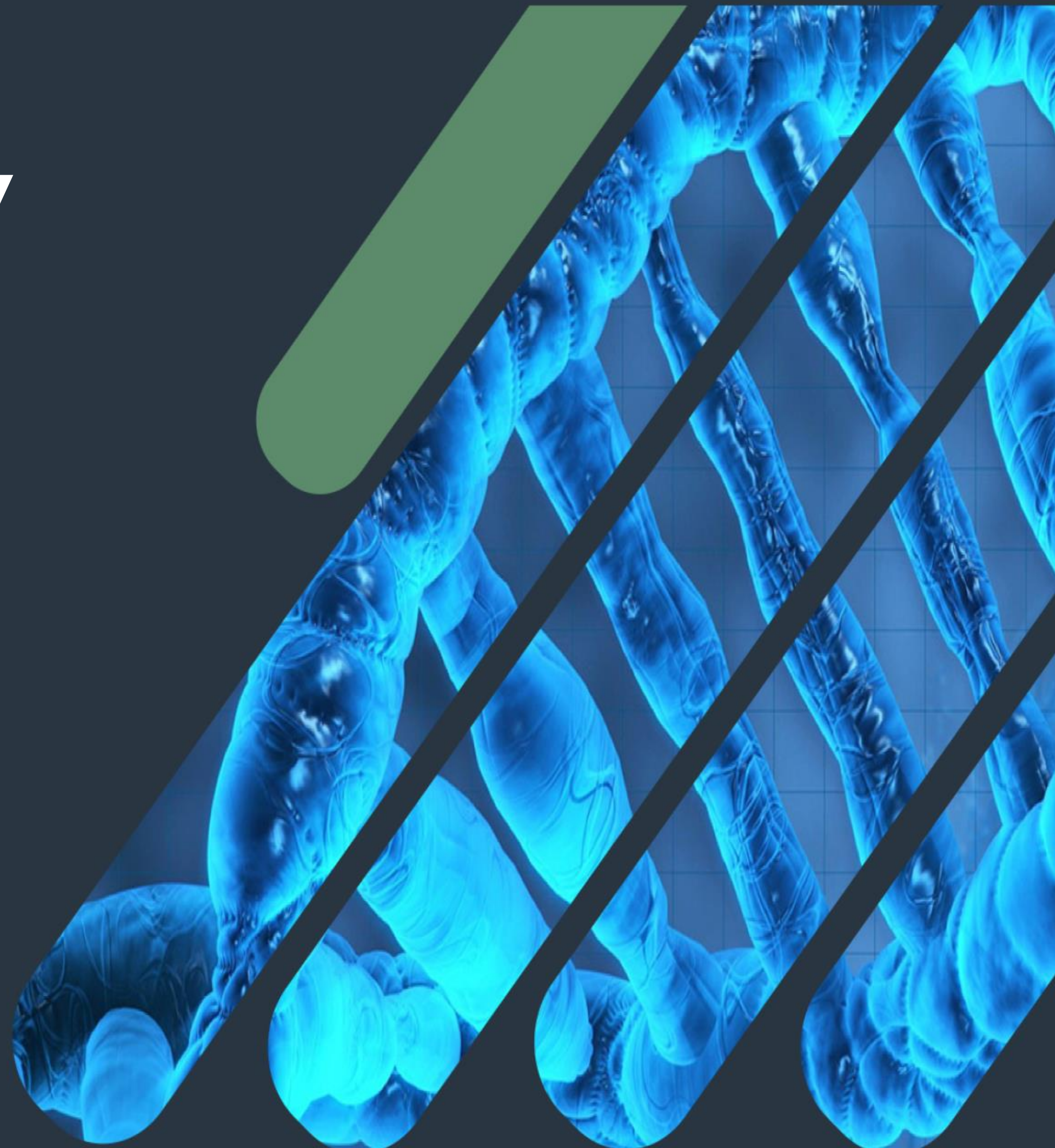
Physiology

Renal plasma clearance



Learning objectives

- Know the clinical significance of GFR measurement.
- State what substances are used to measure GFR and RPF.
- List data required for clearance calculation.
- Predict whether a substance undergoes net reabsorption or net secretion by comparison of its clearance to that of inulin.

CLEARANCE

- **Definition:**

It is the volume of plasma (ml) which is cleared off from a certain substance per minute by both kidneys.

Important Note:

- Clearance is a "**quantitative concept**" which is useful for evaluating several aspects of **renal function**. If one liter of plasma contains one milligram of a substance, and we remove that entire mg, then the *clearance* is **one liter** (**not one mg**). If we removed one tenth of a mg, then the clearance would be one tenth of a liter. ***Renal clearance*** **describes the removal of substances from "a volume of" plasma (excretion) per time unit (usually per minute).**

- **Uses of renal clearance:**

1. Determination of renal blood flow (RBF).
2. Determination of glomerular filtration rate (GFR).
3. To know handling of renal tubules with different substances.
4. Assessment of renal function.
   1. Creatinine clearance
   2. Urea clearance

Clearance Equation

$$C_X = (U_X \text{ X } V) / P_X$$

where

C_X = Renal clearance (ml/min)

U_X X V = excretion rate of substance X

U_X = Concentration of X in urine

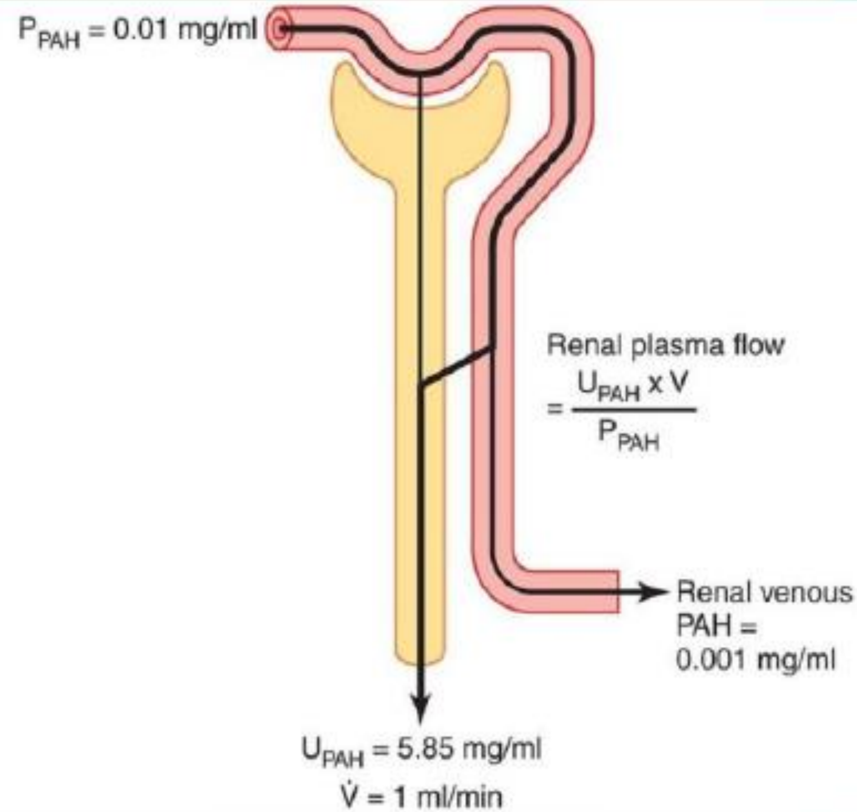
V = urine flow rate in ml/min

Px = concentration of substance X in the plasma

1. 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:

- ***Para-amino hippuric acid or diodrast clearance*** can be used for Determination of renal blood flow because when these substances are present in plasma in certain concentration (not more than 2 mg /dl) they are completely removed by a single circulation through free filtration & complete secretion.

- So the amount of PAHA passed through both kidneys in one minute = the amount of PAHA present in urine of one minute.

Amount = volume x concentration.

- So Volume of plasma passed through both kidneys in one minute (PAHA clearance) x Concentration of PAHA in plasma (P) = Volume of urine in one minute (V) x Concentration of PAHA in urine (U).

- Clearance (C) = $\frac{V \, x \, U}{P}$.

- Clearance of PAHA = RPF =650 ml/min.

- RBF = RPF x $\frac{1}{1-HV}$ = 1200 ml/min.

Actually the clearance of PAHA is slightly less than the RPF because It was found that the renal venous plasma contains about 9% of the PAHA concentration in arterial plasma and exactly zero. Therefore the amount excreted in urine / minute is less than the total amount reaching the kidney / minute i.e. PAHA clearance = only 91% of RPF = about 585 ml/min.

We can measure it by measuring first the extraction ratio.

$$\text{Extraction ratio} = \frac{\text{the amount excreted in urine / minute}}{\text{amount reaching the kidney / minute}} = 91\%.$$

The amount excreted in urine / minute = the total amount reaching the kidney / minute X Extraction ratio.

The amount excreted in urine / minute = RPF X PAHA concentration in arterial plasma X Extraction ratio.

RPF =PAHA clearance / Extraction ratio = 585 X 100 / 91 = 650 ml/min.

2. Examples of a substance used for GFR measurement

1. Creatinine (endogenous):

by-product of skeletal muscle metabolism

2. Inulin (exogenous):

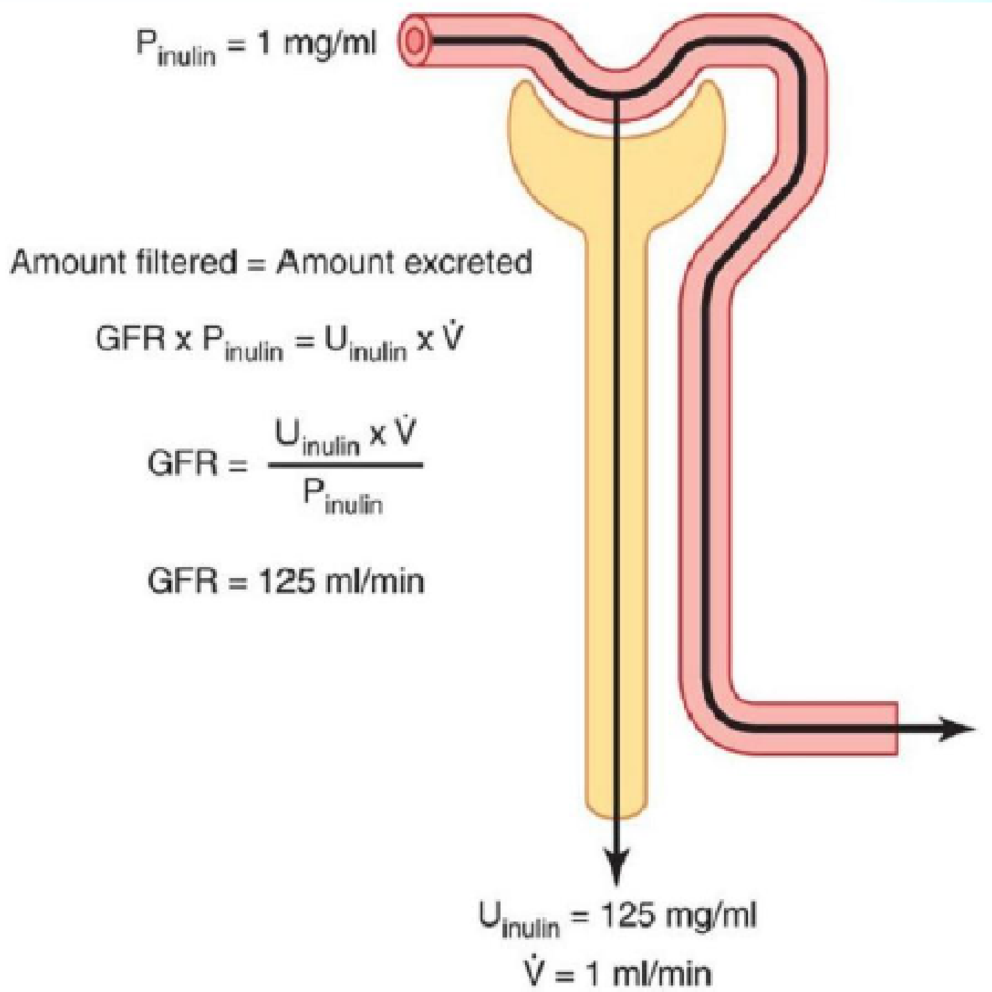
It is a polysaccharide with a molecular weight of about 5200 and it fits all the requirements.

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



➢ Why we measure GFR?

The level of GFR and its magnitude of change over time are vital to:

- The detection of kidney disease.
- Understanding its severity.
- Making decisions about diagnosis, prognosis, and treatment.

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**

3. **Assessment of renal functions**: by measuring →

a) **Creatinine clearance:**

- It is the most common type of clearance used for assessment of renal function.
- Its use is dependent on the fact that daily production of creatinine is constant and little affected by protein intake (unlike urea).

Method:

- Urine is collected for 24 hrs. then the volume of urine in one minute is measured.(V)
- Serum and urinary concentration of creatinine is measured.(P & U)
- Creatinine clearance $= \frac{U \times V}{P}$ =140 ml/min.
- In renal failure creatinine clearance is decreased and serum creatinine is increased.

b) <u>Urea clearance:</u>

1. The bladder is first evacuated and urine is discarded.
2. The subject is given a glass of water at the beginning of the test.
3. He is given another glass of water one hour later.
4. Urine is collected for analysis after the one and two hours (for determination of the urine volume and urea concentration).

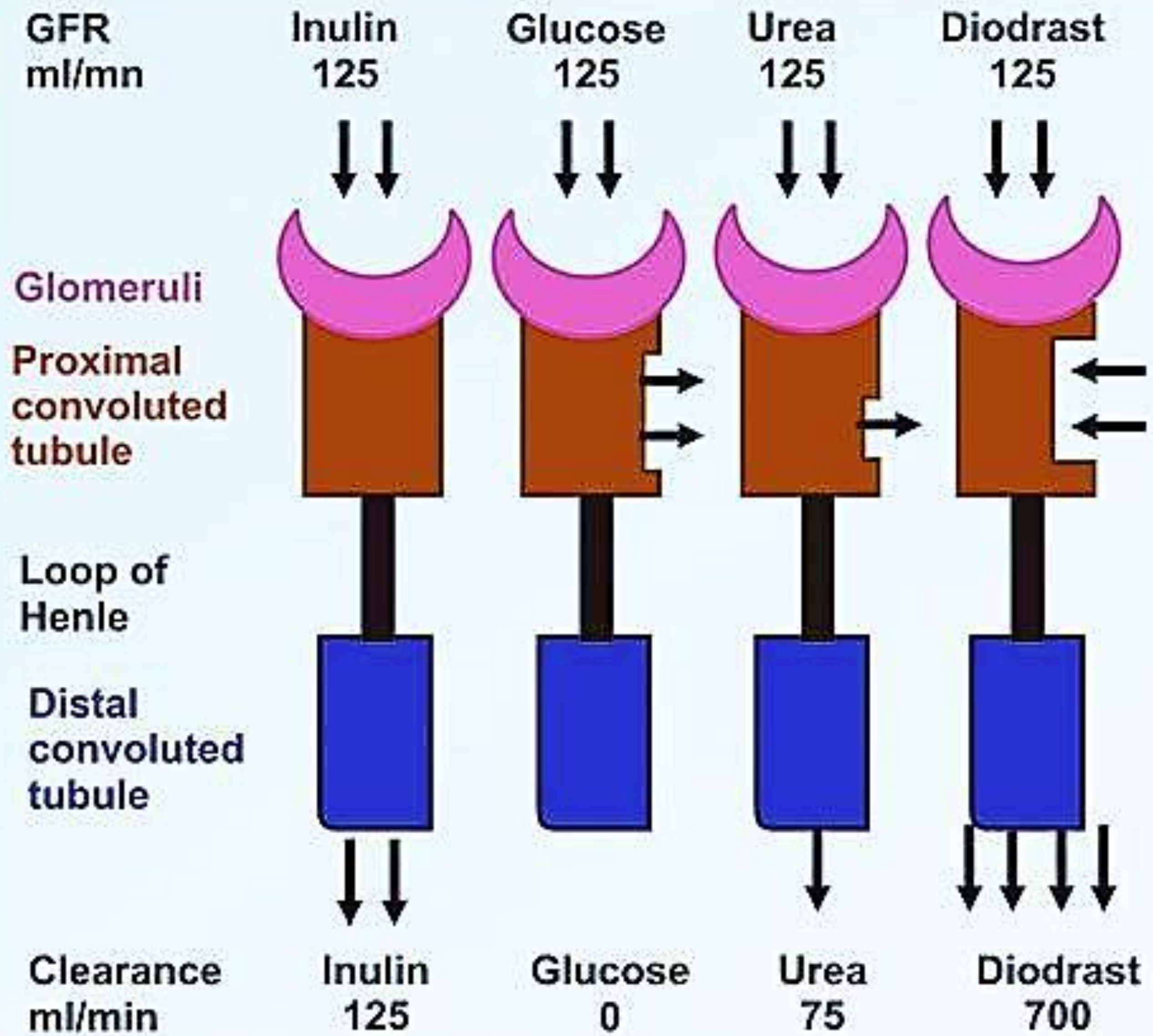
5. Blood sample is withdrawn after the first hour (for analysis of urea concentration).
6. If the urine volume is more than 2 ml/ min. we use the usual formula for determination of urea clearance. $(C) = \dfrac{U \times V}{P}$.
7. But if the urine volume is less than 2 ml/min. the standard clearance formula is used $(C) = \dfrac{U \times \sqrt{V}}{P}$

This is because urea undergoes back diffusion in the tubules. The greater the urine flow the less will be the back diffusion and the more will be the urea excreted.

If the urine volume is 2 ml/min or more the excretion of urea becomes maximal and the usual formula for clearance is used.

4. Handling of renal tubules with different substances

Clearance	Renal handling	Example
If clearance > 650	Completely **secreted** + **synthesized** in renal tubules	Ammonia
If clearance = 650	Completely **secreted**	**PAHA**
If clearance > 125 < 650	Partial **secretion**	Creatinine clearance = 140 ml/min
If clearance = 125	Not **reabsorped**, Not **secreted**	**Inulin**
If clearance < 125	Partial **reabsorption**	Urea
If clearance = Zero	Complete **reabsorption**	**Glucose**



Inulin is neither absorbed nor secreted. Glucose is absorbed completely. Urea is partially absorbed. Diodrast is actively secreted.

Load of substance: It is the amount of substance applied to renal tubules in one minute.

Load of substance (amount) = concentration of the substance in plasma

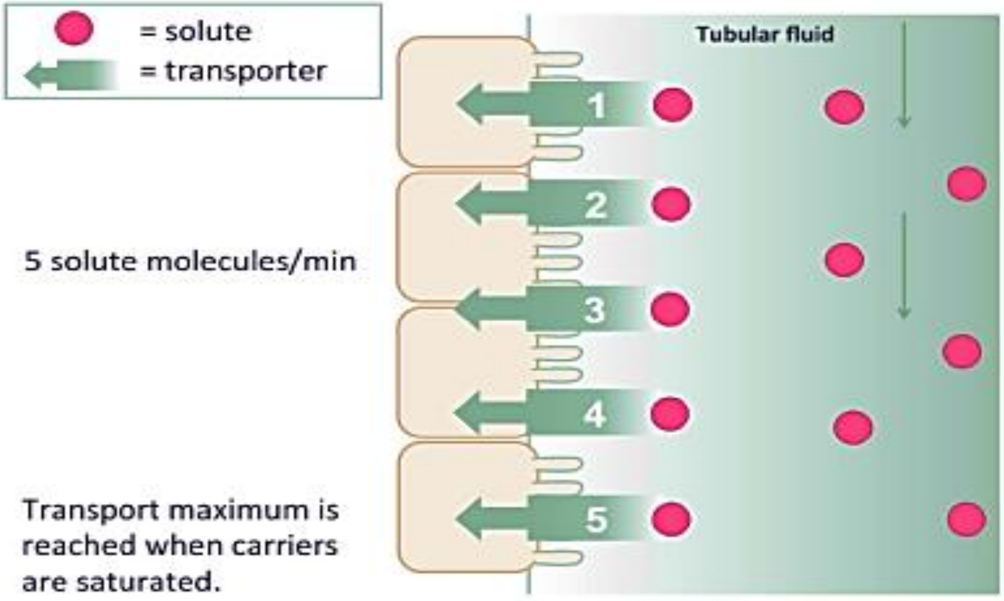
X volume of filtered plasma in one minute (GFR)

i.e. **load of substance = concentration of the substance in plasma X GFR**

Tubular or transfer maximum (Tm):

- It is the maximum amount of the substance in mgs which can be reabsorbed or secreted by renal tubules in one minute.

- It is obtained by increasing the concentration of the substance in blood by gradual continuous infusion and measuring the amount excreted in urine / minute, then calculating the load of substance and the amount excreted each time → the maximal difference will be the Tm of the substance.



For example:

TmG:

- It is the maximum amount of glucose that can be reabsorbed by renal tubules in one minute.
- In males it is 375 mg/min.
- In females it is 305 mg/min.
- Load of glucose at plasma concentration 180 mg/dl = $\frac{180 \, X \, 125}{100}$ = 225 mg/min but at this plasma concentration glucose begins to appear in urine although it is far from TmG ***Why?***
    - ✓ Because not all the 2 million nephrons have the same TmG.

Renal threshold for glucose:

- ➢ It is the plasma level at which glucose first appear in urine.
- ➢ Normally it is 180 mg/dl but in diabetics it may be higher.

Quiz

1) Criteria of a substance used for GFR measurement:
   a) Not freely filtered
   b) Secreted by the tubular cells
   c) Should be toxic
   d) Not reabsorbed by the tubular cells

2) For the measurement of renal plasma flow a substance needs to be:
   a) Not freely filtered
   b) Toxic
   c) Completely secreted
   d) Reabsorbed

3) If the clearance of a substance is less than the clearance of inulin it is?
   a) Only filtered not reabsorbed or secreted
   b) Reabsorbed by nephron tubules
   c) Secreted by nephron tubules
   d) Filtered, reabsorbed, and secreted

4) A substance that is completely reabsorbed from the tubules:
   a) Inulin
   b) Amino acids
   c) Para-Aminohippuric acid (PAH)
   d) Creatinine

5) Amount of substance excreted =
   a) The ratio of GFR to renal plasma flow
   b) Amount filtered-reabsorbed+secreted
   c) Amount filtered+reabsorbed+secreted
   d) Amount filtered-reabsorbed-secreted

6) Substance clearance that is used to measure the renal plasma flow:
   a) Glucose
   b) Inulin
   c) Paraminohippuric acid (PAH)
   d) Na

Q2/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

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


Thank
You!