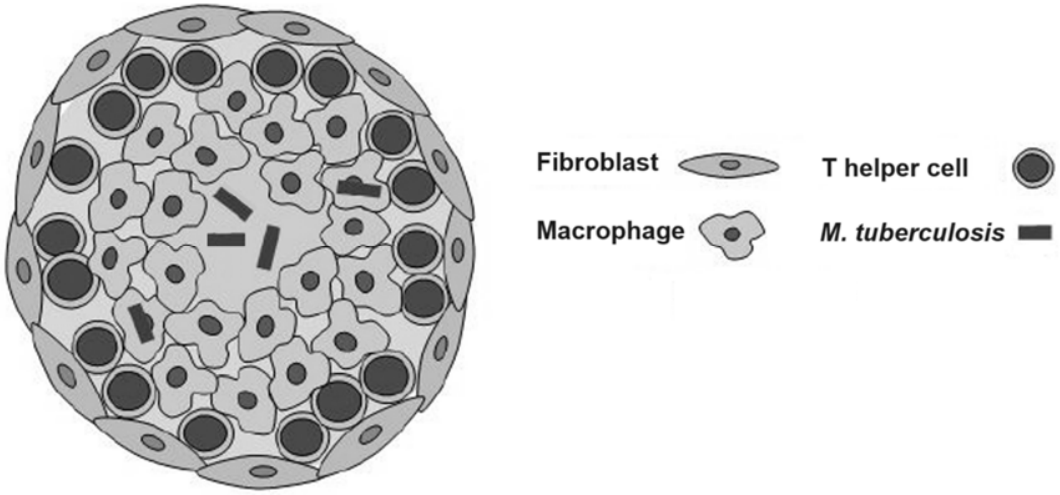

Fig. 2.1

(a) With reference to Fig 2.1, explain how a tubercle is formed during the infection.

1. ***M. tuberculosis*** **cells are engulfed by macrophages through phagocytosis;**
2. ***M. tuberculosis*** **can secrete a protein that inhibits the fusion of phagosomes with lysosomes;**
3. ***M.tuberculosis*** **is also surrounded by a lipid shell comprised of mycolic acid which protects against lysozymes / reactive oxygen radicals in the phagosomes / lysosomes;**
4. **Antigen presentation by macrophages recruit helper T cells;**
5. **At the centre of the tubercle, infected macrophages die due to necrosis, forming a caseous centre;**
6. **Fibroblasts form connective tissue around the tubercle that makes up a fibrous capsule;**

Max 4m

…….. [4]

Vaccines can be used to protect a population against a disease, such as tuberculosis, that has the potential of spreading widely.

The effectiveness of a vaccine containing live attenuated bacteria was compared with another vaccine containing inactivated bacteria. Individuals injected with each type of vaccine are monitored for one year after vaccination. The number of individuals who contracted the disease within one year is shown in Table 2.1.

Table 2.1

type of vaccine	live attenuated vaccine	inactivated vaccine
number of individuals monitored	3916	3936
number of individuals contracting the disease within one year	53	93
percentage of individuals contracting the disease within one year	**1.4 (or 1.35)**	**2.4 (or 2.36)**

(b) (i) Complete Table 2.1 by calculating the percentage of individuals contracting the disease within one year of receiving each type of vaccine. [1]

(ii) Using the results in Table 2.1, calculate how much more likely individuals who received the inactivated vaccine will contract the disease within one year compared to individuals who received the live attenuated vaccine.

Provide your answer as a percentage. Show your workings.

Increased likelihood of contracting disease = (2.4 – 1.4) / 1.4 x 100 = 71%

(OR Increased likelihood of contracting disease = (2.36 – 1.35) / 1.35 x 100 = 74.8%

Individuals who received the inactivated vaccine are …… more likely to contract the disease compared to individuals who received the live attenuated vaccine. [1]

(iii) Suggest why the live attenuated vaccine has a higher effectiveness compared to the inactivated vaccine in protecting against disease.

1. **Live pathogen is able to replicate in the host;**
2. **hence presents a large range/diversity OR large quantity of antigens;**
3. **which stimulates a stronger immune response due to the activation of more B and T cells OR due to more memory cells B and T produced;**

Max 2m

……..... [2]

[Turn over

(iv) Describe the advantages of inactivated vaccines over live attenuated vaccines.

1. **No risk (R! low risk) of reverting to a virulent form due to mutations, which can then cause infections in those vaccinated (whether immunocompromised or not);**
2. **Suitable for individuals who are immunocompromised because they may not even be able to mount an immune response to an attenuated pathogen;**
3. **More stable hence easier to store/handle/distribute;**

Max 2m

……..... [2]

[Total: 10]

3 Viral dengue disease, also known as dengue fever, is caused by an infection by the dengue virus.

(a) Table 3.1 compares some features of the dengue virus with that of the influenza virus, another enveloped virus which infects humans.

Complete Table 3.1 with the features of the influenza virus.

Table 3.1

feature compared	dengue virus	influenza virus
type of genetic material	single-stranded RNA	**single-stranded RNA**
sense of genome	positive-sense	**negative-sense**
envelope proteins	E and M proteins	**neuraminidase, haemagglutinin, M2 channel (any 2)**
mechanism of viral entry into host cells	receptor-mediated endocytosis	**receptor-mediated endocytosis**
mechanism of viral release from host cells	exocytosis	**budding**

Genetic material + genome 1m
Envelope proteins 1m
Mechanism of entry + exit 1m
[3]

In most individuals, symptoms of dengue fever are mild and recovery takes two to seven days. In a small proportion of cases, the disease develops into a more severe form known as dengue haemorrhagic fever. Dengue haemorrhagic fever can be fatal.

Two indicators are measured from the blood tests of patients with milder dengue fever (DF) and dengue haemorrhagic fever (DHF):

- Haematocrit is a percentage of the volume occupied by red blood cells in whole blood. A change in the volume of blood plasma (the cell-free component of blood), but without a change in the volume of red blood cells, will change the haematocrit.
- Platelet count measures the concentration of platelets in whole blood.

The two blood indicators, represented as the mean ± standard deviation, are shown in Table 3.2.

Table 3.2

indicator	patients with DF (number of patients = 11)	patients with DHF (number of patients = 8)
haematocrit / %	37.0 ± 0.1	39.7 ± 2.0
platelet count / x 10^4 mm^{-3}	10.9 ± 0.7	2.6 ± 0.3

[Turn over

(b) (i) A *t*-test can be used to determine whether there is any significant difference in each of the two blood indicators between patients with DF and patients with DHF.

Calculate the value of *t* for each blood indicator and the number of degrees of freedom, using these formulae:

$$t = \frac{|\bar{x}_1 - \bar{x}_2|}{\sqrt{\left(\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}\right)}} \qquad \nu = n_1 + n_2 - 2$$

key to symbols
s = standard deviation
$\bar{x}$ = mean
n = sample size (number of observations)
ν = degrees of freedom

Show your working.

***t* for <u>haematocrit</u> = $\frac{|37.0-39.7|}{\sqrt{\left(\frac{0.1^2}{11}+\frac{2.0^2}{8}\right)}}$ = 3.81 (2 dp);**

***t* for <u>platelet count</u> = $\frac{|10.9-2.6|}{\sqrt{\left(\frac{0.7^2}{11}+\frac{0.3^2}{8}\right)}}$ = 35.14 (2 dp);**

degrees of freedom = 11 + 8 – 2 = 17;

[3]

(ii) Table 3.3 shows the critical values for *t* at several different probabilities and degrees of freedom.

Table 3.3

degrees of freedom	probability, *p*			
	0.5	0.1	0.05	0.01
1	1.00	6.31	12.71	63.66
2	0.82	2.92	4.30	9.92
3	0.76	2.35	3.18	5.84
4	0.74	2.13	2.78	4.60
5	0.73	2.02	2.57	4.03
6	0.72	1.94	2.45	3.71
7	0.71	1.89	2.36	3.50
8	0.71	1.86	2.31	3.36
9	0.70	1.83	2.26	3.25
10	0.70	1.81	2.23	3.17
11	0.70	1.80	2.20	3.11
12	0.70	1.78	2.18	3.05
13	0.69	1.77	2.16	3.01
14	0.69	1.76	2.14	2.98
15	0.69	1.75	2.13	2.95
16	0.69	1.75	2.12	2.92
17	0.69	1.74	2.11	2.90
18	0.69	1.73	2.10	2.88
19	0.69	1.73	2.09	2.86
20	0.69	1.72	2.09	2.85

Use Table 3.3 and your answers to **(b)(i)** to decide whether there is any significant difference in each of the two blood indicators between patients with DF and patients with DHF.

1. **Both the differences in haematocrit and platelet count are significant between DF and DHF patients;**
2. **The calculated *t* value for haematocrit is 3.81 and for platelet count is 35.14, both of which are larger than the critical *t* value of 2.11;**

…… [2]

[Turn over

(iii) Explain what the results indicate about the symptoms of dengue haemorrhagic fever (DHF).

1. **Increased permeability of capillaries / increased plasma leakage / hypovolaemia / decrease in blood or blood plasma volume;**
2. **Inability to form blood clots / bleeding problems / gum bleeding / nose bleeding / bleeding into the skin and internal organs;**

……..... [2]

[Total: 10]

Section B

Answer **one** question in this section.

Write your answers in the spaces provided on the separate Free-response Question Answer Booklet.

Your answers should be illustrated by large, clearly labelled diagrams, where appropriate.

Your answers must be in continuous prose, where appropriate.

Your answers must be set out in parts **(a)** and **(b)**, as indicated in the question.

4 **(a)** Describe the mode of action of insulin in the regulation of blood glucose concentration. [15]

(b) "The future of medical therapy in the treatment of diseases solely depends on finding enzyme inhibitors that targets pathways involved in cell signalling."

Discuss the validity of this statement. [10]

[Total: 25]

5 **(a)** With named examples, outline how environmental factors can cause cancer and explain why it is often challenging to cure cancer. [15]

(b) Discuss whether cancer could act as a selection pressure in the evolution of humans by natural selection. [10]

[Total: 25]

[Turn over

For Examiner Use

4 (a) Describe the mode of action of insulin in the regulation of blood glucose concentration. [15]

1. **Insulin acts on target cells such as muscle cells/ liver cells / adipose or fat cells;**

Reception and Transduction

2. **An increase in blood glucose concentration above set-point / 800 mgdm^{-3} stimulates insulin secretion;**
3. **By β cells of islets of Langerhans;**
4. **Insulin binds to the receptor tyrosine kinase (RTK) / tyrosine kinase receptor on surface of target cells;**
5. **The binding of insulin causes two receptor monomers to aggregate and form a dimer;**
6. **Which activates the tyrosine kinase region of each polypeptide;**
7. **which uses ATP to cross-phosphorylate / autophosphorylate the tyrosine residues on each other's cytoplasmic tails;**
8. **Different relay proteins now bind to specific phosphorylated tyrosine residues on the RTK;**
9. **and become phosphorylated due to the tyrosine kinase activity of the receptor and becomes activated;**
10. **Activated relay proteins causes a phosphorylation cascade / the activation of kinases which phosphorylate and activate other kinases;**
11. **Signal amplification may occur as a result of the phosphorylation cascade / other mechanisms;**

Cellular response and Regulation

12. **Increases the permeability of target cells/ muscle cells/ adipose cells to glucose; R! liver cells**
13. **by increasing the number of glucose transporter / GLUT4 carrier proteins on target cells/ muscle cells/ adipose cells; R! liver cells**
14. **Increases rate of glucose uptake by target cells/ muscle cells/ adipose cells through facilitated diffusion; R! liver cells**
15. **Increased use of glucose as a respiratory substrate, therefore increasing the rate of respiration;**
16. **Leading to increased formation of ATP,**
17. **Increased glycogenesis/ conversion of glucose to glycogen in the liver / muscle for storage; R! if wrong cell**
18. **Increased lipogenesis/ conversion of glucose to fat in adipose tissue / liver for storage; R! if wrong cell**
19. **Increased uptake of amino acid in liver / muscle / adipose tissue; R! if wrong cell**
20. **Increased rate of protein synthesis in liver / muscle / adipose tissue; R! if wrong cell**
21. **Increased formation of DNA/ RNA/ nucleic acid in liver / muscle / adipose tissue; R! if wrong cell**
22. **inhibits glycogenolysis in liver / muscle and gluconeogenesis in liver; R! if wrong cell**
23. **When blood glucose concentration decreases to set point / 800 mgdm^{-3}, secretion of insulin stops;**
24. **Regulatory mechanism for insulin secretion follows a negative feedback loop;**

25. **QWC: At least 2 correct points from each section;**

(b) "The future of medical therapy in the treatment of diseases solely depends on finding enzyme inhibitors that targets pathways involved in cell signalling."

Discuss the validity of this statement. [10]

Valid

1. **Dysfunction in cell signalling pathways can result in a diverse range of diseases + e.g. diabetes, cancer (at least 1);**
2. **Targeting of cell signalling pathways can alter cellular responses + e.g. by activating/inactivating of proteins OR by changing of gene expression;**
3. **Targeting of cell signalling pathways can affect multiple target cells / multiple metabolic pathways simultaneously;**
4. **Targeting of cell signalling pathways may have an amplifying effect, due to these pathways usually resulting in signal amplification;**
5. **Inhibitors that bind to tyrosine kinase domain of receptor tyrosine kinase to prevent cross-phosphorylation and activation of receptor;**
6. **Inhibitors that inhibits GTPase of G protein, to prevent the hydrolysis of GTP to GDP;**
7. **Hence G protein remain activated;**
8. **Inhibitors that inhibits enzymes that synthesises second messenger;**
9. **E.g. adenyl cyclase / adenylyl cyclase;**
10. **Inhibitors that inhibits phosphodiesterase to prevents conversion of cAMP to an inactive product, AMP;**
11. **Inhibitors that inhibits kinases to prevent phosphorylation cascade from occurring / relay proteins from being activated;**
12. **E.g. protein kinase A;**
13. **Inhibitors that inhibit phosphatases to prevent dephosphorylation from occurring;**
14. **Inhibitors that inhibits effector enzymes to prevents them from catalysing a reaction;**
15. **E.g. glycogen phosphorylase;**

Max 6m

Not valid

16. **There are other therapies which do not target cell signalling pathways;**
17. **Antibodies may be injected to provide passive immunity against infectious diseases;**
18. **Antibiotics may be used to treat bacterial infections;**
19. **Phage therapy may be used to treat bacterial infections;**
20. **Genetic engineering / gene editing may be used to treat genetic diseases;**
21. **Bone marrow transplant may be used to treat genetic diseases;**
22. **Stem cells transplant may be used for repair of damaged tissue; R! cell repair**
23. **Blood transfusions may be used to treat anaemia;**
24. **Hormonal therapy may be used to treat metabolic disorders (e.g. diabetes);**

R! vaccines as it is a preventive therapy

25. **Some drugs may target cell signalling pathways but are not enzyme inhibitors;**
26. **E.g. drugs which bind to the receptor to block the original ligand from binding to it / drug may act as enzyme activators instead of inhibitors;**

27. **AVP;**

Max 5m

28. **QWC: At least 1 from correct point from each section;**

[Turn over

For Examiner Use

5 (a) With named examples, outline how environmental factors can cause cancer and explain why it is often challenging to cure cancer. [15]

Environmental factors

Chemical carcinogens:

1. **polycyclic aromatic hydrocarbons (PAHs) / benzo[a]pyrene; R! PAHs, R! nicotine (not a carcinogen)**
2. **can enter the lungs and spread around the rest of the body via the blood stream when smoke is inhaled;**
3. **and bind to DNA to cause damage/ mutation;**
4. **Ethidium bromide;**
5. **intercalates double-stranded DNA;**
6. **thereby deforming the molecule and can affect DNA replication / transcription / gene expression;**

Ionising radiation:

7. **X-rays/ gamma-rays/ radon gas;**
8. **produces free radicals which are chemically very reactive;**
9. **which can interact with DNA to produce double-stranded breaks;**
10. **leading to chromosomal rearrangements and deletions;**

Non-ionising radiation:

11. **Ultraviolet (UV) light; R! UV light**
12. **causing covalent linking of thymine bases that are adjacent OR formation of thymine dimers on a DNA strand;**
13. **which interferes with affect DNA replication / transcription / gene expression;**

Viral and bacterial infection:

14. **Retrovirus may introduce an oncogene to the cell;**
15. **Or viral genome may integrate into host cell DNA at random locations;**
16. **disrupting a cancer-critical gene;**
17. **human papilloma virus;**
18. **produce proteins which inhibit tumour suppressor proteins;**
19. ***Helicobacter pylori* infection;**
20. **which causes ulcers in the stomach, which increases the risk of cancer development;**

Max 8m

How it may cause cancer

21. **Gain in function mutation on proto-oncogene/ loss of function mutation on tumour suppressor gene;**
22. **Leading to uncontrolled cell division;**
23. **Loss of contact inhibition/ density-dependent inhibition OR loss of anchorage dependence;**
24. **Stimulation of angiogenesis whereby there is excessive proliferation of blood vessels around tumour cells;**
25. **Metastasis occurs whereby the cancer cells spread to other locations distant from their original site in the body via lymph vessels or blood vessels, and form secondary tumours;**

Max 4m

Challenges

26. **Many gene mutations / metabolic processes are involved the development of cancer, hence difficult to rectify all;**
27. **Same type of cancer (e.g. gastric cancer) may involve cells with different mutations;**
28. **Cancer cells are able to divide indefinitely, hence difficult to restrict their growth / spread;**
29. **Cancer may be located at sites that are difficult for drugs to gain access;**
30. **Chemotherapy may have different effectiveness in different patients due to genetic variation;**
31. **Cancer cells may be resistant to chemotherapy drugs;**
32. **It is difficult to differentiate between normal and cancer cells, hence difficult to target cancer cells specifically;**
33. **Chemotherapy causes many side effects to the patient;**
34. **Cancer may only show symptoms at late stages, hence difficult to detect;**
35. **Cancer may have metastasised to many locations in the body;**
36. **Cancer cells are difficult to fully eradicate, with the possibility of relapse;**
37. **Cancer may be located in vital tissues / organs, hence cannot be removed without compromising body function;**

Max 5m

38. **QWC: At least 2 points from envt factors, 1 point from cancer devt, 1 point from challenges;**

(b) Discuss whether cancer could act as a selection pressure in the evolution of humans by natural selection. [10]

Yes

1. **Variation in tumour suppressor genes / proto-oncogenes exists in human populations due to mutations;**
2. **These variations are heritable if mutation occurs in the germ cells;**
3. **Some forms of cancer results in early death;**
4. **e.g. brain cancer/ leukaemia;**
5. **Individuals with normal alleles for tumour suppressor genes / proto-oncogenes will be at a selective advantage / selected for;**
6. **And are able to survive till maturity and reproduce / have a higher reproductive success;**
7. **Passing down their normal alleles for tumour suppressor genes / proto-oncogenes to their offspring;**
8. **Over time, this leads to an increase in the allele frequency of normal alleles in the gene pool;**

Max 6m

No

9. **Cancer may only result when mutations occur to both copies of a tumour suppressor gene;**
10. **Cancer is a multi-step process / involves mutations to multiple proto-oncogenes and tumour suppressor genes;**
11. **Cancer may only result when mutations accumulates in a single-cell lineage;**
12. **Chances of developing cancer / acquiring more mutations / dying from cancer increases with age;**
13. **Individuals may be able to reproduce before they develop cancer / die from cancer;**
14. **Some forms of cancer can be fully treated with drugs / chemotherapy / surgical removal of tumour / radiotherapy;**
15. **Or the cancer may be detected early and treated;**
16. **hence cancer survivors may still be able to reproduce;**
17. **Passing down their mutation / mutant alleles of tumour suppressor genes / proto-oncogenes to their offspring;**
18. **Over time, this leads to an increase in the allele frequency of mutation / mutant alleles in the gene pool;**
19. **These variations may also not be heritable if mutation occurs in the somatic cells;**

Max 6m

20. **QWC: 1 correct point from each section;**

[Turn over