Renal Clearance

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Concept of clearance

Clearance is the volume of plasma that is completely cleared of a substance each minute.

Example:

Renal clearance of Substance X is defined as the ratio of excretion rate of substance X to its concentration in the plasma:

$$C_X = (U_X \times V) / P_X$$

Clearance Equation

- $C_X = (U_X \times V) / P_X$
- C_X = Renal clearance (ml/min)
- $U_X \times V$ = excretion rate of substance X
- U_X = Concentration of X in urine
- V = urine flow rate in ml/min

Amount of substance excreted = (filtered – reabsorbed + secreted)

$U_x V = GFR \times P_x \pm T_x$

What is the importance of renal clearance?

To quantify several aspects of renal functions:

- rate of glomerular filtration
- Rate of blood flow
- Assess severity of renal damage
- Tubular reabsorption.
- Tubular secretion of different substances.

Clearance tests

Types of Clearance tests	
Endogenous	**Exogenous**
Creatinine	Inulin
Urea	Para-amino hippuric acid (PAHA)
Uric acid	Diodrast (di-iodo pyridone acetic acid)

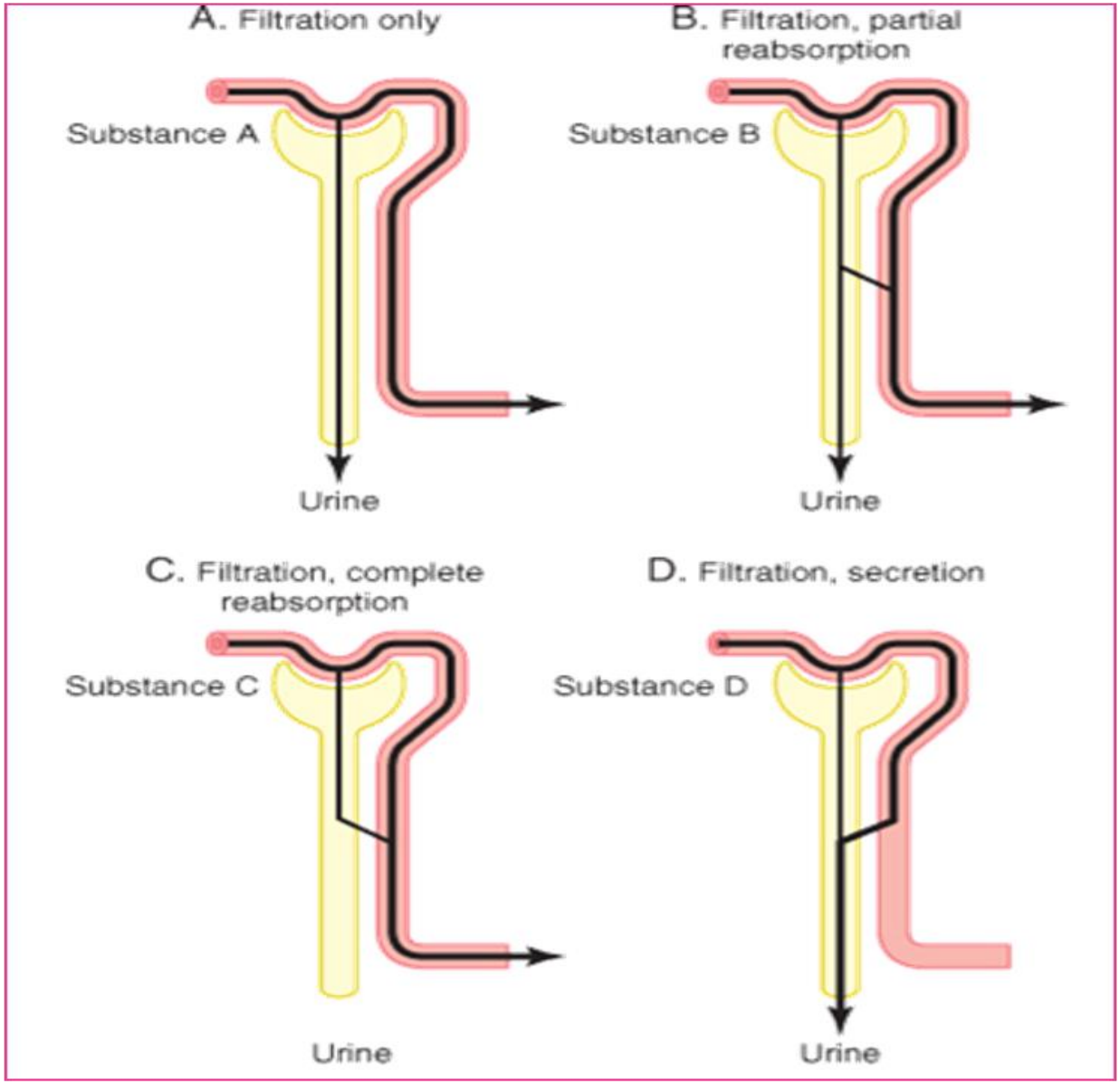
- Calculation: $\frac{U \times V}{P}$

Where:

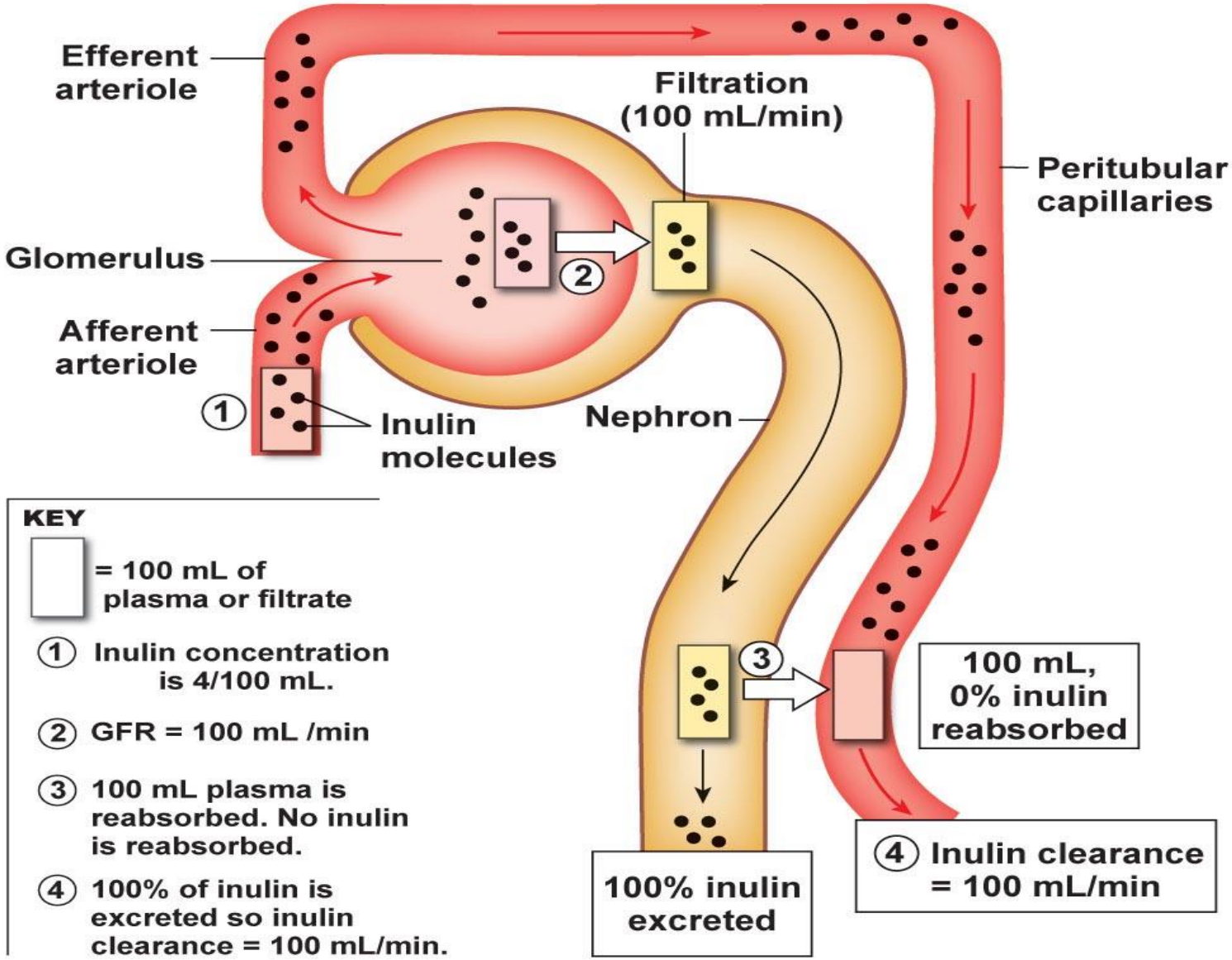
U = concentration of substance in urine (mg/dl)

V = volume of urine excreted per minute (ml/min)

P = concentration of substance in plasma/serum (mg/dl)


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

Nephron Excretion & Clearance

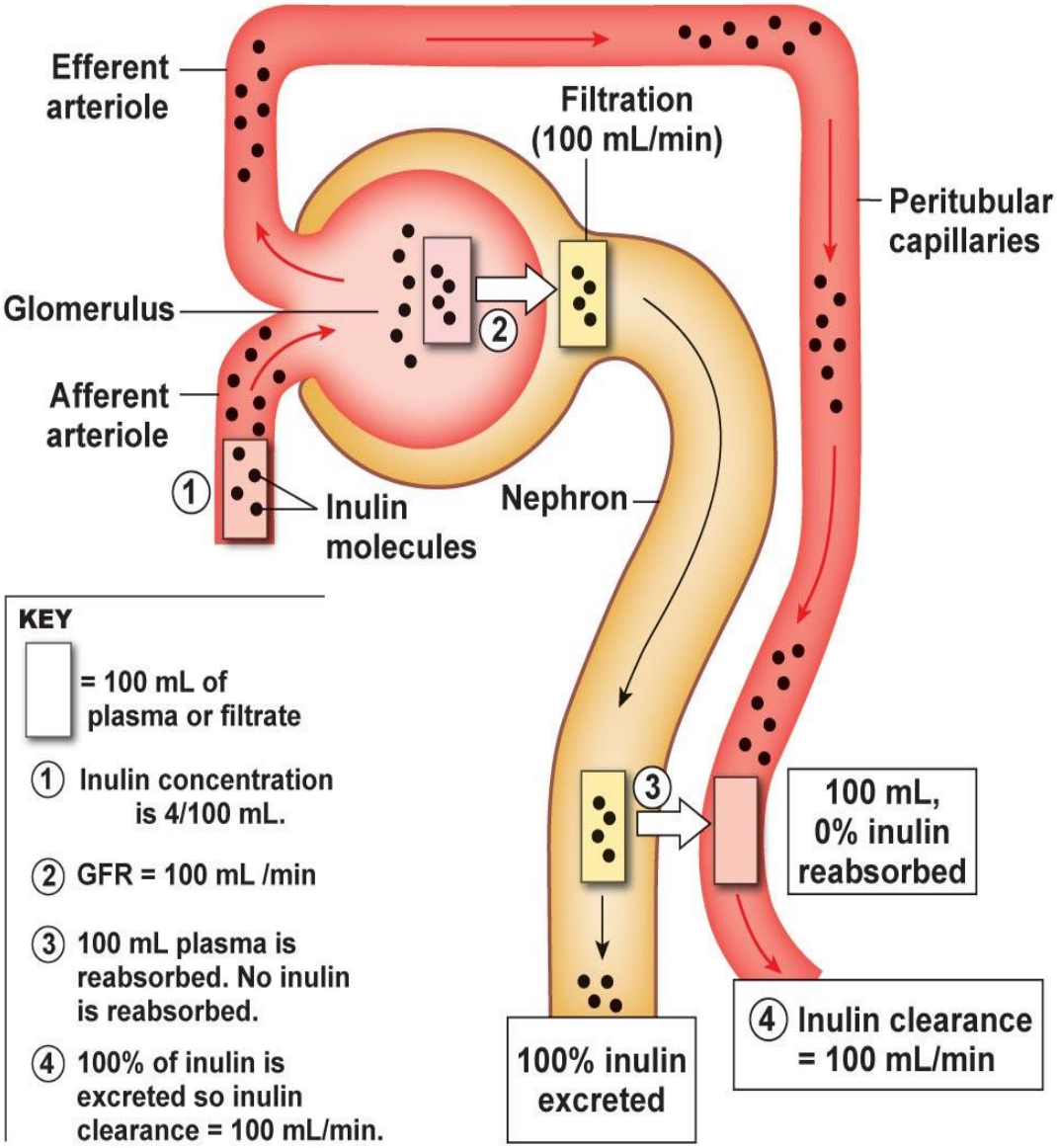


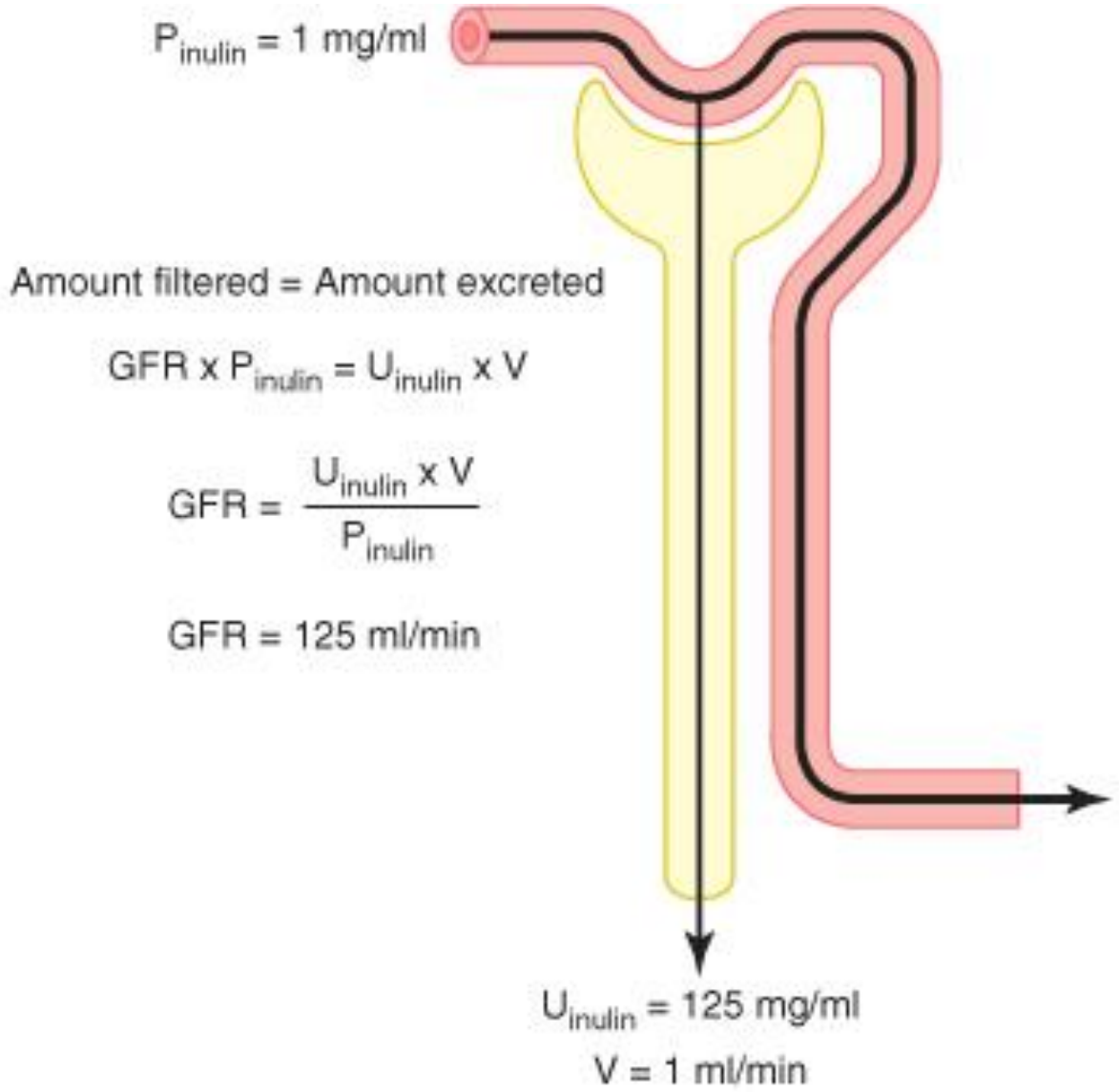
Nephron Excretion & Clearance

Inulin

A plant product that is filtered but not reabsorbed or secreted

Used to determine GFR and therefore nephron function





Example

- if Plasma conc. of inulin = 1mg/100ml
- Urinary conc of Inulin = 120 mg /100ml
- Urine flow (UV) = 1 ml /min then, the clearance of inulin will be?
- C = 120 ml/min

Criteria of a substance used for GFR measurement:

a)freely filtered

b)not secreted by the tubular cells,

c)not reabsorbed by the tubular cells.

d)should not be toxic

e)should not be metabolized

f)easily measurable.

examples of such a substance:

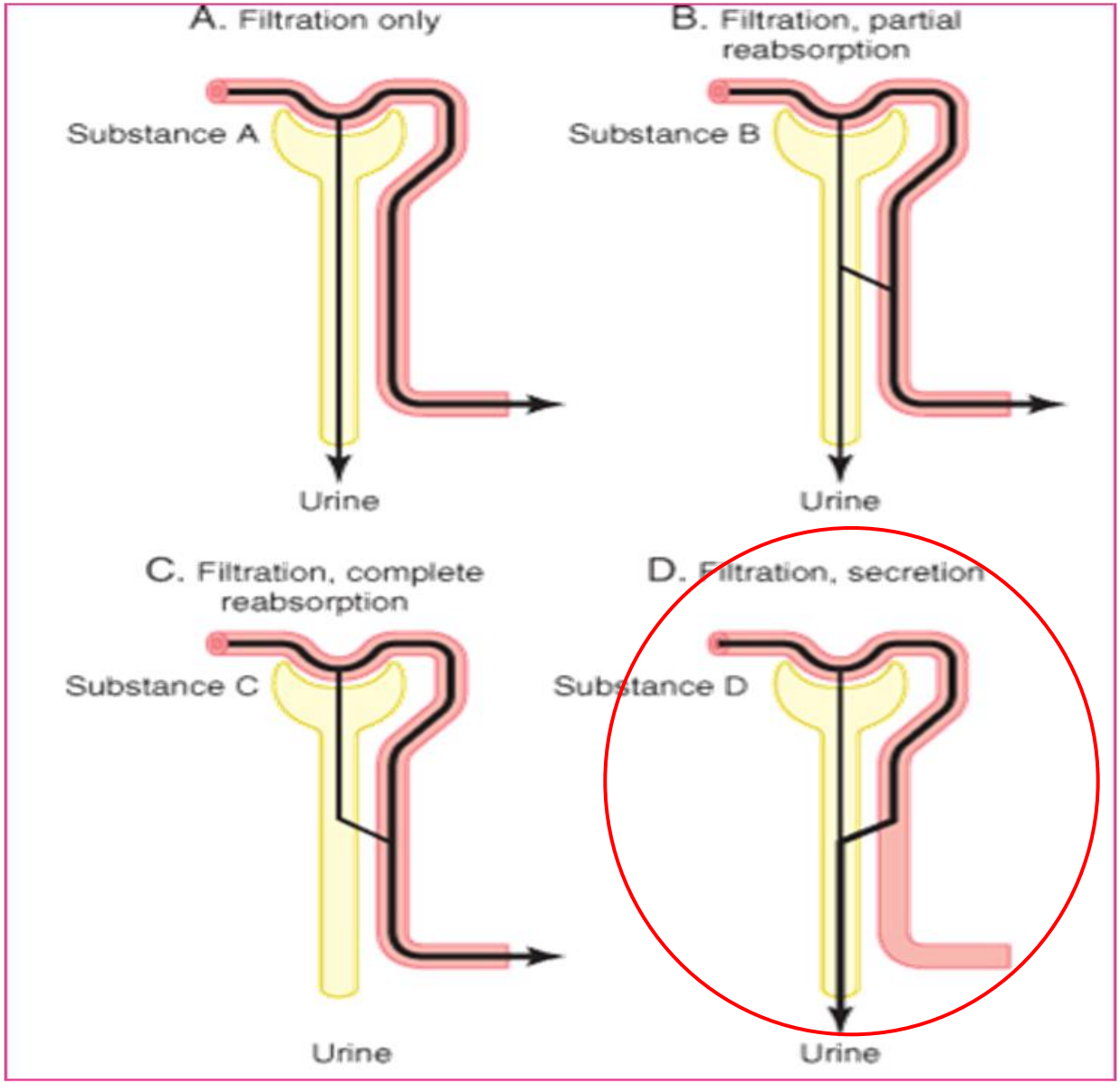
- **Creatinine (endogenous):**

  by-product of skeletal muscle metabolism

Criteria of a substance used for GFR measurement, cont……

Inulin (exogenous):

It is a polysaccharide with a molecular weight of about 5200 and it fits all the above requirements.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Measurement of renal blood flow

Substances used for measurement of GFR are not suitable for the measurement of Renal Blood Flow. Why?

Inulin clearance only reflects the volume of plasma that is filtered and not that remains unfiltered and yet passes through the kidney.

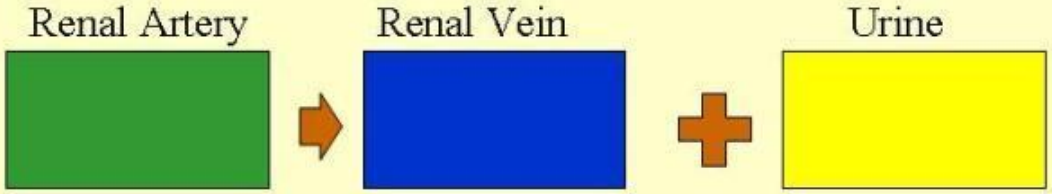
It is known that only 1/5 of the plasma that enters the kidneys gets filtered.
Therefore, other substances to be used with special criteria.

To measure renal blood flow we will have to measure renal plasma flow first and then from the hematocrit we calculate the actual blood flow

Measuring Renal Plasma Flow

- If a substance is not only freely filtered, but also secreted such that all substance reaching the kidney is cleared, then:

$$C_x = RPF$$



- Clearance equals

- Para-amino hippuric acid (PAH) is such a molecule whose clearance equals RPF

Use of PAH Clearance to Estimate Renal Plasma Flow

Paraminohippuric acid (PAH) is freely filtered and secret
and is almost completely cleared from the renal plasma

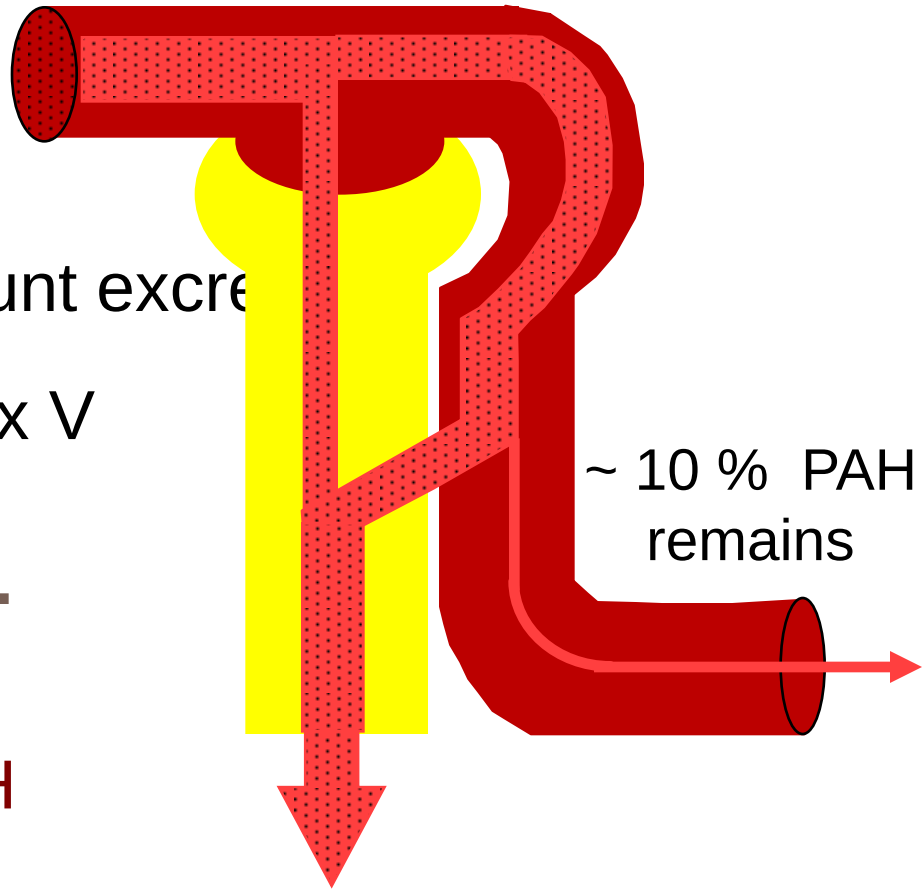
1. amount enter kidney =
   RPF x P_{PAH}

2. amount entered = amount excre

3. ERPF x P_{pah} = U_{PAH} x V

$$ERPF = \frac{U_{PAH} \times V}{P_{PAH}}$$

ERPF = Clearance PAH



Measurement of renal plasma flow:

For the measurement of renal plasma flow, we will again need a substance that is

a)freely filtered

b)rapidly and completely secreted by the renal tubular cells

c)not reabsorbed

d)not toxic

e)and easily measurable

Example of such substance:

Para-aminohippuric acid (PAH)

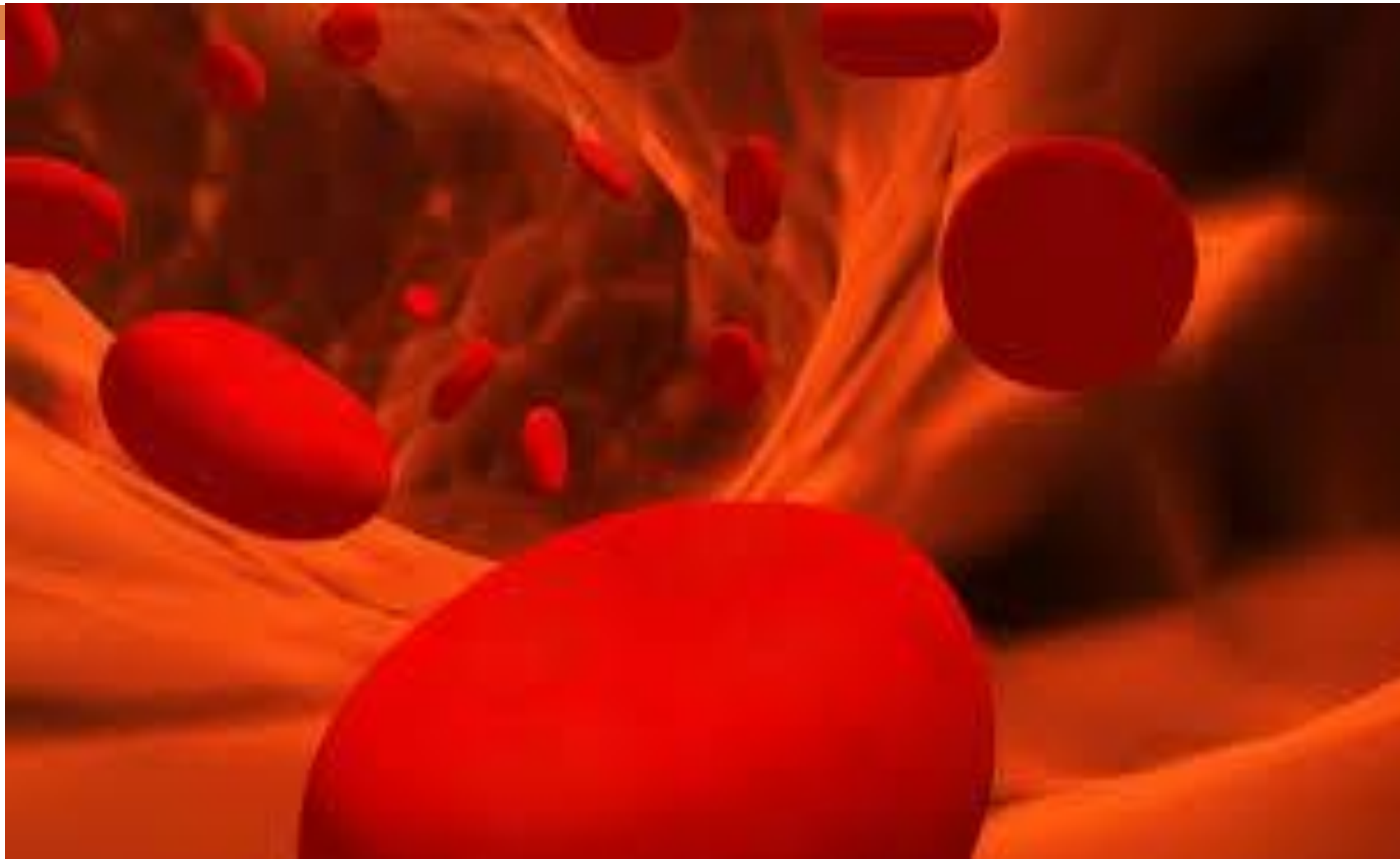
90% of plasma flowing through the kidney is completely cleared of PAH.

PAH clearance: example

- If the concentration of PAH in the urine and plasma and the urine flow are as follows:
- Conc. of PAH in urine=25.2 mg/ml
- Urine flow=1.1 ml/min
- Conc of PAH in arterial blood=0.05 mg/ml
- Then CPAH or Renal Plasma Flow=

$$(25.2 \times 1.1)/0.05 = 560 \text{ ML/ min}$$

How to measure renal bl flow?



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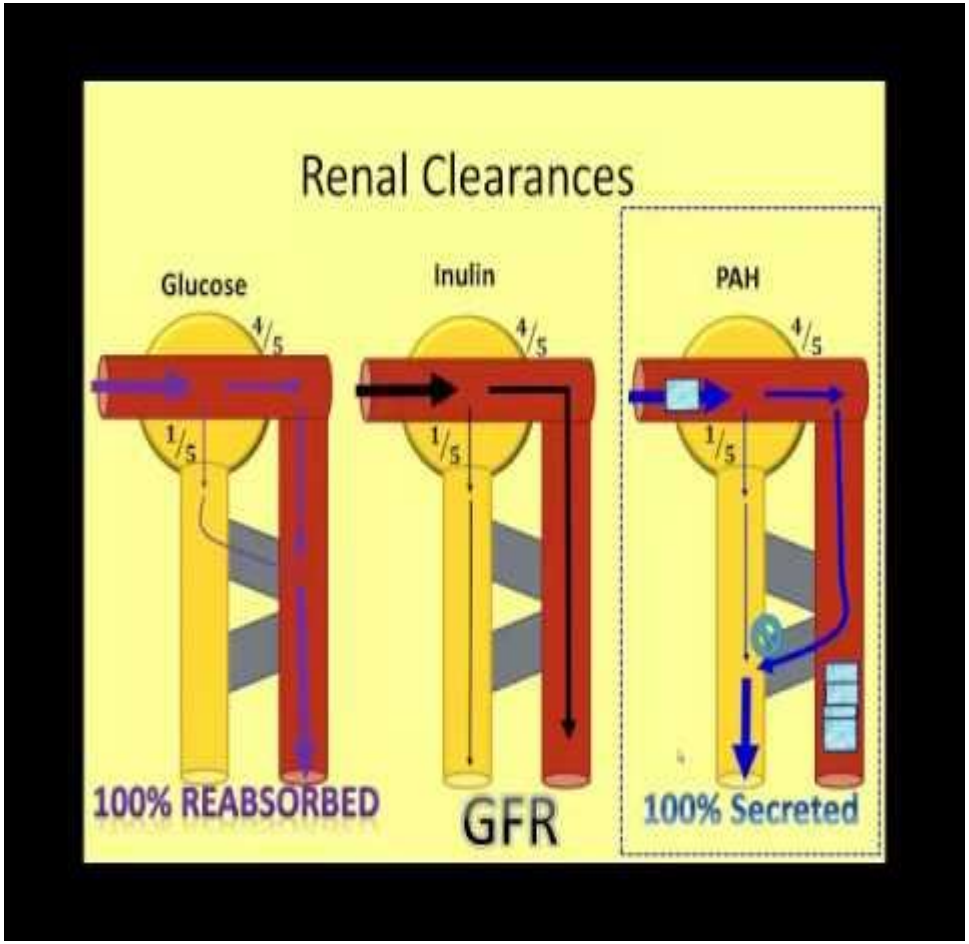
- Lets say the hematocrit is 45%, then renal blood flow will be:

$$(560 \times 100)/(100\text{-}45) = 1018 \text{ ml/min}$$

Renal Clearance gives an indication of the functioning of the kidneys.

- Clearance can also be used to determine renal handling of a substance.
- Clearance values can also be used to determine how the nephron handles a substance filtered into it. In this method the clearance for inulin or creatinine is calculated and then compared with the clearance of the substance being investigated.


Renal Clearances
Glucose
Inulin
PAH
4/5
1/5
100% REABSORBED
GFR
100% Secreted

Comparison of clearance of a substance with clearance of inulin

1) = inulin clearance; only filtered not reabsorbed or secreted

2) < inulin clearance; reabsorbed by nephron tubules

3) > inulin clearance; secreted by nephron tubules

Calculation of tubular reabsorption or secretion from renal clearance

Substances that are completely reabsorbed from the tubules (amino acids, glucose), clearance = zero because the urinary secretion is zero.

Substances highly reabsorbed (Na), its clearance < 1% of the GFR.

Reabsorption rate can be calculated=

Filtration rate- excretion rate

= (GFR X P*)-(U* X V)

* The substance needed to be assessed.

Calculation of tubular reabsorption or secretion from renal clearance, cont…….

- If excretion rate of a substance is greater than the filtered load, then the rate at which it appears in the urine represents the sum of the rate of glomerular filtration + tubular secretion:
- Secretion* = (U* X V)- (GFR X P*).
- * indicate the substance

Filtration fraction

It is the ratio of GFR to renal plasma flow

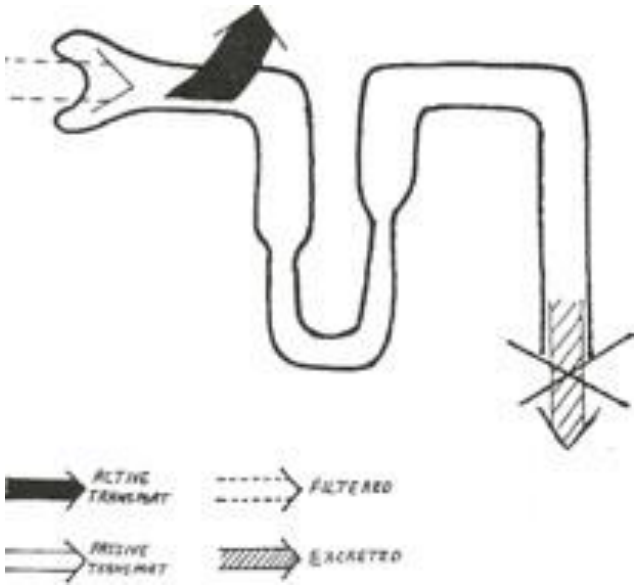
TRANSPORT MAXIMUM

How Many Guys Can Fit In The Back Of A Pick-Up?

Glucose clearance

GLUCOSE CLEARANCE

The glucose clearance is zero at plasma glucose values below the threshold and gradually rises as plasma glucose rises. We can express the excretion of glucose quantitatively at plasma concentrations beyond the threshold, where the glucose reabsorption rate (T_m) has reached its maximum:



TUBULAR TRANSPORT MAXIMUM

- The Maximum limit/rate at which a solute can be transported across the tubular cells of kidneys is called **TUBULAR TRANSPORT MAXIMUM**

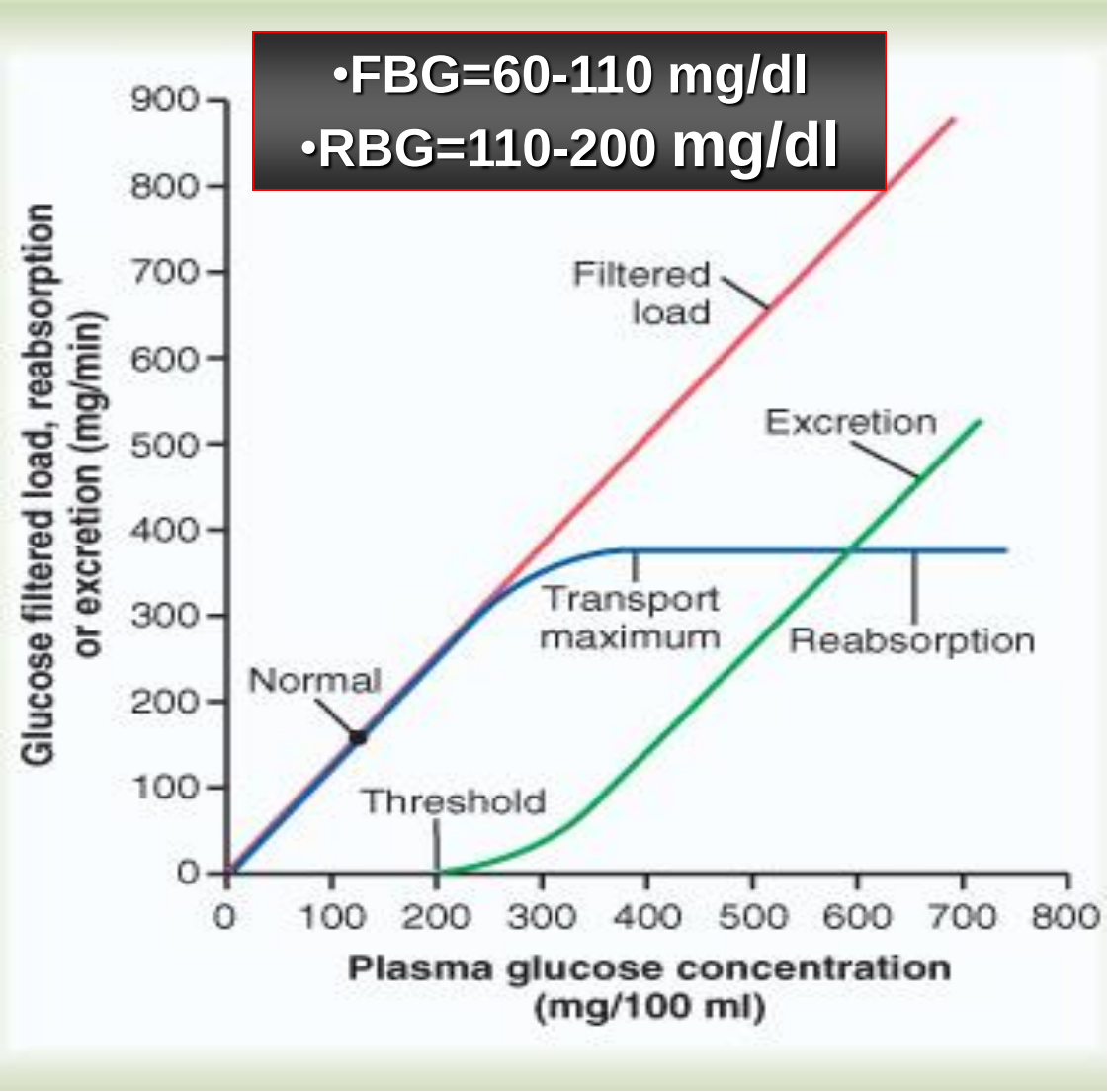
Tm for Glucose is 375 mg/min

GLUCOSE REABSORPTION

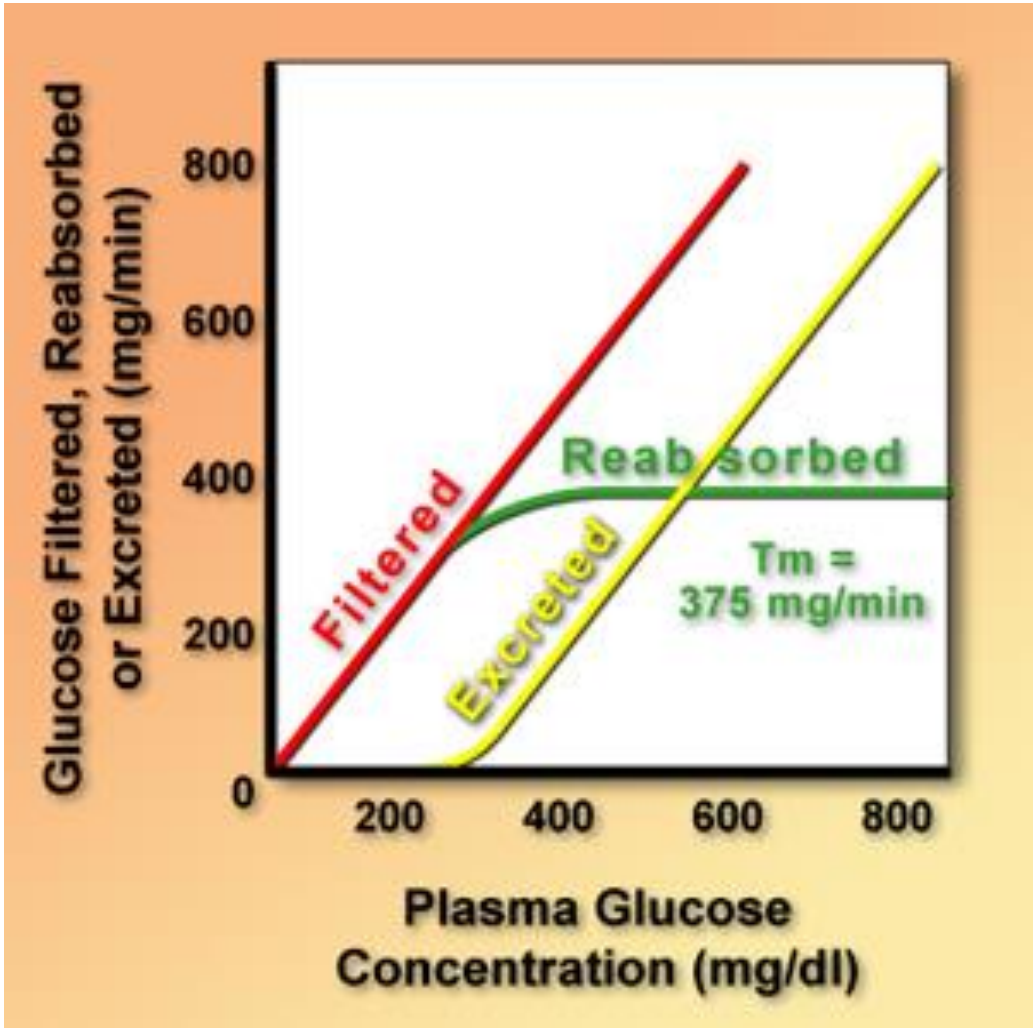
Transport max
375 mg/min

Renal Threshold
200mg/dl

However, when the plasma concentration of glucose rises above about 200 mg/100 ml, increasing the filtered load to about 250 mg/min, a small amount of glucose begins to appear in the urine. This point is termed the *threshold* for glucose. *Note that this appearance of glucose in the urine (at the threshold) occurs before the transport maximum is reached*. One reason for the difference between threshold and transport maximum is that not all nephrons have the same transport maximum for glucose, and some of the nephrons excrete glucose before others have reached their transport maximum. *The overall transport maximum for the kidneys, which is normally about 375 mg/min, is reached when all nephrons have reached their maximal capacity to reabsorb glucose.*



Tubular transport maximum for glucose



Tubular transport maximum for glucose , cont…..

- Filtered Load
  - filtered load = GFR x $[P]_{glucose}$
- Reabsorption
  - plasma [glucose] <200 mg/dL
    - filtered load of glucose is completely reabsorbed
  - 200mg/dL < plasma [glucose]
    - filtered load of glucose is not completely reabsorbed
    - "threshold," or plasma [glucose] at which glucose is first excreted in urine
  - plasma [glucose] > 350 mg/dL
    - filtered load of glucose is not completely reabsorbed
    - Na^+ - glucose (SGLT) cotransporters are completely saturated
    - maximal glucose reabsorption (T_m)

Have a nice weekend