UG MODULE
PHYSIOLOGY(LECTURE 3)
Renal Clearance

BY

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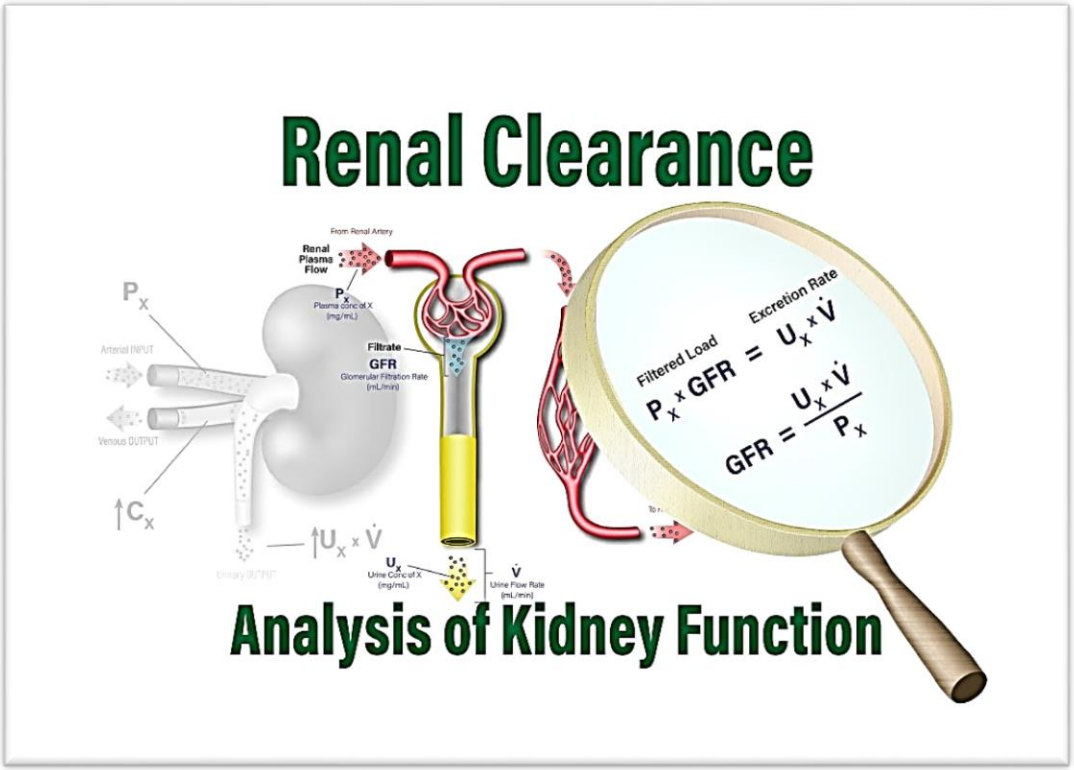
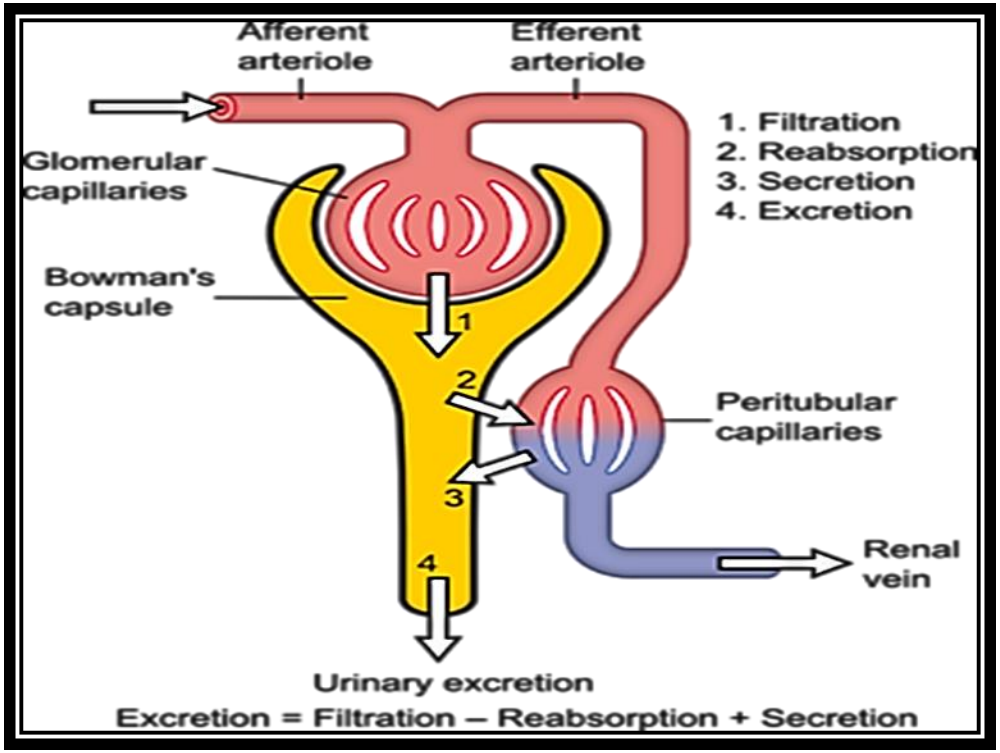


Renal Clearance

The Renal Clearance of a substance is the volume of plasma that is completely cleared of this substance by the kidney /minute.

It is one of renal function tests that depends on combined blood and urine analysis.



Equation of clearance:

Clearance is calculated by using an equation that is determined as follows:

1. The amount of substance (x) cleared from the plasma/minute =the amount of this substance excreted in urine/minute.

N.B: Amount = volume x concentration

2. The amount of substance (x) cleared from plasma/minute= C_x X P_x

C_x = volume of plasma cleared from substance (x) per minute = ml /min

P_x = concentration of substance per ml in plasma = mg /ml

3. The amount of substance (x) excreted in urine/minute= V X U_x, where

V is the volume of urine/minute (ml/minute).

U_x is the concentration of substance/ml urine (mg/ml).

4. Since both amounts are equal, then

C_x X P_x = V X U_x, therefore

$$C_x = \frac{V\ xUx}{P_x}$$

This is the equation of clearance (C) and it shows that the clearance value of any substance is obtained by finding its amount excreted in urine/minute (VxU), then dividing this amount by the concentration of this substance/ml plasma (P).

The clearance of various substances is not the same **depending on the mode of handling of each substances in the nephron** (i.e. what happens to the substance in the nephron).
Substances that are secreted in renal tubules have high clearance, while those reabsorbed have low clearance.

N.B. As the substance is freely filtrated so, its concentration in plasma = its concentration in filtrate = (P_x).

When substance x passes through the renal tubule, the following possibilities can occur before being excreted in urine:

1. **The substance is freely filtered in glomeruli and is neither reabsorbed nor secreted in the renal tubules, so;**

The amount filtered/minute = the amount excreted/ minute

$GFR \times GF_x = V \times U_x$

$$\textbf{GFR} = \frac{V \times Ux}{GFx}$$

Since the substance is freely filtered

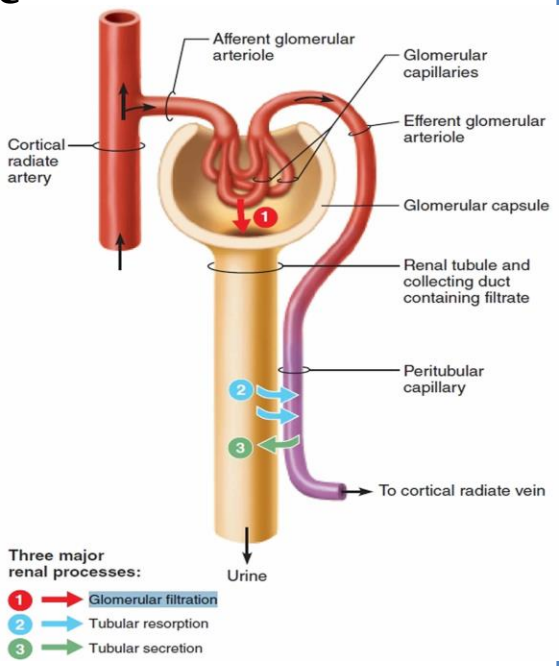
So, its concentration in plasma = its concentration in filtrate

$$P_x = GF_x$$

So,

$$\textbf{GFR} = \frac{V \times Ux}{Px} = C$$

e.g. inulin



Inulin Clearance:

- Inulin is a polysaccharide.
- Its M.W is about 5200.
- Its mode of handling in the nephron is as follows:
  - **It is freely filtered in the glomeruli (i.e. its concentration in plasma= its concentration in glomerular filtrate).**
  - **It is neither reabsorbed nor secreted in the renal tubules, so the amount filtered/minute=the amount excreted in urine/minute.**

Accordingly, the volume of plasma that is cleared from inulin/minute (inulin clearance) is that volume filtered in the glomeruli/minute i.e. the GFR.

For this reason, **determination of inulin clearance is often used for measurement of GFR** as follows:

1. The amount of inulin filtered/minute= GFR X GF_{IN}

And since GFR=C_{IN} and GF_{IN}=P_{IN}

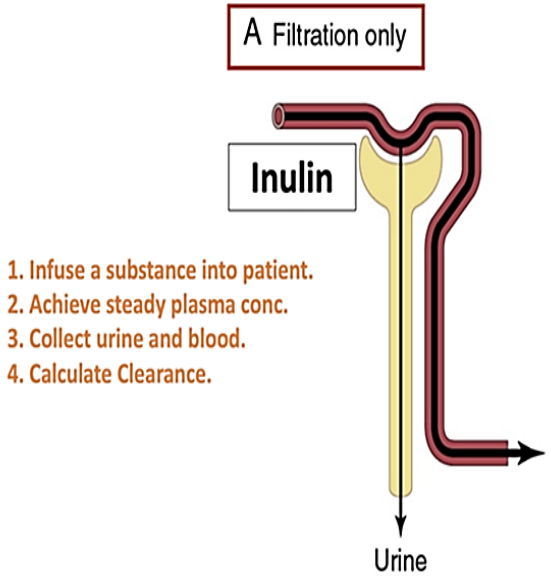
So, the filtered amount= C_{IN} X P_{IN}

2. The amount of inulin excreted/minute= V X U_{IN}

Since 1 and 2 are equal

C_{IN} X P_{IN} = V X U_{IN} and accordingly

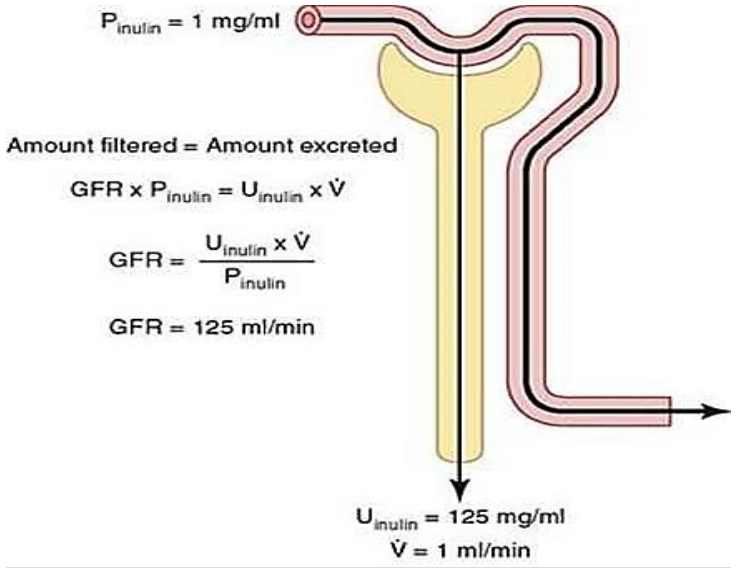
C_{IN} (GFR)= $\frac{V \, X \, UIN}{P_{IN}}$ = about 125 ml/minute.



- **Significance of inulin clearance:**

  - **It measures GFR.**
  - **It is used as a reference value.** Substances having lower clearance than that of inulin (e.g. urea) means that they are reabsorbed in the renal tubules while those having higher clearances (e.g. creatinine) means they are secreted.

Determination of creatinine clearance can also be used for estimating GFR. However, in humans creatinine is secreted in renal tubules but in spite of that endogenous creatinine clearance is frequently used to measure GFR.



Characteristics of substances used for measuring GFR:

- They should be of a small size and not bound to plasma proteins in order to be **freely filtered in the glomeruli**.
- They should be standard substances i.e. cleared from the plasma only by glomerular filtration and are **neither reabsorbed nor secreted**.
- They should be non toxic and not metabolized in the body.
- They should be easy to measure in plasma and urine and have no effect on GFR.
- Does not enter RBCs or leave the circulation to surrounding tissues.

Good examples: Inulin.

2. If the substance is :

Freely filtered (in glomeruli)

Partially reabsorbed and not secreted in the renal tubules:

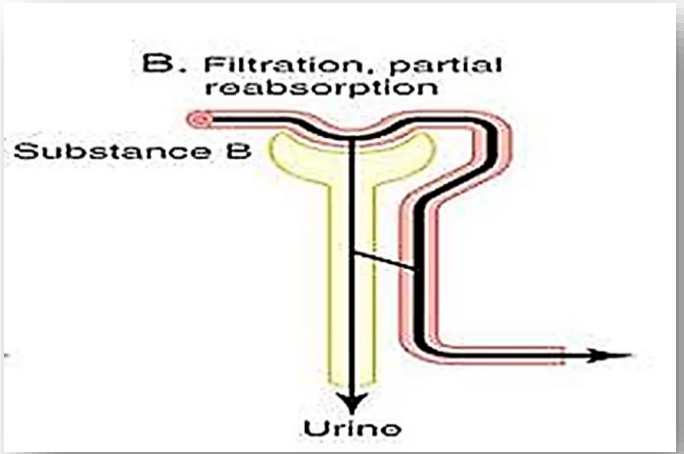
The amount excreted in urine/minute < the amount filtered/minute.

i.e. V x U < GFR x P

So, $\frac{V \times U}{P} <$ GFR i.e. **GFR > clearance of this substance.**

e.g. urea, uric acid, K^+.

Urea clearance is normally about 70 ml/minute.



3. <u>If the substance is:</u>

<u>Freely filtered in glomeruli</u>

<u>Completely reabsorbed and not secreted in the renal tubules :</u>

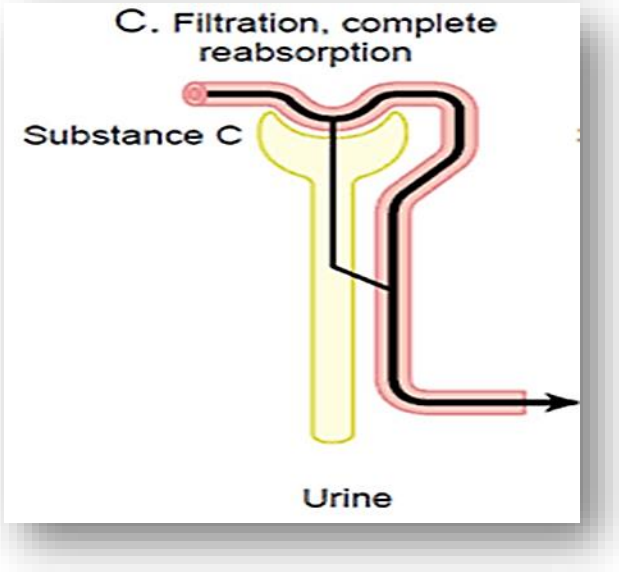
The amount of substance excreted in urine/minute =zero

So, the clearance of this substance **= zero**.

e.g. Glucose

Normally, glucose is completely reabsorbed (PCT) under normal conditions.

This means that all RPF/minute has not been cleared from glucose.



(4) If the substance is

Freely filtered in glomeruli

Partially secreted and not reabsorbed in the renal tubules

then,

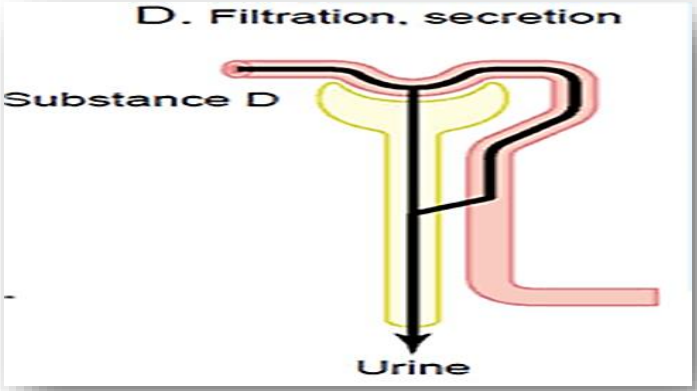
The amount excreted in urine/minute > amount filtered/minute.

i.e. $V \times U > GFR \times P$ so, $\frac{V \times U}{P} > GFR$

The clearance of the substance > GFR.

The clearance of this substance is greater than inulin clearance, meaning that a greater volume of plasma than 125 ml has been cleared from this substance/minute.

e.g. Creatinine clearance (normally about 140 ml/minute).



Creatinine clearance:

- Creatinine is an end product of muscle metabolism and constantly released into the blood .
- As the amount secreted is very low, and also plasma creatinine level is high (so the errors thus tend to cancel) it can be neglected and creatinine clearance is taken an index for **measurement of GFR (endogenous method)**.
- It is better than inulin because it doesn’t represent a load on the kidney.

(5) <u>If the substance is</u>

<u>Freely filtered in glomeruli</u>

<u>Almost completely secreted in the renal tubules and not reabsorbed.</u>

So that the renal venous blood is nearly free of the substance then,

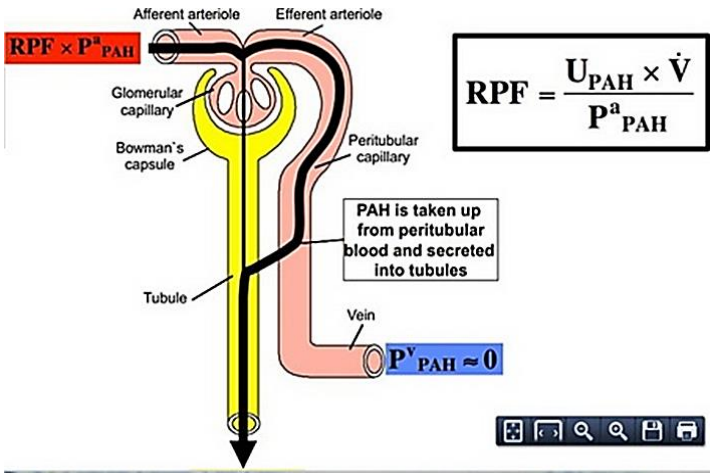
The clearance of this substance = RPF (ml/minute)

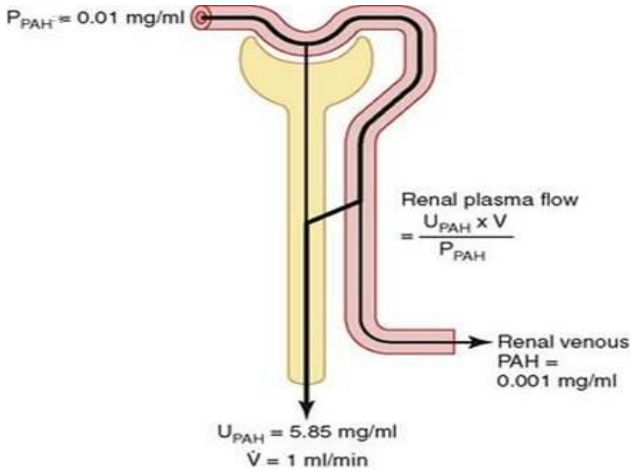
<u>e.g.</u> Para-aminohippuric acid (PAH) and diodrast (85%).

Because PAH (and also diodrast) is almost completely secreted in the renal tubule, its **clearance value equals the ERPF (about 585 ml/minute)**, meaning that all RPF/minute has been cleared from PAH.

Extraction ratio= Percentage of PAH removed from blood (90%).

Actual RPF= 585 X100/90= 650 ml/minute.





Significance of renal clearance:

- It is one of renal function tests.
- Measurement of GFR by inulin clearance.
- Measurement of RPF by PAH clearance.
- Estimation of filtration fraction (FF).

THANK YOU