

Renal Clearance



Concept of clearance

Clearance is the volume of plasma that is completely cleared of a substance each minute.

Example:

Renal clearance of Substance X is defined as the ratio of excretion rate of substance X to its concentration in the plasma:

$$C_x = (U_x \times V) / P_x$$

Clearance Equation

- $C_x = (U_x \times V) / P_x$
- $C_x =$ Renal clearance (ml/min)
- $U_x \times V =$ excretion rate of substance X
- $U_x =$ Concentration of X in urine
- $V =$ urine flow rate in ml/min

Amount of substance excreted = (filtered – reabsorbed + secreted)

$$U_x V = GFR \times P_x \pm T_x$$

What is the importance of renal clearance?

To quantify several aspects of renal functions:

- rate of glomerular filtration
- Rate of blood flow
- Assess severity of renal damage
- Tubular reabsorption.
- Tubular secretion of different substances.

Clearance tests

| Types of Clearance tests | |
|--------------------------|---|
| Endogenous | Exogenous |
| Creatinine | Inulin |
| Urea | Para-amino hippuric acid (PAHA) |
| Uric acid | Diodrast (di-iodo pyridone acetic acid) |

✿ Calculation: $\frac{U \times V}{P}$

P

Where:

U = concentration of substance in urine (mg/dl)

V = volume of urine excreted per minute (ml/min)

P = concentration of substance in plasma/serum (mg/dl)

Clearance

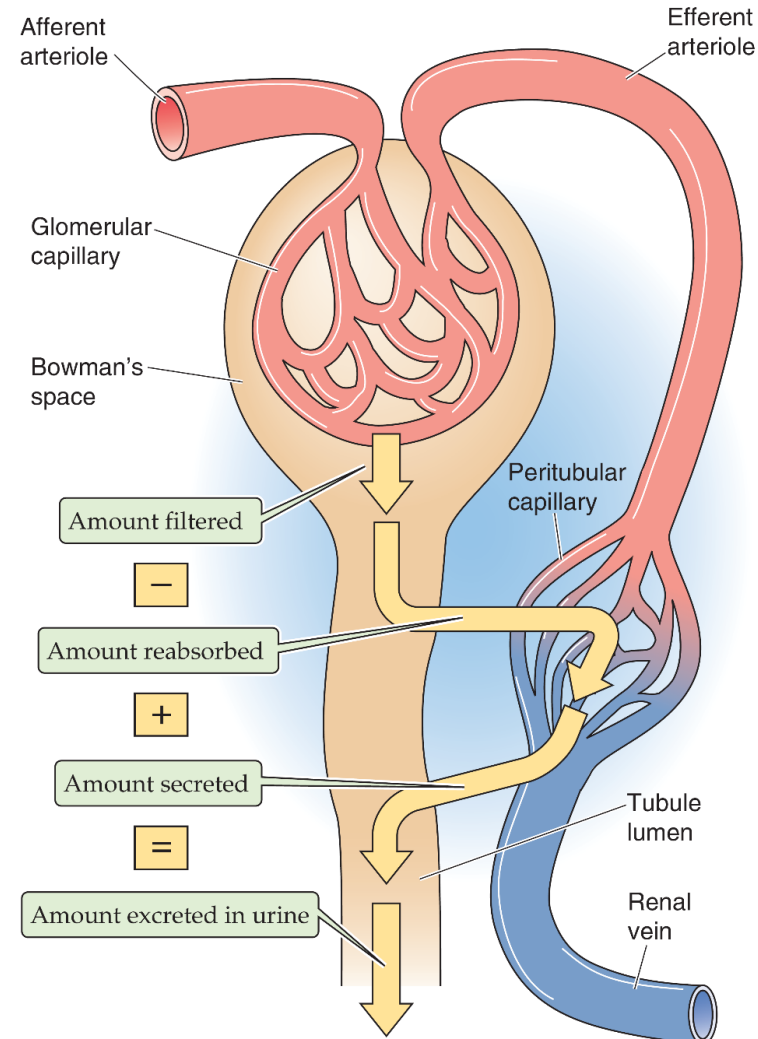
Clearance method

Volume of **plasma** which is completely cleared of a substance per unit time.

amount **excreted** = amount **filtered** – amount reabsorbed + amount secreted

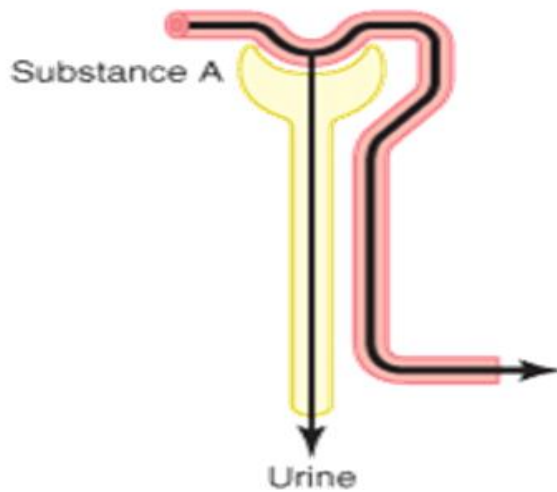
amount **filtered** per minute
= $GFR \cdot P_x$ (filtered load)

amount **excreted** per minute
= $\tilde{V} \cdot U_x$ (excretion rate)

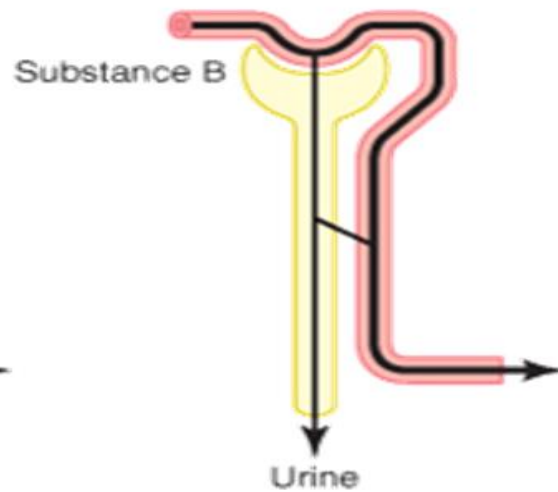




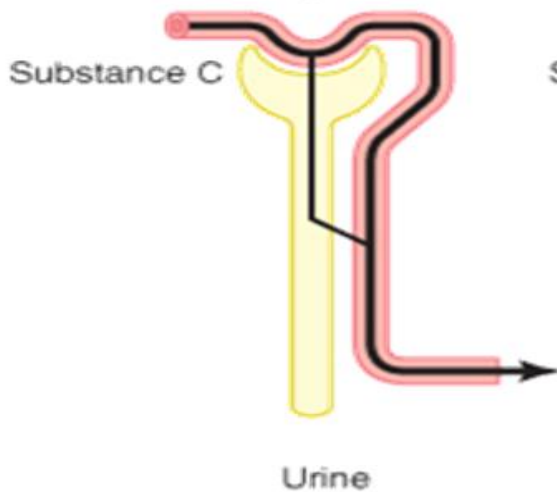
A. Filtration only



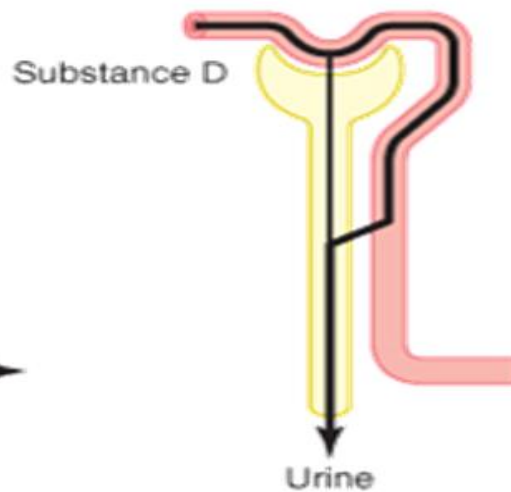
B. Filtration, partial reabsorption



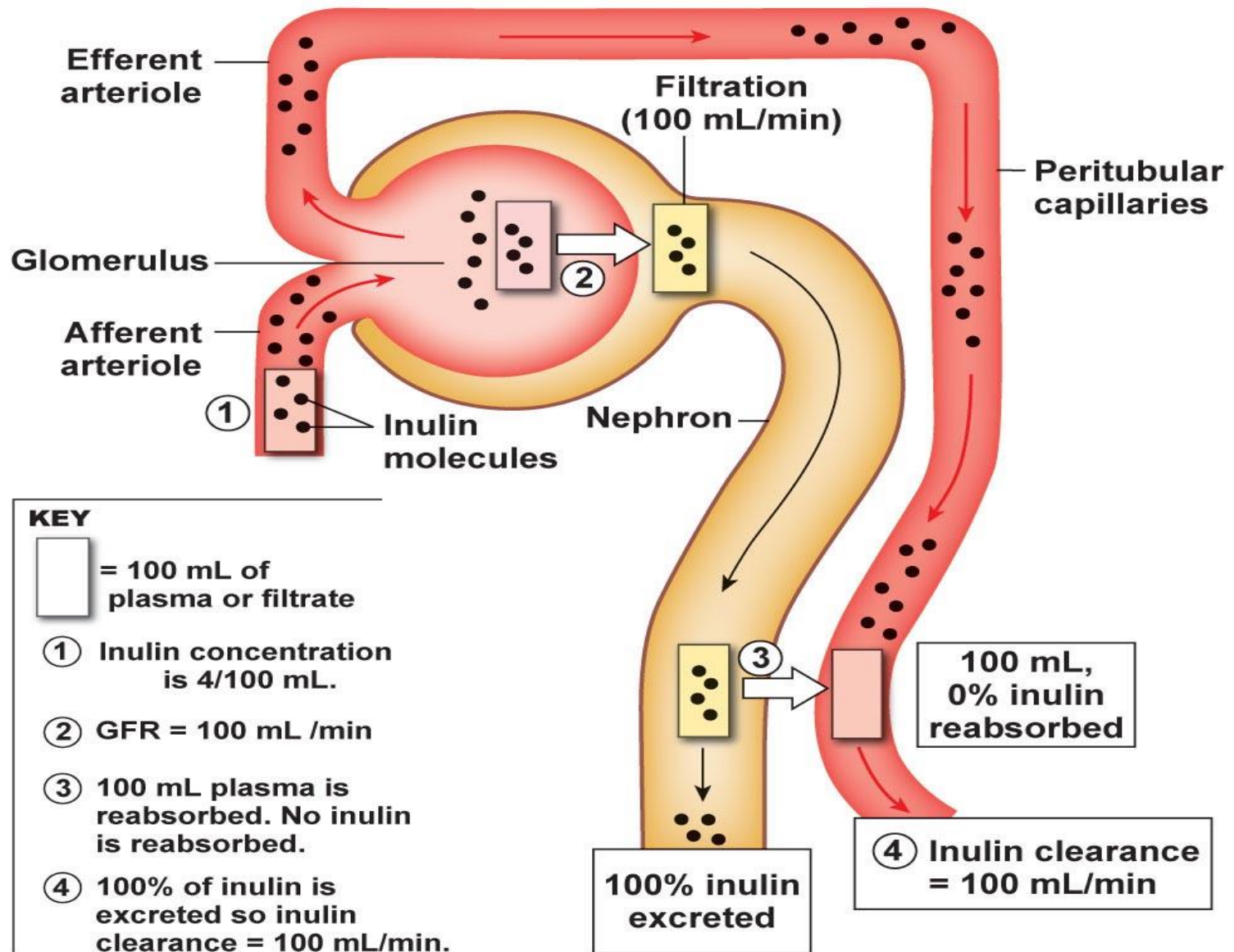
C. Filtration, complete reabsorption



D. Filtration, secretion



Nephron Excretion & Clearance



Nephron Excretion & Clearance

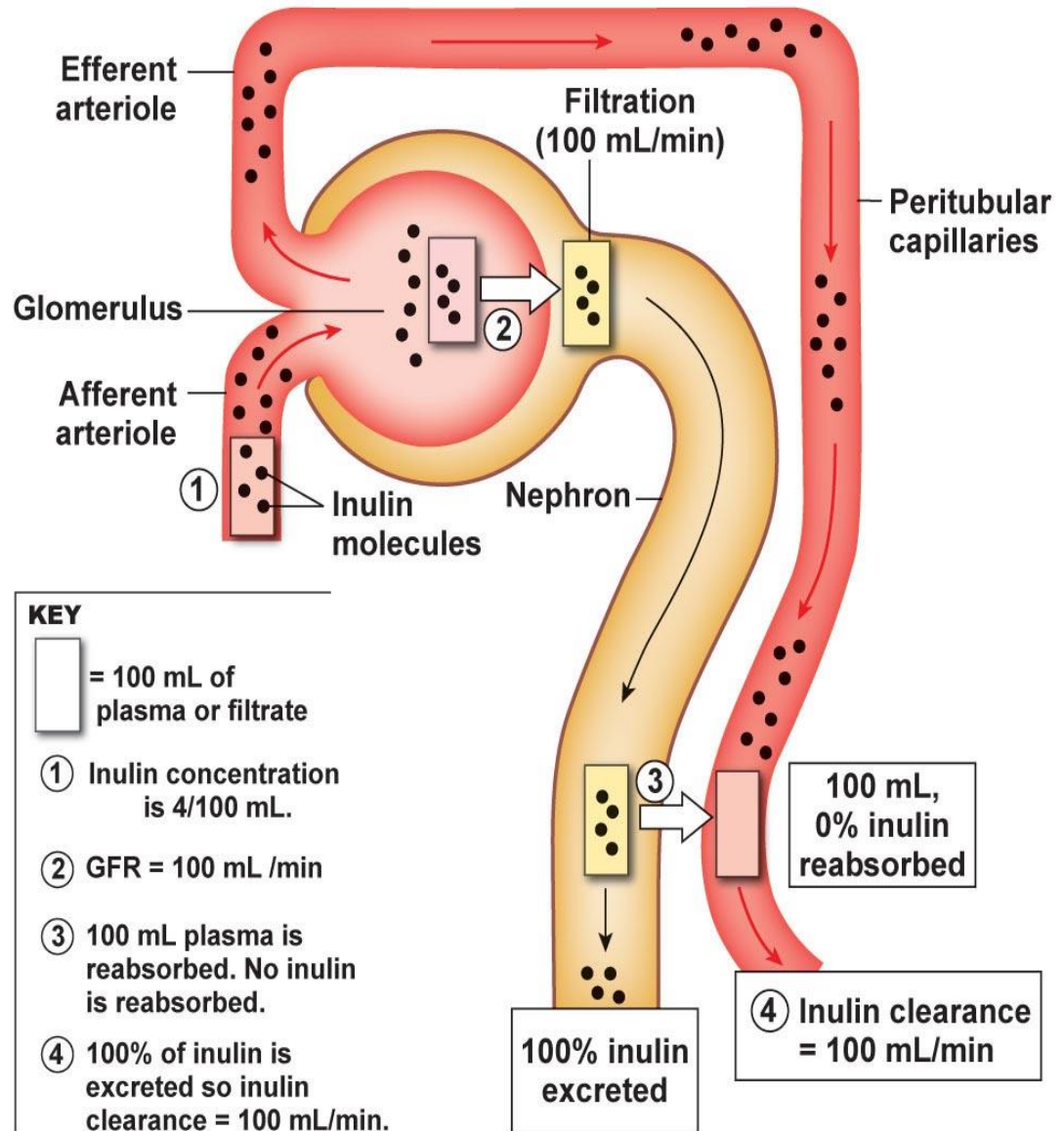
Inulin

A plant product that is filtered but not reabsorbed or secreted

Used to determine

GFR

and therefore nephron function



$P_{\text{inulin}} = 1 \text{ mg/ml}$

Amount filtered = Amount excreted

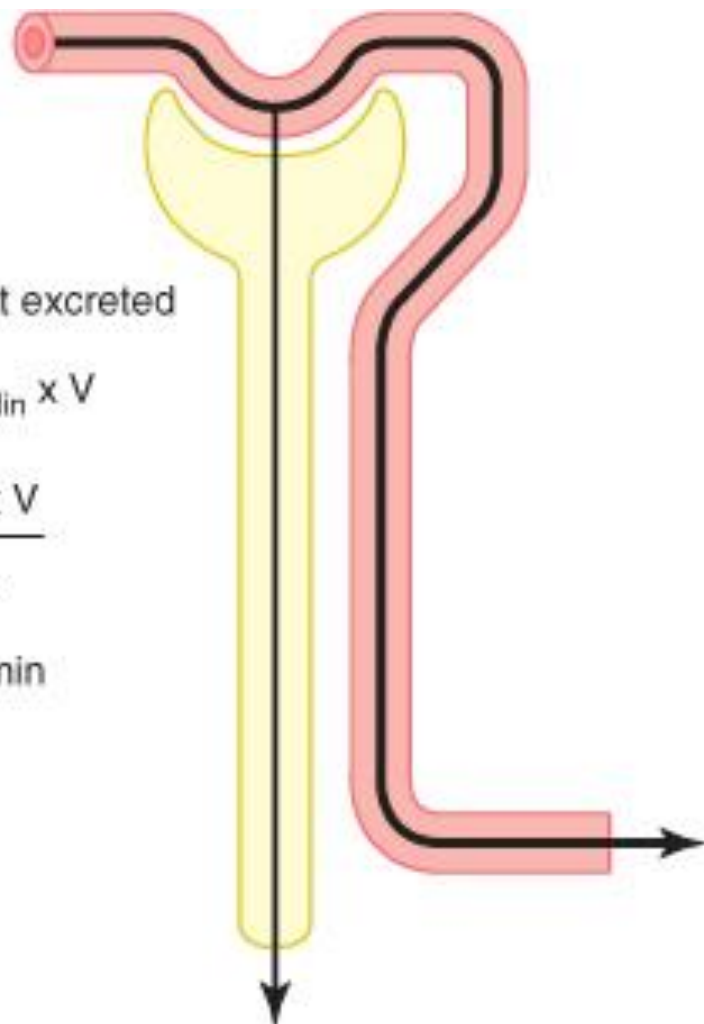
$$\text{GFR} \times P_{\text{inulin}} = U_{\text{inulin}} \times V$$

$$\text{GFR} = \frac{U_{\text{inulin}} \times V}{P_{\text{inulin}}}$$

$$\text{GFR} = 125 \text{ ml/min}$$

$U_{\text{inulin}} = 125 \text{ mg/ml}$

$V = 1 \text{ ml/min}$



Clearance = GFR

Criteria of substance:

1. freely filtered
2. **NOT** reabsorbed, **NOT** secreted or metabolized in the nephron

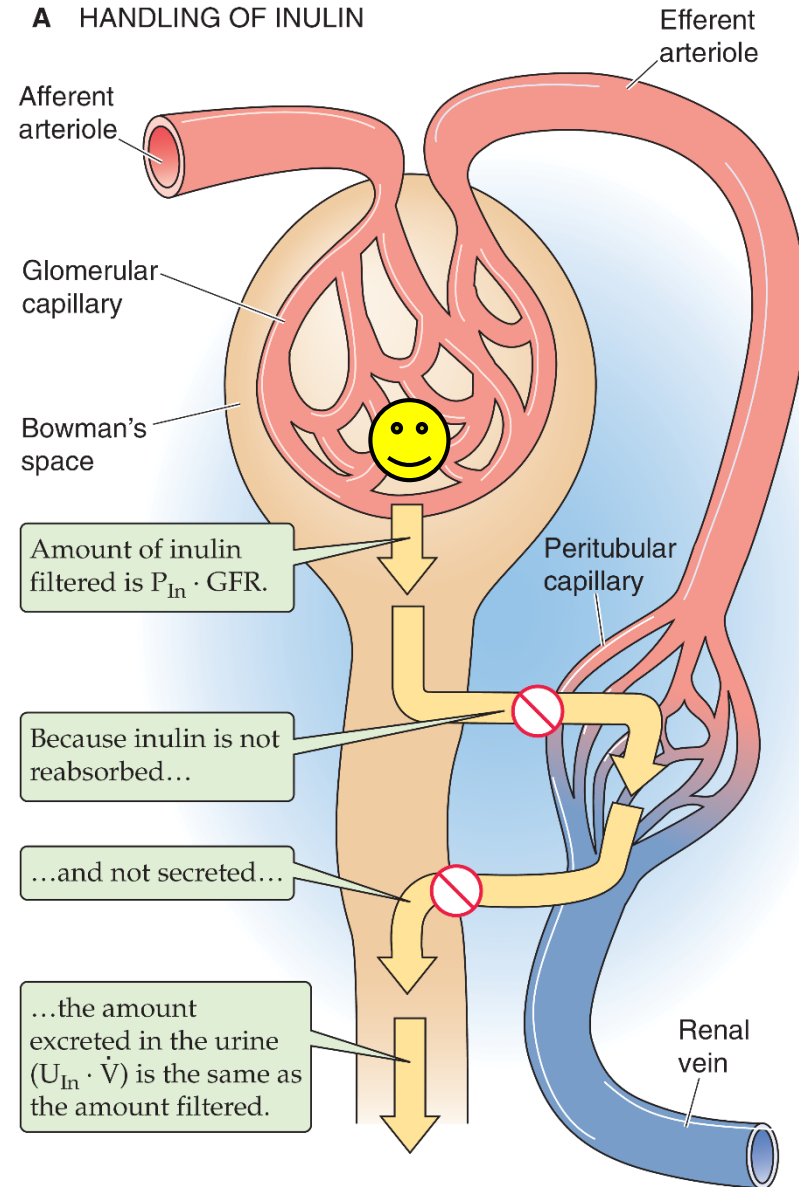
amount **filtered** per minute =
amount **excreted** per minute

■ e.g., inulin

$$\text{GFR} \cdot [P]_{\text{Inulin}} = [U]_{\text{Inulin}} \cdot \tilde{V}$$

$$\text{Cl}_{\text{Inulin}} = \text{GFR} = \frac{[U]_{\text{Inulin}} \cdot \tilde{V}}{[P]_{\text{Inulin}}}$$

A HANDLING OF INULIN



Example

- if Plasma conc. of inulin = 1 mg/100ml
- Urinary conc of Inulin = 120 mg /100ml
- Urine flow (UV) = 1 ml /min then, the clearance of inulin will be?
- $C = 120 \text{ ml/min}$

Criteria of a substance used for GFR measurement:

a)freely filtered

b)not secreted by the tubular cells,

c)not reabsorbed by the tubular cells.

d)should not be toxic

e)should not be metabolized

f)easily measurable.

examples of such a substance:

□ **Creatinine (endogenous):**

by-product of skeletal muscle metabolism

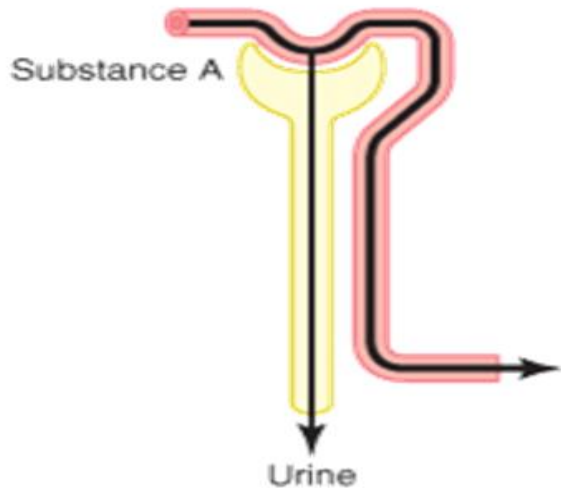
Criteria of a substance used for GFR measurement, cont.....

Inulin (exogenous):

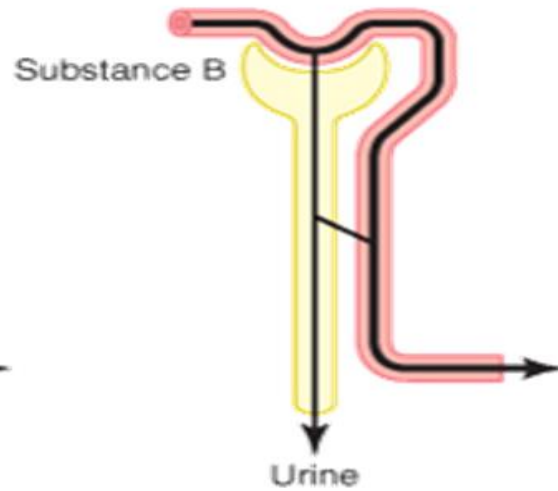
It is a polysaccharide with a molecular weight of about 5200 and it fits all the above requirements.



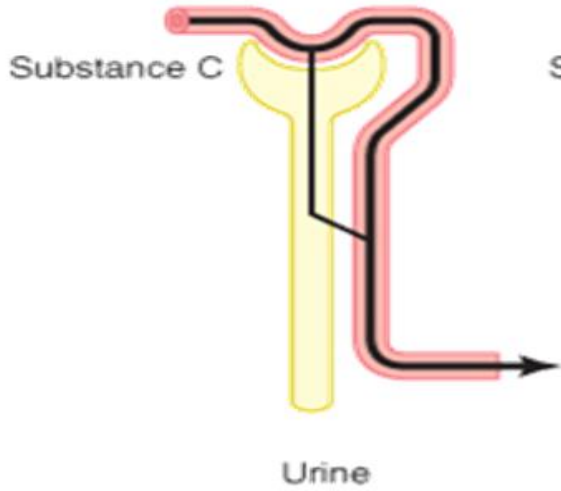
A. Filtration only



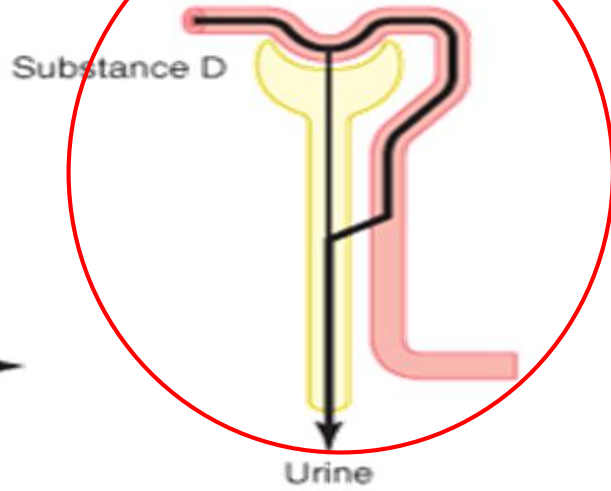
B. Filtration, partial reabsorption



C. Filtration, complete reabsorption



D. Filtration, secretion



Measurement of renal blood flow

Substances used for measurement of GFR are not suitable for the measurement of Renal Blood Flow. Why?

Inulin clearance only reflects the volume of plasma that is filtered and not that remains unfiltered and yet passes through the kidney.

It is known that only $1/5$ of the plasma that enters the kidneys gets filtered.

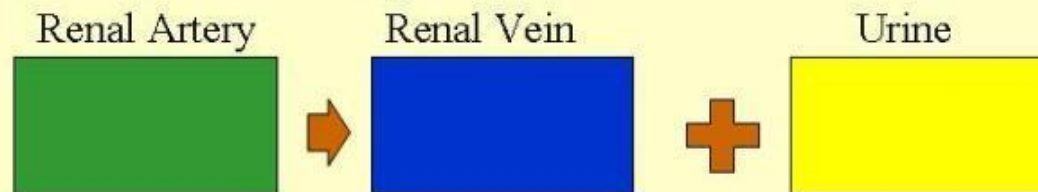
Therefore, other substances to be used with special criteria.

To measure renal blood flow we will have to measure renal plasma flow first and then from the hematocrit we calculate the actual blood flow

Measuring Renal Plasma Flow

- If a substance is not only freely filtered, but also secreted such that all substance reaching the kidney is cleared, then:

$$C_x = RPF$$



- Clearance equals



- Para-amino hippuric acid (PAH) is such a molecule whose clearance equals RPF

Use of PAH Clearance to Estimate Renal Plasma Flow

Paraminohippuric acid (PAH) is freely filtered and secreted and is almost completely cleared from the renal plasma

1. amount enter kidney =

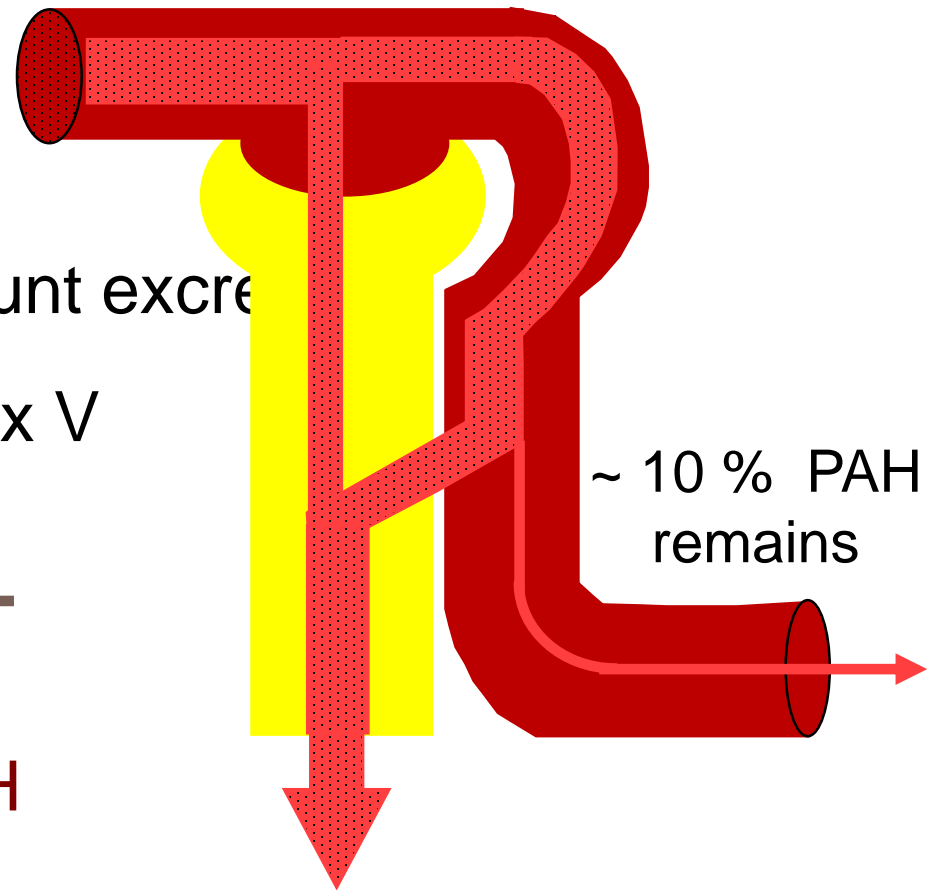
$$RPF \times P_{PAH}$$

2. amount entered = amount excreted

$$ERPF \times P_{pah} = U_{PAH} \times V$$

$$ERPF = \frac{U_{PAH} \times V}{P_{PAH}}$$

$$ERPF = \text{Clearance PAH}$$



Measurement of renal plasma flow:

For the measurement of renal plasma flow, we will again need a substance that is

a)freely filtered

b)rapidly and completely secreted by the renal tubular cells

c)not reabsorbed

d)not toxic

e)and easily measurable

Example of such substance:

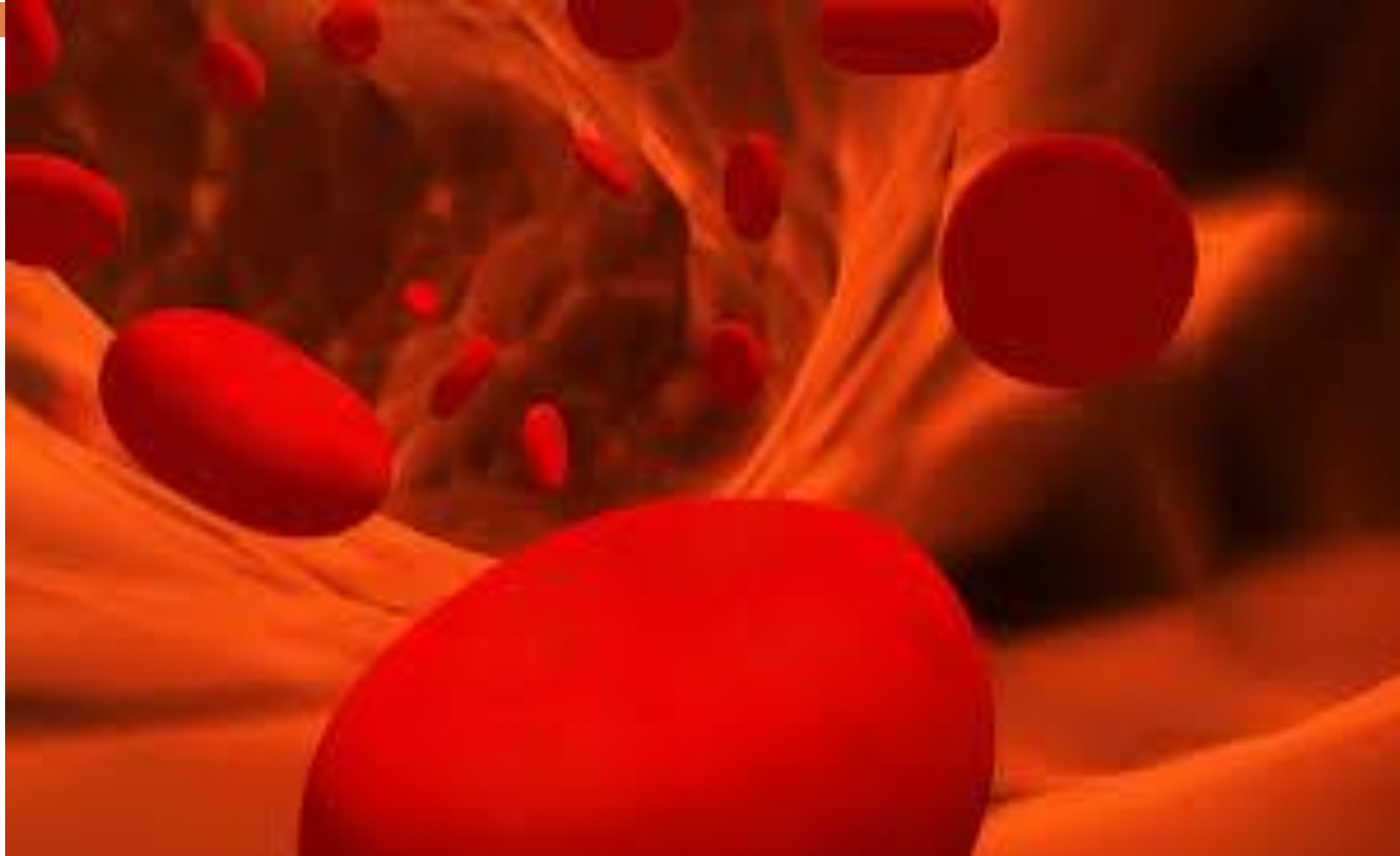
Para-aminohippuric acid (PAH)

90% of plasma flowing through the kidney is completely cleared of PAH.

PAH clearance: example

- If the concentration of PAH in the urine and plasma and the urine flow are as follows:
- Conc. of PAH in urine=25.2 mg/ml
- Urine flow=1.1 ml/min
- Conc of PAH in arterial blood=0.05 mg/ml
- Then CPAH or Renal Plasma Flow=
$$(25.2 \times 1.1)/0.05 = 560 \text{ ML/ min}$$


How to measure renal bl flow?




PAH clearance: example

- If the concentration of PAH in the urine and plasma and the urine flow are as follows:
- Conc. of PAH in urine=25.2 mg/ml
- Urine flow=1.1 ml/min
- Conc of PAH in arterial blood=0.05 mg/ml
- Then CPAH or Renal Plasma Flow=
$$(25.2 \times 1.1)/0.05 = 560 \text{ ML/ min}$$
- Lets say the hematocrit is 45%, then renal blood flow will be:

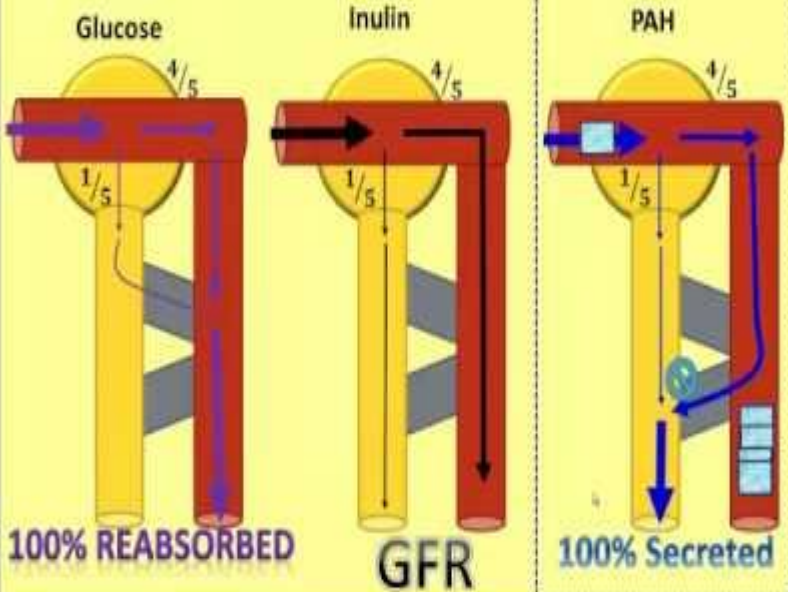
$$(560 \times 100)/(100-45)= 1018 \text{ ml/min}$$



Renal Clearance gives an indication of
kidneys function.

- 
- Clearance can also be used to determine renal handling of a substance.
 - Clearance values can also be used to determine how the nephron handles a substance filtered into it. In this method the clearance for inulin or creatinine is calculated and then compared with the clearance of the substance being investigated.

Renal Clearances



Comparison of clearance of a substance with clearance of inulin

- 1) **= inulin clearance; only filtered not reabsorbed or secreted**
- 2) **< inulin clearance; reabsorbed by nephron tubules**
- 3) **> inulin clearance; secreted by nephron tubules**

Calculation of tubular reabsorption or secretion from renal clearance

Substances that are completely reabsorbed from the tubules (amino acids, glucose), clearance = zero because the urinary secretion is zero.

Substances highly reabsorbed (Na), its clearance < 1% of the GFR.

Reabsorption rate can be calculated=

Filtration rate- excretion rate

$$= (GFR \times P^*) - (U^* \times V)$$

* The substance needed to be assessed.

Calculation of tubular reabsorption or secretion from renal clearance, cont.....

- If excretion rate of a substance is greater than the filtered load, then the rate at which it appears in the urine represents the sum of the rate of glomerular filtration + tubular secretion:
- $\text{Secretion}^* = (U^* \times V) - (\text{GFR} \times P^*)$.
- * indicate the substance

Q: Given the following information for a freely filterable substance

GFR = 120 mL/min

Plasma concentration = 3 mg/mL

Urine flow rate = 2 mL/min

Urine concentration = 10 mg/mL

we can conclude that:

- a) the kidney tubules reabsorbed 340 mg/min
- b) the kidney tubules reabsorbed 200 mg/min
- c) the kidney tubules secreted 200 mg/min
- d) the kidney tubules secreted 340 mg/min
- e) Net transport is 0 mg/min

$$\begin{aligned}\text{Amount Filtered per minute} &= (\text{GFR} \times [\text{Sub}]_{\text{plasma}}) \\ &= 120 \text{ ml/min} \times 3 \text{ mg/ml} = \underline{\underline{360 \text{ mg/min}}}\end{aligned}$$

$$\begin{aligned}\text{Amount excreted per minute} &= ([\text{sub}]_{\text{urine}} \times \text{Urine flow rate}) \\ &= 2 \text{ ml/min} \times 10 \text{ mg/ml} = \underline{\underline{20 \text{ mg/min}}}\end{aligned}$$

Amount Filtered per minute > Amount excreted per minute

$$\begin{aligned}\text{Amount transported per minute} &= \text{Filtered} - \text{Excreted} \\ &= 360 - 20 = \underline{\underline{340 \text{ mg/min}}}\end{aligned}$$

Filtration fraction



It is the ratio of GFR to renal plasma flow



Have a nice week end

