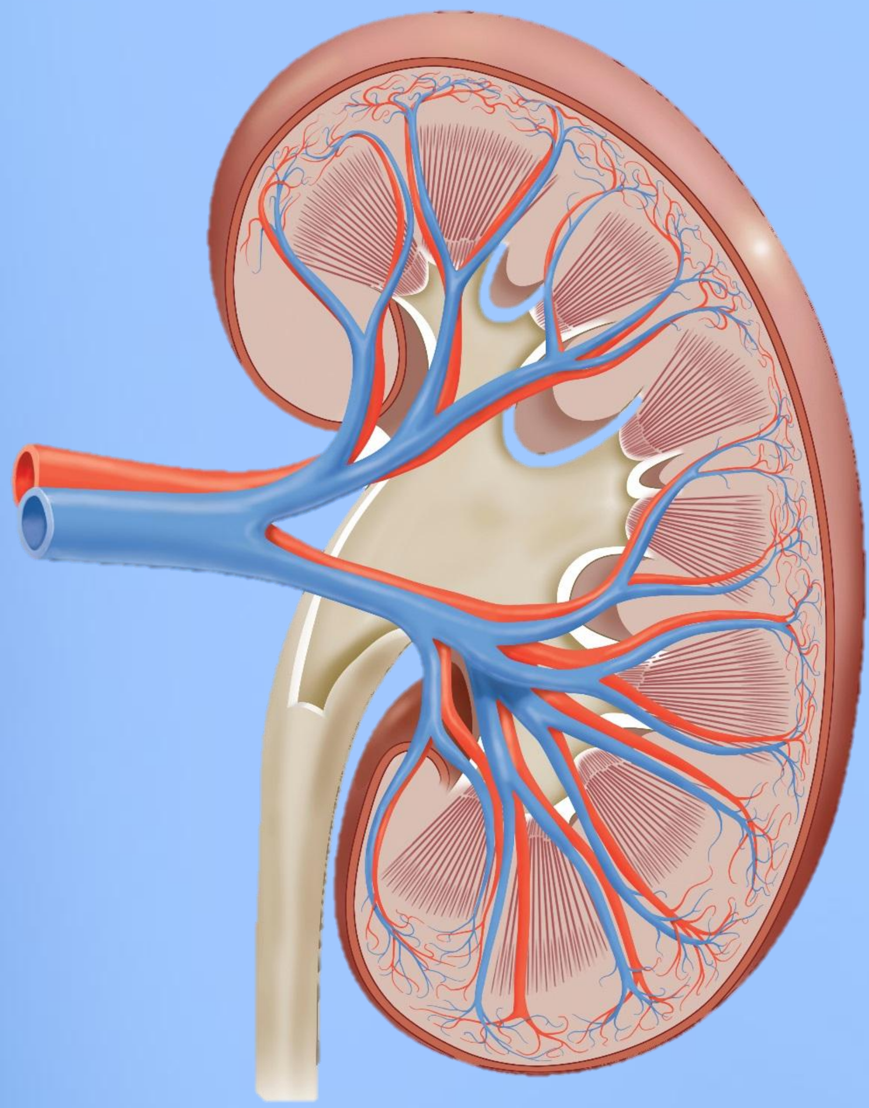
3

RENAL CLEARANCE



Renal Block

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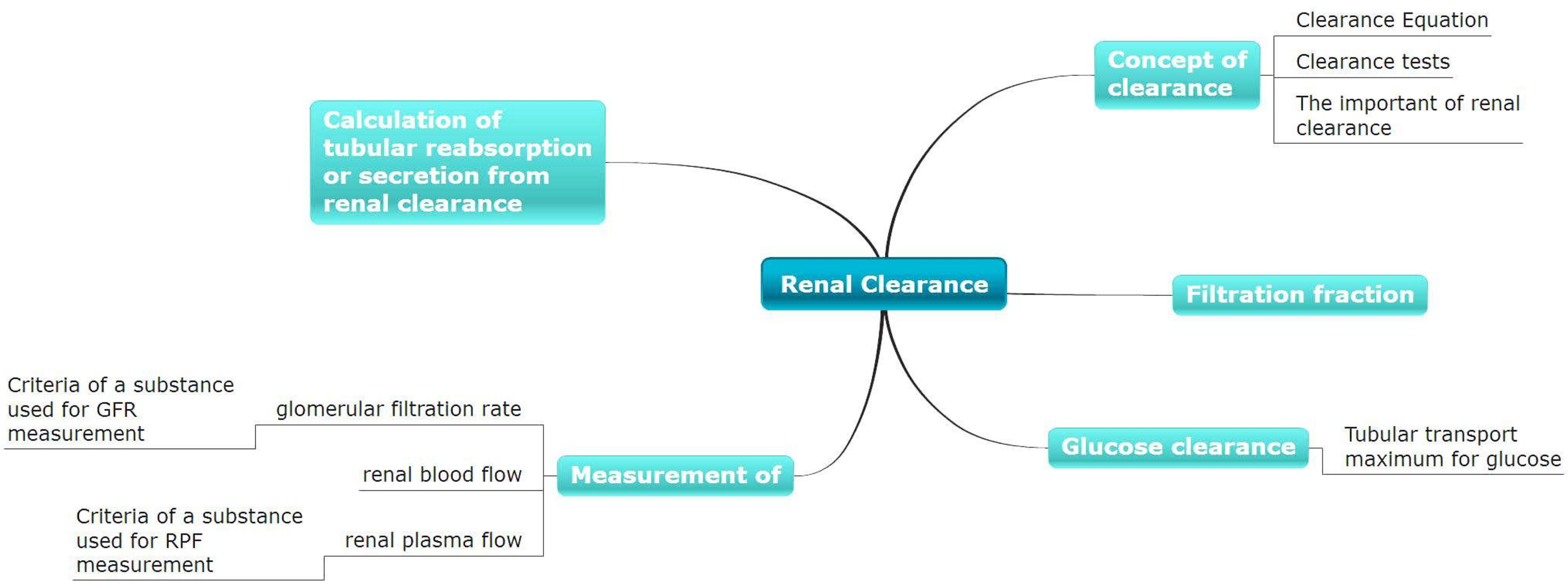
OBJECTIVES:

At the end of this session, the students should be able to:

- ✓ 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

Mind map



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Concept of clearance

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

The important of renal clearance

- rate of glomerular filtration
- Assess severity of renal damage
- Tubular secretion&reabsorption of different substances.

Clearance Equation

$$C_X = (U_X \, X \, V) / P_X$$

where

C_X = Renal clearance (ml/min)

U_X X V = excretion rate of substance X

U_X = Concentration of X in urine

V = urine flow rate in ml/min

Px= concentration of substance X in the plasma

Clearance tests

endogenous		
creatinine	Urea	Uric acid

exogenous		
Inulin	Para amino hippuric acid	Diodrast (di-iodo pyridone acetic acid)

Measurement of glomerular filtration rate (GFR)

GFR is measured by the clearance of a glomerular maker like **Creatinine & Inulin .**

Measurement of renal plasma flow (RPF)

RPF can be estimated from the clearance of an organic acid **Para-aminohippuric acid (PAH)**

Measurement of renal blood flow (RBF)

RBF is calculated from the **RPF** and **hematocrit**

The formula used to calculate GFR or RPF is

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

X could be PAH , creatinine and inulin

The formula used to calculate RBF is

RBF= RPF \ 1-Hct

Or

RBF=RPF% \ 100-Hct

Hematocrit is the fraction of blood volume that is **occupied by red blood cells** and 1-Hct or 100-Hct is the fraction of blood volume that is **occupied only by plasma**

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Criteria of a substance used for GFR measurement

1.freely filtered

2.not secreted by the tubular cells

3.not reabsorbed by the tubular cells.

4.should not be toxic

5.should not be metabolized

6.easily measurable.

Criteria of a substance used for renal plasma flow measurement

1.freely filtered

2.rapidly and completely secreted by the renal tubular cells

3.not reabsorbed

4.not toxic

5.and easily measurable

Examples of a substance used for GFR measurement

1. Creatinine (endogenous):

by-product of skeletal muscle metabolism

2. Inulin (exogenous):

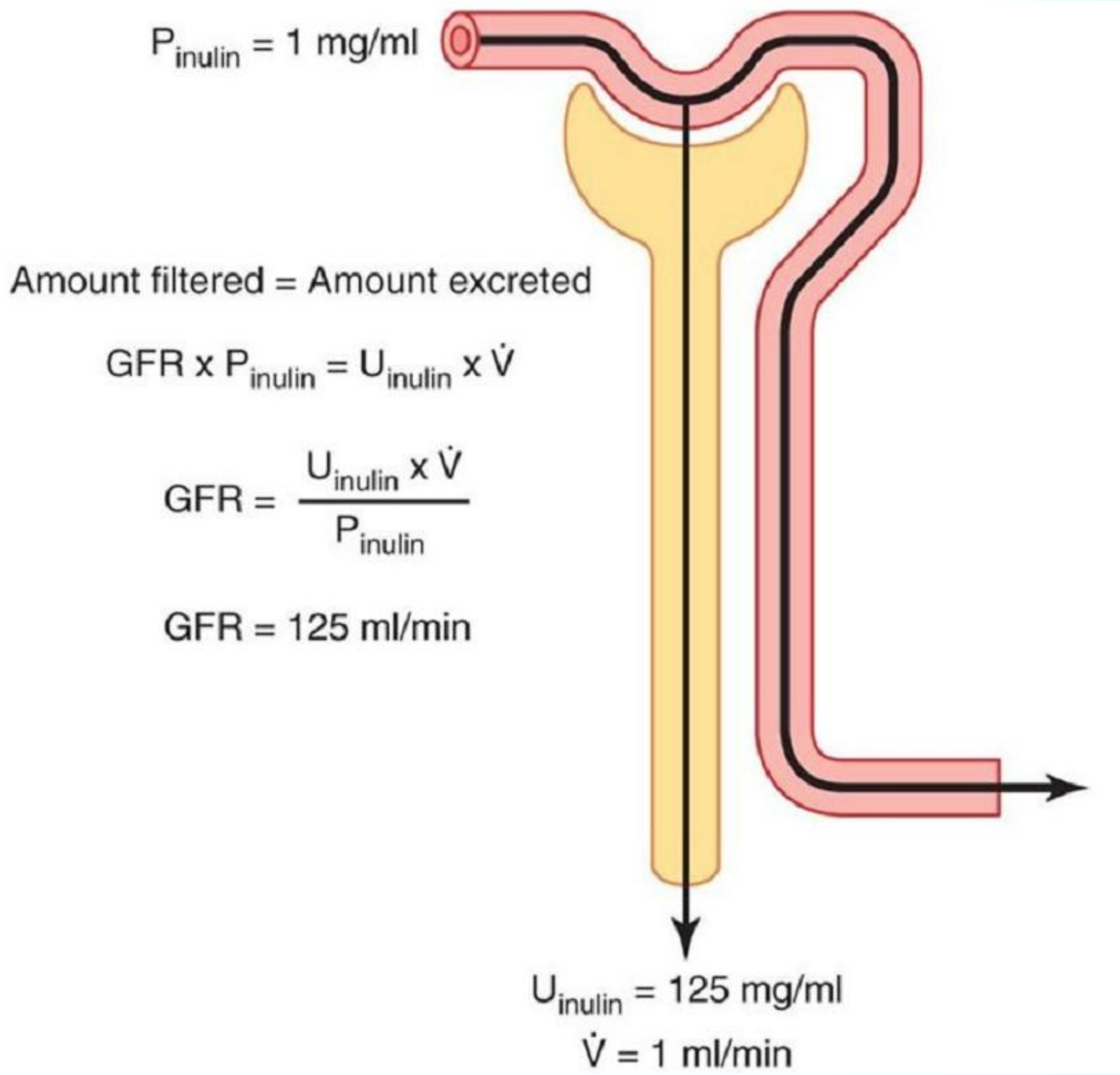
It is a polysaccharide with a molecular weight of about 5200 and it fits all the requirements.

Question ?

If the concentration of Inulin in the urine and plasma and the urine flow are as follows:

- Conc. of inulin in urine = **(U_{inulin}=120 mg/ml)**
- Urine flow = **(V=1 ml/min)**
- Conc. of inulin in arterial blood = **(P_{inulin}=1 mg/ml)**

C_{nulin} = (120 x 1)/1 =**120 ml/min**



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Why it is easier for a physician to use creatinine clearance Instead of Inulin for the estimation of GFR?

Because measurement of creatinine clearance **does not require intravenous infusion** into the patient, this method is much more widely used than inulin clearance for estimating GFR clinically . However ,

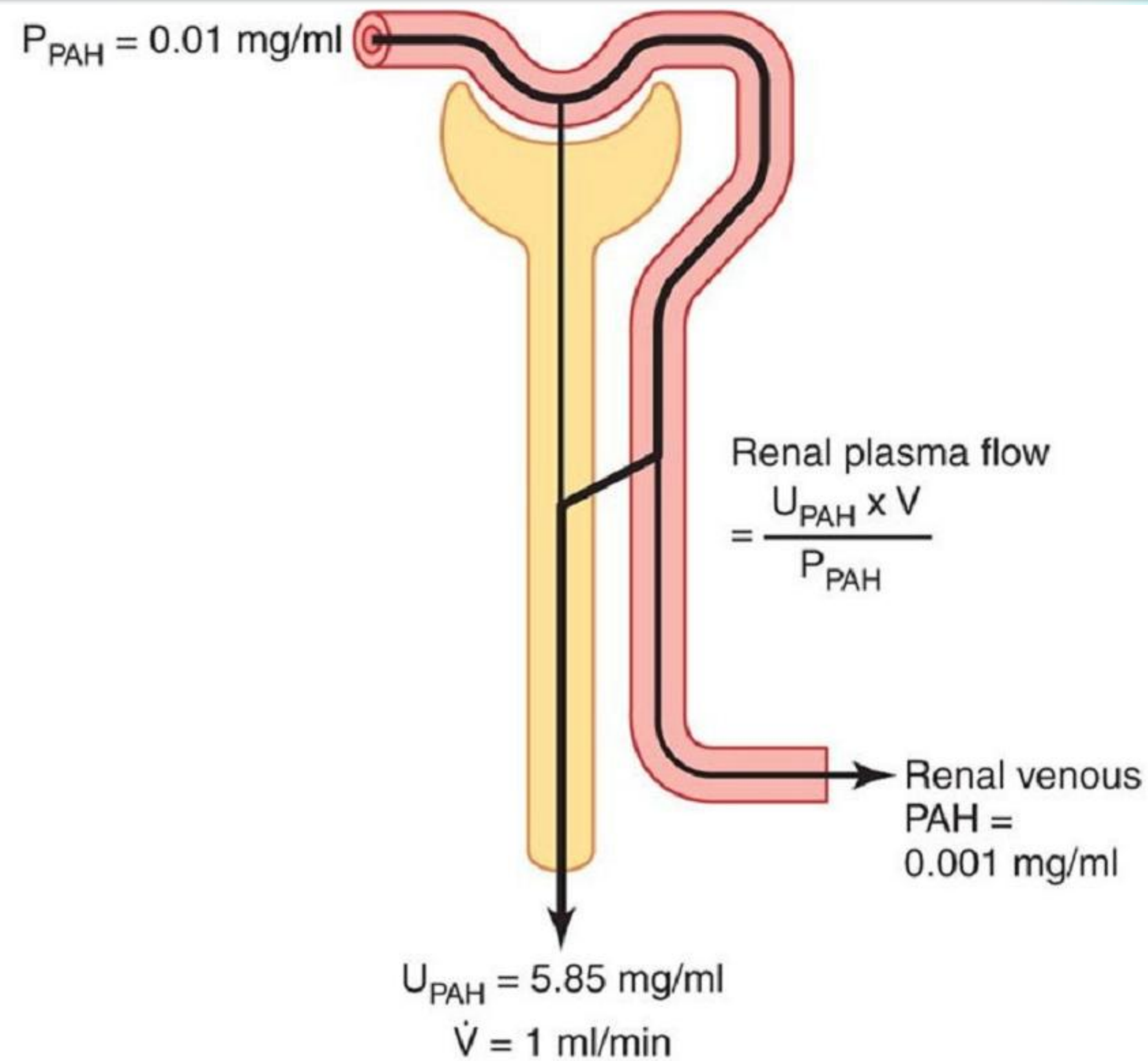
creatinine clearance is not a perfect marker of GFR because a **small amount of it is secreted by the tubules (error1)**, so the amount of creatinine excreted slightly exceeds the amount filtered.

There is normally a slight error in **measuring plasma creatinine that leads to an overestimate of the plasma creatinine concentration (error2)**, and fortuitously , these two errors tend to cancel each other . Therefore, creatinine clearance provides a reasonable estimate of GFR

Examples of a substance used for renal plasma flow and renal blood flow measurement

1.Para-aminohippuric acid (PAH)

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



Question ?

If the concentration of PAH in the urine and plasma and the urine flow are as follows:

- Conc. of PAH in urine = **(U_{PAH}=5.85 mg/ml)**
- Urine flow = **(V=1 ml/min)**
- Conc. of PAH in arterial blood = **(P_{PAH}=0.01 mg/ml)**
- Hematocrit is **45% = (PCV=0.45)**

Effective PAH or Renal Plasma Flow =

C_{PAH} = (5.85 x 1)/0.01 = **585 ML/ min**

Actual PAH or Renal Plasma Flow =

585/0.9 = **650 ML/ min**

Renal blood flow =

650/(1-0.45)= **1182 ml/min**

$$\text{Total renal plasma flow} = \frac{\text{PAH clearance}}{\text{PAH extraction ratio}}$$

If the extraction ratio for PAH is 90 percent, the actual renal plasma flow can be calculated by dividing 585 ml/min by 0.9, yielding a value of 650 ml/min. Thus, total renal plasma flow can be calculated as

$$E_{PAH} = \frac{P_{PAH} - V_{PAH}}{P_{PAH}}$$

The extraction ratio (E_{PAH}) is calculated as the difference between the renal arterial PAH (P_{PAH}) and renal venous PAH (V_{PAH}) concentrations, divided by the renal arterial PAH concentration:

Measurement of renal blood flow

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

Because Inulin clearance only reflects the volume of plasma that is filtered (GFR) and not that remains unfiltered (RBF) and get 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, so 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

We can't measure the renal blood flow directly we have to measure the renal plasma flow first

Filtration fraction

It is the ratio of GFR to renal plasma flow

FF = GFR/RPF = 125/650 = 0.19

To calculate the filtration fraction, which is the fraction of plasma that filters through the glomerular membrane, one must first know the renal plasma flow (PAH clearance) and the GFR (inulin clearance). If renal plasma flow is 650 ml/min and GFR is 125 ml/min, the filtration fraction (FF) is calculated as

Filtration Fraction = 125/650 = 0.19

0.19 * 100 = 19%

Calculation of tubular reabsorption or secretion from renal clearance

Reabsorption rate can be calculated=
Filtration load - excretion rate
= (GFR X P*) - (U* X V)
* The substance needed to be assessed.

Secretion* = (U* X V) - (GFR X P*).
* indicate the substance

Table 19-2 Renal Handling of Solutes

For any molecule *X* that is freely filtered at the glomerulus:	Renal handling of *X* is:
Filtration is greater than excretion	Net reabsorption of *X*
Excretion is greater than filtration	Net secretion of *X*
Filtration and excretion are the same	No net reabsorption or secretion
Clearance of *X* is less than inulin clearance	Net reabsorption of *X*
Clearance of *X* is equal to inulin clearance	*X* is neither reabsorbed nor secreted.
Clearance of *X* is greater than inulin clearance	Net secretion of *X*

1 Substances that are completely reabsorbed from the tubules

Example : amino acids, glucose

clearance = zero because the urinary secretion is zero.

2 Substances highly reabsorbed

Example : Na

its clearance < 1% of the GFR.

3 Waste products as urea are poorly reabsorbed

Have relatively high clearance rates.

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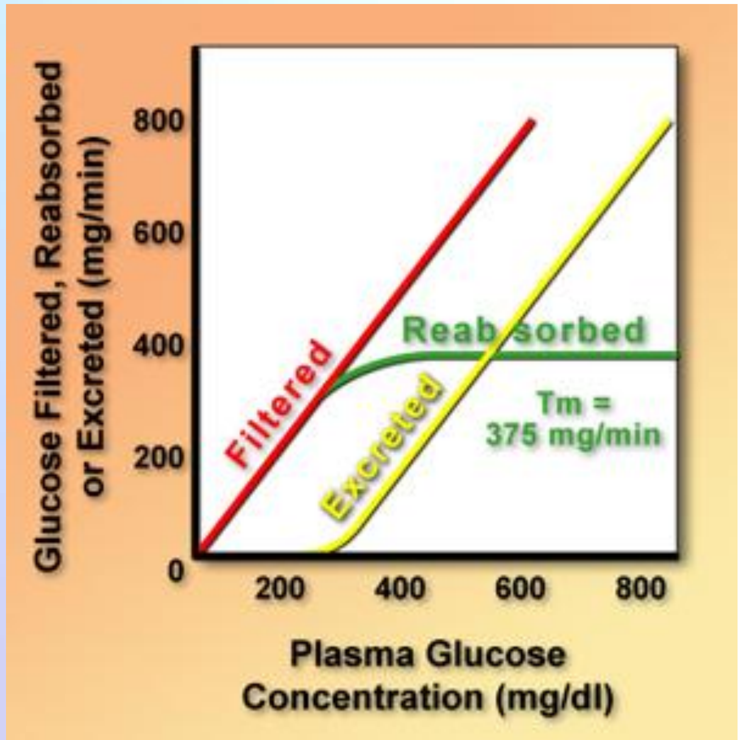
Glucose clearance

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 for glucose



Filtered Load :

filtered load = GFR x $[P]_{glucose}$

Reabsorption :

plasma [glucose] < 160 mg/dL	160 mg/dL < plasma [glucose] < 200 mg/dL	plasma [glucose] > 350 mg/dL
• filtered load of glucose is completely reabsorbed **(no excreted in urine)**	• filtered load of glucose is not completely reabsorbed, • **"threshold," or plasma [glucose] at which glucose is first excreted in urine**	•filtered load of glucose is not completely reabsorbed •Na^+ - glucose (SGLT) co transporters are completely saturated •maximal glucose reabsorption (T_m) = 375

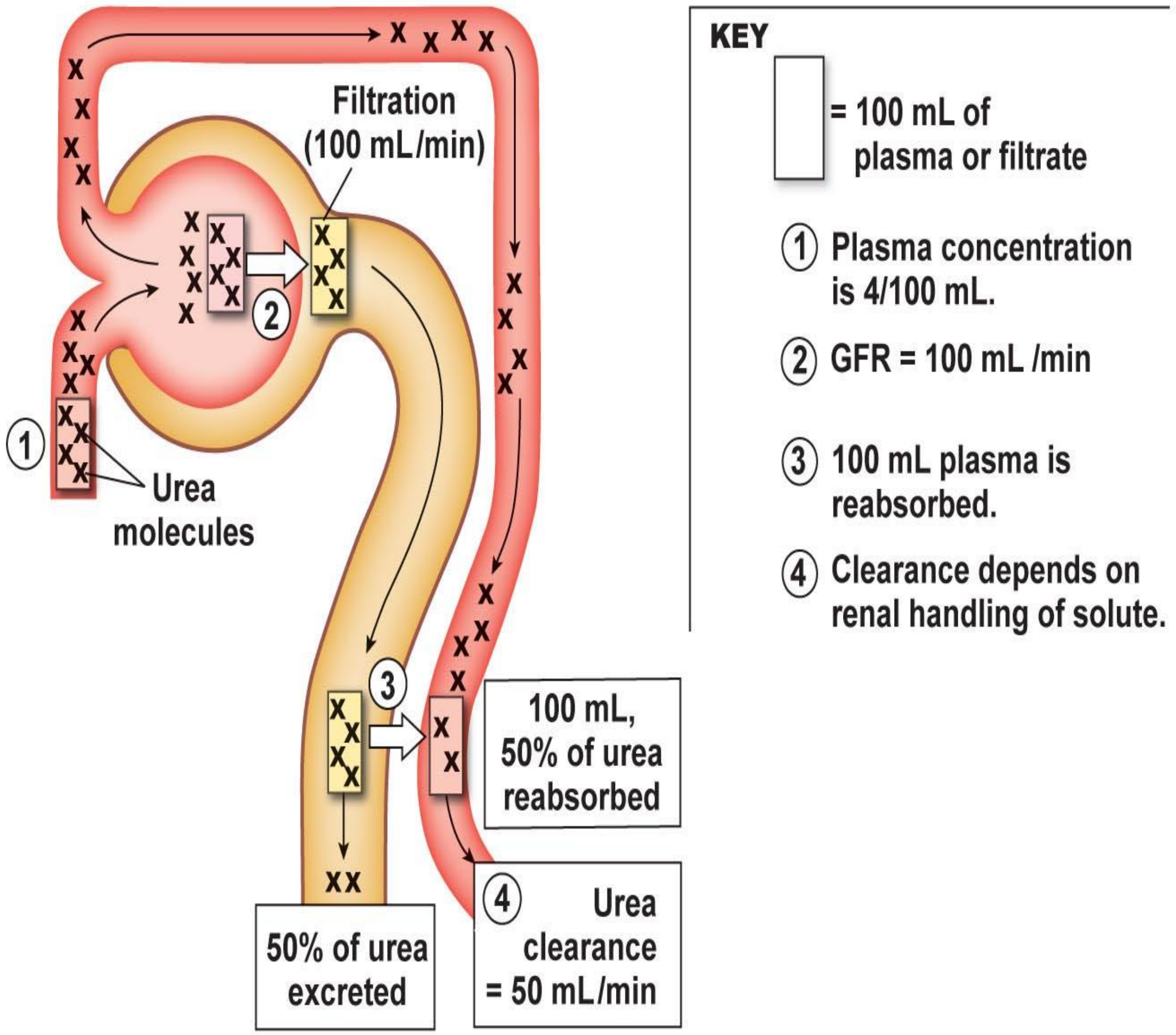
- ↑ uptake glucose → ↑ Filtered rate
- Reabsorption increase with Filtration → glucose is completely reabsorbed

if rise plasma glucose level between 160 and 200 → not completely reabsorbed

if Continue ↑ uptake glucose → ↑ plasma glucose level to 350 is start excreted in urine and Reabsorption is constant (because the maximal glucose reabsorption from kidney = 375)

Urea clearance

100% is filtered and only 50% is reabsorbed



(b) Urea clearance

SUMMARY

Term	Equation	Units
Clearance rate (C_S)	$C_s = \frac{U_s \times \dot{V}}{P_s}$	ml/min
Glomerular filtration rate (GFR)	$GFR = \frac{U_{inulin} \times \dot{V}}{P_{inulin}}$	
Clearance ratio	$\text{Clearance ratio} = \frac{C_s}{C_{inulin}}$	None
Effective renal plasma flow (ERPF)	$ERPF = C_{PAH} = \frac{U_{PAH} \times \dot{V}}{P_{PAH}}$	ml/min
Renal plasma flow (RPF)	$RPF = \frac{C_{PAH}}{E_{PAH}} = \frac{(U_{PAH} \times \dot{V}/P_{PAH})}{(P_{PAH} - V_{PAH})/P_{PAH}} = \frac{U_{PAH} \times \dot{V}}{P_{PAH} - V_{PAH}}$	ml/min
Renal blood flow (RBF)	$RBF = \frac{RPF}{1 - \text{Hematocrit}}$	ml/min
Excretion rate	Excretion rate = $U_S \times V$	mg/min, mmol/min, or mEq/min
Reabsorption rate	$\text{Reabsorption rate} = \text{Filtered load} - \text{Excretion rate} = (GFR \times P_s) - (U_s \times \dot{V})$	mg/min, mmol/min, or mEq/min
Secretion rate	Secretion rate = Excretion rate - Filtered load	mg/min, mmol/min, or mEq/min

S, a substance; U, urine concentration; V, urine flow rate; P, plasma concentration; PAH, para-aminohippuric acid; P_{PAH}, renal arterial PAH concentration; E_{PAH}, PAH extraction ratio; V_{PAH}, renal venous PAH concentration.

SUMMARY

The formula used to calculate GFR or RPF is $C_X = (U_X \times V)/ P_X$ X could be PAH , creatinine and inulin

The formula used to calculate RBF is **RBF= RPF \ 1-Hct** Or **RBF=RPF% \ 100-Hct**

We can't measure the renal blood flow directly we have to measure the renal plasma flow first

Reabsorption rate = Filtration rate - excretion rate = (GFR X P*) - (U* X V)
Secretion* = (U* X V) - (GFR X P*).

Substances that are completely reabsorbed (**amino acids, glucose)**

Substances highly reabsorbed (**Na)**

Waste products as urea are poorly reabsorbed , they

Glucose clearance

plasma [glucose] < 160 mg/dL	160 mg/dL < plasma [glucose] < 200 mg/dL	plasma [glucose] > 350 mg/dL
• filtered load of glucose is completely reabsorbed **(no excreted in urine)**	• filtered load of glucose is not completely reabsorbed,	• filtered load of glucose is not completely reabsorbed • maximal glucose reabsorption (T_m) = 375

MCQs

1. what is the Renal clearance for creatinine, if Concentration of creatinine in urine = 12 , in the plasma = 7 and urine flow rate = 18 ?
a. 31 b. 4.6 c. 10.2 d. 44

2. what is the renal plasma flow and renal blood flow for PAH if hematocrit is 50 % ,Conc. of PAH in urine =30 mg/ml , in arterial blood = 0.5 mg/ml, Urine flow=3 ml/min,?
a. 580 – 1000 b. 110 - 400 c. 180 - 360 d. 100 - 500

3. Substances that are completely reabsorbed from the tubules is :
a. Glucose b. Na c. amino acids d. a and c

4. what is the Reabsorption rate for amino acids if GFR = 1 , Conc. in urine = 0 mg/ml , in arterial blood = 80 mg/ml, Urine flow= 1 ml/min ?
a. 1 b. 80 c. 0 d. 40

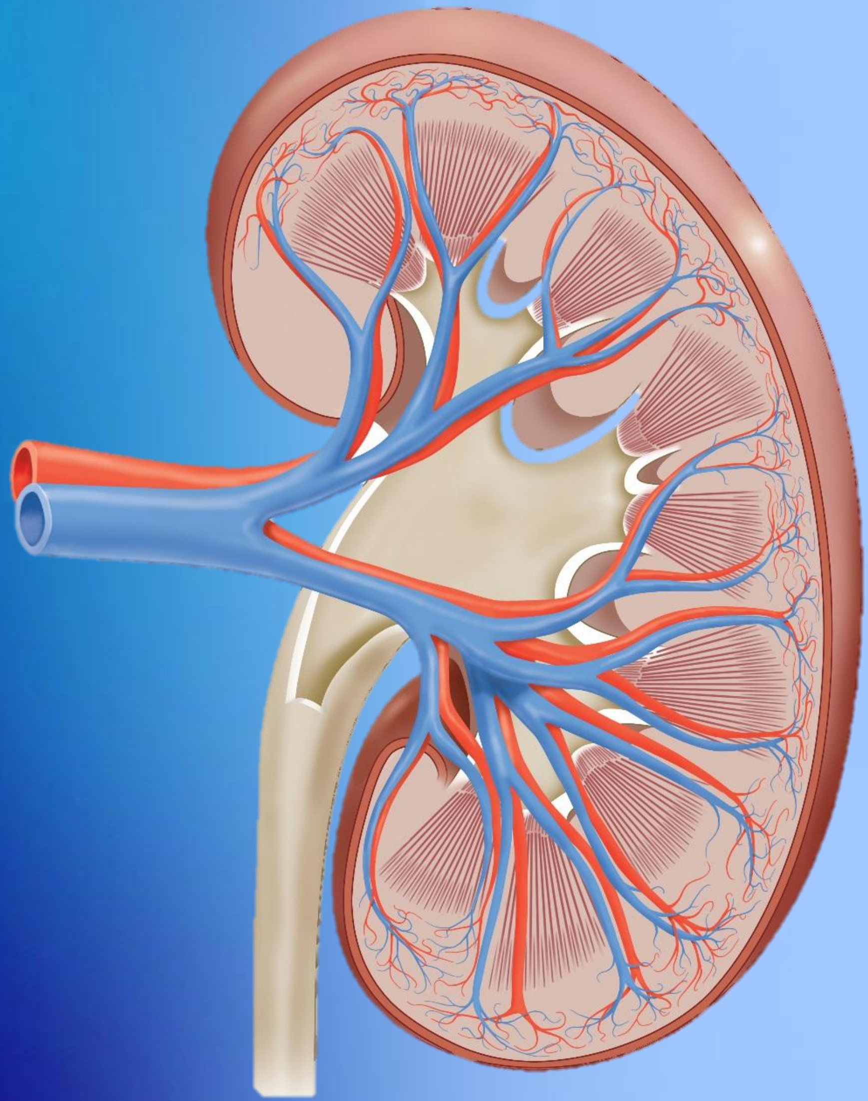
5. maximal glucose reabsorption (T_m) =
a. 350 b. 375 c. 300 d. 200

6. The glucose clearance is
a. 1 b. 4 c. zero d. 0.1

7. Substances used for measurement of GFR are suitable for the measurement of Renal Blood Flow
a. T b. F

8. We can use the Na to measurement of GFR
a. T b. F

Ans. : 1.a , 2.c , 3.d , 4.b , 5.b , 6.c , 7.b , 8.b



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