Deacon's Challenge

No 147 - Answer

It has been suggested that a simple delta-check using serial plasma creatinine measurements be used to detect acute kidney injury (AKI). If the within-subject biological coefficient of variation (CV) for plasma creatinine is 5.0% what minimum analytical CV is required to detect a percentage increase in plasma creatinine of 20% with 95% certainty?

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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If x_1 is the initial creatinine result, x_2 the second result and s_1 and s_2 their respective standard deviations then the differences between the two results $(x_2 - x_1)$ can be considered as a normally distributed variable with mean $m_{1,2}$ and standard deviation of their differences $s_{1,2}$. If x_1 and x_2 are not significantly different then measured differences $(x_2 - x_1)$ would belong to a distribution with a mean of zero and combined standard deviation of $s_{1,2}$. A *z*-score can be calculated for any value of $(x_2 - x_1)$ in order to determine the likelihood that this value is significantly different from zero at any desired level of probability:

$$z = \frac{(x_2 - x_1)}{s_{1,2}}$$

If both the numerator and the denominator on the right hand side of the equation are multiplied by 100 and divided by x_1 then $(x_2 - x_1)$ becomes the percentage increase in creatinine and assuming the *CV* is the same at both concentrations, $s_{1,2}$ becomes $\%CV_{1,2}$:

$$z = \frac{\%\ \text{change}}{\%CV_{1,2}}$$

If a *z*-score of 1.96 is used and there is no real change in *x* (i.e. the mean percentage difference is zero) then on 95% of occasions these differences would fall within the $1.96s_{1,2}$ range with 2.5% of results less than $-1.96s_{1,2}$ and 2.5% greater than $+1.96s_{1,2}$. However, since we only wish to detect an *increase* in plasma creatinine (when the % change is positive) only the positive side of the curve is used and we instead adopt a *z*-score of 1.65 so that the $\pm1.65s_{1,2}$ range includes 90% of results with 5% less than $-1.65s_{1,2}$ and 5% greater than $+1.65s_{1,2}$. Therefore any value greater than the $+1.65s_{1,2}$ would indicate a rise in creatinine with at least 95% certainty.

Substitute $z = 1.65$ and % increase = +20% then solve for $CV_{1,2}$:

$$1.65 = \frac{20}{\%CV_{1,2}}$$

$$\%CV_{1,2} = \frac{20}{1.65} = 12.12\%$$

The %*CV* of the increase in creatinine ($\%CV_{1,2}$) is related to the %*CV*s of the individual measurements ($\%CV_1$ and $\%CV_2$) by the expression:

$$\%CV_{1,2}^2 = \%CV_1^2 + \%CV_2^2$$

Since the two measurements were made on specimens from the same individual using the same method, $\%CV_1 = \%CV_2$, this expression can be simplified:

$$\%CV_{1,2}^2 = 2 \times \%CV^2$$

and taking square roots:

$$\%CV_{1,2} = \sqrt{2} \times \%CV = 1.414\ \%CV$$

Substituting $\%CV_{1,2} = 12.12\%$ and solving for %*CV*:

$$12.12 = 1.414\ \%CV$$

$$\%CV = \frac{12.12}{1.414} = 8.57\%$$

This %*CV* of the individual measurements ($\%CV_{Total}$) is made up of two components, the intra-subject biological %*CV* ($\%CV_{Biological}$) and the analytical %*CV* ($\%CV_{Analytical}$):

$$\%CV_{Total}^2 = \%CV_{Biological}^2 + \%CV_{Analytical}^2$$

Substituting $\%CV_{Total} = 8.57\%$ and $\%CV_{Biological} = 5.0\%$ and solving for $\%CV_{Analytical}$:

$$8.57^2 = 5.0^2 + \%\%CV_{Analytical}^2$$

$$73.44 = 25 + \%CV_{Analytical}^2$$

$$\%CV_{Analytical}^2 = 73.44 - 25 = 48.44$$

$$\%CV_{Analytical} = \sqrt{48.44} = \mathbf{7.0\%} \quad \text{(2 sig figs)}$$

N.B. It is possible to combine the above expressions so that the calculation can be performed in a single step:

$$\%\ \text{change} = 1.44 \times z \times \sqrt{(\%CV_{Biological}^2 + \%CV_{Analytical}^2)}$$

Question 148

It is becoming increasingly common practice to replace pH with hydrogen ion concentration when reporting acid-base data. Analysis of cord blood in a neonate gave a hydrogen ion concentration of 66 nmol/L, with a pCO_2 of 7.4 kPa and an actual bicarbonate of 20 mmol/L. After taking steps to improve ventilation and circulation the end-expiration pCO_2 is 5.1 kPa and the actual bicarbonate of 16 nmol/L. Calculate the new hydrogen ion concentration in nmol/L, stating any assumptions made.

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