Renal Block

Physiology Team

3rd Lecture

Renal clearance

This Lecture is Done By:

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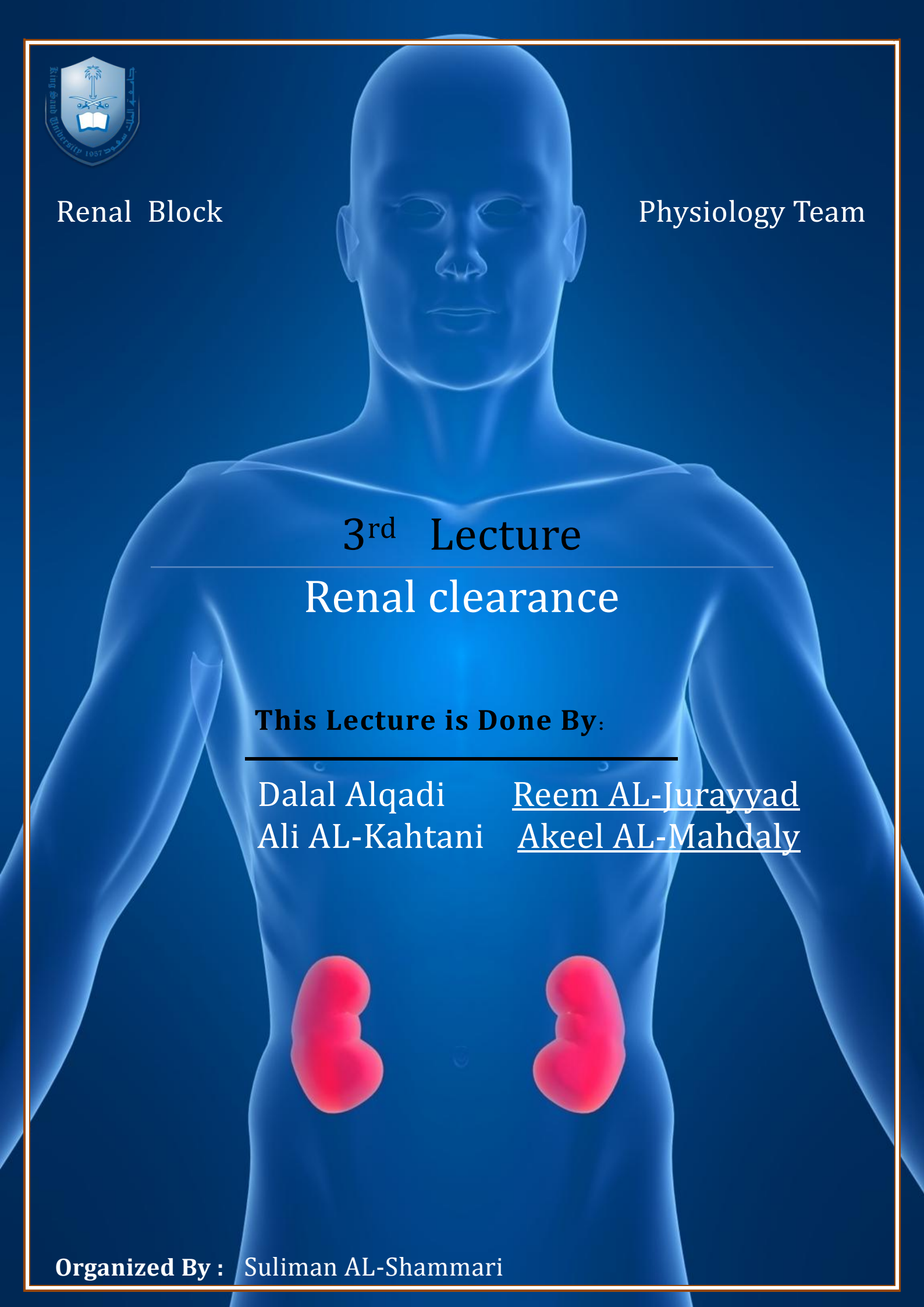

Organized By : Suliman AL-Shammari

●**In average adult renal blood flow** to both kidneys = 1.1l/min (or RBF= 22-25% of cardiac output) which is considered high compared to their size.

●**To measure RBF: an organic acid** (containing carbon) which is called paraaminohippurate acid PAH is used.

●**the reason why PAH was chosen for measuring RBF** is that In one renal circulation/min PAH is almost completely removed from the plasma & excreted in urine (i.e. about 90% of PAH is removed by the kidney in one renal circulation).

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$$\textbf{Clearance of PAH} = \frac{[U]PAH \times V\ min}{[P]PAH} = 630ml/min = RPF\ (renal\ plasma\ flow)$$

U: urine PAH P: plasma PAH V: urine volume
Clearance of PAH means excretion of it.

●**renal blood flow (RBF) =** plasma flow / plasma volume ×100
=700/55 × 100= 1.2 l/min

●**Actual renal <u>plasma</u> flow (RPF) =** ERPF/ extraction ratio
= 630 / 90 * 100 = 700ml/min

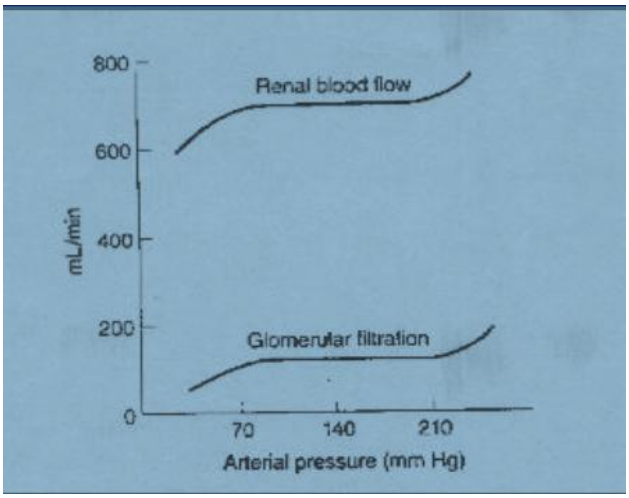
• $RBF = \frac{RAP - RVP}{\text{Total Renal vascular pressure}}$ (the doctor said it's not imp.)

Auto-regulation:-

Feedback mechanism to keep RBF and GFR relatively constant even if marked changes in ABP occurred, it can perform regulation if the pressure is still within 75-160 mmHg ABP. However if BP drops to 60 mmHg → ↓ blood flow to glomeruli → ↓ GFR ➔ kidneys shut down (acute renal injury).
And if BP raises to more than 210 mmHg → damage GFR ➔ leak of proteins in urine.

Changes in diameter of afferent, efferent and glomerular capillaries:-

- drop pressure results in dilation of afferent arteriole, dilation of glomerular capillaries and constriction of efferent arteriole, the mechanism is not known but it results in ↑ GFR (notice that the drop in pressure must not decrease more than 60, otherwise GFR will ↓).
- Rises in pressure results in constriction of afferent arteriole only.



GFR & RBF remain constant in range of 70 – 210 mmHg

GFR regulation :

There are 3 mechanisms control GFR :

1- Renal autoregulation
2- Neural control
3- Rennin-angiotesin system (hormonal mechanism)

Renal Autoregulation

1- intrinsic factors:

- myogenic :

- The ability of blood vessels to resists stretching by recoiling.
- ↑ Hydrostatic pressure → stretching vessel's wall → reflex contraction (recoil)
- Reducing the increase in BP and increase GFR

- **tubuloglomerular feedback :** senses change in the Jaxtaglomerular apparatus

- **↓ GFR will cause slow blood flow which will ↑NaCl reabsorption → ↓ NaCl in filtrate**

- **macula densa senses the low Na and stimulates:**

1. ↑ rennin → ↑Angiotensin II → efferent vasoconstriction → ↑ GFR
2. Afferent dilation → ↑ GFR

GFR is autoregulated by tubuloglomerular feedback :

afferent arteriolar vasodilator feedback mechanism :

- decrease ionic concentration causes afferent arteriolar dilation
  → increase blood flow
  → increase glomerular pressure
  → increase GFR

efferent arterioles vasoconstrictor :

- low concentration of ions causes Jaxtaglomerular cells to release renin
  → angiotensin II
  → constrict efferent arterioles and that will lead to increase glomerulas pressure → GFR will return back normal

2- extrinsic factors :

sympathetic innervations. Angiotensin II and nitric oxide "NO"

■ Neural regulation :

Sympathetic :

- In normal conditions, the nervous system has little influence
- In cases of emergency stress, there will be a ↓ in BP due to hemorrhage which ↑ the sympathetic tone → vasoconstriction of all arteries including the renal artery → ↓ RBF → vasoconstriction of afferent artery → ↓ GFR

Note : SNS also stimulates renin-angiotensin mechanism

■ Hormonal

Renin angiotensin mechanism :

- Renin release is stimulated by:
  - ↓ ECF Na → ↓ ECV
  - hypotension → ↑ sympathetic tone
  - ↓ in afferent pressure
- Renin acts on Angiotensinogen converting is to Angiotensin I
- Angiotensin converting enzyme (ACE) converts Angiotensin I to Angiotensin II (vasoconstrictor) so it increases the BP.
- Angiotensin II act on adrenal cortex and stimulates aldostrone secretion, which acts on the kidney to increase Na reabsorption in the distal & collecting duct of the nephron because of the low Na level in the blood.
- The kidney will increase the secretion of H+ and K+ so more H+ and K+ are available for exchange with Na, which will increase Na reabsorption.

Regulation	Stimulated when	mechanism	Effect on GFR
Angiotensin II	↓ Blood Volume ↓ Blood Pressure	Constriction of : Afferent & Efferent arterioles	↓
Atrial Natriuretic peptide	Arterial wall stretch (due to blood Volume)	Relaxation of Mesangial cells Leading to ↑ filtration surface	↑

↘ **Hormonal factors Decrease GFR :**

- Norepinephrine , Epinephrine
- Adrenaline, noradrenaline
- Endothelin
- Angiotensin II

↗ **Hormonal factors Increase GFR :**

- Endothelial-derived nitric oxide
- Prostaglandins
- bradykinin

Factors affecting GFR :

Increase	Decrease
↑ Renal blood flow	↑ Plasma colloid osmotic pressure
↑ glomerular pressure	↑ Bowman's capsule
↑ Blood pressure	Afferent constriction
↑ Efferent constriction	Sympathetic stimulation

Pathological Factors decrease the glomerular filtration rate :

- Renal diseases , diabetes mellitus , hypertension
- Urinary tract obstruction (Kidney stones)
- Decreased renal blood flow , increased plasma proteins
- Decreased arterial pressure (small effect)
- Decreased angiotensin II (due to drugs that block it's formation)
- Increased sympathetic activity , vasoconstrictor hormones

Clearance :

Concept of clearance:

It is the volume of plasma completely cleared of any substance by both kidneys per unite time.

***Clearance equation*:**

$$C = Us \times V / P s$$

$$\mathbf{Ps \times Cs = Us \times V}$$

[P]s = conc. of substance in plasma.
[U]s = conc. of substance in urine.
V = volume of urine
amout of S excreted= $filterd - reabsorbed - secreted$

- **Renal clearance for different substances varies between 0 – 600 mL/min.**
  - It is 0 mL/min when the substance is not cleared into urine.
  - 600 mL/min is the maximum in plasma

- **Clearance of Inulin: 120 ml/min = GFR.**
- **Clearance of PAH = 630 ml/min.**

Inulin Clearance & GFR:

- The amount of inulin cleared = GFR

- **As inulin is:**
  1. Freely filtered.
  2. Not reabsorbed or secreted.

(Filtered inuline = excreted inuline)

- Inulin clearance = GFR = 120 ml/min

Creatinine clearance & GFR: *(simpler than inulin)*

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

Note: in the labs they don't measure inuline because it is a synthesis substance. So it must be injected. Creatinine is the best substance to be measured.

Glucose & Urea clearance:

- Renal clearance of glucose = zero (does not appear in urine) It is filtered & completely reabsorbed.
- Glucose is filtered and then completely reabsorbed, so no glucose in urine
- [U]s x Vmin = zero.
- Urea clearance = 60 ml/min.
- Urea filtered is partially reabsorbed.

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Inulin clearance Vs. clearance of other substance:

There are 4 possibilities of filtration in a normal person:

1- Freely filtered, not reabsorbed, not secreted. **Ex. : Inuline**

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. : creatinine**

substance clearance	possibilities of filtration	Example
120 = inulin	not reabsorbed or secreted	Creatinine
< 120	filtered & partially reabsorbed	urea
> 120	filtered & secreted	Para amine, puric acid
= 0	filtered and completely reabsorbed	Glucose