



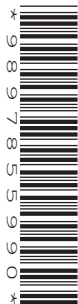
Oxford Cambridge and RSA

Friday 16 June 2023 – Morning

A Level Biology B (Advancing Biology)

H422/02 Scientific literacy in biology

Time allowed: 2 hours 15 minutes



You must have:

- a clean copy of the Advance Notice Article (inside this document)
- the Insert (inside this document)

You can use:

- a scientific or graphical calculator
- a ruler (cm/mm)



Please write clearly in black ink. **Do not write in the barcodes.**

Centre number

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Candidate number

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First name(s)

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Last name

StemUp Model Solution

INSTRUCTIONS

- Use black ink. You can use an HB pencil, but only for graphs and diagrams.
- Write your answer to each question in the space provided. If you need extra space use the lined pages at the end of this booklet. The question numbers must be clearly shown.
- Answer **all** the questions.
- Where appropriate, your answer should be supported with working. Marks might be given for using a correct method, even if your answer is wrong.

INFORMATION

- The total mark for this paper is **100**.
- The marks for each question are shown in brackets [].
- Quality of extended response will be assessed in questions marked with an asterisk (*).
- This document has **28** pages.

ADVICE

- Read each question carefully before you start your answer.

- 1 This question is based on the Advance Notice Article 'Development of therapeutic antibodies for the treatment of disease'.

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

A substance (e.g. a protein or glycoprotein) on the surface of a pathogen that stimulates an immune response. [1]

- (ii) Scientists can combine antibody fragments using phage display to produce many different antibodies, each specific to a different antigen.

Using the abbreviations from **Fig. 1** in the Advance Notice Article, explain how combining antibody fragments allows scientists to produce many different antibodies, each specific to a different antigen.

The antigen-binding site is formed by VL and VH, which are complementary to one specific antigen (epitope). Combining different VL and VH regions (with constant regions) produces millions of different Fab or scFv fragments, each with a different binding site, specific to a different antigen. [2]

- (iii) The B cell receptor is an IgG molecule with the same structure as the human IgG shown in **Fig. 1** in the Advance Notice Article.

Use an abbreviation from **Fig. 1** to identify the part of the B cell receptor that will be attached to the cell surface membrane of a B cell.

CH3 [1]

- (b) (i) Explain why mouse monoclonal antibodies (mAbs) have been largely replaced as therapeutic antibodies by humanised or fully human mAbs.

Mouse mAbs are recognised as foreign (non-self), so they stimulate a HAMA (immune, allergic) response: they are removed from the blood and can cause allergic reactions. Humanised or fully human mAbs contain little or no mouse protein, so they reduce the HAMA (immune, allergic) response. [2]

- (ii) Explain why the Fab and scFv antibody fragments shown in **Fig. 1** are effective as neutralizing or agglutinating antibodies but are less effective as opsonins or in activation of complement.

They have the variable regions, so they bind antigens, clumping pathogens (agglutination) and blocking their adhesion to and entry into cells. But they lack the full constant region (CH2, CH3), which is needed to bind to phagocytes (opsonisation) and activate complement. [2]

- (c) (i) Describe how therapeutic mAbs can be used in cancer treatment.

mAbs are specific to antigens on cancer cells, so they target them.
 Some bind to cell-surface receptors (e.g. Herceptin), blocking growth factors and inhibiting cell division.
 Others deliver anti-cancer drugs or radioisotopes, e.g. a mAb-enzyme conjugate activating a cytotoxic pro-drug at the tumour (ADEPT), or drug-filled liposomes.
 mAbs can also mark cancer cells for destruction.

[3]

- (ii) The cost of treating a patient with advanced cancer using therapeutic mAbs can be extremely high. In some cases, the treatment can increase survival time by just a few months.

Pharmaceutical companies justify the high cost of treatment based on the high costs of developing and testing therapeutic mAbs.

Discuss whether the use of therapeutic mAbs to treat cancer justifies the high costs.

For: there may be no other treatments for advanced cancer, and mAbs are proven to be effective, with fewer side effects.
 It is hard to put a value on human life: a few extra months may be very valuable to the patient.
 Against: the increase in survival time may be very short, and the money might be better spent on other, more cost-effective treatments.
 High costs also cause health inequality, as many patients cannot afford the treatment.

[3]

(d)* Describe the role of T and B lymphocytes in the development of long-term immunity.

Macrophages and dendritic cells act as antigen-presenting cells (APCs). T helper cells with complementary receptors bind the antigen and are selected (clonal selection), then divide by mitosis (clonal expansion). T helper cells release cytokines, which activate B cells and cytotoxic (killer) T cells. A B cell with complementary antibody receptors binds the antigen, engulfs it and acts as an APC (clonal selection). Stimulated by cytokines it divides (clonal expansion) and differentiates into plasma cells, which secrete specific antibodies. Cytotoxic T cells kill infected cells; regulatory T cells suppress the response. Some B and T cells differentiate into memory cells, which survive for many years or decades: this gives long-term immunity. On reinfection with the same antigen, memory cells divide rapidly: the secondary response is faster and larger, so the pathogen is destroyed before it can reproduce and cause symptoms. [6]

Additional answer space if required.

.....

.....

.....

.....

.....

- 2 Aerobic fitness and muscle mass decrease as humans age. Both of these changes have an adverse effect on our general health.

(a) VO_2 max is a measure of aerobic fitness.

(i) State the definition of VO_2 max.

The maximum rate (volume per minute) at which oxygen can be taken in and used (utilised) by the body. [1]

(ii) Describe how VO_2 max is measured.

The subject does a graded exercise test: exercising on an exercise bike or treadmill with the intensity (workload) increased progressively. The ventilation (breathing) rate is measured, and the O_2 and CO_2 concentrations of the inhaled and exhaled air are measured with a mask and gas analyser. VO_2 max is reached when oxygen consumption stays steady even though the workload (intensity) increases.

[3]

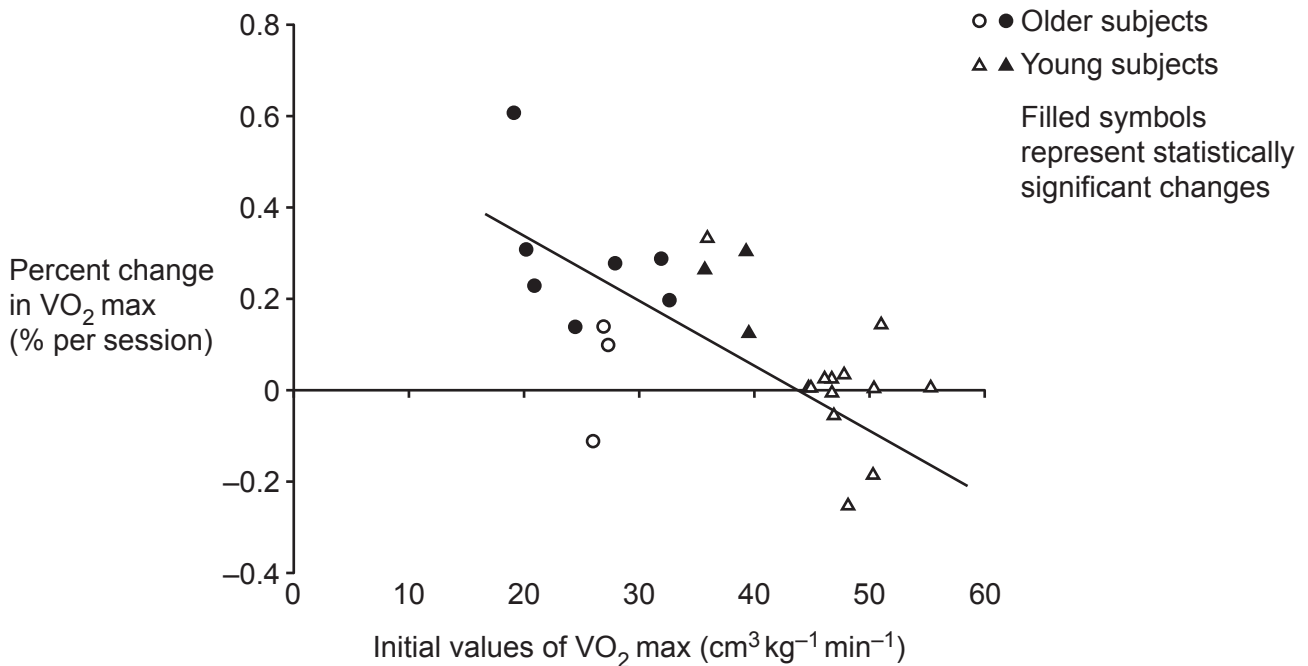
- (b) In older people (over 60 years) resistance training (lifting or pulling against a resistance) is a way of increasing muscle mass and improving bone strength. These changes reduce the risks associated with osteoporosis, falls and bone fractures.

Aerobic training might not be advisable in some older people and can also inhibit the development of muscle mass through resistance training.

A group of scientists reviewed published studies of the effect of resistance training on aerobic fitness in both young people and older people. They calculated the percentage increase in VO_2 max after a course of resistance training.

Because the different studies used training courses of different lengths, they expressed their results as 'percentage change in VO_2 max per session'. Their results are shown in **Fig. 2.1**. Each symbol in **Fig. 2.1** represents the result of one study.

Fig. 2.1



The scientists concluded that resistance training increases aerobic fitness in subjects of all ages who had a low starting level of aerobic fitness.

(i) Evaluate this conclusion.

Supports: there is a negative correlation: the lower the initial $\text{VO}_2 \text{ max}$, the greater the percentage increase in $\text{VO}_2 \text{ max}$ per session, and an increase in $\text{VO}_2 \text{ max}$ shows increased aerobic fitness.

All the statistically significant increases (filled symbols) were in subjects with a low initial $\text{VO}_2 \text{ max}$, in both older and young subjects.

Undermines: these are secondary data, with no information about the size or methodology of the studies.

[3]

(ii) Suggest why an increase in muscle mass might lead to an increase in $\text{VO}_2 \text{ max}$.

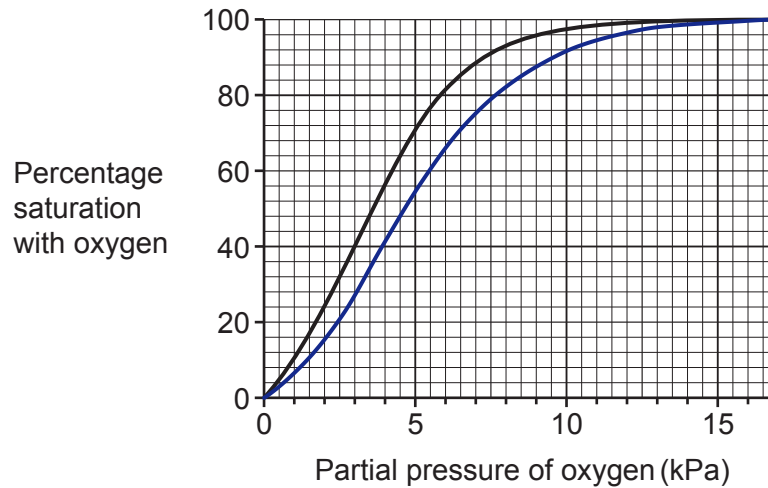
More muscle means more mitochondria and more aerobic respiration, so greater O_2 consumption.

[1]

- (c) High intensity interval training (HIIT) can increase VO_2 max to a greater extent than traditional, long aerobic exercise.

Fig. 2.2 shows the oxygen dissociation curve of an adult male at rest.

Fig. 2.2



- (i) Sketch the curve you would expect when the same person is undergoing a period of HIIT.

Answer on Fig. 2.2.

[1]

- (ii) Explain how the curve you have sketched on **Fig. 2.2** helps improve this person's performance.

The curve has shifted to the right (Bohr effect), so haemoglobin has a lower affinity for oxygen. So more oxygen dissociates from oxyhaemoglobin in the respiring muscles (at low $p\text{O}_2$), making more oxygen available for aerobic respiration, so a higher rate of respiration is maintained.

[2]

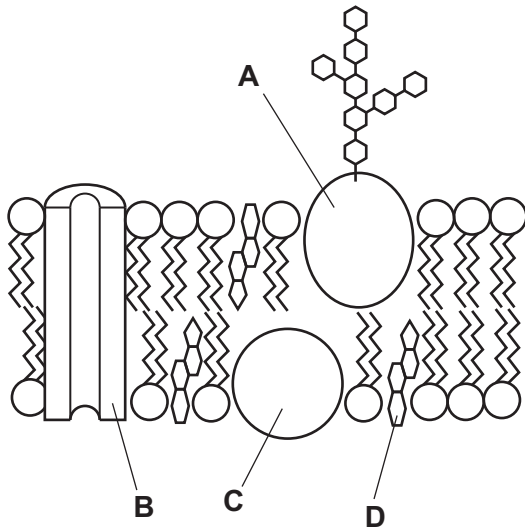
- 3 TLRs are receptors found on macrophages and are involved in the non-specific immune response.

Gram-negative bacteria have lipopolysaccharide (LPS) in their cell walls.

When Gram-negative bacteria infect a host, such as a human, they release LPS which binds to TLRs on macrophages. This causes the macrophages to release cytokines.

- (a) Fig. 3.1 shows a section of the plasma membrane of a macrophage.

Fig. 3.1



- (i) State the letter on Fig. 3.1 that identifies the component of the membrane that binds to LPS.

A [1]

- (ii) Explain why the membrane is described as a fluid mosaic.

Fluid: the phospholipids (and proteins) can move about within the bilayer.

Mosaic: the proteins (glycoproteins) are scattered randomly through the bilayer, like a mosaic.

..... [2]

- (iii) Describe **two** effects of cytokine release by macrophages.

Cytokines attract more macrophages (phagocytes) to the site of infection and stimulate phagocytosis.

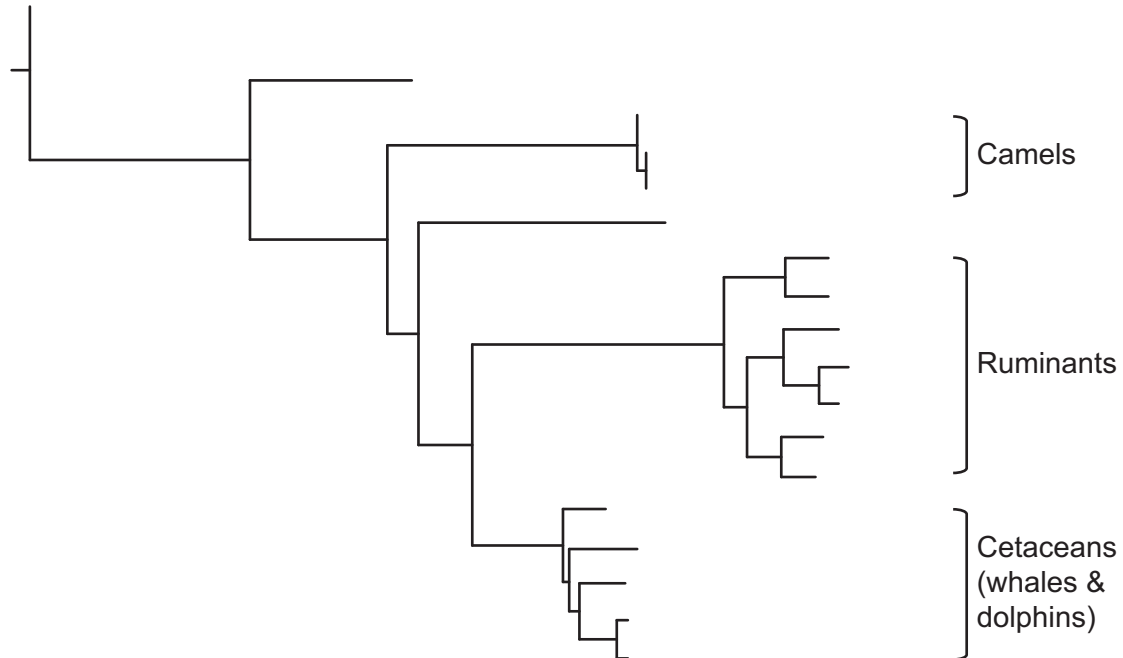
They activate lymphocytes (B and T cells), causing them to proliferate.

..... [2]

- (b) TLRs have been used to study the evolutionary relationships between ungulates, a group of mammals. Many species of ungulate have hooves.

Fig. 3.2 shows the evolutionary relationships in ungulates.

Fig. 3.2



- (i) State the name given to the study of evolutionary relationships.

Phylogeny..... [1]

- (ii) Explain how the relationships shown in **Fig. 3.2**, based on TLRs, could have been worked out.

The DNA base sequences of the TLR genes (or the amino acid sequences of the TLR proteins) were compared between species......

The more similar the sequences, the more closely related the species......

..... [2]

- (iii) Camels and ruminants are herbivores and both groups have an even number of toes. This led a student to conclude that camels and ruminants are the most closely related groups of ungulates.

Discuss whether the results support the student's conclusion.

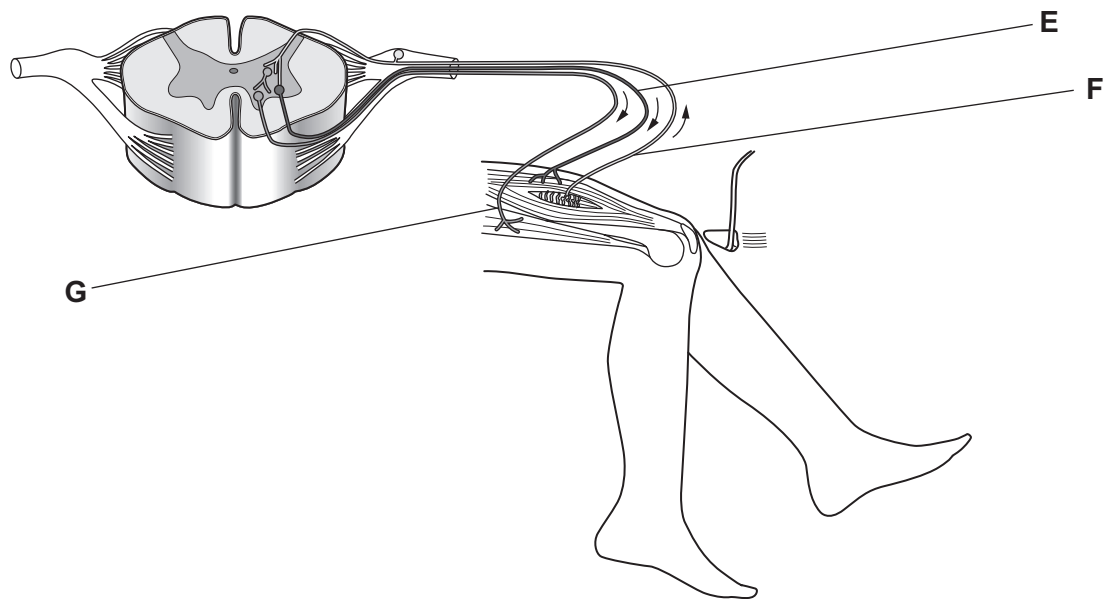
Supports: camels and ruminants share anatomical and behavioural evidence (herbivores with an even number of toes) and both live on land, whereas cetaceans are aquatic.

Does not support: Fig. 3.2 shows that ruminants and cetaceans are the most closely related, because they share the most recent common ancestor.

Camels are less closely related to ruminants, as they share a less recent common ancestor, so the conclusion is not supported. [3]

- 4 The knee jerk reflex is used to identify disorders of nervous conduction. The kneecap is struck with a rubber hammer and the lower leg responds by flexing in a kicking action.

(a) The neurones involved in the knee jerk reflex are shown in the diagram.



- (i) Identify structures **E** and **F** on the diagram.

E *motor neurone*

F *sensory neurone*

[2]

- (ii) The neurone labelled **G** inhibits muscle contraction.

Suggest the advantage of this inhibition.

It prevents contraction of the opposing (antagonistic) muscle, so it does not work against the kick (the leg can extend).

[1]

- (iii) Explain why reflexes give animals a survival advantage.

Reflexes are rapid (fast), involuntary (automatic) responses to stimuli, as no conscious decision in the brain is needed. So an animal can respond quickly to stimuli that threaten survival, e.g. withdrawing from a hot object or the blink reflex, preventing injury.

[2]

- (b) Physiotherapists use the knee jerk reflex to identify possible nerve damage in patients.

Based on the physiotherapist's assessment of the speed of response, the knee jerk reflex responses are categorised as:

- Level 0: No evidence of contraction
- Level 1: Decreased, but still present (hyporeflexia)
- Level 2: Normal
- Level 3: Super-normal (hyperreflexia)
- Level 4: Clonus (repetitive shortening of the muscle after a single stimulation).

- (i) Explain the limitations of this method for collecting data.

It does not collect quantitative data: the speed of response is not measured, only judged.

It is subjective: it depends on the interpretation of the observer, so different assessors may give different scores for the same response; the hammer force may also vary. [2]

- (ii) Suggest improvements to this method for collecting data for analysis.

Measure the speed of the response (time it) with a timer or sensor, so the data are quantitative.

Measure the degree of movement of the leg (knee jerk angle), e.g. by video analysis.

Make sure the hammer blow is the same strength each time, e.g. use a machine to keep the tap force the same.

Measure reaction times in different (healthy) patients for comparison. [3]

- (c) An investigation into reaction times was performed in a school laboratory.

The subjects sat in front of a laptop computer with a touchscreen. A blue square was shown on the screen. The subject was told to tap the screen as soon as the square changed colour to green. The computer measured the subject's reaction time as the time between the change of colour and the screen being tapped.

The study tested three groups, with 10 participants in each group:

- group 1 were all 16 – 18 year old male students
- group 2 were all 16 – 18 year old female students
- group 3 was a mixture of male and female staff members.

The results are shown in **Table 4.1**.

Table 4.1

	Reaction time (ms)		
	Group 1	Group 2	Group 3
	150	170	150
	158	225	275
	174	220	280
	186	205	350
	196	210	220
	205	195	195
	202	185	205
	188	206	320
	195	222	160
	179	199	153
Mean	183.3	203.7	230.8
Standard deviation	18.2640	17.2694	77.1303

A t-test was carried out to compare the reaction times of male and female students.

- (i) State the null hypothesis that should be used.

..There is no significant difference between the mean reaction times of.....
 ..male and female students.....
 [1]

- (ii) Use the data in **Table 4.1** to calculate a value for t .

Use the formula: $t = \frac{|\bar{x}_A - \bar{x}_B|}{\sqrt{\frac{s_A^2}{n_A} + \frac{s_B^2}{n_B}}}$

$$\begin{aligned} t &= |183.3 - 203.7| \div \sqrt{(18.264^2/10 + 17.2694^2/10)} \\ &= 20.4 \div \sqrt{(33.357 + 29.823)} \\ &= 20.4 \div \sqrt{63.18} = 20.4 \div 7.949 \\ &= 2.566 \end{aligned}$$

$$t = \dots\dots\dots 2.57 \dots\dots\dots [3]$$

- (iii) **Table 4.2** shows the critical values for t .

Table 4.2

Degrees of freedom	p values			
	0.10	0.05	0.01	0.001
1	6.31	12.71	63.66	636.60
2	2.92	4.30	9.92	31.60
4	2.13	2.78	4.60	8.61
6	1.94	2.45	3.71	5.96
8	1.86	2.31	3.36	5.04
10	1.81	2.23	3.17	4.59
16	1.75	2.12	2.92	4.02
18	1.73	2.10	2.88	3.92
20	1.72	2.09	2.85	3.85

Use your value for t and **Table 4.2** to explain the conclusions the researchers would have reached when comparing the reaction times of males and females.

Degrees of freedom = 10 + 10 - 2 = 18, so the critical value at p = 0.05 is 2.10. t = 2.57 is greater than 2.10, so the null hypothesis can be rejected.

There is less than 5% probability (p < 0.05) that the difference is due to chance: male students have significantly shorter reaction times. [2]

- (iv) State the conclusion that can be drawn about group 3 compared with groups 1 and 2, based on the standard deviations shown in **Table 4.1**.

There is much more variability among the participants in group 3 (their reaction times are much more spread out).

[1]

- (v) Suggest an explanation for the difference between group 3 and the other two groups.

Group 3 staff have a greater range of ages (and of health) than the 16 to 18 year old students.

[1]

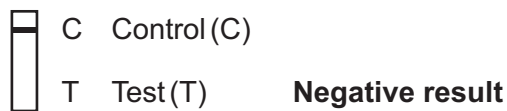
- 5 Ovulation lateral flow test kits are used by women who are trying to become pregnant.

The kits work on the same principle as pregnancy test kits. They show the presence of LH in urine, which coincides with ovulation.

The base of the test strip contains monoclonal antibodies specific to LH.

The test strip is dipped into a urine sample, and the results are read after a few minutes.

- (a) The diagram shows the possible results of ovulation lateral flow tests.



- (i) The control and test lines also have monoclonal antibodies attached.

State what would bind to the antibodies on each line.

Control line ..labelled antibodies with no LH attached.....

Test line ..labelled antibodies with LH attached.....

[2]

- (ii) Explain why no lines means that the result is **not** valid.

..The labelled antibodies have not moved up (along) the strip, so the

test has not worked.....

[1]

(b) Describe **one** cause of infertility in males and **one** in females.

Males *Low sperm count; too few sperm are produced to fertilise an egg.*

Females *Blocked oviducts (fallopian tubes), so sperm cannot reach the egg.*

[2]

(c)* Discuss the different treatments for infertility.

You should include the ethical issues **and** draw conclusions based on risks and benefits associated with the different treatments in your answer.

Ovulation induction (FSH) treats failure to ovulate; risk of multiple births.

Artificial (intrauterine) insemination places sperm from the partner or a donor into the uterus; it may cause uterine cramping and has a low success rate. Donor children may not know their genetic background.

In IVF eggs are collected after hormone treatment and fertilised in a dish, then embryos are placed in the uterus; spare embryos can be frozen (frozen embryo replacement). In ICSI one sperm is injected into the egg (with surgical sperm retrieval if needed), treating non-motile sperm.

Benefits: a couple can have their own biological child rather than adopt, reducing effects on mental health and relationships; IVF embryos can be screened for inherited disorders.

Risks: IVF is invasive and stressful with a low success rate, and transferring several embryos increases multiple births, miscarriage, stillbirth and maternal mortality. ICSI may pass on genes for non-motile sperm and increase autism risk.

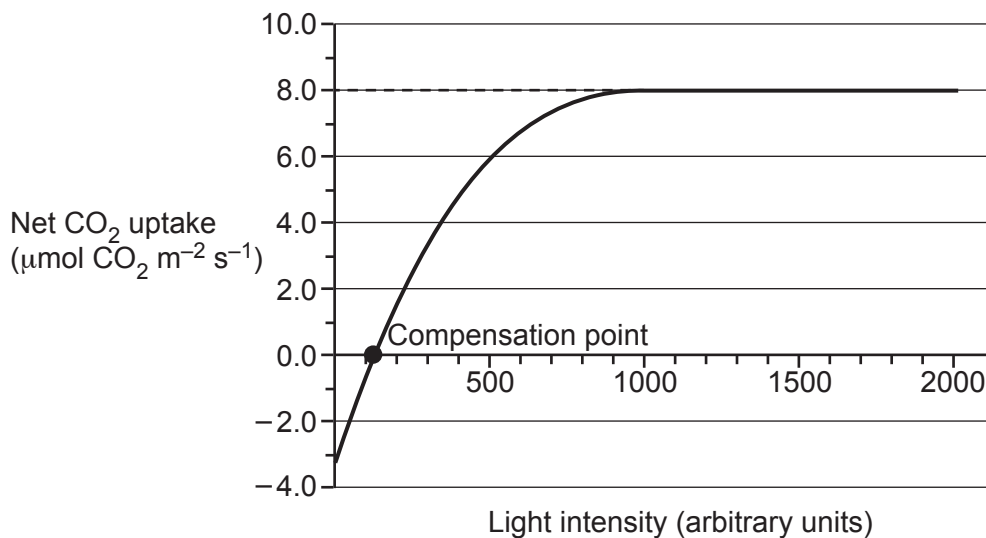
[6]

Additional answer space if required.

- 5(c) *Ethics: spare IVF embryos are destroyed or used in research, and treatment is expensive, diverting resources from other healthcare.*
- Conclusion: less invasive treatments should be tried first; IVF and ICSI give the best chance of a child but their risks and ethical issues must be weighed, e.g. limiting embryos transferred.*

- 6 (a) **Fig. 6.1** shows the relationship between light intensity and the net rate of photosynthesis, measured as net CO₂ uptake, in a plant growing at atmospheric CO₂ concentration (0.04%).

Fig. 6.1



- (i) Explain the significance of the compensation point shown on **Fig. 6.1**.

Rate of photosynthesis = rate of respiration: CO₂ taken up in photosynthesis equals CO₂ released in respiration. [1]

- (ii) Use the data in **Fig. 6.1** to explain why crops growing in greenhouses during the winter months are often grown under artificial lights.

In winter the light intensity is lower and the duration of daylight is shorter.
At low light intensity, below the compensation point, respiration is faster than photosynthesis, so there is a net loss of CO₂ and sugars.
Artificial light means the compensation point is reached and passed: photosynthesis is faster than respiration, and above about 900 AU net CO₂ uptake is at its maximum of 8.0 μmol CO₂ m⁻² s⁻¹.
So there is more sucrose (energy) available for growth. [3]

- (b) A student used hydrogen carbonate indicator solutions to investigate the compensation point in leaf samples from two different species of crop plant.

Leaf extracts were prepared and placed in glass bottles containing hydrogen carbonate indicator solution. The bottles were exposed to light for a fixed period of time, and the colours were compared with a set of standards, shown in **Fig. 6.2** on the Insert.

- (i) Explain **two** steps that the student should take to ensure an accurate comparison of compensation points.

1 *Keep the light intensity the same for both plants (light source at the same distance), because light intensity affects the rate of photosynthesis but not respiration.*

2 *Keep the temperature the same (water bath), because temperature affects the rate of respiration more than photosynthesis, which would change the compensation point.*

[4]

- (ii) The colour of the hydrogen carbonate indicator after each plant extract was exposed to light is indicated by the labels **H** and **J** in **Fig. 6.2** on the Insert.

On the basis of this result, the student concluded that crop plant **J** would be more suitable for growing in the winter months than crop plant **H**.

Evaluate the student's conclusions.

Supports: the purple indicator colour with J shows more CO₂ is being used (photosynthesis) than produced (respiration); the orange-yellow with H shows the opposite.

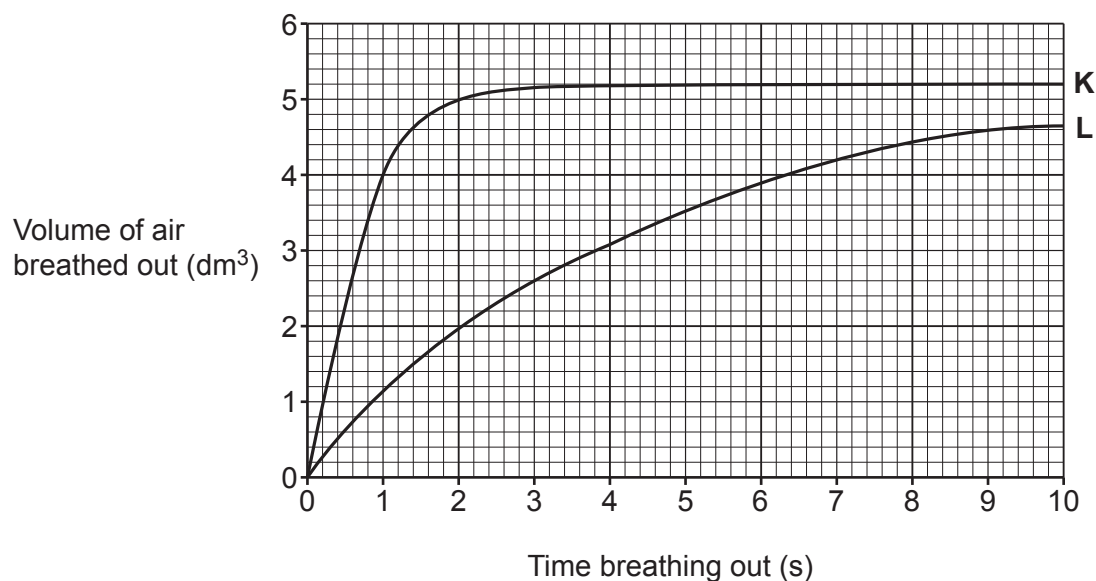
So plant J has a lower compensation point (a higher rate of photosynthesis at this light intensity), so J would grow faster in winter.

Undermines: there is no information about the light intensity used, so the result may not be relevant to winter conditions.

Leaf extracts in bottles may not reflect whole plants in actual greenhouse conditions, and there is only one result.

[4]

- 7 (a) The graph shows data recorded during forced expiration (breathing out) in two subjects, **K** and **L**. One subject is a patient with chronic obstructive pulmonary disease (COPD) and the other is a normal control.



The table shows the effects of COPD on the vital capacity and forced expiratory volume in one second (FEV₁).

Measurement	Normal range	COPD
Vital capacity	3 – 5.5 dm ³	May be reduced
FEV ₁	Calculation based on height and age	Reduced
Ratio of FEV ₁ to vital capacity	Approximately 0.7 – 0.8	<0.7

- (i) A student said that it was not possible to estimate vital capacity for subject **L** on the basis of the graph.

Evaluate the student's conclusion.

The student is partly right: curve L has not completely flattened off (reached a plateau) by 10 s, so vital capacity cannot be read directly. However, the curve can be extrapolated (continued) until it levels off, to estimate vital capacity (about 4.7 dm³ or more).

[2]

- (ii) With the aid of a calculation, show that it is possible to identify which of the two curves, **K** and **L**, is the normal control and which is the patient with COPD.

K: $FEV_1 = 4.0 \text{ dm}^3$, $VC = 5.2 \text{ dm}^3$, ratio = $4.0 \div 5.2 = 0.77$
L: $FEV_1 = 1.2 \text{ dm}^3$, $VC \geq 4.7 \text{ dm}^3$, ratio = $1.2 \div 4.7 = 0.26$ (or less)
K is in the normal range (0.7 to 0.8), so K is the normal control; L is below 0.7, so L is the patient with COPD.
 [3]

- (iii) FEV_1 is calculated using the formula:
 $(4.3 \times \text{height}) - (0.029 \times \text{age}) - 2.49$
 where height is in m and age is in years.

Use this formula to estimate the age in years of a healthy subject with $FEV_1 = 4.4$ and height = 1.76 m.

$$4.4 = (4.3 \times 1.76) - (0.029 \times \text{age}) - 2.49$$

$$0.029 \times \text{age} = 7.568 - 2.49 - 4.4 = 0.678$$

$$\text{age} = 0.678 \div 0.029 = 23.4$$

Age = ...23..... years [2]

- (b) Asthma is another obstructive respiratory disease in which breathing out can be difficult. A severe asthma attack can lead to respiratory arrest, where the person stops breathing.

The first aid treatment for respiratory arrest is to administer expired air resuscitation (EAR).

- (i) Explain the reasons for the following aspects of EAR.

1. Gloves and a mask should be worn.

To protect yourself and the patient from infection by pathogens in body fluids.

2. The patient's head should be held back.

To move the tongue away from the back of the throat, opening the airway.

3. Watch to see if the chest rises whilst blowing into the mouth.

To check that the airway is clear (not obstructed) and air is reaching the lungs.

4. If there is no pulse after two breaths, you must perform cardiopulmonary resuscitation (CPR).

With no pulse, CPR pumps blood so the brain is not starved of oxygen (brain death).

[4]

- (ii) Suggest how EAR would differ if you were performing it on a small child.

Cover both the child's mouth and nose with your mouth. (mouth-to-nose-and-mouth).

Reduce the force and volume of each breath (use small puffs), because a child's lungs are smaller.

[2]

- (c) Lung surfactant is a mixture of phospholipids and proteins that helps the alveoli stretch and expand during breathing in and prevents them collapsing when breathing out.

The following sentences compare the synthesis and secretion of lung surfactant proteins with other types of protein secreted by cells.

Complete the sentences using the most appropriate words or terms.

All secreted proteins are produced on*ribosomes*..... attached to the rough endoplasmic reticulum (RER). The assembled protein in the RER is then pinched off in*transport*..... vesicles and moved to the*Golgi apparatus*..... where it is processed and packaged into*secretory*..... vesicles.

In alveolar epithelial cells these are known as lamellar bodies. These move to the cell surface membrane and the surfactant is released by*exocytosis*..... .

Movement of these organelles requires motor proteins to move them along the*cytoskeleton*..... .

[4]

END OF QUESTION PAPER

[illegible]

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