# Renal Function Tests

## 430 Biochemistry Team

Done By:-

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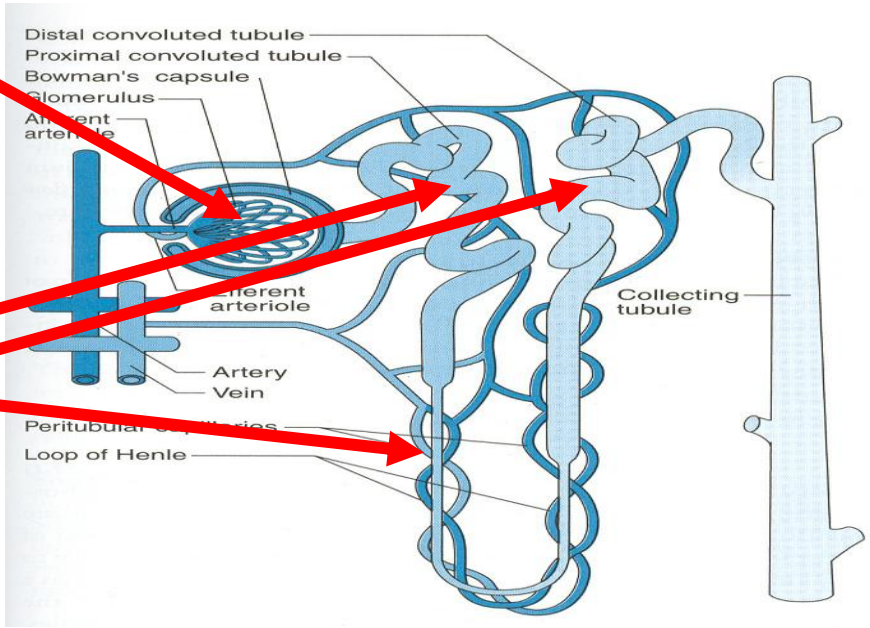
## - Functional Units (General Information):-

- The Uriniferous tubule (nephron and collecting tubule) 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 (tuft of fenestrated capillaries "without diaphragm) and renal tubules ( proximal convoluted tubles + loop of Henli + distal convoluted tuble) .
- The nephron does its job by *1- ultra filtration* ( is the filtration of all plasma components except plasma proteins through the filtration barrier by hydrostatic pressure) at *glomerulus* *2- Secretion and re absorption* at renal tubules

**Ultra Filtration**

**Secretion and reabsorption**



# What are the functions of the kidney?

1- **Regulation of :** By – (these are all homeostatic functions by the angiotensin-aldosterone system in kidneys)

- water and electrolyte balance, e.g. ( Na+, K+, Cl-)
- acid base balance. Of blood, NOT urine.
- arterial blood pressure.

2- **Excretion of :-** metabolic waste products and foreign chemicals, e.g. creatinine and Urea

3- **Hormonal Function :**

**- Secretion of rennin >>** Renin is an enzyme , not a hormone , that is secreted by the Juxtaglomeular cells when the blood pressure is low to maintain normal pressure (vasoconstriction)

**- Erythropoietin >>** is a hormone the controls the production of RED blood cells

**- 1,25 DHCC >>** in the kidney the PTH convert vitamen D to 1,25 dihydroxycholecalciferol(active form)

**Note:- Vitamen D:- regulates plasma levels of calcium and phosphorus . Cholesterol is the pre-curser of Vitamin D.**

4- **Metabolic Function :** site for gluconeogenesis. >> is a metabolic pathway that results in the generation of glucose from non-carbohydrate and kidneys can participate in gluconeogenesis in starvation or sever states.

## - Renal diseases ( General Information ):-

- Many disease cause effect the renal function, e.g. heart failure, glomuerularnephritis.

- In renal disease :-

  **1-** In some, several functions of the kidneys are effected

  **2-** In others, there is selective impairment of:-

  - glomerular function

  - tubular function

- Most types of renal diseases cause destruction of complete nephron.

**Note:- The end stage for many renal diseases is acute renal failure, Nowadays "Acute kidney injury" is being used to describe acute renal failure.**

## - What are Kidney function tests?

Kidney function tests are common lab tests used to evaluate how well the kidneys are working

## - What is the purpose of kidney function tests?

1- Confirm the diagnosis of renal disease

2- Give an idea about the severity of the disease

3- Follow up the treatment. That is, to see if there is any response from the treatment given.

## - What are the Kinds of kidney function tests?

Routine Kidney function Tests: include the measurement of:-

1- Serum creatinine. **First line**

2- Creatinine clearance. **Second line**

3- Serum urea. **Third line**

Both Serum creatinine and creatinine clearance are the most commonly used Kidney Function Tets.

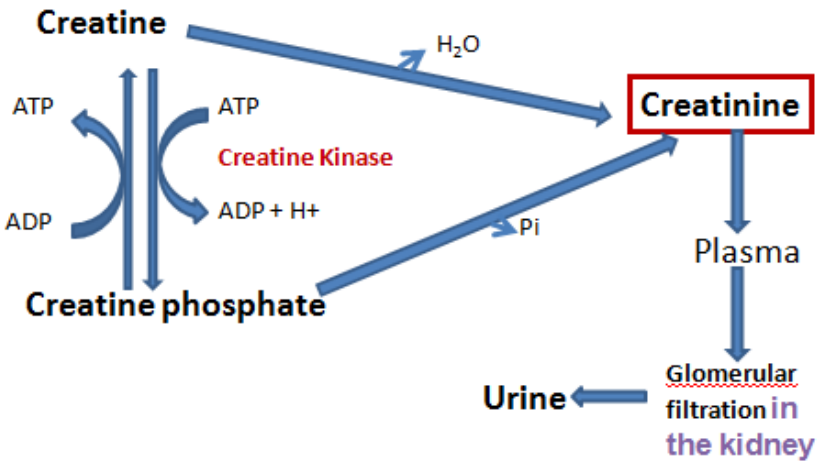
**Note:- The gold standard testing of kidney function is inulin clearance, which is basically the same process used in creatinnie clearance, but the only difference is that it is an Exogenous substance (Inulin) that is injected in the patient . However it is not used because it may lead to further complications such as anaphylactic shock also it is very cost effective. It is usually used in medical researches and under monitoring.**

## - How to assess the kidney function?

- 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.

**Before we start talking about each test individually there is a couple points we would like you to keep in mind before moving on ☺ here we go :-**

1. Creatine and creatine phosphate spontaneously form creatinine as an end product




2. **The difference between GFR and Creatinine clearance :-**

- **Creatinine clearance :-** It is the volume of plasma that is cleared from creatinine by the kidney per unit of time.

- **GFR :-** is the volume of fluid filtered from the renal (kidney) glomerular capillaries into the Bowman's capsule per unit time. It is the best estimate of the number of functioning nephrons or functional renal mass. Accurate measurement of GFR is time-consuming and expensive, but a number of filtered substances may be measured to estimate GFR, including blood urea nitrogen (BUN) and serum creatinine and measurement of creatinine clearance by the kidney.

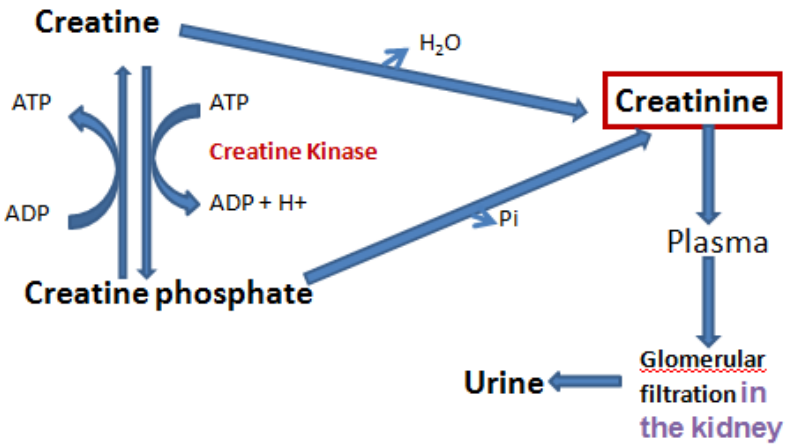
- **Remember :** both of GFR and Creatinine clearance have the same **unit (ml/min)**

- Finally we can conclude that: ***"creatinine clearance is a useful tool for approximating the GFR"***

## A-First Line test:- Serum Creatinine (55-120 µmol/L in adult):

It is all about measuring the creatinine level in blood. If it's **above** the normal value it indicates renal failure

- 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. **( Explanation was mentioned previously and we took it in Muscloskeletal Block)**
- 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. In other words, creatinine is physiologically produced by our bodies regardless (not being affected by) the food we eat or the drugs we take.
- Plasma creatinine remains fairly constant throughout adult life.

## B-Second Line test:- Creatinine clearance

Accurate measurement of GRF by **clearance tests** requires determination of the concentration in plasma and urine of a substance that is "in other words, the following is the criteria for the substance that is used to measure its clearance to get an accurate GFR".

1- Freely filtered at glomeruli. ( small sized and can pass through the GF barrier)

2- Neither reabsorbed nor secreted by tubules.

3- Its concentration in plasma needs to remain constant throughout the period of urine collection. ( which means its concentration is not affected by the metabolic out comes)

4- Better if the substance is present endogenously. (why? to lessen the risk of complication or eliminate it , like it was said previously Inulin is an Exogenenous substance which may cause anaphylactic shock)

5- Easily measured.

**So , based on the previous criteria Creatinine meets most of these points**

1- It is filtered in the plasma freely at the glomerulus.

2- is not reabsorbed by the renal tubules **BUT secreted by renal tubules** (10 % of urinary creatinine).

3- Plasma creatinine is an endogenous substance not affected by diet.

4- Plasma creatinine remains fairly constant throughout adult life.

## So , Creatinine clearance test is :-

- is the volume of plasma that is cleared from creatinine, and is excreted in urine per minute.
- It could be calculated from the following equation:

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

U = Concentration of Creatinine in urine μ mol /l

V = Volume of urine per min

P = Concentration of the Creatinine in plasma μ mol /l

- 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 80 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.
- The creatinine clearance is measured using a 24-hour urine collection. This holds a high percentage of errors in terms of completion of the collection.

## Cockcroft-Gault Formula for Estimation of GFR

- As indicated above, the creatinine clearance is measured by using a 24-hour urine collection. However this introduces us to 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. Remember: no need for 24- hours collection in the formula.

- An example is the Cockcroft-Gault Formula:

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

**No need to memorize the formula**

- 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.

- **This formula overestimates the GFR if the patient is obese. (one of it's limitations, or cons).**

➢ **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. Serum creatinine will only be positive if 50 % of total kidney function (GFR) is lost.
- Assessment of possible kidney donors.
- Detection of renal toxicity of some nephrotoxic drugs. ( Which means before giving a patient a drug with possible renal toxicity, his creatinine clearance is measured before and after admission.)

➢ **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

(Males) : 90 – 140 ml/min/1.73 m2

(Females) : 80 – 125 ml/min/1.73 m2

## C- Third Line Test:- Serum Urea ( 2.5-6.6 mmol/L) in adult:

- Same as BUN (Blood Urea Nitrogen)
- Urea is formed in the liver from ammonia released from deamination of amino acids. Generally : ( Proteins >> ammonia "precursor of urea" >> Urea)
- 50 % or more of urea filtered at the glomerulus is passively reabsorbed by the renal tubules. ( so they can never be used as a clearance test , "go back to the criteria")
- As a kidney function test, urea is inferior to serum creatinine because **high protein diet increases urea formation.**

**Some conditions increase serum urea with normal serum creatinine:**

1. **High protein diet increases urea formation.**
2. **Any condition of ↑ proteins catabolism (Cushing syndrome, diabetes mellitus, starvation, thyrotoxicosis) →↑ urea formation.**
3. **Dehydration (vomiting, diarrhea, ECF losses)**

**Note:- If tests results for a patient show High Urea Serum and normal creatinine serum or normal creatinine clearance , that patient doesn't have a kidney impairment… please read the following case for a clear explanation.**

# Clinical case

**If we draw a blood sample from a healthy patient and find that ( urea is elevated, serum creatinine is normal) could that indicate a renal pathology, knowing that the patient has not eaten a protein rich diet on the day the sample was drawn?**

- **Answer:**

**first of all, we exclude any condition that would elevate protein levels and urea formation, like Cushing syndrome, thyrotoxicosis …)"healthy patient". Secondly, we exclude urea coming from dietary sources, "as mentioned in the question".**

**In renal pathologies (renal failure), urea is elevated along with serum creatinine (both elevated).**

**Finally let's consider dehydration as the underlying pathology. Dehydration usually results from hypovolemia. In hypovolemia, less blood is being filtered (decreased GFR), therefore creatinine and urea clearance will decrease. First we have to remember here that creatinine is not reabsorbed but partially (10%) secreted in the tubules. However, urea is extensively reabsorbed. That will lead to remarkable increase in urea's concentration compared to that of creatinine. Therefore, the most probable diagnosis is dehydration ( urea is an early indicator for dehydration).**