Deacon's Challenge No. 61 Answer

A laboratory using a method with an analytical coefficient of variation of 5% at a concentration of 100 mmol/L for a serum constituent examined samples from a healthy population and found a Gaussian distribution with a 95% reference range of 74-126 mmol/L. If the method coefficient of variation had been 22%, what reference range would the laboratory have found?

The total variation contributing to the reference range is composed of both biological variation and analytical imprecision. Their variances (i.e. their SDs squared) or CVs squared are additive.

If SD_T = total SD of the reference range
SD_{Biol} = SD of biological variation alone
SD_{Anal} = SD due to analytical imprecision

Then $SD^2_T = SD^2_{Biol} + SD^2_{Anal}$

One way to approach the problem would be to substitute values for SD_T and the original SD_{Anal}, solve for SD_{Biol} then calculate the new SD_T from the SD_{Biol} and the new SD_{Anal}. Alternatively, the new SD_T resulting from a change to the new SD_{Anal} ($SD_{Anal.New}$) can be determined by subtracting the original SD^2_{Anal} ($SD^2_{Anal.Old}$) then adding the new SD^2_{Anal}:

$$SD^2_{T.New} = SD^2_{Biol} + SD^2_{Anal.Old} - SD^2_{Anal.Old} + SD^2_{Anal.New}$$

Substituting: $SD^2_{T.Old} = SD^2_{Biol} + SD^2_{Anal.Old}$

and $\Delta SD^2_{Anal} = SD^2_{Anal.New} - SD^2_{Anal.Old}$ ....(i)

gives: $SD^2_{T.New} = SD^2_{T.Old} + \Delta SD^2_{Anal}$ ....(ii)

The original reference range (74-126 mmol/L) is the mean ±2SD i.e. spans 4SD units. Therefore $SD_{T.Old}$ is obtained by dividing the range by 4:

$$SD_{T.Old} = \frac{126-74}{4} = 13 \text{ mmol/L}$$

The analytical imprecision is given as CV(%), not SD. The relationship between CV(%) and SD is:

$$CV(\%) = \frac{SD \times 100}{Mean}$$

Which can be rearranged to give an expression for SD:

$$SD = \frac{CV(\%) \times Mean}{100}$$

The mean (i.e. midpoint of the reference range) is (126 +74)/2 = 100 mmol/L. Therefore the mean and 100 cancel and SD = CV(%).

Therefore substituting $SD^2_{Anal.Old}$ and $SD^2_{Anal.New}$ into expression (i) gives:

$$\Delta SD^2_{Anal} = 22^2 - 5^2 = 484 - 25 = 459$$

Next substitute for $SD_{T.Old}$ and ΔSD^2_{Anal} into expression (ii) and solve for $SD_{T.New}$:

$$SD^2_{T.New} = 13^2 + 459 = 169 + 459 = 628$$

$$SD_{T.New} = \sqrt{628} = 25 \text{ mmol/L (2 sig figs)}$$

Lower limit of reference range = mean - 2SD = 100 - (2 x 25)
= 100 - 50 = 50 mmol/L

Similarly upper limit of reference range = mean + 2SD = 100 + 50 = 150 mmol/L

Reference range (if analytical CV = 22%) = 50-150 mmol/L

Question 62

As Duty Biochemist you encounter a sample with an apparent plasma sodium concentration of 152 mmol/L. You discover that the blood was taken in error into an 'anticoagulation' Vacutainer tube containing 0.5 mL trisodium citrate solution (citrate concentration 0.105 mol/L). The total volume of anticoagulated blood in the tube is 4.5 mL. Assuming that the result is analytically correct, what is the true plasma sodium concentration?

MRCPath, November 2005