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.
- Show your working in any calculation questions and include units in your answer where appropriate.
- Answer the questions in the spaces provided
  - *there may be more space than you need.*
- You may use a scientific calculator.
- 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.

Information

- The total mark for this paper is 100.
- The marks for each question are shown in brackets
  - *use this as a guide as to how much time to spend on each question.*

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.
The internal conditions within the body are maintained by homeostatic mechanisms. The regulation of blood glucose involves homeostatic mechanisms.

(a) The diagram shows part of the sequence of events when there is an increase in blood glucose levels.

1. Increase in blood glucose levels
2. Beta cells in the pancreas secrete insulin
3. Insulin stimulates facilitated diffusion of glucose into cells
4. Glucose used in cellular respiration
5. Glucose converted to fatty acids and glycerol
6. Glucose converted to glycogen

(i) Describe how glucose moves into cells by facilitated diffusion.

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(ii) Explain how the structure of glycogen allows it to be an energy store.

(b) Beta cells in the pancreas produce insulin when there is an increase in glucose levels in the blood.

   Transcription factors are involved in the activation of the insulin gene.

   Explain how transcription factors could activate insulin gene expression in beta cells.

(Total for Question 1 = 8 marks)
Obesity can be affected by both genetic and environmental factors. An indicator of obesity is the body mass index (BMI).

The effects of a gene called FTO, saturated fats and physical exercise on BMI were investigated.

There are two alleles (FTO\textsuperscript{T} and FTO\textsuperscript{C}) at the FTO locus.

(a) (i) Which of the following describes what is meant by the term locus?

☐ A genetic code for a protein
☐ B holds together sister chromatids
☐ C location of a gene on a chromosome
☐ D paternal part of a genome

(ii) Compare and contrast the structures of a saturated fatty acid and an unsaturated fatty acid.
(b) The effects of saturated fats in the diet on the BMI in individuals with different FTO genotypes are shown in the graph.

![Graph showing BMI for different genotypes and diet types]

Deduce the effect of environmental and genetic factors on BMI.

(Total for Question 2 = 7 marks)
3 Sepsis is a bacterial infection in the bloodstream. Sepsis can cause tissue death in limbs. This may require parts of a limb to be removed (amputation).

(a) Open wounds can become infected by bacteria, leading to sepsis.

Explain why bacteria are able to multiply in the bloodstream when they enter the body.

(b) Sepsis can cause blood clots to form and block the supply of blood to tissues in the limbs.

Explain why blood clot formation in capillaries could cause tissues to die.
(c) Extensor and flexor muscles are involved in the movement of the lower leg as shown in the diagrams.

(i) Explain how the extensor and flexor muscles bring about movement of the lower leg.

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(ii) Individuals who have had limbs amputated can use prostheses to compete in athletic events.

A transtibial amputation involves the removal of part of the lower leg below the knee. Extensor and flexor muscles are still attached to the parts of the lower leg bones (the tibia and fibula) that remain.

The photograph shows Paralympic athletes competing in the 100m final in London 2012. The three athletes shown have all had transtibial amputations.

Deduce how athletes with transtibial amputations are able to move their prosthetic limbs during a race.

(Total for Question 3 = 8 marks)
4 Visual development requires exposure of the visual cortex to environmental signals during a critical period.

The diagram shows parts of the brain, including the visual cortex.

(a) The visual cortex processes information received from the retina.

(i) The non-protein part of the light-absorbing pigment in the rod cells of the retina is called

- [ ] A IAA
- [ ] B ops in
- [ ] C retinal
- [ ] D rhodopsin

(ii) The part of the brain involved in interpreting the information processed in the visual cortex is

- [ ] A
- [ ] B
- [ ] C
- [ ] D
(b) Describe the role of visual stimulation on the development of the visual cortex during the critical period.

(iii) Explain how fMRI can be used to identify the part of the brain involved in interpreting information from the visual cortex.

(Total for Question 4 = 8 marks)
Athletic competitions often take place during the summer months when ambient temperatures are high.

High ambient temperatures affect marathon runners.

Heat stress occurs when the core body temperature rises above 40 °C.

(a) Describe how thermoregulatory mechanisms are controlled to help marathon runners avoid heat stress.
(b) Physical and physiological differences between males and females affect thermoregulation.

The graph shows the effect of a mean increase in body temperature on the rate of sweat production by males and females.

Female marathon runners have smaller bodies, with a larger ratio of skin surface to body mass than males.

Male marathon runners have less body fat than females: 5–11% compared with 10–15%.

Comment on how gender could affect thermoregulation in marathon runners.

(4)
When running a marathon, both heart rate and stroke volume increase.

The graph shows the effect of exercise intensity on stroke volume for marathon runners.

(i) Cardiac output is the product of stroke volume and heart rate.

During a race, a marathon runner’s exercise intensity increased from 0 to 100%. The table shows the effect on the runner’s heart rate.

<table>
<thead>
<tr>
<th>Exercise intensity (%)</th>
<th>Heart rate / bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>55</td>
</tr>
<tr>
<td>100</td>
<td>160</td>
</tr>
</tbody>
</table>

Calculate the increase in cardiac output for a marathon runner during a race.

Give your answer in dm³ min⁻¹.

.............................................................. dm³ min⁻¹
(ii) Explain why it is necessary for the cardiac output of marathon runners to increase during a race.

(Total for Question 5 = 12 marks)
Anabolic steroids and testosterone have been used as performance-enhancing drugs by some athletes. These drugs can increase muscle mass and strength.

(a) An investigation was carried out to assess the effect of doses of testosterone on muscle size.

A group of men was randomised into four groups: A, B, C and D. Groups A and B were given a placebo. Groups C and D were both given doses of testosterone. Groups A and C had no exercise training. Groups B and D were given exercise training.

The cross-sectional area of the triceps muscle of each individual was measured at the start of the investigation and after 10 weeks.

The results are shown in the table.

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Mean cross-sectional area of muscle / mm$^2$ ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A Placebo without exercise</td>
</tr>
<tr>
<td>Triceps – at the start</td>
<td>3621 ± 213</td>
</tr>
<tr>
<td>Triceps after 10 weeks</td>
<td>3539 ± 226</td>
</tr>
</tbody>
</table>

(i) Deduce the effect of testosterone on the size of the triceps muscle. 

(2)
(ii) The purpose of the placebo is to

- A increase the accuracy of the measurements
- B increase the reproducibility of the data
- C show that exercise has an effect
- D show that testosterone has an effect

(b) In another investigation, groups of men were given either a placebo or 300 mg of testosterone per week for two weeks. The concentrations of different lipoproteins (HDL and LDL) in the blood were measured at the start of the investigation and after two weeks.

The results of the investigation are shown in the graph.

![Graph showing lipoprotein concentrations](image)

(i) The ratio of total cholesterol to HDL is used as an indicator of the risk of cardiovascular disease. The higher the ratio of total cholesterol to HDL, the greater the risk.

In this investigation, the men given the placebo had a total cholesterol to HDL ratio of 4.2:1 after two weeks.

Calculate the ratio of total cholesterol to HDL for those taking testosterone after two weeks.

Ratio of total cholesterol to HDL 

\[
\text{Ratio} = \frac{\text{Total Cholesterol}}{\text{HDL}}
\]

(2)
*(ii) Doses of testosterone are used to enhance performance in sports by increasing muscle mass and therefore strength.

- Testosterone increases the activity of an enzyme in the liver that breaks down HDL.
- The production of cholesterol is catalysed by the enzyme HMG CoA reductase (HMGCR).
- Testosterone increases levels of mRNA for HMGCR.

Explain why using testosterone as a performance-enhancing drug is unacceptable in terms of risks to health.

(Total for Question 6 = 11 marks)
The arctic ground squirrel (*Spermophilus parryii*) lives in Alaska. It has small ears, a cylindrical body and a shorter tail than other species of ground squirrel.

The arctic ground squirrel can survive cold winters by hibernating for up to eight months per year. When hibernating, arctic ground squirrels use stored fat supplies as an energy source.

(a) Which combination of adaptations shown by the arctic ground squirrel have been described?

- A anatomical and behavioural only
- B anatomical and physiological only
- C anatomical, behavioural and physiological
- D behavioural and physiological only
(b) During hibernation, the core body temperature of an arctic ground squirrel can fall from 37 °C to −3 °C.

The table shows the effect of air temperature on the metabolic rate in the arctic ground squirrel.

<table>
<thead>
<tr>
<th>Air temperature / °C</th>
<th>Metabolic rate / cm³ oxygen g⁻¹ hour⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>−16</td>
<td>0.18</td>
</tr>
<tr>
<td>−8</td>
<td>0.08</td>
</tr>
<tr>
<td>−4</td>
<td>0.04</td>
</tr>
<tr>
<td>0</td>
<td>0.02</td>
</tr>
<tr>
<td>4</td>
<td>0.02</td>
</tr>
<tr>
<td>8</td>
<td>0.02</td>
</tr>
<tr>
<td>12</td>
<td>0.02</td>
</tr>
</tbody>
</table>

(i) Calculate the change in metabolic rate for an arctic ground squirrel, with a body mass of 850g, as the air temperature increases from −16 °C to 4 °C.

Give your answer in dm³ oxygen day⁻¹. (3)
(ii) When the air temperature was −4 °C, the respiratory quotient (RQ) for the arctic ground squirrel was calculated as 0.77.

The RQ value can indicate the respiratory substrate as shown in the table.

<table>
<thead>
<tr>
<th>RQ value</th>
<th>Respiratory substrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>Carbohydrate</td>
</tr>
<tr>
<td>0.9</td>
<td>Protein</td>
</tr>
<tr>
<td>0.7</td>
<td>Lipid</td>
</tr>
</tbody>
</table>

Intermediate values indicate a mixture of respiratory substrates.

Which of the following respiratory substrates were used by the arctic ground squirrel when the air temperature was −4 °C?

☐ A carbohydrate and protein
☐ B lipid only
☐ C lipid and protein
☐ D protein only
(iii) The data for calculating metabolic rate are collected using a respirometer.

The rate of respiration for small mammals can be measured using a continuous flow respirometer. A continuous flow respirometer circulates air through a chamber containing the animal. The rate of air flow can be measured using flowmeters on the inlet and outlet tubes.

![Diagram of a continuous flow respirometer with an animal inside a chamber connected by inlet and outlet tubes with flowmeters.]

Devise a procedure using a continuous flow respirometer to collect the data required to calculate the metabolic rate of an arctic ground squirrel.

(Total for Question 7 = 9 marks)
People with Guillain-Barré syndrome (GBS) suffer from a rapid onset of muscle weakness. It is thought that GBS is caused by damage to the peripheral nervous system.

(a) The diagram shows some typical neurones.

(i) Which of these is a sensory neurone?

- [ ] A  W
- [ ] B  X
- [ ] C  Y
- [ ] D  Z

(ii) The axons of some neurones are surrounded by a myelin sheath.

The main component of myelin is a glycolipid.

Glycolipids are formed from lipids attached to a chain of

- [ ] A  amino acids which are joined by glycosidic links
- [ ] B  amino acids which are joined by peptide bonds
- [ ] C  sugar molecules which are joined by ester bonds
- [ ] D  sugar molecules which are joined by glycosidic links
(iii) Describe the role of the dendrites in a neurone.

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(b) The speed of conduction along a motor neurone can be calculated.

The time taken for a stimulus (S) to produce a response (R) further along the neurone is recorded.

Using two stimuli, a known distance apart, allows the speed of conduction to be calculated.

Calculate the speed of conduction for the neurone shown.

(2) \[ \text{cm s}^{-1} \]
In individuals with GBS, the immune system attacks and destroys the myelin sheath surrounding some neurones.

Neurone conduction was studied in an individual with GBS and in an individual without GBS. The results are shown in the table.

<table>
<thead>
<tr>
<th>Individual</th>
<th>Sensory neurone</th>
<th>Motor neurone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Speed of conduction / metres per second</td>
<td>Size of action potential / mV</td>
</tr>
<tr>
<td>With GBS</td>
<td>54</td>
<td>35</td>
</tr>
<tr>
<td>Without GBS</td>
<td>58</td>
<td>33</td>
</tr>
</tbody>
</table>

Explain why GBS caused muscle weakness in this individual.

(Total for Question 8 = 11 marks)
9 Plasmin is an enzyme that digests fibrin.

Plasmin is produced, in the blood, from an inactive form of the enzyme called plasminogen.

\[
\text{plasminogen} \quad \xrightarrow{\text{enzymatic activity}} \quad \text{plasmin}
\]

\[
\text{fibrin} \quad \xrightarrow{\text{digestion}} \quad \text{digested fibrin}
\]

Pharmaceutical companies have developed drugs that inhibit the activity of plasmin. One of these drugs, tranexamic acid, is used in surgery to reduce blood loss.

(a) Explain why tranexamic acid will result in reduced blood loss during surgery. (3)
(b) The active site of the plasmin enzyme binds to the amino acid lysine on the fibrin protein molecule.

Plasmin binds to part of the fibrin molecule in order to break down the fibrin. The diagrams show the structure of lysine in the fibrin polypeptide and the structure of tranexamic acid.

Deduce why tranexamic acid prevents plasmin breaking down fibrin. (3)
(c) The activity of plasmin in a sample can be determined using fibrin plates.

Fibrin plates are produced by mixing thrombin and fibrinogen into molten agar and pouring the mixture into a Petri dish.

Once the agar has set, wells are cut in the fibrin plate and solutions containing plasmin are placed in the wells.

The effect of different plasmin concentrations on the fibrin plates is shown in the diagram and the photograph. The numbers on the diagram indicate the plasmin concentration.

(i) The relationship between plasmin concentration and fibrin digestion shows

- A inverse correlation
- B negative correlation
- C no correlation
- D positive correlation
*(ii)* Scientists are developing new plasmin inhibitors.

Devise an investigation, using fibrin plates, to compare the effectiveness of a new inhibitor with tranexamic acid.

(Total for Question 9 = 13 marks)
10 Glucosaminoglycans (GAGs) are the by-products of chemical reactions inside cells. GAGs are broken down by enzymes inside lysosomes in cells.

Mucopolysaccharidosis type I (MPS I) is a genetic condition that results in the build-up of GAGs inside cells.

MPS I affects the production of enzyme G that breaks down GAGs inside lysosomes.

(a) Enzymes work by

☐ A increasing the activation energy of a reaction
☐ B lowering the activation energy of a reaction
☐ C providing energy to the reactants
☐ D removing energy from the products

(b) Describe what happens to lysosomes once their contents have been digested.

(c) More than 50 different mutations in the gene for enzyme G have been found to result in MPS I. Most of these mutations involve changing a single base in the gene.

(i) Explain how a single base mutation can lead to an altered primary structure of enzyme G.
(ii) Explain how human genome sequencing can be used to identify the mutations associated with MPS I.

(3)
(d) A biotechnology company is developing a method of repairing the mutations in the gene for enzyme G.

The method being developed is called CRISPR-Cas9.

In this method, a short sequence of RNA binds to the DNA containing the mutation responsible for MPS I.

This RNA acts as a guide to enable the Cas9 enzyme to bind to DNA.

This enzyme can then cut and repair the DNA, removing the mutation.

(i) Describe how scientists could produce this short sequence of RNA needed to treat someone with MPS I.

(ii) Explain why the use of CRISPR-Cas9 technology can be described as personalised medicine.

(Total for Question 10 = 13 marks)