Please check the examination details below before entering your candidate information

Candidate surname	Other names

Centre Number | Candidate Number

Pearson Edexcel International Advanced Level

Time 1 hour 45 minutes

Paper reference **WBI15/01**

Biology

International Advanced Level
UNIT 5: Respiration, Internal Environment, Coordination and Gene Technology

You must have:
Scientific article (enclosed), scientific calculator, ruler, HB pencil

Total Marks

Instructions

- Use **black** ink or ball-point pen.
- **Fill in the boxes** at the top of this page with your name, centre number and candidate number.
- Answer **all** questions.
- Answer the questions in the spaces provided – *there may be more space than you need.*
- **Show all your working out** in calculations and **include units** where appropriate.

Information

- The total mark for this paper is 90.
- The marks for **each** question are shown in brackets – *use this as a guide as to how much time to spend on each question.*
- In questions marked with an **asterisk** (*), marks will be awarded for your ability to structure your answer logically, showing how the points that you make are related or follow on from each other where appropriate.

Advice

- Read each question carefully before you start to answer it.
- Try to answer every question.
- Check your answers if you have time at the end.

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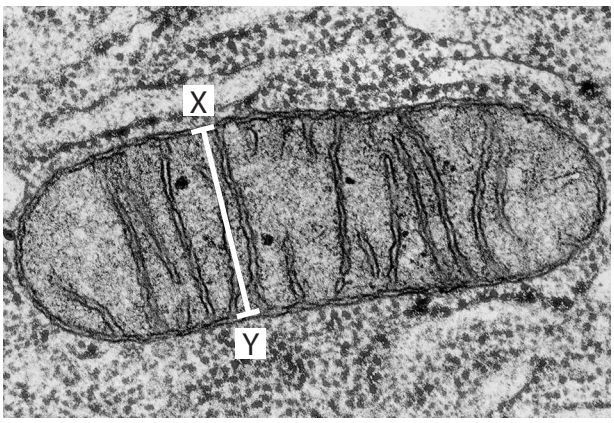
Answer ALL questions. Write your answers in the spaces provided.

Some questions must be answered with a cross in a box ☒. If you change your mind about an answer, put a line through the box ☒ and then mark your new answer with a cross ☒.

1 The photograph shows a transmission electron micrograph of a mitochondrion and surrounding cytoplasm.



(Source: © CNRI / SCIENCE PHOTO LIBRARY)

(a) The mitochondrion shown in the diagram is 2000 nm in length.

Calculate the width of this mitochondrion between X and Y.

(2)

Answer ..... nm

(b) Describe how ATP is synthesised by oxidative phosphorylation in the mitochondrion.

(3)

(c) Describe how ATP is used to supply energy for biological processes.

(2)

(Total for Question 1 = 7 marks)

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2 Muscles, bones and joints enable movement of the skeleton.

(a) (i) Which structure attaches one bone to another bone at a flexible joint?

(1)

- ☒ **A** actin
- ☒ **B** ligament
- ☒ **C** synapse
- ☒ **D** tendon

(ii) How many of the statements about joints are correct?

(1)

- antagonistic pairs of muscles move the bones at a joint
- muscles acting on a joint are myogenic
- tendons are more elastic than ligaments

- ☒ **A** 0
- ☒ **B** 1
- ☒ **C** 2
- ☒ **D** 3

(b) Usain Bolt's world record of 9.58 seconds for the 100 m men's sprint is unbeaten.

(Source: © Ian MacNicol / Getty Images)

(i) What is the role of myoglobin in muscle fibres?

(1)

- ☒ **A** it is an enzyme that reacts with myosin
- ☒ **B** it is part of the sarcolemma involved in the release of calcium ions
- ☒ **C** to act as an immediate source of energy
- ☒ **D** to provide oxygen for muscles

(ii) Explain why the muscles of a sprinter have a high percentage of fast twitch fibres.

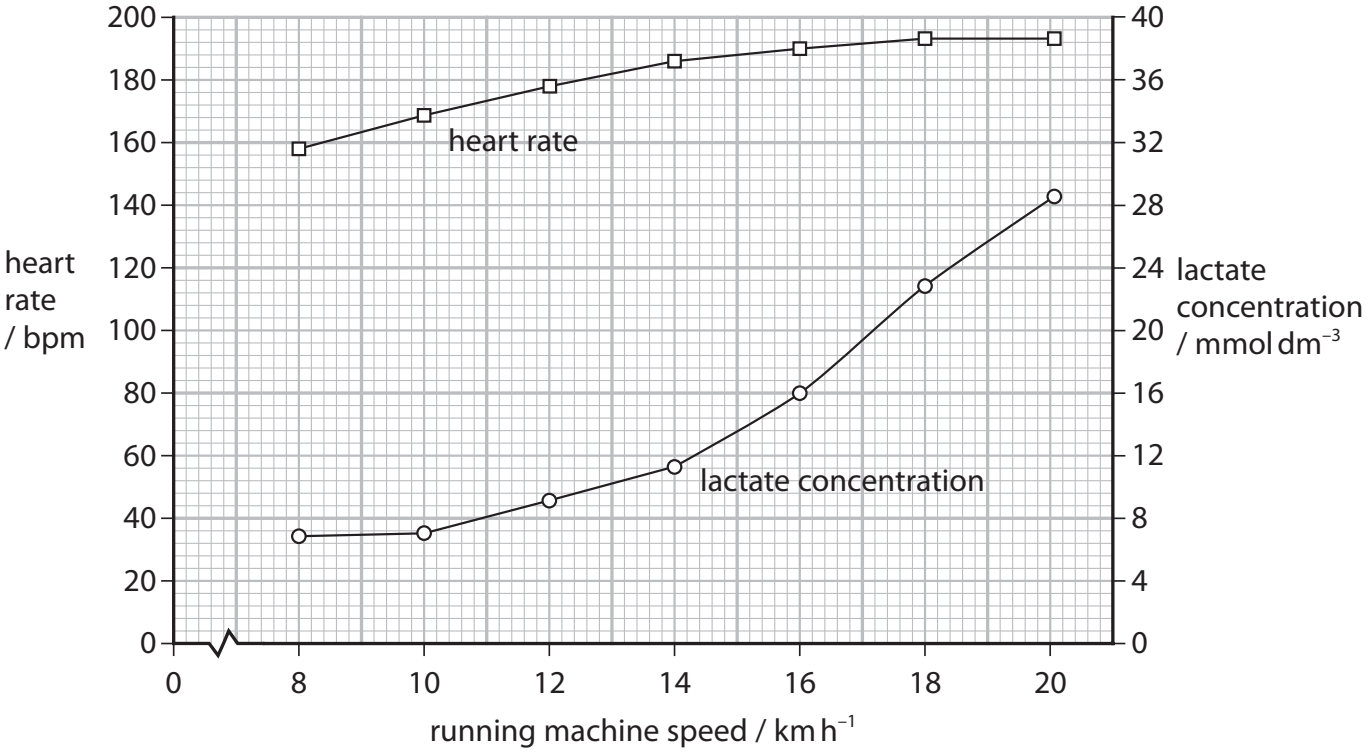
(3)

(c) In an investigation, an athlete ran for 10 minutes on a running machine moving at constant speed.

The investigation was repeated at seven running speeds.

At each speed, the heart rate and lactate concentration in the blood of the athlete were measured.

The results are shown in the graph.



Comment on the results of this investigation.

(3)

(Total for Question 2 = 9 marks)

3 Whales are large mammals.

The photograph shows a beluga whale and a human diver.

(Source: © Andrey Nekrasov/Alamy Stock Photo)

(a) (i) A beluga whale can become habituated to human divers.

How many of the following statements about habituation are correct?

(1)

- habituation is an example of anatomical adaptation
- habituation is only observed in mammals
- habituation only occurs after repeated exposure to the same stimulus

☒ **A** 0

☒ **B** 1

☒ **C** 2

☒ **D** 3

(ii) A beluga whale can respond to a stimulus using a spinal reflex arc.

Which row is correct?

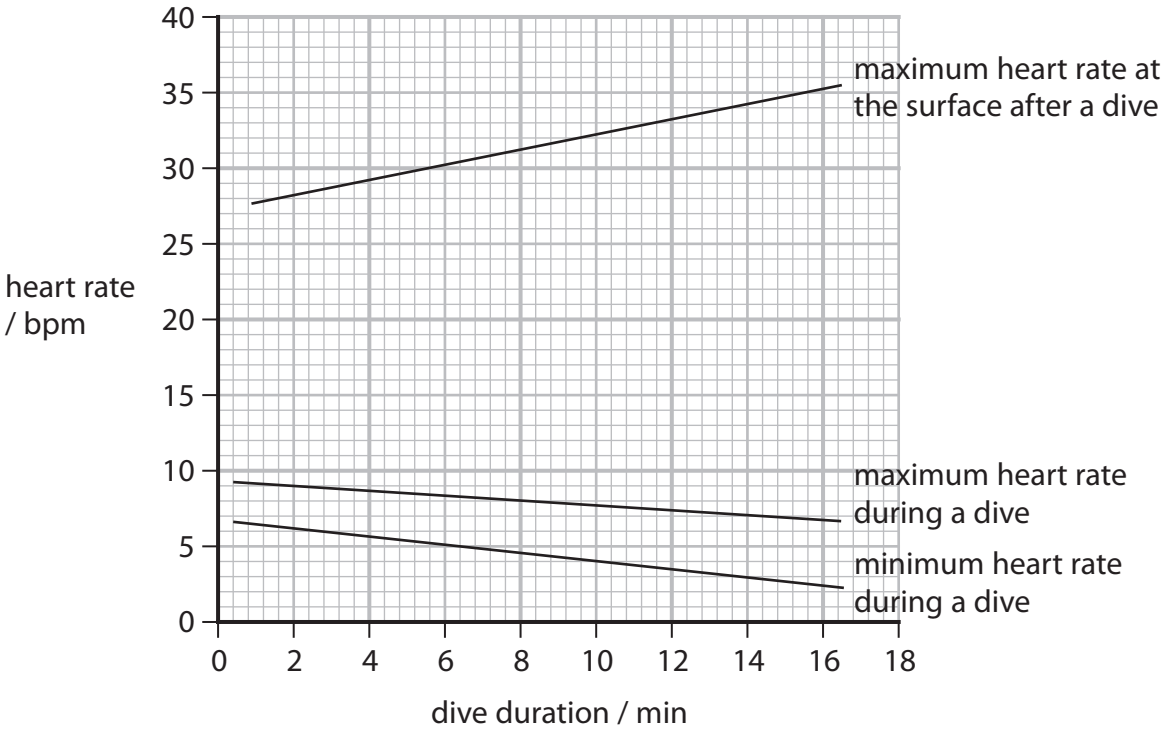
(1)

		Location of relay neurone	Location of cell body on the sensory neurone
☒	**A**	grey matter of spinal cord	at the end of the axon
☒	**B**	grey matter of spinal cord	in the middle of the axon
☒	**C**	white matter of spinal cord	at the end of the axon
☒	**D**	white matter of spinal cord	in the middle of the axon

(b) The heart rate of a whale changes when it is diving.

The graph shows the changes in heart rate that occur during dives of different durations.

The maximum heart rate at the surface is when the whale returns to the surface after a dive.



(i) Comment on the changes in heart rate of the whale when diving.

(3)

(ii) Explain how the changes in heart rate are controlled when the whale returns to the surface immediately after the dive.

(3)

(Total for Question 3 = 8 marks)

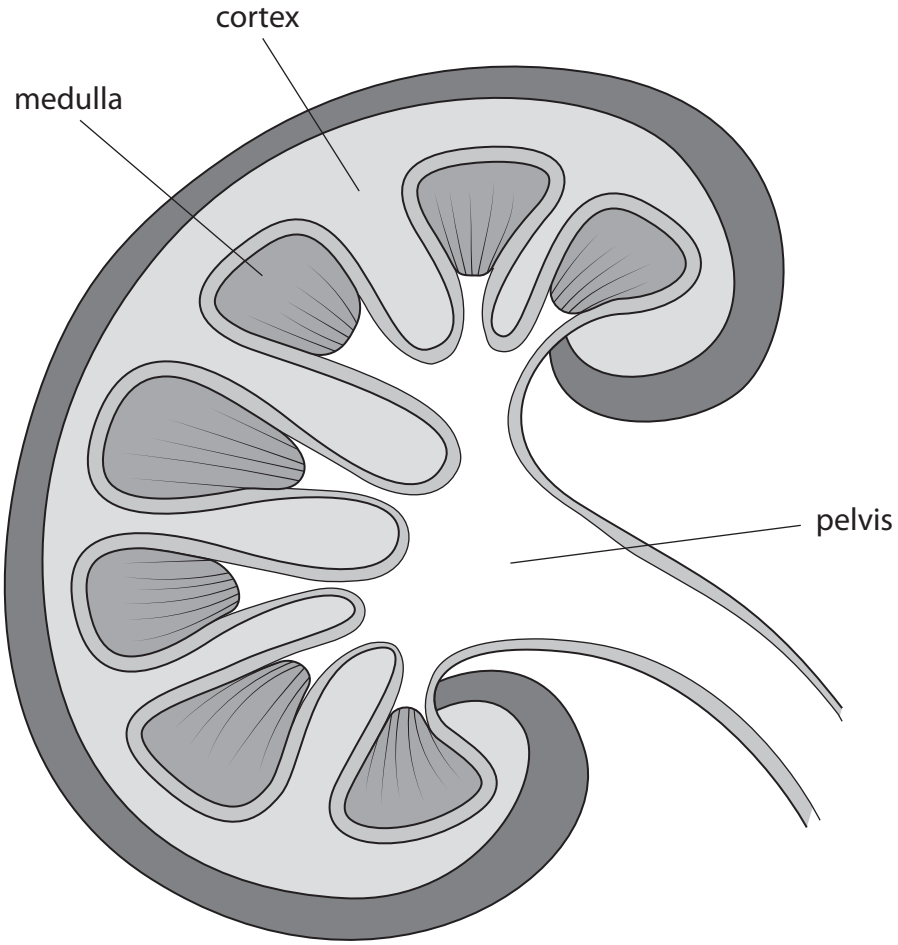
4 The kidneys perform important roles in filtering the blood and maintaining fluid levels in the body.

Each kidney contains up to a million functioning units called nephrons.

Each nephron consists of a filtering unit of tiny blood vessels called a glomerulus that is attached to a tubule.

(a) The diagram shows part of a human kidney.

(i) Draw an arrow on the diagram to show the location of a single Bowman's capsule (renal capsule).



(1)

(ii) Where in the kidney are most amino acids reabsorbed from the nephron?

(1)

- ☒ **A** collecting duct
- ☒ **B** distal tubule
- ☒ **C** loop of Henle
- ☒ **D** proximal tubule

(iii) Which row shows the correct pathway taken by a water molecule through the kidney nephron?

(1)

		Route through nephron ⟶			
☒	**A**	collecting duct	proximal tubule	distal tubule	glomerulus
☒	**B**	glomerulus	proximal tubule	distal tubule	collecting duct
☒	**C**	glomerulus	distal tubule	collecting duct	proximal tubule
☒	**D**	proximal tubule	glomerulus	distal tubule	collecting duct

(b) Explain how the loop of Henle acts as a countercurrent multiplier to produce concentrated urine.

(4)

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(c) Describe how ADH is involved in the control of the water potential of the blood.

(4)

(Total for Question 4 = 11 marks)

5 Animals and plants can detect and respond to light.

(a) Rod cells respond to light by producing action potentials in the optic nerve.

(i) In which structure are rod cells located?

(1)

☒ **A** iris

☒ **B** pupil

☒ **C** retina

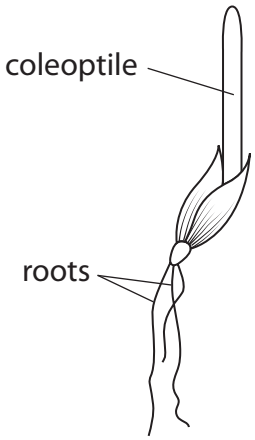
☒ **D** spinal cord

(ii) Describe the role of rhodopsin in rod cells.

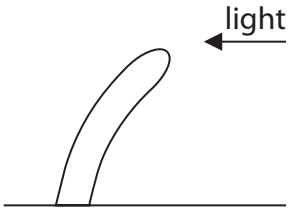
(3)

*(b) The drawing shows the results of some experiments investigating phototropisms.

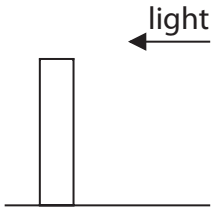
The diagram shows a coleoptile of a seedling.



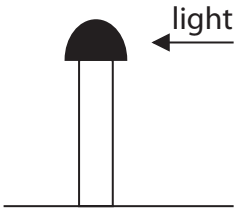
Experiment 1:



intact coleoptile illuminated from one side

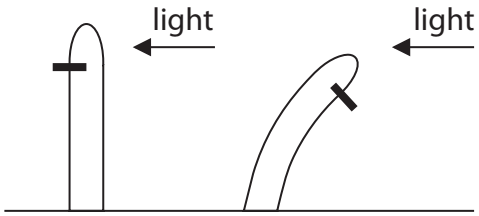


tip of coleoptile removed and remaining coleoptile illuminated from one side



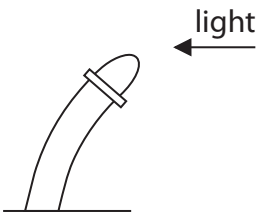
black cap placed on tip of coleoptile and coleoptile illuminated from one side

Experiment 2a:



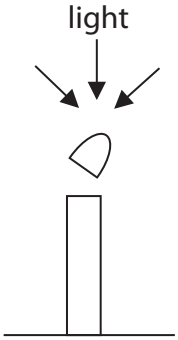
plastic sheet inserted below the tip of the coleoptile and the coleoptile illuminated from one side

Experiment 2b:



gel layer placed below the tip of the coleoptile and the coleoptile illuminated from one side

Experiment 3:



coleoptile illuminated and the tip removed

tip replaced on one side of the remaining coleoptile that is then kept in the dark

Scientists concluded that these results suggest a plant growth substance is involved in regulating the phototropic response.

Discuss how the results of these experiments support the role of a plant growth substance in the phototropic response of plants.

Use the information for these experiments and your own knowledge to support your answer.

(6)

(Total for Question 5 = 10 marks)

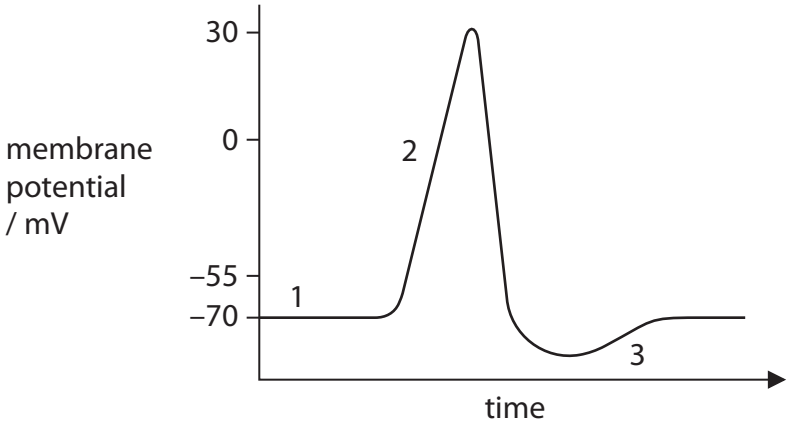
6 The nervous system is a complex collection of neurones and specialised cells that transmit impulses between different parts of the body.

(a) Which substance can transmit a nerve impulse from one neurone to the next one?

(1)

- ☒ **A** acetylcholine
- ☒ **B** ADP
- ☒ **C** cholesterol
- ☒ **D** NADP

(b) The diagram shows the change in membrane potential as an action potential is transmitted in a motor neurone.

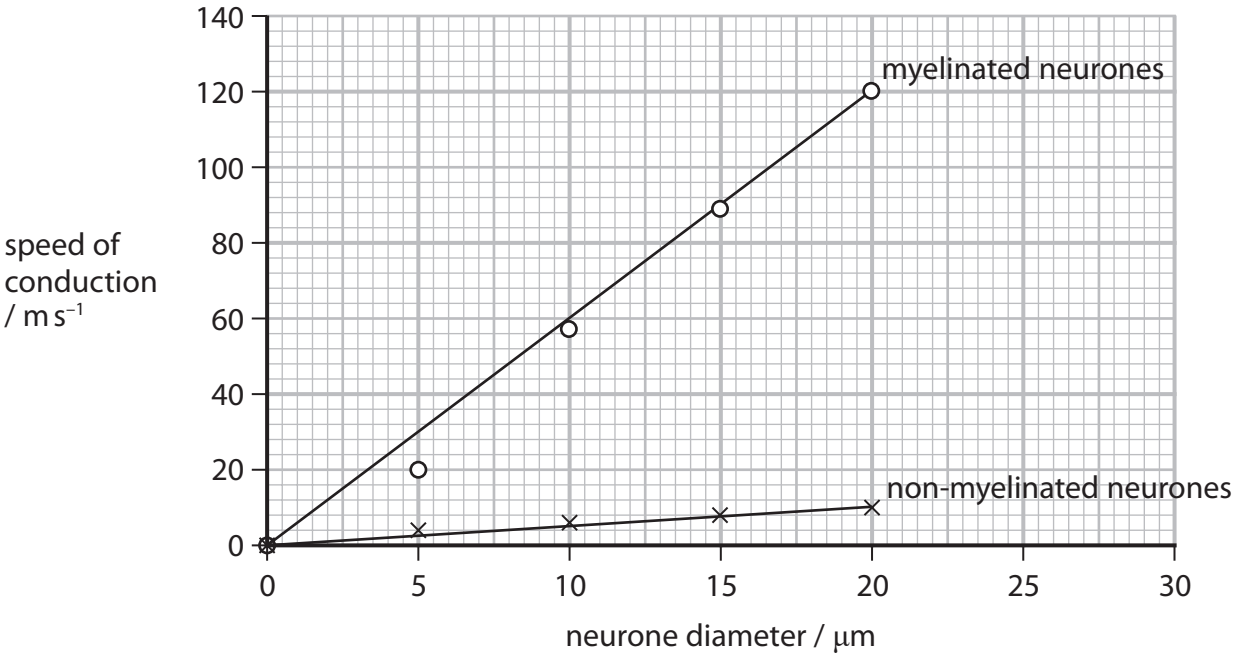


Explain why the membrane potential changes between 1 and 2.

(2)

(c) Myelinated neurones are surrounded by a fatty sheath.

The graph shows the speed of conduction in myelinated neurones and non-myelinated neurones.



(i) Calculate the percentage difference in the gradient of the myelinated and non-myelinated neurones.

The gradient for non-myelinated neurones is 0.5.

The equation for a straight line is $y = mx + c$.

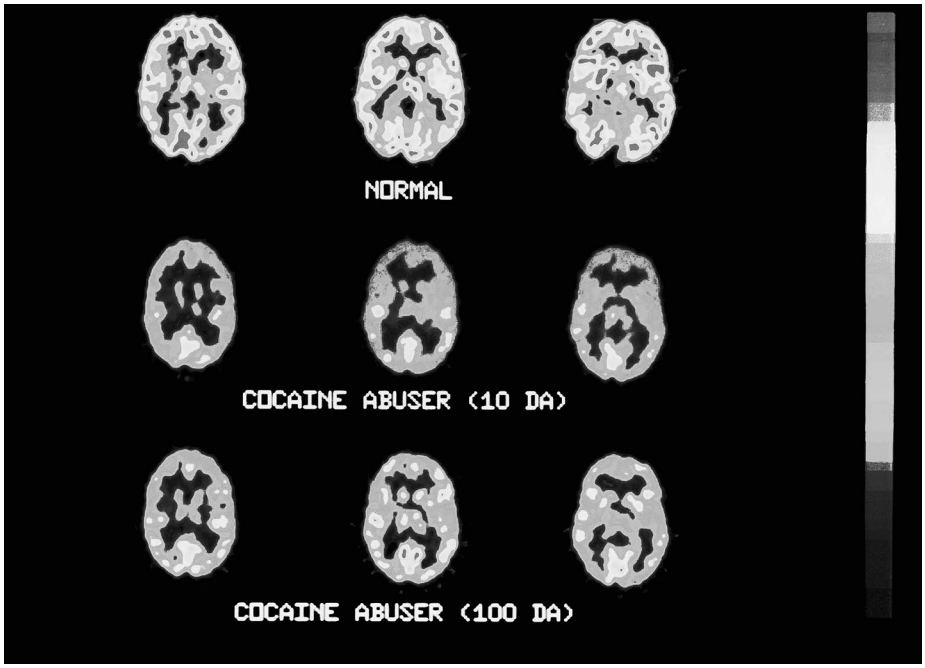
(3)

Answer ..... %

(ii) Explain why the speed of conduction differs in myelinated and non-myelinated neurones.

(3)

(d) The positron emission tomography (PET) images show the brain of an individual before (control) and after taking the drug cocaine.



(Source: © BROOKHAVEN NATIONAL LABORATORY / SCIENCE PHOTO LIBRARY)

Explain how positron emission tomography (PET) can be used to identify the change in activity in the brain after taking this drug.

(4)

(Total for Question 6 = 13 marks)

7 Alpha-1 antitrypsin (AAT) deficiency is an inherited disease that can affect different organ systems.

Alpha-1 antitrypsin (AAT) is a protein produced in the liver.

(a) Investigation of the breathing of a patient with AAT deficiency found that the:

- resting tidal volume (V_T) was 500 cm^3
- dead space (DS) was 150 cm^3
- resting respiratory rate (RR) was 12 breaths per minute.

Calculate the volume of air that enters the alveoli (A_V) **each hour**.

$$A_V = (V_T - DS) \times RR$$

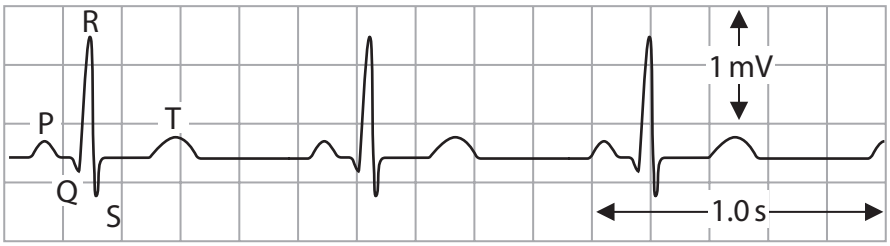
Give your answer to 2 significant figures with appropriate units.

(3)

Answer .....

(b) Activity of the heart was investigated in the same patient.

The trace shows a normal electrocardiogram (ECG).

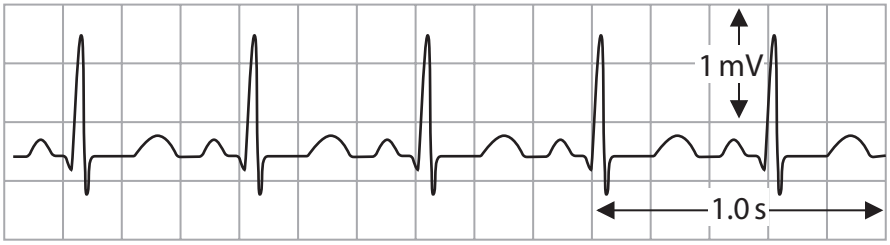


(i) Name the stage of the cardiac cycle at T on this ECG.

(1)

.....

(ii) The ECG of the patient with AAT is shown in the trace.



Calculate the mean heart rate shown in this ECG trace.

(1)

Answer .....

(iii) Compare and contrast the ECG trace of this patient with the normal ECG trace.

(3)

.....

.....

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.....

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.....

.....

(c) One potential treatment for AAT deficiency uses adenoviruses to genetically modify cells in an affected person.

Adenoviruses contain double-stranded DNA.

Explain how adenoviruses can be used to treat AAT deficiency in a person.

(4)

(Total for Question 7 = 12 marks)

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8 The scientific document you have studied is adapted from an article in Science Direct: *Assessment of food toxicology* by Alexander Gosslau.

Use the information from the scientific article and your own knowledge to answer the following questions.

(a) Explain how toxicants in food could cause Parkinson's disease (paragraph 3).

(3)

(b) Suggest how the genes affected by toxicants can be identified (paragraph 4).

(2)

(c) Explain how scientists could determine the high degree of homology of genes between humans and zebrafish (paragraph 5).

(3)

(d) Suggest how electrophilic species (ES) of free radicals could be "involved in the modulation of gene expression" (paragraph 6).

(3)

(e) Suggest how ES can damage mtDNA (paragraph 7).

(3)

(f) In the MTT assay, reduced NAD converts an MTT solution from yellow to purple.

Describe how the MTT assay could be used to show which of two drugs is more toxic to cells (paragraph 10).

(4)

(g) Explain the advantages of reprogramming ordinary somatic cells to behave like embryonic stem cells for use in stem cell-based assays of toxicants (paragraph 11).

(2)

(Total for Question 8 = 20 marks)

TOTAL FOR PAPER = 90 MARKS

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Time 1 hour 45 minutes

Paper reference **WBI15/01**

Biology

International Advanced Level
UNIT 5: Respiration, Internal Environment, Coordination and Gene Technology

Scientific article for use with Question 8

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Scientific article for use with Question 8

Assessment of food toxicology by Alexander Gosslau

1. The history of food toxicity might have started as early as Hippocrates made the statement "Let food be thy medicine and medicine thy food" which presaged the modern science by over two millennia ago. With the development of modern biochemistry, molecular biology, cell culture techniques, computer science and bioinformatics, it has been possible to identify and characterize potential toxicants in food.

2. There are two different related areas in the measurement of toxicants and toxicity in food: (1) actual measurements of the effects of toxicants in different models ranging from *in vitro* biochemical systems, cell-based *in vitro* systems, animal *in vivo* models to clinical settings analyzing systemic or organ-specific toxicity and (2) assessment and/or predictions of potential toxicants in food.

3. The mechanisms of toxicant effects are multifactorial interacting intrinsically and extrinsically with key molecules which play major roles in cell integrity, metabolism, signaling pathways, gene expression and translation. For a variety of toxicants their effects appear to converge on the generation of electrophilic species (ES) leading to oxidative stress and chronic inflammation. Oxidative reactions induced by toxicants lead to an accumulation of damaged macromolecules thus harming cells, tissues and organs. Therefore, toxicants may play central roles in cell death, chronic inflammation, aging and degenerative diseases such as Alzheimer's, Parkinson's and Huntington's diseases, as well as multiple sclerosis, myocardial infarction, arteriosclerosis, diabetes, rheumatoid arthritis, sterility, cataracts and many others.

4. For *in vitro* assessment a variety of biochemical systems have been developed to analyze damaging effects on integrity or activity of key biomolecules. Such molecules are important in cell integrity, metabolism, signaling pathways, as well as gene expression and translation. The list of affected molecules is extensive and includes enzymes, receptors, membrane lipids, nucleic acids and/or factors involved in gene expression. On a cellular level, a variety of viability assays are routinely used to quantify effects of potential food toxicants for extrapolation of a range of dosages used for maximal tolerated concentrations for *in vivo* animal models and also clinical settings. *In vivo* rodent models still appear to be the gold standard for toxicity assessment but there are limitations of such traditional testing such as high costs, low throughput readouts, inconsistent responses, ethical issues and concerns of extrapolability to humans.

5. Another refinement in toxicity assessment is the installation of alternative lower hierarchy surrogate animal models such as zebrafish (*Danio rerio*), fruit flies (*Drosophila melanogaster*) or nematodes (*Caenorhabditis elegans*). These models offer an advantage in terms of ethical concerns, high throughput and genetic manipulation over traditional rodent models. The value of using alternative sub-mammalian vertebrate and invertebrate models became evident by the surprising discovery of the high degree of homology of genes between humans and zebrafish, fruit flies or nematodes.

6. Although the mechanisms leading to toxic effects in humans are multifactorial, the majority of toxic effects appear to converge on the generation of free radicals. Different electrophilic species (ES) such as reactive oxygen species (ROS) or reactive nitrogen species (RNS) are capable of oxidizing virtually all biomolecules. Whereas a variety of toxicants generate ES directly, others induce a secondary response leading indirectly to generation of ES by immunocompetent leukocytes which play a key role in the inflammatory cascade. ES are also involved in the modulation of gene expression by interfering with transcription factors and/or DNA which can lead to mutations and carcinogenesis. The accumulation of damage to membrane lipids, cellular proteins, carbohydrates as well as nucleic acids harm the functioning of cells, tissues and organs. These and other observations strengthen the hypothesis that toxicants leading to oxidative stress and chronic inflammation play central roles in cell death, aging and degenerative diseases.

7. The oxidation of lipids, proteins, nucleic acids and carbohydrates generate a variety of damaging breakdown products which thus can lead to the onset of many degenerative diseases. Lipid peroxidation of cell structures containing lipids can lead to the generation of different toxic products including alcohols, ketones, alkanes, aldehydes and ethers which have the potential to contribute to cell damage, necrosis or apoptosis. Nucleic acids are delicate targets of ES leading to mutations. Damage of nucleic acids by ES may result in single and double strand breaks, DNA–DNA, DNA–protein, DNA–lipid adducts or numerous base modifications. Mitochondrial DNA (mtDNA) is particularly susceptible to oxidative damage because of the absence of associated histones, an incomplete mitochondrial DNA repair system and the generation of free radicals through electron leakage from the respiratory chain.

8. Testing whether a chemical can modulate the activity of particular enzyme or binding affinities to a particular receptor or other biomolecule is the most direct way to gain mechanistic insights into action at the molecular level. There are different biochemical *in vitro* assays which analyze the integrity or mutation of DNA and RNA, membrane lipids, as well as the binding and activity of various receptors, enzymes involved in signaling transduction, drug or neurotransmitter metabolism and many others.

9. The use of cellular models provides a much higher level of complexity than simple biochemical assays. A huge number of human cell lines are available and a variety of different cell-based *in vitro* assays have been developed for screening of food toxicants.

10. For general assessment of cytotoxicity an indirect measure of cell viability is usually performed and several cellular bioassays are routinely used integrating different cytotoxicity endpoints such as membrane leakage or cellular activity. Whereas the trypan blue, propidium iodide, crystal violet or lactate dehydrogenase assays are analyzing membrane integrity based on exclusion, other viability assays such as the neutral red, alamar blue or MTT assay are metabolic measures of cellular activity. Inhibitory concentrations (IC values) obtained by viability assays are then used for initial dose selection in testing on animals and humans.

    In addition to the measurement of dyes, activity analysis of enzymes is also an established technique used to determine membrane integrity. Leakage of intracellular enzymes such as lactate dehydrogenase (LDH) or others into the extracellular medium is thus employed as indicator of cell membrane damage.

    Damage of mitochondria is a major contributor to organ toxicity, such as of the liver, kidney, heart, muscle and the central nervous system, and mitochondrial dysfunction is increasingly implicated in a growing list of degenerative diseases.

11. Recently, stem cell-based assays are being discussed as source for various toxicological applications thanks to the Nobel Prize-winning discovery of how to reprogram ordinary somatic cells to behave like embryonic stem cells. Human-induced pluripotent stem cells (iPSCs) allow assays to consider an individual's genetic background and potential epigenetic influences that affect the variability of the toxicity response. Stem cell-based models are also of particular interest for toxicity measurements which either lack extrapolability in rodent models such as for genotoxicity, cardiotoxicity, respiratory toxicity or for different stages of disorders which largely remain unknown such as neurological disorders (depression, anxiety, Alzheimer's and Parkinson's disease), autoimmune diseases (multiple sclerosis, type I diabetes, asthma), systemic infection, cancer and others.

12. While complex cell culture systems can provide unique insights into *in vivo* toxicology, they will never completely model the higher level interactions present in an intact organism. Therefore, the gold standard for toxicity assessment has been *in vivo* toxicology, where a particular molecule or complex food ingredients are given to animals to evaluate acute, subacute and chronic effects.

13. The majority of animals used are rodents and to derive statistically significant results the numbers of animals needed for testing are enormous with an estimation of 7000 animals and tens of millions of dollars for each test compound in the pharmaceutical industry. Although the numbers of animals involved in food toxicity screening are decreasing, the numbers of compounds or food ingredients to be tested as well as the costs of the current *in vivo* assessment systems are exploding.

14. More recently, the zebrafish *D. rerio* has been used as a vertebrate model organism for a wide variety of research including drug discovery and toxicology. The increased usage of zebrafish as *in vivo* model system reflects the striking similiar toxicity profile between humans and zebrafish due to substantial physiological, anatomic and genetic homology. The zebrafish model is also amenable to gene manipulation, is low in cost, has a short generation time and is particularly well suited for high-throughput screening as well as microarray and proteomic studies. Since zebrafish larvae are transparent they are ideal for studies on organ morphology by *in vivo* imaging techniques in addition to more detailed studies by immunohistochemistry or *in situ* hybridization.

15. Toxicity assessment in humans involves different fields such as clinical, forensic, environmental and regulatory toxicology. A systemic determination of toxicants in body tissues is usually obtained by biopsy or by analyzing body fluids such as blood and urine.

16. A great deal of knowledge on toxicity in humans has been obtained by post mortem molecular and anatomic analysis of cells, tissues and organs. Forensic toxicology is very related to toxicologic pathology but focusing more on the application to the purposes of the law. By virtue of advances in nanotechnology and its application in food industry, the newly created discipline of nanotoxicology investigates safety or potential hazards of nanoparticles. Another dimension refers to genetically modified organisms (GMO) or genetically modified food (GMF) as potential sources of toxicity. All the different disciplines of toxicity assessment in humans are not mutually exclusive but rather highly interconnected. The goal is to identify and understand the molecular mechanisms of toxicants causing adverse effects in order to ultimately prevent their intake thus increasing food safety.