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?

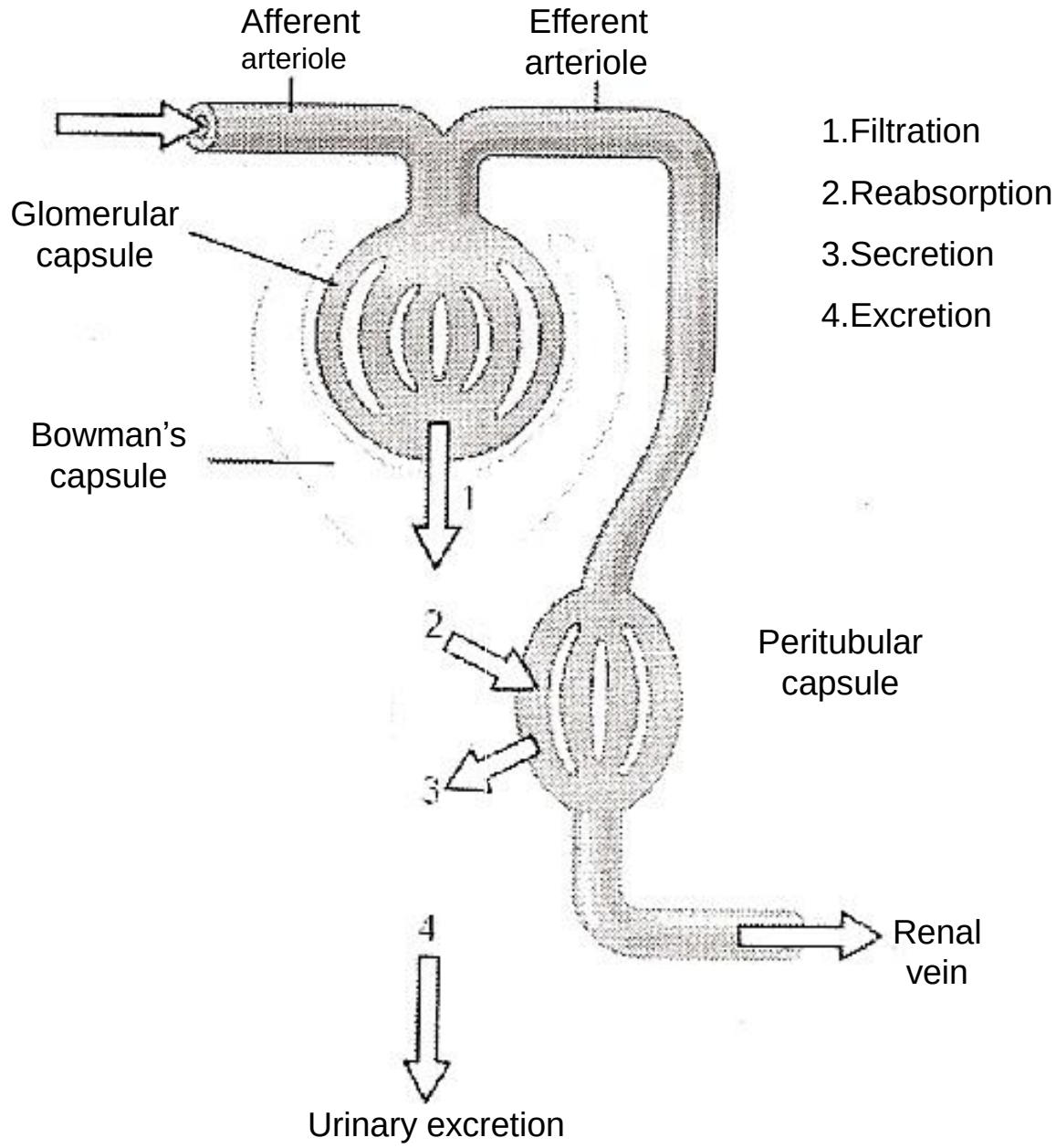
Through this equation:

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

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.**



1.Filtration

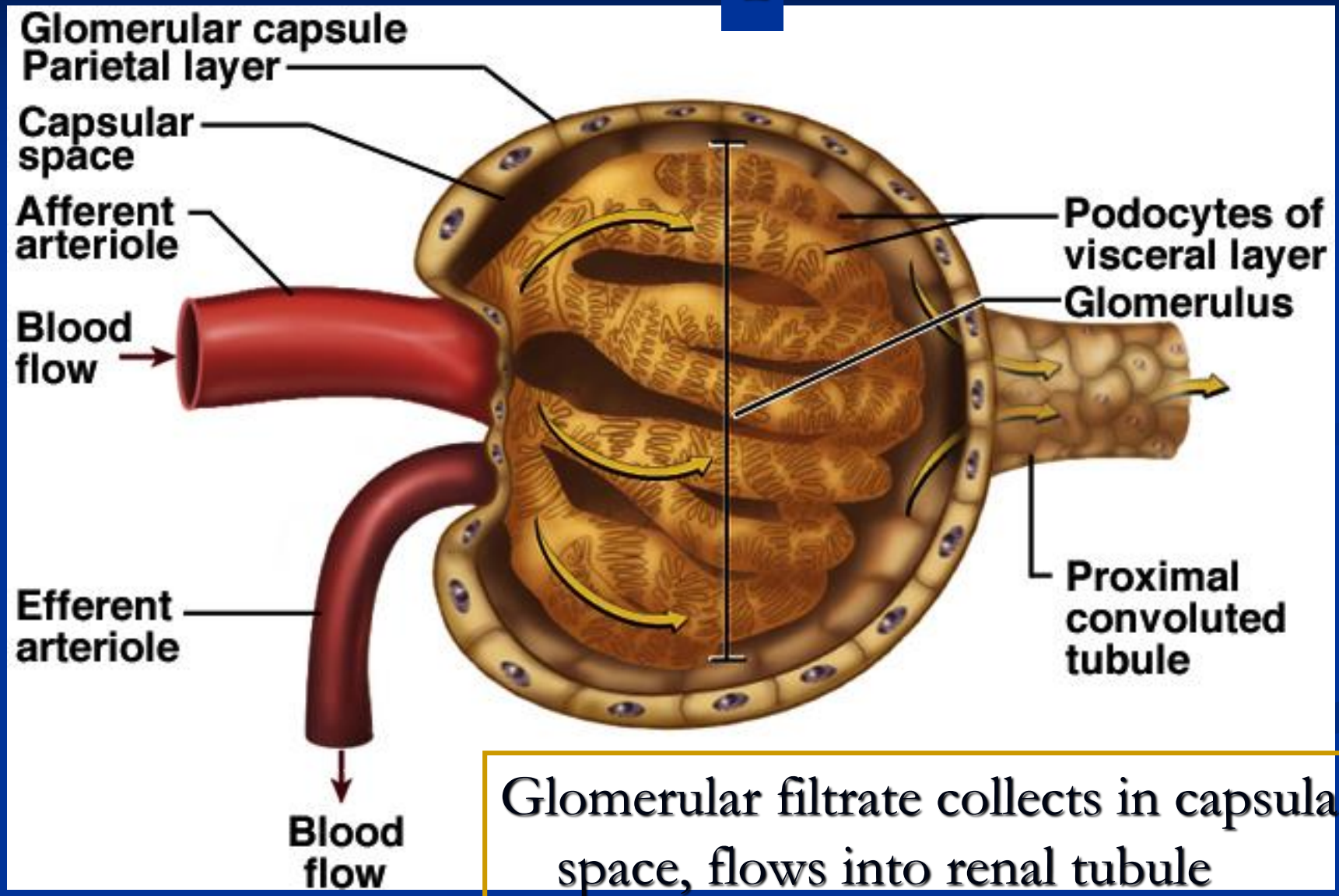
2.Reabsorption

3.Secretion

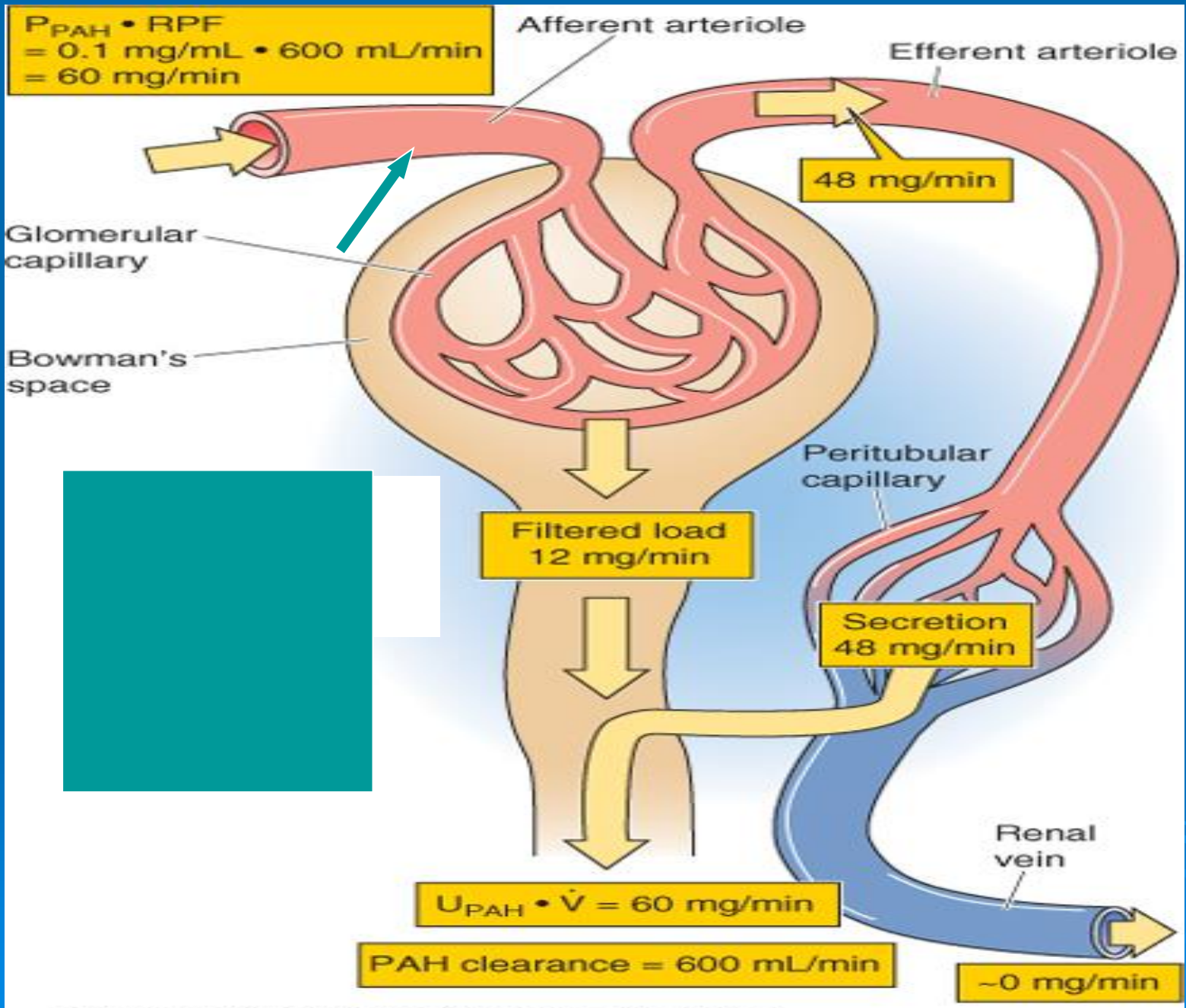
4.Excretion

Excretion = Filtration – Reabsorption + Secretion

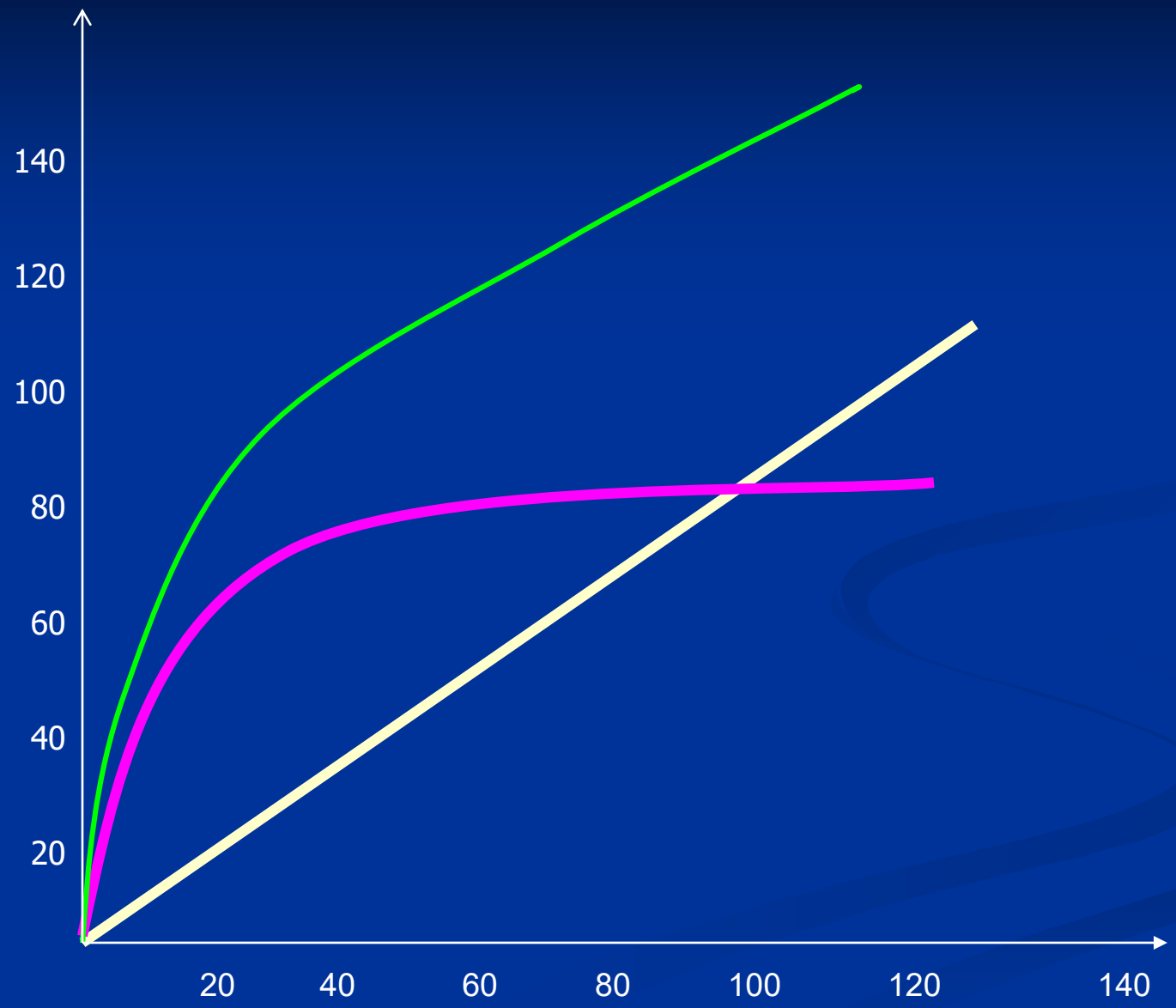
Renal Corpuscle



Glomerular filtrate collects in capsular space, flows into renal tubule



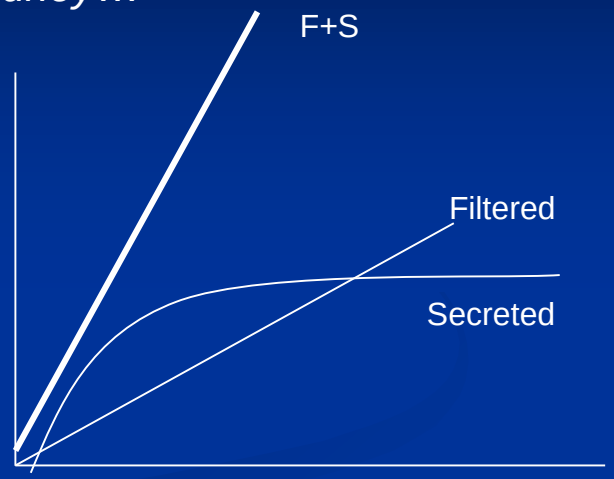
PAH CURVE for FILTRATION and SECRETION :



Remember:

PAH is completely cleared (cleaned) from plasma in the kidney…

But only 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 Tmax…. 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 (Cr).

- If PAH delivered to the peritubular capillaries exceeds Tmax (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
- Ux: is the amount of X leaving the kidneys through urine ren

- "X" leaves the kidney through: 1. renal vein or 2. through urine
Thus: Ax = Vx (we consider this portion equals zero) + Ux

• *Conditions must be met before using "x" as RPF marker: "X" does not accumulate, made, or catabolized by the kidney*

If we assume that Vx equals zero, then:

Ux = Ax

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

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

So…

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*)

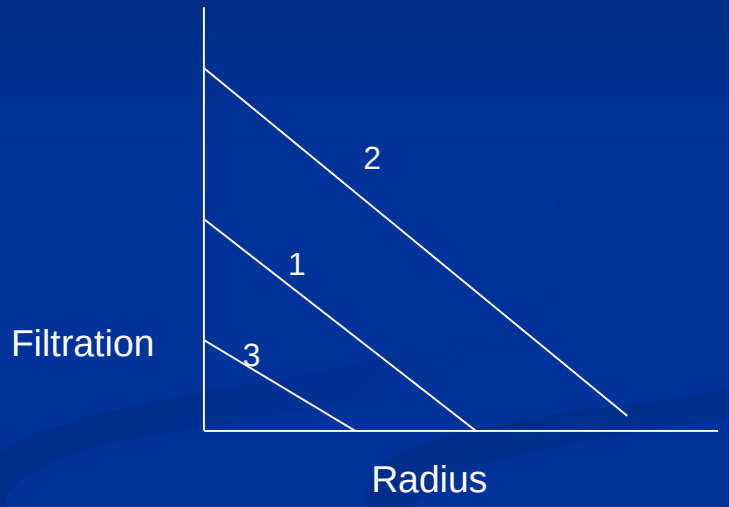
Inulin is a Glomerular marker. (Inulin clearance = GFR)

Excreted amount/min = amount provided for excretion/min

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

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

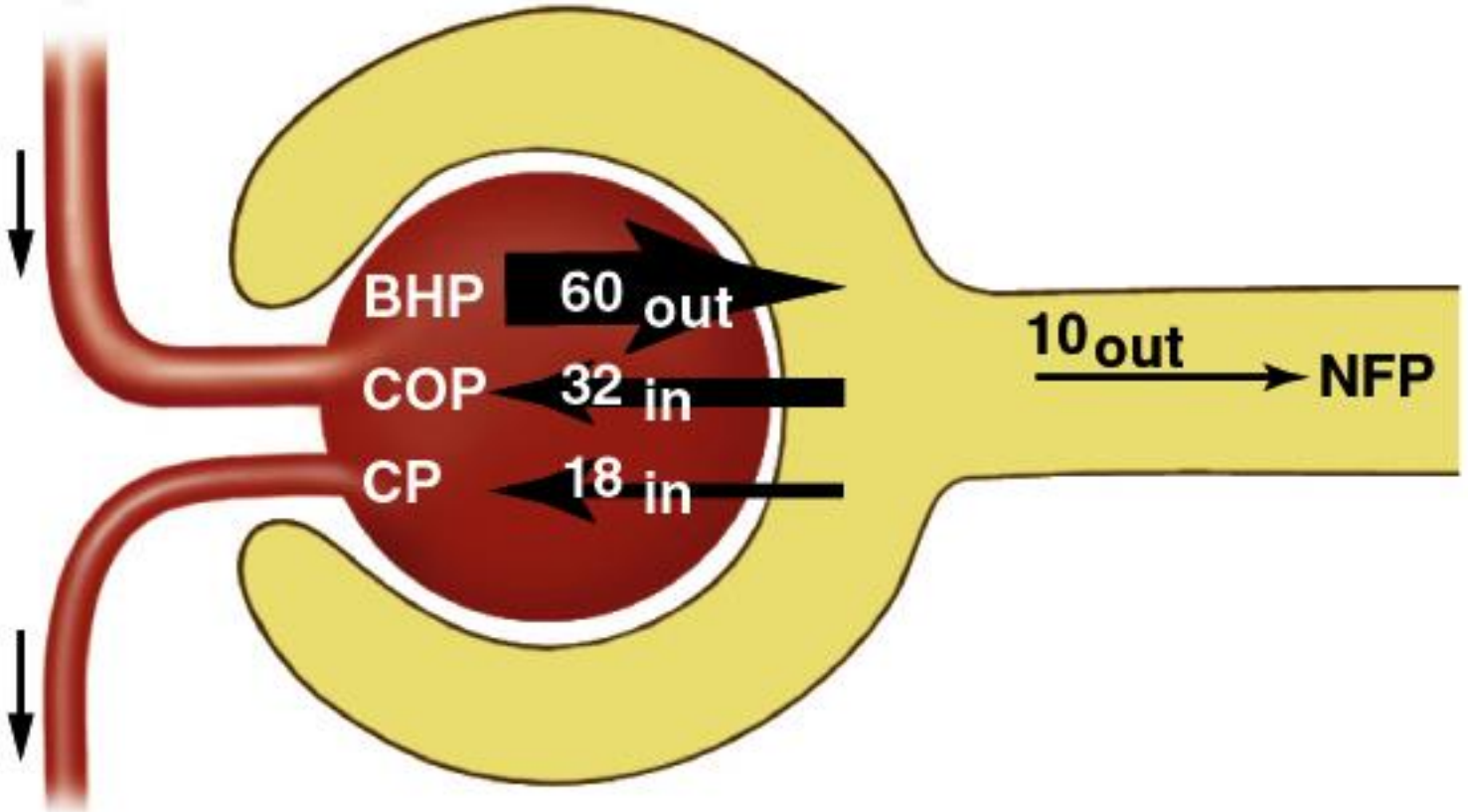
(1) a neutral substance
(2) Is a cation substance: because it'll attach to the –ve basement membrane, more filtration.
(3) Anion: less filtration



Note:

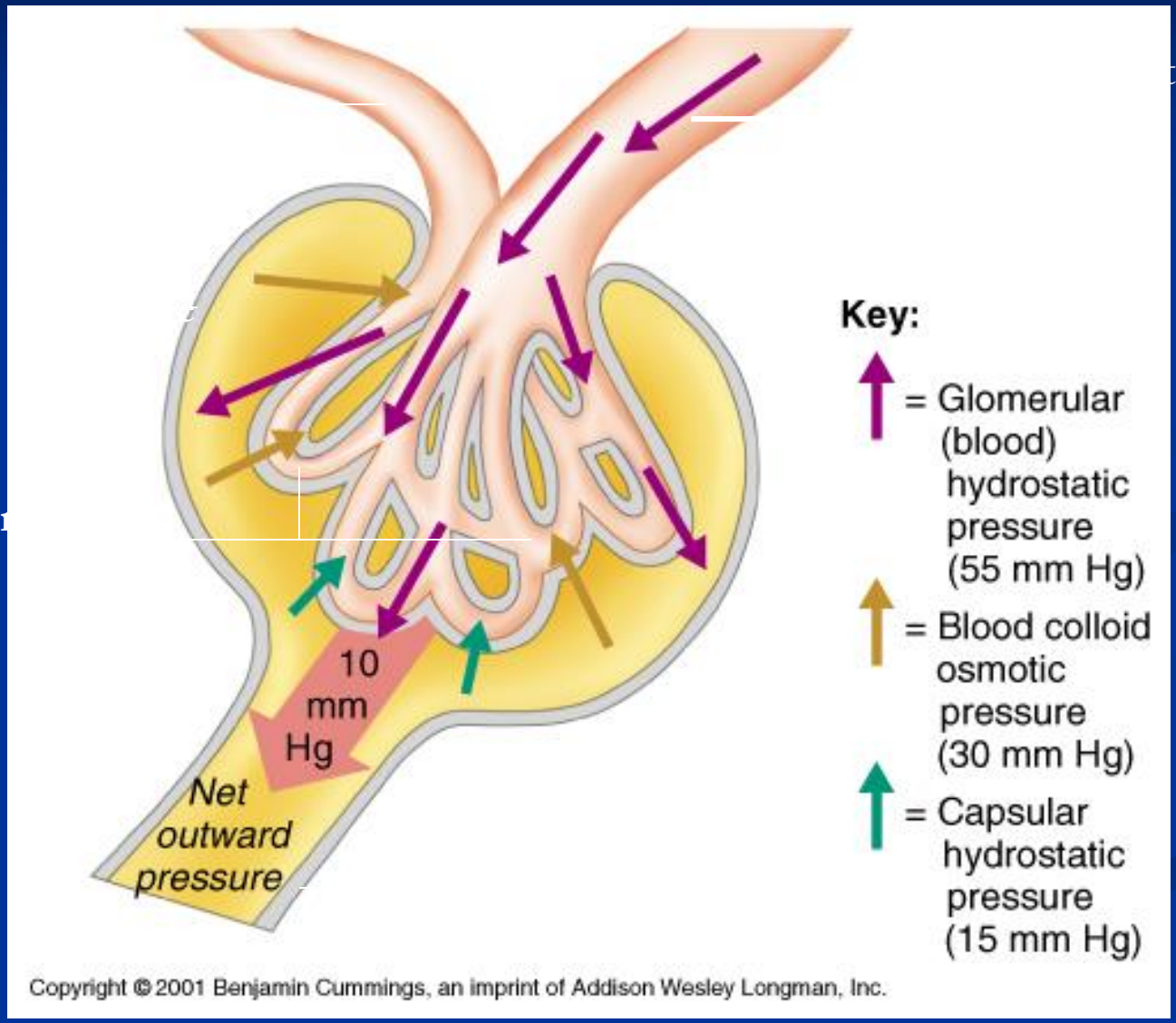
Hemoglobin MW is less than 70 K. However, it is not filtered because Hb is bounded to protein: in hemolysis we can see Hb in the urine (pink urine).

Filtration Pressure



Blood hydrostatic pressure (BHP)	60 mmHg out
Colloid osmotic pressure (COP)	–32 mmHg in
Capsular pressure (CP)	–18 mmHg in
Net filtration pressure (NFP)	10 mmHg ou

Location of the Glomerulus



- 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 μmol /l of creatinine to mg/dl, divide by 88.4.

To convert mg/dl of creatinine to μmol/l, multiply by 88.4

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

- Creatinine: Comes from high energy bound, 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:

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

Last point to describe which is the To answer the question I asked earlier:
10% of Cr in urine is secreted which overestimates the GFR. But it was found that 10% of Cr in plasma is bounded to protein… it is the total Cr we measure and not only the free portion. (so, both factors cancel each others).

Ccr is good estimation of GFR.

Objective 9

Given the concentration of a substance in the plasma and the amount of the substance excreted in the urine per minute, you will compute the plasma clearance rate.

Plasma Clearance

Plasma clearance is defined as **the amount of plasma** that is **cleared or "cleansed" of a particular substance in one minute**. The **kidneys** will **carry out this** clearance process through the use of **filtration**, **reabsorption** and **secretion.**

Plasma Clearance

Filtration will **directly** affect clearance. As filtration increases, more material will be removed from the blood plasma. Reabsorption is **indirectly** proportional to clearance. As reabsorption increases, less material will be removed from the blood plasma. Secretion will **directly** affect clearance. As secretion increases, more material will be removed from blood plasma.

Plasma Clearance

The formula used to calculate plasma clearance is:

$$C = V \times U/P$$

C = plasma clearance rate in ml/min

V = urine production rate in ml/min

U = the concentration of a substance in the urine in mg/ml

P = the concentration of a substance in the plasma in mg/ml

As you track the units in the equation, you will notice that mg/ml cancel out, leaving ml/min.

Plasma Clearance

Let us practice calculating plasma clearance using the clearance equation. In all your calculations, assume that the urine production rate (V) is 2 ml/min. Let's start with the substance inulin (not insulin!). If after a dose of inulin, your urine has 30 mg/ml and your plasma has 0.5 mg/ml of this substance, what is the inulin clearance rate? If you got 120ml/min, you are correct!

Plasma Clearance

If you did not get 120ml/min, look at the following calculation and recheck your work.

120 ml/min = 2 ml/min x 30 mg/ml/ 0.5 mg/ml

Plasma Clearance

Test your ability to conduct further calculations by calculating the clearance rate for the following substances:

Substance	Urine concentration	Plasma concentration
Urea	7.0 mg/ml	0.2 mg/ml
Glucose	0.0 mg/ml	1.0 mg/ml
Penicillin	298 mg/ml	0.7 mg/ml

Remember that the urine production rate (2ml/min) will be the same for all of the above calculations. The clearance rate for each of the above substances will be: **Urea** = 70 ml/min; **Glucose** = 0 ml/min; **Penicillin** = 851 ml/min**!!!**. Were you able to get the right answers? If not, go back and restudy the clearance process.