Renal function test

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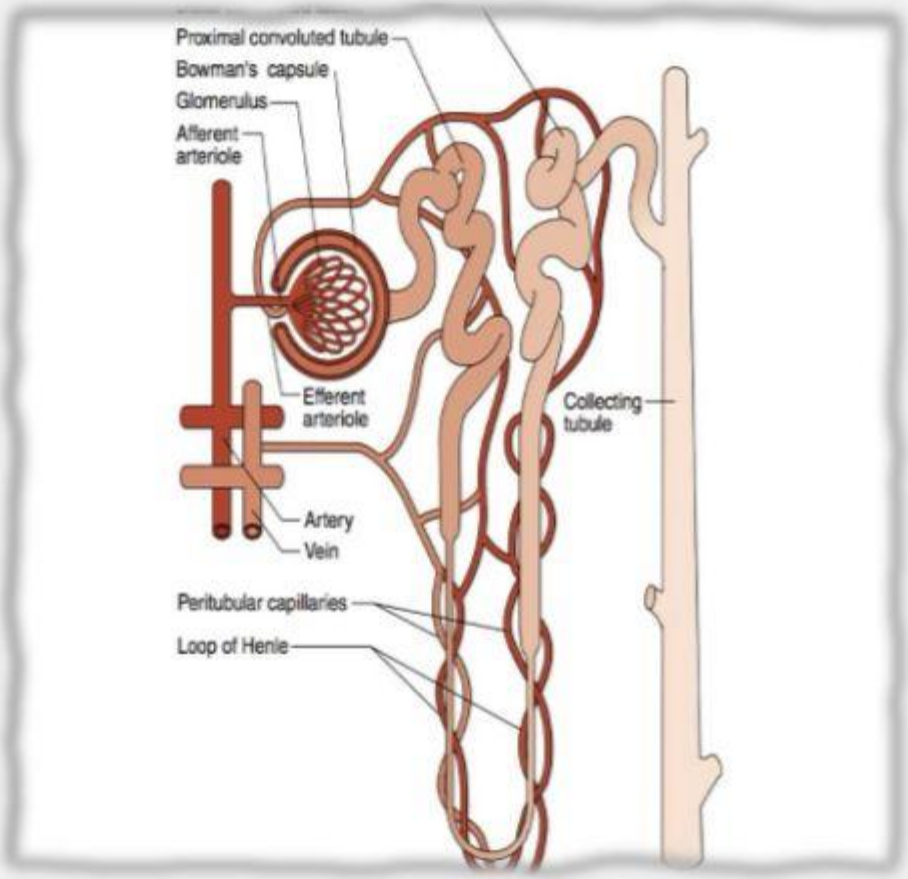
Functional unit of kidney

- The nephron is the functional unit of the kidney.
- Each kidney contains about one million nephrons.

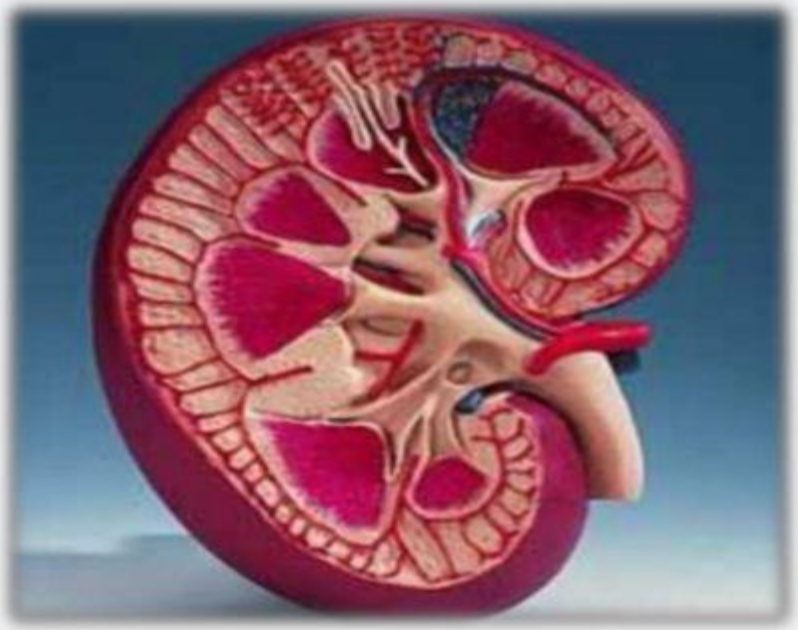
- The nephron is composed of glomerulus (network of capillaries), bowman capsule and renal tubule, containing the proximal, and distal tubules, loop of Henle and collecting duct.
- The nephron performs its homeostatic function by ultra filtration at glomerulus and secretion and reabsorption at renal tubules.



Representation of a nephron and its blood supply

Functions of the Kidney:

- Regulation: e.g. Maintenance of homeostasis,
  - Water and electrolyte balance.
  - Acid base balance.
  - Arterial blood pressure.



- Excretion: of metabolic waste products and foreign chemicals e.g. uric acid, urea, creatinine and retention of substances vital to the body: glucose, amino acids etc.
- Hormonal or Endocrine: e.g. Secretion of erythropoietin, renin & activation of vitamin D (1,25 dihydroxycholecalciferol- conversion only in kidney).
- Metabolic Function: site for gluconeogenesis.

Renal Diseases:

- Many diseases affect renal function.
- In some, several functions are affected. In others, there is selective impairment of glomerular function or one or more of tubular functions.
- Most types of renal diseases cause destruction of complete nephron.

- Major causes of renal diseases:
  - Pre-renal diseases
  - Glomerular diseases
  - Tubular & interstitial diseases
  - Obstructive uropathies

When should you assess renal function?

- Indications for assessing renal functions:
  - Older age
  - Family history of Chronic Kidney disease (CKD)
  - Decreased renal mass
  - Diabetes Mellitus (DM)
  - Hypertension (HTN)
  - Autoimmune disease
  - Systemic infections
  - Urinary tract infections (UTI)
  - Nephrolithiasis (renal stones)
  - Obstruction to the lower urinary tract (e.g. prostatic causes)
  - Drug toxicity

Assessment of Kidney Functions:

❑ Assessment of Glomerular Functions

➢ Assessment of glomerular filtration rate (GFR) is used an index of glomerular functions.

➢ Measurement of GFR:

- Clearance tests
- Blood creatinine
- Blood urea
- Blood uric acid
- Blood β2-microglobulin.

❑ Assessment of Tubular Functions

➢ Renal tubular functions is assessed by:

- Urine osmolarity measurements
- Urine PH
- Urine volume
- Urine specific gravity
- Urine appearance and color
- Urine protein amount
- Urine glucose amount measurement (glucosuria)
- Urine amino acids (aminoaciduria)

Some of Routine kidney function test include the measurement of:

- Serum creatinine.
- Clearance test.
- Serum urea.

- Both serum creatinine and clearance test are used as kidney function tests to:

  - Confirm the diagnosis of renal disease.
  - Give an idea about the severity of the disease.
  - Follow up the treatment.

Serum creatinine:

- Creatine is synthesized in the kidneys and liver.
- It is then transported in blood to other organs such as muscle and brain.
- 98% of the body creatine present in the muscles is phosphorylated to phosphocreatine, which represent as store of a high-energy compound.
- About 1-2 % of total muscle creatine or creatine phosphate pool is converted daily to creatinine through the spontaneous, non enzymatic loss of water or phosphate.
- Creatinine is a non-protein nitrogen waste product formed in muscle. It is the end product of creatine catabolism.
- Creatine is synthesized in liver from some amino acids (glycine, methionine, arginine).

- Creatinine in the plasma is filtered freely at the glomerulus and secreted by renal tubules (10% of urinary creatinine).
- Creatinine is not reabsorbed by the renal tubules.
- Plasma creatinine is an endogenous substance not affected by diet.
- Plasma creatinine remains fairly constant throughout adult life.
- The plasma levels of creatinine are related to the muscle mass (the production varies with age and sex).
- It is generally a more sensitive and specific test for renal function than the BUN.

Clearance test:

- Clearance is defined as the volume of plasma completely cleared from a substance excreted in urine per minute
- Normal range: is usually about 110 ml/min in the 20–40-year-old adults.
- It falls slowly but progressively to about 70 ml/min in individuals over 80 years of age.

- It could be calculated from the following equation:

$$\text{Clearance (ml/min)} = \frac{U \times V}{P}$$

U = Concentration of creatinine in urine µmol/l.

V = volume of urine (in ml/min)

P = Concentration of creatinine in serum µmol/l.

- The most frequently used clearance test is based on the measurement of creatinine.
- The glomerular filtration rate (GFR): the amount of filtrate that flows out of all the renal corpuscles of both kidneys every minute.
- It provides a useful index of the number of functioning glomeruli. It gives an estimation of the degree of renal impairment by disease.

- Accurate measurement of GFR by clearance tests requires determination of the creatinine concentration in plasma and urine.

- It should be noted that the GFR decline with age (to a greater extent in males than in females) and this must be taken into account when interpreting results.

Why Creatinine is used for testing clearance?

- Accurate measurement of GFR by clearance tests requires determination of the concentration in blood & urine of a substance that is:
  - Freely filtered at glomeruli
  - Neither reabsorbed nor secreted by tubules.
  - Its concentration in plasma needs to remains constant throughout the period of urine collection.
  - Better if the substance is present endogenously
  - Easily measured.

Creatinine meets most of these criteria.

Normal adult reference values

- Urinary excretion of creatinine is 0.5 - 2.0 g/24 hours in a normal adult, varying according to muscular weight.
  - Serum Creatinine: 55 – 120 µmol/L
  - Creatinine clearance: 90 – 140 ml/min (Males)
    80 – 125 ml/min (Females)

- A raised serum creatinine is a good indicator of impaired renal function
- But normal serum creatinine does not necessarily indicate normal renal function as serum creatinine may not be elevated until GFR has fallen by as much as 50%.

Cockcroft-Gault Formula for Estimation of GFR

- The creatinine clearance is measured by using a 24-hour urine collection, but this does introduce the potential for errors in terms of completion of the collection.
- An alternative and convenient method is to employ various formulae devised to calculate creatinine clearance using parameters such as serum creatinine level, sex, age, and weight of the subject.

$$GFR = \frac{K \times (140 - age) \times \text{Body weight}}{\text{Serum creatinine } (\mu mol/L)}$$

where K is a constant that varies with sex:

1.23 for male & 1.04 for female.

The constant K is used as females have a relatively lower muscle mass.

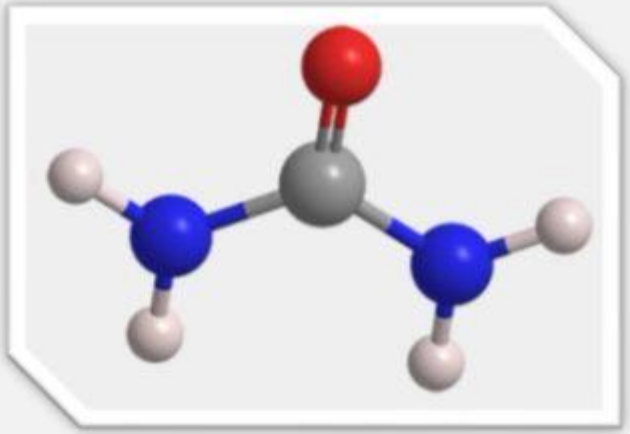
❑ Serum creatinine is a better kidney function test than creatinine clearance because :

- ✓ Serum creatinine is more accurate.
- ✓ Serum creatinine level is constant throughout adult life.

❑ Creatinine clearance is only recommended in the following conditions:

- ✓ Patients with early (minor) renal disease.
- ✓ Assessment of possible kidney donors.
- ✓ Detection of renal toxicity of some nephrotoxic drugs.

Serum Urea:



❑ Urea is a relatively nontoxic nitrogen containing substance made by the liver to dispose of ammonia resulting from protein metabolism (deamination of amino acids).

❑ Urea is filtered freely by the glomeruli

❑ Plasma urea concentration is often used as an index of renal glomerular function.

❑ Non renal factors can affect the urea level as:

- High protein diet increases urea formation (exogenous production factor).
- Increased protein catabolism (Cushing syndrome, diabetes mellitus, starvation) increased urea formation.
- Mild dehydration.
- Reabsorption of blood proteins after a GIT hemorrhage

- 50% or more of urea filtered at the glomerulus is passively reabsorbed by the renal tubules.

- ❑ Accordingly, measurement of plasma creatinine provides a more accurate assessment than blood urea because there are many factors that affect urea level rather than renal causes

- ❑ Its elimination in the urine represents the major route for nitrogen excretion.
- ❑ Serum Urea in adult: (2.5-6.6 mmol/L)
- ❑ BUN = (blood urea nitrogen) test measures the amount of nitrogen in the blood that comes from the waste product urea.
- ❑ The real urea concentration is BUN x 2.14


THANK
YOU