3. Renal Clearance

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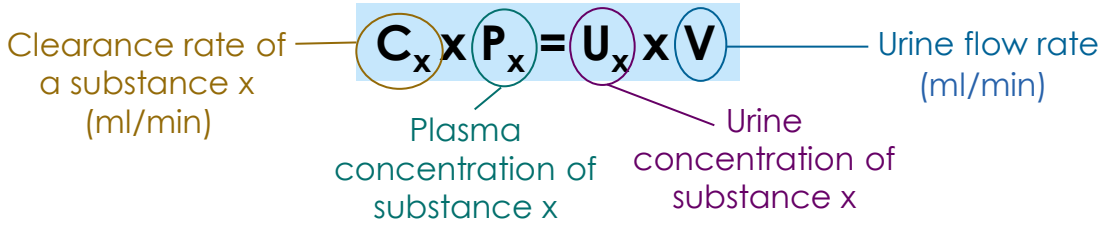
Renal Clearance

of a substance is the volume of plasma that is completely cleared of the substance by the kidneys per unit time.

Importance of Renal Clearance

- **Rate of glomerular filtration(GFR)**
- **Tubular reabsorption of different substance**
- **Tubular secretion of different substance**
- **Assess severity of renal damage**
- **Rate of blood flow**

Clearance refers to the volume of plasma that would be necessary to supply the amount of substance excreted in the urine per minute. **Stated mathematically:**



Accordingly Clearance can be expressed as:

$$C_x = \frac{U_x \times V}{P_x}$$

Urinary Excretion Rate

Renal Clearance of Substance x is defined as the ratio of excretion rate of substance x to its concentration in the plasma.

Clearance Tests

Types	
Endogenous	**Exogenous**
Creatinine	Inulin
Urea	Para-aminohippuric Acid(PAHA)
Uric Acid	Diodrast (di-ido pyridone acetic acid)

Recall the equation we mentioned previously it's used for **calculation** of the test

$$C = \frac{U \times V}{P}$$

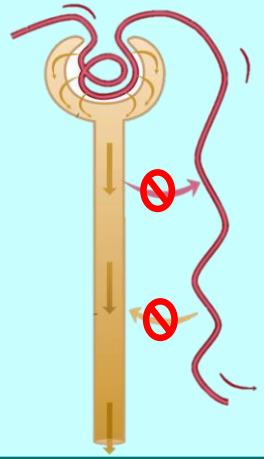
Where:

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

V = Volume of urine excreted per mintue (ml/min)

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

Different Types of Substances' Clearance

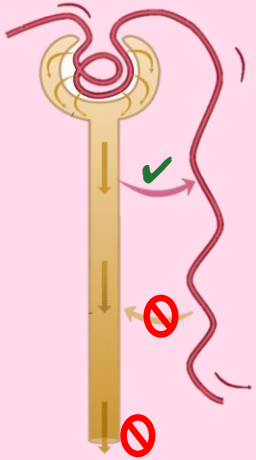


✧ **Neither secreted nor reabsorbed.**

✧ Excretion = Filtration

Clearance = GFR

Examples:
Inulin & Creatinine

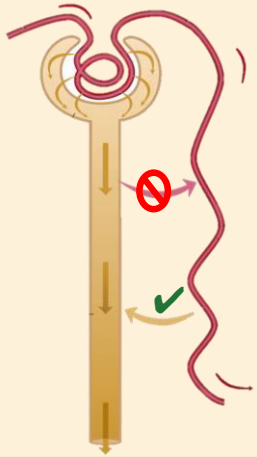


✧ **Neither secreted nor excreted.**

-Fully reabsorbed-

✧ Execration = 0
Clearance = Zero

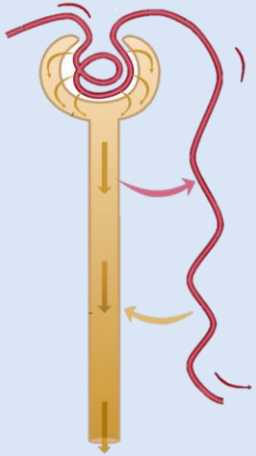
Examples:
Amino Acids& Glucose



✧ **Not reabsorbed.**

✧ Amount excreted = amount Filtered + amount secreted

Clearance = Renal Plasma Flow
Example:
PAH



✧ **Partial reabsorption**

✧ Excretion = Filtration – Reabsorption + Secretion

Clearance < 1%

Examples:
Cl , Na and urea

Additional

<table>
<tr><th>Estimation of Glomerular Filtration Rate (GFR)</th><th>Estimation of Renal Plasma Flow (RPF)</th></tr>
<tr><td colspan="2">Substances Used</td></tr>
<tr><td>Exogenous</td><td rowspan="5">Paraminohippuric Acid (PAH)

✧ *PAH, is about 90% cleared from the plasma. Therefore, the clearance of PAH can be used as an approximation of renal plasma flow.
✧ ~10% PAH remains
* : Extra note: Because the GFR is only about 20% of the total plasma flow, a substance that is completely cleared from the plasma must be excreted by tubular secretion as well as glomerular filtration . There is no known substance that is completely cleared by the kidneys</td></tr>
<tr><td>Inulin</td></tr>
<tr><td>Determine clearance rate and therefore nephron function.</td></tr>
<tr><td>Not produced in the body, is found in the roots of certain plants (polysaccharides) and must be administered intravenously to a patient to measure GFR.</td></tr>
<tr><td>Endogenous</td></tr>
<tr><td>Creatinine</td><td></td></tr>
<tr><td>By-product of muscle metabolism.(Endogenous)</td><td></td></tr>
<tr><td colspan="2">Freely filtrated.</td></tr>
<tr><td colspan="2">Not reabsorbed</td></tr>
<tr><td>Not secreted</td><td>Rapidly and completely secreted</td></tr>
<tr><td colspan="2">Should not be toxic</td></tr>
<tr><td>Should not be metabolized</td><td>-</td></tr>
<tr><td colspan="2">Easily measurable</td></tr>
</table>

Examples

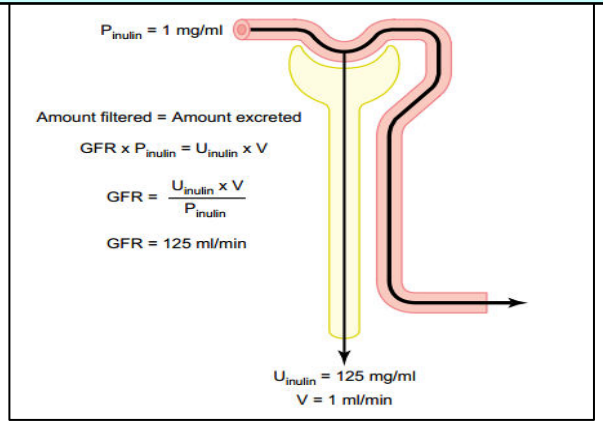
Estimation of Glomerular Filtration Rate (GFR)	Estimation of Renal Plasma Flow (RPF)
Inulin (Exogenous)	**Paraminohippuric Acid (PAH)**
If the plasma concentration (P) of inulin is **1** mg/ml. Urine concentration of inulin (U) is **125** mg/ml. Urine flow rate (V) is **1** ml/ min. **Calculate the GFR or the inulin Clearance?**	Arterial blood concentration of PAH (P) is **0.01** mg/ml. Urine concentration of PAH (U) is **5.85** mg/m. Urine flow rate (V) is **1** ml/min. **Calculate the RPF or the PAH Clearance?**

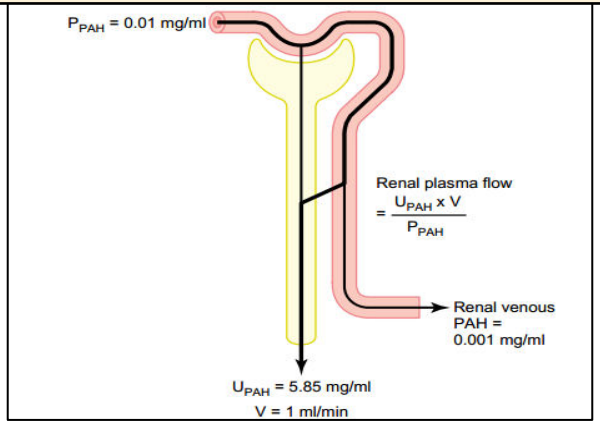
$$C = \frac{U \times V}{P}$$

بالتعويض بالقانون اللي عرفناه مسبقا!

$$C_{inulin}\ (GFR) = \frac{125 \times 1}{1} = \underline{125\ ml/min}$$

$$C_{PAH}\ (RPF) = \frac{5.85 \times 1}{0.01} = \underline{585\ ml/min}$$





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 filtrated and not that remains unfiltrated and yet passes through the kidney.
- ✧ It is known that only 1/5 of the plasma that enters the kidneys gets filtrated therefore, other substance to be used with special criteria.

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

Previous Example

Estimation of Renal Plasma Flow (RPF)
Paraminohippuric Acid (PAH)
Arterial blood concentration of PAH (P) is **0.01** mg/ml. Urine concentration of PAH (U) is **5.85** mg/m. Urine flow rate (V) is **1** ml/min. **Calculate the RPF or the PAH Clearance?**
$C_{PAH}(RPF) = \frac{5.85 \times 1}{0.01} = \underline{585\ ml/min}$

That was the renal PLASMA flow if you want to measure the renal BLOOD flow you need to consider the hematocrit (the percentage of red blood cells in the blood) = 45%

Then renal blood flow will be:

$$RBF = \frac{585 \times 100}{100 - 45} = \underline{1063\ ml/min}$$

Renal clearance gives an indication of the function of the kidneys.

Clearance can also be used to determine renal handling of substance

It's how the nephron handles a substance filtered into it. In this method clearance for inulin or creatinine is calculated and then compared with the clearance substance being investigated.

Comparison of clearance of substance with clearance of inulin:

- = inulin clearance; only filtrated not reabsorbed or secreted.
- < inulin clearance; reabsorbed by nephron tubules. e.g. glaucous
- > inulin clearance; secreted by nephron tubules. e.g. PAH

Calculation of Tubular Reabsorption From Renal Clearance

Unlike glomerular filtration, which is relatively nonselective, *tubular reabsorption is highly selective* which makes the rate of reabsorption varies for each substance:

1- Some substances, such as glucose and amino acids, are almost completely reabsorbed from the tubules, so the urinary excretion rate is essentially zero.

(clearance = zero because the urinary secretion is zero & complete reabsorption).

2-Many of the ions in the plasma, such as sodium, chloride, and bicarbonate, are also highly reabsorbed, but their rates of reabsorption and urinary excretion are variable, depending on the needs of the body.

(its clearance < 1% of the GFR.)

3-Waste products, such as urea and creatinine, are poorly reabsorbed from the tubules and excreted in relatively large amounts.

(They have relatively high clearance rates)

Therefore, by controlling the rate at which they reabsorb different substances, the kidneys regulate the excretion of solutes independently of one another, a capability that is essential for precise control of the body fluid composition.

"Reabsorption rate can be calculated= Filtration rate- excretion rate

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

(*) :The substance needed to be assessed (To determine the amount of).

Calculation of Tubular Secretion From Renal Clearance

For many substances, tubular reabsorption plays a much more important role than secretion in determining the final urinary excretion rate. However, tubular secretion accounts for significant amounts of potassium ions, hydrogen ions, and a few other substances that appear in the urine.

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*)"

Filtration fraction

It is the ratio of GFR to renal plasma flow

$$\text{Filtration fraction} = \frac{\text{GFR}}{\text{RPF}}$$

(*) :indicate the substance

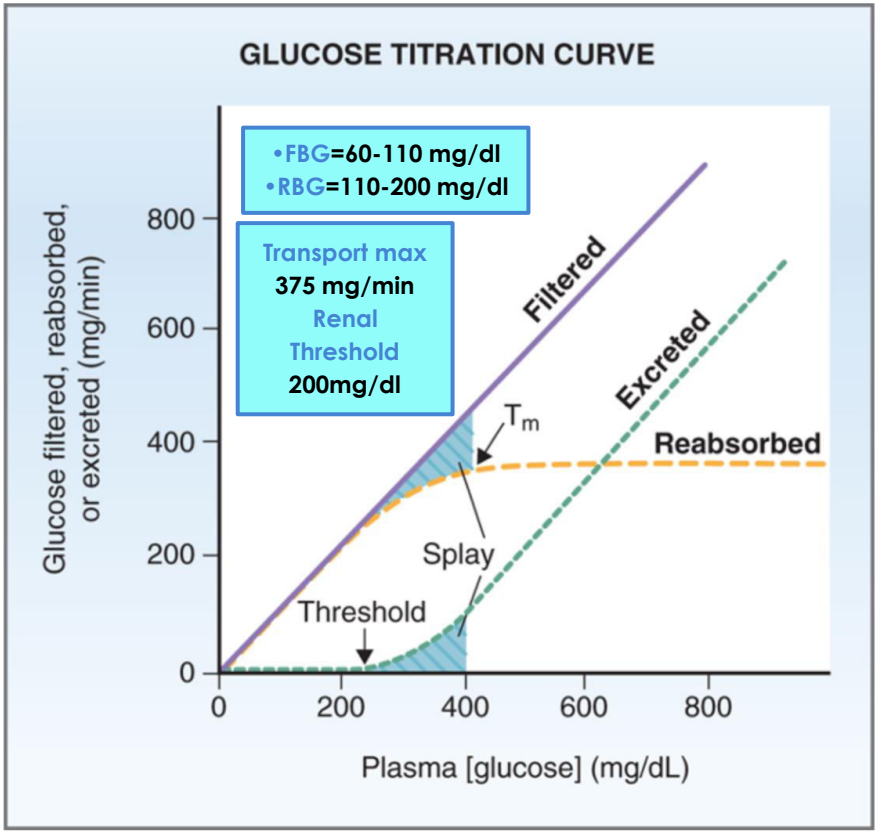
Glucose Clearance

The glucose clearance is zero at plasma glucose values below the threshold and gradually rises as plasma glucose rises.

And that means that we can express the excretion of glucose quantitatively when plasma concentrations has become 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



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.*

Further Explanation

In conclusion the Glucose clearance is as following:

Filtered Load*:

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

Reabsorption:

Plasma [glucose] < 200 mg/dL

-Filtered load of glucose is completely reabsorbed.

200 mg/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)

* Quantity of a substance filtered at the glomeruli per min

	Clearance Equation	Substance used	Criteria Substance	Example
GFR Measurement	$GFR = \frac{[U] \times UV}{[P]}$	•Inulin (exogenous) •Creatinine (endogenous)	•NOT secreted •NOT reabsorbed	**IF** $[P]_{Inulin}$ = 1 mg/100ml $[U]_{Inulin}$ = 120 mg /100ml (UV) = 1 ml /min **Then, the clearance of inulin will be?** C = 120 ml/min
RPF[1] Measurement	$ERPF = \frac{[U] \times UV}{[P]}$	•Paraminohippuric Acid (PAH)	•Rapidly and completely secreted	**IF** $[U]_{PAH}$ = 25.2 mg/ml (UV) =1.1 ml/min $[AB]_{PAH}$ = 0.05 mg/ml **Then CPAH of RPF** = (25.2 x 1.1)/0.05 = 560 ML/ min

Glucose Clearance	Glucose Reabsorption	
	Transport max	Renal Threshold
The glucose clearance is **zero** at plasma glucose values	375 mg/min	200mg/dl

1: Renal Plasma Flow

Summary

1-Which one of the following clearance tests is considered as an exogenous type?
A. Uric acid
B. Inulin
C. Urea
D. Creatinine

2-Tubular transport maximum for glucose is:
A. 375 mg/min
B. 200 mg/min
C. 125 mg/min
D. 250 mg/min

3-The ratio of GFR to renal plasma flow is:
A. Clearance rate
B. Excretion rate
C. Tubular reabsorption
D. Filtration fraction

4-If the substance is freely filtered, rapidly and completely secreted by the renal tubular cells. We can use it to quantify:
A. Rate of glomerular filtration
B. Rate of blood flow
C. Tubular reabsorption
D. Tubular secretion

5-When we compared the clearance of a substance with the clearance of inulin, and the result was inulin clearance < substance clearance. That means the substance is :
A. only filtered not reabsorbed or secreted
B. Reabsorbed by nephron tubules
C. Secreted by nephron tubules

6-Substance that is completely reabsorbed from the tubules, clearance = zero:
A. PAH
B. Insulin
C. Glucose
D. Creatinine

7- If: $[P]_{inulin}$= 1mg/100ml , $[U]_{inulin}$= 125 mg /100ml , (UV) = 1 ml /min then, the clearance of inulin will be?
A.120 ml/min
B.125 ml/min
C.130 ml/min

8-If: $[U]_{PAH}$=27 mg/ml , (UV) =1.3 ml/min , $[AB]_{PAH}$=0.07 mg/ml, Then the Renal Plasma Flow will be?
A. 501 ml/ min
B. 610 ml/min
C. 1120 ml/min

1.B
2.A
3.D
4.B
5.C
6.C
7.B
8.A

MCQs

1- The clearance of X substance is zero. What's the best example of substance X?
Glucose

2- Mention tow important parameters that could be measured through their clearance?
*GFR *RPF

3- Clearance of PAH can estimate the renal 'plasma' flow, how is it possible to indicate the renal 'blood' flow?
considering the hematocrit

4- Urinary excretion rate can be measured by multiplying...?
U = Concenteration of substance in urine **& V** = Volume of urine excreted per mintue

5- Substance X is freely filtered and Rapidly and completely secreted. What's the best example of substance X?
Paraminohippuric Acid (PAH)

6- Mention an endogens substance that is used to measure the GFR?
Creatinine

7- Filtration fraction is the ration of ?
GFR to renal plasma flow

8- In what portion of the glucose titration curve, is the renal vein glucose concentration equal to renal artery concentration?

At all plasma glucose concentrations below threshold

9- When the clearance of PAH is used to measure effective RPF, is the measurement done at plasma concentration of PAH that are above or below T_m for secretion?

Below T_m (Hint: More fluid filtered out of glomerular capillaries leads to increased plasma protein concentration.)

10- If GFR is constant and there is an increase in urine flow, how does the plasma inulin concentration change :increased, decreased or unchanged?

Unchanged (Hint: if GFR in constant and urine flow rate increases, urine inulin concentration decreases.)

11-What are the units of glucose T_m ?

mg / min (or amount / time)

12- GFR is 120mL/min, the plasma concentration of X is 10mg/mL, the urine concentration of X is 100mg/mL and urine flow rate is 1mL/min. Assuming that X is freely filtered, is there net reabsorption or net secretion of X and what is the rate?

Net reabsorption, 1100mg/min

13- Which is highest clearance of PAH below T_m, clearance of glucose below threshold clearance of inulin? Clearance of PAH below T_m (Hint: Clearance of glucose below threshold is zero; clearance of inulin is GFR; clearance of PAH below T_m is RPF.)

THANK YOU FOR CHECKING OUR WORK!

BEST OF LUCK

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