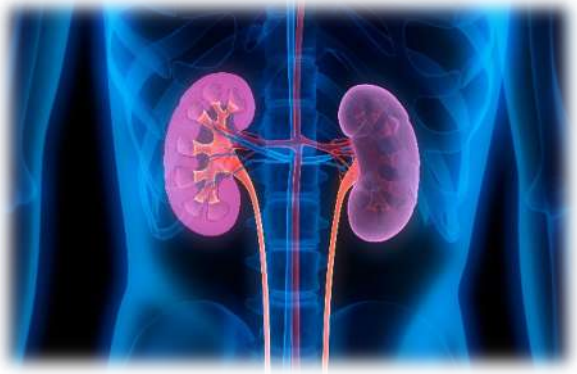
Estimation of Serum Creatinine, Urine Creatinine and Creatinine Clearance

Kidney functions:

The kidneys serve three essential functions:

1. **They function as filters**, removing waste 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 erythrogenesis, 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 :**

Clearance (ml/min) = U.V/ P

➔Where:

U= concentration of any substance in urine.

P= concentration of the same substance in plasma.

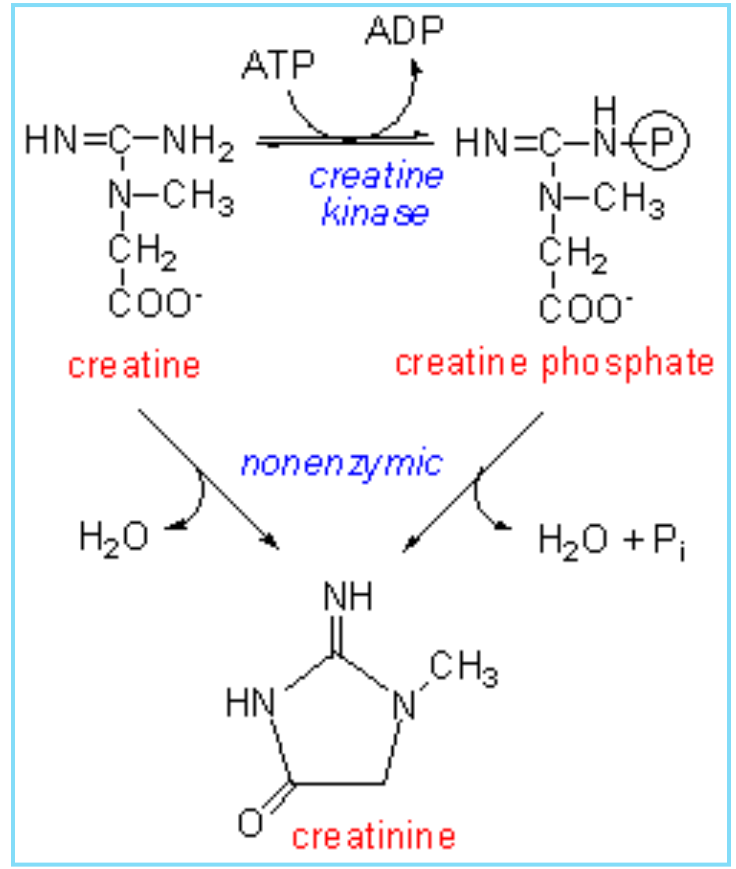
V= volume of urine (ml/min).

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.	End-product of protein metabolism.
Advantages	Not reabsorbed or secreted.	An endogenous product of muscle metabolism; near constant production.	An endogenous 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 by-product 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/1.73m^2

Note:

What 1.73 m^2 means?

- Kidney function is proportional to kidney size, which is proportional to body surface area. A of 1.73 m^2 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/1.73m²)
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:

Creatinine + picric acid ⟶ Creatinine picrate (orange)

Absorbance at 520nm

Method:

1- Set up a series of 8 test tube as shown in the table:

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- Cover the tubes with foil and Mix well, then put the tubes carefully in the boiling water bath for 40 seconds.

4- Pipette 0.6 ml of NaOH to all tubes.

5- Let the tubes stand for 20 min.

6- Read the absorbance at 520 nm.

Results & Calculation :

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

Patient information: 24h urine volume = 100ml, gender: women, body surface: 1.6m^2, DF=10.

1-Serum creatinine (S-Cr) =

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

2-Urine creatinine (U-Cr) =

(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

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

B ----------> 1.6 m^2 (person surface area)

? ----------> 1.73 m^2

-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 mg/dl ÷2.32 mg/dl) × (100÷1440*)= 14.6 ml/min

14.6 ml/ min in 1.6 m2, find the creatinine clearance for 1,73 m2 surface area :

=(14.6 ×1.73)÷1.6= **15.8 ml /min/1.73m2**

--------OR-------

➔ Creatinine Clearance: = (U XV X1.73)/ (P X 1440 X A)

= (488 mg/dl× 100× 1.73)/ (2.32× 1440× 1.6)

= **15.8 ml/min /1.73m^2**

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

References:

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