Deacon's Challenge No. 43 Answer

In 1976 Cockroft and Gault studied the relationship between creatinine excretion, age and body weight. They plotted the 24 h urinary creatinine excretion (mmol/24h) divided by body weight (in Kg) on the y axis against age on the x axis. The intercept on the y axis (i.e. y value when x = 0) was 0.248, whereas the slope was -0.0018. Derive an equation which can be used to calculate creatinine clearance (in mL/min) from plasma creatinine (µmol/L), body weight (in Kg) and age (in years).

The general expression for creatinine clearance is:

$$\text{Creatinine clearance} = \frac{U \times V}{P} \text{ mL/min}$$

where U and P are the creatinine concentrations in urine and plasma respectively in the SAME units and V is the urine flow rate in mL/min (assuming that the clearance is to be expressed as mL/min).

The data of Cockroft and Gault relate urine creatinine excretion to body weight and age so as to avoid the inconvenience (and inaccuracy) of a timed urine collection. The slope and intercept can be used to write a simple linear equation:

$$\text{Rate of urinary creatinine excretion (mmol/Kg/24h)} = 0.248 - (0.0018 \times \text{age})$$

If both sides are multiplied by the body weight (in Kg), then the body weight is transferred to the right hand side of the equation:

$$\text{Urine creat (mmol/24h)} = \text{Body Wt (Kg)} [0.248 - (0.0018 \times \text{age})]$$

To make the expression easier to manage, 0.0018 is moved outside the brackets; 0.248 then becomes 0.248/0.0018 = 138, and 0.0018 becomes 0.0018/0.0018 = 1:

$$\text{Urine creat (mmol/24h)} = \text{Body Wt} \times 0.0018 (138 - \text{age})$$

Since plasma creatinine (P) is to be expressed as µmol/L then this expression is multiplied by 1000 so that both U and P will be in the same units, and since the clearance is to be expressed per min, the expression is also divided by 24 (to convert to hours) then 60 (to convert to minutes):

$$\text{Urine creat (µmol/min)} = \frac{0.0018 \times \text{Body Wt} (138 - \text{age}) \times 1000}{24 \times 60}$$

$$\text{Urine creat (µmol/min)} = 0.00125 \times \text{Body Wt} (138 - \text{age})$$

Division by the plasma concentration (P) then gives the creatinine clearance:

$$\text{Creatinine clearance (L/min)} = \frac{0.00125 \times \text{Body Wt} (138 - \text{age})}{P}$$

Note that since the plasma concentration is in µmol/L, the clearance is in L/min. Multiplication by 1000 converts it to mL/min:

$$\textbf{Creatinine clearance} = \frac{\textbf{1.25} \times \textbf{Body Wt} (\textbf{138} - \textbf{age})}{\textbf{P}}$$

In most textbooks 1.25 is truncated to 1.2 and 138 is rounded to 140:

$$\textbf{GFR (mL/min)} = \frac{\textbf{(140 – age in yrs)} \times \textbf{Body Wt (Kg)} \times \textbf{1.2}}{\textbf{Plasma creatinine (µmol/L)}}$$

The above data were validated for men, it is common practice to multiply this value by 0.85 for women in order to correct for a lower muscle mass.

It is a common misconception that, since body weight is used in the formula, that the clearance is corrected for surface area. This is NOT the case, body weight (and age) is only used to predict urine creatinine output – a fact that is not obvious when looking at the formula. If a corrected clearance is required then this value must be divided by the body surface area (obtained from height and weight) then multiplied by the average surface area in the usual manner. ■

Question 44

Reproduced below are peak area data from an HPLC analytical run set up to measure plasma phenylalanine. The assay is used to monitor adequacy of dietary control in patients with phenylketonuria. Good control being regarded as maintaining plasma phenylalanine between 120 and 360 µmol/L.

N-methyl L-phenylalanine has been used as the internal standard. 200 µL of internal standard has been added to 200 µL aliquots of samples and standards prior to analysis.

Standard concentration = 500 µmol/L
N-methyl L-phenylalanine (NMP) concentration = 100 µmol/L
QC target: 180-210 µmol/L

Sample	Peak area	
	NMP	Phenylalanine
Standard	20,000	81,000
QC	22,000	35,000
Patient	21,000	140,000

a) Is the assay in control?
b) What was the patient's phenylalanine concentration?
c) What comment would you make about the patient's control from this result?

MRCPath, May 2004