Kidney Function Tests (KFTs)

Objectives

Upon completion of lectures, students should be able to:

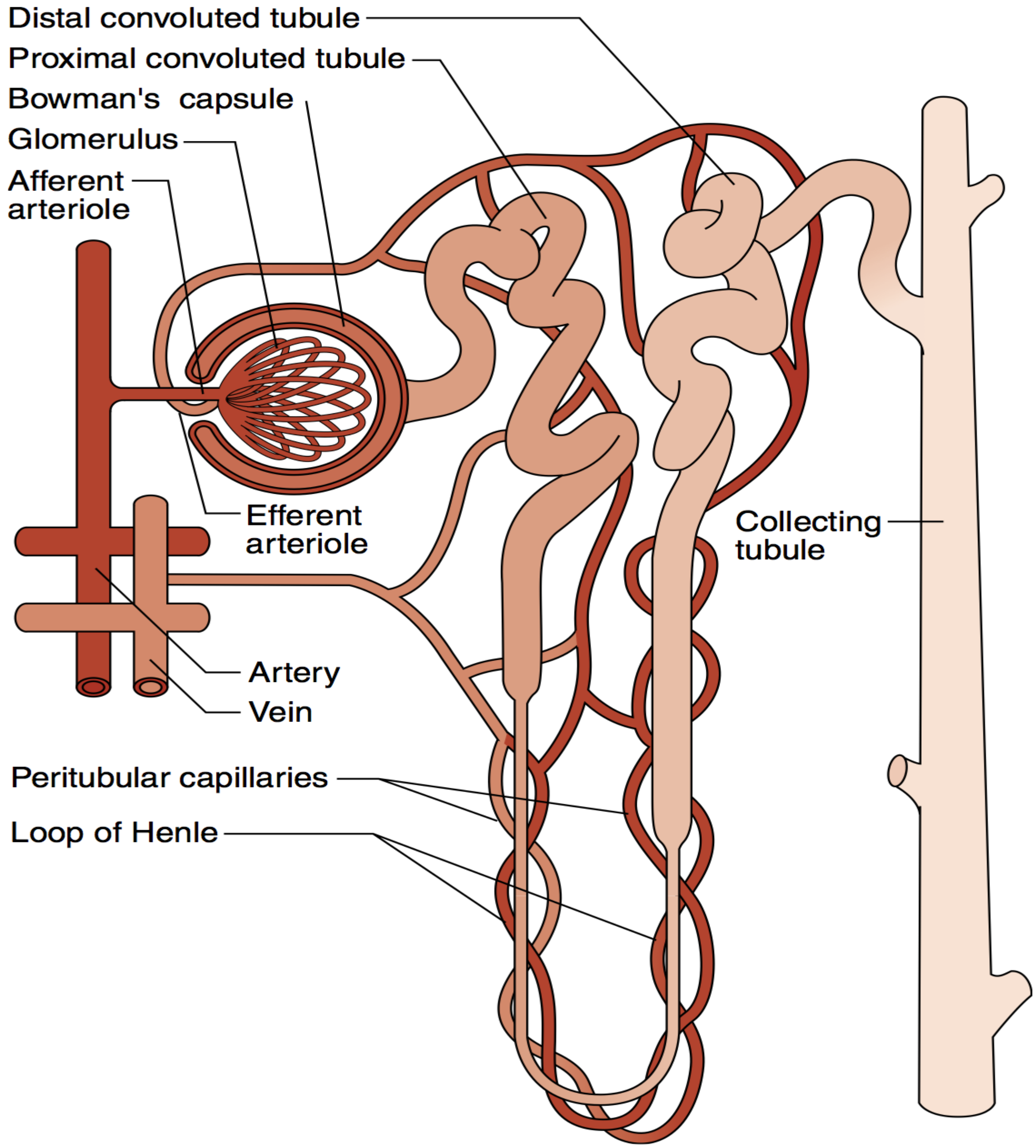
1. know the physiological functions of the kidney.
2. describe the structure and function of the nephron.
3. identify the biochemical kidney function tests with special emphasis on when to ask for the test, the indications and limitations of each kidney function tests.
4. interpret the kidney function tests properly.

Contents:

- Functional units
- Kidney functions
- Routine kidney function tests (KFTs):
  - Serum creatinine
  - Creatinine clearance
  - Cockcroft-Gault formula for GFR estimation
  - Serum Urea

Functional units :

- The nephron is the functional unit of the kidney
- Each kidney contains about 1,000,000 to 1,300,000 nephrons.
- The nephron is composed of glomerulus and renal tubules.
- 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

Each nephron is a complex apparatus comprised of five basic parts:

1. **Glomerulus:** functions to filter incoming blood.

   - **Factors facilitate filtration:**

     - high pressure in the glomerular capillaries, which is a result of their position between two arterioles.

     - the semipermeable glomerular basement membrane, which has a molecular size cutoff value of approximately 66,000 Da.

*The volume of blood filtered per minute is the **glomerular filtration rate (GFR)**, and its determination is essential in evaluating renal function.*

Each nephron is a complex apparatus comprised of five basic parts:

2. **Proximal convoluted tubule:**

   - Returns the bulk of each valuable substance back to the blood circulation.
     - 75% of the water, sodium, and chloride.
     - 100% of the glucose (up to the **renal threshold**)
     - almost all of the amino acids, vitamins, and proteins
     - varying amounts of urea, uric acid, and ions, such as magnesium, calcium and potassium.

     With the exception of water and chloride ions, the process is active; that is, the tubular epithelial cells use energy to bind and transport the substances across the plasma membrane to the blood.

   - Secretes products of kidney tubular cell metabolism, such as hydrogen ions, and drugs, such as penicillin.

Each nephron is a complex apparatus comprised of five basic parts:

3. Loop of Henle:

- Facilitates the reabsorption of water, sodium, and chloride.

The osmolality in the medulla in this portion of the nephron increases steadily from the corticomedullary junction inward

Each nephron is a complex apparatus comprised of five basic parts:

4. Distal convoluted tubule:

- The filtrate entering this section of the nephron is close to its final composition.
- Effects small adjustments to achieve electrolyte and acid-base homeostasis (under the hormonal control of both antidiuretic hormone (ADH) and aldosterone).

The distal convoluted tubule is much shorter than the proximal tubule, with two or three coils that connect to a collecting duct.

Each nephron is a complex apparatus comprised of five basic parts:

5. **Collecting duct:**

   - The collecting ducts are the final site for either concentrating or diluting urine.
   - The hormones ADH and aldosterone act on this segment of the nephron to control reabsorption of water and sodium.
   - Chloride and urea are also reabsorbed here.

Kidney functions :

- **Regulation of :**
  - water and electrolyte balance.
  - acid base balance.
  - arterial blood pressure.
- **Excretion** of metabolic waste products and foreign chemicals.
- **Hormonal Function**: Secretion of erythropoietin & activation of vitamin D and activation of angiotensinogen by renin
- **Metabolic Function**: site for gluconeogenesis

Why to test the renal functions?

- 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.

Routine KFTs include the measurement of :

- Serum creatinine (Cr).
- Creatinine clearance.
- Serum urea.

Both serum Cr and creatinine clearance 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 (55-120 μmol/L in adult):

- Creatinine is the end product of creatine catabolism.
- 98% of the body creatine is present in the muscles where it functions as store of high energy in the form of creatine phosphate.
- 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.

Serum creatinine (55-120 μmol/L in adult):

- 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.

Creatinine clearance:

- The glomerular filtration rate (GFR) 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 concentration in plasma and 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.

- Creatinine clearance 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 8o years of age.

- In children, the GFR should be related to surface area, when this is done, results are similar to those found in young adults.

- Clearance is the volume of plasma cleared from the substance excreted in urine per minute.

- 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 per min

P = Concentration of creatinine in serum μmol/l

Cockcroft-Gault Formula for Estimation of GFR

- As indicated above, 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.

- An example is **the Cockcroft-Gault Formula**:

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

- **where K is a constant that varies with sex:**
  1.23 for male & 1.04 for females.

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

Cockcroft-Gault Formula for Estimation of GFR: Limitations

- **It should not be used if**
  - Serum creatinine is changing rapidly
  - the diet is unusual, e.g., strict vegetarian
  - Low muscle mass, e.g., muscle wasting
  - Obesity

Serum Cr is a better KFT 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.

Normal adult reference values:

Urinary excretion of creatinine is 0.5 - 2.0 g per 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%

Serum Urea (2.5-6.6 mmol/L) in adult:

Urea is formed in the liver from ammonia released from deamination of amino acids.

As a kidney function test, serum urea is inferior to serum creatinine because:

- High protein diet increases urea formation.
- Any condition of ↑ proteins catabolism *(Cushing syndrome, diabetes mellitus, starvation, thyrotoxicosis)* →↑ urea formation.
- 50 % or more of urea filtered at the glomerulus is passively reabsorbed by the renal tubules.

Normal values of Internal Chemical Environment controlled by the Kidneys:

SODIUM	135 to 145 mEq/L
POTASSIUM	3.5 to 5.5 mEq/L
CHLORIDES	100 to 110 mEq/L
BICARBONATE	24 to 26 mEq/L
CALCIUM	8.6 to 10 mg/dl
MAGNESIUM	1.6 to 2.4 mg/dl
PHOSPHORUS	3.0 to 5.0 mg/dl
URIC ACID	2.5 to 6.0 mg/dl
pH	7.4
CREATININE	0.8 to 1.4 mg/dl
BUN (Blood Urea Nitrogen)	15 to 20 mg/dl

References :

- Clinical Chemistry: Techniques, Principles, Correlations. 6th ed, Michael L. Bishop, Edward P. Fody, Larry E. Schoeff. C hapter 26, 2010, pp 557-577