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Candidate surname	Other names

Centre Number | Candidate Number

Pearson Edexcel International Advanced Level

Time 1 hour 45 minutes

Paper reference **WBI15/01**

Biology

International Advanced Level
UNIT 5: Respiration, Internal Environment, Coordination and Gene Technology

You must have:
Scientific article (enclosed), scientific calculator, ruler, HB pencil

Total Marks

Instructions

- Use **black** ink or ball-point pen.
- **Fill in the boxes** at the top of this page with your name, centre number and candidate number.
- Answer **all** questions.
- Answer the questions in the spaces provided – *there may be more space than you need.*
- **Show all your working out** in calculations and **include units** where appropriate.

Information

- The total mark for this paper is 90.
- The marks for **each** question are shown in brackets – *use this as a guide as to how much time to spend on each question.*
- In 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.

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 Skeletal muscle is made of bundles of fibres.

(a) Describe the role of calcium ions in producing contraction of a muscle fibre.

(2)

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(b) The table shows some features of slow and fast twitch muscle fibres.

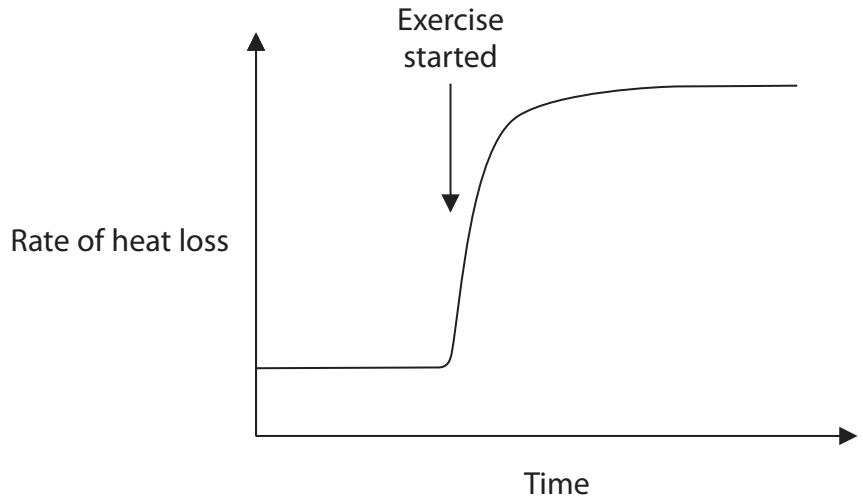
Feature of fibre	Slow twitch fibre	Fast twitch fibre
Number of mitochondria per fibre	Many	Few
Number of myoglobin molecules per fibre	Many	Few
Capillary network	Larger	Smaller
Contraction	Slow and sustained	Rapid and intense

Olympic marathon runners have a high proportion of slow twitch fibres in their muscles.

Explain how the features of slow twitch fibres, shown in the table, are of benefit to an Olympic marathon runner.

(4)

(c) The graph shows the rate of heat loss at rest and during exercise.



Comment on the rate of heat loss during exercise.

(2)

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(Total for Question 1 = 8 marks)

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2 Vitamin A is an essential component of the human diet.

Rice is a staple food in parts of the world where a lot of people have vitamin A deficiency.

Rice contains no β-carotene or vitamin A.

Cells in the human intestine can convert β-carotene from the diet to vitamin A.

Some soil bacteria can produce large quantities of β-carotene.

(a) Describe how genetic engineering could be used to produce rice that contains β-carotene.

(4)

(b) (i) Describe the possible risks of growing genetically modified rice plants.

(3)

(ii) Suggest how one of these risks could be reduced.

(1)

(Total for Question 2 = 8 marks)

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3 The mammalian retina is a tissue that detects light.

(a) Rod cells and bipolar neurones are cell types found in the retina.

(i) What is the name of the chemical formed when light is absorbed by the photopigment found in rod cells?

(1)

☒ **A** cis-retinal

☒ **B** phytochrome

☒ **C** rhodopsin

☒ **D** trans-retinal

(ii) Which row in the table shows the effects of light absorption on cells in the retina?

(1)

		Rod cell	Bipolar neurone
☒	**A**	hyperpolarised	hyperpolarised
☒	**B**	hyperpolarised	depolarised
☒	**C**	depolarised	hyperpolarised
☒	**D**	depolarised	depolarised

(b) An investigation studied the effects of light intensity on the mammalian retina.

Samples of retina were exposed to different light intensities and the mean potential difference of the bipolar neurones was recorded.

The results are shown in the table.

Light intensity / a.u.	Mean potential difference / mV
2	11
4	17
8	19
12	20
16	20
20	20

(i) Describe the effect of light intensity on the mean potential difference of bipolar neurones.

(2)

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(ii) Calculate the percentage change in the mean potential difference when the light intensity increases from 4 to 12 a.u.

(2)

Answer .....%

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(iii) Give **two** reasons why some people might have objections to the use of mammalian retinas in this investigation.

(2)

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(c) Which statement describes the response of the muscles in the iris to increasing light intensity?

(1)

☒ **A** circular and radial muscles contract

☒ **B** circular and radial muscles relax

☒ **C** circular muscles contract and radial muscles relax

☒ **D** circular muscles relax and radial muscles contract

(Total for Question 3 = 9 marks)

4 Homeostasis is the state maintained by living systems.

(a) Feedback mechanisms are involved in maintaining homeostasis.

Describe the difference between a negative feedback mechanism and a positive feedback mechanism.

(2)

(b) Which statement about the homeostasis of thermoregulation when the human body temperature is 37 °C is correct?

(1)

☒ **A** thermoregulation is no longer required

☒ **B** the body no longer generates any heat

☒ **C** the body will be generating more heat than it can lose

☒ **D** the body temperature is maintained in a dynamic equilibrium

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(c) The health of a kidney can be determined by measuring the glomerular filtration rate (GFR).

This method measures the rate at which a small molecule called creatinine is filtered from the blood.

(i) Explain how small molecules like creatinine are filtered from the blood in the glomerulus.

(3)

(ii) In 15 hours, a person excreted 1960 mg of creatinine in the urine.

Calculate the GFR for this person.

Give your answer to 3 significant figures.

(1)

Answer .....

(d) In type II diabetes, body cells take up less glucose in response to insulin.

Many people with type II diabetes are overweight or obese.

Some of these individuals have been given surgery to help weight loss.

A clinical trial investigated the effect of surgery on the uptake of glucose by body cells in the presence of insulin.

This trial used groups of people who were non-diabetic, people in the early stage of diabetes (pre-diabetic) and people who were type II diabetics.

Group	Mean uptake of glucose / a.u.	
	Before surgery	After surgery
Non-diabetic	1.07 ± 0.29	1.39 ± 0.58
Pre-diabetic	0.55 ± 0.32	1.30 ± 0.88
Type II diabetic	0.40 ± 0.24	1.10 ± 0.87

(i) Comment on the results of this trial.

(3)

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(ii) Calculate the difference that surgery makes to the mean uptake of glucose in the non-diabetic group and the type II diabetic group.

(2)

Answer .....

(Total for Question 4 = 12 marks)

5 Animals use aerobic and anaerobic respiration to produce ATP.

(a) Aerobic respiration has three stages where reactions occur between enzymes and substrates.

(i) Which row of the table shows the location of each stage?

(1)

		Glycolysis	Link reaction	Krebs cycle
☒	**A**	cytoplasm	cytoplasm	cytoplasm
☒	**B**	cytoplasm	mitochondrial matrix	mitochondrial matrix
☒	**C**	mitochondrial matrix	cytoplasm	cytoplasm
☒	**D**	mitochondrial matrix	mitochondrial matrix	mitochondrial matrix

(ii) A student calculated the volume of oxygen used by a cockroach as 1.7 cm^3 $hour^{-1}$. The same cockroach produced 1.3 cm^3 $hour^{-1}$ of carbon dioxide in the same time.

What is the respiratory quotient (RQ) of this cockroach?

(1)

☒ **A** 0.7

☒ **B** 0.8

☒ **C** 1.3

☒ **D** 2.2

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(iii) Hydramethylnon is an insecticide that is used to treat termite infestations.

Hydramethylnon inhibits the electron transport chain.

Which row of the table shows the expected changes caused by hydramethylnon?

(1)

		Oxygen consumption	Lactate production
☒	**A**	decrease	decrease
☒	**B**	decrease	increase
☒	**C**	increase	decrease
☒	**D**	increase	increase

(b) The table shows the oxygen consumption and body mass of two animals.

Animal	Oxygen consumption / $cm^3\ h^{-1}$	Body mass / g
Southern elephant seal	1.82×10^4	5.00×10^6
Field mouse	20.00	10.00

These figures can be used to calculate the metabolic rate of each animal in $cm^3\ g^{-1}\ h^{-1}$.

Calculate how many times greater the metabolic rate of the field mouse is compared with that of the southern elephant seal.

(2)

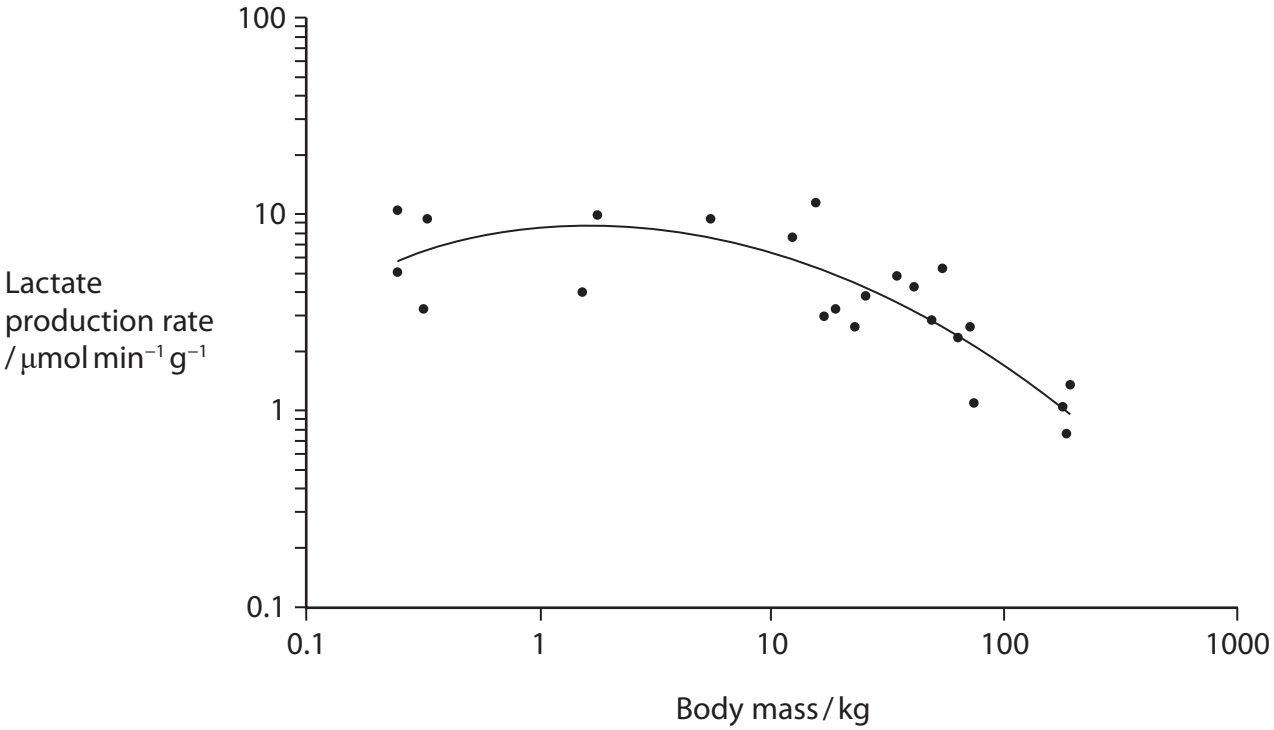
Answer .....

*(c) The photograph shows a crocodile (*Crocodylus porosus*) that lives in saltwater habitats.

(Source: © Danny Ye/Shutterstock)

An investigation measured the lactate production rate of these crocodiles when they were active.

The graph shows the results of this investigation.



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Each plotted point on the graph represents a single crocodile.

Discuss the roles of the different types of respiration in these active crocodiles.

Use the information in the graph and your own knowledge to support your answer.

(6)

(Total for Question 5 = 11 marks)

6 When activated, T lymphocytes can divide rapidly and secrete proteins called cytokines.

These cytokines will activate different types of lymphocyte.

(a) (i) Which is the function of tRNA in cytokine synthesis?

(1)

- ☒ **A** identifies an amino acid and transports it to a ribosome
- ☒ **B** identifies a base and transports it to a ribosome
- ☒ **C** forms a template for DNA polymerase
- ☒ **D** forms a template for RNA polymerase

(ii) Which organelle is involved in chemically modifying cytokine proteins before they are secreted?

(1)

- ☒ **A** Golgi apparatus
- ☒ **B** ribosome
- ☒ **C** smooth endoplasmic reticulum
- ☒ **D** vesicle

(b) Describe the role of DNA polymerase in DNA replication during cell proliferation.

(2)

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(c) Explain how cytokine genes can be expressed in an activated T lymphocyte.

(3)

(d) T lymphocytes produce different types of cytokine.

Some of these cytokines activate T killer cells and some activate B cells.

Explain why different cytokines can activate different cells.

(3)

(e) CD45 is a protein found on the surface of lymphocytes. Different forms of the CD45 protein are found on the surface of different lymphocytes.

Describe how different forms of the CD45 protein can be produced from a single CD45 gene.

(3)

(Total for Question 6 = 13 marks)

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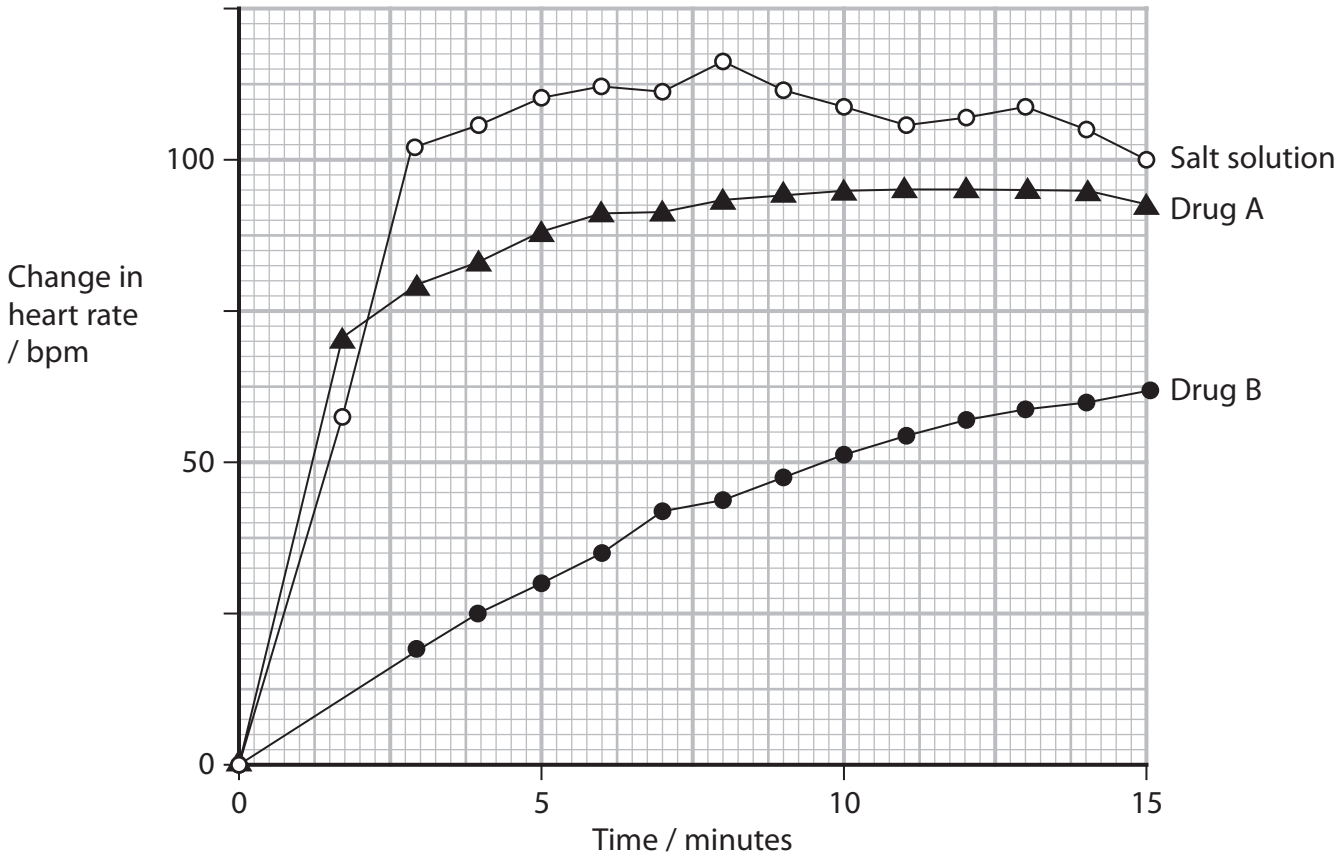
7 Researchers investigated how groups of rats, treated with drugs, responded to stress.

Groups of rats were stressed by moving them into a new environment. The rats were then treated with a salt solution, drug A or drug B.

Group	Treatment
1	Salt solution
2	Drug A
3	Drug B

The graph shows the change in mean heart rate measured over a 15-minute period.



(a) Calculate the percentage difference in the change in heart rate when using drug B between 5 and 12.5 minutes.

(3)

Answer .....%

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(b) Compare and contrast the effects of drug A and drug B on the heart rate during the investigation.

(3)

(c) Explain the effect of these drugs on the control of the heart rate.

(3)

(Total for Question 7 = 9 marks)

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8 The scientific article you have studied is adapted from *Rethinking Alzheimer's* in *New Scientist* (February 2019).

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

(a) Memory and cognitive function are two processes that occur in the brain (paragraphs 2 and 13).

Different parts of the brain are responsible for specific functions.

Complete the table showing which parts of the brain are responsible for different functions.

(2)

Part of brain	Function
cerebellum	
	interpretation of information from the retina
medulla oblongata	
	secretion of ADH

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(b) Some forms of dementia can be diagnosed using brain scans.

Compare and contrast the use of functional magnetic resonance imaging (fMRI) and computed tomography (CT) scans to identify structures like plaques in the brain (paragraph 6).

(4)

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(c) Suggest how the amyloid protein may prevent bacterial infection in the brain (paragraphs 7 and 22).

(4)

(d) Explain how the bacterium *Porphyromonas gingivalis* that causes gum disease may invade the brain and cause inflammation in brain regions affected by Alzheimer's disease (paragraphs 10, 20 and 21).

(4)

(e) Suggest how gingipains may have a degrading effect on the memory of a person suffering from Alzheimer's disease (paragraph 12).

(3)

(f) The team found genetic material from *P. gingivalis* in the cerebral cortex (paragraph 13).

Describe how the team could show that this genetic material is active.

(3)

(Total for Question 8 = 20 marks)

TOTAL FOR PAPER = 90 MARKS

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Time 1 hour 45 minutes

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Biology

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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

Rethinking Alzheimer's

A landmark study suggests mouth bacteria may be to blame, reports Debora MacKenzie. New Scientist, vol 241, issue 3215, Feb 2019

1. After decades of disappointment, we may have a new lead on fighting Alzheimer's disease. Compelling evidence that the condition is caused by a bacterium involved in gum disease could prove a game-changer in tackling one of medicine's biggest mysteries, and lead to effective treatments or even a vaccine.

2. As populations have aged, dementia has skyrocketed to become the fifth biggest cause of death worldwide. Alzheimer's constitutes some 70 percent of these cases, yet we don't know what causes it. The condition, which results in progressive loss of memory and cognitive function, usually over a decade or so, is devastating both to those who have it and to their loved ones.

3. The condition often involves the accumulation of two types of proteins – called amyloid and tau – in the brain. As these are among the earliest physical signs of the disease, the leading hypothesis since 1984 has been that the condition is caused by the defective control of these proteins, especially amyloid, which accumulates to form large, sticky plaques in the brain.

4. The bulk of research into understanding and treating Alzheimer's has centred on this "amyloid hypothesis". Huge sums of money have been invested in experiments involving mice genetically modified to produce amyloid, and in developing drugs that block or destroy amyloid proteins, or sometimes degraded tangles of tau.

5. It has become clear that this approach isn't working. In 2018 alone, the US National Institutes of Health spent $1.9 billion on Alzheimer's research. But according to a recent study, the failure rate of drug development for Alzheimer's has been 99 percent.

What is Alzheimer's disease?

There are many types and causes of dementia, but Alzheimer's disease is the most common form, accounting for between 60 and 70 percent of all cases.

Common early symptoms of Alzheimer's include short-term memory loss, apathy and depressed mood, but these symptoms are often just seen as being a part of normal ageing, making early diagnosis difficult.

Doctors diagnose Alzheimer's on the basis of medical examination, patient history and cognitive tests, and can use imaging to rule out other forms of dementia. However, a definitive diagnosis of Alzheimer's is only possible after death, when examination of brain tissue can reveal whether a person had the deposits of amyloid and tau proteins (see main story) that are characteristic of the condition.

The vast majority of people with Alzheimer's are diagnosed with the condition after the age of 65, but clumps of amyloid protein can begin to build up in the brain some 15 or 20 years before symptoms appear. We have long hoped for diagnostic tests that can determine if someone has Alzheimer's before death and spot the condition before extensive brain damage has occurred.

Donna Lu

6. Some have begun to question the amyloid hypothesis. The lack of results has been compounded by the discovery that people – including some in their 90s with exceptional memories – can have brain plaques and tangles without having dementia. In a review of the research to date last year, Bryce Vissel at the University of Technology Sydney, Australia, concluded that there isn't sufficient data to suggest that "amyloid has a central or unique role in Alzheimer's".

7. In 2016, researchers discovered that amyloid seems to function as a sticky defence against bacteria. They found that the protein can act as an anti-microbial compound that kills bacteria, and when they injected bacteria into the brains of mice engineered to make Alzheimer's proteins, plaques developed round bacterial cells overnight.

8. At the time, the team said it still believed that amyloid itself went on to cause the brain damage of Alzheimer's, not bacteria. But a spate of subsequent studies have looked at microbes.

9. Bacteria have been found in the brains of people who had Alzheimer's when they were alive. But it hasn't been clear whether the bacteria caused the disease or were simply able to enter brains damaged by Alzheimer's.

10. Multiple teams have been researching *Porphyromonas gingivalis*, the main bacterium involved in gum disease, which is a known risk factor for Alzheimer's. So far, teams have found that *P. gingivalis* invades and inflames brain regions affected by Alzheimer's; that gum infections can worsen symptoms in mice genetically engineered to have Alzheimer's; and that it can cause Alzheimer's-like brain inflammation, neural damage and amyloid plaques in healthy mice.

A whole new hypothesis

11. "When science converges from multiple independent laboratories like this, it is very compelling", says Casey Lynch of Cortexyme, a pharmaceutical firm in San Francisco.

12. Now researchers from Cortexyme and several universities have reported finding the two toxic enzymes that *P. gingivalis* uses to feed on human tissue in 99 and 96 percent of 54 human Alzheimer's brain samples taken from the hippocampus – a brain area important for memory. These protein-degrading enzymes are called gingipains, and they were found in higher levels in brain tissue that also had more tau fragments and thus more cognitive decline.

13. The team also found genetic material from *P. gingivalis* in the cerebral cortex – a region involved in conceptual thinking – in all three Alzheimer's brains they looked for it in.

14. "This is the first report showing *P. gingivalis* DNA in human brains, and the associated gingipains co-localising with plaques", says Sim Singhrao at the University of Central Lancashire, UK, who wasn't involved in the study. Her team has previously found that *P. gingivalis* actively invades the brains of mice with gum infections.

15. When Lynch and her colleagues looked at brain samples from people without Alzheimer's, they saw that some had *P. gingivalis* and protein accumulations, but at low levels. We already know that amyloid and tau can accumulate in the brain for 10 or 20 years before Alzheimer's symptoms begin. This, says the team, shows that *P. gingivalis* doesn't get into the brain as a result of Alzheimer's – but could be the cause.

16. When the team gave *P. gingivalis* gum disease to mice, it led to brain infection, amyloid production, tangles of tau protein and neural damage in the regions and nerves normally affected by Alzheimer's. This suggests causation, says Lynch.

17. She adds that *P. gingivalis* fulfils an updated set of criteria for attributing a disease to a particular pathogen. These conditions are named Koch's postulates, after Robert Koch, a founder of the germ theory of disease.

18. "The study does address most of Koch's postulates", says Robert Genco of the University at Buffalo, New York. "Future studies need to be in humans to be convincing."

19. We don't know how *P. gingivalis* gets into the brain, but there are plausible routes it could take. Your mouth normally hosts a diverse and relatively stable community of bacteria, but when dental plaque builds under the edge of your gums, it can form inflamed pockets in which *P. gingivalis* can thrive and release toxins.

20. This inflammation can lead to chronic periodontitis and tooth loss and some studies have shown that people with fewer teeth are more likely to have dementia. The inflammation and toxins caused by *P. gingivalis* damage the lining of your mouth, which may make it possible for oral bacteria to enter the bloodstream and then other organs. Even if you don't have disease, transient damage to your mouth lining from eating or tooth-brushing can let mouth bacteria into your blood, says Lynch.

21. The blood-brain barrier should protect your brain from microbes, but *P. gingivalis* can invade white blood cells and the cells lining blood vessels, so might cross it that way. It may also invade cranial nerves near the mouth, then spread from cell to cell towards the brain over a period of years.

22. As to how *P. gingivalis* might cause dementia after it arrives in the brain, there are two clear possibilities. It may trigger the release of amyloid, the brain's method of trying to contain the infection, and this may then kill neurons.

23. Or *P. gingivalis* may directly damage the brain. We already know that Alzheimer's involves inflammation, an excessive immune response that ends up killing neurons instead of protecting them. *P. gingivalis* is known to cause inflammation in gum tissue, and it may do so in the brain as well.

24. In response to the new findings, David Reynolds of the Alzheimer's UK charity said he is dubious that *P. gingivalis* causes Alzheimer's, because of the evidence showing that a person's genes play a crucial role in the disease. "Strong genetic evidence indicates that factors other than bacterial infections are central to the development of Alzheimer's, so these new findings need to be taken in the context of this existing research", he said in a statement.

25. But a bacterial hypothesis for Alzheimer's doesn't conflict with genetic evidence. The human body's propensity for inflammation can vary according to genetic variations that affect our immune systems, and this may influence how much damage *P. gingivalis* induces in a brain.

26. The biggest genetic risk factor for Alzheimer's is a variant of the gene that makes the ApoE immune protein. Last year, a team in Sweden found that the gingipains released by *P. gingivalis* break up the ApoE protein into fragments, cleaving it at the site of a particular amino acid within the protein, and that these fragments may harm nerves. The ApoE4 variant of this protein contains more of this amino acid, suggesting that the reason people who make this variant are at higher risk of developing Alzheimer's may be because harmful levels of ApoE protein fragments build up more quickly in their brains than in those of other people.

Hope for treatments

27. The speed at which damage accumulates is a key factor in the disease. Although many people harbour *P. gingivalis* in their mouths, only some develop Alzheimer's. Because it can be decades before Alzheimer's symptoms appear, whether a person develops the condition could come down to how much damage occurs before they die of other causes.

28. "Alzheimer's strikes people who accumulate gingipains and damage in the brain fast enough to develop symptoms during their lifetimes", says Lynch. She says her team's findings are a "universal hypothesis of pathogenesis fully explaining the causes of Alzheimer's disease."

29. But Vissel warns that Alzheimer's is a complex disease. "The answer is unlikely to be one-cause-fits-all. We need to keep open eyes."

30. However, the new study is very exciting, he says. "Alzheimer's is so common in people at advanced age that I think it can only be either some intrinsic property of the brain or an infection."

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