PHYSIOLOGY TEAM 432

LECTURE : 3

Renal Blood flow and Renal Clearance

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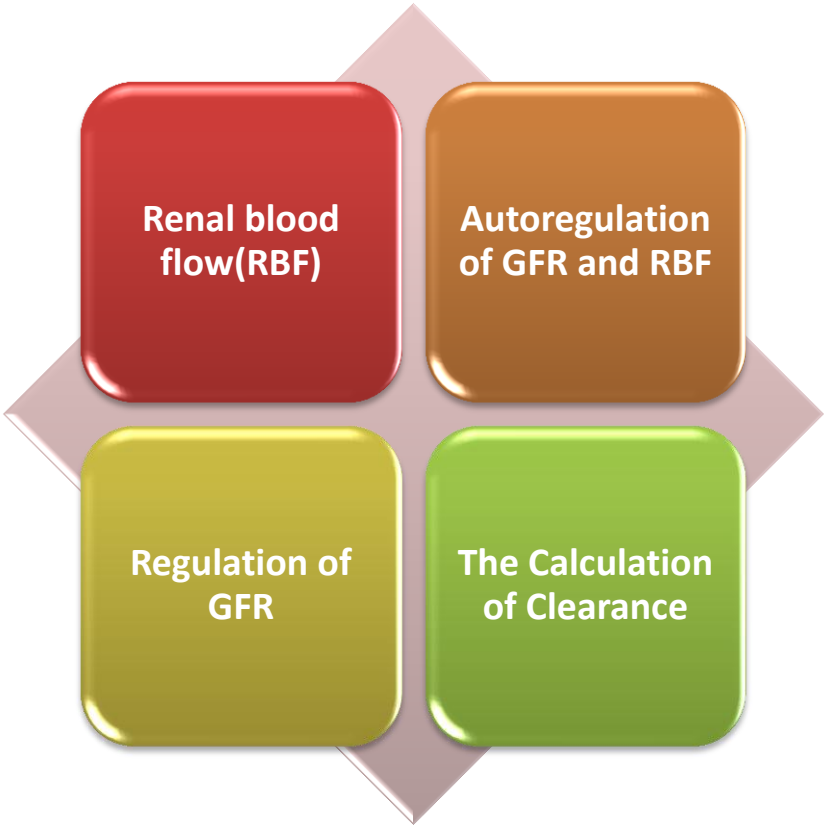
OBJECTIVES

At the end of this lecture student should be able to describe:



MIND MAP

RBF

- PAH CLEARANCE
- CALCULATION OF RBF
- AUTOREGULATION OF :
  - RBF
  - GFR IN 3 METHODS:
    1-hormonal regulation.
    2-Myogenic autoregulation.
    3-Autonomic Regulation (extrinsic).

clearance

- Inulin clearance & GFR
- Creatinine clearance &GFR
- Glucose & urea clearance

Renal Blood Flow (RBF):

In average adult:	• **RBF = 1.1 L/min.**
Para aminohippuric acid (PAH):	• **It is an organic acid.** • **And used for measurement of RBF (PAH is approximately equivalent to RBF).**
In one renal circulation/min:	• **PAH is almost completely removed from the plasma & excreted in urine (removed by filtration &secretion).**
PAH clearance	• **= volume of plasma cleared from PAH/min = RPF/min.**

RPF: renal plasma flow

Use of PAH Clearance to Estimate RPF:

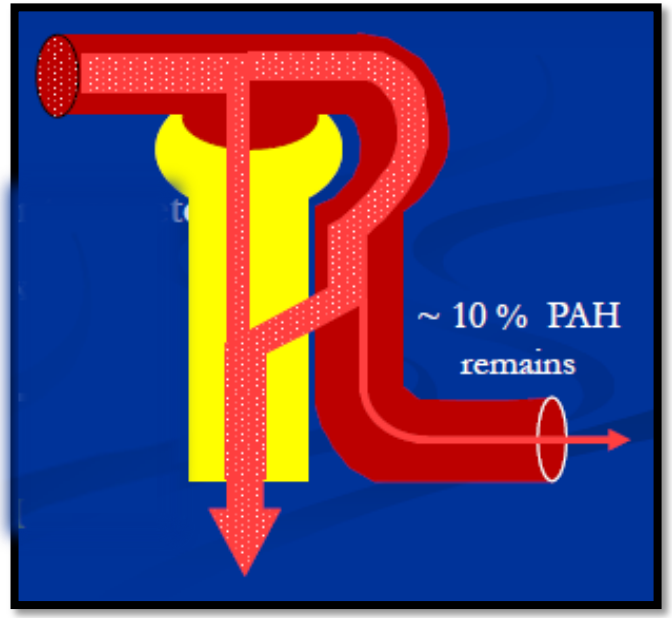
- PAH is **freely filtered and secreted** and is almost **completely cleared** from the renal plasma.

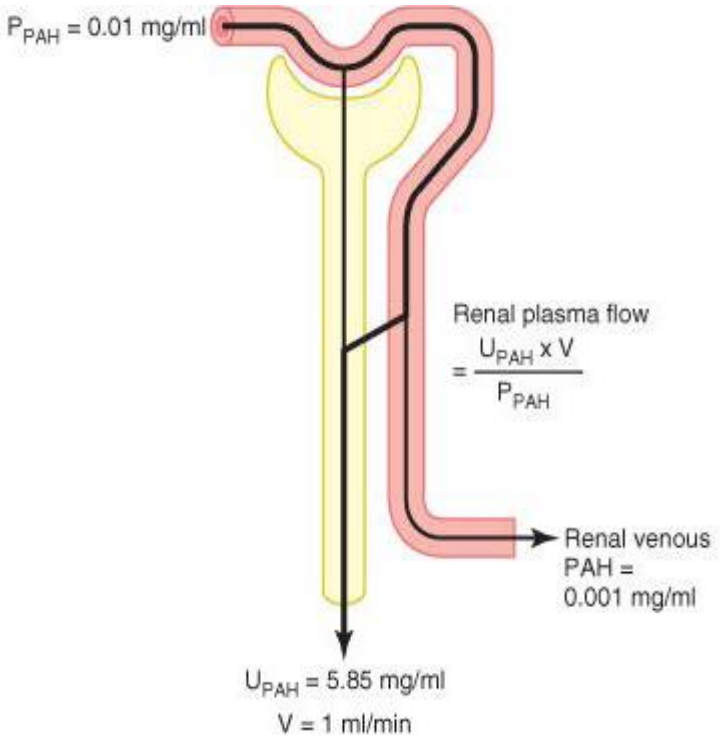
1- Amount enter kidney = RPF X $P_{(PAH)}$

2- Amount entered ≈ Amount excreted

3- Effective RPF (ERPF) X $P_{(PAH)}$ = $U_{(PAH)}$ X V.

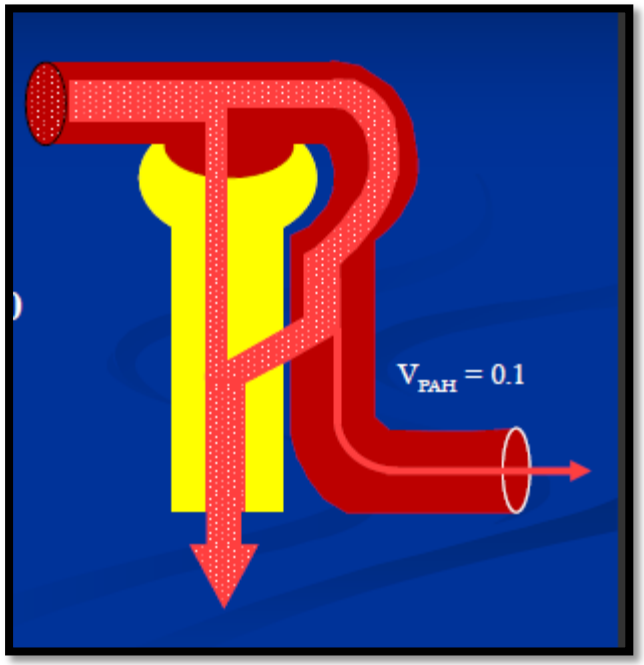
❑ ERPF = Clearance PAH.





To calculate actual RPF, one must correct for incomplete extraction of PAH (extraction ratio)

- E (PAH) = 0.9
- PAH is 90% extracted.
- Actual RPF (ARPF) = (ERPF \ 90) X 100
- RBF = (ARPF \ 55) X 100



Extraction ratio (EPAH) is calculated as the difference between the renal arterial PAH (PPAH) and renal venous PAH the (VPAH) concentrations, divided by renal arterial PAH concentration (90%)

Calculation of Renal Blood Flow:

Definition of Renal Plasma Flow (RPF)	Percentage	Formula (Equation)
• The amount of a PAH excreted per unit time.	• **~ 90%** of PAH in arterial blood **is removed by the kidney (10% remains in blood).**	• **Clearance of PAH** = $\frac{[U]PAH \times Vmin}{[P]PAH}$ = **585** ml/min = **effective renal plasma flow (ERPF) [which is the 90% of cleared PAH].**

الناتج بالتعويض بالقيم الموجوده في الصورة في السلايد الخامس

- **Actual RPF** = ERPF / extraction ratio
  = (585 / 90) X 100 = 650 ml/min.
- **Calculate the RBF**:

1. = (650 / 55) X 100 = 1.2 L/min.
2. = $\frac{\text{RAP} - \text{RVP}}{\text{Total renal vascular pressure}}$

OR

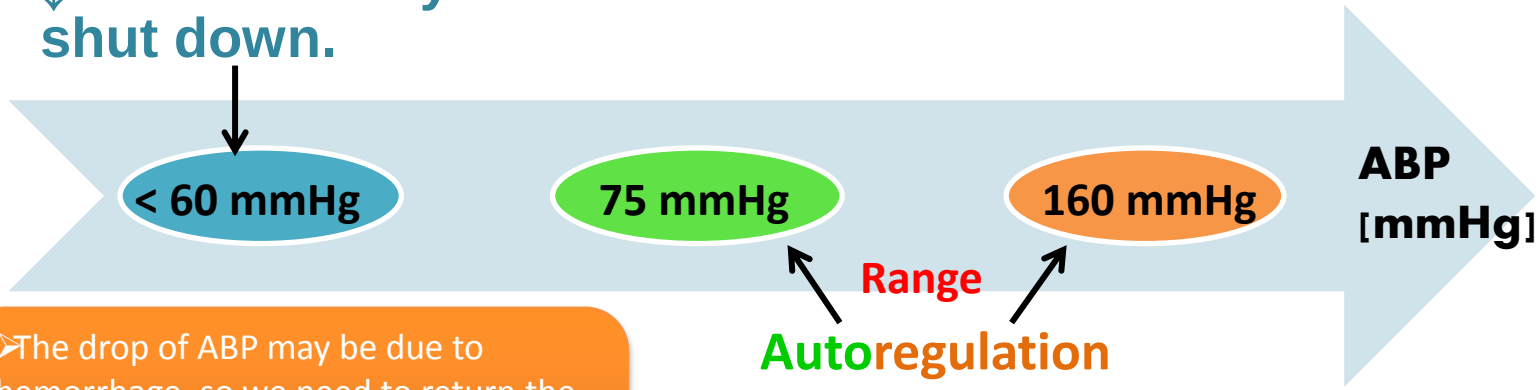
Blood contains 55% of plasma

Autoregulation:

Its range is between 75-160 mmHg ABP

➢It is a feedback mechanism to keep **RBF & GFR relatively constant** despite marked changes in ABP.

↓ GFR & kidney shut down.



➢The drop of ABP may be due to hemorrhage, so we need to return the blood volume back to normal as soon as possible to avoid the shut down of the kidney thus acute renal failure.

Autoregulation of GFR:

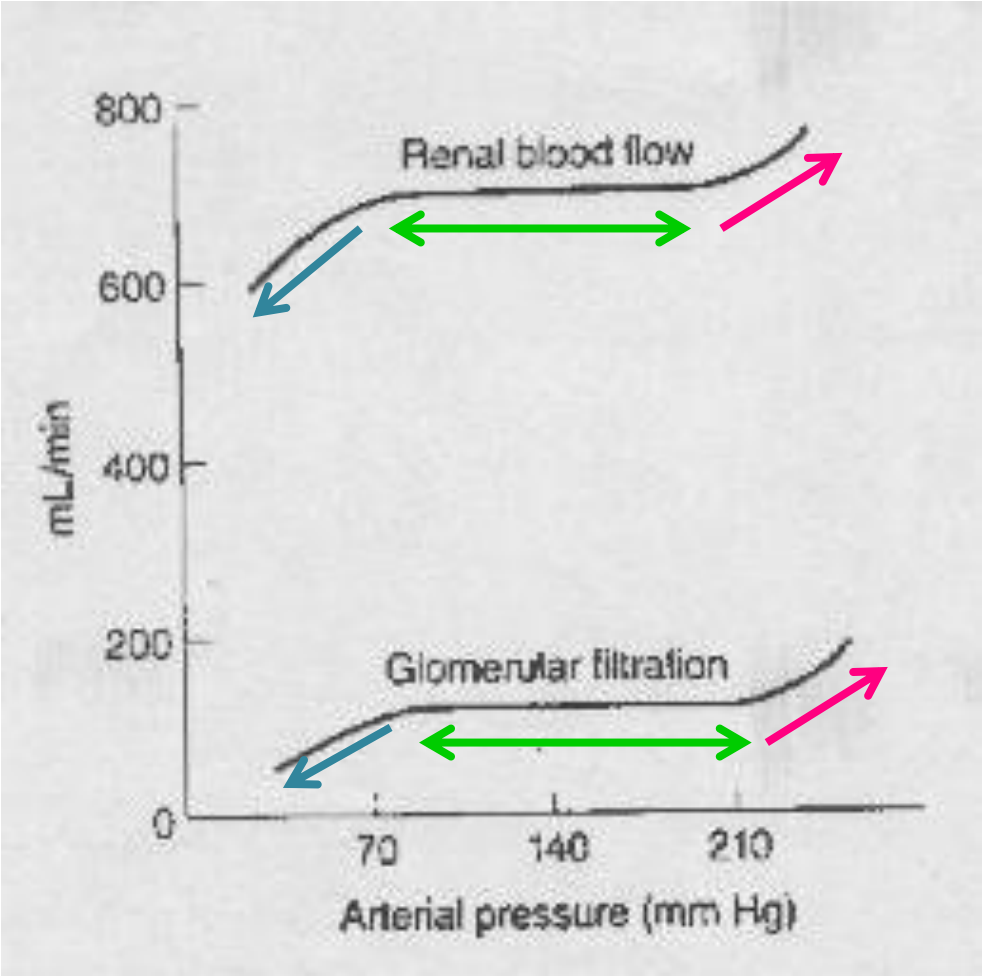
➢Changes diameters of **afferent**, **efferent** arterioles, & **glomerular capillaries**.
➢↑ BP → vasoconstriction of **afferent arteriole**.
➢↓ BP → dilation of **afferent arteriole** & dilation **glomerular capillaries** BUT constriction in **efferent arteriole**.

Autoregulation of RBF & GFR:

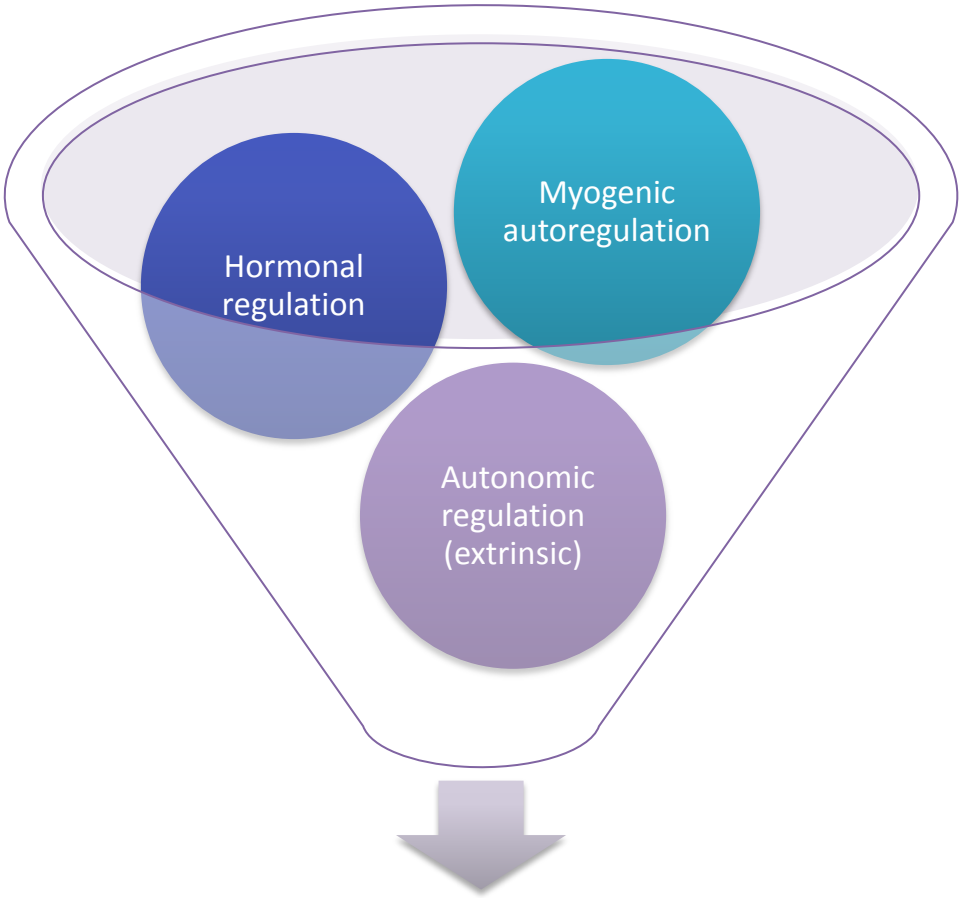
Note:

1. The **range of ABP** that makes **GFR & RBF relatively constant.**
2. The **drop of ABP** which leads **to ↓ GFR & RBF.**
3. The **elevation of ABP** & **↑ GFR & RBF.**

❖ **The drop of ABP affects more on kidney than elevation.**



Autoregulation of GFR by the kidney in three methods.



Autoregulation of GFR

1. Myogenic autoregulation

- The ability of blood vessels to resist stretching.
- ↑ hydrostatic Pressure → stretching vessels wall → reflex contraction.

Ex. Afferent:
↑BP → more blood to the kidney → afferent dilates and immediately constricts to prevent the high BP from going to the glomeruli which leads to ↑ GFR

2. Hormonal Regulation

" Next slides "

Tubuloglomerular feedback

Renin-angiotensin Aldosterone

Other Hormones

3. Autonomic Regulation of GFR

- In normal condition Sympathetic NS has *little influence* on GFR.

↓ BP (hemorrhage) → ↑ sympathetic → vasoconstriction of **renal artery** →↓RBF → vasoconstriction of **afferent** →↓ GFR

TO DIVERT BLOOD TO VITAL ORGANS

Sympathetic has little influence on GFR in **normal conditions** [**autoregulation** is taking the upper hand; **dilation of afferent arteriole**] **unless** there is a life-threatening condition! In that condition it will **constrict** the vessels in kidneys by **SNS** because we don't need to make urine, we need O2 to supply the brain!

Tubuloglomerular feedback

The slower the more Na will be reabsorbed

↓GFR → Slow flow *of filtration* → ↑NaCl reabsorption → ↓NaCl at macula densa:

Senses the level of Na

1.
- ↑ Renin
- ↑ Angiotensin II
- Efferent vasoconstriction
- ↑ GFR

2.
- Afferent dilation
- ↑ GFR

Unknown mechanism!

Renin-angiotensin Aldosterone

Renin is released into plasma in the **following conditions**:

- Low ECF Na or low ECV
- ↑ Sympathetic (hypotension)
- ↓ Afferent pressure

Angiotensinogen → By Renin → Angiotensin I → By ACE → Angiotensin II

Angiotensin II acts on adrenal cortex

Aldosterone secretion

↑ Na reabsorption in distal & collecting duct of nephron

◆ ↑ H and K secretion in exchange for Na.

The more you reabsorbed Na the more H and K will be secreted.

Other Hormonal Regulation of GFR

1. Adrenaline, noradrenaline → **afferent** vasoconstriction → ↓ GFR
2. Angiotensin II → **efferent** Vasoconstriction → ↑ GFR
3. Prostaglandins and bradykinin → **afferent** vasodilator → ↑ GFR

Clearance

- Volume of plasma completely cleared of a substance by both kidneys per unit time.
- Clearance equation $C = \frac{[U]_s \times V/min}{[P]_s} = ml/min$
- Renal clearance for different substances various between 0-600 ml/min.

Why 0-600 ? Because the maximum plasma that inters the kidney is about 600 ml/min.

Inulin clearance & GFR

- 120-125 ml/min.
- As inulin is:

1. freely filtered.
2. not reabsorbed or secreted.

Inulin clearance = GFR

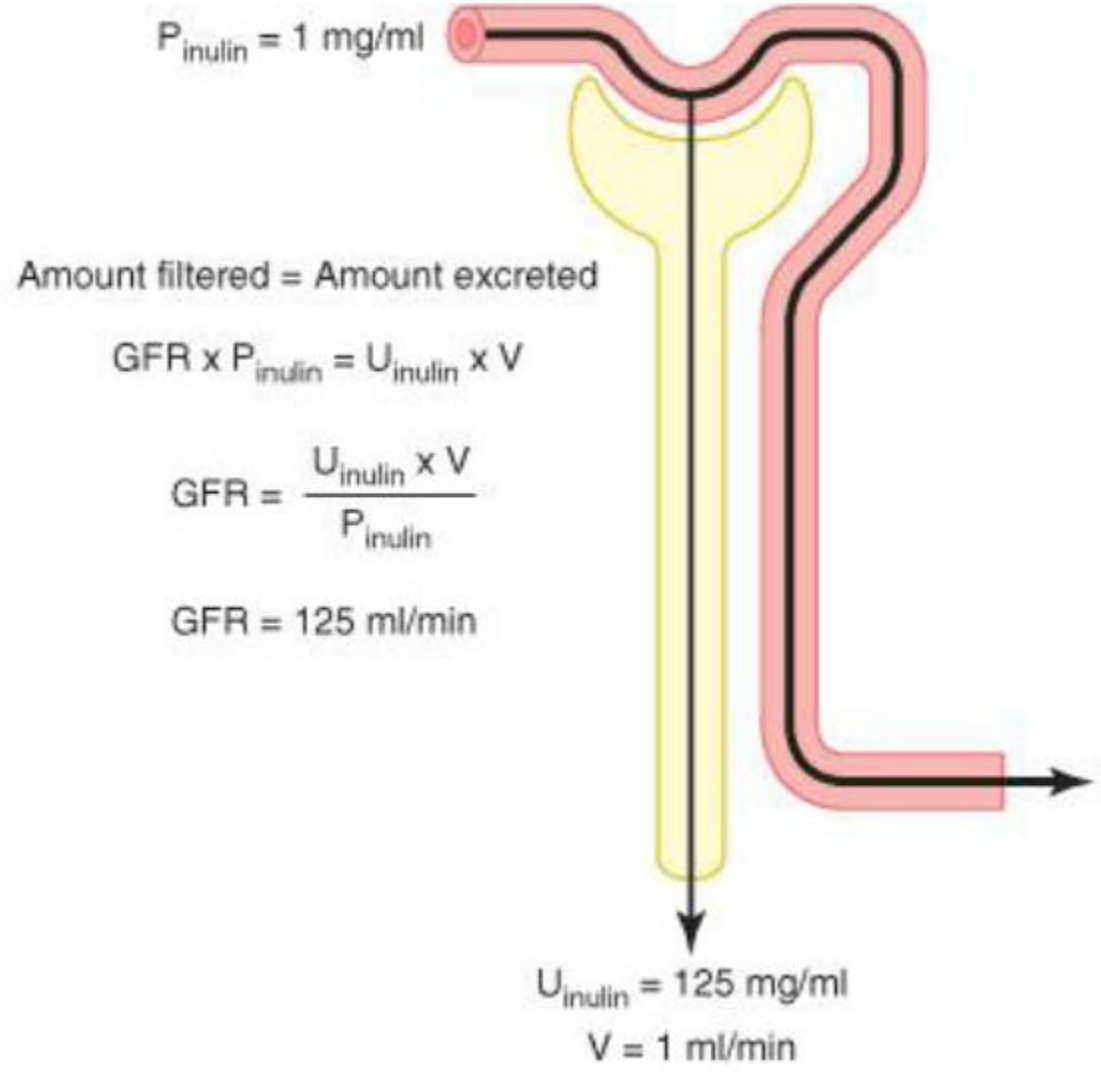
Creatinine clearance &GFR

- Creatinine is an **endogenous substance** used routinely to measure GFR.
- **Completely filtered,** but **secreted** in small quantity.
- Inverse relationship between GFR & plasma creatinine.

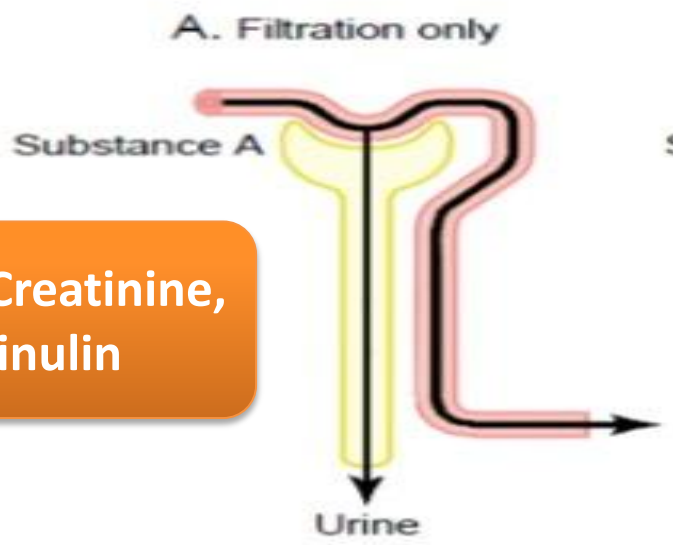
Glucose & urea clearance

- glucose clearance = **zero**.
- **Filtered, completely absorbed**, no glucose in urine.
- $[U]_g \times V_{min} =$ zero
- Urea clearance = 60 ml/min, urea **filtered, partially reabsorbed**

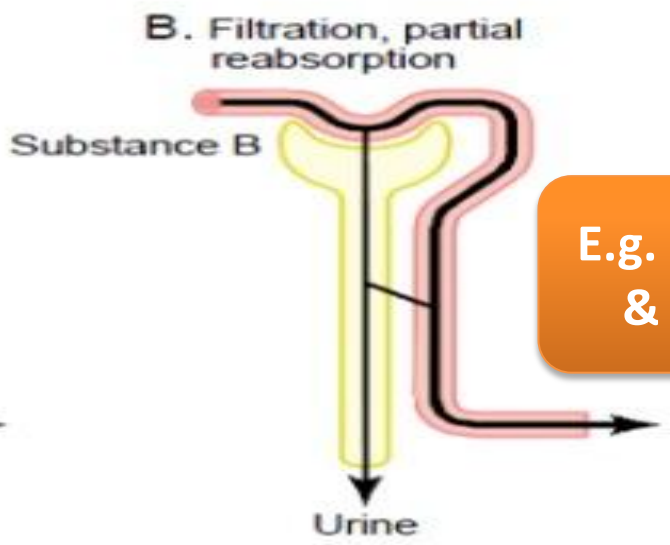
This diagram shows inulin which is freely filtered and not reabsorbed nor secreted



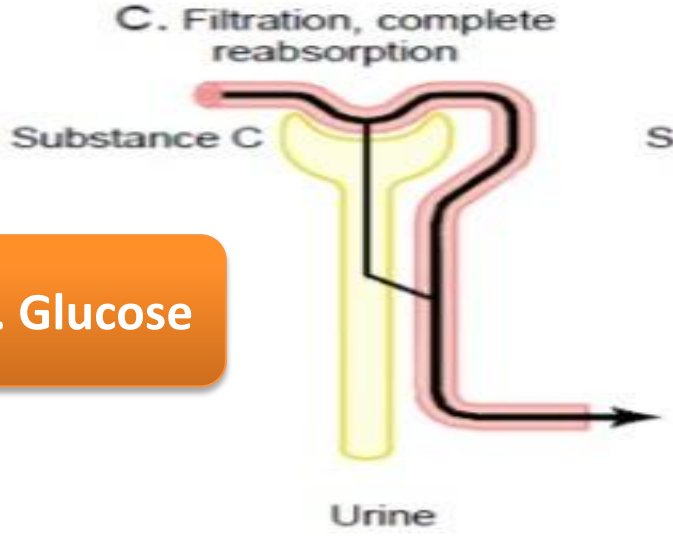
The diagram shows the renal handling of four hypothetical substances (A, B, C, & D).



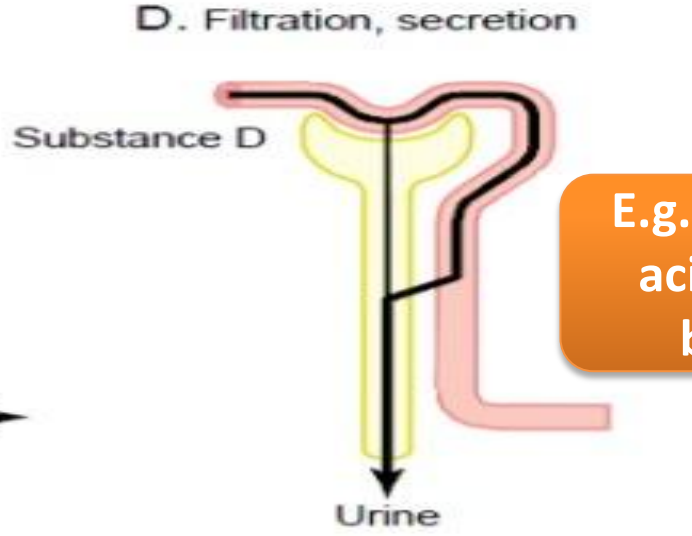
E.g. Creatinine, inulin



E.g. Urea, Na & Cl ions

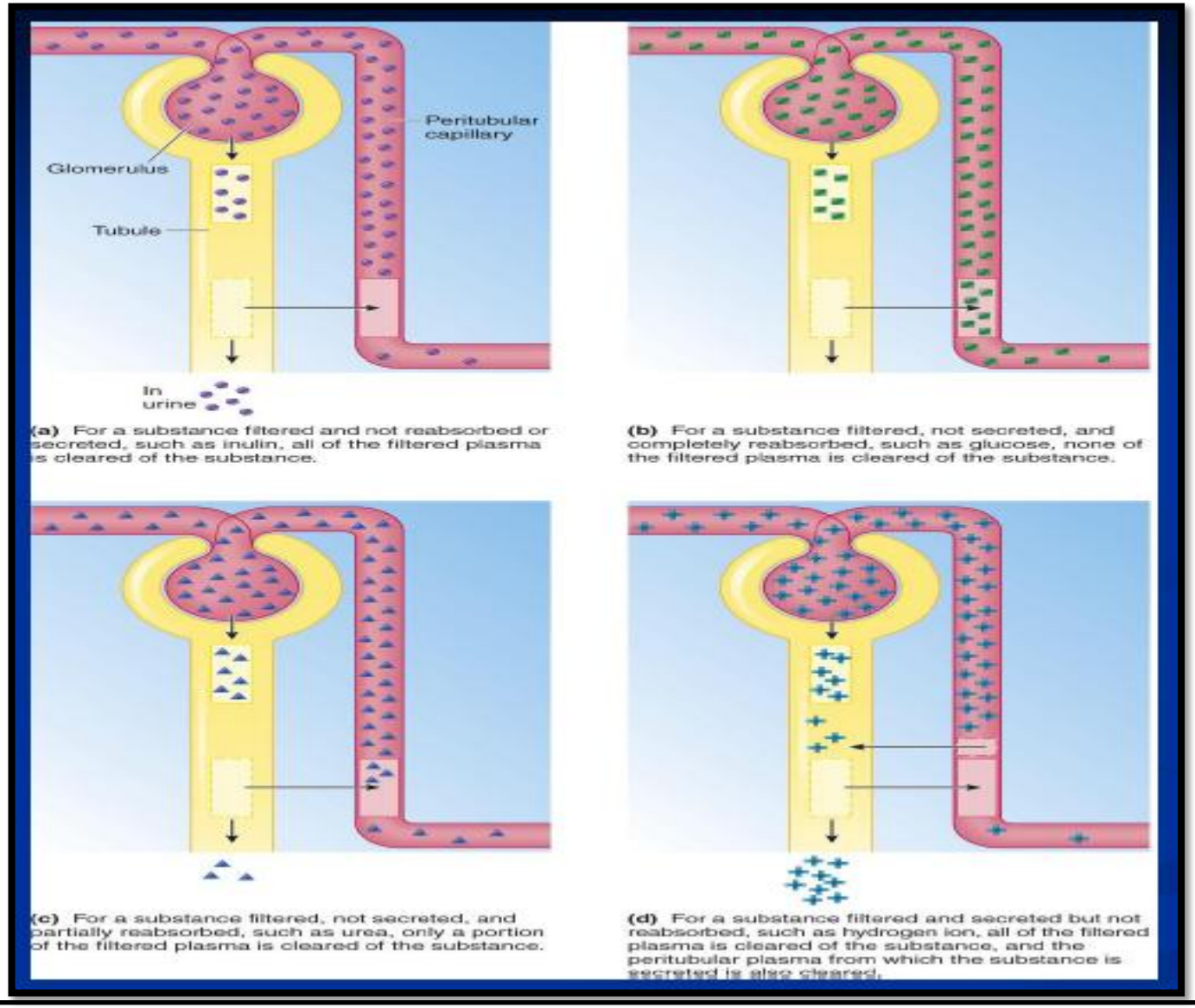


E.g. Glucose



E.g. Organic acids and bases

Another diagram shows the renal handling of four hypothetical substances (A, B, C, & D).



Inulin Clearance

VS.

Clearance of other substance (S)

1. C**x** = inulin clearance → Substance x is **filtered** but ***not*** **absorbed or secreted**.

2. C**y** < inulin clearance → Substance y is **filtered and partially absorbed**.

3. C**z** > inulin clearance → Substance z is **filtered and secreted**.

Sample Problem

Q: In a 24hr period, 1.44 L of urine is collected from a man receiving an infusion of inulin.

- **In his urine, the [inulin] is 150mg/ml, and [Na+] is 200 mEq/L.**
- **In his plasma, the [inulin] is 1mg/mL, and the [Na+] is 140 mEq/L.**

What is the clearance ratio for Na+, and what is the significance of its value?

Try to solve it then check your answer in the next slide

Answer

The clearance ratio for Na+ is the clearance of Na+ relative to the clearance of inulin. The clearance equation for any substance is C = [U] × V̇/[P]. All of the values needed are provided in the description, although urine flow rate (V̇) must be calculated.

The calculated clearance ratio for Na+ of 0.01 (or 1%) provides a great deal of information about the renal handling of Na+. Since Na+ is freely filtered across the glomerular capillaries, it also must be extensively reabsorbed by the renal tubule, making its clearance much less than the clearance of inulin. The clearance ratio of 0.01 means that only 1% of the filtered Na+ is excreted. Stated differently, 99% of the filtered Na+ must have been reabsorbed.

$$\dot{V} = \text{Urine volume/time}$$
$$= 1.44\ \text{L/24 hr}$$
$$= 1440\ \text{mL/1440 min}$$
$$= 1.0\ \text{mL/min}$$
$$C_{Na^+} = \frac{[U]_{Na^+} \times \dot{V}}{[P]_{Na^+}}$$
$$= \frac{200\ \text{mEq/L} \times 1\ \text{mL/min}}{140\ \text{mEq/L}}$$
$$= 1.43\ \text{mL/min}$$
$$C_{inulin} = \frac{[U]_{inulin} \times \dot{V}}{[P]_{inulin}}$$
$$= \frac{150\ \text{mg/mL} \times 1\ \text{mL/min}}{1\ \text{mg/mL}}$$
$$= 150\ \text{mL/min}$$
$$\frac{C_{Na^+}}{C_{inulin}} = \frac{1.43\ \text{mL/min}}{150\ \text{mL/min}}$$
$$= 0.01 \text{ or } 1\%$$

SUMMARY

1- PAH : used for measurement of RBF.

-PAH clearance= volume of plasma cleared from PHA/min = RPF/min.

2-Calculation of renal blood flow:

CPAH = UPAH x V/ PPAH=ERPF

Actual Renal Plasma Flow = ERPF/ Extraction Ratio

RBF = (ARPF \ 55) X 100

3.Autoregulation: It is a feedback mechanism to keep **RBF & GFR relatively constant** despite marked changes in ABP.

- Myogenic: The ability of blood vessels to resist stretching.
- Hormonal regulation (tubuloglomerular & renin-angiotensin).(next slide)
- Autonomic regulation: In normal condition Sympathetic NS has *little influence* on GFR.

4.Clearance: FOUR POSSIBILITIES:

1. **Freely filtered – Not Reabsorbed – Not Secreted .. Ex: inulin.**
2. **Freely filtered – All Reabsorbed – Not Secreted .. Ex: Glucose.**
3. **Freely filtered – Partially Reabsorbed – Not Secreted .. Ex: urea.**
4. **Freely filtered – Not Reabsorbed –Secreted .. Ex: hydrogen ion.**

SUMMARY

Table 26-4 Hormones and Autacoids That Influence Glomerular Filtration Rate (GFR)

Hormone or Autacoid	Effect on GFR
Norepinephrine	↓
Epinephrine	↓
Endothelin	↓
Angiotensin II	↔ (prevents ↓)
Endothelial-derived nitric oxide	↑
Prostaglandins	↑

SUMMARY

From 431

Indicate wither in of the following factors would (A) increase (D) decrease the GFR:

factors	A/D
1.Tubuloglomerular feedback response to decreased salt delivery to the distal tubule	A
2.Affernt arteriole vasoconstriction	D
3.A dramatic fall in arterial pressure following sever hemorrhage (<80 mmHg)	D
4.A fall in plasma protein concentration resulting from loss of these proteins from a large burned surface of skin	A
5.Contraction of podocyte	D
6.Contraction of mesengial cells	D
7.A rise in bowman's capsule pressure resulting from ureteral obstruction by kidney stone	D
8.Myogenic response of an afferent arteriole stretched as a result of an increased driving blood pressure	D
9.Increase in sympathetic activity to the afferent arterioles	D

SUMMARY

Important questions from Dr. Sitelbanat:

Q1: How to find RBF?

By finding the clearance of **PAH**, then write the related equations & follow the steps.

Q2: How to find GFR?

By finding the clearance of **inulin**, then write the related equations & follow the steps.

Q3: Glucose clearance = 0, WHY?

Because it's completely reabsorbed.

U X V = 0 indicating no glucose in urine [U = 0].

Q4: Urea clearance = 45 – 60 % WHY?

Because it's partially reabsorbed.

THE END

If there are any problems or suggestions
Feel free to contact:

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THANK YOU

Actions speak louder than Words