Deacon's Challenge

No 192 - Answer

A metabolic disease is known to result in decreased plasma activity of enzyme X. X was measured in 100 normal subjects and 100 individuals with the disease. A reasonable Gaussian distribution was obtained for each population with the following statistics:

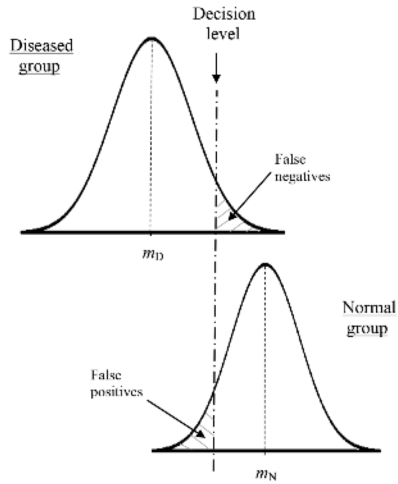
	Mean (m)	*Standard deviation (s)*
Normal subjects	*1025 U/L*	*100 U/L*
Diseased group	*530 U/L*	*200 U/L*

Find the decision level at which sensitivity is equal to specificity? What is the sensitivity (and hence specificity) at this decision level?

Two-tailed values of the normal deviate (z-score) and probability (P) are:

P(%)	*10*	*5*	*2*	*1*	*0.2*	*0.1*
z	*1.65*	*1.96*	*2.33*	*2.58*	*3.09*	*3.29*

These data form two overlapping normal probability distributions in which the mean of the normal group (m_N) is higher than the mean of the diseased group (m_D). The decision level (*DL*) divides the normal group into true negatives and false positives. The diseased group is divided into true positives and false negatives:



If the sensitivity (proportion of true positives in the diseased group) equals the specificity (the proportion of true negatives in the normal group) then the proportion of each group in the shaded area must also be equal. If the data is normalised (by subtracting the mean from each value and dividing the difference by the standard deviation) then the normal deviates (*z*-scores) at the point of intersection with the decision level with each distribution must also be equal:

$$\frac{DL - m_D}{s_D} = \frac{m_N - DL}{s_N}$$

which can be re-arranged to give an expression for *DL*:

$$s_N (DL - m_D) = s_D(m_N - DL)$$

$$s_N.DL - s_N.m_D = s_D.m_N - s_D.DL$$

$$s_N.DL + s_D.DL = s_D.m_N + s_N.m_D$$

$$DL (s_N + s_D) = s_D.m_N + s_N.m_D$$

$$DL = \frac{s_D.m_N + s_N.m_D}{s_N + s_D}$$

Substitute m_D = 530 U/L, s_D = 200 μ/L, m_N = 1025 U/L and s_N = 100 U/L to evaluate *DL*:

$$DL = \frac{(200 \times 1025) + (100 \times 530)}{100 + 200} = \frac{205{,}000 + 53{,}000}{300} = \mathbf{860\ U/L}$$

The sensitivity can be calculated from the *z*-score of the diseased group:

$$z = \frac{DL - m_D}{s_D} = \frac{860 - 530}{200} = \frac{330}{200} = 1.65$$

From the table of *z*-scores a *z* of 1.65 corresponds to a probability of 0.1 (10%). Therefore 10% of results will fall outside the mean±1.65*s* range, with half of these (5%) being above the mean+1.65s. Therefore 95% of results in the disease group will be below the decision level of 860 U/L. The sensitivity (the % of diseased individuals below the DL) is therefore 95%.

Similarly the specificity can be calculated from the z-score of the normal group:

$$z = \frac{m_N - DL}{s_N} = \frac{1025 - 860}{100} = \frac{165}{100} = 1.65$$

Again 5% of results in the normal group will be less then mean-1.65*s* and 95% will be above the decision level of 860 U/L so that the specificity (% of normals above the DL) is also **95%**.

Question 193

A patient in A&E with suspected adrenal crisis was given an iv dose of hydrocortisone at 18.00. The medical team on take wish to carry out a short synacthen test to confirm the diagnosis but there will be a significant contribution from the administered drug until its concentration has fallen to 10% of the peak value. Assuming that hydrocortisone elimination follows a single compartment (first order) model with a half-life of 2 h, what is the earliest time at which the test can be carried out?