Practical Kidney 2

Renal function and renal physiologic reserve involves the ability to filter and clear unwanted substances, and to reabsorb essential, though filtered, material. Ideally, we would like to measure the plasma level of a substance that is neither secreted nor reabsorbed by the kidney, measure the urinary concentration and volume, and calculate the clearance of the substance and thus the glomerular filtration rate (GFR). No such substance is readily and inexpensively available. Consequently, physicians have had to "make do" with urea and creatinine in the blood and also use their clearance as a measure of the GFR.
Renal clearance of a certain substance can be defined as the ml of blood (plasma or serum) which contain that certain substance excreted in a minute by the kidneys. This is given by the formula:

Clearance of substance X = U x V/P
= substance conc. in urine (mg/dl) x urinary volume (ml/min) / substance conc. in plasma (mg/dl)

OR
The clearance of any substance is defined as the number of ml of plasma which contains the same amount of that substance, as that excreted in urine in one minute.
The clearance carried out after giving inulin, mannitol and sodium thiosulfate gives accurate glomerular filtration rate since they are filtered at the glomeruli and they are neither reabsorbed nor secreted by the renal tubules. Its clinical application is limited, since the tests are cumbersome, time consuming, expensive and uncomfortable to the patient. The clearance of creatinine has been held to approximate to the inulin clearance and it is widely used as a measure of the glomerular filtration rate (normal average GFR = 125 ml)

Urea clearance

Urea is produced as a break down product of protein. It is completely filtered by the kidney, but is also reabsorbed. Thus urea clearance grossly underestimates GFR. In addition, the amount of urea reabsorbed increases with dehydration.
Clearance ureea = (U x V / P) = Urine urea (mg/dl) × V (ml/min) / Plasma urea (mg/dl)
Clinical significance: The urea clearance values fall progressively with increasing renal failure. If clearance falls below 20%, it is considered to be due to severe renal failure. Below 5%, uremic coma may be present.

Normal values: urea clearance = 60-95 ml/min (Average : 75 ml/min)

Procedure

1. Determine serum (or plasma) urea nitrogen
2. Determine urine urea nitrogen.
3. Calculate urea clearance according to urine excretion per minute (V/min.).

This method is based on the decomposing of urea $(NH_2)_2CO$ into N_2, H_2O and Na_2CO_3 by sodium hypobromite. The resulting N_2 is measured into the Kowarski apparatus. The N_2 volume is transformed into N_2 grams (Avogadro's law) and the N_2 grams into urea grams.

1. Determine urine urea nitrogen
    - Add tricloracetic acid to urine to precipitate the proteins (2.5 ml +2.5 ml)
    - Fill the apparatus with Kowarski solution over the superior tap and close it
    - Add 3 ml of urine, open the tap and let only 2,5 ml flow
    - Add 7 ml of sodium hypobromite and let only 6 ml flow
    - After each operation clean the reservoir of the apparatus
    - There will be a gas buildup at the top of the apparatus that you will read as N_2 volume (cm^3) after 10-15 minutes

- Calculus:

  Note the N_2 resulted from the reaction with V; in the reacton there were 1.25 ml of urine involved (and 1.25 ml of tricloracetic acid)

  V ml N_2.....1,25 ml urine

  X ml.....1000 ml urine X= V x 800

  28g N_2.....22400 ml N_2

  Y mg.....V x 800 Y= V

  As there are 2 N_2 in urea, in 1000ml of urine there are 2 x Vgrams of urea.

  Normal value: 15-35 g/l

2. Determine blood urea nitrogen.
   - Adopt the same procedure
   - 4 ml of blood with 4 ml of tricloracetic acid
   - Use 5 ml in the reaction (2,5 ml of blood)
   - Same calculus but there will rezult V/2 grams of N_2, so V grams of urea.
3. Calculate urea clearance according to urine excretion per minute (V/min.).

Normal volume is around 2 ml/min, and for this volume the renal clearance of urea is 75 ml/min.

Creatinine Clearance

Creatinine is a metabolic by product of muscle metabolism (it is derived from creatine and phosphocreatine). For the majority of patients the muscle turnover varies little from day to day, and the serum creatinine is more or less constant. Creatinine is filtered and excreted by the kidney. Serum creatinine is probably the most widely used indirect measure of glomerular filtration rate; it is easy and inexpensive to measure.

This test gives relatively accurate and useful measure of the glomerular filtration rate and also the excretory capacity of the kidney. The reasons for the greater degree of accuracy of creatinine clearance are (1) creatinine is not absorbed by the tubules (2 The effect of fluid intake and excretion on creatinine clearance is much less than that of urea and (3) The blood creatinine values are relatively stable. The creatinine clearance values may be greater than the actual glomerular filtration rate, when plasma creatinine levels increase considerabIy above the normal range.

This is given by the formula

Clearance = UV / P

Normal values

a) For males : 105 ± 20 ml/min
b) For Females: 95 ± 20 ml/min

Determination of Creatinine Clearance

1) Measure volume of the collected urine specimen.
2) Determine serum creatinine
3) Determine urine creatinine
4) Calculate creatinine clearance from the following formula:

Creatinine clearance (ml) = urine creatinine (mg/dl) × V (ml/min) / serum creatinine (mg/dl)

This method is based on the reaction between creatinine and picric acid that results in a redish-orange compound (Jaffe reaction). The extinction of the compound resulted from the sample is read at 520 nm on a spectrophotometer against a blanc and compared to a standard compound to obtain the concentration of the sample.

Generaly used in the clinic:

Creatinine (Cr) Clearance ml/min = ((140 - Age) · (Wt))/(72 · Cr), multiply by 0.85 if female.