

Review of the previous lecture:

- Kidney's function is to clean the blood by removing waste products.
- kidney failure will lead to death for many reasons, for example:
 - Electrolyte imbalance
 - * K imbalance: lead to cardiac arrhythmias
 - * Ca imbalance: affects bone (kidney is the major organ for Ca homeostasis)
 - pH disturbance: acidosis, alkalosis.
 - Kidney secret erythropoietin→ therefore, kidney failure leads to anemia
 - Kidney regulates the volume of blood: kidney failure→hypertension, malignant hypertension→pulmonary edema

Today's Lecture:

- **Renal Blood Flow (RBF)**
- **Glomerular Filtration Rate (GFR)**

How to measure Renal Blood Flow?

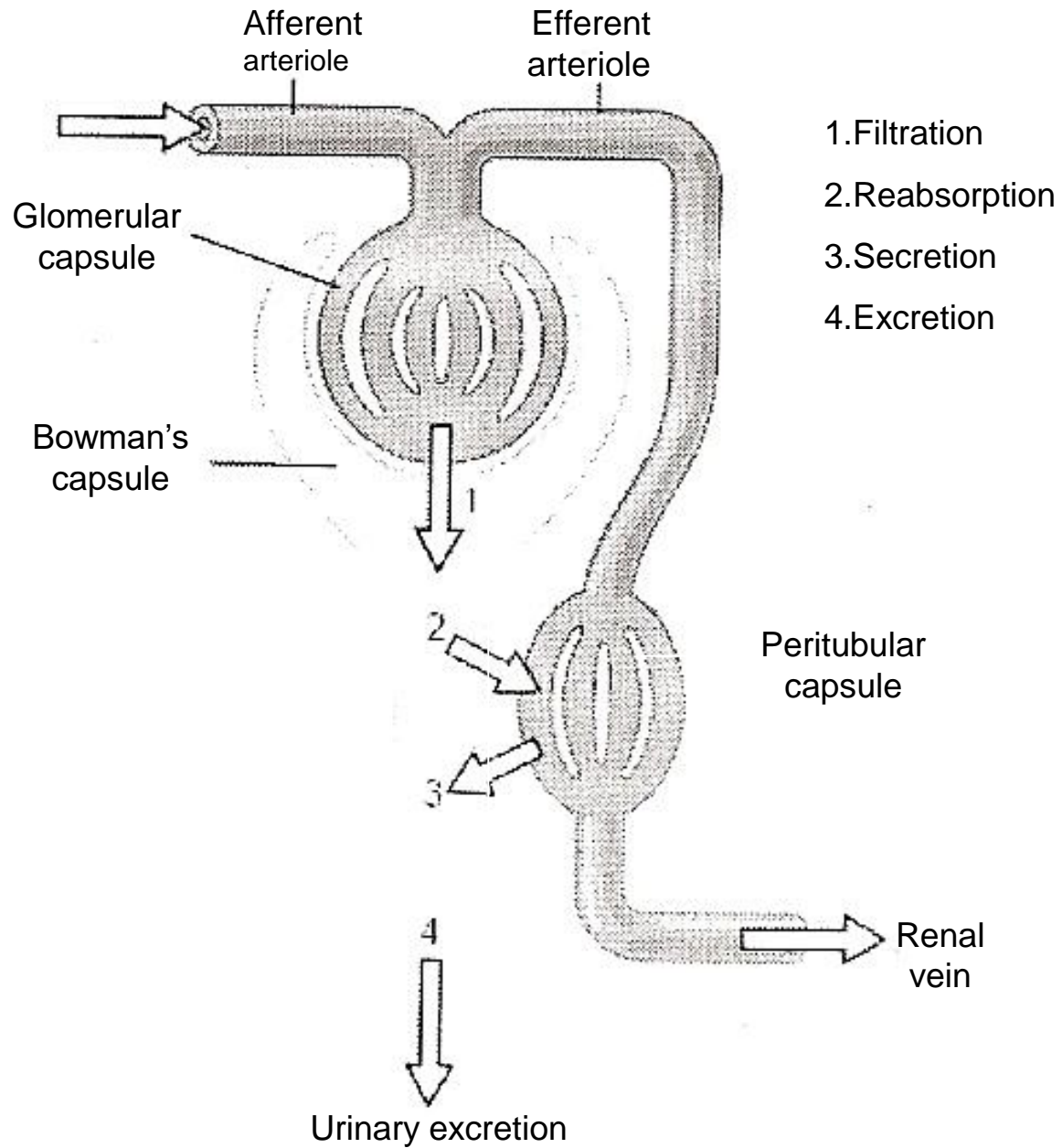
Through this equation:

$$\text{RBF} = \frac{\text{Renal Plasma Flow}}{1-\text{Hct}}$$

So, if we assume that the RBF is 1250 ml and the Hct is 45%, the Renal Plasma Flow is **≈ 685 ml.**

The source of PAH in the urine:

- 1. filtration 20%**
- 2. secretion 80%**
- 3. without any reabsorption.**

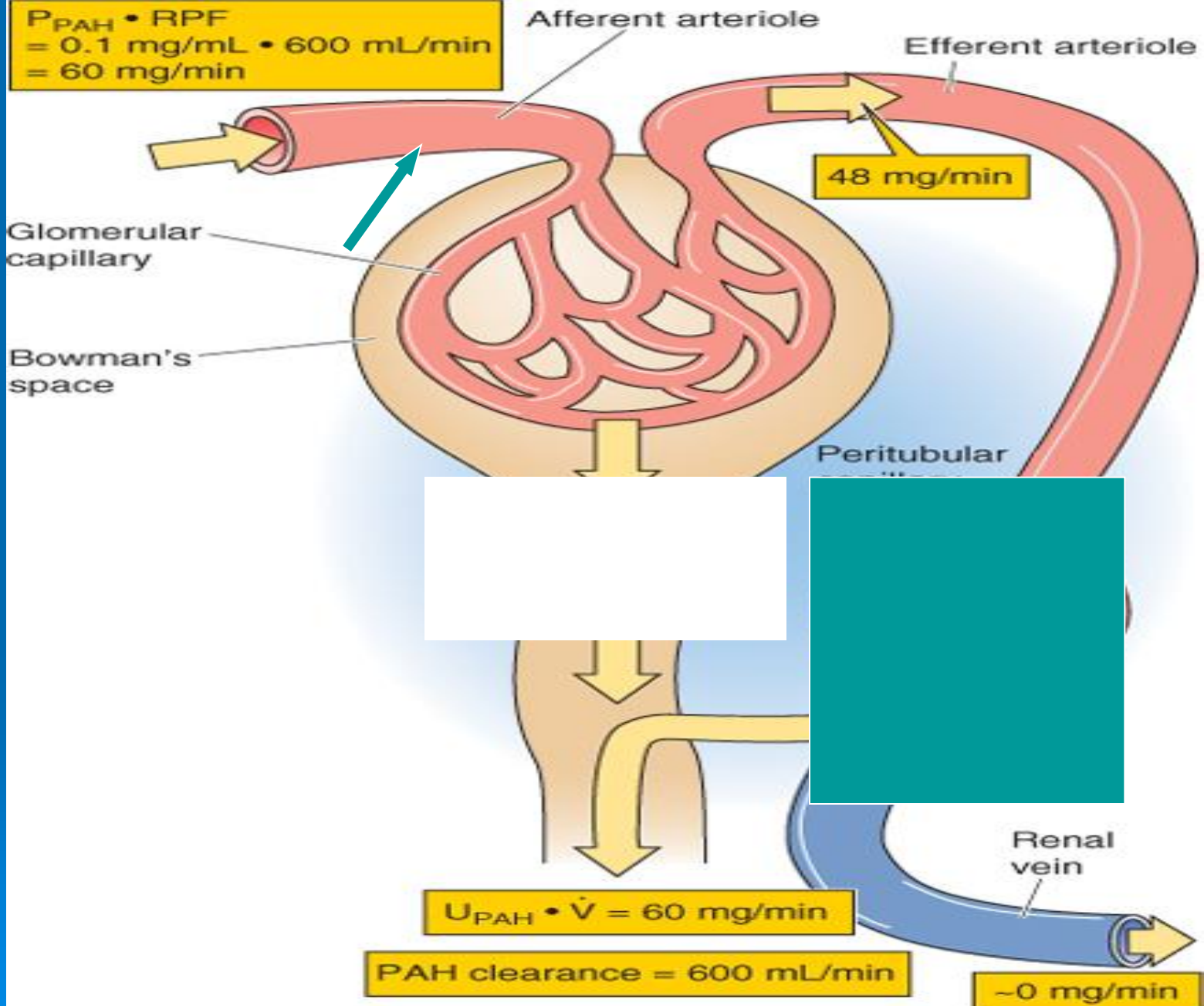


$$\text{Excretion} = \text{Filtration} - \text{Reabsorption} + \text{Secretion}$$

$$P_{PAH} \cdot RPF$$

$$= 0.1 \text{ mg/mL} \cdot 600 \text{ mL/min}$$

$$= 60 \text{ mg/min}$$



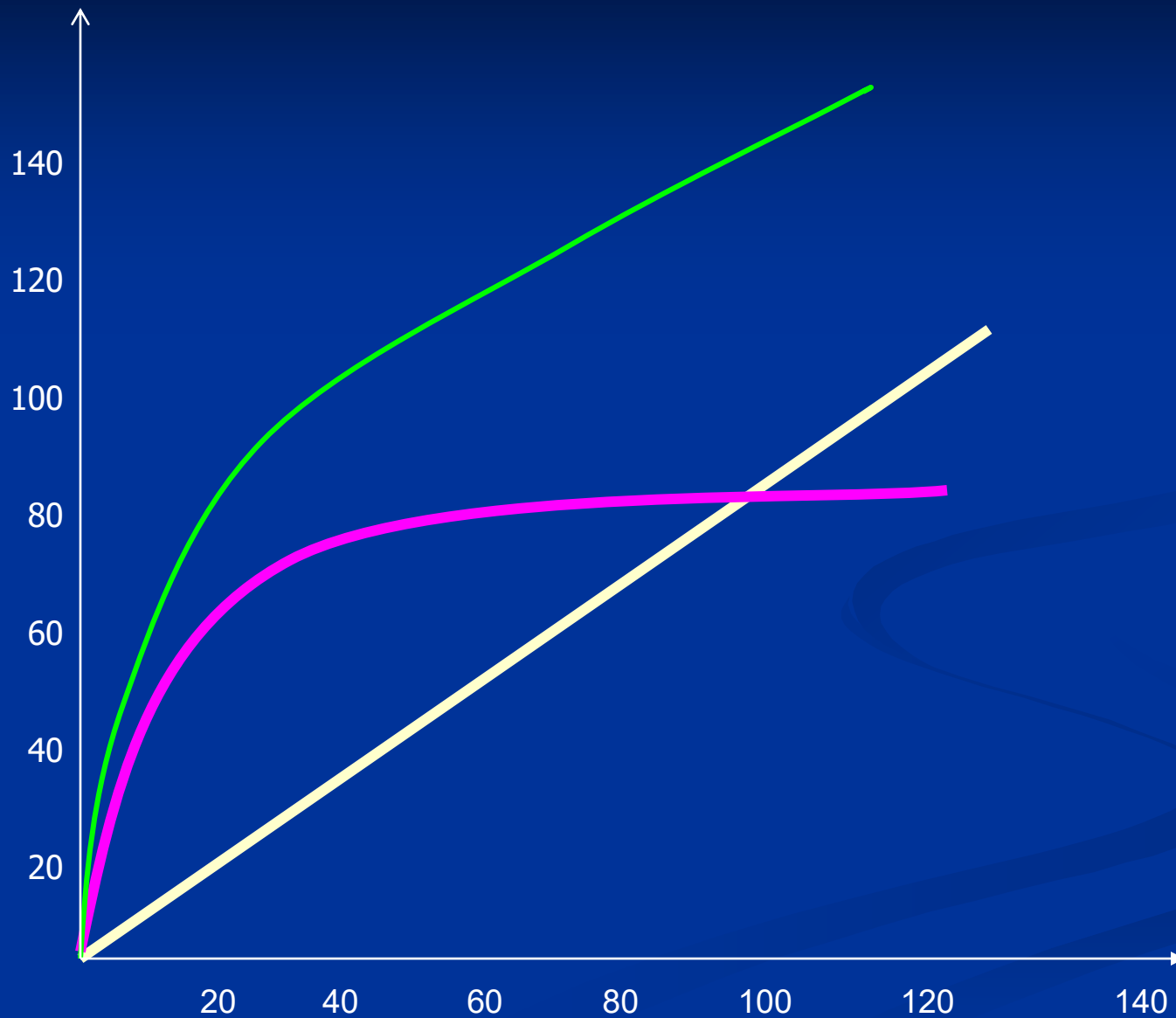
$$U_{PAH} \cdot \dot{V} = 60 \text{ mg/min}$$

$$PAH \text{ clearance} = 600 \text{ mL/min}$$

$$-0 \text{ mg/min}$$

PAH CURVE for FILTRATION and SECRETION

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Remember:

PAH is completely cleared from plasma in the kidney...

under one condition...name it

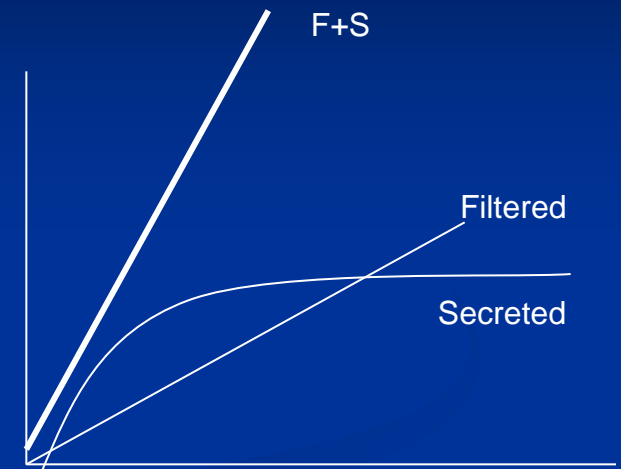
- When we increase the PAH in the plasma, the filtration will increase proportionally (because filtration is a passive process).

(remember: 20% of the PAH is filtered)

- But in the case of secretion (which is an active process) after reaching T_{max} No more increase in secretion...plateau phase

- So at a certain concentration the kidney will not be able to clear the whole plasma from that substance.

- **If PAH delivered to the peritubular capillaries exceeds T_{max} (80 mg/min) →→ PAH clearance becomes less than RPF (underestimation of RPF)**



Let us look at it from different angle:

We will use “Law of Conservation of Mass”:

Amount excreted in the urine/min = Amount provided for excretion (by artery)/min

- A_x : is the amount of X entering the kidneys through the renal artery

- “X” leaves the kidney through: 1. renal vein or 2. through urine Thus:

$$A_x = V_x + U_x$$

• *Conditions must be met before using “x” as RPF marker: X is not accumulated in the kidney.*

• *Is not catabolized by the kidney.*

• *Is not produce by the kidney itself.*

If we assume that V_x equals zero, then:

$$U_x = A_x$$

Amount Excreted of X (mg/min) = Urine output (V) * U_x

Amount provided for excretion (mg/min) = RPF * P_x P=plasma

So...

$$\mathbf{RPF = (U_x/P_x) * V}$$

PAH :

Paramino hippuric acid

A substance used to measure RBF (RBF marker),
how?

Through the equation, the amount of the substance that enters the kidney has to be excreted in the urine, so we need a substance that is totally excreted by filtration and secretion without any reabsorption to the vein and these criteria are found in PAH.

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Clearance:

-Cx: Is volume of plasma/min provide X for excretion.

-Unit of clearance: [Volume/time]

Examples:

- We have 650 ml plasma with specific amount of X, after leaving the kidney all of the plasma was cleaned from X. 100% of 650 ml/min $C_x = 650$ ml/min
- We have 650 ml plasma with specific amount of Y, after leaving the kidney we find the same amount of Y. 0% of 650 ml plasma $C_y = 0$ ml/min
- We have 650 ml plasma with specific amount of Z, after leaving the kidney we find half of the amount of Z. Clearance will be 50% of the 650 $C_z = 325$ ml/min

GFR

* When 125ml/min of plasma is filtered in Bowman's capsule, 1 ml of urine will be excreted and 124 ml will be reabsorbed (99.2%).

* How to measure GFR?

- We need a substance that is: freely filtered, not secreted and not reabsorbed.

- INULIN is an exogenous substance that meets these criteria

Filtrate Load of Inulin: the amount of Inulin filtered in Bowman space per min which is equal to the same amount *excreted in the urine/min*)

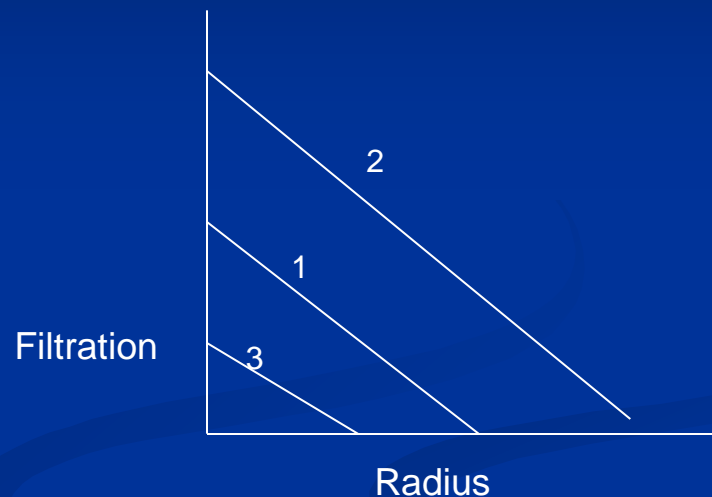
Inulin is a Glomerular marker. (Inulin clearance = GFR)

Excreted amount/min = amount provided for excretion/min

$$U_{\text{inulin}} * V = P_x * \text{GFR}$$

- Any substance with a MW less than 70 K can be filtered, and the filtration is inversely related with the radius:

- (1) a neutral substance
- (2) Is a cation substance: because it'll attach to the -ve basement membrane, more filtration.
- (3) Anion: less filtration



Note:

Hemoglobin MW is less than 70 K. However, it is not filtered because Hb is bounded to protein: in hemolysis we can see Hb in the urine (pink urine).

- Since Inulin is an exogenous substance it is only used for research purposes and not as a clinical test.

We need an endogenous substance: **Creatinine.**

- *Is muscle protein*
- *Small molecule (MW is 114)*
- *Its concentration does not fluctuate from day to day in plasma*
- *Freely filtered, not reabsorbed but **SLIGHTLY SECRETED***

To convert $\mu\text{mol/l}$ of creatinine to mg/dl , divide by 88.4.

To convert mg/dl of creatinine to $\mu\text{mol/l}$, multiply by 88.4

Creatinine in the urine comes from 90% filtered and 10% through secretion. This has the potential to overestimate GFR by 10%. But in actuality it does not...why? In fact, it does overestimate GFR in end-stage renal failure...again WHY?

- Creatinine: Comes from high energy bond, muscle phosphocreatinine (PC)
- Plasma creatinine by itself (without creatinine clearance) is a good indicator of renal function because it does not relate to food intake or level of exercise.

Through this equation:

$$\text{Creatinin Clearance (GFR)} = \frac{U_{Cr} * V}{P_{Cr}}$$

Last point to describe which is the answer to the previous question I asked you:

10% of Cr in urine is secreted which overestimates the GFR.

But it was found that 10% of Cr in plasma is bounded to proteins (so, they canceled each others). We actually measure total plasma creatinine and not just free creatinine in plasma.

Ccr is good estimation of GFR.