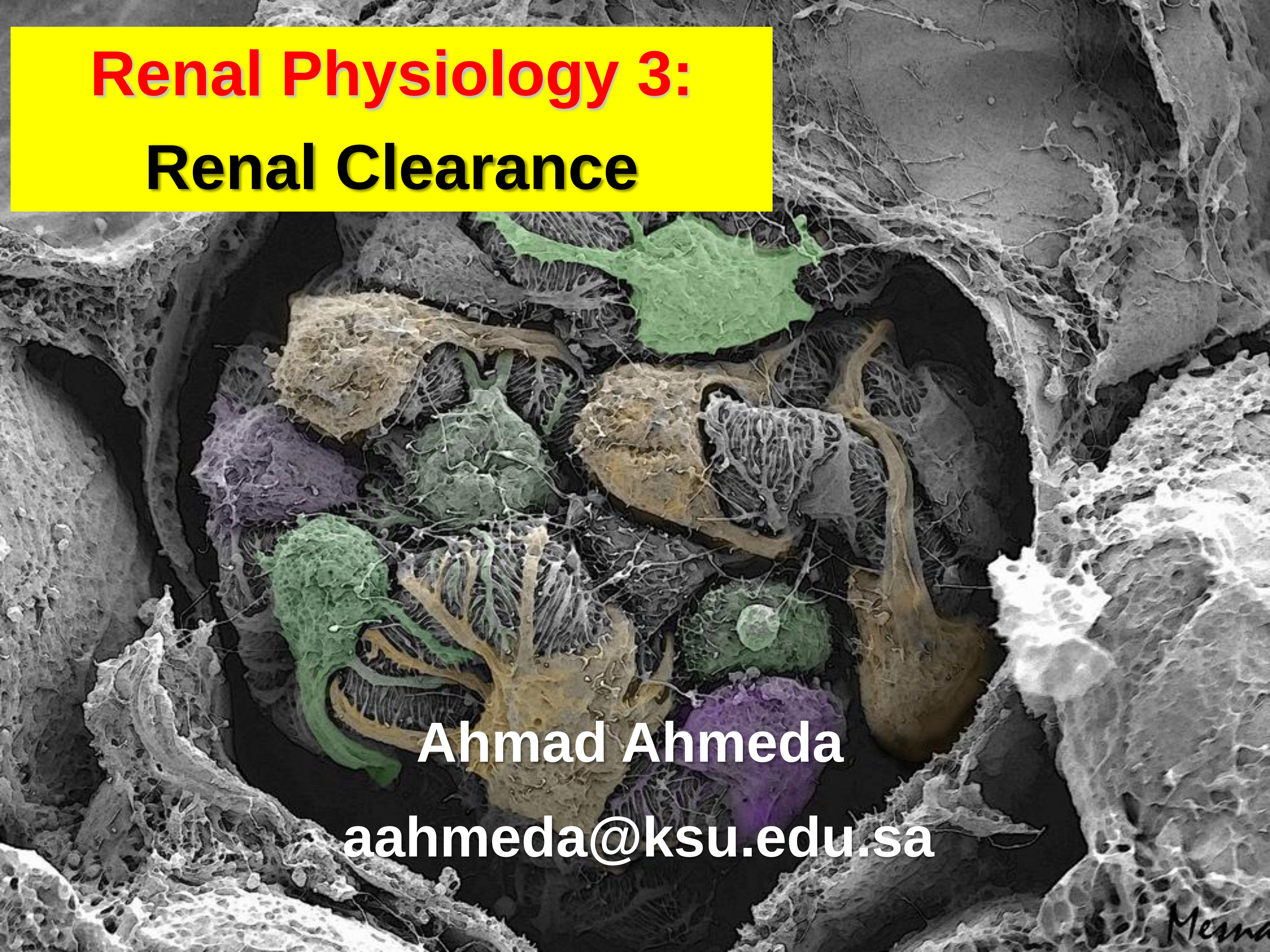

Renal Physiology 3:
Renal Clearance

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Learning Objectives:

- Describe the concept of renal plasma clearance.
- Use the formula for measuring renal clearance.
- Use clearance principles for inulin, creatinine etc. for determination of GFR.
- Explain why it is easier for a physician to use creatinine clearance Instead of Inulin for the estimation of GFR.
- Describe glucose and urea clearance.
- Explain why we use of PAH clearance for measuring renal blood flow.

How to measure GFR?

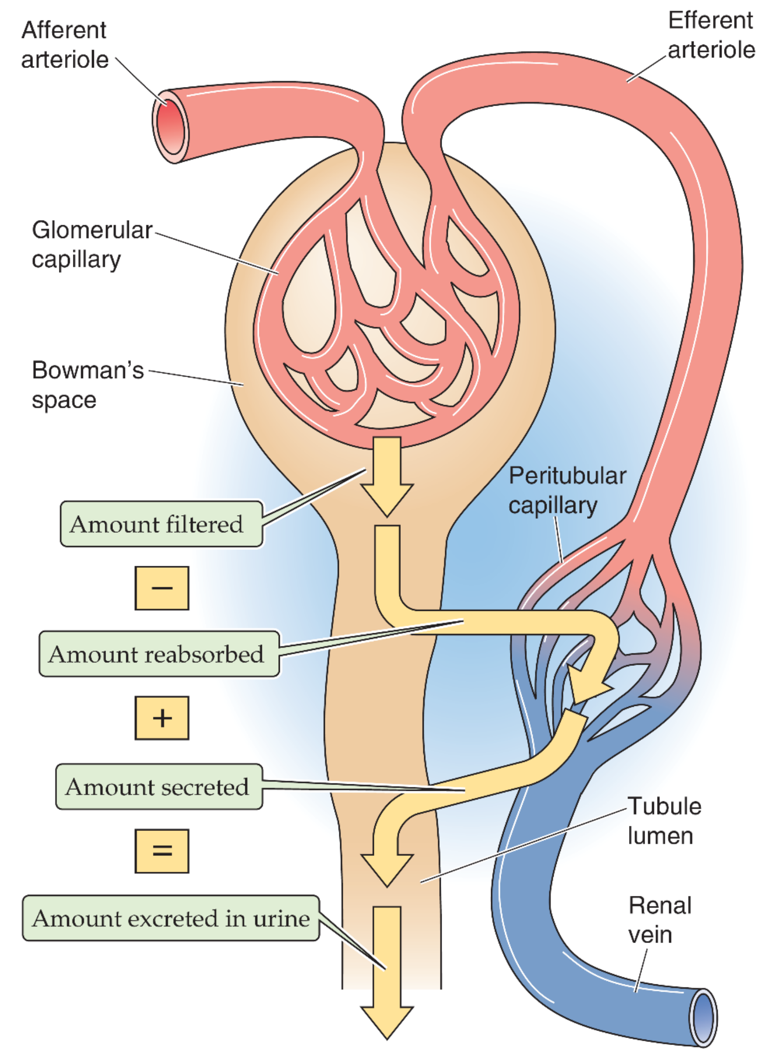
Clearance method

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
$= GFR \, . \, P_x$ (filtered load)

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



Clearance = GFR

<u>Criteria of substance:</u>

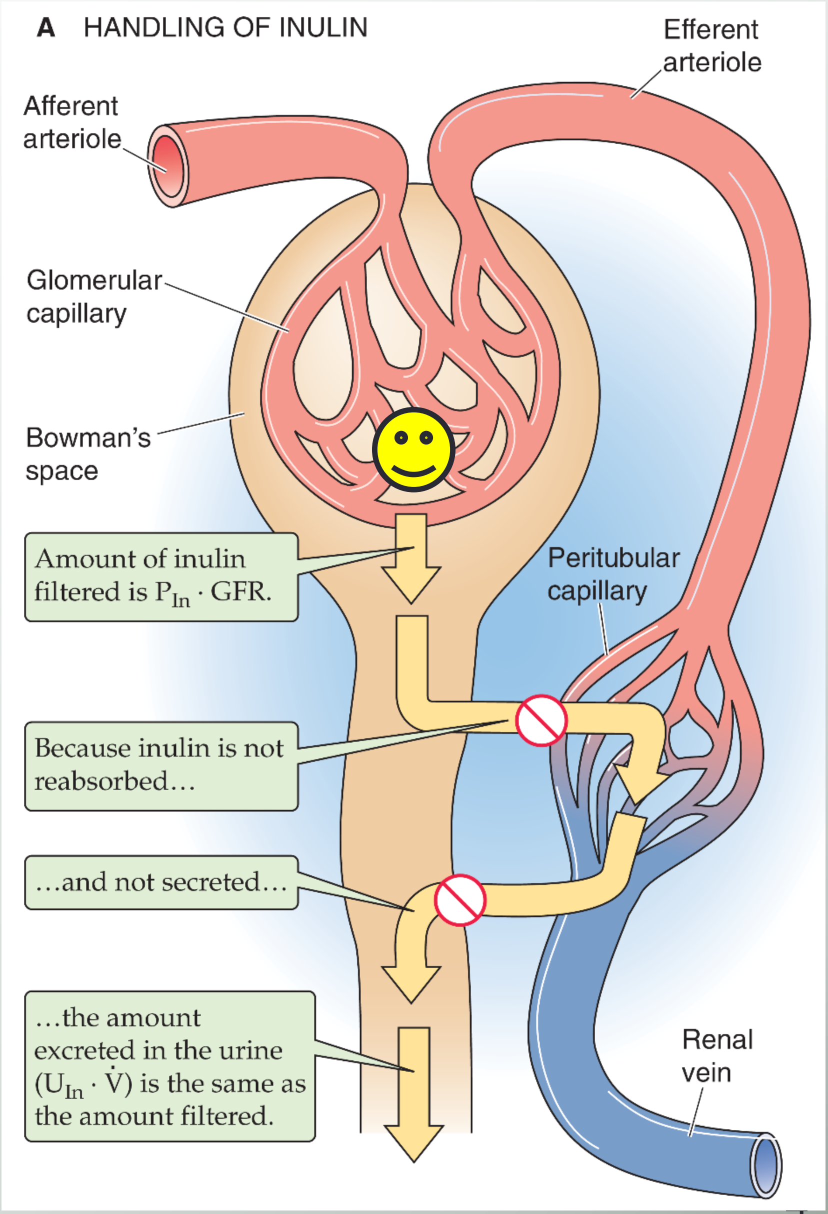
1. freely filtered
2. **NOT** reabsorbed, **NOT** secreted or metabolized in the nephron

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

- e.g., inulin

$$GFR \, . \, [P]_{Inulin} = [U]_{Inulin} \, . \, \tilde{V}$$

$$Cl_{Inulin} = GFR = \frac{[U]_{Inulin} \, . \, \tilde{V}}{[P]_{Inulin}}$$



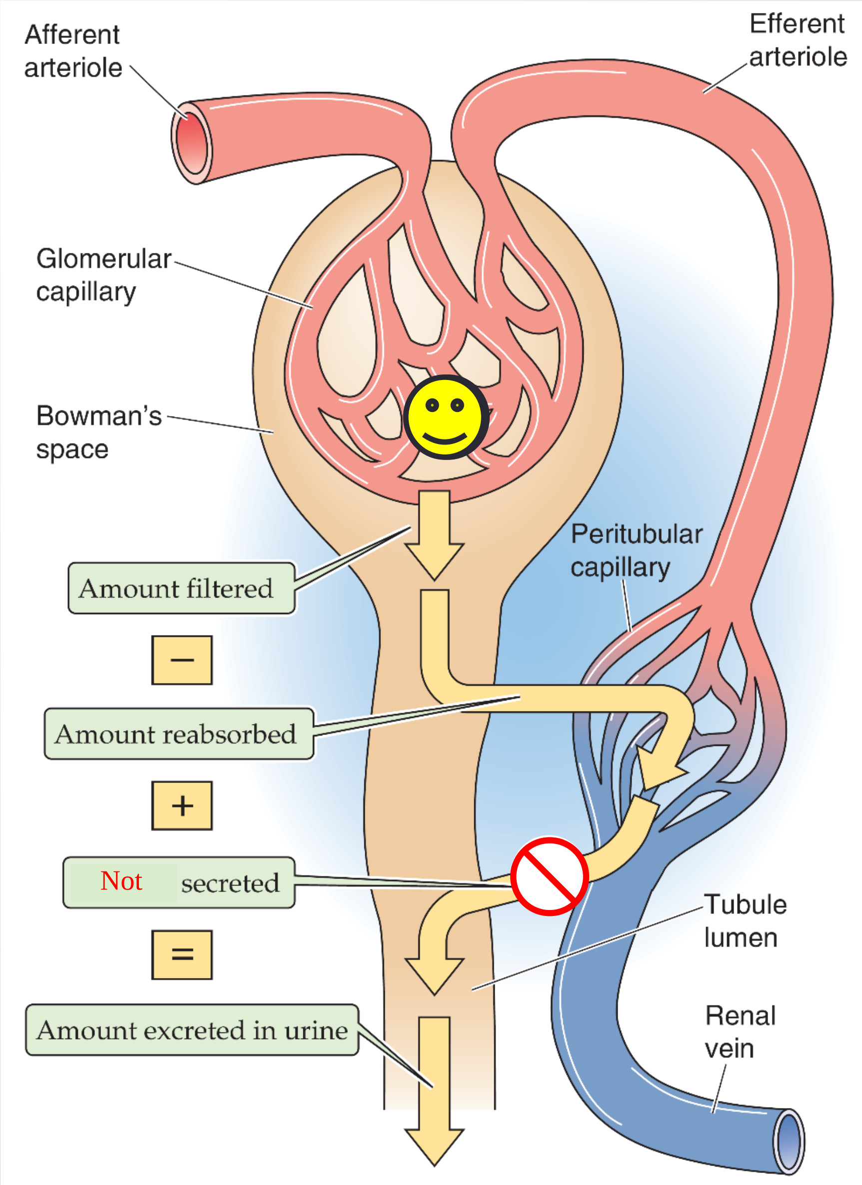
- For substances **reabsorbed** by the kidney:

amount **filtered** per minute > amount **excreted** per minute

$$GFR \,.\, [P]_x \quad > \quad [U]_x \,.\, \tilde{V}$$

$$GFR \,.\, [P]_x - \text{Absorbed 'T'} = [U]_x \,.\, \tilde{V}$$

- $Cl_{sub} < Cl_{inulin}$ Absorption from nephrons is occurring
- Cl = **0** for glucose & amino acids (normally).
- e.g., glucose, sodium, urea.



- For substances **secreted** by the kidney:

PAH, creatinine.

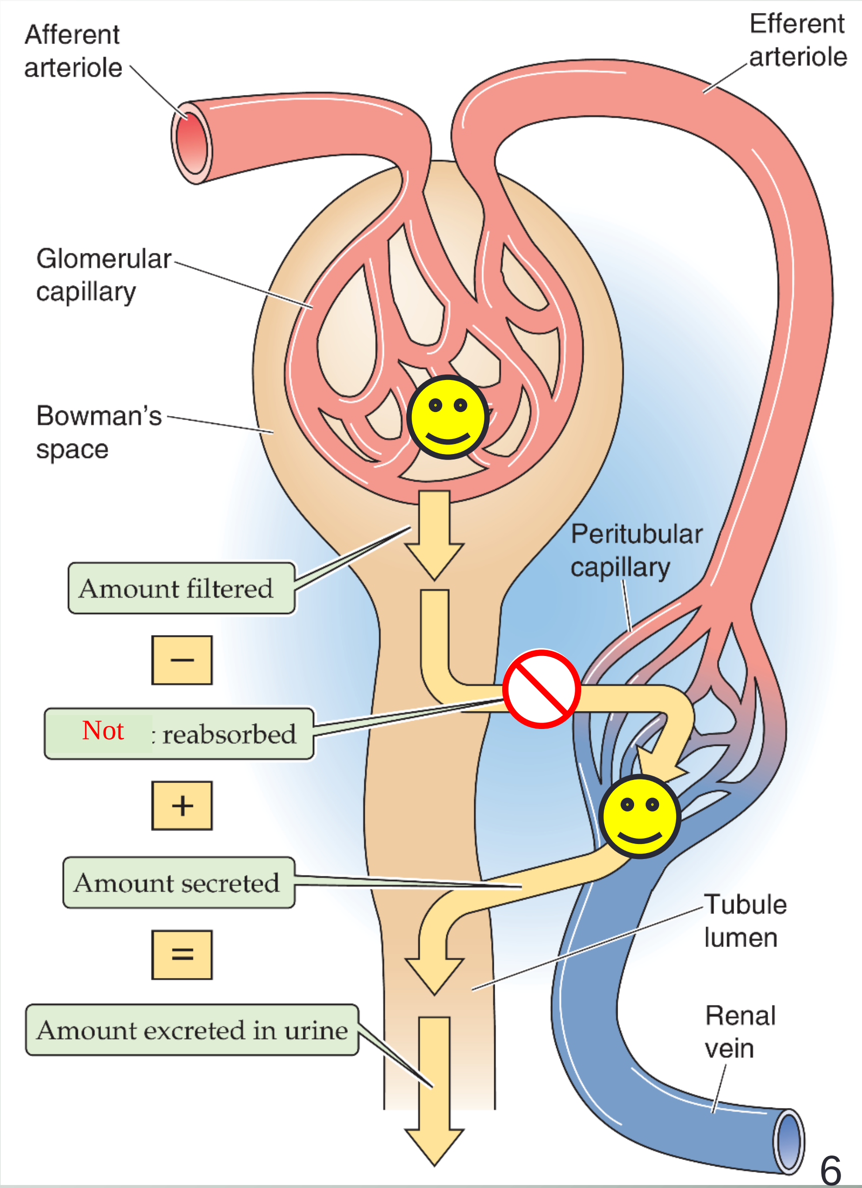
amount **filtered** per minute < amount **excreted** per minute

$$GFR \,.\, [P]_x \quad < \quad [U]_x \,.\, \tilde{V}$$

$$GFR \,.\, [P]_x + \text{Secreted 'T'} = [U]_x \,.\, \tilde{V}$$

12 mg/min < 60 mg/min

- $Cl_{sub} > Cl_{inulin}$ Secretion into nephrons is occurring



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

Amount Filtered per minute = (GFR X $[Sub]_{plasma}$)

= 120 ml/min X 3 mg/ml = **360 mg/min**

Amount excreted per minute = ($[sub]_{urine}$ X Urine flow rate)

= 2 ml/min X 10 mg/ml = **20 mg/min**

Amount Filtered per minute > Amount excreted per minute

Amount transported per minute = Filtered – Excreted

= 360 - 20 = **340 mg/min**

Clearance method to measure RPF

Criteria of *substance used*

- *filtered + secreted*
- **NOT *reabsorbed***

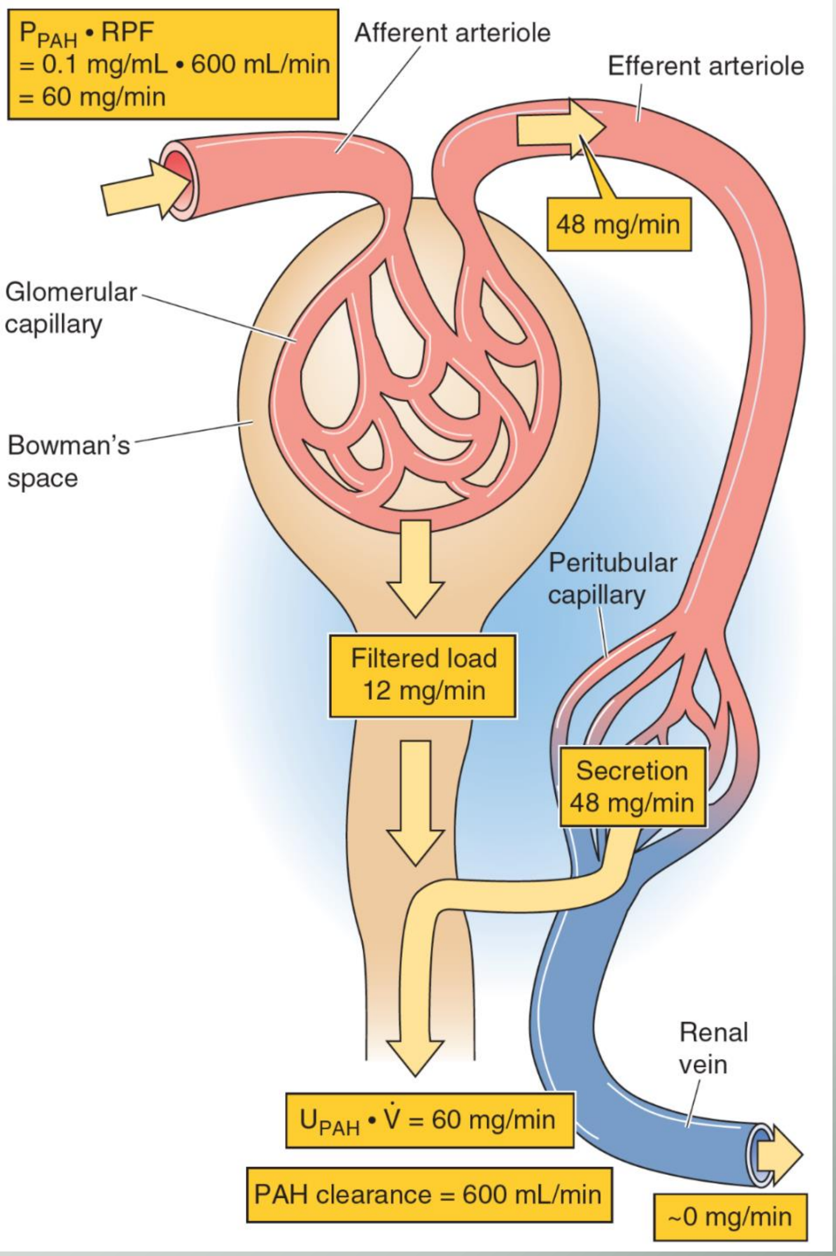
- **PAH**

Amount of PAH excreted = Amount filtered + amount secreted

- **100%** removed on passage through the kidney:

$$Cl_{PAH} = RPF = \frac{[U]_x \cdot \tilde{V}}{[P]_x}$$

RPF = RBF × (1-hematocrit)



A patient is infused with PAH to measure renal blood flow. She has a urine flow rate of **1 mL/min**, a plasma [PAH] of **1 mg/mL**, a urine [PAH] of **600 mg/mL**, and a hematocrit of **45%**. What is her RBF?

a) 555 mL/min
b) 600 mL/min
c) 660 mL/min
d) 1,091 mL/min
e) 1,333 mL/min

$$Cl_{PAH} = RPF = \frac{[U]_x \cdot \tilde{V}}{[P]_x} = \frac{600 \text{ mg/mL} \times 1 \text{ mL/min}}{1 \text{ mg/min}} = 600 \text{ mL/min}$$

$$RPF = RBF \times (1\text{-hematocrit})$$

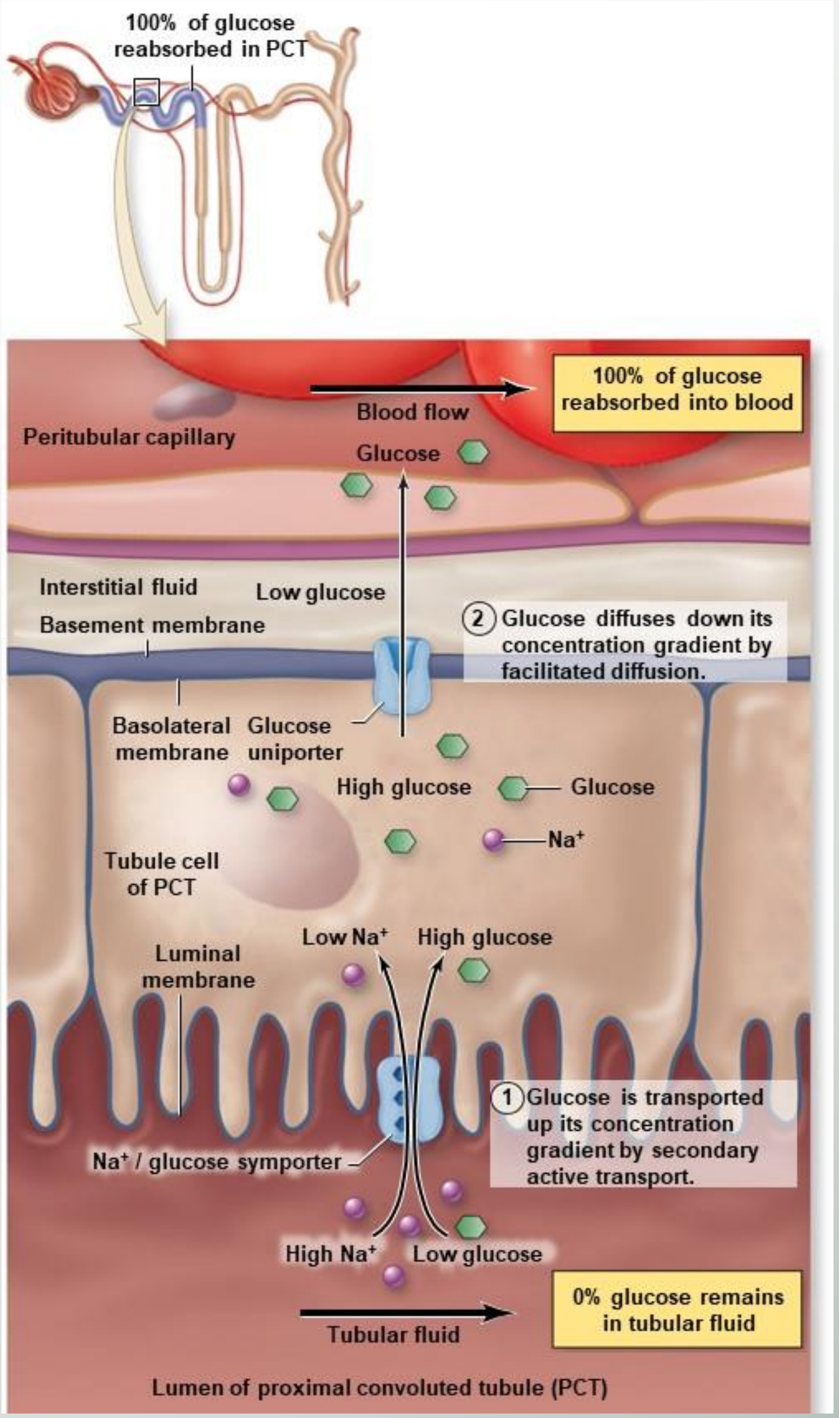
RBF = 600 / (1-0.45) = 1,091 mL/min

Glucose Reabsorption

- From tubular lumen to tubular cell: Sodium co-transporter (**Carrier-mediated secondary active transport**).
  - Uphill transport of glucose driven by electro-chemical gradient of sodium, which is maintained by Na-K pump presents in basolateral cell membrane.

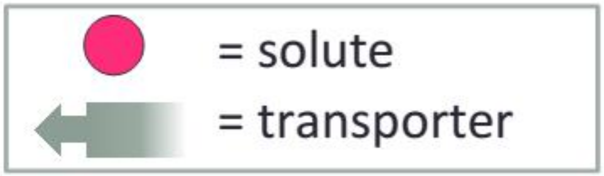
- From tubular cell to peritubular capillary: Facilitated diffusion (**Carrier-mediated passive transport**)

Glucose Reabsorption

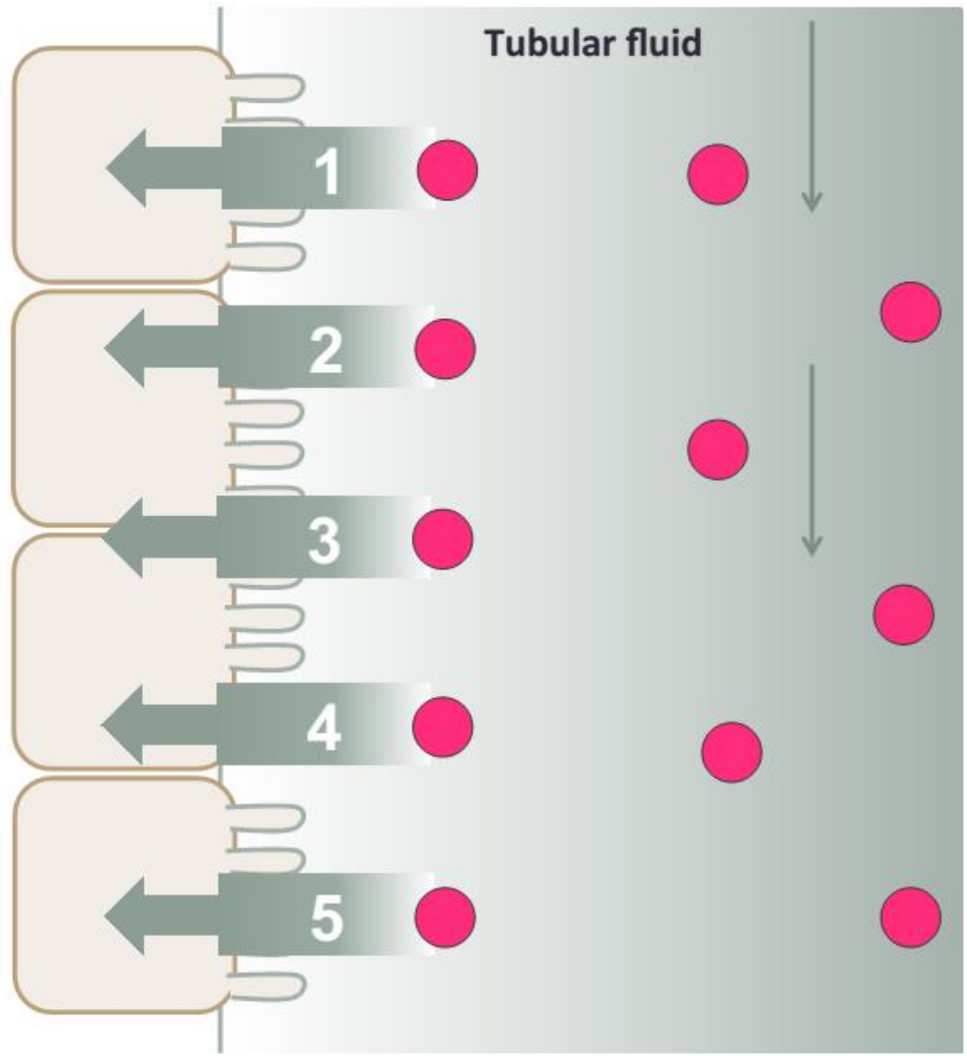


Tubular transport maximum

- It is the maximal amount of a substance (in mg) which can be transported (reabsorbed or secreted) by tubular cells/min.
- Many substances are reabsorbed by carrier mediated transport systems e.g. glucose, amino acids, organic acids…
- Carriers have a maximum transport capacity (**T_m**) which is due to **saturation** of the carriers. If T_m is exceeded, then the excess substrate enters the urine.
- Glucose is **freely filtered**, so whatever its [plasma] that will be filtered.

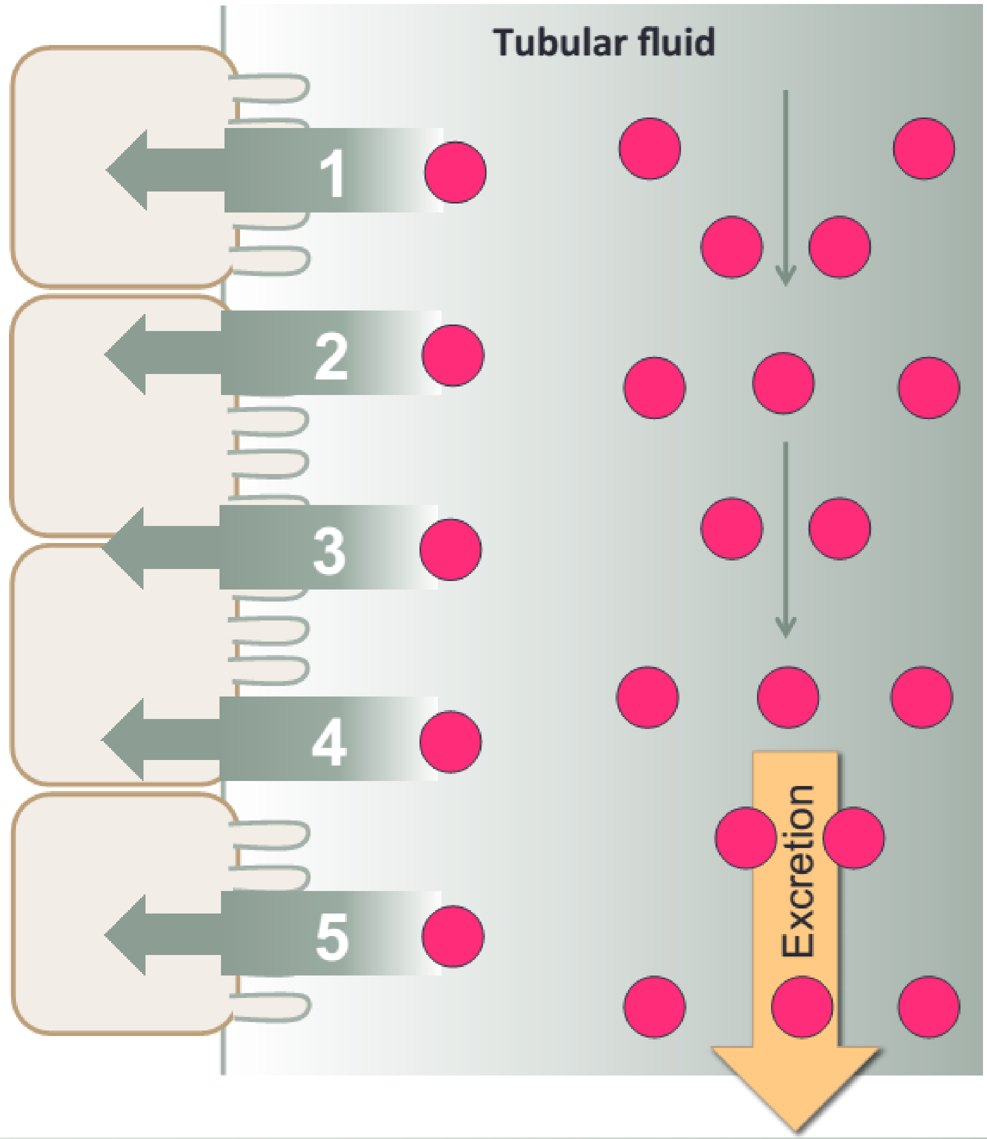


5 solute molecules/min



Transport maximum is reached when carriers are saturated.

= solute
= transporter



5 solute molecules/min

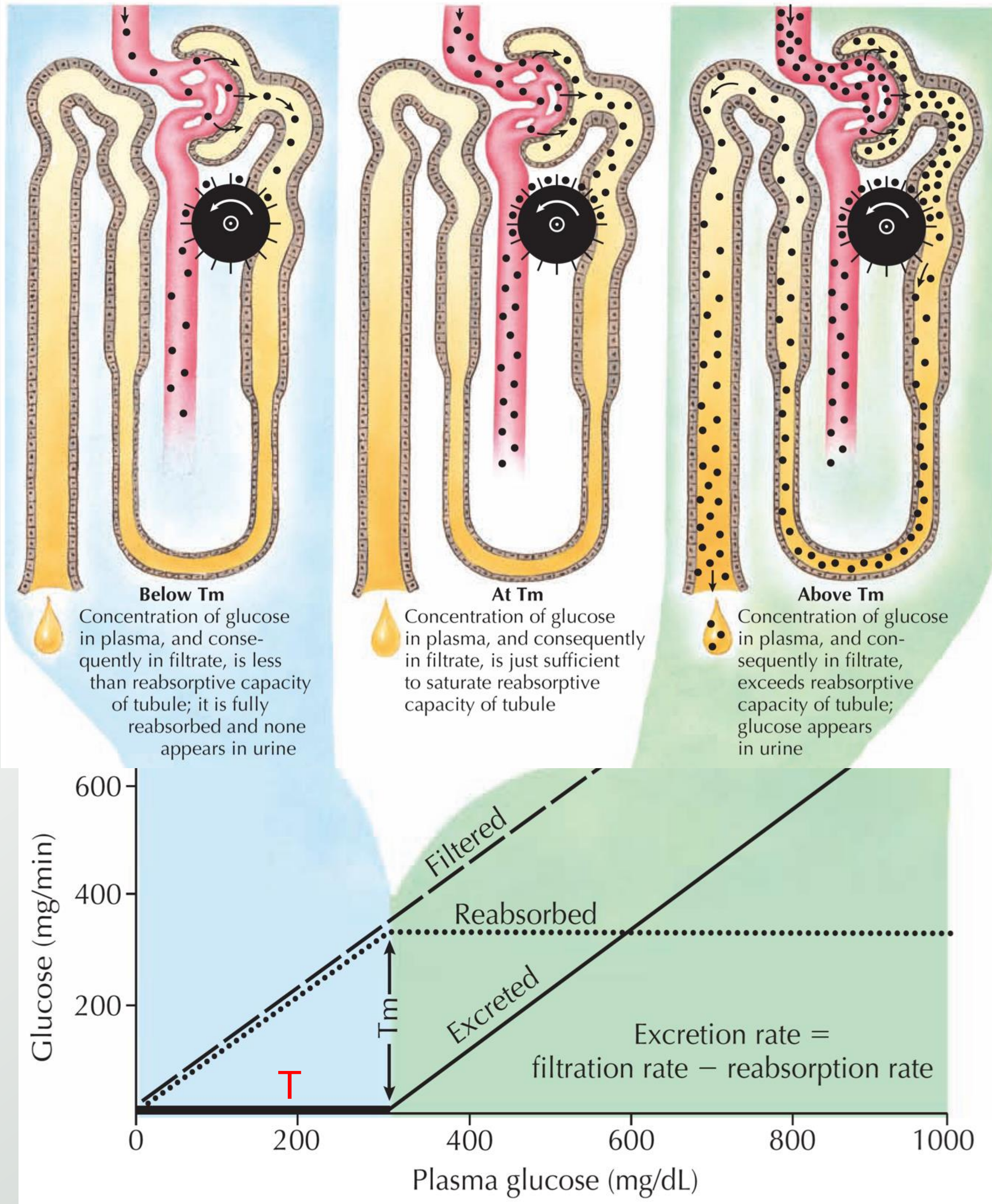
Saturation is reached,
Maximum speed, T_m

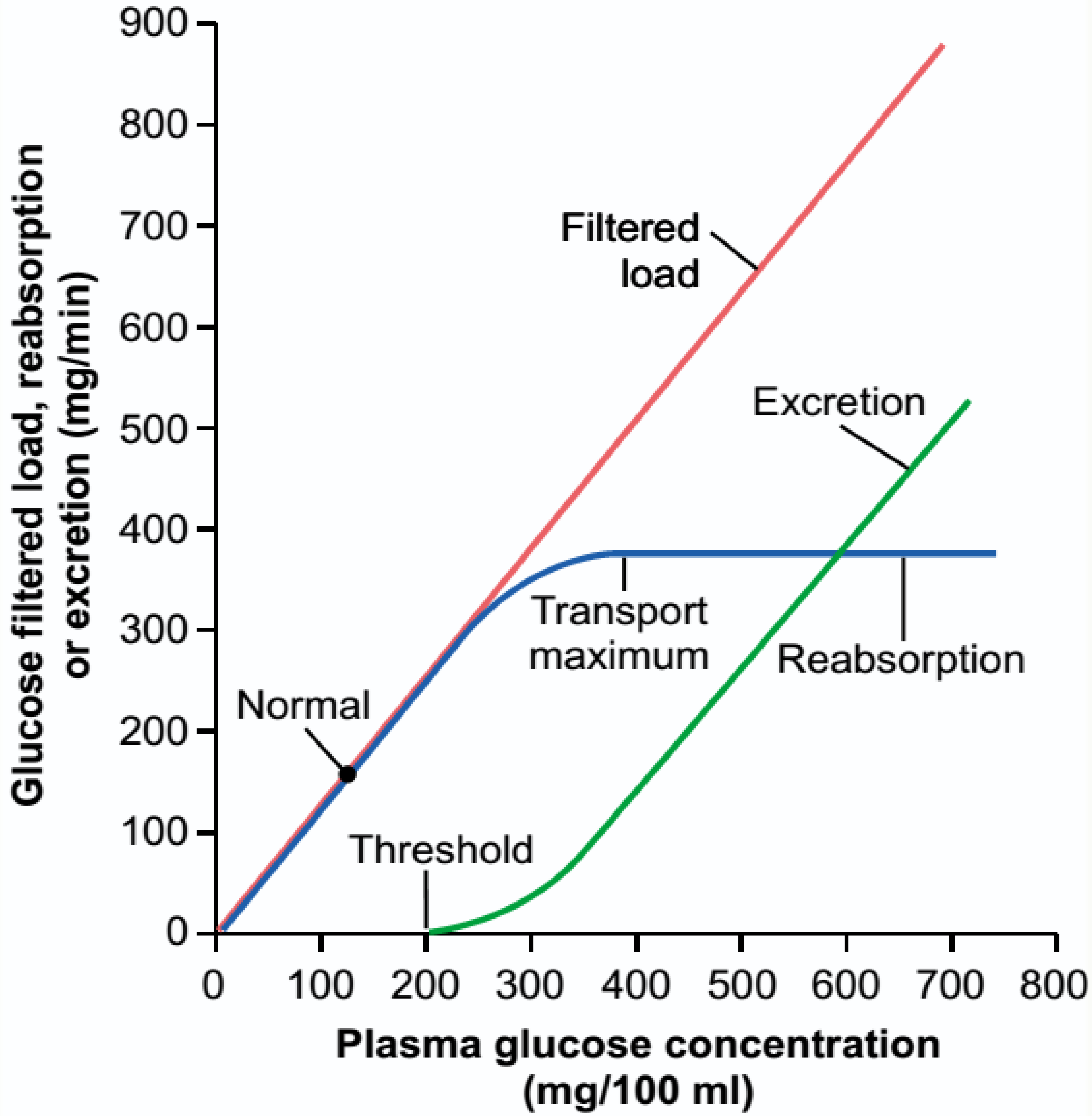
Tubular Transport Maximum

- The plasma concentration at which the Tmax of glucose is reached and the glucose is first appearing in the urine is called Renal Plasma Threshold of glucose.
- (If plasma [glucose] = 275 mg/dl, 275 mg/dl will be filtered, 180mg/dl reabsorbed and 95 mg/dl may be excreted.)
- Kidney does NOT regulate [glucose], (insulin and glucagon). Normal [glucose] of 90 mg/dl, so T_m is set way above any possible level of (non-diabetic) [glucose] at 375 mg/min. Thus, ensure that all this valuable nutrient is normally reabsorbed. The appearance of glucose in the urine of diabetic patients = glycosuria, is due to failure of insulin, NOT, the kidney.

Once T_m is reached for all nephrons, further ↑ in tubular load are not reabsorbed, but are then excreted.

Threshold (T) is the plasma conc. at which tubular load just exceeds T_m for reabsorption, where below threshold all solute molecules are reabsorbed, and above threshold, some solutes are not





Glucose filtered load, reabsorption or excretion (mg/min)
900
800
700
600
500
400
300
200
100
0
Filtered load
Excretion
Transport maximum
Reabsorption
Normal
Threshold
0
100
200
300
400
500
600
700
800
Plasma glucose concentration (mg/100 ml)

Thanks