

Please check the examination details below before entering your candidate information

Candidate surname		Other names	
Pearson Edexcel		Centre Number	Candidate Number
Level 3 GCE			
Time 2 hours	Paper reference	9BN0/03	
Biology A (Salters Nuffield) Advanced PAPER 3: General and Practical Applications in Biology			
You must have: Ruler, HB pencil and scientific calculator and a copy of the scientific article adapted from National Geographic (enclosed)			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.
- 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.
- Good luck with your examination.

Turn over ►

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Scientific article for use with Question 8

How the DNA Revolution is Changing Us

1. The ability to quickly alter the code of life has given us unprecedented power over the natural world. The question is: Should we use it?
2. If you took a glance around Anthony James's office, it wouldn't be hard to guess what he does for a living. The walls are covered with drawings of mosquitoes. Mosquito books line the shelves.
3. Hanging next to his desk is a banner with renderings of one particular species – *Aedes aegypti* – in every stage of development, from egg to pupa to fully grown, enlarged to sizes that would even make fans of Jurassic Park blanch. His license plates have a single word on them: AEDES.
4. There are approximately 3,500 species of mosquito, but James pays attention to just a few, each of which ranks among the deadliest creatures on Earth. They include *Anopheles gambiae*, which transmits the malaria parasite that kills hundreds of thousands of people each year. For much of his career, however, James has focused on *Aedes*. Historians believe the mosquito arrived in the New World on slave ships from Africa in the 17th century, bringing with it yellow fever, which has killed millions of people. Today the mosquito also carries dengue fever, which infects as many as 400 million people a year, as well as such increasingly threatening pathogens as chikungunya, West Nile virus, and Zika.
5. In a widening outbreak that began last year in Brazil, Zika appears to have caused a variety of neurological disorders, including a rare defect called microcephaly, where babies are born with abnormally small heads and underdeveloped brains.
6. The goal of James's lab, and of his career, has been to find a way to manipulate mosquito genes so that the insects can no longer spread such diseases. Until recently, it has been a long, lonely, and largely theoretical road. But by combining a revolutionary new technology called CRISPR-Cas9 with a natural system known as a gene drive, theory is rapidly becoming reality.
7. CRISPR places an entirely new kind of power into human hands. For the first time, scientists can quickly and precisely alter, delete, and rearrange the DNA of nearly any living organism, including us. In the past three years, the technology has transformed biology. Working with animal models, researchers in laboratories around the world have already used CRISPR to correct major genetic flaws, including the mutations responsible for muscular dystrophy, cystic fibrosis, and one form of hepatitis. Recently several teams have deployed CRISPR in an attempt to eliminate HIV from the DNA of human cells. The results have been only partially successful, but many scientists remain convinced that the technology may contribute to a cure for AIDS.
8. In experiments, scientists have also used CRISPR to rid pigs of the viruses that prevent their organs from being transplanted into humans. Ecologists are exploring ways for the technology to help protect endangered species. Moreover, plant biologists, working with a wide variety of crops, have embarked on efforts to delete genes that attract pests. That way, by relying on biology rather than on chemicals, CRISPR could help reduce our dependence on toxic pesticides.
9. No scientific discovery of the past century holds more promise – or raises more troubling ethical questions. Most provocatively, if CRISPR were used to edit a human embryo's germ line – cells that contain genetic material that can be inherited by the next generation – either to correct a genetic flaw or to enhance a desired trait, the change would then pass to that person's children, and their children, in perpetuity. The full implications of changes that profound are difficult, if not impossible, to foresee.

10. "This is a remarkable technology, with many great uses. But if you are going to do anything as fateful as rewriting the germ line, you'd better be able to tell me there is a strong reason to do it," said Eric Lander, who is director of the Broad Institute of Harvard and MIT and who served as leader of the Human Genome Project. "And you'd better be able to say that society made a choice to do this – that unless there's broad agreement, it is not going to happen."
11. "Scientists do not have standing to answer these questions," Lander told me. "And I am not sure who does."
12. CRISPR-Cas9 has two components. The first is an enzyme – Cas9 – that functions as a cellular scalpel to cut DNA. (In nature, bacteria use it to sever and disarm the genetic code of invading viruses.) The other consists of an RNA guide that leads the scalpel to the precise nucleotides – the chemical letters of DNA – it has been sent to cut. (Researchers rarely include the term "Cas9" in conversation, or the inelegant terminology that CRISPR stands for: "clustered regularly inter-spaced short palindromic repeats.")
13. The guide's accuracy is uncanny; scientists can dispatch a synthetic replacement part to any location in a genome made of billions of nucleotides. When it reaches its destination, the Cas9 enzyme snips out the unwanted DNA sequence. To patch the break, the cell inserts the chain of nucleotides that has been delivered in the CRISPR package.
14. By the time the Zika outbreak in Puerto Rico comes to an end, the U.S. Centers for Disease Control and Prevention estimates that, based on patterns of other mosquito-borne illnesses, at least a quarter of the 3.5 million people in Puerto Rico may contract Zika. That means thousands of pregnant women are likely to become infected.
15. Currently the only truly effective response to Zika would involve bathing the island in insecticide. James and others say that editing mosquitoes with CRISPR – and using a gene drive to make those changes permanent – offers a far better approach.
16. Gene drives have the power to override the traditional rules of inheritance. Ordinarily the progeny of any sexually reproductive animal receives one copy of a gene from each parent. Some genes, however, are "selfish": Evolution has bestowed on them a better than 50 percent chance of being inherited. Theoretically, scientists could combine CRISPR with a gene drive to alter the genetic code of a species by attaching a desired DNA sequence onto such a favored gene before releasing the animals to mate naturally. Together the tools could force almost any genetic trait through a population.
17. Last year, in a study published in the *Proceedings of the National Academy of Sciences*, James used CRISPR to engineer a version of *Anopheles* mosquitoes that makes them incapable of spreading the malaria parasite. "We added a small package of genes that allows the mosquitoes to function as they always have," he explained. "Except for one slight change." That change prevents the deadly parasite from being transmitted by the mosquitoes.
18. "I'd been laboring in obscurity for decades. Not anymore, though – the phone hasn't stopped ringing for weeks," James said, nodding at a sheaf of messages on his desk.
19. Combating the *Ae. aegypti* mosquito, which carries so many different pathogens, would require a slightly different approach. "What you would need to do," he told me, "is engineer a gene drive that makes the insects sterile. It doesn't make sense to build a mosquito resistant to Zika if it could still transmit dengue and other diseases."

20. To fight off dengue, James and his colleagues have designed CRISPR packages that could simply delete a natural gene from the wild parent and replace it with a version that would confer sterility in the offspring. If enough of those mosquitoes were released to mate, in a few generations (which typically last just two or three weeks each) entire species would carry the engineered version.
21. James is acutely aware that releasing a mutation designed to spread quickly through a wild population could have unanticipated consequences that might not be easy to reverse. "There are certainly risks associated with releasing insects that you have edited in a lab," he said. "But I believe the dangers of not doing it are far greater."
22. The potential for CRISPR research to improve human medicine would be hard to overstate. The technology has already transformed cancer research by making it easier to engineer tumor cells in the laboratory, then test various drugs to see which can stop them from growing. Soon doctors may be able to use CRISPR to treat some diseases directly.
23. Stem cells taken from people with hemophilia, for example, could be edited outside of the body to correct the genetic flaw that causes the disease, and then the normal cells could be inserted to repopulate a patient's bloodstream.
24. In the next two years we may see an even more dramatic medical advance. There are 120,000 Americans on waiting lists to receive organ transplants, and there will never be enough for all of them. Thousands of people die every year before reaching the top of the list. Hundreds of thousands never even meet the criteria to be placed on the list.
25. For years, scientists have searched for a way to use animal organs to ease the donor shortage. Pigs have long been considered the mammal of choice, in part because their organs are similar in size to ours. But a pig's genome is riddled with viruses called PERVs (porcine endogenous retroviruses), which are similar to the virus that causes AIDS and have been shown to be capable of infecting human cells. No regulatory agency would permit transplants with infected organs. And until recently, nobody has been able to rid the pig of its retroviruses.
26. Now, by using CRISPR to edit the genome in pig organs, researchers seem well on their way to solving that problem. A group led by George Church, a professor at Harvard Medical School and MIT, used the tool to remove all 62 occurrences of PERV genes from a pig's kidney cell. It was the first time that so many cellular changes had been orchestrated into a genome at once.
27. When the scientists mixed those edited cells with human cells in a laboratory, none of the human cells became infected. The team also modified, in another set of pig cells, 20 genes that are known to cause reactions in the human immune system. That too would be a critical part of making this kind of transplant work.
28. Church has now cloned those cells and begun growing them in pig embryos. He expects to start primate trials within a year or two. If the organs function properly and are not rejected by the animals' immune systems, the next step would be human trials. Church told me he thinks this could happen in as few as 18 months, adding that for many people the alternative to the risk of the trial would surely be death.
29. Church has always wanted to find a way to provide transplants for people who aren't considered healthy enough to receive them. "The closest thing we have to death panels in this country are the decisions made about who gets transplants," he said. "A lot of these decisions are being made based on what else is wrong with you. Many people are rejected because they have infectious diseases or problems with substance abuse – a whole host of reasons. And the conceit is that these people would not benefit from a transplant. But of course they would benefit. And if you had an abundance of organs you could do it for everyone."

30. The Black-footed Ferret is one of ten most endangered mammals in North America. Twice in the past 50 years, wildlife ecologists assumed that the animals, which were once plentiful throughout the Great Plains, had gone extinct. They came close; every black-footed ferret alive today descends from one of seven ancestors discovered in 1981 on a cattle ranch near Meeteetse, Wyoming.
31. But the ferrets, inbred for generations, lack genetic diversity, which makes it harder for any species to survive.
32. “The ferrets are a classic example of an entire species that could be saved by genomic technology,” said Ryan Phelan of the group Revive & Restore, which is coordinating efforts to apply genomics to conservation. Working with Oliver Ryder at the San Diego Frozen Zoo, Phelan and her colleagues are attempting to increase the diversity of the ferrets by introducing more variable DNA into their genomes from two specimens preserved 30 years ago.
33. Phelan’s work can address two immediate and interlocking threats. The first is lack of food: Prairie dogs, the ferrets’ main prey, have been decimated by sylvatic plague, which is caused by the same bacterium that gives rise to bubonic plague in humans. And the plague is also fatal to the ferrets themselves, which become infected by eating prairie dogs that have died of the disease. A vaccine against human plague developed in the 1990s appears to provide lifelong immunity in ferrets. Teams from the Fish and Wildlife Service have captured, vaccinated, and released as many of the ferrets (a few hundred exist in the wild) as they can. But such a ferret-by-ferret approach cannot protect the species.
34. A more sophisticated solution has been proposed by Kevin Esvelt, an assistant professor at the MIT Media Lab, who developed some of the CRISPR and gene drive technology with Church. Esvelt describes his work as sculpting evolution. “All you need to do is provide resistance,” he explained – by encoding antibodies generated by vaccination and then editing them into the ferrets’ DNA.
35. Black-footed ferrets are hardly the only endangered animals that could be saved through a CRISPR gene drive. The avian population of Hawaii is rapidly disappearing, largely because of a type of malaria that infects birds. Before whalers brought mosquitoes in the early 19th century, birds in the Hawaiian Islands had no exposure to the diseases that mosquitoes carry, and therefore no immunity. Now only 42 of more than a hundred species of birds endemic to Hawaii remain, and three-quarters of those are listed as endangered. The American Bird Conservancy has referred to Hawaii as “the bird extinction capital of the world.” Avian malaria is not the only threat to what remains of Hawaii’s native birds, but if it cannot be stopped – and gene editing seems to be the best way to do that – they will likely all disappear.
36. In February of this year, U.S. Director of National Intelligence James Clapper warned in his annual report to the Senate that technologies like CRISPR ought to be regarded as possible weapons of mass destruction. Many scientists considered the comments unfounded, or at least a bit extreme. There are easier ways for terrorists to attack people than to conjure up new crop plagues or deadly viruses.
37. The more rapidly science propels humanity forward, the more frightening it seems. This has always been true. Do-it-yourself biology is already a reality; soon it will almost certainly be possible to experiment with a CRISPR kit in the same way that previous generations of garage-based tinkerers played with ham radios or rudimentary computers. It makes sense to be apprehensive about the prospect of amateurs using tools that can alter the fundamental genetics of plants and animals.

38. But the benefits of these tools are also real, and so are the risks of ignoring them. Mosquitoes cause immense agony throughout the world every year, and eradicating malaria or another disease they carry would rank among medicine's greatest achievements. Although it is clearly too soon to contemplate using CRISPR in viable human embryos, there are other ways of editing the human germ line that could cure diseases without changing the genetic lineage of our species.
39. Children born with Tay-Sachs disease, for instance, lack a critical enzyme necessary for the body to metabolize a fatty waste substance found in the brain. The disease is very rare and occurs only when both parents transmit their defective version of the gene to a child. With CRISPR it would be easy to treat one parent's contribution – say, the father's sperm – to ensure that the child did not receive two copies of the faulty gene. Such an intervention would clearly save lives and reduce the chance of recurrence of the disease. A similar outcome can be achieved already through in vitro fertilization: implanting an embryo free of the defective gene ensures that the child won't pass the disorder on to a future generation.
40. When faced with risks that are hard to evaluate, we have a strong tendency to choose inaction. But with millions of lives at stake, inaction presents its own kind of danger. Last December scientists from around the world met in Washington to discuss the difficult ethics of these choices. More discussions are planned. There will never be simple answers, but without any regulatory guidance – and there is none yet for editing human DNA – the tremendous potential of this revolution could be overshadowed by fear.
41. "With gene drives and CRISPR we now have a power over species of all kinds that we never thought possible," says Hank Greely, director of Stanford's Center for Law and the Biosciences. "The potential good we can do is immense. But we need to acknowledge that we are dealing with a fundamentally new kind of power, and figure out a way to make sure we use it wisely. We are not currently equipped to do that, and we have no time to lose."

Source

Michael Specter, National Geographic, August 2016 pp.30-55

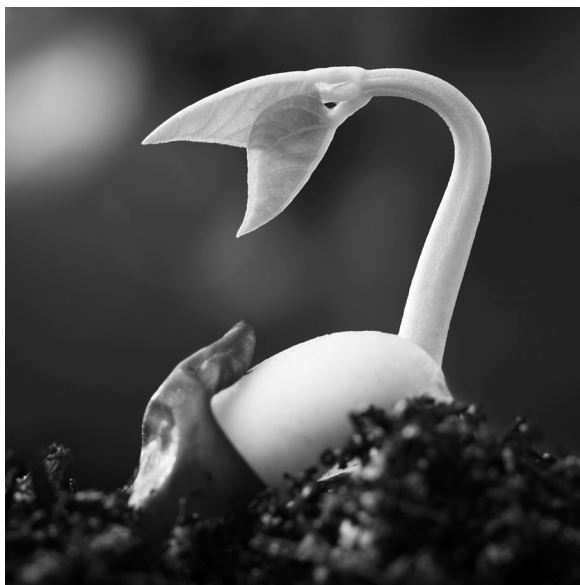
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Answer ALL questions.

Write your answers in the spaces provided.

- 1** Plants can respond to and use light.

The photograph shows a seedling starting to grow from a germinating seed.



- (a) Explain why the seedling needs a supply of magnesium ions.

(2)

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(b) Describe the role of IAA (auxin) in the phototropic response of plants.

(4)

(Total for Question 1 = 6 marks)

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2 Acetylcholinesterase is an enzyme involved in regulating the transmission of nerve impulses across some synapses.

- (a) Acetylcholinesterase is found on the cell surface membranes of neurones and red blood cells.

These acetylcholinesterase molecules have different primary structures.

In humans, a single gene codes for acetylcholinesterase.

- (i) Explain how a single gene can give rise to acetylcholinesterase molecules with different primary structures.

(2)

- (ii) Explain how the acetylcholinesterase gene can be expressed in some tissues but not others.

(3)

- (b) Alzheimer's disease is associated with the loss of neurones that produce acetylcholine.

It has been suggested that inhibitors of acetylcholinesterase may be useful in the treatment of Alzheimer's disease.

- (i) Explain why inhibitors of acetylcholinesterase could be useful in the treatment of Alzheimer's disease.

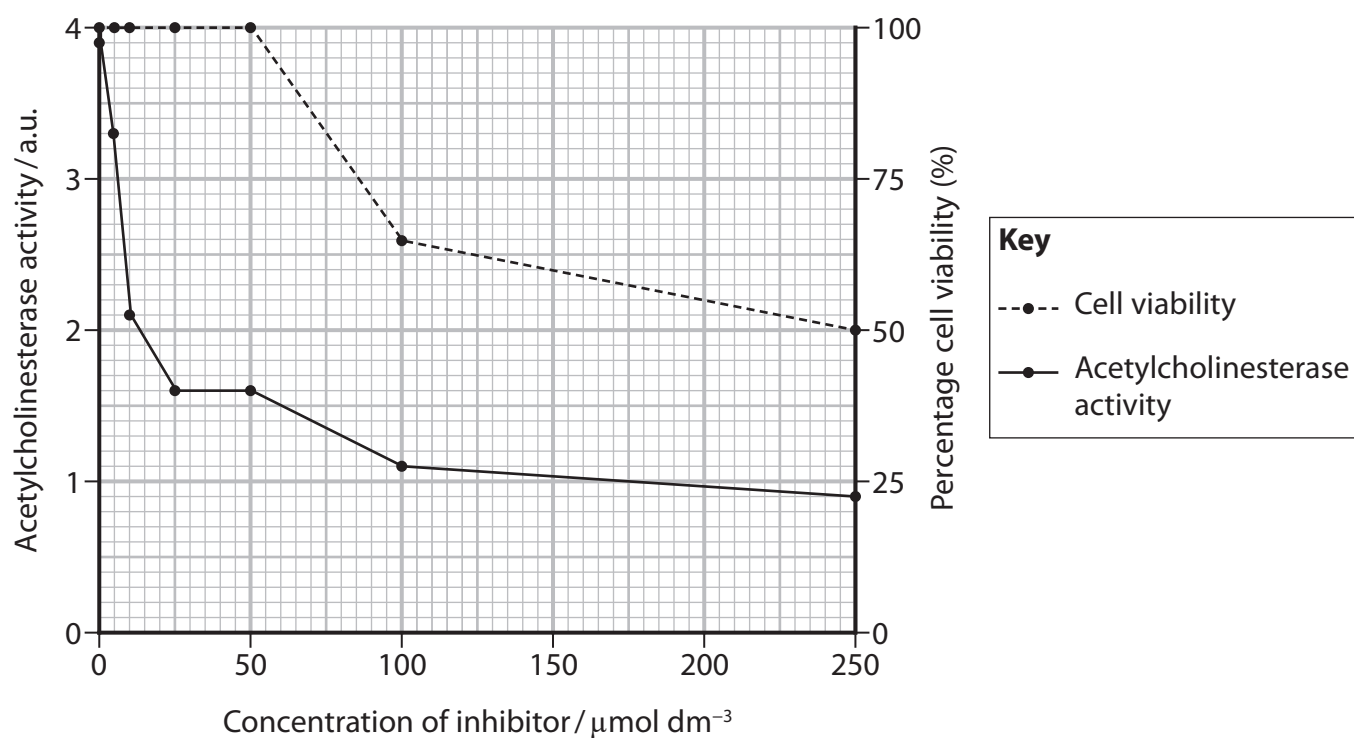
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(ii) Trials of a new inhibitor were carried out using tissue cultures.

The effect of the concentration of the inhibitor on acetylcholinesterase activity and cell viability was measured.

Percentage cell viability was measured as the percentage of cells that were not killed by the inhibitor.

The graph shows the results for this inhibitor.



State and justify a suitable concentration of inhibitor to use in clinical trials.

(3)

(Total for Question 2 = 11 marks)

3 Doctors sometimes prescribe beta-blockers for their patients.

Beta-blockers are a type of drug with antihypertensive properties.

- (a) In one study, the effect of beta-blockers on the heart rate during exercise was investigated.

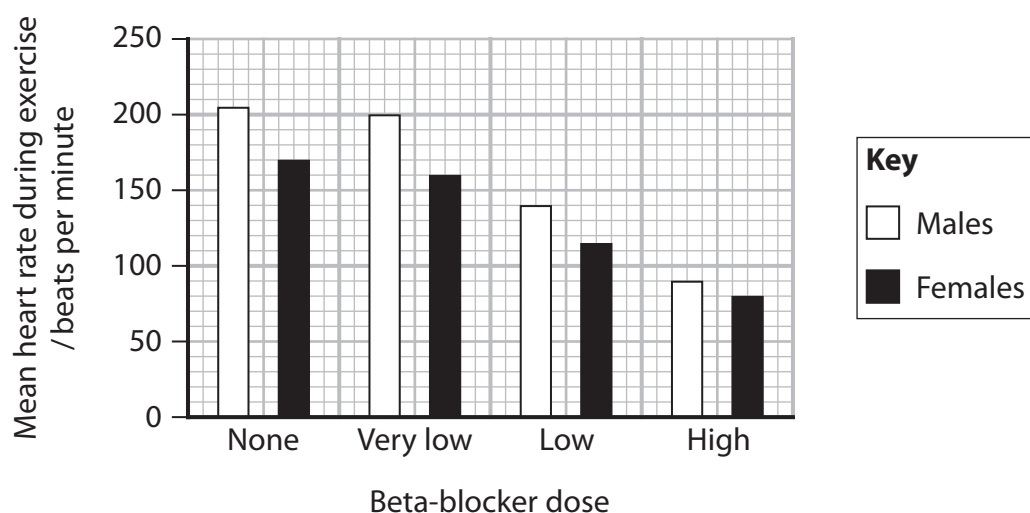
In this study, volunteers were placed randomly into one of four groups shown in the table.

Group	Dose of beta-blocker
A	none
B	very low
C	low
D	high

The heart rate of each volunteer was recorded during a period of exercise.

A mean value was calculated separately for the males and females in each group.

The graph shows the results of this study.



- (i) Calculate the percentage change in male heart rate caused by increasing the dose of beta-blocker from very low to high.

(2)

Answer

(ii) Deduce the effect of beta-blockers on the supply of blood to muscle during exercise.

(4)

(b) Explain why beta-blockers are prescribed for some people.

(2)

(c) Beta-blockers work by blocking the effects of a hormone called adrenaline.

Adrenaline is produced by the adrenal glands located on top of each kidney.

Adrenaline acts on the heart to cause changes in heart rate.

Deduce how adrenaline can cause a change in heart rate.

(4)

(Total for Question 3 = 12 marks)

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4 Lipoprotein lipase is an enzyme found in different tissues including the brain.

(a) The enzyme lipoprotein lipase is involved in the metabolism of lipids in the brain.

The effect of temperature on lipid metabolism in the brain tissue of a species of fish was investigated.

The results of this investigation are shown in the table.

Temperature /°C	Lipoprotein lipase mRNA /a.u.	Triglyceride concentration /mmol mg ⁻¹	Fatty acid concentration /μmol mg ⁻¹	Lipoprotein lipase activity per milligram of tissue /a.u.
5	4.50	0.58	0.84	1.70
17	1.00	0.60	0.69	1.55
30	1.10	0.70	0.64	0.99

Comment on the effect of temperature on lipid metabolism in this species of fish.

(3)

(b) Lipoprotein lipase can be extracted from brain tissue to investigate the effect of temperature on the rate of reaction of this enzyme.

(i) State what is meant by the term Q_{10} temperature coefficient.

(1)

(ii) Devise an investigation to determine Q_{10} for an extract of lipoprotein lipase enzyme.

(5)

(Total for Question 4 = 9 marks)

5 Forests are important habitats.

(a) The effect of cutting down trees on the number of bird species observed in two different forest habitats was investigated.

- (i) Give two biotic factors, other than cutting down trees, that could affect the number of bird species observed in a forest.

(2)

(ii) Some of the results of the investigation are shown in the table.

Forest	Number of bird species in areas of the forest where no trees are cut down	Number of bird species in areas of the forest where some trees are cut down
A	35	19
B	16	10

Calculate the Chi-squared value (χ^2) for forest B using the formula shown.

$$\chi^2 = \sum \frac{(O - E)^2}{E}$$

(3)

Answer

(iii) The table gives some critical values for the Chi-squared test.

Probability level	Critical value
0.05	3.84
0.01	6.64
0.001	10.83

The Chi-squared value for forest A is 4.74.

Deduce the effect of some trees being cut down on the number of species of birds in these two forests.

(2)

(b) Many forests are exploited by humans.

(i) Describe how forests can be managed as a sustainable resource.

(2)

(ii) Explain the impact of cutting down trees on climate change.

(4)

(Total for Question 5 = 13 marks)

- 6 The neurones of the central nervous system contain TAU proteins. These proteins help to maintain cell structure.

In humans, six different TAU proteins can be produced from a single gene.

Parkinson's disease has been linked to the different forms of the TAU proteins present in neurones.

Scientists are studying the effect of these different TAU proteins in animal models.

One model used is the fruit fly, *Drosophila*.

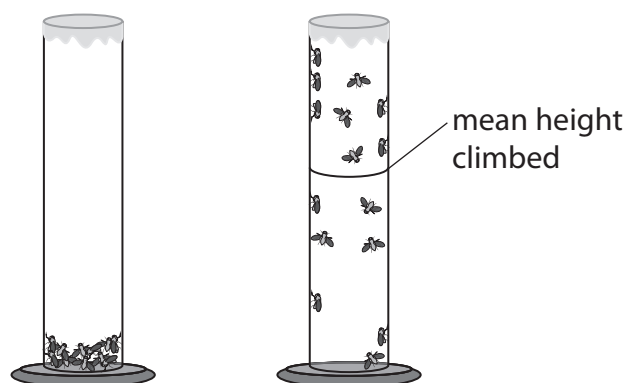
- (a) Describe how *Drosophila* flies could be genetically modified to produce one form of the human TAU protein.

(4)

(b) In one investigation, the effect of ageing on *Drosophila* making different human TAU proteins was studied.

Flies making different forms of human TAU protein were tested in a climbing test.

- Fifteen one-day-old *Drosophila* flies were placed at the bottom of a measuring cylinder.
- A video recording was carried out and paused at 10 seconds. The height climbed by each fly was recorded.
- The test was repeated for flies of different ages.



time = 0 seconds time = 10 seconds

The table shows the results of this investigation.

Age of flies / days	Mean height climbed at 10 seconds / mm		
	Control (no human TAU protein)	0N3R TAU protein	0N4R TAU protein
1	60 ± 6	52 ± 5	54 ± 5
7	61 ± 4	43 ± 1	50 ± 4
14	53 ± 3	18 ± 2	28 ± 8
21	45 ± 9	12 ± 4	18 ± 5
28	32 ± 8	10 ± 5	19 ± 1
35	26 ± 9	3 ± 1	11 ± 1
42	15 ± 3	1 ± 1	3 ± 1

Comment on the effect of TAU proteins on the ability of *Drosophila* flies to climb.

(3)

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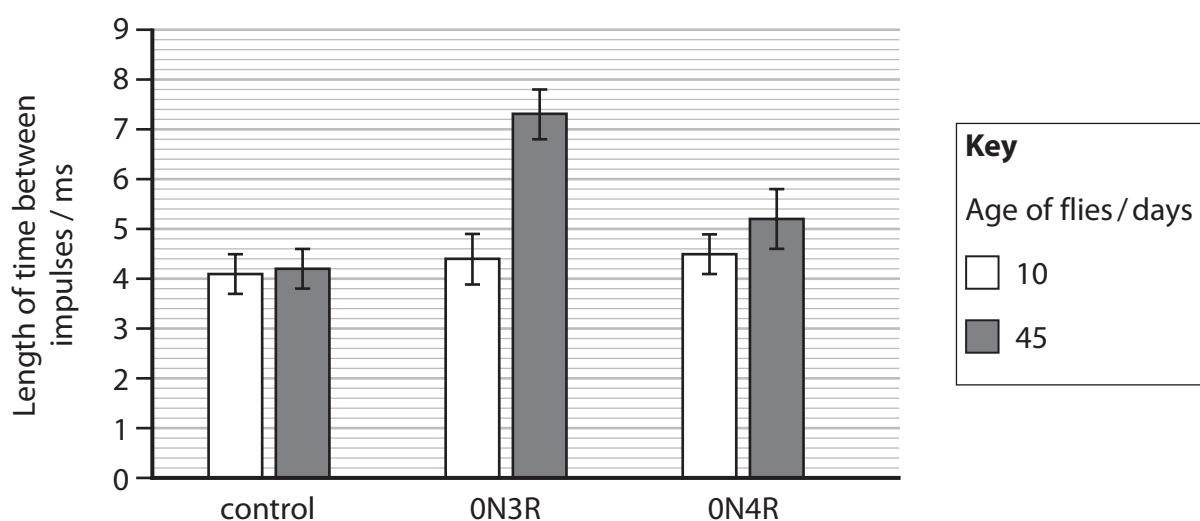
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- (c) In another investigation, the effect of these TAU proteins and age on the conduction of nerve impulses along the axon of neurones was studied.

The length of time between impulses was measured for *Drosophila* flies of different ages.

The results are shown in the graph.



Determine the effect of these TAU proteins on the maximum frequency at which nerve impulses can be conducted along the axon of the neurone.

(4)

(Total for Question 6 = 11 marks)

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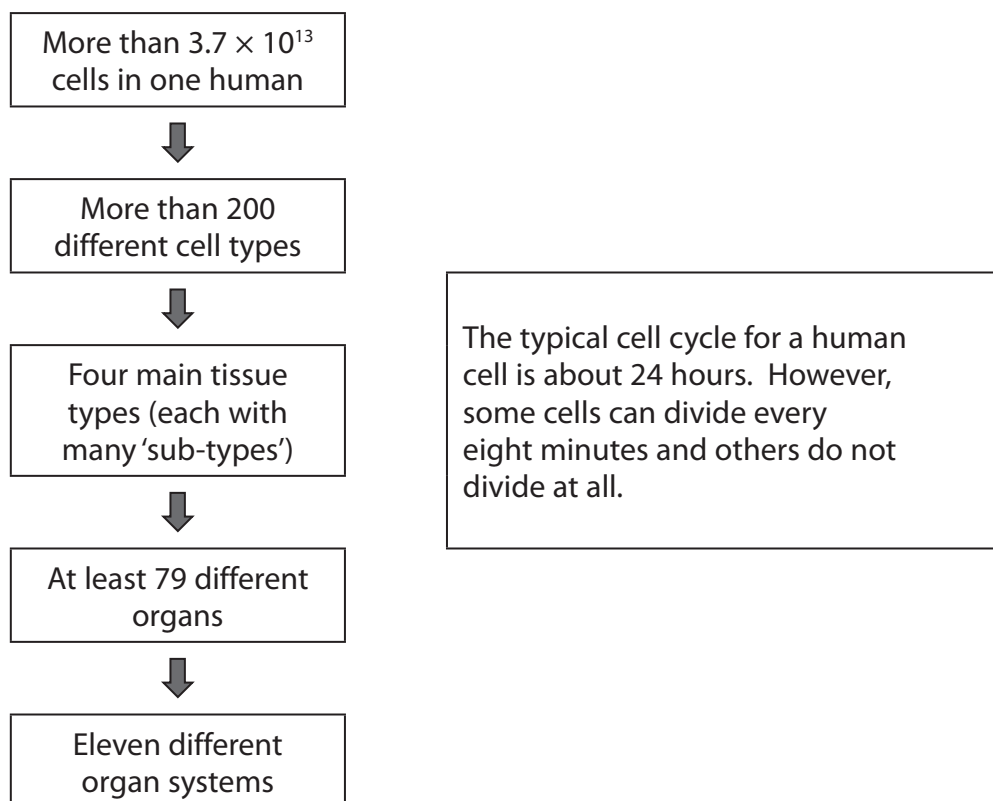
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***7** Humans are complex multicellular organisms.

Cell division is involved in:

- the production of gametes
- the development of tissues
- the development of tumours
- the response to infection in humans.

The figure summarises some information about the organisation of cells in a human.



The table summarises some information about human genetics and cancers.

Number of protein coding genes	Approximately 20 000
Number of different genetic disorders	Approximately 2200
Proportion of cancers caused by an inherited genetic defect	5 to 10%

Evaluate the role of cell division in processes affecting human health and disease.

(9)

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(Total for Question 7 = 9 marks)

- 8 The scientific article you have studied is adapted from *National Geographic*.

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

- (a) Explain how two populations of mosquito could be shown to belong to different species (paragraph 4). (2)

- (b) Explain why scientists believe CRISPR could be used to prevent AIDS developing in people infected with HIV (paragraph 7). (4)

- (c) Describe how plant biologists could demonstrate the effect of deleting genes that attract pests to crops (paragraph 8).

(3)

- (d) Explain why the editing of the germ line of a human embryo would result in the changes being inherited by the next generation (paragraph 9).

(2)

- (e) Explain why an RNA guide can be used to identify the precise nucleotides that Cas9 has been sent to cut (paragraph 12).

(2)

- (f) Gene drives can be used to 'force almost any genetic trait through a population' (paragraph 16).

Multiple genetic crosses were carried out between individuals homozygous for a recessive allele and individuals heterozygous for the same gene.

Describe how the outcome of these crosses would be affected if a gene drive was used with the recessive allele.

(3)

(g) Dengue is a disease caused by a virus carried by *Aedes aegypti*.

Using CRISPR and a gene drive, it may be possible to stop the reproduction of *Aedes aegypti* mosquitoes (paragraphs 20 and 21).

Explain why stopping the reproduction of this species of mosquito might not stop the spread of this disease.

(3)

(h) Deduce how PERVs present in pig tissues could infect human cells (paragraph 25).

(2)

- (i) Explain why some pig genes can cause reactions in the human immune system (paragraph 27).

(3)

- (j) Explain how a vaccine developed against human plague can provide lifelong immunity to sylvatic plague in the black-footed ferret (paragraph 33).

(3)

(k) State what is meant by the term endemic (paragraph 35).

(1)

(l) Deduce the pattern of inheritance for Tay-Sachs disease (paragraph 39).

(1)

(Total for Question 8 = 29 marks)

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