Review question on cystic fibrosis

Introduction

This is an exam style question which reviews the genetics of cystic fibrosis, the process of PGD, screening procedures for cystic fibrosis and false positives.

Suggested answers

a	i	1:4 / 25%	*for 1 mark*	1
	ii	• chance is 1:4 for <u>each</u> child • previous conception does not affect chances	*any 1 for 1 mark*	1
b	i	D – need for several to select/ IVF so that embryo can be sampled C – one cell to provide DNA for testing A – to identify CF alleles present in embryo B - only embryos without 2 CF genes used	*2 marks for correct order* *1 mark for each reason*	6
	ii	20% (any value from 15 to 30%)	*for 1 mark*	1
c	i	• sample is 1/60th of total number of babies in a year • variation in actual number means <u>average</u> not necessarily whole number • two unusual CF mutations very rare/ 6 a year therefore average (0.1) less than a whole number in sample of 10 000 • 3.5 x 60 = 210 actual babies a year (or other similar calculation showing how sample gives non-integer values)	*any 2 for 1 mark each*	2
	ii	• (50 –4.1) x 100 / 50 • 92%	*any 1 for 1 mark*	1
	iii	• lower value would increase false negatives • IRT test not very accurate • false negatives would mean babies with CF not identified. • this would be more serious further tests can produce more accurate results	*any 2 for 2 marks*	2
	iv	• 0.6 babies • 0.5 have one mutation undetected • 0.1 have 2 mutations undetected	*any 2 for 1 mark each*	2
	v	• carrier is perfectly healthy • at least one parent is carrier • need to check both parents • risk for future children if both parents carriers • possibility of second rare mutation	*for 1 mark each*	2
				18

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Cystic Fibrosis is one of the commonest inherited diseases in the UK. It is caused by mutations in the CTFR gene. These mutated alleles are recessive.

(a) Before the faulty gene was identified affected families had no way of preventing the birth of children with the disease, except by not having children at all.

(i) What is the chance of two carrier parents having a child with the disease?

(1 mark)

(ii) In one family of five children, four had cystic fibrosis. Explain why this sad, unusual result is so different from that predicted in (i) .

(1 mark)

(b) Now it is possible to identify carriers before they conceive a child. Carrier parents can opt to use pre-implantation genetic diagnosis, PGD, to prevent the birth of a baby with CF.

(i) Put the following procedures in the order in which they would take place during PGD and explain the purpose of each.

A) Genetic analysis of chromosomes
B) Selection and implantation of an embryo
C) Removal of one cell from embryos
D) In vitro fertilisation, IVF, of several eggs

Procedure	Purpose

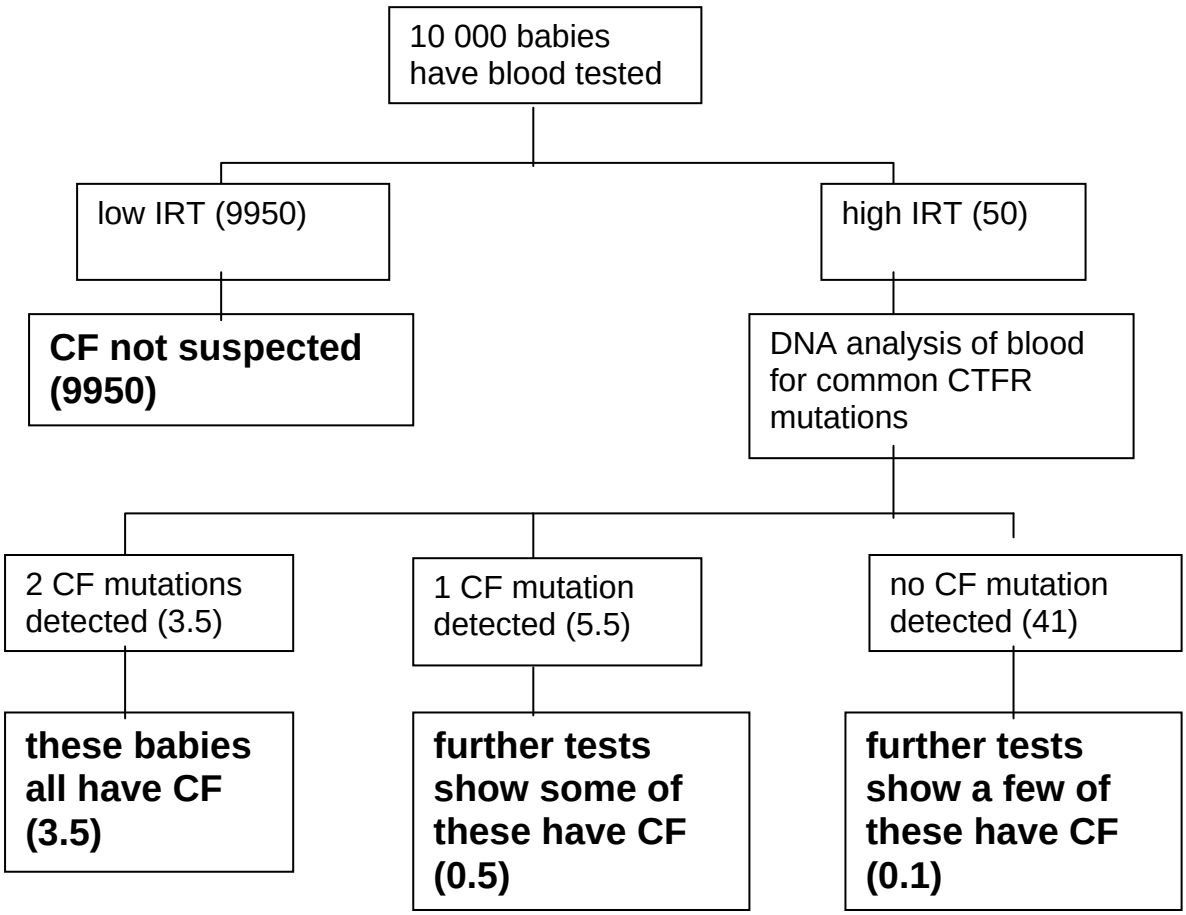
(6 marks)

(ii) This procedure does not guarantee that the couple will have a baby. About what proportion of implanted IVF embryos result in the birth of a baby?

(1 mark)

(c) In the UK today nearly all newborn babies are screened for cystic fibrosis, using a test for chemicals in the blood, called IRT. This screening test identifies about 50 per 10 000 babies as needing further investigation. The procedures followed are shown in Figure 1.

Figure 1 Procedures used for newborn screening for CF



Numbers in brackets give the average number of babies in each category, from any original group of 10 000 babies.

This diagram is a simplified version adapted from 'A laboratory guide to newborn screening for cystic fibrosis' http://www.ich.ucl.ac.uk/newborn/download/laboratory_guide_cystic_fibrosis.pdf

(i) Why does Figure 1 show numbers of babies that are not whole numbers? About 600 000 babies are born in Britain each year.

(2 marks)

(ii) Only 4.1 of the 50 babies with high IRT are finally found to have CF. What percentage of positive results from IRT screening are false positives?

(1 mark)

(iii) IRT levels show a range of values and the test itself is not very accurate. The cut-off point for calling an IRT result 'high', a positive result, could be chosen at any value. Using a higher value would reduce the number of false positives.

Suggest why a cut-off point has been chosen which gives a large number of false positives.

(2 marks)

(iv) There are many possible CF mutations, far more than those tested in the DNA analysis. Some are very rare and some of these are not yet identified. How many of the babies in Figure 1 must have at least one of these rare mutations? Explain your answer.

(2 marks)

(v) Parents of all children who are identified as having one CF mutation are referred to a genetic counsellor. Describe **two** of the issues they would discuss with the parents.

(2 marks)

(Total 18 marks)