MED439
KING SAUD UNIVERSITY

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PHYSIOLOGY

RENAL CLEARANCE

Black: in male AND female slides
Red : important
Pink: in female slides only
Blue: in male slides only
Green: Notes
Gray: extra information

Editing file

Important note: if you understand the equations you will understand the whole lecture.

Renal Clearance

Definition:
the **volume of plasma** that is completely cleared of a substance each minute.

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

$$C_x = (U_x \times V) / P_x$$

C_x = Renal clearance (**ml/min**)

$U_x \times V$ = excretion rate of substance X

U_x = Concentration of X in urine (mg/dL)

V = urine flow rate (ml/min)

P_x = concentration of X in plasma (mg/dL)

x= substance

• The importance of renal clearance:

<u>To quantify several aspects of renal functions:</u>

- rate of glomerular filtration
- rate of blood flow
- assess severity of renal damage
- tubular reabsorption
- tubular secretion of different substances

• Clearance Method :

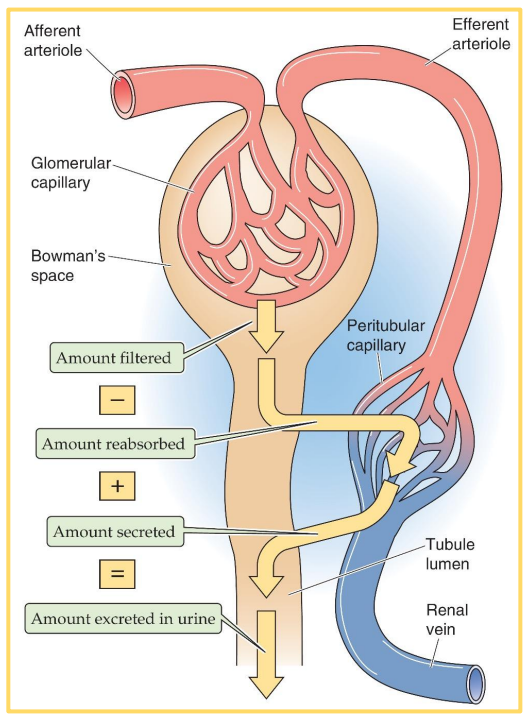
amount excreted = amount filtered – amount reabsorbed + amount secreted

let's compensate in the equation:

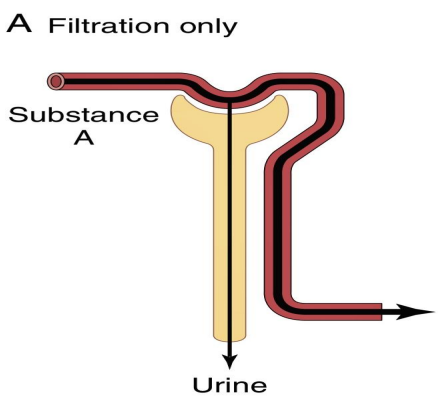
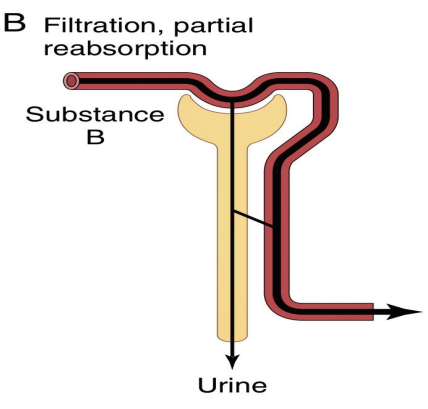
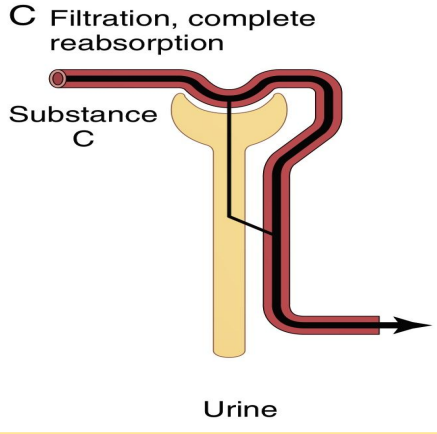
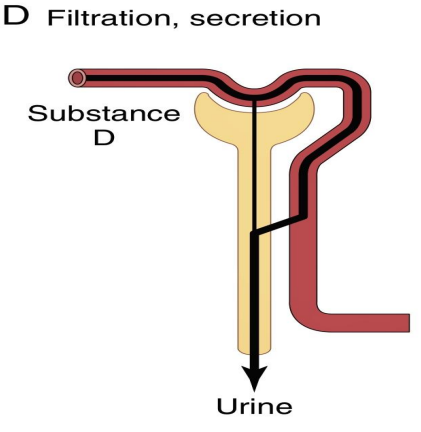
$$U_x \cdot V = GFR \cdot P_x \pm T_x$$

- Amount **excreted** per minute **(excretion rate)**
- Amount **filtered** per minute **(Filtered load)**
- tubular activity: - Reabsorption / + Secretion

For each substance in the plasma, a particular combination of filtration, reabsorption, and secretion occurs. The rate at which the substance is excreted in the urine depends on the relative rates of these three basic renal processes.



Renal handling of four hypothetical substances:

A Filtration only	B Filtration, partial reabsorption	C Filtration, complete reabsorption	D Filtration, secretion
			
is freely filtered by the glomerular capillaries but is **neither reabsorbed nor secreted.**	is freely filtered but is also **partly reabsorbed** from the tubules back into the blood.	is freely filtered but is not excreted into the urine because all the filtrate is **reabsorbed**	is freely filtered and is not reabsorbed but additional quantities are **secreted** from the peritubular capillary into the renal tubules.
Excretion rate = filtration rate Eg: creatinine, inulin	Excretion rate = filtration rate - reabsorption rate Eg: Na, urea	Amount excreted= 0 Eg: amino acids, glucose	Excretion rate = filtration rate + secretion rate Eg: PAHA

Clearance tests

- **endogenous substances**
  - creatinine
  - urea
  - uric acid
- **exogenous substances**
  - para-aminohippuric acid (PAHA)
  - inulin
  - diodrast (di-iodo pyridone acetic acid)

Criteria of a substance used for GFR measurement:

01 freely filtered

02 not secreted by tubular cells

03 should not be metabolized

04 should not be toxic

05 not reabsorbed by tubular cells

06 easily measurable

examples

Creatinine (endogenous):
by-product of skeletal muscle metabolism

Inulin (exogenous):
It is a polysaccharide with a molecular weight of about 5200 and it fits all the above requirements. Used to determine GFR and therefore nephron function

Inulin clearance

- if Plasma conc. of inulin = 1mg/100ml
- Urinary conc of Inulin = 125/120 mg/100ml
- Urine flow (UV) = 1 ml /min then, the clearance of inulin will be?

Calculation:

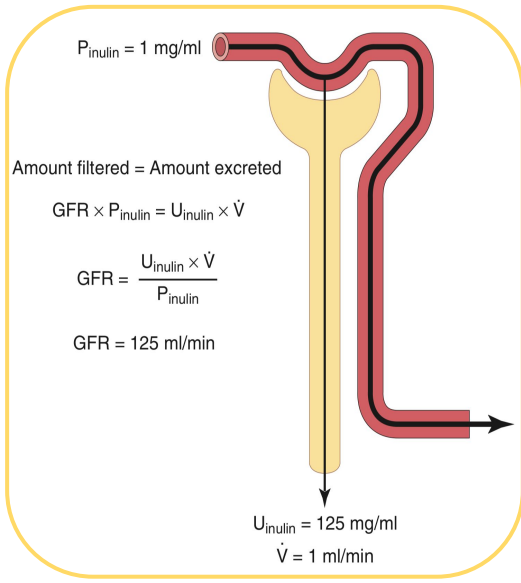
Amount filtered per minute = Amount excreted per minute

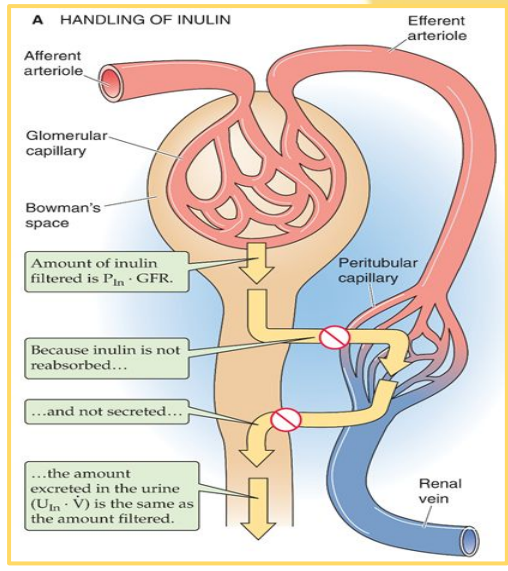
$$GFR \cdot [P]_{Inulin} = [U]_{Inulin} \cdot \dot{V}$$

$$Cl_{Inulin} = GFR = \frac{[U]_{Inulin} \cdot \dot{V}}{[P]_{Inulin}} = \frac{(125/120) \times 1}{1}$$

- The Answer: C = (125/120) ml/min = GFR

It could be 120 or 125 normally and both numbers mentioned in the slides



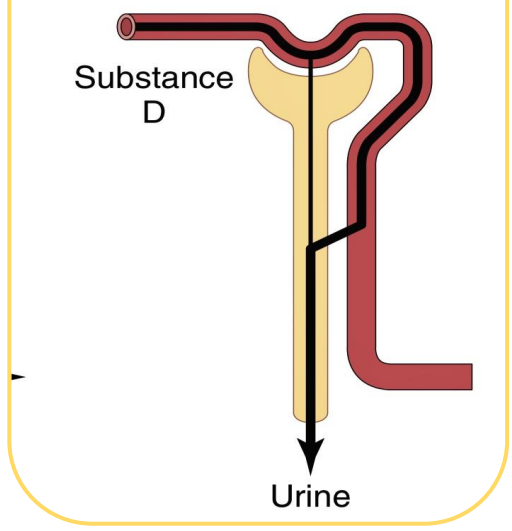


Inulin A plant product that is filtered but not reabsorbed or secreted Used to determine GFR and therefore nephron function.

Remember that the kidney handles Inulin as substance A from the previous slide.
Inulin, which is not produced in the body, must be administered intravenously to a patient to measure GFR.

Renal blood flow (RBF)

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** and **not** that **remains unfiltered (RBF)** 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.

- the substance we will be using for RBF is PAHA (Para aminohippuric acid)
- To measure renal blood flow we will have to measure renal plasma flow first and then from the hematocrit value we calculate the actual blood flow. more details on next slides

NOTE THAT if you want the RBF (Renal Blood Flow) value you will need to get the RPF (Renal Plasma Flow) first then we divide it by (1 – Hct%) that will get us RBF

- **Measurement of renal plasma flow then using it to get RBF :**

$$RPF = \frac{(UPAH \times V)}{P_{PAH}}$$

$$RBF = \frac{RPF}{(1 - Hct\%)}$$

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

01 freely filtered

02 rapidly and completely secreted by the renal tubular cells

03 easily measurable

04 not toxic

05 not reabsorbed

Para-aminohippuric acid (PAH):
is freely filtered and secreted and is almost (90%) **completely cleared** from the renal plasma.
Therefore: **ERPF= Clearance PAH** (ERPF means effecting renal plasma flow or you can say Renal plasma flow)

- **PAH clearance**

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

- **Conc. of PAH in urine**= 25.5 mg/ml
- **Urine flow**= 1.1 ml/min
- **Conc of PAH in arterial blood** = 0.05 mg/ml
- The Answer: **CPAH** or **Renal Plasma Flow** = (25.5 x 1.1)/0.05 = 560 ML/ min

using the same equation mentioned at the top of this page we use the RPF which is 560ml/min we can get the RBF

- Let's say the hematocrit is 45%, then **renal blood flow** will be:

ضربوا البسط والمقام بـ١٠٠ بس لتسهيل عملية القسمة إذا كانت يدوية

(560 x 100)/(100-45)= 1018 ml/min

You can use this equation
To calculate RBF from RPF

$$RBF = \frac{RPF}{(1 - Hct\%)} \longrightarrow RBF = \frac{560}{1-(0.45)} = \textbf{1018 ml/min}$$

NOTE: usually the Hct equals 0.45 but the values might change also note the variables if it was given in L you turn it to mL and so on

• Renal Clearance gives an indication of kidneys function.

Renal clearance and kidneys function

Clearance can also be used to determine **renal handling of a substance.** (how the nephron handles a substance filtered into it).

أي أن الكلية ما تتعامل مع كل substances بنفس الطريقة

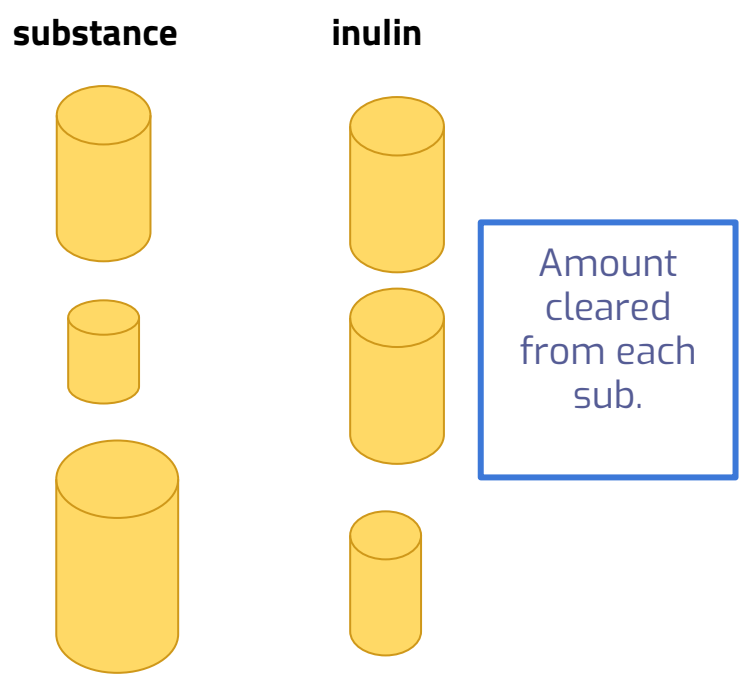
In this method the clearance for inulin or creatinine is calculated and then compared with the clearance of the substance being investigated.

• Comparison of clearance of a substance with clearance of inulin

01 if the clearance is = inulin clearance;
only filtered not reabsorbed or secreted

02 if the clearance is < inulin clearance;
reabsorbed by nephron tubules

03 if the clearance is > inulin clearance;
secreted by nephron tubules



• Calculation of tubular reabsorption or secretion from renal clearance

Reabsorption

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

02 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.**

Secretion

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

Useful video :
about renal clearances

Example: Given the following information for a freely filterable substance

GFR = 120 mL/min
Plasma concentration = 3 mg/mL
Urine flow rate = 2 mL/min
Urine concentration = 10 mg/mL
we can conclude that:
a) the kidney tubules reabsorbed 340 mg/min
b) the kidney tubules reabsorbed 200 mg/min
c) the kidney tubules secreted 200 mg/min
d) the kidney tubules secreted 340 mg/min
e) Net transport is 0 mg/min

Calculation:

- Amount Filtered per minute = (GFR X [Sub]plasma)
= 120 ml/min X 3 mg/ml = 360 mg/min

- Amount excreted per minute = ([substance]urine X Urine flow rate)
= 2 ml/min X 10 mg/ml = 20 mg/min

Amount Filtered per minute > Amount excreted per minute

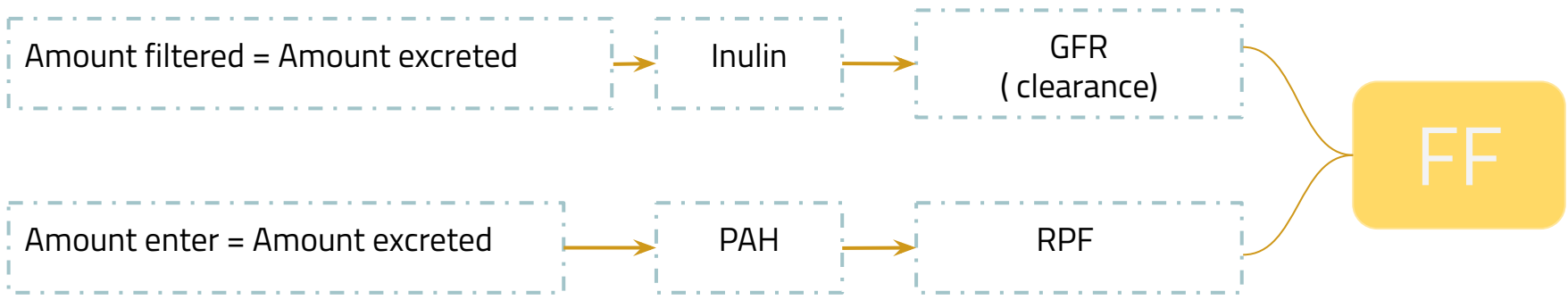
Amount transported per minute = Filtered – Excreted

= 360 - 20 = 340 mg/min

Filtration fraction:

It is the ratio of GFR to renal plasma flow
GFR/RPF

Summary:



Summary

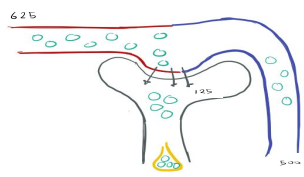
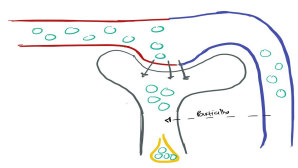
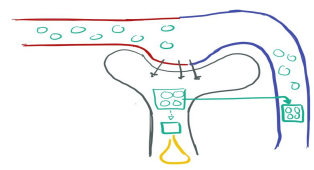
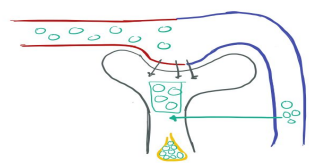
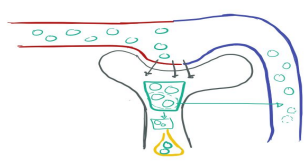
extra information found in the notes of the lecture pp presentation.

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.

Clearance of a solute is the volume of plasma (per unit time) needed to supply the amount of solute that appears in the urine. This CLEARANCE method uses the amount balance of an I.V. injected test substance such as inulin.

Summary of important points:
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 period (usually per minute).

If a substance is not excreted then the renal clearance is zero. If a substance could be 100% removed from plasma, then the clearance would be the entire volume of plasma processed by the kidneys (= renal plasma flow, ml/min !!).
Para-amino-hipuric acid (PAH) is almost entirely removed from plasma by the kidneys (85-90%), so the clearance of PAH is almost equal to RPF (actually 85-90% of RPF). Similarly, if a substance (like inulin) is freely filtered, but not reabsorbed or secreted, then the amount excreted (removed) = the amount filtered. Thus the clearance of inulin is equal to the volume filtered, the glomerular filtration rate (GFR).

Example of substance	Renal mechanism	Clearance ml/min	Importance	
Inulin	-No reabsorption -No secretion -amount filtered = amount excreted	125	Measure GFR	
Creatinine	-Partially secreted	↑ 125	Measure GFR	
Glucose	-Completer reabsorption	Zero		
PAHA	-Completely secreted -amount excreted = amount filtered +amount secreted	625	Measure RPF then we can measure RBF	
k , urea	-Partially reabsorption	↓125		

Summary here Dr.Manan Notes

MCQ & SAQ

Q1: what does the concentration of a substance in urine multiplied by urine flow rate represent?

A. Filtration rate
B. Reabsorption rate
C. Secretion rate
D. Excretion rate

Q2: which is NOT a criteria for a substance used for GFR measurement?

A. Freely secreted
B. Not reabsorbed
C. Not toxic
D. Easily measured

Q3: which clearance equation represents a substance that is freely filtered and is not reabsorbed but additional quantities are secreted

A. Excretion = filtration - reabsorption
B. Excretion= filtration + secretion
C. Excretion = secretion - reabsorption
D. Excretion = filtration - reabsorption + secretion

Q4: If the clearance of a substance is less than inulin clearance then what's true?

A. substance was reabsorbed
B. sub. was filtered and reabsorbed
C. sub. got secreted
D. Non of this

Q5: what does FF depends on.

A. Inversely proportional to GFR
B. Inversely Proportional to RPF
C. Inversely for BOTH
D. Proportion of Both

Q6: Which one of the following provides an estimation of the GFR?

A. Inulin
B. PAHA
C. Manulin
D. Non

answer key:
1: D
2: A
3:B
4: A
5: B
6: A

1- GFR is 120 mL/min, the plasma concentration of X is 10 mg/mL, the urine concentration of X is 100 mg/mL, and urine flow rate is 1.0 mL/min. Assuming that X is freely filtered, is there net reabsorption or net secretion of X, and what is the rate?

2- Calculate clearance for substance X (CX) using the data: Urine flow (V) = 1.2 mL/min Urine concentration of X (U x) = 40 mg/mL Plasma concentration of X (P x) = 0.6 mg/mL

3-question in slide 7

4-Why we use para aminohippuric acid (PAHA) for RPF?

A1: net reabsorption. 1100 mg/min -Linda

A2: Cx= 40x1.2/0.6 = 80 mL/min -Lippincott flashcards

A4: Freely filtered,rapidly and completely secreted by the renal tubular cells,Easily measurable not toxic not reabsorbed.

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