RENAL CLEARANCE

Physiology Practical-1

What are we going to discuss?

What is it?

- Definition.
- Equation.

What are its limitations?

Renal Clearance

Some exercises!

What is its significance?

- Relation to GFR.
- Relation to RPF & RBF.
- Other uses.

What is Renal Clearance?

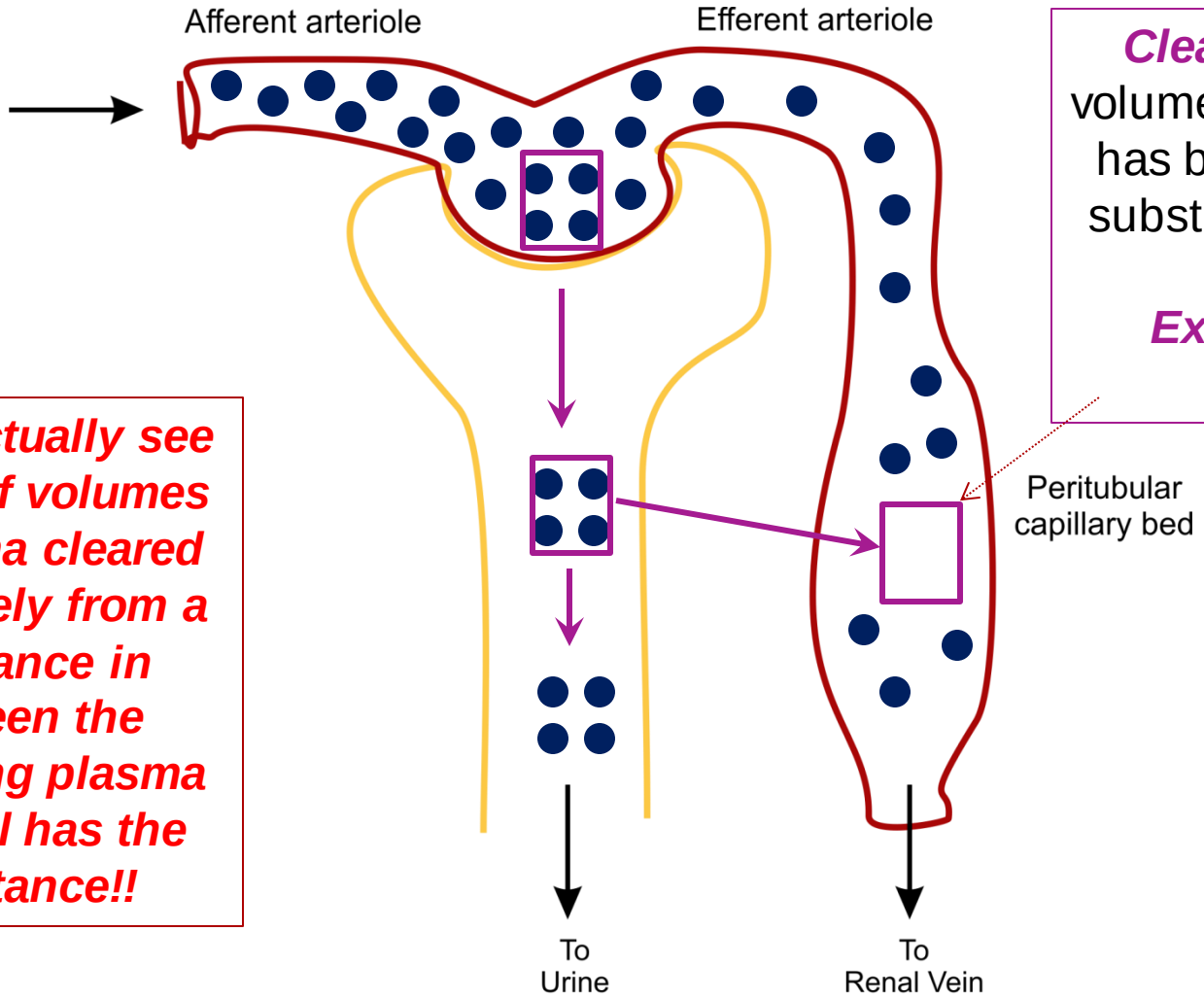
Clearance is defined as:

- "The volume of plasma from which a particular substance is completely removed (cleared) by the kidneys in a given amount of time (usually a minute)".

- "The volume of plasma passing through the kidneys that has been totally cleared of a substance per unit time".

Let's try to visualize the definition!

Trying to Visualize the Definition of Renal Clearance



Clearance is this volume of plasma that has been cleared of substance ● per unit time.

Expressed as **ml/min**

Do we actually see blocks of volumes of plasma cleared completely from a substance in between the remaining plasma that still has the substance!!

(Adapted with modification from Human Physiology by Sherwood, 7e)

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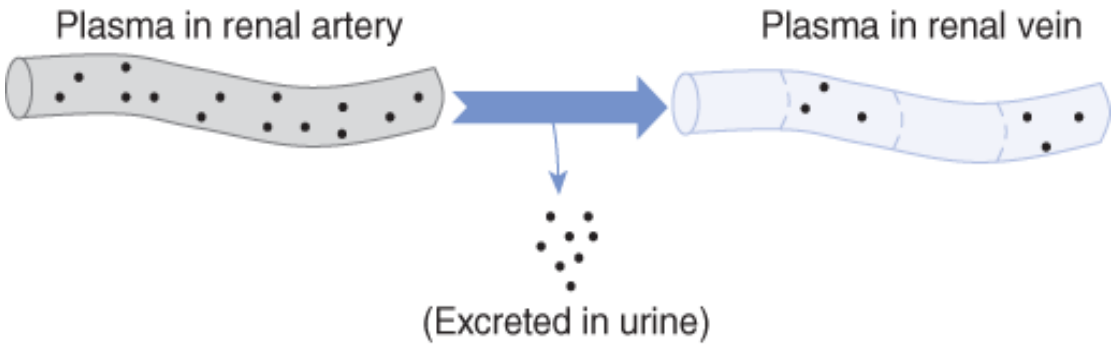
Let's Revise the Definition of Renal Clearance

Clearance can be defined as the ***virtual*** volume of plasma cleared of a substance per unit time.



(Vander's Renal Physiology, 8e)

How is the Renal Clearance of a Substance Calculated

$$C_x = \frac{U_x \, X \, \dot{V}}{P_x}$$

C_x is the clearance of substance x.
U_x is the urine concentration of substance x.
V' is the urine flow rate.
P_x is the plasma concentration of substance x.

Where did this equation come from?

Two points we want to make sure you know before we move on:

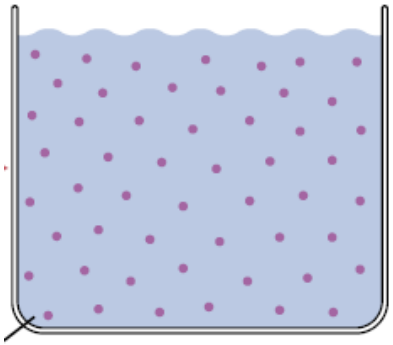
To understand how was the clearance equation derived we need to make sure that you understand:

1-"**Conservation of Mass**"

Mass is conserved-it cannot be destroyed or created.

المادة لا تفنى ولا تستحدث من العدم.

2-How to calculate the amount of a substance.

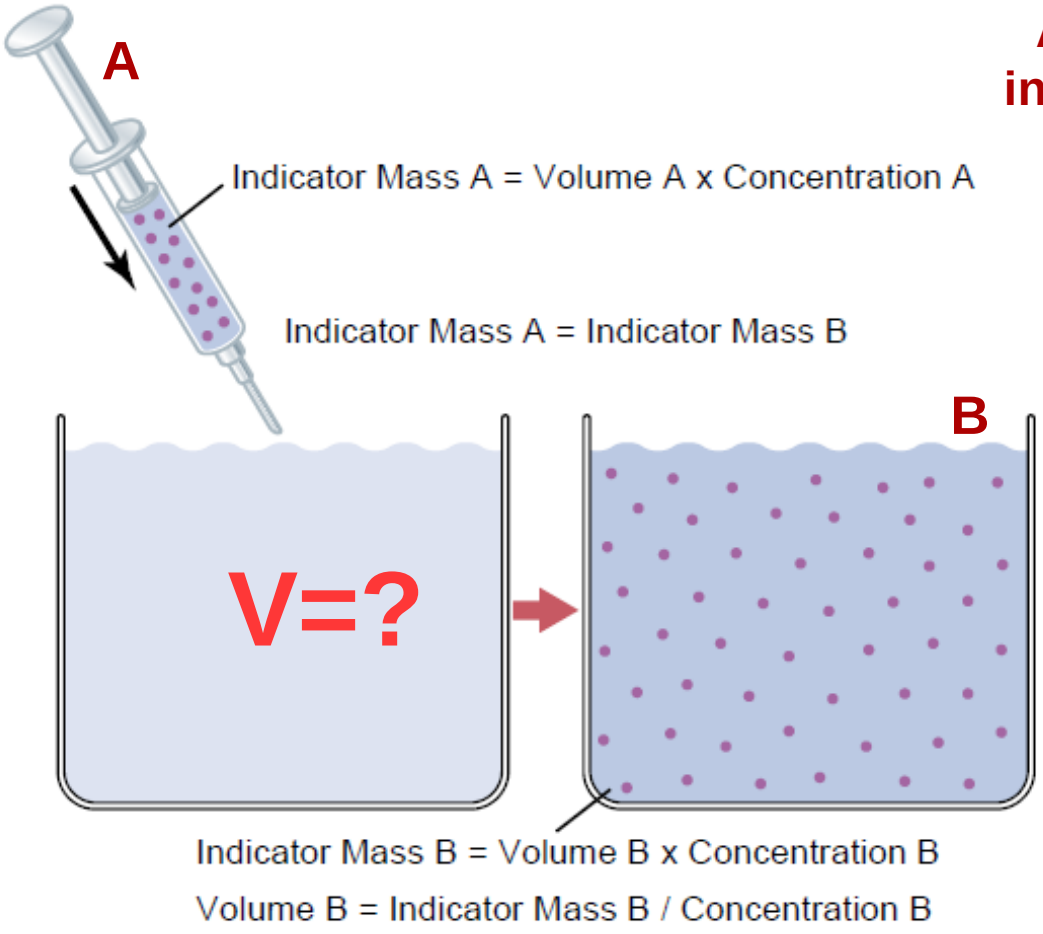


If $[Na^+]$=140 mmol/L, and the volume of container = 3L. ***What is the total amount of Na^+ in the container?***

Amount of Na^+= Concentation X volume = 140 X 3 = 420mmol.

Indicator-Dilution Method

One of the most widely used applications of this law is the **"Indicator-dilution method"**



Amount of indicator in A = **Amount of indicator in B**

$C_A \times V_A = C_B \times V_B$

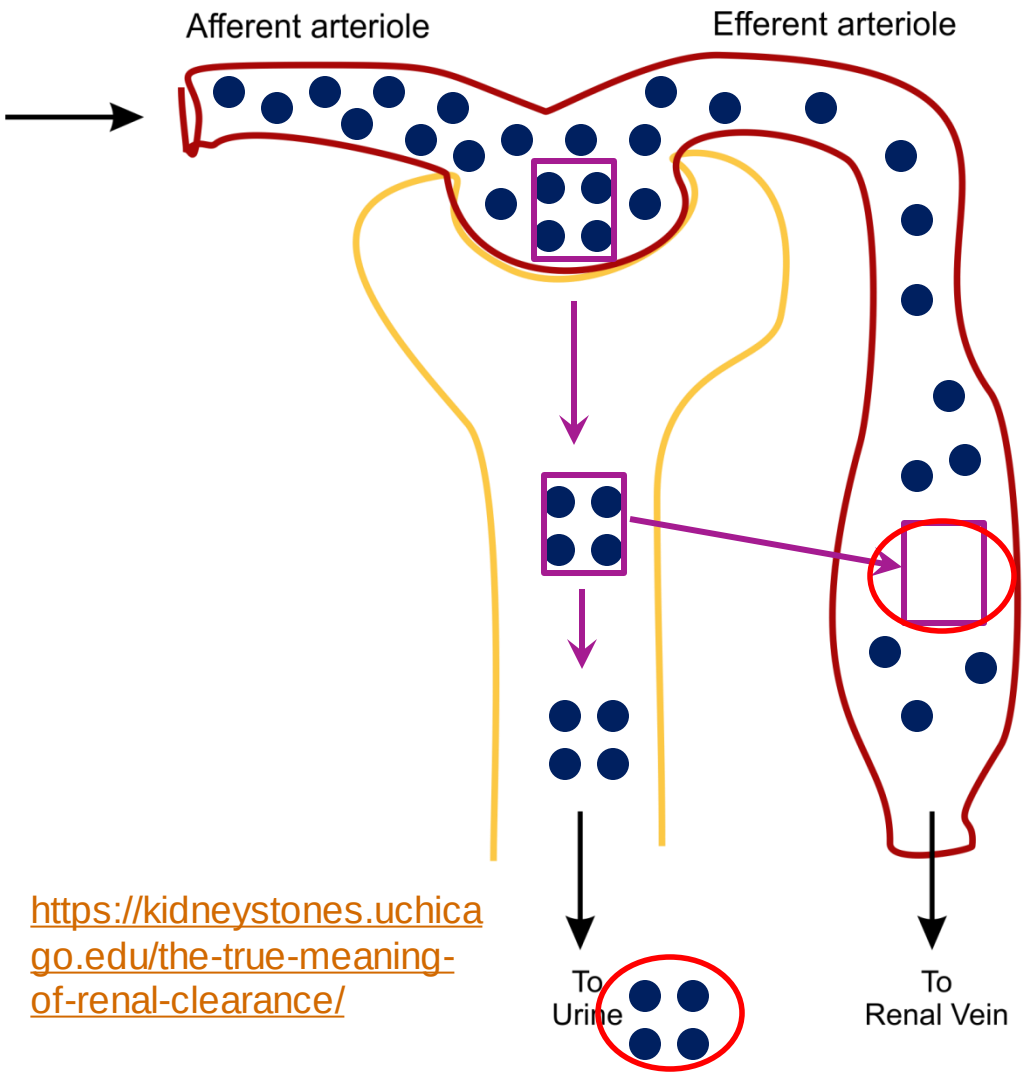
$$V_B = \frac{C_A \times V_A}{C_B}$$

Abbreviations;

- Concentration (C)
- Volume (V)

(Guyton & Hall. Medical Physiology, 12e)

How Does This Apply to Clearance?



https://kidneystones.uchicago.edu/the-true-meaning-of-renal-clearance/

Whatever substance (x) that appears in urine must have come from blood (plasma)

✗ ***Not*** synthesized.

$$Amount\ excreted = Amount\ cleared$$

Urine flow rate — Clearance

$$U_x X V_{excreted} = P_x X V_{cleared}$$

Instead of using volumes we will use rate (volume/time)

$$U_x X \dot{V} = P_x X C_x$$

$$C_x = \frac{U_x X \dot{V}}{P_x}$$

(Adapted with modification from Human Physiology by Sherwood, 7e)

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THE SIGNIFICANCE OF RENAL CLEARANCE

The Significance of Renal Clearance

- Renal clearance was used to calculate:
  - ✓ GFR.
  - ✓ RPF.
  - ✓ RBF.
- It also gives us an idea on how long does a substance stay in the body before it is removed.
- It can also give us an idea on how the kidney handles a substance.

(Guyton & Hall. Medical Physiology, 12e) https://kidneystones.uchicago.edu/the-true-meaning-of-renal-clearance/

Using Clearance to Measure GFR

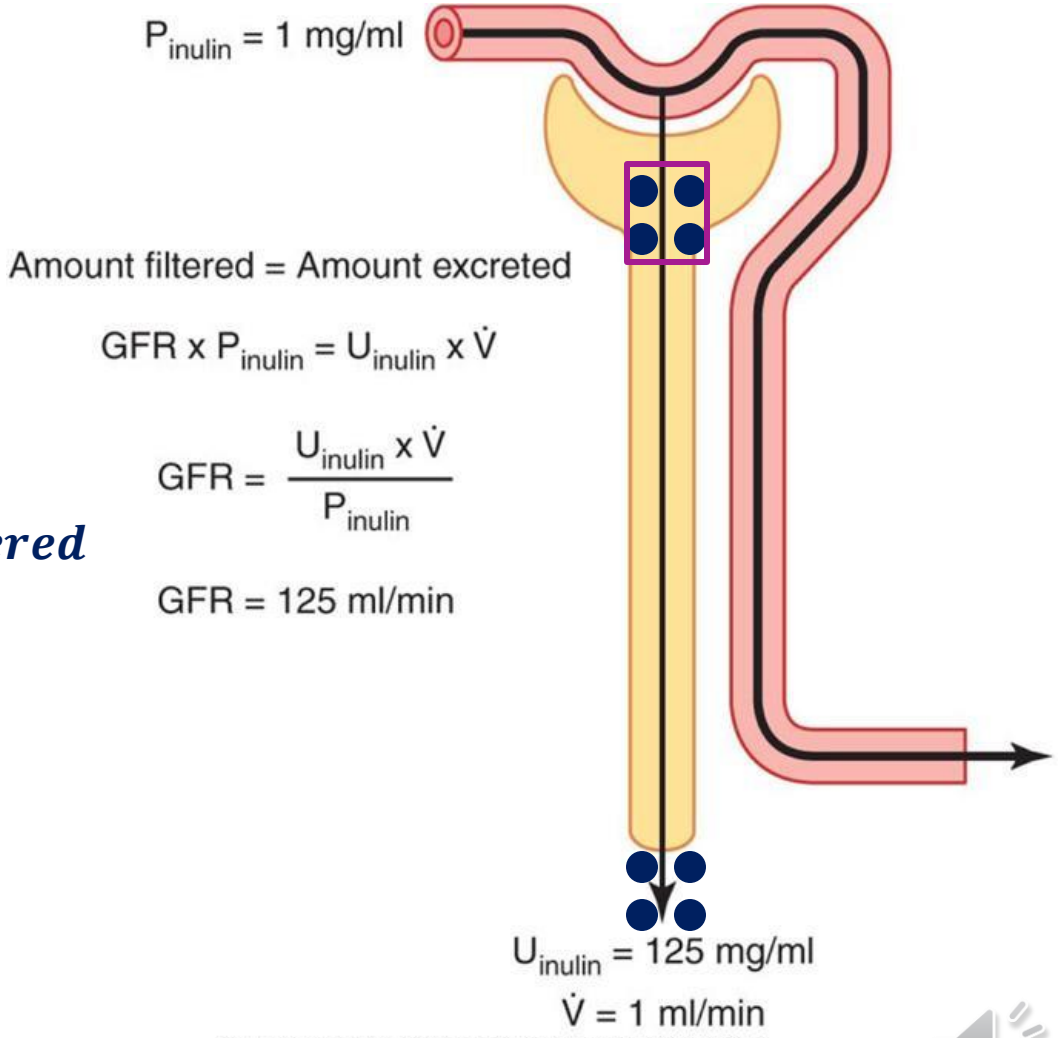
- It is through clearance that scientists were able to calculate GFR.

- ***How??***

$$\boldsymbol{Amount\ excreted = Amount\ filtered}$$

$$\boldsymbol{U_x X\ \dot{V} = P_x X\ GFR}$$

$$\boldsymbol{GFR = \frac{U_{inulin} X\ \dot{V}}{P_{inulin}}}$$



(Guyton & Hall. Medical Physiology, 12e)

Using Clearance to Measure GFR

- Inulin is not used clinically to measure GFR.. ***Why??***

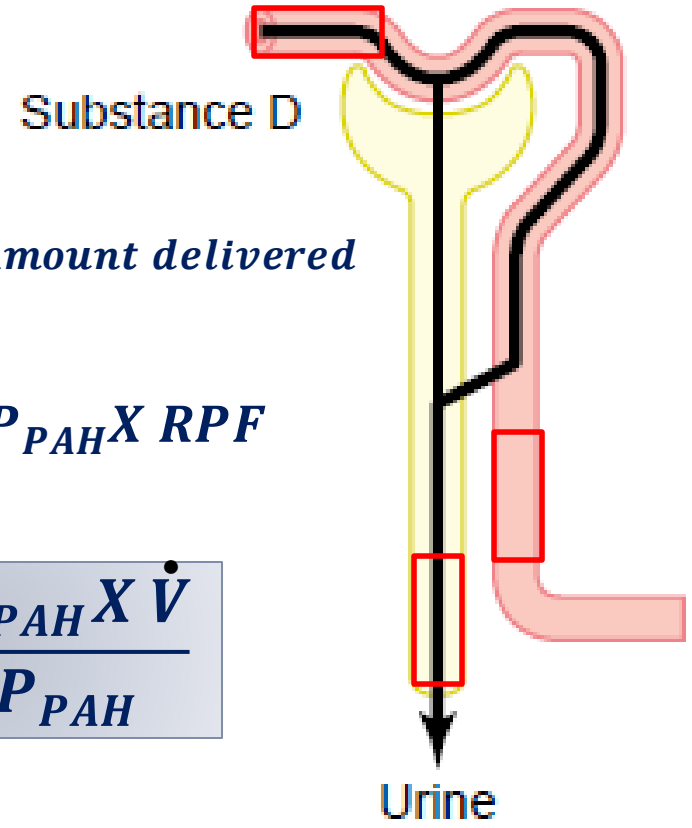
- ***What is used to measure GFR clinically?***
  - ✓ **Creatinine.**
  - ✓ **C_{Cr} = GFR.**

$$GFR = C_{Cr} = \frac{U_{Cr} \, X \, V}{P_{Cr}}$$

Using Clearance to Measure RPF

- Also through clearance, scientists were able to calculate RPF.
- ***How??***
- If a substance is completely cleared from plasma passing through the kidney then, its clearance = RPF.
- ***PAH***.

D. Filtration, secretion



$$Amount\ excreted = Amount\ delivered$$

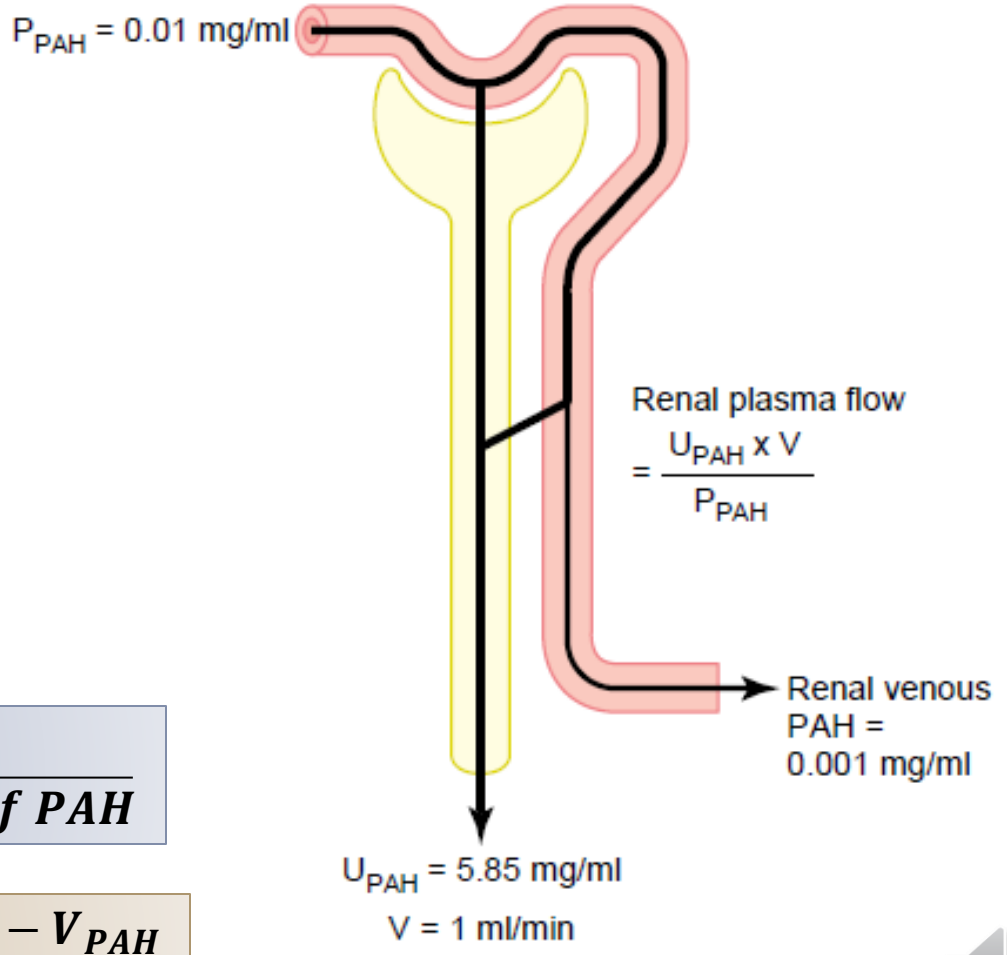
$$U_{PAH} X \dot{V} = P_{PAH} X\ RPF$$

$$RPF = \frac{U_{PAH} X \dot{V}}{P_{PAH}}$$

(Guyton & Hall. Medical Physiology, 12e)

Using PAH Clearance to Measure RPF

- However, not all PAH is removed by passing through the kidneys.
- Approximately 90% is removed = ***extraction ratio of PAH (0.9)***.
- C_{PAH} = Effective RPF.



$$Total\ RPF = \frac{C_{PAH}}{Extraction\ ratio\ of\ PAH}$$

$$Extration\ ratio\ of\ PAH = \frac{P_{PAH} - V_{PAH}}{P_{PAH}}$$

Determining RBF

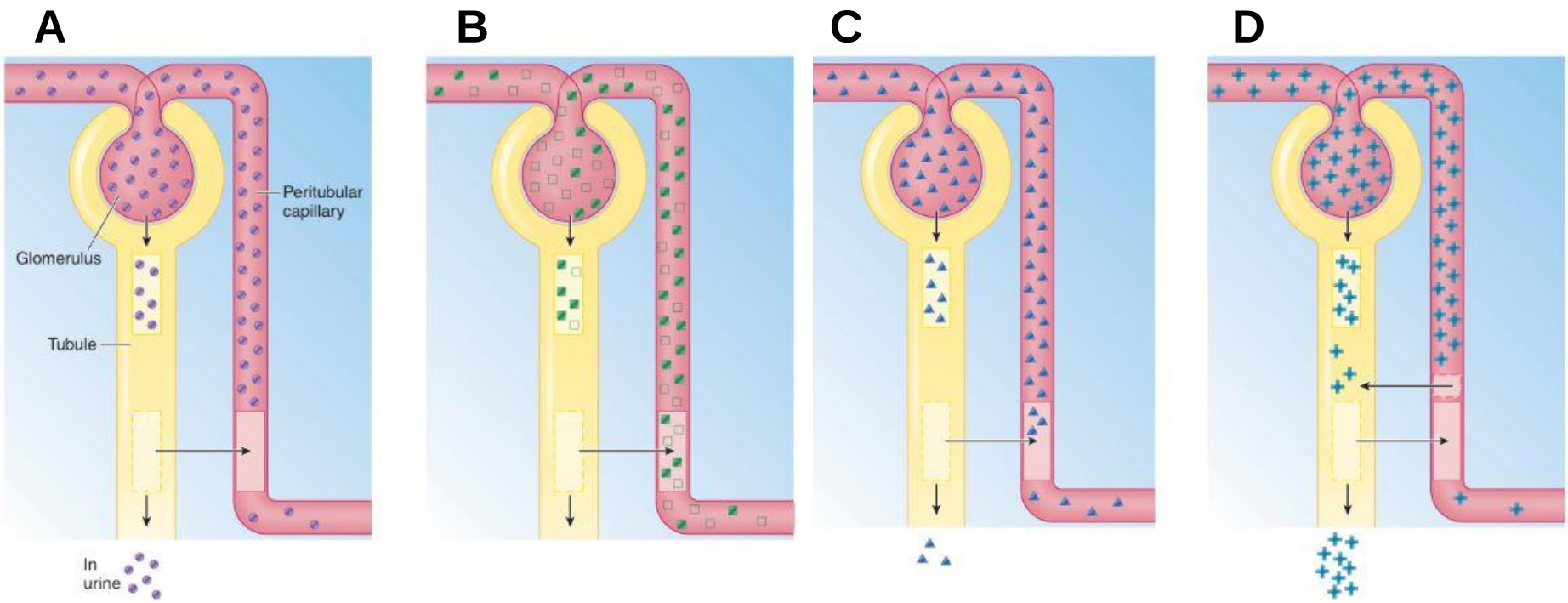
- RBF is not measured directly.
- It can be calculated from RPF using the following equation:

$$RBF = \frac{RPF}{1 - Hematocrit}$$

- Units are ml/min.

(Guyton & Hall. Medical Physiology, 12e)

Using Clearance to Infer the Renal Handling of a Substance



How can the clearance of a substance inform us on the possible ways by which the kidney is handling the substance?

(Human Physiology by Sherwood, 7e)

Calculation of Reabsorption & Secretion Rates

$$Excretion\ rate = U_s\ X\ V$$

$$Reabsorption\ rate = Filtered\ load - Excretion\ rate$$
$$= (P_s\ X\ GFR) - (U_s\ X\ V)$$

$$Secretion\ rate = Excretion\ rate - Filtered\ load$$

Unit = mg/min

Some Exercises

- What is the clearance of substance x if you know that its plasma concentration is 0.01 mg/ml, its urine concentration is 5.85 mg/ml and the urine flow rate is 1ml/min?

- By comparing the clearance of the following substances with that of inulin, what do you understand?
  - Glucose clearance= 0 ml/min.
  - Urea clearance =65 ml/min.
  - PAH clearance = 625 ml/min.

More Exercises

- Use the data provided in the table to answer the questions:

Parameter	Value
Urine flow rate	1 ml/min
Plasma concentration of inulin (P_{in})	100 mg/ml
Urine concentration of inulin (U_{in})	12 g/ml
Renal artery concentration of PAH (P_{PAH})	1.2 mg/ml
Renal vein concentration of PAH (V_{PAH})	0.1 mg/ml
Urine concentration of PAH (U_{PAH})	650 mg/ml
Plasma concentration of A (P_A)	10 mg/ml
Urine concentration of A (U_A)	2 g/ml
Hematocrit	0.45

(Linda Costanzo. Cases & Problems Physiology, 4e)

Continue Exercise

1. What is the value for GFR?

2. What is the value of the “true” renal plasma flow? What is the value of the “true” renal blood flow? What is the value of the effective renal plasma flow? Why is the effective renal plasma flow different from the true renal plasma flow?

3. What is the value of the filtration fraction?

4. Assuming Substance A is freely filtered, what is the filtered load of substance A? Is it reabsorbed or secreted? What is the reabsorption rate?

5. What is the clearance of substance A? Is this value consistent with the conclusion you reached in Q4?

(Linda Costanzo. Cases & Problems Physiology, 4e)

References

- This link is from the webpage of Professor Fredric Coe who's work in 1965 laid the ground for renal clearance as we know it today.

https://kidneystones.uchicago.edu/the-true-meaning-of-renal-clearance/

- Guyton & Hall Medical Physiology, 12e.
- Human Physiology by Sherwood, 7e.
- Linda Costanzo Cases & Problems Physiology, 4e.

THANK YOU