RIVER VALLEY HIGH SCHOOL

JC 2 PRELIMINARY EXAMINATION

CANDIDATE NAME										
CENTRE NUMBER	S					CLASS	23J	INDEX NUMBER		

BIOLOGY **9744/03**

Paper 3 Long Structured and Free-response Questions **13 September 2024**

2 hours

Candidates answer on the Question Paper.
No Additional Materials are required.

READ THESE INSTRUCTIONS FIRST

Write your Centre number, index number and name 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.
DO **NOT** WRITE ON ANY BARCODES.

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 Question Paper.

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.

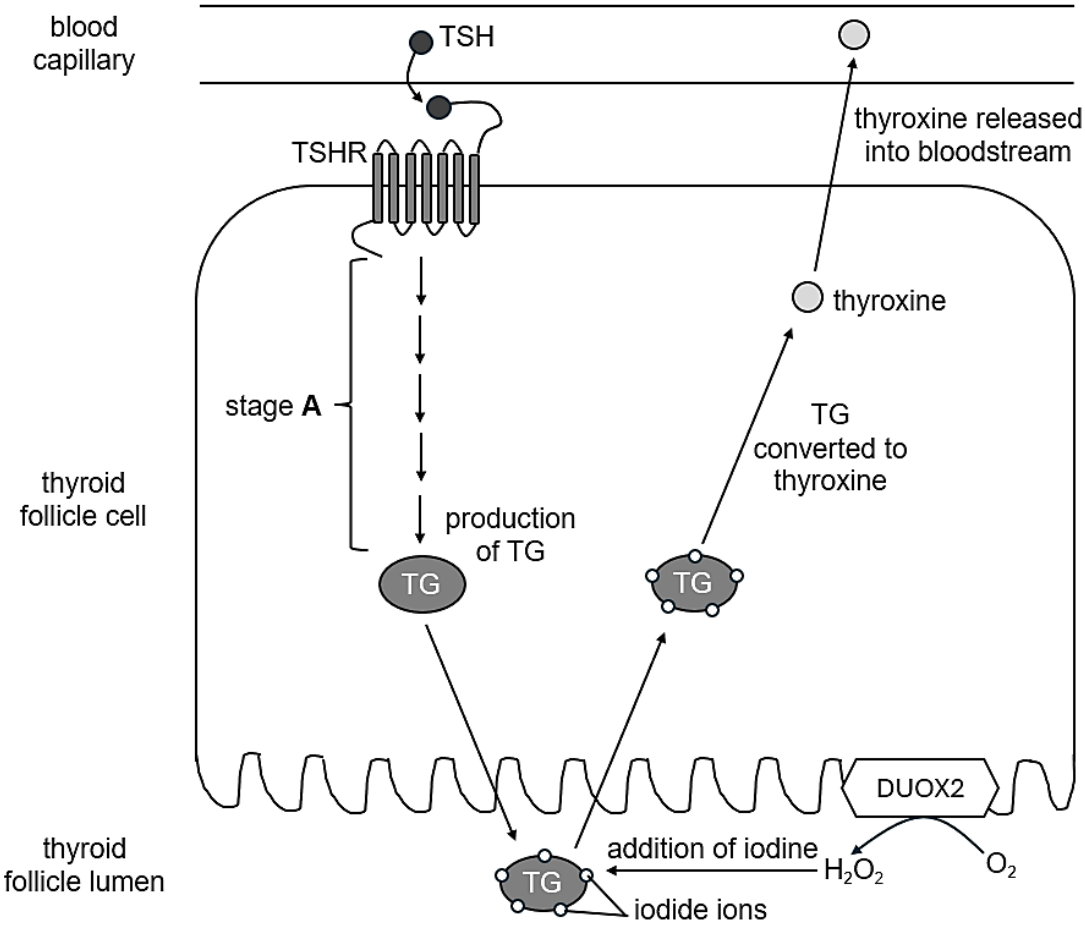
The number of marks is given in brackets [ ] at the end of each question or part question.

For Examiner's Use	
Section A	
1	
2	
3	
Section B	
Total	

Section A

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

1 Thyroid hormones, such as thyroxine, play crucial roles in regulating metabolism and brain development. Fig 1.1 shows how the thyroid-stimulating hormone (TSH) from the pituitary gland stimulates the thyroid follicle cell to produce thyroxine.



key
TSHR – thyroid-stimulating hormone receptor
TG – thyroglobulin
DUOX2 – dual oxidase 2 enzyme

Fig. 1.1

(a) Name the receptor type to which TSHR belongs and describe the role of protein kinases in stage **A.** [3]

1. G-protein coupled receptor;; AO A
2. protein kinases transfer phosphate group (from ATP) to substrate (other protein kinases);
3. inducing conformational change;
4. of substrate into its active form;
5. initiating phosphorylation cascade / within a phosphorylation cascade;

6. allows for signal amplification;
7. max 3

Congenital hypothyroidism (CH) is a common endocrine metabolic disease caused by insufficient thyroxine secretion in a patient at birth.

In a genetic study on CH, blood samples of patients were analysed and two gene mutations associated with the disease were identified. The results for a healthy individual and two patients with CH are shown in Table 1.1. The partial gene sequences shown are found at the start of each gene.

Table 1.1

individual	blood TSH / mU L^{-1}	partial gene sequence	
		TSHR locus (triplets 4 to 6)	*DUOX2* locus (triplets 6 to 10)
healthy	<15.0	3'-TAGTGGCAT-5'	3'-TGCACCGACTCTATA-5'
patient 1	44.3	3'-TAGTCGCAT-5'	3'-TGCACCGACTCTATA-5'
patient 2	>50.0	3'-TAGTGGCAT-5'	3'-TGCACTGACTCTATA-5'

(b) (i) Using Fig. 1.1 and Table 1.1, predict which patient will show lower blood thyroxine levels and explain how the mutation in this patient will affect the function of the corresponding TSHR or DUOX2 protein. [4]

AO B

1. Patient 2;
2. Base pair substitution in *DUOX2* locus;
3. cytosine replaced with thymine; [A: C replaced with T]
4. change in 7th mRNA codon from UGG to UGA;
5. production of a stop codon;
6. premature termination of translation / producing truncated polypeptide chain;
7. non-functional DUOX2 produced;
8. DUOX2 unable to convert oxygen to hydrogen peroxide;

OR

9. Patient 1;
10. Base pair substitution in *TSHR* locus;
11. guanine replaced with cytosine; [A: G replaced with C]
12. change in 5th mRNA codon from ACC to AGC;
13. amino acid has a different R group property;
14. polypeptide chain folds differently;
15. TSHR has a different 3-dimensional conformation / non-functional TSHR produced;

16. TSH unable to bind to ligand-binding site of TSHR;

[A: cytoplasmic domain of TSHR unable to bind to G-protein]

(ii) Predict the TG levels in the thyroid follicle lumen in patient 1 and patient 2 by placing a tick (✓) in the appropriate box. [2]

AO B

	high	normal	low
patient 1			✓
patient 2	✓		

(iii) TG polypeptide is synthesised at the rough endoplasmic reticulum.

Describe **two** other roles of the rough endoplasmic reticulum. [2]

1. Facilitation of folding of polypeptide chain;;
2. Transport proteins via transport vesicle;;

AO A

A family with a history of a different type of hypothyroidism was studied. Table 1.2 shows the genotype at the *DUOX2* locus and the iodine intake in diet for each individual in the family.

The normal allele at the *DUOX2* locus contains one restriction site. A mutation in the allele resulted in the loss of that restriction site.

Table 1.2

individual	genotype at *DUOX2* locus	iodine intake in diet	hypothyroidism
P	+/+	optimal	nil
Q	+/-	optimal	mild
R	+/-	insufficient	severe
S	-/-	optimal	severe

key

\+ = normal *DUOX2* allele

\- = mutant *DUOX2* allele

(c) **(i)** Outline how the genotype of each individual was determined from each of their DNA samples. [4]

1. DNA was amplified with polymerase chain reaction (PCR); AO A
2. using forward and reverse (DNA) primers that flank;
3. the *DUOX2* gene locus / alleles;
4. PCR products digested with restriction enzymes;
5. before being separated by gel electrophoresis;

OR

6. genomic DNA digested with restriction enzymes;
7. before being separated by gel electrophoresis;
8. a Southern blot is then performed;
9. and a radioactive (single-stranded DNA) probe;
10. complementary / specific to the *TSHR / TG / DUOX2* allele is introduced;
11. and a piece of photographic film is placed over the DNA fragments;

max 2½ (for pts 6 to 11)

12. homozygotes with 2 normal alleles will show 2 bands;
13. homozygotes with 2 mutant alleles will show 1 band;
14. heterozygotes will show 3 bands;

(ii) Evaluate whether the data in Table 1.2 indicates a genetic or an environmental influence on hypothyroidism. [4]

Influence of genotype on hypothyroidism AO B

1. number of copies of mutant DUOX2 allele affects the extent of hypothyroidism;;
2. ref. individual P (0 copy, no disease) vs individual Q/R/S;;

OR

3. ref. individual Q (1 copy, optimal iodine intake, mild) vs individual S (2 copies, optimal, severe);;

Influence of environment on hypothyroidism

4. iodine intake in diet affects the extent of hypothyroidism;;
5. ref. individual Q (1 copy, optimal iodine intake, mild) vs individual R (1 copy, insufficient iodine intake, severe);;

(d) Stem cell transplants can be used to treat hypothyroidism. In this treatment, adult stem cells taken from the skin of patients with hypothyroidism are artificially transformed into pluripotent stem cells (iPSCs).

Using your knowledge of stem cells, suggest **one advantage** and **one limitation** of using iPSCs to treat hypothyroidism. [2]

advantage
1. Less risk of immune rejection;;
2. No need to destroy human embryos to obtain ESC;;

max 1

limitation
3. Adult cells e.g. skin cells may have accumulated mutations resulting in increased risk of cancer;;
4. iPSCs may still carry the allele for hypothyroidism;;
5. Difficulty in ensuring iPSCs can differentiate into thyroid cell / genes related to thyroid function will be expressed;;

max 1

AO B

Fig. 1.2 shows the effects of thyroid hormones on glucose metabolism in the body.

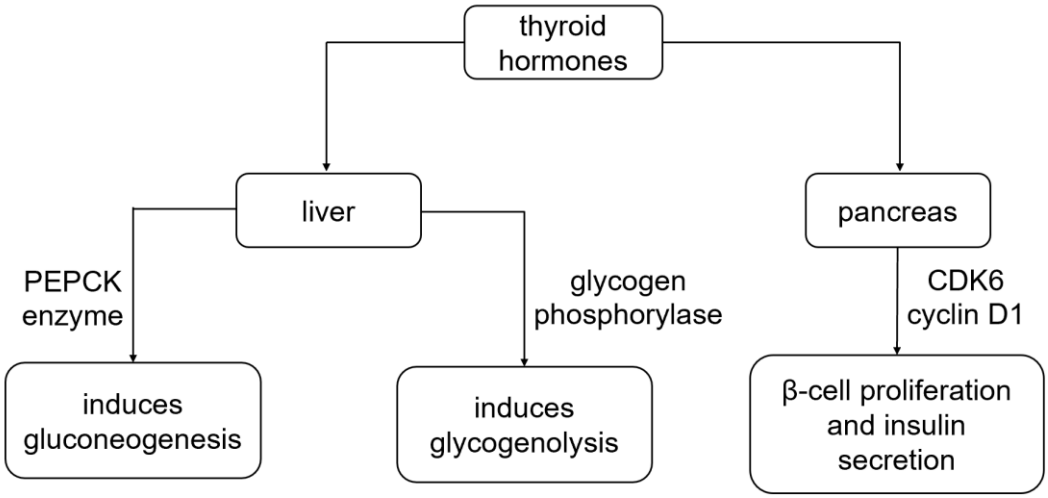


Fig. 1.2

(e) Hyperinsulinemia is a condition associated with abnormally high levels of insulin in the blood.

With reference to Fig. 1.2, explain how high levels of thyroid hormones may result in hyperinsulinemia. [4]

AO B

High levels of hydroid hormones will

1. PEPCK enzyme / glycogen phosphorylase activated;
2. in the liver;
3. result in more gluconeogenesis / production of glucose / glycogenolysis;
4. blood glucose concentration elevated / higher than normal;
5. CDK6 and cyclin D1 activated;
6. in the pancreas;
7. more β-cells undergo proliferation and secrete more insulin;
8. increase blood insulin concentration;

9. more insulin secreted than normal to reduce elevated blood glucose concentration;

max 4

[Total: 25]

AOA – 9

AOB – 16

2 In a person with active tuberculosis (TB), the bacteria, *Mycobacterium tuberculosis*, can be present in airborne droplets that are exhaled. A healthy person who inhales these droplets has effective defence mechanisms in the gas exchange system to prevent infection.

(a) One example of this defence mechanism involves the action of macrophages and lymphocytes.

Describe how these cells are formed from blood stem cells. [3]

1. lymphoid cells further differentiate into lymphocytes;; AO A
2. in lymph nodes / spleen / thymus;
3. myeloid cells differentiate to form macrophages;;
4. in bone marrow;

The Mantoux test is used to detect if a person has previously contracted TB.

A summary of the Mantoux test is given below.

- A small amount of tuberculin, a protein extracted from *M. tuberculosis*, is injected under the skin.
- The site of the injection is examined 48 hours later.
- An immune response causes a red lump to develop:
  - If the red lump is more than 6 mm in diameter, the test is positive.
  - If the red lump is less than 6 mm in diameter, the test is negative.

(b) **(i)** Explain why a positive test result develops in a person who has previously contracted TB. [2]

if person has previously contracted TB, AO B

1. rapid response due to the presence of memory B cells / antibodies;
2. memory cells / antibodies bind to tuberculin at the site of injection;
3. (faster) recruitment of phagocytes to remove the tuberculin/antigen;
4. more intense / stronger inflammatory response;
5. increased blood flow to the site, causing more swelling/ larger lump;

Max 2

(ii) Suggest how the following test results may occur: [1]

false positive test result may occur due to:

1. If a person who had a TB vaccination/ exposure to other *Mycobacteria* species;; AO B

false negative test result may occur due to: [1]

1. If a person who has weakened immune response/ HIV/ immunosuppressive medication/ old TB infection/ malnutrition;; AO B

The researchers investigated the effect of two different drugs, **J** and **K**, on *M. tuberculosis*.

Table 2.1 summarises the mode of action of each drug.

Table 2.1

drug	required treatment duration	target cell	nature of drug
J	6 months	bacteria	single-stranded RNA binds to promoter of genes
K	2 months	bacteria and eukaryotes	an analog of aminoacyl-tRNA, which has a modified amino acid without the carboxyl group

(c) With reference to Table 2.1, explain how drug **K** inhibits the growth of *M. tuberculosis*. [2]

1. Drug K enter the A site of ribosome; AO B
2. is incorporated into the polypeptide chain;
3. unable to form peptide bond with the incoming amino acid (in A site due to the lack of carboxyl group) /;
4. resulting in premature termination of translation;
5. no protein for growth;

Max 2

Fig. 2.1 shows the effect of the two drugs, both individually and in combination, on the relative population size of *M. tuberculosis*, expressed as a percentage of the initial population.

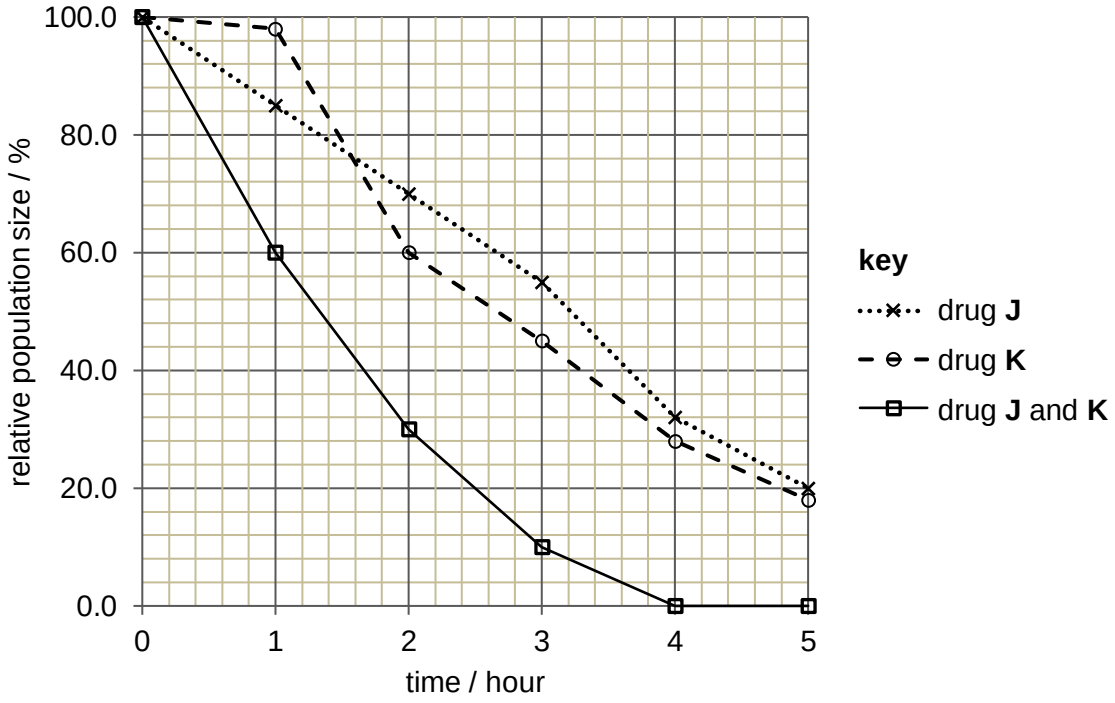


Fig. 2.1

(d) *M. tuberculosis* can be killed by either drug **J** or drug **K**. However, a combination treatment is preferred to reduce the risk of drug resistance.

Using Table 2.1 and Figure 2.1, suggest and explain **two** reasons why using a combination of drugs **J** and **K** over single-drug treatment is more likely to reduce drug resistance. Ensure that one advantage is supported by data from Table 2.1 and the other from Figure 2.1. [3]

reason 1

reason 2

Table 2.1 [Max 1.5] AO B

nature of drug

1. [R] drugs have different modes of action to kill bacteria + quote data (drug J blocks transcription, drug K blocks translation);;
2. [E] if resistance / mutation occurs, unlikely to be against all drugs;

or

treatment duration

3. [R] combination treatment allows for shorter duration of treatment than using drug J + quote data (drug J requires 6 month of treatment but drug J requires 2 months of treatment);;
4. [E] it kills bacteria quickly, reduces the time available for mutations that confer resistance;

Fig. 2.1 [Max 1.5]

5. [R] combination treatment results in a faster reduction in bacterial growth compared to using either drug alone + quote data;;

   or

6. [R] combination treatment results in a greater extent of reduction in bacterial growth compared to using either drug alone + quote data;;
7. [E] by killing bacteria quickly, reduces the time available for mutations that confer resistance;

(g) Describe **two** differences between transcription and DNA replication. [2]

AOB

	Factors	Transcription	DNA replication
1	No. of template strand	one	two
2	Monomers	free ribonucleoside triphosphates	free deoxyribonucleoside triphosphates
3	Enzymes involved in polymerisation	RNA polymerase	DNA polymerase
4	Products	single-stranded RNA	double-stranded DNA
5	RNA primer	not required	required
6	Synthesis	continuous synthesis of mRNA	discontinuous for lagging strand synthesis
7	AVP		

1 mark for each comparative statement

Max 2

[Total: 14]

AOA - 3

AOB - 11

3 **(a)** Describe how electron movement in the electron transport chain results in ATP production in the mitochondrion. [3]

1. Electrons from NADH and $FADH_2$; AO A
2. are passed down electron carriers (of lower energy levels through a series of redox reactions) in ETC;
3. free energy is released;
4. is used to generate a proton gradient through pumping protons;
5. from matrix into intermembrane space; R: stroma into thylakoid lumen
6. movement of H^+ through the ATP synthase;
7. is coupled to phosphorylation ADP to ATP;

Max 3

Mitochondria produce ATP or release heat depending on the movement of protons from the intermembrane space to the matrix.

Fig 3.1 shows how heat is released in the mitochondrion through uncoupling proteins.

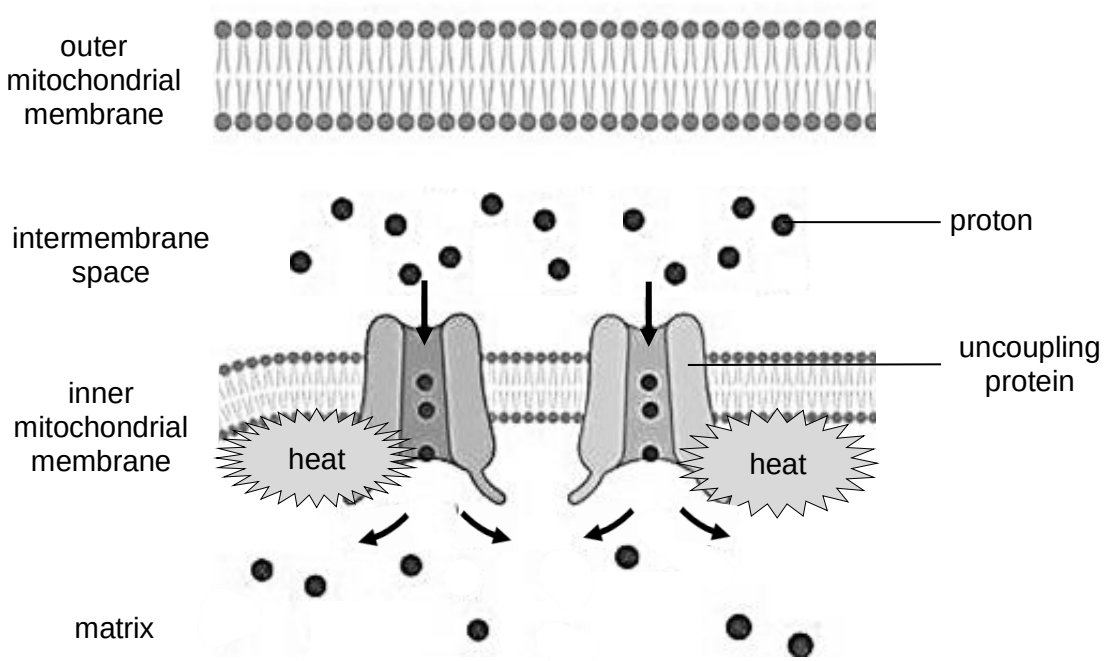


Fig 3.1

Adapted from El-Gammal, et. al, Regulation of mitochondrial temperature in health and disease, European journal of physiology, 474(10), 2022.

(b) Explain how the release of heat affects ATP production. [2]

1. Heat release decreases ATP production; R: not awarded if explanation is because of denaturation of ATP synthase AO B
2. As H^+ moves from intermembrane space to matrix;
3. through the uncoupling proteins;
4. Less protons are available to pass through ATP synthase;

(c) Describe how the inner mitochondrial membrane is adapted to its function. [3]

1. (S) Large surface area of the highly folded mitochondrial inner membrane / numerous infoldings; AOA

   (F) accommodates large numbers of Electron Transport Chain/ ATP Synthase;

2. (S) inner membrane consist of hydrophobic core / is impermeable to charged particles such as H^+;

   (F) thus allow the generation of proton gradient;

3. (S) inner membrane contains ATP synthase;

   (F) which phosphorylates ADP to ATP;

R: generic membrane structure and properties as qtn is specific about inner mitochondrial membrane

Climate change causes ocean warming, leading to heat stress in fish. Recent research indicates that mitochondrial responses under heat stress may determine species survival.

Fig. 3.2 shows the number of protons moving across the inner mitochondrial membrane through either ATP synthases or uncoupling proteins in treated and control *Notolabrus fucicola*, a fish native to the cold waters around New Zealand.

Fig 3.2

Adapted from Fathima I. Iftikar, Julia R. MacDonald, Daniel W. Baker, Gillian M. C. Renshaw, Anthony J. R. Hickey; Could thermal sensitivity of mitochondria determine species distribution in a changing climate?. J Exp Biol 1 July 2014

(d) With reference to the information in this question and Fig 3.2, explain why the *N. fucicola* is predicted to survive the ocean warming. [3]

1. There was significant reduced heat generation; AOB
2. With 170 to 90 H^+ going to uncoupling proteins per unit time upon heat stress;; (±10)
3. There was significant increased ATP production, giving extra energy for the fishes to swim to deeper / cooler waters to escape warming oceans
4. As number of H+ going through ATP synthase increased from 160 to 290 per unit time;; (±10)

[Total: 11]

AOA – 6

AOB – 5

Section B

Answer **one** question in this section.

Write your answers on the lined paper provided at the end of this Question Paper.

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 how the structures of constituent biomolecules in the cell surface membrane contribute to the movement of substances across the membrane.	[15]
		1. Phospholipids;; 2. (S) Hydrophilic phosphate group of phospholipids face outwards to interact with aqueous environment and non-polar / hydrophobic hydrocarbon tails face inwards (F) creating a hydrophobic core;; 3. (F) prevents large, charged and polar substances from passing through;; 4. (F) allows for small, uncharged and non-polar substances to pass through via diffusion through transient gaps;; 5. (S) unsaturated fatty acid tails of phospholipids hinder hydrocarbon chains from packing closely together (F) increases membrane fluidity;; [A: reverse argument] 6. (F) allows for breaking and reforming of the phospholipid bilayer;; 7. (F) during endocytosis / exocytosis / receptor-mediated endocytosis / vesicle formation (any 2) to transport large substances;; **8. Channel and carrier proteins;;** 9. (S) hydrophobic portion / amino acids with non-polar R groups found on the exterior of the protein (F) allow protein to be embedded in the membrane via hydrophobic interactions;; 10. (S) hydrophilic portion / amino acids with polar R groups found on the interior of the protein; (F) provides a hydrophilic channel / pathway to transport polar substances;; 11. (S) contains a specific binding site / binding site with complementary shape to the substance (F) allows specific substance to bind and be transported;; 12. ref. facilitated diffusion and active transport;; **13. Glycoproteins / glycolipids;;** 14. (S) carbohydrate chains (F) serve as specific receptor sites for receptor-mediated endocytosis;; **15. Cholesterol;;** 16. (S) steroid ring and hydrocarbon tail 17. (F) allow molecule to be wedged between phospholipid molecules;; 18. (F) limiting membrane permeability;; 19. (F) at high temperatures, cholesterol immobilises adjacent phospholipid molecules, limiting membrane fluidity;; 20. (F) at low temperatures, cholesterol interferes with the close packing of phospholipids, enhancing membrane fluidity;; QWC – address both parts of the question;;	AO A – 10 AO B – 5

(b) Outline how HIV causes disease in humans and distinguish between the use of vaccines and antibiotics in enhancing immune protection against pathogens. [10]

How HIV causes disease in humans [max 5]

1. Human Immunodeficiency Virus (HIV) causes Acquired Immunodeficiency Disease;;
2. HIV infects T helper cells that contain the CD4 cell surface protein;
3. T helper cells are involved in recognising pathogens; and
4. activating and directing other immune cells;
5. to bring about an immune response to combat these pathogens;
6. HIV infection causes destruction of T helper cells;

7. Viral reproduction occurs and large number of viral particles are released;
8. Hijacking of cellular machinery and resources towards producing new viral particles disrupts normal activities needed for cell survival;
9. budding off of a large amount of viral particles from the cell surface might disrupt the cell surface membrane;
10. causing cell death / apoptosis;
11. functional T helper cell levels decline to a critical point;
12. T cell count falls below 200 cells/ mm^3;
13. unable to effectively recognise various pathogens and trigger an efficient immune response against them;
14. Opportunistic infections by pathogens that bypass the immune system;
15. Increased risk of developing various cancers due to inability of the immune system to remove cancer cells;
16. or to ward off infections by oncogenic viruses;

Distinguish between vaccines and antibiotics [max 4]

	feature	vaccines	antibiotics
D1	target pathogen	Bacteria and viruses	Bacteria only
D2	treatment course	Not given as a course / given once or a few times	Given as a course / over many days
D3	specificity	specific to a particular pathogen	can act on a range of pathogens
D4	activation of immune response	activates immune response	does not activate immune response
D5	production of antibodies	yes	no
D6	production of memory cells	yes	no
D7	duration of immunity / protection	long term immunity / protection	Does not provide long term immunity / protection
D8	when it is administered	before infection [A: preventative]	during infection [A: not preventative]

QWC – address both parts of the question;;

AO A – 5

AO B – 5

5	**(a)**	The mitotic cell cycle is tightly regulated by proteins to ensure accurate transmission of genetic information and to maintain stability in humans. However, not all cells within the body are genetically identical. Describe the roles of proteins involved in the formation of genetically identical cells during the mitotic cell cycle and explain why not all cells in humans are genetically identical.	[15]
		DNA replication 1. semi-conservative DNA replication; 2. during S phase of interphase; 3. DNA polymerase; replicates DNA/add nucleotides; 4. via complementary base pairing; 5. contributes to accuracy by proof-reading; 6. produces genetically identical DNA/sister chromatids; **Checkpoints** 7. CDK and cyclins regulate control of checkpoints; 8. allows cell cycle to proceed when internal and external conditions are favourable; 9. provide time for errors or malfunctioning cellular machinery to be repair; 10. prevent errors in cell division that may result if the cell cycle progressed prematurely to the next stage; 11. DNA repair enzymes; 12. excised the faulty or damaged section of the DNA; (the gap is filled by DNA polymerase) **Condensation of chromosomes** 13. Histone proteins; 14. for chromatin condensation; 15. Scaffold proteins; 16. aids in formation of loop domain; 17. Prevent entangling of chromosomes during separation; 18. Protect DNA from cellular enzymes; 19. Prevents chromosomal mutation; **Kinetochore proteins** 20. Kinetochore proteins; 21. attached at centromeres; 22. Allows attachment of kinetochore microtubules to centromere; **Tubulins** 23. Tubulins; 24. form spindle fibres; 25. Allows alignment of chromosomes on metaphase plate; 26. allows sister chromatids to move to opposite poles of the cell; (to form genetically identical daughter cells) **Actin** 27. Actins form microfilaments; 28. These enable the formation of a contractile ring; 29. The ring contracts, pinching the cell into two; [Max 10] **Cells are not genetically identical**	AO A – 10 AO B – 5

30. Gametes/sperm/egg, the number of chromosomes is halved compared to somatic cells / underwent crossing over and independent assortment to result in haploid cells that are different from each other;;
31. Mature red blood cells, these cells lack a nucleus;;
32. B lymphocytes, somatic recombination occurs in these cells;;
33. B lymphocytes, hypermutation occurs in these cells;;
34. Cancer cells, these cells may have gene mutations or chromosomal aberrations (excluding inversions);;
35. Actively dividing cells (excluding stem cells and germline cells), telomeres shorten with each round of DNA replication;;
36. Cells infected by retroviruses, viral DNA integrates into the chromosomes of the human host cell;;
37. Ref. mutations (point or chromosomal) and how it results in non-genetically identical cells;;

[Max 4]

QWC: Address roles of proteins in interphase and mitosis, and give at least 1 example of cells that are not genetically identical;;

(b) Viruses and prokaryotes can cause diseases. However, environmental factors such as temperature and rainfall can significantly influence disease transmission.

Contrast the structure and organisation of the genomes of HIV and prokaryotes and explain how seasonal changes in environmental factors contribute to the increased transmission of the dengue disease. [10]

Differences [Max 5]

		HIV genome	Prokaryote genome
D1	DNA/RNA	RNA	DNA
D2	structure of genome	linear	circular
D3	Number of strands	single-stranded	doube-stranded
D4	Number of genome	two RNA	one
D5	Presence of plasmid	Absent	Present
D6	Association with proteins	nucleoprotein	DNA packing protein (non-histone protein)
D7	Levels of packing	No packing	supercoiled
D8	Origin of replication	None	one
D9	Clustering of genes/operon	No	Yes (Related genes are clustered into operons)
D10	Number of genes	Less genes, ~200	More genes, ~4000 in *E. coli*
D11	Size of genome	Small (2kb- over 1 million bp)	Larger (a few million bp)

AO A – 5

AO B – 5

Temperature [Max 3]

1. warmer temperatures, increase metabolic rates;
2. by increasing rates of enzyme-catalysed reactions;
3. shorten life cycle/shorten development time/faster development rate;
4. increase in the mosquito vectors population;
5. increase rate of digestion; □
6. female mosquitoes feed/bite more frequently;

		7. increase in the transmission of the dengue virus; 8. shorter virus replication cycle; 9. shorten extrinsic incubation period for dengue virus; 10. increase in virus level in a shorter time; 11. increases transmission of virus to another person during feeding; (award once) **Rainfall [Max 2]** 12. increase in rainfall results more flooding/stagnant water; 13. increase the number of breeding sites available; 14. for eggs and larval development; 15. hydrate the eggs /water covers the eggs for hatching; 16. increase in mosquito population; QWC – address both parts of the question;;	
			[Total: 25]