Renal Physiology 3:
Renal Clearance

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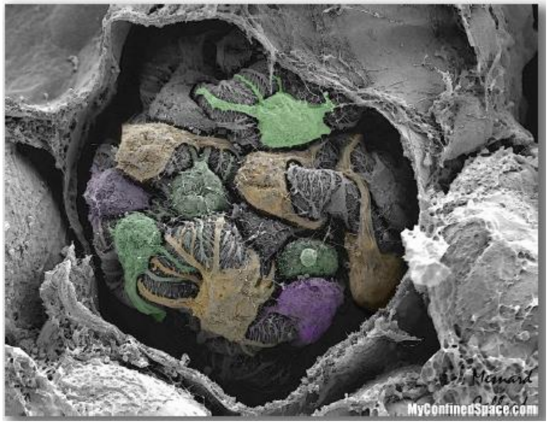
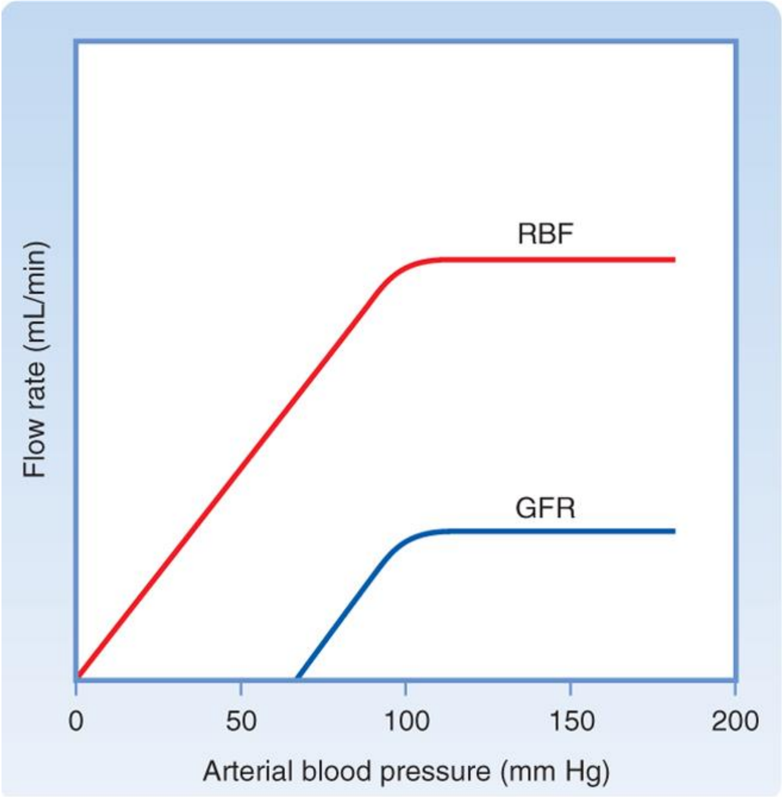


1) Myogenic mechanism

- normal response of vascular smooth muscle
- that is, increased stretch due to pressure rise depolarises the cells, calcium enters and causes a vasoconstriction
- well developed in the kidney

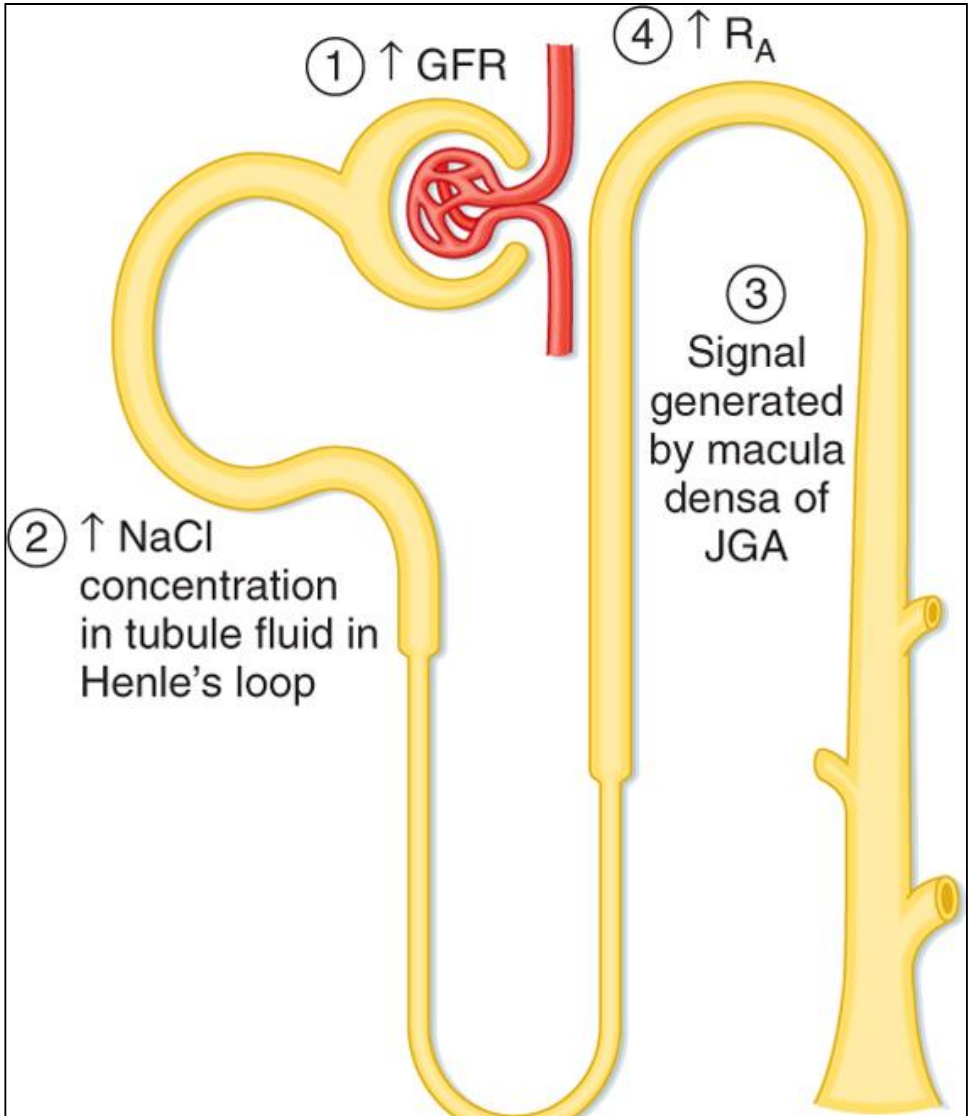


2) Tubuloglomerular feedback

- [NaCl] dependent mechanism
- macula densa cells in JGA detect [NaCl] send signals to afferent arteriole

- e.g. ↑ GFR = ↑ [NaCl] filtrate
- sensed by JGA ⇒ arteriole constricts
- (resistance ↑ ⇒ ↓ blood flow)

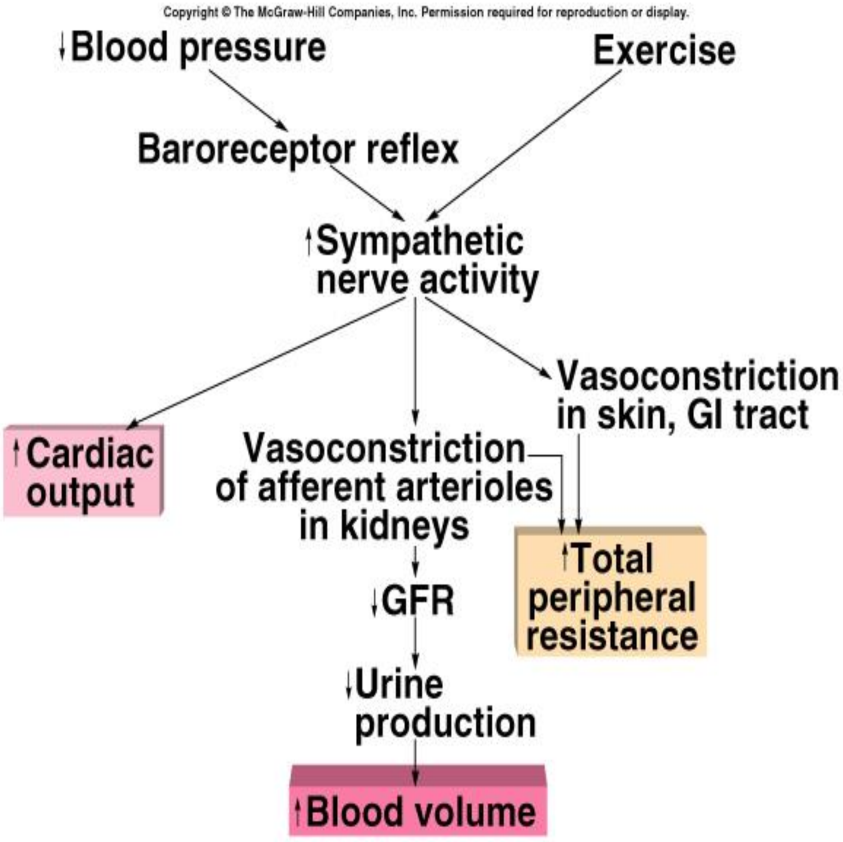
mediator unknown ?? Adenosine/Renin



(1) ↑ GFR
(4) ↑ R_A
(3) Signal generated by macula densa of JGA
(2) ↑ NaCl concentration in tubule fluid in Henle's loop

Sympathetic Regulation of GFR

- Stimulates vasoconstriction of afferent arterioles.
  - Preserves blood volume to muscles and heart.
- Cardiovascular shock:
  - Decreases glomerular capillary hydrostatic pressure.
  - Decreases urine output (UO).



Extrinsic Regulation

1) Neurogenic factors

- Sympathetic Nerve Fiber: is the major NF to kidney. Stimulation of sympathetic NF causes renal vasoconstriction and results in decrease of RBF and GFR.
- There are some parasympathetic NF to efferent arterioles, most predominantly to juxtamedullary nephrons and sphincters of vasa recta. Stimulation of parasympathtic NF causes renal vasodilation and results in increase in RBF and GFR.

Extrinsic Regulation

2) Humoral and pharmacological factors:

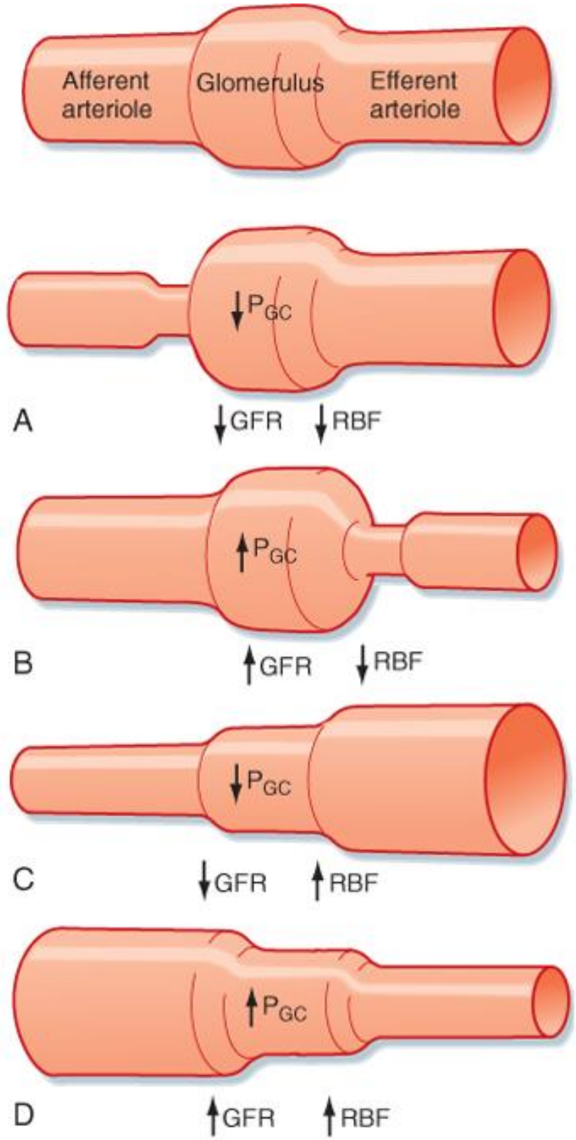
- Epinephrine, Nor-Epinephrine, Angiotensin II, Prostaglandin (F), and Thromboxane cause renal vasoconstriction and results in decrease in RBF and GFR.
- Acetylcholine, Bradykinin, Prostaglandin (D, E, and I), and bacterial pyogens cause renal vasodilation and results in increase in RBF and GFR.

Extrinsic Regulation

3) Physiological Stress: cold, deep anesthesia, fright, sever exercise, hypoxia and ischemia stimulate sympathetic NF leading to renal vasoconstriction and decrease in RBF.

4) Posture: RBF increase in supine than sitting than standing.

Changing the posture from lying to standing leads to a decrease of about 15% in RBF due to the stimulation of sympathetic NF.



Koeppen & Stanton: Berne and Levy Physiology, 6th Edition.

- **Normal**
- **Afferent arteriolar constriction**
- **Efferent arteriolar constriction**
- **Efferent arteriolar dilatation**
- **Afferent arteriolar dilatation**

Plasma Clearance

Definition:

- The clearance value of a certain substance ⇒ (means the vol. of plasma which is cleared from this substance by the kidney (in urine) /min.

Calculation:

- It is calculated by applying the formula U x V / P where:
  - (V) = Vol. of urine (ml) /min.
  - (U) = Conc. of the substance mg/ml urine.
  - (P) = Conc. of the substance mg/ml plasma.

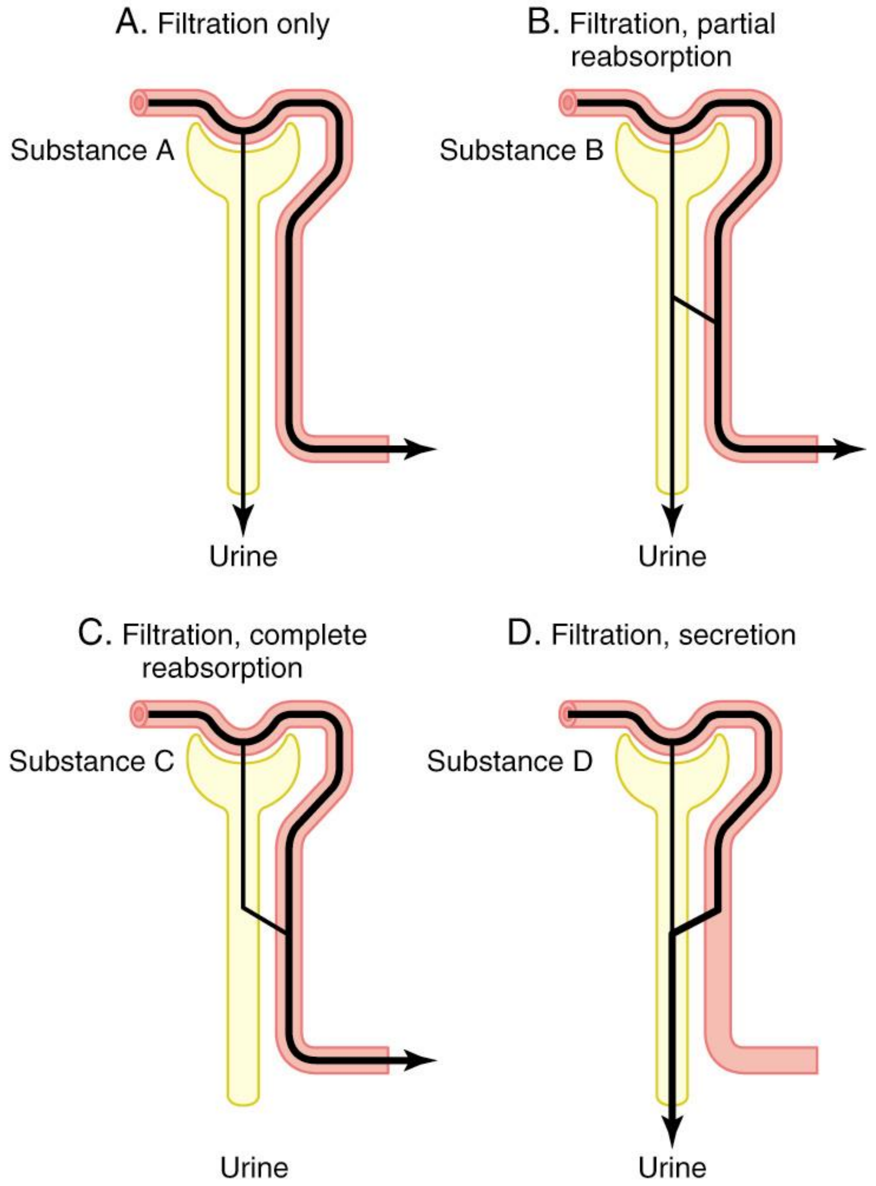
Plasma Clearance

Any exogenous substance used in plasma clearance tests should have the following properties:

- Stays in the plasma i.e. does not enter the RBC’s.
- Does not affect the renal functions.
- Not metabolized by the kidney.
- Easily measured in plasma & urine.
- Non toxic.

Renal Clearance

- If the substance is freely filtered at the glomeruli and is not reabsorbed, secreted or metabolized in the nephron, then
  - – amount filtered per minute = amount excreted per minute
  - - $[sub]_{plasma}$ x glomerular filtration rate = $[sub]_{urine}$ x urine flow rate


A. Filtration only
Substance A
Urine
B. Filtration, partial reabsorption
Substance B
Urine
C. Filtration, complete reabsorption
Substance C
Urine
D. Filtration, secretion
Substance D
Urine

Renal Clearance

Advantages:

- Plasma clearance tests can be used for:
  - Measurement of the glomerular filtration rate.
  - Measurement of the renal plasma flow rate (& from there we can calculate the renal blood flow rate).
  - Determining the renal handling of the different substances; whether or not the substance is reabsorbed or secreted by the renal tubules.

- Clearance measurements are also used to examine renal management of substances absorbed or secreted by the kidney.

For substances secreted by the kidney

- GFR.Ps + T = Us.V (T = amount transported)

What goes into the nephrons — What leaves the nephrons

- C = UV/P

Cs > Cin Secretion into nephrons is occurring

For substances absorbed by the nephrons

- $GFR.P_s$ = $T + U_s.V$ (T = amount transported)

What goes Into the nephrons — What leaves the nephrons

$GFR.P_s - U_s.V = T$

$C = UV/P$

$C_{subs} < C_{inulin}$ Absorption from nephrons is occurring

$U_s.V$ = normally zero for glucose & amino acids.

P.A.H.A

- Used to measure the RBF.

Properties of P.A.H.A:

1) When present below a certain conc. in the blood
   - They are completely removed by a single circulation through the kidney. This is because:
     - They are easily filtered.
     - They are secreted by renal tubules.
     - They are not reabsorbed after filtration.
2) Not enter RBC's or other tissue cells.
3) Not metabolized by tissues. 4) Not toxic.
5) Not adsorbed to the unfiltrated plasma proteins.

Renal Threshold

- Is the concentration of a substance dissolved in the blood above which the kidneys begin to remove it into the urine.
- After this level $\Rightarrow$ the filtered load exceeds the absorptive capacity of the tubules.
- Substances of high threshold: glucose, amino acids & vitamins.
- Substances of medium threshold: K^+ & urea.
- Substances of low threshold: phosphate & uric acid.
- Substances of no threshold: creatinine, mannitol & inulin.

Tubular transport maximum

- **Definition:**

  It is the maximal amount of a substance (in mg) which can be transported (reabsorbed or secreted) by tubular cells/min.

Notice:

•Appearance of glucose in urine before the transport maximum is reached is termed “Splay” and results from:

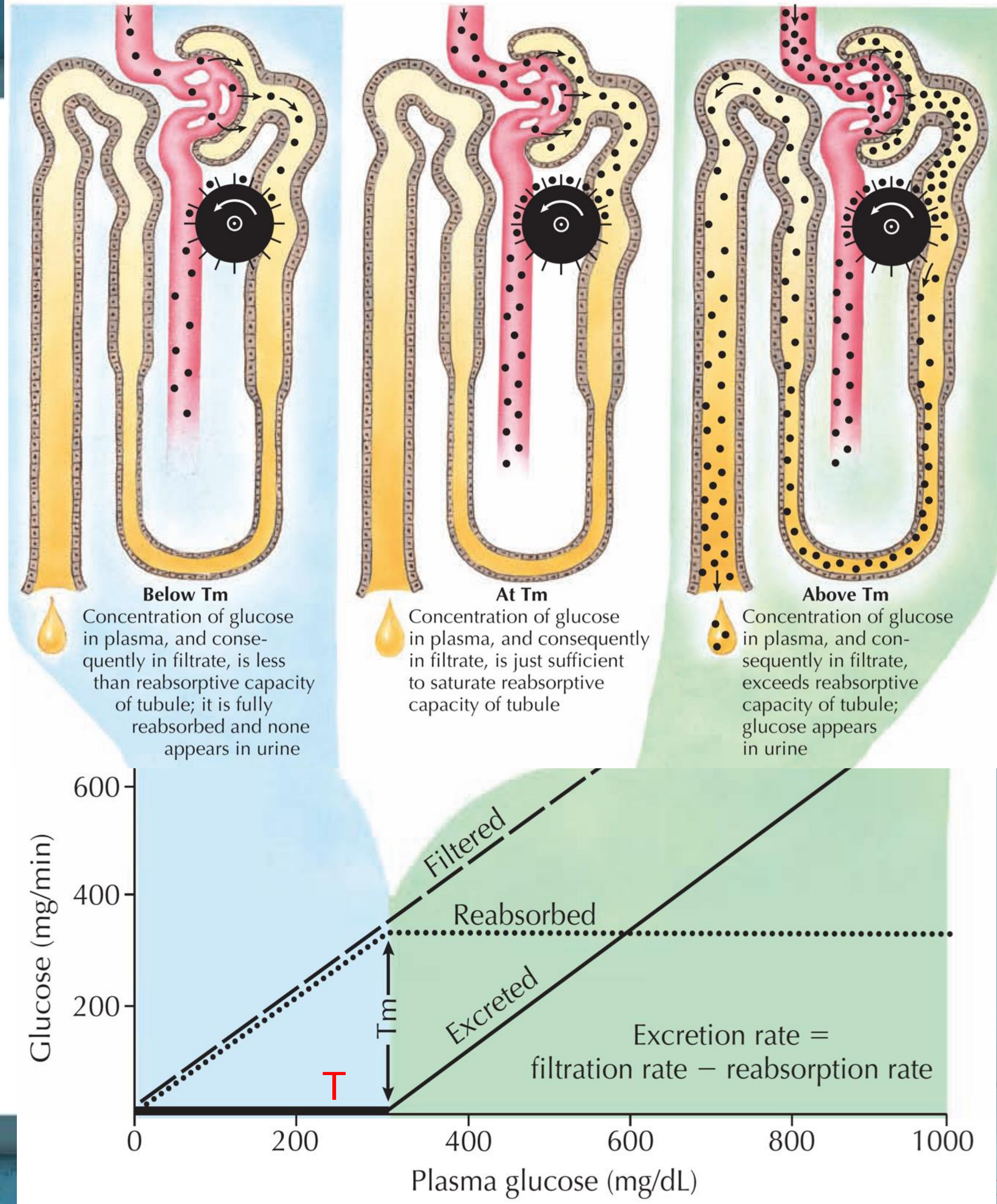
- Nephron variability: “in glomerular size & tubular length”.
- Variability in the number of glucose carriers & the transport rate of the carriers.

Tubular Transport Maximum

- Many substances are reabsorbed by carrier mediated transport systems e.g. glucose, amino acids, organic acids, sulphate and phosphate ions.
- 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.
- For amino acids, T_m also very high $\rightarrow$ no urinary excretion occurs.

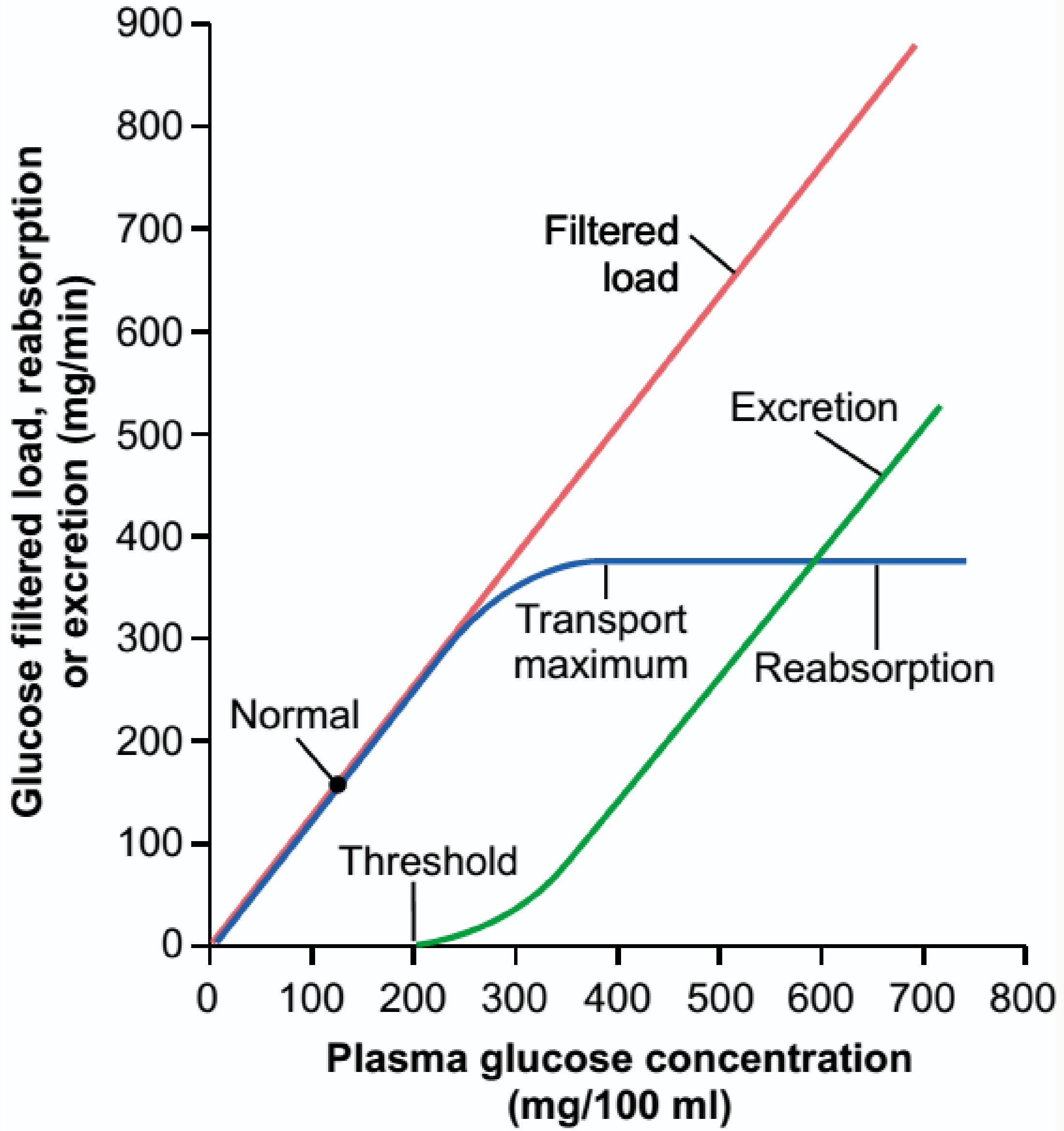
Once T_m is reached for all nephrons, further ↑ in tubular load are not reabsorbed, but are then excreted.

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



Tubular Transport Maximum

- In man for plasma glucose up to 180 mg/dl, all will be **reabsorbed**. Beyond this level of plasma [glucose], it appears in the urine = Renal plasma threshold for glucose.
- (If plasma [glucose] = 275 mg/dl, 275 mg/dl will be filtered, 180mg/dl reabsorbed and 95 mg/dl 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 380 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.



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)