



## Biochemistry Teamwork

### -Kidney Function Test-

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### Functional units of Kidney :

- 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.

### Kidney functions :

- Regulation of:
  - Water and electrolyte balance.
  - Acid base balance. ( $H^+$  - bicarbonate)
  - Arterial blood pressure. (Renin Angiotensin Aldosterone System)
- 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 (normally 90% in liver and 10% at kidney but in prolonged fasting 40-50% in kidney)

Ex: At hypotension the kidney tubules would increase reabsorption of Na taking with it water from the filtrate, for body fluid homeostasis.

### 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.

### Routine kidney function test include the measurement of: (listed by importance)

- Serum creatinine.
- Creatinine clearance.
- Serum urea.

Routine test is the U/E and CBC test (urea and electrolytes)

### Both serum creatinine 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.

Dr.Rana said that we don't have to memorize any numbers

Serum Urea (2.5-6.6 mmol/L). Urea is more than Creatinine normally. Differentiate between  $\mu$  and  $m$ .  
 $1\text{ mmol} = 1000\ \mu\text{mol}$

### Serum creatinine (55-120 $\mu\text{mol/L}$ 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.
- Creatinine in the plasma is filtered freely at the glomerulus and secreted by renal tubules (10% of urinary creatinine). We usually disregard the 10% that is secreted (freely = no oxygen consumption).
- 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?

It is an important feature of creatinine to be formed spontaneously, meaning there is no chance of enzyme defect and it can only indicate kidney injury.  
-Endogenous: made in the body

### Creatinine Clearance:

Because muscles of children are still growing so we measure the surface of their bodies with GFR.

- The glomerular filtration rate 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 GRF 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 remain constant throughout the period of urine collection.
- Better if the substance is present endogenously.
- Easily measured.

Differentiate between creatinine concentration and clearance in terms of units ( $\mu\text{mol/L}$ ) and (ml/min), respectively.

**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 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.
- 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  $\mu\text{mol/l}$

V = Volume of urine per min (ml/min)

P = Concentration of creatinine in serum  $\mu\text{mol/l}$

Cockcroft-Gault Formula for Estimation of GFR:

First we take a serum sample from the patient and get the concentration of creatinine, then we have a 24 hour urine collection and we instruct the patient what to do (here it is dependent to patient compliance, the patient might not understand the instructions or they may tamper with the sample) and we see the volume and concentration of the urine sample. [The volume is the limitation of this test because of patient compliance and this is why this test is inaccurate]

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

K = constant that varies with sex: 1.23 in males and 1.04 in females.

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

DR. Amr said this **Formula** is not important . but you need to know where should we use it

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 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.

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  $\mu\text{mol/L}$
- Creatinine clearance: 90 – 140 ml/min (Males)  
80 – 125 ml/min (Females)

We are not required to know the numbers, just know which is more and which is less

A raised serum creatinine is a good indicator of impaired renal function.

- But a 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: **important**

- High protein diet increases urea formation.
- Any condition of ↑ proteins catabolism (*Cushing syndrome, diabetes mellitus, starvation, thyrotoxicosis, dehydration (due to vomiting or diarrhoea) –mentioned by the doctor, but not in the slides*) → ↑ 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:**

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

DR. Amr says you don't need to memorize these values

## Questions

1. Which of the following tests gives a useful index of the number of functioning glomeruli?

- a) Serum creatinine
- b) Creatine clearance
- c) Serum urea

2. Which of the following is true about serum creatinine?

- a) It is more than serum urea
- b) It is affected by diet
- c) It is not reabsorbed by renal tubules

3) Which test is the most accurate?

- A) Serum creatinine
- b) Creatinine clearance
- c) Serum urea

4- patient with dehydration ,vomiting ,and diarrhea .. With normal serum Creatinine, but increased Serum Urea ... does it indicate renal impairment ?

- No . But because of loose of fluid "this question motioned by DR. Amr"

1b,2c,3a