Deacon's Challenge

No 130 - Answer

Haemochromatosis, a cause of abnormal liver function tests (LFTs), has a UK allele frequency of 0.07. Iron overload due to haemochromatosis can be demonstrated in 80% of men aged over 40, using a raised serum transferrin saturation. A commoner cause of abnormal LFTs is non-alcoholic fatty liver disease (NAFLD), with a reported prevalence of 5%. Unfortunately, raised TSat has also been reported in 7.4% of patients with abnormal LFTs due to NAFLD (and there is no association between NAFLD and haemochromatosis). Assuming that there are no other causes of raised TSat, in what percentage of male patients over 40 with abnormal LFTs will a raised TSat indicate haemochromatosis? State any assumptions made.

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If the allele frequency (p) is 0.07 and we are only considering the autosomal recessive forms of hereditary haemochromatosis, then the prevalence of affected individuals (homozygotes for the defective gene) is p^2.

$$\text{Prevalence} = 0.072^2 = 0.0049$$

We have to assume that the prevalence is the same in patients with abnormal LFTs (it is probably much higher) as it is in the general population.

We need to calculate the proportions of true positives (TP) and false positives (FP).

Sensitivity of TSat is given as 80%

$$\text{TP} = \text{Prevalence} \times \text{Sensitivity}$$

$$= 0.0049 \times \frac{80}{100} = 0.00392$$

False positives only occur with NAFLD.

$$\text{FP} = \text{Prevalence of NAFLD} \times \text{False positive rate}$$

Since the prevalence of NAFLD is 5% of all patients with abnormal LFTs and the false positive rate in this group is 7.4%:

$$\text{FP} = \frac{5}{100} \times \frac{7.4}{100} = 0.0037$$

The percentage of all patients with abnormal LFTs in which raised TSat indicates haemochromatosis is the positive predictive value of the test – PV(+):

$$\text{PV(+)} = \frac{\text{TP} \times 100}{(\text{TP} + \text{FP})} = \frac{0.00392 \times 100}{(0.00392 + 0.0037)} = \frac{0.00392 \times 100}{0.00762} = \mathbf{51\%} \text{ (to 2 sig figs)}$$

Question 131

A patient is admitted to ITU with a blood hydrogen ion concentration of 105 nmol/L, pCO_2 of 5.9 kPa and an actual bicarbonate of 10.2 mmol/L. After taking steps to improve ventilation and circulation a second set of blood gases were: pCO_2 5.1 kPa and bicarbonate 20 mmol/L. Calculate the new hydrogen ion concentration in nmol/L.

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