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 the question labelled 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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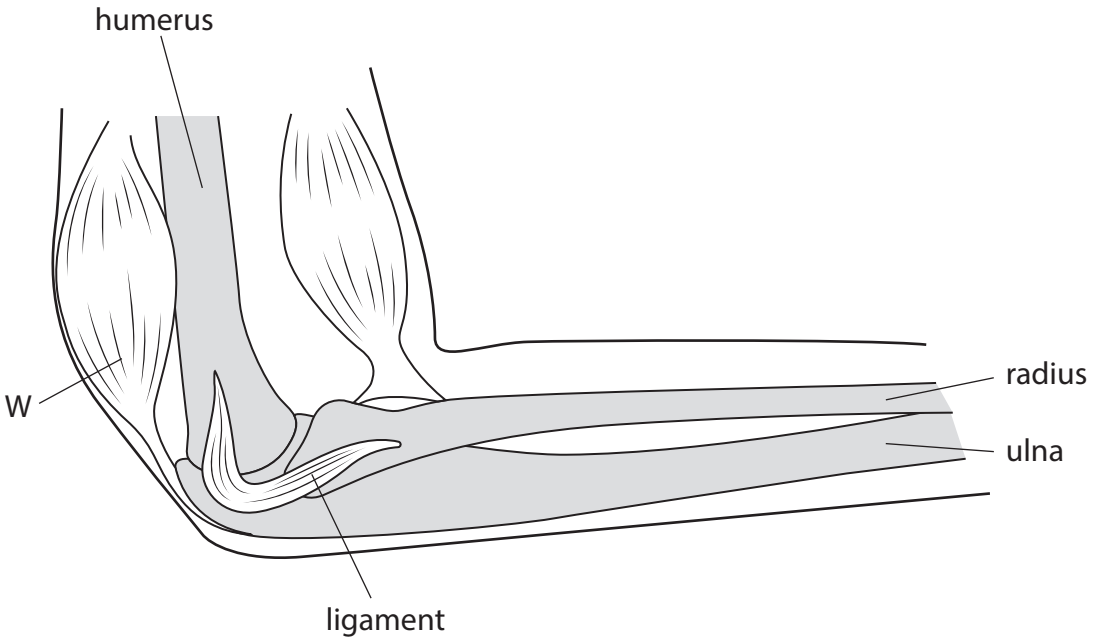
Answer ALL questions.

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 diagram shows an elbow joint.



(a) (i) Which structure contains actin and myosin?

(1)

☒ **A** bone

☒ **B** ligament

☒ **C** muscle

☒ **D** tendon

(ii) What is the function of the part of the joint labelled W?

(1)

- ☒ **A** it acts as an extensor
- ☒ **B** it acts as a flexor
- ☒ **C** it acts as a ligament
- ☒ **D** it acts as a tendon

(b) (i) Explain the role of the ligament labelled on the diagram.

(2)

(ii) Suggest **one** possible cause of damage to this ligament.

(1)

(Total for Question 1 = 5 marks)

2 Different techniques can be used in the investigation of the activity of the brain.

(a) Which type of scan can be used to study changes in brain function as they happen?

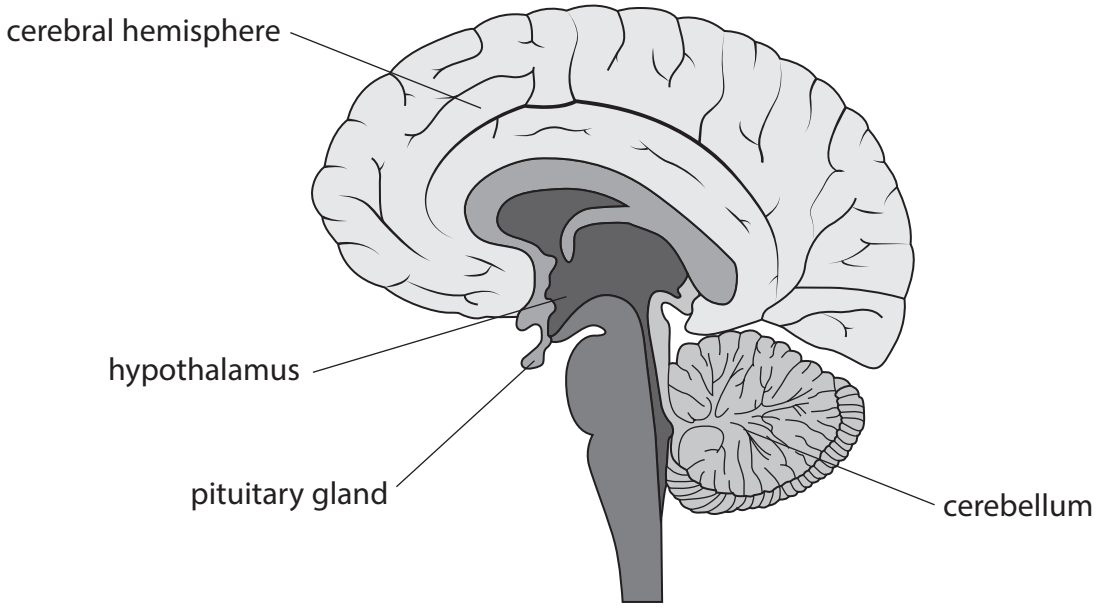
(1)

- ☒ **A** computed tomography (CT)
- ☒ **B** electrocardiogram (ECG)
- ☒ **C** functional magnetic resonance imaging (fMRI)
- ☒ **D** polymerase chain reaction (PCR)

(b) Describe the advantages and disadvantages of using positron emission tomography (PET) and magnetic resonance imaging (MRI) to investigate brain function.

(3)

(c) The diagram shows a section through the human brain.



Complete the table to show **one** function for each part of the brain.

(3)

Part of brain	Function
cerebellum	
cerebral hemisphere	
hypothalamus	

(Total for Question 2 = 7 marks)

3 Nervous communication involves neurones and changes in ion concentrations.

(a) (i) Which description of the movement of ions will produce an action potential in an axon?

(1)

☒ **A** K^+ ions move into the axon

☒ **B** K^+ ions move out of the axon

☒ **C** Na^+ ions move into the axon

☒ **D** Na^+ ions move out of the axon

(ii) Which row describes the events that occur during repolarisation of a neurone?

(1)

		Sodium ion channel	Membrane potential
☒	**A**	closed	decreasing
☒	**B**	open	decreasing
☒	**C**	open	increasing
☒	**D**	closed	increasing

(b) Describe the structure of a spinal reflex arc.

(3)

(c) Explain how the nerve impulse is transmitted across a synapse.

(4)

(Total for Question 3 = 9 marks)

4 Cancers can develop as a result of mutations or epigenetic modifications.

(a) (i) State what is meant by the term **mutation**.

(1)

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.....

.....

(ii) Name the type of nuclear division taking place as a tumour develops.

(1)

.....

(b) How many of the following statements about epigenetic modification are correct?

(1)

- It can result in a change in the base sequence of a gene
- It can involve histone modification
- It can result in an altered phenotype
- It can involve DNA methylation

☒ **A** 1

☒ **B** 2

☒ **C** 3

☒ **D** 4

(c) Oestrogen stimulates some types of breast cancer to proliferate.

Oestrogen is a steroid hormone found in mammals.

Oestrogen affects up to 100 different genes.

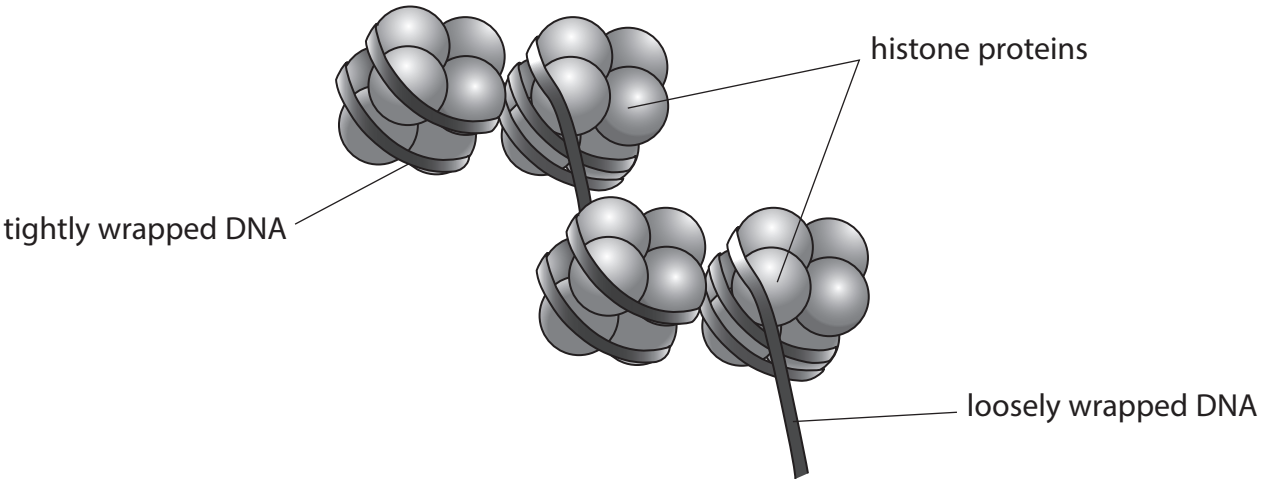
Explain how oestrogen may result in the proliferation of some breast cancer cells.

(4)

(d) The expression of genes in cancer cells can be regulated by histone modification.

DNA that is not being transcribed is tightly wrapped around histone proteins.

The diagram shows DNA wrapped around histone proteins.



Acetylation of histones is one example of histone modification. Acetyl groups are added to histone proteins.

Suggest how acetylation of histone proteins could result in increased gene expression.

Use the information in the diagram to support your answer.

(2)

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(Total for Question 4 = 9 marks)

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5 Aerobic respiration is a metabolic process involving a series of chemical reactions.

(a) How is water formed during aerobic respiration?

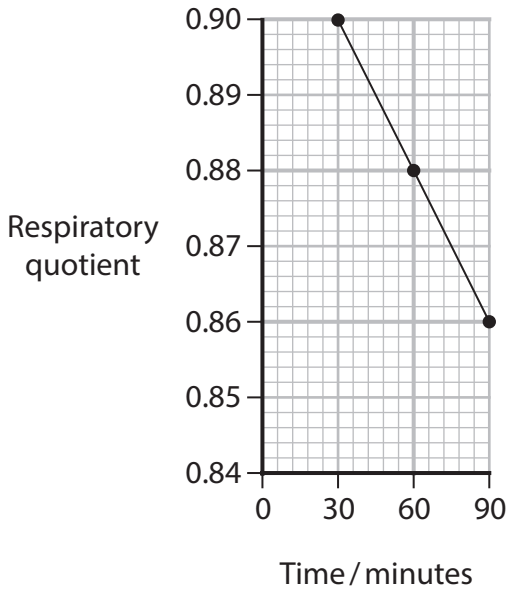
(1)

- ☒ **A** reduction of carbon
- ☒ **B** reduction of oxygen
- ☒ **C** phosphorylation of ADP
- ☒ **D** phosphorylation of glucose

(b) The effect of exercise on the respiratory quotient of a cyclist was investigated.

The cyclist undertook moderate exercise for 90 minutes.

The graph shows the respiratory quotient for the cyclist during this investigation.



(i) The rate of oxygen uptake by the cyclist at 60 minutes was 2.20 $dm^3 min^{-1}$.

Which is the rate of carbon dioxide production by the cyclist at 60 minutes?

(1)

- ☒ **A** 1.30 $dm^3 min^{-1}$
- ☒ **B** 1.94 $dm^3 min^{-1}$
- ☒ **C** 2.50 $dm^3 min^{-1}$
- ☒ **D** 3.08 $dm^3 min^{-1}$

(ii) The table gives the respiratory quotient for aerobic respiration using fats or carbohydrates as respiratory substrates.

Substrate	Respiratory quotient
Fat	0.7
Carbohydrate	1.0

Explain the changes in respiratory quotient in this person during the exercise period of this investigation.

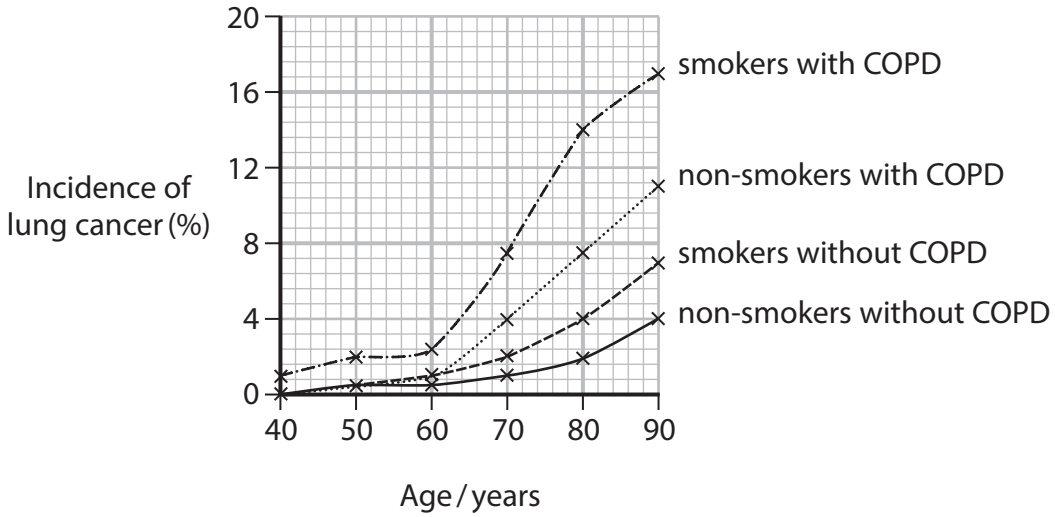
Use the information in the table and the graph to support your answer.

(2)

(c) Chronic obstructive pulmonary disease (COPD) is a life-threatening illness.

This disease greatly reduces the ability to take in oxygen in the lungs and is a risk factor for lung cancer.

The graph compares the incidence of lung cancer in smoking and non-smoking individuals with and without COPD.



In South Korea there are 105 500 males and 158 600 females in the 80-year-old age group.

(i) Calculate the total number of people in this age group that will have lung cancer who are non-smokers with COPD.

Give your answer in standard form.

(2)

Answer .....

(ii) Cigarette smoking causes inflammation in the lungs. This can result in damage to the walls of the alveoli and lead to COPD.

Cigarette smoking also causes the production of thick mucus in the lungs.

Deduce the effects on the heart rate and ventilation rate in a person who smokes and has COPD.

(4)

(Total for Question 5 = 10 marks)

6 Skeletal muscle contains slow twitch and fast twitch muscle fibres.

(a) The table compares the percentage of slow twitch fibres in different types of athlete.

Type of athlete	Range of percentages of slow twitch fibres in muscle (%)
100 m runner	12 to 30
1500 m runner	30 to 65
10 000 m runner	60 to 95
marathon (42 200 m) runner	60 to 95

Explain the importance of slow twitch muscle fibres in these types of athlete.

(3)

(b) Name the basic unit of contraction in a skeletal muscle.

(1)

.....

(c) The heart pumps oxygen rich blood to the tissues.

Cardiac output and cardiac index can show how effectively the heart is working.

(i) A patient had a heart rate of 65 beats min^{-1} and a stroke volume of 57 cm^3 per beat.

Calculate the cardiac output for this individual.

Use the equation:

stroke volume = cardiac output ÷ heart rate

Give your answer in $dm^3\ min^{-1}$.

(2)

Answer .....

The cardiac index can be calculated using the formula:

$$\text{cardiac index} = \frac{\text{stroke volume} \times \text{heart rate}}{\text{body surface area}}$$

The table shows data for two patients.

Patient	heart rate /bpm	stroke volume /dm^3	body surface area /m^2
A	79	0.057	1.54
B	79	0.075	2.39

(ii) The cardiac index for patient A was 2.92 $dm^3\ min^{-1}\ m^{-2}$

Which is the correct cardiac index for patient B?

(1)

- ☒ **A** 1.24
- ☒ **B** 2.48
- ☒ **C** 2.92
- ☒ **D** 5.21

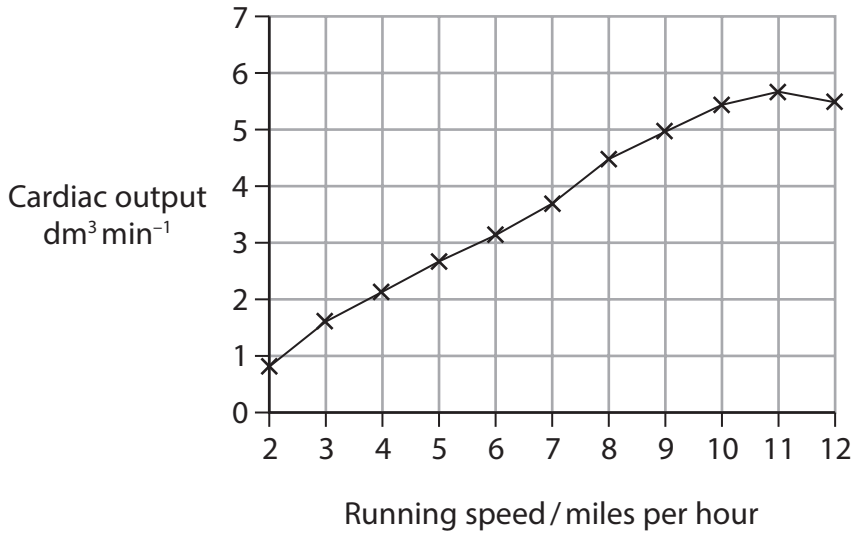
(iii) State the ratio of the body surface area of patient A to patient B.

(1)

Answer .....

(d) The cardiac output changes in an athlete as their running speed increases.

The graph shows cardiac output for an athlete running at different speeds.



(i) Comment on the effect of running speed on cardiac output.

(2)

(ii) Exercise increases the rate of respiration in muscles.

Explain how an increase in the rate of respiration causes an increase in the heart rate of an athlete.

(3)

(iii) Anaerobic respiration produces lactate.

Describe what happens to this lactate.

(2)

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(Total for Question 6 = 15 marks)

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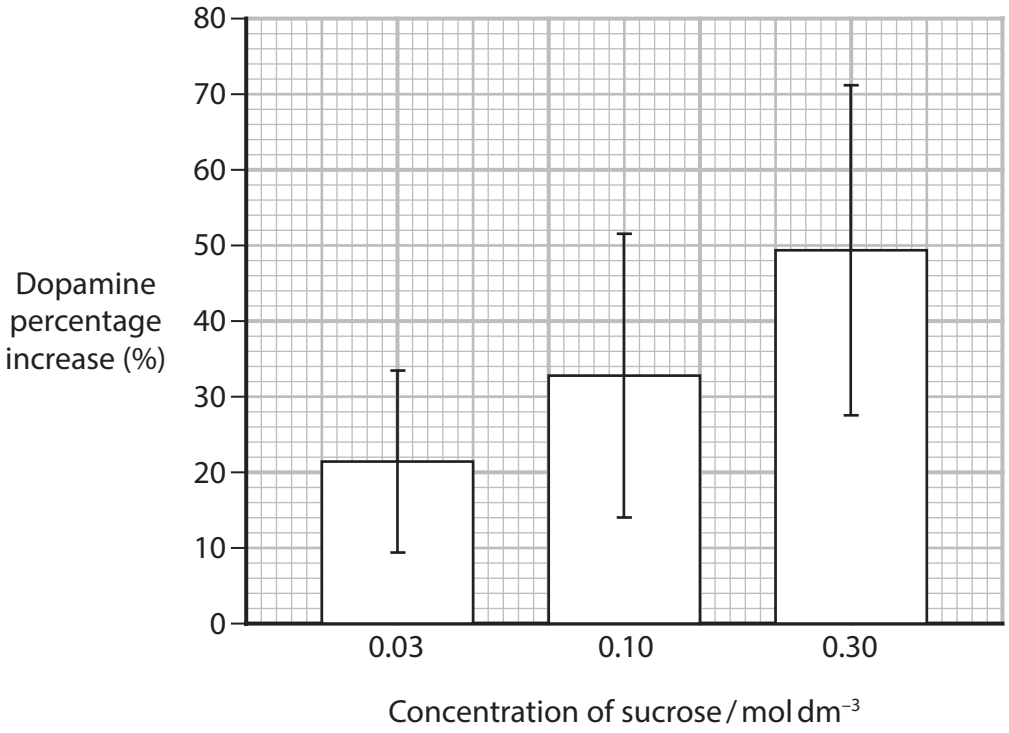
7 (a) Scientists investigated the effect of sucrose solutions on the desire of rats to eat.

The release of dopamine in some areas of the brain increases the desire of the rat to eat.

Scientists measured increases in the release of dopamine in the brain of rats given different concentrations of sucrose solutions to drink.



The scientists concluded that drinking a sucrose solution had an effect on the desire of the rats to eat.

(i) Comment on the results shown in the bar chart and how they support this conclusion.

(4)

(ii) The table gives the results for a sucrose concentration of 0.4 mol dm^{-3}.

Complete the table to calculate the standard deviation (S) for these results.

$$S = \sqrt{\frac{\sum(x - \bar{x})^2}{n - 1}}$$

Give your answer to two significant figures.

(2)

result (*x*)	***x* – $\bar{x}$**	**$(x - \bar{x})^2$**
45	–15	225
63	3	9
74	14	196
58		
	$\sum(x - \bar{x})^2$ =	
	***n* – 1 =**	
	S =	

(b) When humans are in danger or under stress they respond by activating the 'fight or flight' response.

Describe the role of adrenaline in the fight or flight response.

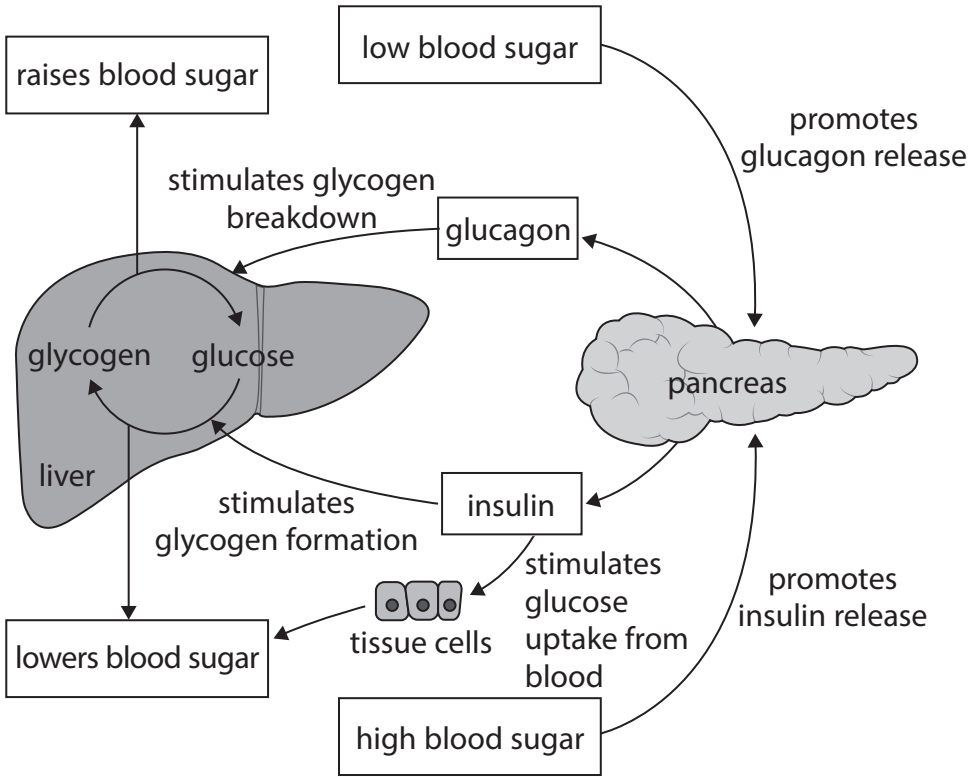
(3)

*(c) Negative feedback is involved in maintaining systems within narrow limits.

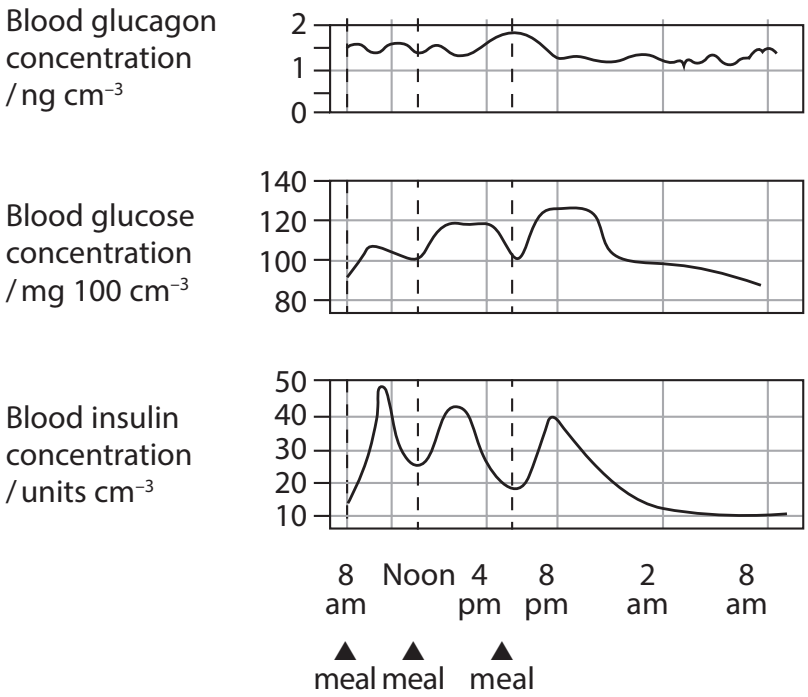
The blood glucose concentration has to be maintained within narrow limits.

Insulin and glucagon are hormones involved in the control of blood glucose levels.

The diagram shows how blood glucose concentrations are controlled in the body.



The graphs show the daily changes in the concentrations of insulin, glucagon and glucose.



Discuss how negative feedback is involved in the control of blood glucose concentrations.

Use the information in the diagram and the graphs to support your answer.

(6)

(Total for Question 7 = 15 marks)

8 The scientific document you have studied is adapted from the article '*Brain aging and neurodegeneration: from a mitochondrial point of view*' by Amandine Grimm and Anne Eckert.

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

(a) Suggest why there is a relationship between the ageing process and neurodegeneration (paragraphs 1 and 2).

(3)

(b) Describe how energy released from glucose is used in oxidative phosphorylation (paragraph 2).

(3)

(c) Explain how free radicals (reactive oxygen species, ROS) can cause damage to mitochondrial DNA (paragraphs 2 and 4).

(3)

(d) "The brain is a remarkable organ composed by highly differentiated cells… with different morphology, according to their role and their localization" (paragraph 6).

Describe how this differentiation can occur.

(3)

(e) Explain what is meant by the phrase 'mitochondrial proteome' (paragraph 7).

(2)

(f) Explain why synaptic mitochondria are more susceptible to ageing than the mitochondria found in other parts of a neurone (paragraph 9).

(2)

(g) Explain why the mitochondrial genome is essential for oxidative phosphorylation (paragraph 10).

(2)

(h) Suggest how damaged mitochondria are removed by 'autophagy' (paragraph 11).

(2)

(Total for Question 8 = 20 marks)

TOTAL FOR PAPER = 90 MARKS

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

Scientific article for use with Question 8

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Scientific article for use with Question 8

Brain aging and neurodegeneration: from a mitochondrial point of view

1 Aging is defined as a progressive time-related accumulation of changes responsible for or at least involved in the increased susceptibility to disease and death. The brain seems to be particularly sensitive to the aging process since the appearance of neurodegenerative diseases, including Alzheimer's disease, is exponential with the increasing age. The aging process was defined by Harman as a 'progressive accumulation of changes with time that are associated with or responsible for the ever-increasing susceptibility to disease and death which accompanies advancing age'. Indeed, age is the main risk factor for prevalent diseases, including neurodegenerative disorders.

2 The brain is a high energy consuming organ that requires about 20% of body basal oxygen to fulfill its function. Thus, it is not surprising that disturbances in brain energy metabolisms lead to disease, ranging from subtle alterations in neuronal function to cell death and neurodegeneration. Cellular energy is mainly produced via oxidative phosphorylation (OXPHOS) taking place within mitochondria. These organelles are often compared to powerhouses, providing cellular energy under the form of ATP molecules. Mitochondria produce the energy required for almost all cellular processes, from cell survival and death, to the regulation of intracellular calcium homeostasis, synaptic plasticity and neurotransmitter synthesis. However, when mitochondria fulfill their physiological functions, they can also be compared to a double-edged sword that, on one hand, produces the energy necessary for cell survival, and on the other hand, induces the formation of reactive oxygen species (ROS) that can be harmful for cells when produced in excess with mitochondria as the first target of toxicity.

Mitochondria and the free radicals theory of aging

3 The 'free-radicals theory of aging' was stated for the first time by Harman in 1956, and postulates that aging, as well as age-associated degenerative diseases, is a consequence of free radicals attacks on cells and tissues. But how these 'harmful' molecules are they generated?

ROS derive mainly from the OXPHOS taking place within mitochondria. Indeed, the production of ATP by mitochondria requires about 85% of oxygen (O_2) consumed by cells. Mitochondrial complex IV reduces O_2 into H_2O using electrons derived from NADH or $FADH_2$ driven in the respiratory chain. An inevitable byproduct of electron transport chain (ETC) activity is the formation of superoxide anion radicals ($O_2^{\cdot -}$), mostly by complexes I and III.

4 In physiological conditions, ROS are involved in processes such as immune response, inflammation, as well as synaptic plasticity, learning and memory. However, when produced in excess, those molecules can induce oxidative stress, damaging proteins and DNA, and inducing lipid peroxidation, with the corresponding mitochondrial structures as the first targets of toxicity. Furthermore, since mitochondrial DNA (mtDNA) is localized close to free radical production sites, it is directly in contact with those molecules and can exhibit oxidative damages. Oxidative stress can trigger cell death and has been implicated in the pathogenesis of many neurodegenerative diseases, such as Alzheimer's disease.

Redox homeostasis and mitochondrial bioenergetics in brain aging

5 A growing body of evidence highlights bioenergetic impairments as well as disturbances in the reduction-oxidation (redox) homeostasis in the brain with increasing age.

Neuronal mitochondria: what makes our brain so special?

6 The brain is a remarkable organ composed by highly differentiated cells that populate different anatomical regions. Neurons are polarized cells with different morphology, according to their role and their localization. These post-mitotic and excitable cells have really high energy requirements: (i) to maintain their membrane potential allowing the propagation of electric signals, (ii) to re-establish the ion balance after the firing of action potential (e.g. via the Na^+/K^+ ATPase activity), (iii) to trigger the release of neurotransmitters by fusion of vesicles to the plasma membrane, (iv) to allow the recapture of neurotransmitters from the synaptic cleft. Glucose oxidation is the most relevant source of energy in the brain, since other fuel sources, such as fatty acid oxidation, have an ATP generation rate too slow to sustain neuronal energy demands, and produce too much ROS that may cause oxidative stress. In consequence, neurons rely almost exclusively on the mitochondrial OXPHOS system to fulfill their energy needs supplied under the form of ATP.

7 Some studies aimed to compare mitochondrial properties in different organs, including the brain. For instance, mitochondria isolated from rat liver, kidney, brain and skeletal muscle showed significant and similar proton leak, but the phosphorylating systems appeared to be more active in the brain and the muscle. Differences in the rat mitochondrial proteome were also observed when comparing the kidney, liver, heart, skeletal muscle, and brain. Moreover, each organ possesses different protein composition, especially in the expression of proteins involved in the OXPHOS system.

8 It is important to note that neurons are post-mitotic cells with a life span similar to that of the whole organism. Unlike in other organs, such as the skin or the liver, damaged neurons are not (or rarely) replaced during life, stressing the importance of protecting systems, including antioxidant defenses, to maintain neuronal integrity and survival. Post-mitotic cells, such as neurons, seem to be more sensitive to the accumulation of oxidative damages compared to dividing cells, and are more prone to accumulating defective mitochondria during aging.

9 In addition, to bring a higher degree of complexity, neurons are exceedingly compartmentalized, comprising structures like: cell body, axon, dendrites, and even more specific compartments that are the synapses. Consequently, a proper mitochondrial distribution is paramount to sustaining the energy requirement at specific locations within the different neuronal compartments. Thus, it is not so surprising that synaptic mitochondria, which need to sustain the energy required for synaptic activity, present functional differences when compared to non-synaptic mitochondria. Indeed, peroxide production was found higher in synaptic mitochondria of rats, compared to non-synaptic ones. Interestingly, aging seems to accentuate the differences between these two populations of mitochondria. In 14-month-old rats, respiration was significantly decreased only in synaptic mitochondria, when compared with 3-month-old rats. Besides, a higher susceptibility to calcium insult was observed only in synaptic mitochondria of old animals. In non-synaptic mitochondria, oxygen consumption was not significantly affected by aging, and both populations of mitochondria generated higher levels of peroxide in 14-month-old animals compared to young animals.

Age-related mitochondrial defects and the importance of mitochondrial dynamics in aging

Mitochondrial fusion/fission and mitophagy

10 Mitochondria possess a residual genome (approximately 16 kilobase) coding for 13 proteins essential for mitochondrial respiratory chain function, which make them unique organelles carrying autonomous DNA. It appears that the quality control of mtDNA replication is not as efficient as nuclear DNA (nDNA), resulting in an increased risk of mtDNA mutations. Fortunately, to avoid the accumulation of such mutations, mitochondria are remarkably dynamic organelles that divide and fuse in order to maintain a homogenous mitochondrial population by content mixing (mtDNA, metabolites, and proteins), quality control and distribution of mitochondria within the cell.

11 Fusion/fission activity is also integrated with mitochondrial quality control pathways allowing the detection and removal of aged or damaged mitochondria through a specific form of autophagy, termed mitophagy. The exact mechanism underlying mitophagy, more specifically what triggers mitophagy, remains to be elucidated in more detail.

12 In summary, when mitochondria fuse, they mix their membranes, matrix and inter-membrane space, including all their content (lipids, proteins, metabolites and mtDNA). After this mixing, mitochondria can divide, sharing equally their new content between two daughter organelles. When a damaged mitochondrion is detected, it is eliminated from the fusion/fission cycle by mitophagy, guaranteeing a homogenous and healthy mitochondrial population. Thus, it is not surprising that defects in mitochondrial dynamics and mitochondrial quality control system may lead to cellular impairments, and was proposed to be involved in the process of aging and neurodegeneration.

Conclusions

13 In this review, we aimed to look at brain aging processes from a mitochondrial point of view, and we showed that:

- Mitochondria are at the center of the free radicals theory of aging by being a source and target of ROS. The age-related increase in brain oxidative stress may lead to protein, lipid as well as DNA oxidation, which in turn affects mitochondrial function. When a pathological threshold is passed, this may trigger cell death by apoptosis.
- Mitochondrial dynamics play an important role in maintaining a healthy organelle population. Impairments in this quality control system may lead to the accumulation of defective mitochondria, as well as inefficient mitochondrial transport and distribution, again leading to synaptic and neuronal degeneration.
- Neurons are particularly vulnerable to oxidative insults and mitochondrial dysfunction given that they are post-mitotic differentiated cells relying almost exclusively on the OXPHOS system to sustain their high energy needs. Besides, distinct mitochondrial populations can be observed in different neuronal compartments (e.g., synaptic vs. non-synaptic), highlighting the importance of proper mitochondrial distribution in these highly compartmentalized cells.