Deacon's Challenge No. 38 Answer

A man has a PSA of 5 µg/L. 22% of patients with benign prostatic hypertrophy and 38% of patients with prostatic cancer have concentrations of PSA between 4.1 and 10 µg/L. What is the positive predictive value for a diagnosis of cancer of the result for this man in this range, if the prevalence of cancer in his age group is 5% and benign prostatic hypertrophy is 20%? Assume 2% of patients without any prostatic pathology have a PSA >4.1 µg/L.

MRCPath, May 2003

This question differs from previous problems on sensitivity and specificity in that there are three, not two, groups of patients. However, there are only two groups as far as the disease in question (prostatic cancer) is concerned – those with cancer and those without. The only difference is that the group without disease is made up of two populations:

- those with benign prostatic hypertrophy (BPH)
- those without either BPH or prostatic cancer (CAP).

For those patients with CAP, let TP = number with raised PSA who have CAP
FN = number with normal PSA who have CAP

Incidence of CAP in the population is 5% = (TP + FN)

The proportion of CAP patients with raised PSA (sensitivity) = 38%

Therefore, Sensitivity = $\frac{TP}{TP + FN} = \frac{TP}{5\%} = 38\%$

Rearrange and solve for TP: TP = 38% x 5% = 1.9%

Next calculate the percentage of false positives for both the BPH and normal groups.

BPH group
22% of the patients with BPH have raised PSA. Therefore the false positive rate (FP) for the BPH group is 22%.

The incidence of PBH in the population (TN + FP) is 20%.
Substitute (TN + FP) = 20% into the expression for false negative rate and solve for FP:

FP rate (BPH) = $\frac{FP}{(TN + FP)} = \frac{FP}{20\%} = 22\%$

Therefore, FP = 22% x 20% = 4.4%

Normal group
Similarly, 2% of the normal group have raised PSA. Therefore the false positive rate (FP) for the normal group is 2%.

The incidence of normals is 100 - (% with CAP + % with BPH)
= 100 - (5 + 20)
= 100 - 25 = 75 %

Again, this proportion is equal to (FP + TN).

FP rate (normals) = $\frac{FP}{(TP + FN)} = \frac{FP}{75\%} = 2\%$

so that FP = 75% x 2% = 1.5%

The positive predictive value (PV+) of the PSA test is the proportion of the positive results which are due to CAP (the remainder being due to false positives from both the BPH and normal group).

PV(+) = $\frac{TP\ (CAP)}{TP\ (CAP) + FP\ (BPH) + FP\ (normal)}$

Substitute for TP(CAP), FP(BPH) and FP(normal):

PV(+) = $\frac{1.9}{1.9 + 4.4 + 1.5} = \frac{1.9}{7.8} = 0.24$ (or 24%)

Therefore only about 1 in 4 positive results will be due to prostatic cancer. ■

Question No. 39

A 33 year old woman investigated for subfertility had a mildly elevated serum prolactin level varying between 800 and 1400 mIU/L on three occasions over three months. The next specimen received in the laboratory a year later gave a prolactin result of 1900 mIU/L (Bayer Centaur ref range 59-619 mU/L). The possibility of macroprolactin was considered.

250 µL of serum was mixed with 250 µL polyethylene glycol (PEG 6000), centrifuged at 3000 rpm for 30 min and the supernatant re-analysed, the result being compared to a 1:1 dilution in Centaur diluent.

The result following PEG treatment was 354 mIU/L.

The result of the diluted specimen was 948 mIU/L.

Calculate the recovery of prolactin in the presence of PEG and comment on the result.

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