Deacon's Challenge

No 93 - Answer

A 25-year old married woman in good health has just discovered that her brother is homozygous for the C282Y haemochromatosis gene mutation. Her sister has been tested and has the normal genotype. Her own genotype is as yet unknown. The population gene frequency for C282Y is 8%.

a) Calculate the probability that the woman is a homogygote.

b) Calculate the probability that her husband is a homozygote.

c) If the woman were subsequently tested and found to be a heterozygote, calculate the probability that their son will be a homozygote.

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a) Let A be the mutated gene for haemochromatosis and a the normal gene. For her brother to be homozygous for the mutation (genotype *AA*) he must have inherited one mutated gene from each parent. Since her sister is normal (homozygous for the normal gene, genotype *aa*) she must have inherited one normal gene from each parent. Therefore each parent must have both a normal (*a*) and mutated gene (*A*) i.e. they must be heterozygotes (genotype *Aa*). The results of a cross between both parents is:

		Male gametes	
		A	*a*
Female gametes	*A*	*AA*	*Aa*
	a	*aA*	*aa*

Therefore the probability of this lady being homozygous for the haemochromatosis mutation (*AA*) is 1 in 4 i.e. 0.25 (or 25%).

b) Since we have no information on the husband's family the chance of him being homozygous for the haemochromatosis gene is the same as for any member of the general population where the gene frequency is 8%. If the frequency of the haemochromatosis gene is 8% (i.e. 0.08) then the frequency of the homozygous state (*AA*) is the square of this:

Probability of a homozygote = $(0.08)^2$ = **0.0064** (i.e. 0.64 % or 1 in 156)

c) If the woman is a heterozygote (*Aa*) then the probability of her producing an *A* gamete is 0.5.
We do not know the genotype of her husband so the probability of him producing a gamete with the mutated gene (*A*) is the same as its incidence in the general population i.e. 8% (0.08).

Therefore probability of a son being homozygous (*AA*)

= 0.5 x 0.08 = **0.04** (4% or 1 in 25).

No 94 - Question

Serum AFP levels are being monitored following curative surgery for hepatoblastoma in a two-year old boy. Samples are normally being taken at weekly intervals but a repeat sample is taken in error two days after the routine week 4 sample. The requesting clinician is concerned that this sample appears to show evidence of disease recurrence. Assuming a biological variation of 12% and an analytical CV of 6% for this assay, determine whether this concern is justified.

Day	**AFP** (kIU/L)
7	1,613,000
14	723,000
21	329,000
28	145,000
30	149,000

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