

Estimation of Serum Creatinine, Urine Creatinine and Creatinine Clearance

-Kidney functions:

The kidneys serve three essential functions:

1. **They function as filters**, removing metabolic products and toxins from the blood and excreting them through the urine.
2. **They regulate the body's** fluid status, electrolyte balance, and acid-base balance.
3. **The kidneys produce or activate hormones** that are involved in erythropoiesis, Ca^{2+} metabolism, and the regulation of blood pressure and blood flow.



-Renal function tests (RFT):

- Are used to detect the presence of **renal diseases** and assess their progress.
- The most widely used test is to measure the glomerular filtration rate (GFR), that is, the rate of filtrate formation by the kidneys.

-Glomerular Filtration Rate (GFR):

- Under **normal** conditions, approximately 625 mL of plasma flow through the kidneys each minute and the volume of plasma **filtered** is 125 ml/ min which is called the **glomerular filtration rate**.
- Glomerular filtration rate (GFR): is the volume of plasma filtered by the kidneys per unit of time.
- GFR is an **important** and the **best** overall measurement in the evaluation of kidney function.

-Measuring the GFR:

- Accurate measurement of the GFR by **clearance tests** requires determination of the concentration, in plasma and urine, of a substance is known to be **completely filtered** from the plasma at the glomerulus.
- This substance **must not be reabsorbed nor secreted by renal tubules**, broken down, or accumulated by the tubules and must remain at a **constant concentration** in the plasma throughout the period of urine collection.

- **Clearance is given by :**

$$\text{Clearance} = U.V / P$$

→ Where:

U= concentration of any substance in urine.

P= concentration of the same substance in plasma.

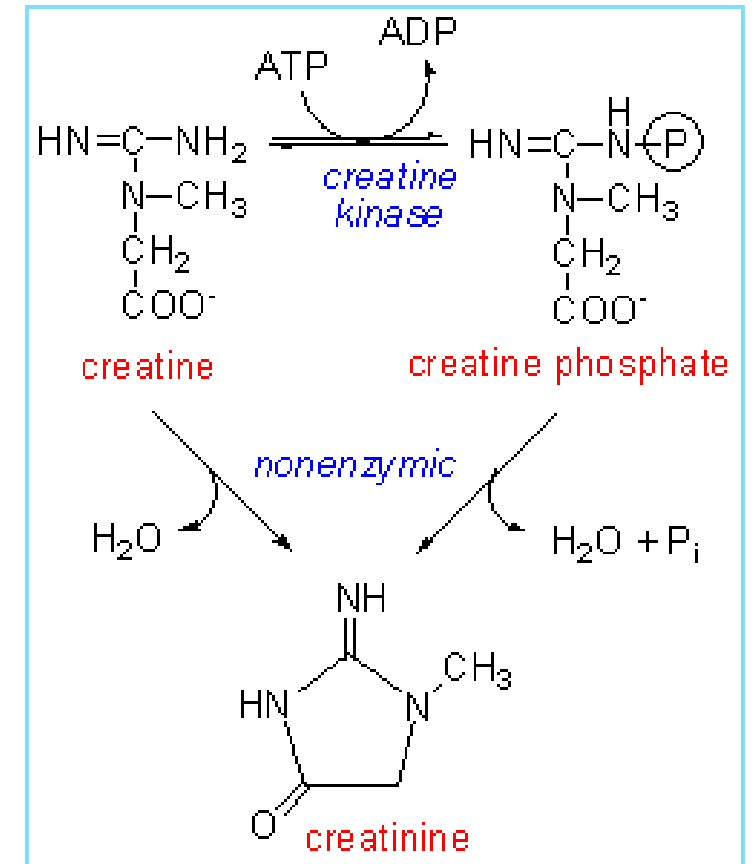
V= volume of urine (ml/min).

Substances used for Measuring GFR (clearance test)

	Inulin Clearance	Creatinine Clearance	Urea Clearance
Source	Non-toxic fructose polymer.	End-product of skeletal muscle creatine metabolism.	Endproduct of protein metabolism.
Advantages	Not reabsorbed or secreted.	An <u>endogenous</u> product of muscle metabolism; near constant production.	An <u>endogenous</u> product of protein.
Disadvantages	Not made by body; must be injected (exogenous).	Small amount is secreted.	-Partially reabsorbed. -Synthesis varies with diet.

-Creatinine:

- Creatinine is derived from “**creatine**” which is synthesized in the liver, kidney and pancreas it moves through the circulation and is taken up entirely by muscles.
- Creatinine is a substance that, in health, is easily excreted by the kidney. It is the byproduct of muscle energy metabolism and is produced at a **constant rate according to the muscle mass of the individual**.
- Endogenous creatinine production is **constant** as long as the muscle mass remains constant.



Creatinine clearance :

- A measure of the amount of creatinine eliminated (filtered) from the blood by the kidneys.
- Creatinine is cleared from the body fluids **almost entirely** by glomerular filtration (small amount is secreted by kidney tubules).
- Therefore, the clearance of creatinine can be used to assess GFR.
- Because measurement of creatinine clearance does not require intravenous infusion into the patient, this method is much more widely used than inulin clearance for estimating GFR clinically.
- **Tubules to variable degree secrete creatinine**, which by itself, would lead to an ~20% overestimate of GFR in humans.

Serum Creatinine:

- **High plasma creatinine:**

Plasma creatinine tends to be higher in subjects with a **large muscle mass**.

- Other **non-renal** causes of increased plasma creatinine include the following :

1. A high meat intake can cause a temporary increase.
2. Transient, small increases may occur after vigorous exercise .

➔ If non-renal cause can be excluded, an increased plasma creatinine indicates a fall in GFR (renal disease).

Urine Creatinine:

- **Decreased urine creatinine is found in:**

- Advanced renal disease.

- Renal stenosis.

- **Increased urine creatinine is found in:**

- Diabetes mellitus.

-Clinical Implications of creatinine clearance:

- **Decreased creatinine clearance is found in any condition that decreases renal blood flow:**
 - a. Impaired kidney function.
 - b. Shock, dehydration.
 - c. Hemorrhage.
 - d. Hypothyroidism.
- **Increased creatinine clearance is found in:**
 - a. Pregnancy.
 - b. Hyperthyroidism

-Reference Values:

- Urine creatinine :1- 2 g/24h
- Serum creatinine: 0.6–1.2 mg/dL
- Creatinine clearance: 100-130 ml/min/1.73m²

Note:

What 1.73 m² means?

- Kidney function is proportional to kidney size, which is proportional to body surface area. A of 1.73 m² is the normal mean value for young adults.
- Adjustment for body surface area is necessary when comparing a patient's estimated GFR to normal values or to the levels defining the stages of Chronic kidney disease (CKD).

Chart 2 - Chronic kidney disease staging

Stage	Description	GF (ml/min/1.73m ²)
I	Kidney lesion with normal or increased GF	≥ 90
II	Kidney lesion with mild GF decrease	60-89
III	Kidney lesion with moderate GF decrease	30-59
IV	Kidney lesion with marked GF decrease	15-29
V	Functional kidney failure or undergoing SRT	< 15

SRT- substitutive renal therapy. Source: National Kidney Foundation, 2002.

Practical Part

-Objectives:

- 1- To estimate creatinine in serum and urine.
- 2- To calculate creatinine clearance value.

-Principle:

(Jaffe's method):

Colorimetric estimation of creatinine using the alkaline picrate method:



-Method:

1- Set up a series of 8 test tube as follows:

Chemical	Standard (3mg/dl)		Test (serum)		Test (urine)		Blank
	(A)	(B)	(C)	(D)	(E)	(F)	
Water	1.5 ml	1.5 ml	1.5 ml	1.5 ml	1.5 ml	1.5 ml	2 ml
Standard	0.5 ml	0.5 ml	-	-	-	-	-
Serum Sample	-	-	0.5 ml	0.5 ml	-	-	-
Urine Sample	-	-	-	-	0.5 ml	0.5 ml	-
Picric acid	6 ml	6 ml	6 ml	6 ml	6 ml	6 ml	6 ml

2- Immerse the Tubes carefully in the boiling water bath for 40 seconds.

4- Pipette 0.6 ml of NaOH to all tube.

5- Let the tubes stand for 20 min.

6- Read the absorbance at 520 nm.

-Results:

Tube	Standard		Test (Serum)		Test (Urine)	
	(A)	(B)	(C)	(D)	(E)	(F)
Absorbance at 520 nm						
Average (Mean of Absorbance)						

-Calculation:

Patient information: 24h urine volume = 100ml, gender: women, body surface: 1.6m², DF=100.

1-Serum creatinine =

(Mean Absorbance of serum test ÷ Mean Absorbance of Standard) X concentration of standard = mg / dl

2-Urine creatinine =

(Mean Absorbance of Urine test ÷ Mean Absorbance of Standard) X concentration of standard X DF= mg / dl

(To compare with normal range, convert from mg/dl to g/24 h)

3- Creatinine Clearance :

$$=U.V/ P$$

$$= [(\textit{Urinary creatinine (mg/dl)}) / (\textit{plasmac creatinine (mg/dl)})] \times \textit{Urine volume(ml/min)} = \mathbf{B}$$

$$\mathbf{B} \text{ -----} > 1.6 \text{ m}^2 \text{ (person surface area)}$$

$$? \text{ -----} > 1.73 \text{ m}^2$$

$$\text{-Corrected for surface area= ml/min/1.73 m}^2$$

-Example:

Find the Creatinine Clearance if you know that the Urine creatinine $U = 488$ mg/dl , Serum creatinine $P = 2.32$ mg/dl, Volume of urine in 24 h = 100 ml and A "surface area" = 1.6 m^2 ?

→ Creatinine Clearance: = $U.V / P$

$$= (488 \text{ mg/dl} \div 2.32 \text{ mg/dl}) \times (100 \div 1440^*) = 14.6 \text{ ml/min}$$

14.6 ml/ min in 1.6 m^2 , find the creatinine clearance for 1.73 m^2 surface area :

$$= (14.6 \times 1.73) \div 1.6 = \underline{15.8 \text{ ml /min/1.73m}^2}$$

-----OR-----

→ Creatinine Clearance: = $(U \times V \times 1.73) / (P \times 1440 \times A)$

$$= (488 \text{ mg/dl} \times 100 \times 1.73) / (2.32 \times 1440 \times 1.6)$$

$$= \underline{15.8 \text{ ml/min /1.73m}^2}$$

* To convert 24 hour to min (24x60 = 1440)

-Discussion:

- Comment on the concentration of creatinine in serum and urine.
- Comment on the value of **Creatinine Clearance .**

-Home work:

A man aged 40 years with surface area of 1.8m^2 has a serum creatinine of 6 mg/dl. A 24 h urine of 2100 ml is collected and the creatinine concentration found to be 450 mg/dl.

- Calculate the Creatinine Clearance ?

-References:

- <http://www.nlm.nih.gov/medlineplus/ency/article/003435.htm>
- [http://www.mayoclinicproceedings.org/article/S0025-6196\(11\)60609-5/fulltext](http://www.mayoclinicproceedings.org/article/S0025-6196(11)60609-5/fulltext)
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