Alzheimer’s disease (AD) is a non-reversible brain disorder that develops over a

number of years. At the start of 2014 the number of Americans with AD was

estimated to be 5.4 million. Every 30 seconds another person in America

develops AD.

5        In the brain of a person with AD there is a lower concentration of acetylcholine.

This affects communication between nerve cells and initially results in memory

loss and confusion. Some of the symptoms of AD that are associated with

communication between nerve cells are reduced by taking the drug donepezil.

Donepezil inhibits the enzyme acetylcholinesterase.

10      A gene mutation called E280A found on chromosome 14 causes early-onset AD

at a mean age of 49 years. The age at which the E280A mutation is expressed

to cause AD varies.

Yaramul is a town in a historically isolated region of the Andes Mountains. The

population of this town has the highest frequency of the E280A mutation in the

15      world. The origin of the E280A mutation in this population has been traced back

to a common ancestor in the 17th century. Natural selection has not reduced

the frequency of the E280A mutation in the population.

This autosomal dominant mutation involves a change in triplet 280 from GAA to

GCA. Scientists analysed chromosome 14 from 102 individuals from Yaramul.

20      They recorded a sample size of 204 and detected 75 E280A mutations but only

74 potential AD cases. The scientists identified individuals with the mutation by

whole genome sequencing. They had decided that a DNA probe would not be a

suitable method to detect the E280A mutation.

(a)     Assuming no one with AD died in 2014, calculate the annual percentage increase in AD cases in America for 2014 (lines 2–4).

Answer = \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ %

**(2)**

(b)     Explain how donepezil could improve communication between nerve cells (lines 7–9).

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**(3)**

(c)     Suggest and explain **two** reasons why there is a high frequency of the E280A mutation in Yaramul (lines 13–15).

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2. \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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**(2)**

(d)     Explain why natural selection has **not** reduced the frequency of the E280A mutation in the population (lines 16–17).

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**(2)**

(e)     The age at which the E280A mutation is expressed to cause AD can vary (lines 11–12).

Suggest and explain **one** reason for this.

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**(2)**

(f)      One scientific study which analysed chromosome 14 involved 102 individuals. The scientists recorded a sample size of 204. In this sample they detected 75 E280A mutations but only 74 potential AD cases (lines 19–21).

Suggest explanations for the figures the scientists recorded.

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**(2)**

(g)     Suggest why a DNA probe for the mutated triplet was **not** considered a suitable method for detection of the E280A mutation (lines 22–23).

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**(2)**

**(Total 15 marks)**

**Mark Scheme**

(a)     1.      Correct answer of 19.4 / 19.41%

**OR**

19.47 / 19.5% = **2 marks**;

2.      Incorrect answer but shows increase of

1,048,320 **OR** 1,051,200 = one mark;

*Accept: 19.46% for one mark.*

**2**

(b)     1.      Less / no acetylcholine broken down;

2.      Acetylcholine attaches to receptors;

3.      (More) Na+ enter to reach threshold / for depolarisation / action potential / impulse;

*1.      Accept: more acetylcholine present / remains.*

*1 and 2. Accept: remains attached for longer = 2 marks.*

*3.      Must be sodium ions.*

**3**

(c)     1.      Isolated **so** inbreeding / low genetic diversity / small gene pool;

2.      Allele inherited (through generations) from (common) ancestor;

*1.      Ignore: Founder effect.*

*1.      Accept: no interbreeding with other populations.*

*1.      Reject: interbreeding within the population.*

**2**

(d)     1.      AD / symptoms develops late / at 49;

2.      Have already reproduced;

*Note: ‘It’ is not equivalent to AD / symptom as the question stem relates to the mutation.*

**2**

(e)     1.      Epigenetics / environment / named factor e.g. stress, alcohol, toxins, diet, exercise, smoking;

2.      methylation (of genes)

**OR**

acetylation (of histones);

*1.      Ignore: gender and lifestyle.*

*2.      If further details are provided the context must be correct e.g. increased methylation or decreased acetylation inhibit gene expression / transcription.*

**2**

(f)      1.      One person was homozygous dominant / has two dominant alleles = **2 marks**;

2.      For one mark has two alleles / chromosomes;

*1.      Accept; homozygous dominant genotype e.g. ‘one person has AA’ for 2 marks.*

*2.      Accept: is diploid or has two copies of the gene.*

**2**

(g)     1.      (GCA / triplet) is common / found in other places;

2.      Would not know if it was the mutation / allele / gene

**OR**

Produces ‘false positives’

*1.      Accept: Probe will bind elsewhere.*

**2**

**[15]**

**Examiner report**

(a)     Over a third of students obtained both marks for this question, for answers of 19.41 / 19.4% or 19.47 / 19.5%, depending on whether the student used 7 x 52 (weeks) or 365 as the number of days in a year. Almost a third of students gained one mark for correctly calculating the increase in AD cases per year as being 1 048 320 or 1 051 200, depending on the number of days used. Incorrect rounding to give 19.46% was quite common, to gain one mark.

(b)     The majority of students gained at least one mark for stating that less acetylcholine would be broken down, or that more acetylcholine would be present. Almost half of these students obtained a second mark for stating that the acetylcholine binds to receptors. However, only 10% of students obtained maximum marks by describing how an impulse would be produced in the postsynaptic neurone. Many students did appreciate that sodium ion channels would open, but then failed to mention that sodium ions would then enter to cause depolarisation.

(c)     Over 50% of students scored zero for this question, usually due to answers lacking complete explanations for the valid suggestions they outlined. Less than 2% of students gained both marks. The most frequently credited response was that isolation had resulted in a small gene pool or low genetic diversity. Poor use of terminology also prevented many students gaining both marks. Invariably, students referred to the gene or mutation, rather than the allele being inherited from a (common) ancestor. There was also considerable confusion in the use of the terms inbreeding and interbreeding. There were also many responses which referred to genetic bottlenecks, the Founder effect, and an increase in the rate of mutation in isolated areas. A significant number of students suggested that the late onset of AD enabled individuals still to reproduce and pass on the mutation. This would explain why the frequency of the mutation had not been reduced (part d), rather than why there is a high frequency of this mutation to begin with.

(d)     Almost a third of students obtained both marks, clearly expressing the idea that, due to the symptoms of AD developing late on, affected individuals would have already reproduced. Over 50% of students scored zero, often providing responses that suggested that the mutation was not harmful, or indeed that it was beneficial. An improvement in health care was also provided as an explanation for the frequency of the mutation not being reduced. Students obtaining one mark often did not refer to the late onset of AD, but did understand that individuals with the mutation could still reproduce and pass on the allele.

(e)     Over 50% of students scored zero on this question. Many of these responses suggested that differences in the ‘level’ of acetylcholine, or exposure to mutagenic agents, caused the variation in the age at which the mutation is expressed. Over a third of students obtained one mark, usually by naming an environmental factor such as diet, smoking or stress. Answers specifically referring to epigenetics for at least one mark were infrequent. These responses often gained a second mark, 10% of students, for mentioning methylation or acetylation. Students who described these processes generally provided correct details.

(f)      Almost three out of ten students obtained one mark for explaining the sample size of 204 in terms of two copies of chromosome 14 or two copies of an allele. A common error was to refer to two chromatids. Explaining why there were only 74 potential AD cases when 75 mutations had been detected proved very challenging, with only 2% of students gaining this second mark. Many students suggested that the allele causing AD is recessive, despite line 18 of the comprehension passage stating that it is dominant. A common misconception was that one individual was heterozygous for the condition. Other incorrect responses focused on AD not having yet developed, or attempted to explain the data in relation to the degeneracy of the genetic code.

(g)     Over 10% of students did not attempt this question, and over 5% omitted the parts (e) and (f). It seems likely that some students had difficulty completing the paper, but it was also evident that these last three questions were demanding. Only 25% of students obtained a mark on this question. Almost all of these students gained one mark for realising that the GCA triplet would occur in a number of different places. Half of these students then explained that you could not then determine if the mutation was present or not. As in part (f), a number of incorrect ideas were linked to the degenerate nature of the genetic code. The misconception that probes were being used to sequence the whole genome arose, so lots of different primers would be needed and it would be very time consuming and costly. The probe was sometimes thought only to be able to identify the mutation if the gene had been expressed to cause the disease, or that the probe would not bind because the mutation had not occurred yet. A surprising number of students said the sequence of the mutation was not known, so therefore a probe could not be made, or that the mutation was different in different people.