Deacon's Challenge

No 165 - Answer

An inherited metabolic disease is due to a gain in function of enzyme X. The erythrocyte activity of X was measured in 100 normal subjects and 100 patients with the disease. The 95% confidence limits of the two groups are:

Unaffected: 89 – 901 IU/L red cells
Diseased: 830 – 5260 IU/L red cells

The data from the unaffected group showed a normal Gaussian distribution. However, the data from the diseased group were markedly skewed but a simple logarithmic transformation produced a reasonable Gaussian distribution.

It is proposed to use the assay of X in erythrocytes as a screening test for the disease. Calculate the decision level which will result in a sensitivity of 95%. What specificity will this achieve?

Two tailed z-distribution:

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

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The sensitivity is the percentage of results above the decision level (*DL*) in the diseased group.

First convert the 95% confidence limits of the diseased group to logarithmic units:

$\text{Log}_{10}\,830 = 2.92 \qquad \text{Log}_{10}\,5260 = 3.72$

Next calculate the mean (m) and standard deviation (s) in logarithmic units:

$$\text{Mean} = \frac{2.92 + 3.72}{2} = 3.32$$

The 95% confidence limits include the mean ± 1.96s

$$\text{therefore } s = \frac{3.72 - 2.92}{1.96 \times 2} = 0.20$$

To obtain a sensitivity of 95% select a P value of 10% so that a half of values will be less than 5%. i.e. use $z = 1.65$:

$$z = \frac{m - DL}{s}$$

$$1.65 = \frac{3.32 - DL}{0.20}$$

$$DL = 3.32 - (1.65 \times 0.20) = 2.99$$

This value is in logarithmic units so take the antilog to obtain DL in enzyme units:

$DL = \text{antilog}_{10}\,2.99 =$ **977 IU/L red cells**

The specificity is the percentage of normal individuals with values below the DL.

First calculate m and s for the unaffected group:

$$m = \frac{89 + 901}{2} = 495 \text{ IU/l red cells}$$

$$s = \frac{901 - 89}{2 \times 1.96} = 207 \text{ IU/L red cells}$$

Calculate z to determine the percentage results outside m ± DL range:

$$z = \frac{DL - m}{s} = \frac{977 - 495}{207} = 2.33$$

From z-table, 2% of values will fall outside the m ± 2.33s range and half of these (1%) will be above the DL.

Therefore specificity = 100 – 1 = **99%**

Question 166

A patient is found to have a serum digoxin concentration of 3.8 µg/L. Digoxin was stopped. Assuming a half life of digoxin in the serum of 40 hours, how long would it take for the serum digoxin concentration to fall to 2.0 µg/L?

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