

Please check the examination details below before entering your candidate information

Candidate surname

Other names

Centre Number

Candidate Number

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**Pearson Edexcel International Advanced Level**

**Thursday 24 October 2024**

Morning (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.*

## 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 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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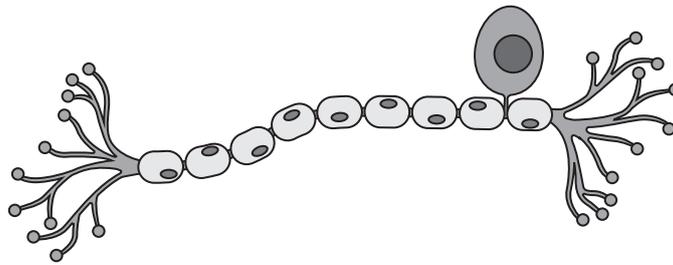
Answer ALL questions.

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 Neurones transmit impulses between receptors and effectors.

The diagram shows a neurone.

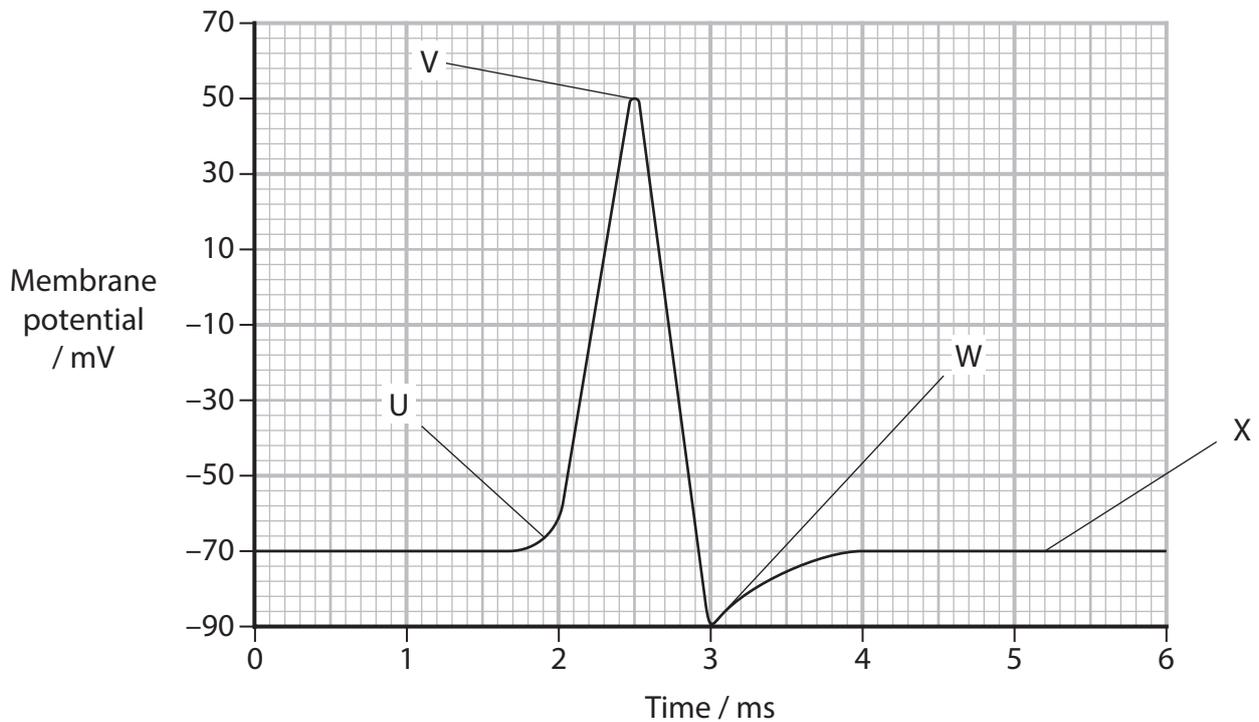


(a) Draw an arrow on the diagram to show the direction of a nerve impulse.

(1)

(b) Nerve impulses travel along axons due to changes in membrane potentials.

The graph shows an action potential in a neurone.



(i) Which is the resting potential for this neurone?

(1)

- A -90 mV
- B -70 mV
- C +48 mV
- D +70 mV

(ii) Which letter on the graph shows where the neurone is hyperpolarised?

(1)

- A U
- B V
- C W
- D X

(iii) Which is the difference in membrane potential between points V and W on the graph?

(1)

- A 40 mV
- B 50 mV
- C 90 mV
- D 140 mV

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(c) Give **two** differences between the **functions** of a motor neurone and a sensory neurone.

(2)

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**(Total for Question 1 = 6 marks)**



2 Plants and animals use chemicals to co-ordinate metabolic activities and development.

(a) (i) Which is a function of gibberellins in plants?

(1)

- A hydrolyse starch to release glucose
- B inhibit elongation of cells
- C regulate the translation of DNA
- D regulate the transcription of genes

(ii) Which is produced by an animal in a 'fight or flight' response?

(1)

- A adenine
- B adrenaline
- C amylopectin
- D antihypertensive



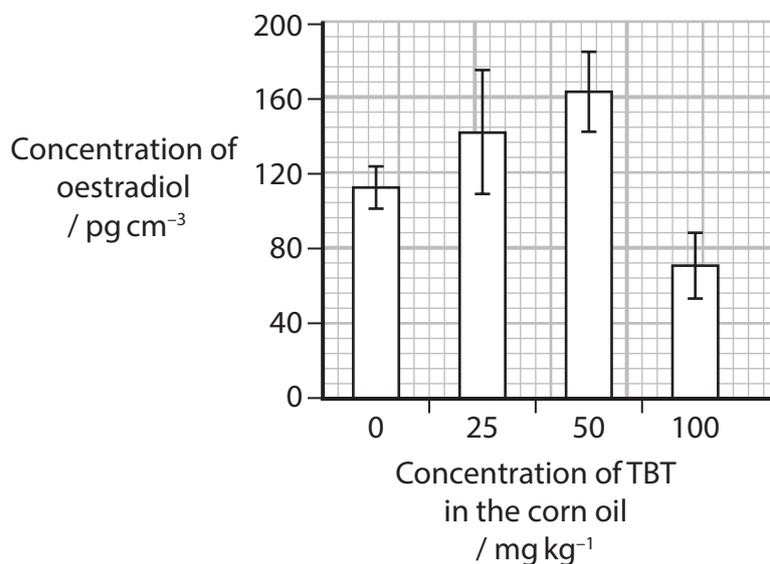
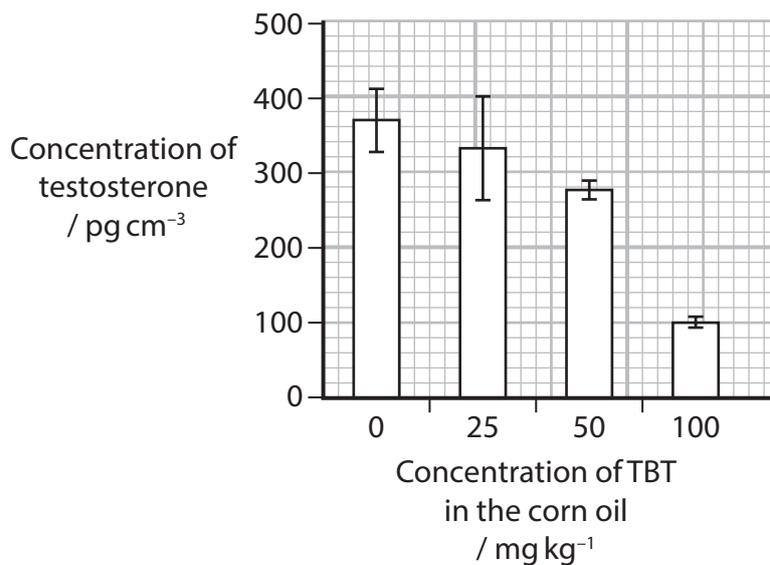
(b) Tributyltin (TBT) is a commonly used chemical in boat building.

The effect of TBT on the blood levels of two steroid hormones, testosterone and oestradiol, was investigated.

Groups of male mice were fed corn oil alone, or corn oil containing different concentrations of TBT.

The concentrations of testosterone and oestradiol in the blood of the mice was measured.

The results are shown in the graphs.





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3 Endurance athletes may suffer from muscle fatigue when contraction of the muscle fibres is disrupted.

It is thought that the disruption of the contraction of muscles is caused by a lack of calcium ions within the muscle fibre.

(a) Explain why a decrease in calcium ions could disrupt the contraction of muscles.

(3)

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(b) The body controls the concentration of calcium ions circulating in the blood.

This concentration is kept within the range 80 to 100 mg dm<sup>-3</sup>.

(i) Name the type of process involved in maintaining calcium ion concentrations within this range.

(1)

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- (ii) The calcium ion concentration in the blood is kept within a range of 6% above and below the mean concentration.

The mean calcium ion concentration in the blood of a person was  $91 \text{ mg dm}^{-3}$ .

Calculate the **maximum** possible difference in the calcium ion concentration in the blood of this person.

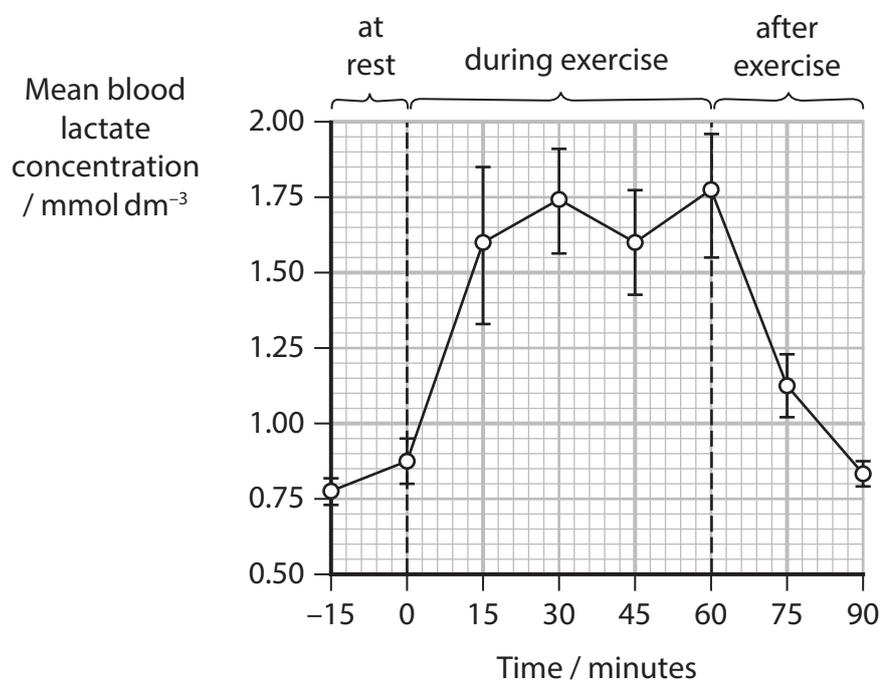
(2)

Answer .....  $\text{mg dm}^{-3}$

- (c) In an investigation, a group of cyclists completed a 30 km time trial in a simulator.

The blood lactate concentration was measured at rest, during exercise and after exercise.

The results are shown on the graph.



(i) Explain the effect on the lactate concentration from 15 minutes to 60 minutes on the graph.

(2)

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(ii) State **one** reason why the lactate concentration was measured 15 minutes before starting the exercise.

(1)

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(iii) State **one** variable that would need to be controlled in this investigation and how this would be achieved.

(1)

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**(Total for Question 3 = 10 marks)**

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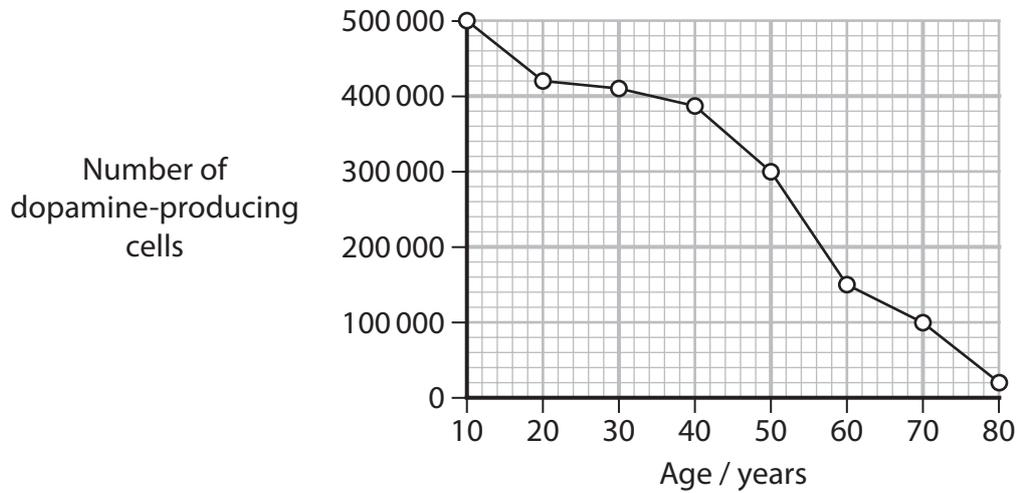
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4 Parkinson's disease is caused by a lack of specific neurotransmitters.

The graph shows the effect of age on the number of dopamine-producing cells in people who develop Parkinson's disease.



(a) In people without Parkinson's disease, the number of dopamine-producing cells rarely falls below 350 000.

Explain why the symptoms of Parkinson's disease increase with age.

Use the graph to support your answer.

(4)

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(b) The drug L-DOPA is used in tablet form to treat Parkinson's disease.

This drug is converted to dopamine by an enzyme found in the digestive system and the brain.

Carbidopa is an inhibitor of the enzyme found in the digestive system.

Suggest why carbidopa is given to patients when they are treated using L-DOPA in tablet form.

(2)

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5 Pronghorns are similar to antelopes and are native to North America.

They live in open areas of grasslands.

The photograph shows a pronghorn.



(Source: © Paul Tessier/Shutterstock)

(a) These pronghorns can run long distances at speeds of 90 km per hour.

(i) Which of the following features of pronghorns is an adaptation for running long distances at high speeds?

(1)

- A** decreased glomerular filtration rate
- B** increased number of slow twitch muscle fibres
- C** narrower airways
- D** smaller cardiac output





- (b) Scientists measured the mass, resting metabolic rate and pulse rate of five mammals.

The table shows the results.

Mammal	Mass / kg	Resting metabolic rate / joules second <sup>-1</sup>	Pulse rate / beats per minute
rat	0.260	1.45	420
dog	16.0	20.0	100
sheep	45.0	50.1	70
human	70.0	87.0	72
cow	400	267	40

- (i) Describe the relationships between mass, resting metabolic rate and pulse rate shown in the table.

(3)

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- (ii) When a human exercises, the metabolic rate is increased and heat energy is released.

Describe how the body temperature of a human is maintained at 37°C during exercise.

(3)

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**(Total for Question 5 = 11 marks)**

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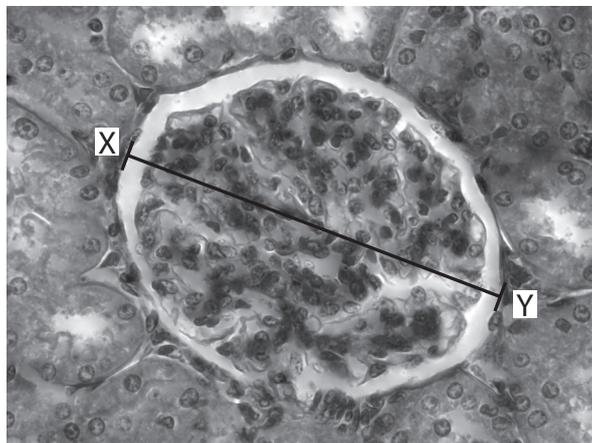
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- 6 The kidney has an important role in the regulation of the plasma concentration and blood volume.

The photograph shows a Bowman's capsule (renal capsule).

The line from X to Y shows the diameter of the Bowman's capsule.



(Source: © Science Photo Library/Alamy Stock Photo)

- (a) The diameter from X to Y is 70 nm.  
(i) Calculate the magnification of this photograph.

Give your answer in **standard form**.

(2)

Answer .....



(ii) Calculate the volume of this Bowman's capsule.

Assume that this Bowman's capsule is spherical.

Use the equation:

$$V = \frac{4}{3}\pi r^3$$

Give your answer to **two** significant figures.

(2)

Answer..... nm<sup>3</sup>

(b) (i) Which is the specialised receptor that detects changes in the plasma solute concentration?

(1)

- A baroreceptor
- B chemoreceptor
- C osmoreceptor
- D thermoreceptor

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- (ii) The Bowman's capsule of a healthy kidney filters up to 7.5 g of glucose per hour.

Calculate the rate of glucose filtration in **milligrams per second**.

(2)

Answer..... mg s<sup>-1</sup>

**(Total for Question 6 = 13 marks)**

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- 7 Some diseases, and certain cancers, are thought to be caused by a lack of specific neurotransmitters.

This means they can be treated using drugs which increase the concentration of these neurotransmitters.

Some of these drugs are manufactured using genetically modified (GM) organisms.

- (a) Which is a description of a GM organism?

(1)

- A an amplified sequence of nucleic acid
- B an organism containing genetic material from another species
- C a virus containing DNA
- D DNA that contains a mutation

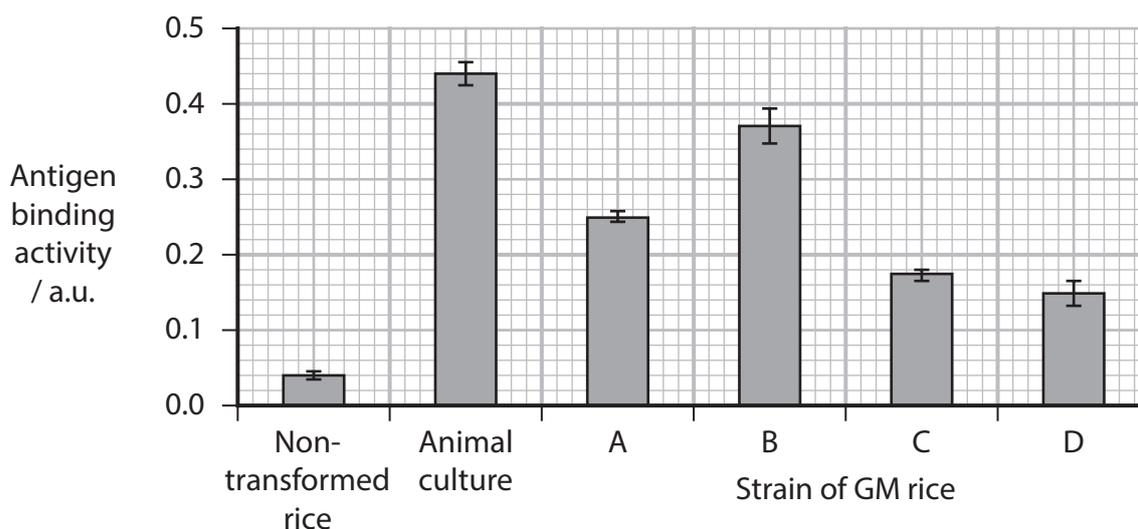
- (b) Bevacizumab (BVZ) is an antibody used to treat brain cancer patients.

This antibody is produced using animal cell cultures.

A new method of producing BVZ has been developed using genetically modified (GM) rice.

The graph compares the antigen binding activity of a BVZ antibody produced using:

- a control using non-transformed rice
- animal cell culture
- four strains of GM rice (A, B, C and D).



(i) Describe **three** conclusions that can be made from these results.

(3)

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(ii) Explain how BVZ antibodies can cause the destruction of cancer cells.

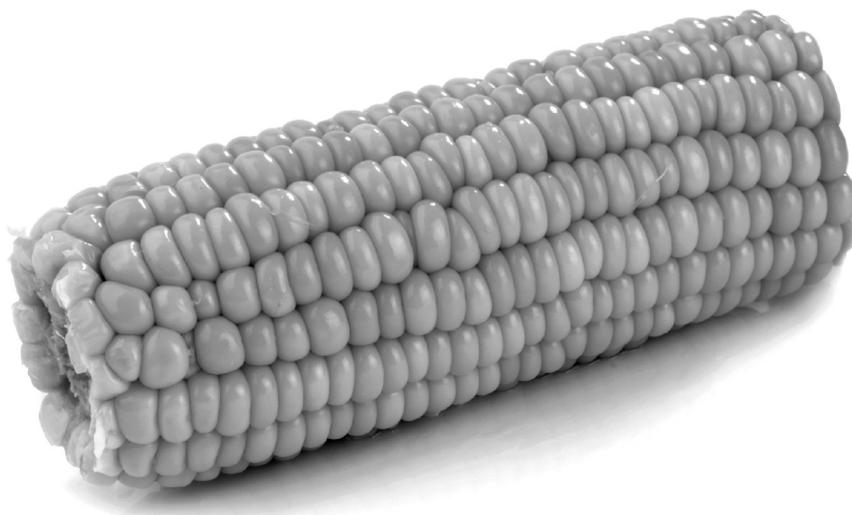
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\*(c) Maize is a major food crop.

The photograph shows a maize cob with rows of grains.



(Source: © art nick/Shutterstock)

Maize can be infected by a fungus.

This fungus produces a toxin that affects plant growth and is poisonous to animals.

This fungus can be genetically modified (GM).

In an investigation, maize plants were infected with normal fungus or infected with GM fungus.

The table shows the mean and standard deviation for growth measurements of the maize and the concentration of toxin.

Crop infected with	Plant height / cm	Number of grains per cob	Concentration of toxin / a.u.
Normal fungus	$285.0 \pm 60$	$113 \pm 2$	$530 \pm 100$
GM fungus	$320.0 \pm 33$	$117 \pm 2$	$270 \pm 35$





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(Total for Question 7 = 12 marks)



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8 The scientific article you have studied is adapted from articles about Alzheimer's disease published in *The Conversation*: August 31, 2023 and November 13, 2022

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

(a) Describe the possible role of hypertension (high blood pressure) in causing dementia (Paragraphs 2 and 19).

(2)

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(b) Suggest why the protein beta-amyloid from the fatty membranes surrounding nerve cells 'is chemically sticky, gradually clumping together' (Paragraph 7).

Use your knowledge of protein structure to support your answer.

(3)

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(c) Describe the information that would be obtained from using a combined MRI and PET scan of the brain (Paragraph 13).

(2)

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(d) State **one** reason why it might be considered unethical to tell people they are at risk of developing cognitive impairment (Paragraph 15).

(1)

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(e) Explain why a 'falling blood pressure' might result in poor brain health (Paragraph 20).

(3)

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(f) Some genes may be linked to an increase in the risk of dementia.

Describe how scientists could identify the link between these genes and the risk of dementia (Paragraph 28).

(3)

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(g) Describe what is meant by the term 'monoclonal antibody' (Paragraph 31).

(2)

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(h) Give **one** reason why a placebo was used in the donanemab trial (Paragraph 33).

(1)

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(i) Swelling is a symptom of inflammation.

Explain why lecanemab may result in 'brain swelling' (Paragraph 35).

(2)

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(j) Successfully clearing amyloid from the brain had only a small effect.

Suggest **one** reason why researchers are suggesting the need to start using the drugs even 'earlier in the disease' (Paragraphs 44 and 45).

(1)

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**(Total for Question 8 = 20 marks)**

**TOTAL FOR PAPER = 90 MARKS**



# Pearson Edexcel International Advanced Level

**Thursday 24 October 2024**

Morning (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

### Article 1

#### **We've been studying the same people for 76 years – this is what we've found out about Alzheimer's disease.**

1. In 2016, a sub-study of 502 people from the cohort, known as Insight 46, was started specifically to address brain ageing and dementia, and their life course influences. Using cutting-edge imaging and AI technology, we have been observing their brains ever since.
2. The results from our studies have revealed several important insights, including:
  1. Cognitive function in childhood relates to cognitive performance 70 years later.
  2. Education does not just increase opportunities but is significantly associated with brain health in later life.
  3. Midlife appears to be the time when hypertension and cardiovascular risk may influence dementia risk.
  4. While weight gain in midlife has many adverse health implications, weight loss in later life may in some cases be a sign of impaired brain health.

#### **Tracking subtle variations**

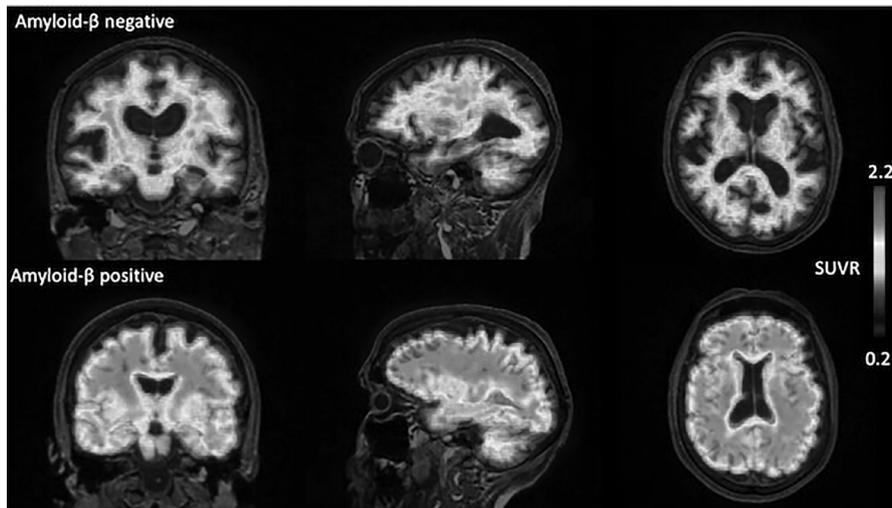
3. When members of the cohort reached their mid-30s, Mike Wadsworth, the then director of the NSHD {National Survey of Health and Development}, focused the study on physical and mental health, particularly the measures that show subtle variation in the general population, such as blood pressure, lung function, physical performance and emotional symptoms. This approach was enhanced by the subsequent directors, Diana Kuh and Nish Chaturvedi.
4. Cognitive function was picked up again at age 43 with a new emphasis on skills vulnerable to decline, such as memory, concentration and mental speed. These measures, along with those of physical and psychiatric health and their life course influences, form the platform on which we built our brain study, Insight 46.

#### **What is dementia?**

5. Dementia is an ancient word meaning "out of mind", but today it refers to a syndrome of acquired (not present from birth), progressive cognitive impairment, severe enough to interfere with everyday activities such as planning meals, managing bills and medicines, and housekeeping.
6. As cognitive impairment worsens, these activities become more impaired, eventually disrupting basic self-care such as dressing and bathing. Sometimes this is accompanied by depression, paranoia, aggression, wandering or reversed sleep-wake cycles. Dementia is therefore very different from the mild cognitive changes that occur in normal ageing.
7. Alzheimer's disease is the commonest form of dementia. On a biological level, a key process is the depositing of beta-amyloid protein in the brain. This is a protein that comes from the fatty membrane surrounding nerve cells. It is chemically sticky, gradually clumping together and interfering with nerve function and triggering inflammation. These clumps gradually gather between the nerve cells in the brains of people with Alzheimer's disease and become plaques – hard, insoluble accumulations of beta-amyloid proteins.
8. These plaques are thought to be an early hallmark microscopic feature of Alzheimer's. However amyloid plaques in themselves are not sufficient to cause dementia which is more closely related to accumulation of another, likely downstream, protein called tau which clumps within nerve cells in the form of tangles.



9. Accumulation of these proteins leads to nerve cell death which leads to brain shrinkage (atrophy) which can be seen using MRI scans. The diagnosis of Alzheimer's dementia remains predominantly clinical, requiring evidence of decline over time in at least two cognitive areas, such as memory, language, attention or problem solving. Contemporary criteria also involve investigations including MRI or CT brain scanning and, in some cases, spinal fluid or positron emission tomography (PET) scans. PET scans can be used both to visualise and quantify abnormal protein deposition within the living brain. For Insight 46, we use a tracer that is injected into the body, enters the brain and which highlights where any amyloid is accumulating.



(Source: © Marcus Richards and Jonathan M Schott, The Conversation)

A PET scan. The top row is of a normal participant and below is one showing beta-amyloid

10. Alzheimer's disease is only one of many forms of dementia. Other causes include other neurodegenerative disorders due to the accumulation of different proteins, and cerebrovascular disease where the blood supply to the brain is interrupted, for example, from blood vessel narrowing, blockage or bleeding.

### The beginning of Insight 46

11. While developing what was to become the mental ageing research programme for our team, we acknowledged that it would be an exciting new direction to scan the brains of NSHD participants.
12. Previous work at the Dementia Research Centre at the University College London Institute of Neurology had shown that MRI scans from patients with rare genetic forms of Alzheimer's disease showed excess brain shrinkage occurred before symptoms started.
13. In addition, UCL had installed the UK's first scanner that allowed MRI and PET to be measured simultaneously. As NSHD participants were approaching the age of 70 and still relatively healthy, this raised an exciting possibility: our two teams could combine forces and combine the uniquely rich life course data with state-of-the-art scanning to explore the brain changes that occur before symptoms become apparent in a birth cohort – something that had never been done before.



(Source: © horsemen / Alamy Stock Photo)

PET-MRI scanner

## What have we found so far?

### One, Amyloid accumulation starts before symptoms

14. We found that around 18% of “cognitively normal” people from the cohort had amyloid PET scans like those seen in people with Alzheimer’s disease – a finding that tallies with other studies in people around the world who don’t have symptoms. These individuals also had slightly lower performance on sensitive tests of cognition and slightly increased rates of brain shrinkage.
15. While the significance of the finding for amyloid frequency is unclear – and hence our protocols and consent processes mean that unlike some MRI findings we do not give the results to participants – we think that these individuals are at higher risk of developing cognitive impairment in the future, something we plan to look out for closely in the years to come.

### Two, Child cognitive tests indicate brain function later in life

16. We found that cognition assessed in childhood predicted cognition around 60 years later. This is consistent with earlier findings for the whole cohort, suggesting that some aspects of cognitive performance are stable over a lifetime. This matters because cognitive function is not just about the mind – it helps to shape everyday skills, supports quality of life and ultimately predicts how long we live.
17. However, the level of cognitive performance can be potentially improved. In the same report, education and occupation in midlife predicted later cognition after taking account of childhood cognitive scores. We had seen this in the whole cohort too, which counters an old argument, still sometimes made, that education is nothing more than a marker of IQ. In other words, level of education and type of occupation can positively affect cognitive performance in later life regardless of cognitive skills in early childhood.
18. It also emphasises that education does not just increase opportunities but has a significant effect on brain health.



### Three, Importance of early heart health checks

19. Some of the first publications from Insight 46 showed that high and rising blood pressure in those aged in their 40s and – in some cases their 30s – predicted smaller brain volume. There are several possible mechanisms for this, including microstructural damage from high blood pressure and a higher burden of small blood vessel damage in the brain. The latter is thought to be a marker of brain frailty, raising the risk of stroke, dementia, depression, impaired mobility and death.
20. Similar outcomes were seen in relation to heart health in general, using an index that includes blood pressure, use of anti-hypertension medication, diabetes, smoking and high body weight. Conversely, falling blood pressure in later life may in some cases be a marker of poor brain health.
21. Similar findings may also apply to body weight. A follow-up analysis found that declining body weight in the two years before the scan predicted the presence of amyloid.
22. These findings have significant implications for public health, suggesting that routine checking of heart health, and blood pressure, in particular, may need to start much younger than is typically recommended – probably at or before the age of 40.

### Four, A blood test for Alzheimer's disease

23. Most experts will agree that when we have new drugs for Alzheimer's disease, they are likely to have maximum benefits if taken early in the disease, and preventing the onset of cognitive decline would clearly be preferable to trying to slow or halt memory decline that has already started. It is unlikely that the expensive PET scans we are conducting in Insight 46 will be able to screen whole populations, so there is much interest in developing blood tests instead.
24. Using state-of-the-art methods sensitive enough to detect 1g of salt dissolved in one million trillion litres of water, we were able to show that a blood marker is capable of detecting amyloid in the brain with about 85% accuracy. We are currently looking at a range of new blood tests that seem to be even better at detecting amyloid, and at even lower cost.
25. The prospect of new drugs that can clear amyloid from the brain provide even more reason to intensify efforts to identify amyloid pathology early, cheaply and at scale.
26. Studies using the whole NSHD cohort have also shown complex relationships between cognitive function and several bodily functions, including those of the lungs, bones and kidneys. This probably reflects biology shared between the brain and these organs. We are currently looking to see how these findings relate to the brain health measures we have made in Insight 46. A similar "common cause" story applies to depression and cognitive function, and we are currently looking into how depression relates to the brain.
27. On the other hand, health-related behaviour such as smoking, physical exercise and healthy diet genuinely seem to predict cognitive function (negatively for smoking, positively for exercise and diet).
28. We have been emphasising prediction of health problems, but it's equally important to understand resilience. Why can some people navigate through or escape these problems altogether even though they are apparently at risk, from genes or certain disadvantages in life? Does it come down to pure luck? But luck is, of course, just another way of saying we don't know something.

## Article 2

### New Alzheimer's drugs don't deserve the hype – here's why.

29. A prominent childhood memory is of my grandparents living with and then dying from dementia. As is universal with dementia, there was a double blow: watching my grandparents lose their identity and seeing the suffering of those closest to them.
30. As a junior doctor on a specialist dementia ward when I was in my 20s, I watched the same stories play out for family after family, feeling largely powerless to help. Now in my 30s, I conduct public health research to understand what we can do to prevent, delay or improve the experience of dementia – the leading cause of death in England.
31. Naturally, this makes me desperate for good news on treatment options for Alzheimer's disease – the main cause of dementia. Enter three drugs (aducanumab (trade name Aduhelm), lecanemab (Leqembi) and donanemab) that remove amyloid, the protein thought to cause Alzheimer's disease. Unlike their many predecessors, that also successfully removed amyloid from the brain, these drugs were the first to slow cognitive decline.  
[drugs with an ending of mab are whole monoclonal antibodies]
32. This breakthrough was hailed as “the beginning of the end for Alzheimer's disease”, but how useful are these drugs going to be? There are four key shortcomings to consider:

#### One, Tiny benefits

33. In the donanemab trial, the people taking the drug declined on average by ten points on a 144-point cognitive scale. The placebo group declined by 13 points.
34. Consistent with the patterns in the trials of the other two drugs, this tells us that all groups in all these trials declined and the amount of decline that was avoided by taking the drug – in this case donanemab – (three points) was a lot smaller than the amount of decline that still occurred (ten points). The difference in the amount of decline was so small that it would probably not be noticeable to the doctors looking after these patients.

#### Two, Side-effects

35. Through regular magnetic resonance imaging (MRI) scans, one in six people taking lecanemab was found to have evidence of brain bleeding, and one in eight had brain swelling.
36. Regular scans will sometimes pick up these pathologies in dementia patients. And, indeed, one in 11 of those in the placebo group had evidence of bleeding, while one in 59 had swelling. For most people, these events were only detectable by MRI and not through showing any specific symptoms. However, the effects of this drug's damage to the brain, particularly the long-term effects, are unknown.
37. Sadly, there have also been a few deaths attributed to these drugs.

#### Three, Very expensive

38. Aducanumab was marketed in the US for US\$45,000 (£35,000) per patient per year (later reduced to US\$20,000 to increase demand), and lecanemab for US\$26,500. This is just for the drug itself. Health systems also need to pay for additional scans to test for eligibility, monitoring and management of side-effects, and staff to run infusion clinics.
39. The donanemab trial suggested that treatment could end when brain scans showed sufficient amyloid clearance. But we don't know if amyloid will return after some time. Regular monitoring for amyloid recurrence and repeated bouts of treatment would add further costs.



40. There are other impositions for patients: attending centres every two to four weeks for drug infusions and regular monitoring and worrying about side-effects.



(Source: © Dragon Images/Shutterstock)

Patients would need regular infusions.

#### **Four, Highly selective trials**

41. It is accepted that not all trial “efficacy” (the effect seen in a specialised trial context, designed to maximise the likelihood of treatments working, such as including only uncomplicated cases) will convert into clinical “effectiveness” (the effect seen when drugs are given to relatively more complex patients in busy, real-world clinical settings). This is concerning, because there’s little wiggle room before the effects become undetectable. And, while this is the case for all diseases, Alzheimer’s is likely to be an extreme example.
42. For every ten patients that doctors thought might be eligible for these trials, seven or eight were rejected. People with brain pathologies other than amyloid, such as vascular damage or Lewy bodies, and those with significant other medical problems, which might have clouded the trial results and increased the risk of side-effects, were excluded.
43. If the drug eligibility is restricted to match the trial eligibility, then very few people will be eligible. If eligibility is broader, then already small effects are likely to be even smaller and side-effects more pronounced.

#### **Profound shortcomings**

44. There’s more. The trials selected people at the earliest stages of the disease – that is, when symptoms had only recently developed – and successfully cleared amyloid, yet patients still declined almost as fast. So inevitably, researchers ask: maybe we need to start the drugs even earlier? But how?
45. People in the trials were, on average, five to ten years younger than most people are at Alzheimer’s diagnosis in the US and UK. And catching people earlier in the disease is problematic because most people with amyloid but no cognitive symptoms won’t get dementia before they die.

46. Sadly, I don't think these drugs can make a big difference for people currently, or soon to be, living with Alzheimer's disease. Also, the shortcomings are so profound, despite decades of expensive trials and patient sacrifice, I think it's time to take the amyloid blinkers off and prioritise exploring other, neglected, options for treating dementia.

This isn't the beginning of the end of Alzheimer's, but perhaps it should be the end of the anti-amyloid drug pathways.

**Sources:**

**Article 1**

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**Article 2**

New Alzheimer's drugs don't deserve the hype – here's why. S Walsh. *The Conversation*. Published: August 31, 2023 2.46pm BST

