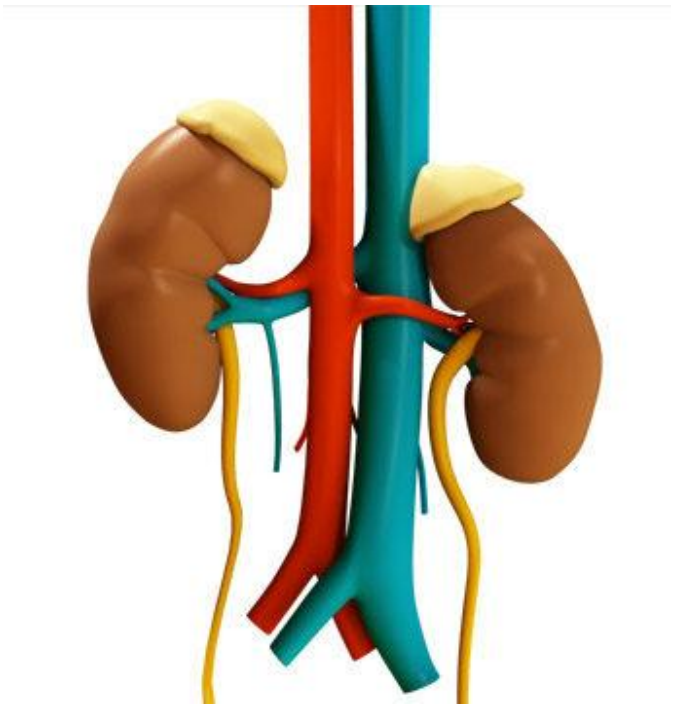
PHY
LL

The Renal Block

Chapter I



Created by

JU READ

يُريد

429

Prof. Sultan Meo

Dr. Shahed Habeeb

Head writers

Muhammed Al Watban

Abdullah Al Faris

Notes

Abdulmuhsen Al Mfarredj

Abdulla Al Agayiel

Press

Ahmed Al Duraihem

Editor

Aban Bahabri

Supervisor

Ismael Raslan

Special thanks to :

428 people

To contact with the team :

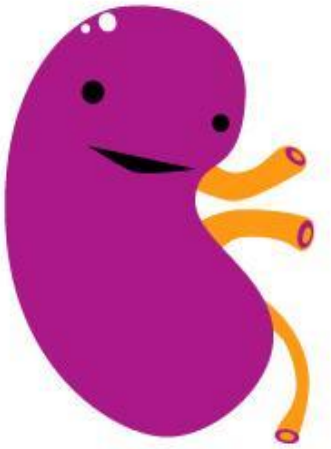
ThePhyllteam@yahoo.de

First Version

1430-1431

First of all ..

The functions of kidneys consist of :



✱Clear the body from waste products :

- urea
- uric acid
- creatinine
- drugs
- metabolic wastes .. as rapidly as they are produced.

✱ *Homeostatic function* : maintain the body fluids in regular amount :

↑ intake = ↑excretion

✱ Regulate the arterial pressure in two manners:

- Long term regulation by : blood pressure and rennin.
- Short term regulation by : nervous system.

✱ Regulate the acid-base balance by : excreting acids and regulating the body fluid buffer stores.

✱Erythrocytes production , **how ?**
When kidneys are exposed to hypoxia , they secrete **erythropoietin**
(90% of erythropoietin is from the kidneys)

✱Regulate vitamin D production by hydroxylating it at

- number 1 position.

E.K Functions of vitamin D :

- Deposition of Ca in bone.
- Absorption of Ca from GIT
- Regulating of Ca and phosphate

✱ Glucose synthesis during fasting by gluconeogenesis

E.K : extra knowledge

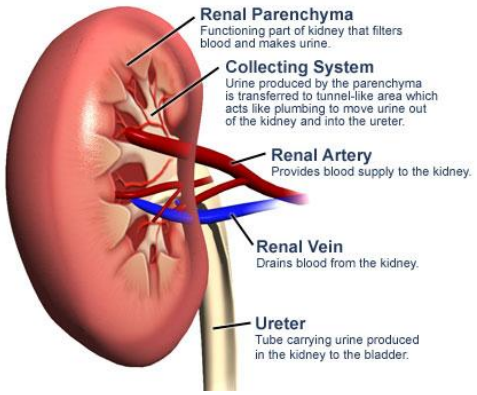
Physiological Anatomy of the Kidney

Kidney is located in the lumber region in the posterior wall of the body

NUMB3RS of kidney :

- 12 cm long
- 6 cm wide
- 3 cm thick
- 150 gm weight

The renal artery and vein, lymphatic, nerve supply and ureter pass through The medial side which called the *hilum*



Nephron:

- .. is usually the structional function unit of the kidney
- we have 1- 1.3 million nephrons in each kidney .
- each decade we lose 10% of nephrons ,that happens after the age of 40
- Kidneys cannot regenerate new nephrons

Types of nephron :

- Cortical nephrons: taxt
- Juxtamedullary nephrons

Nephron consist of :

➔Glomerular corpuscle :

Glomerulas

⮌Afferent arterioles :

- Has larger diameter than efferent that's why blood pressure is high in glomerulus.
- The elevated (high) Blood pressure is needed to force fluid out of bloodstream into the nephron.

↳ Efferent arterioles :

- Has narrowe diameter then afferent : keeps glomerular pressure high
- carry the clean filtered blood away from the glomerulus .

Bowman's Capsule

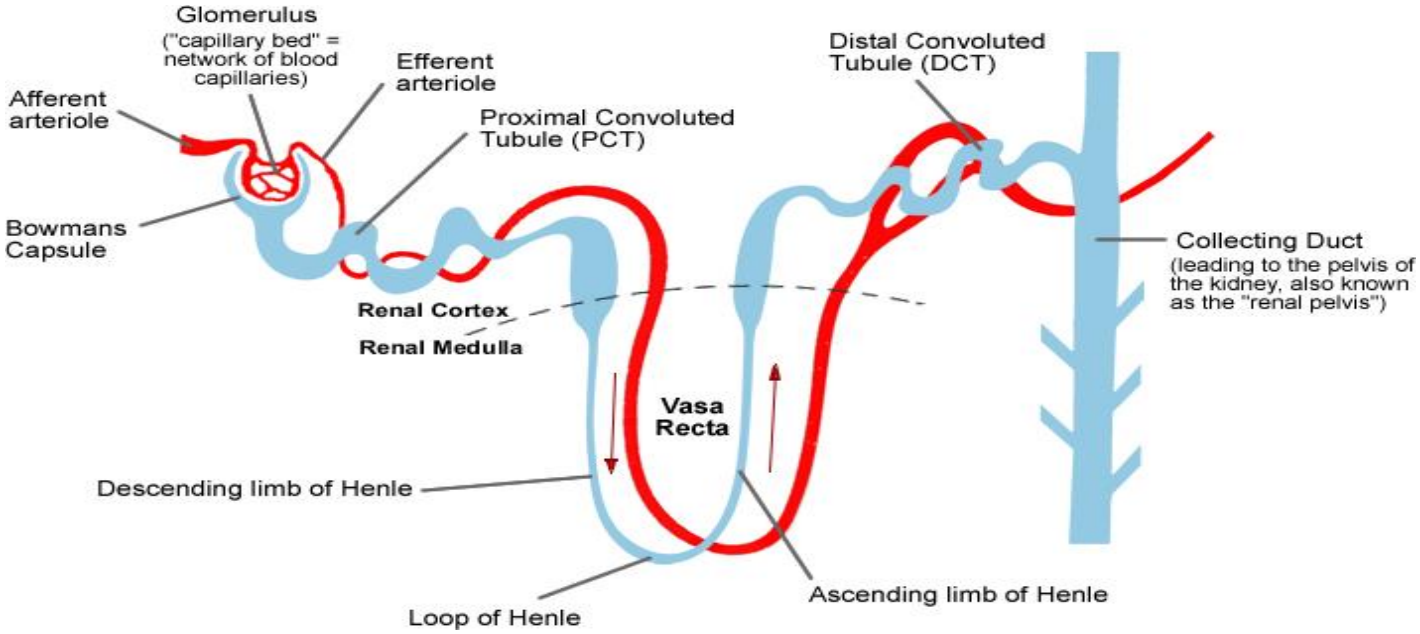
- Cup shaped structure
- It's the first portion of the nephron pathway that moves fluid out of the body

➔Proximal Convoluted Tubules

➔Loop of Henle , divides into two parts :

- Thin descending limb.
- Ascending limb, has thin and thick segments.

➔Late (distal) convoluted tubules



Juxta Glomular Apparatus JGA

It's combination of cells lying close to the glomerulas.

it is composed of :

- afferent arteriole cells
- cells of the angle between afferent and efferent arterioles

it 's structure consist of :

- Macula densa
- Lacis cells
- JG cells

Macula densa

- It's a group of modified epithelial cells in the portion of the distal convoluted tubule lying in contact with afferent g vessels to the same nephrons
- It works as sensory cells detects the changes in NACL

Lacis Cells

AKA : Polkissen cells or Goor maghtigh's cells

- Formed mainly by : granular
- they lie close contact with the macula densa , within the vascular pole

JG Cells

- It's a group of modified epithelial cells in the portion of the distal convoluted tubule lying in contact with afferent g vessels to the same nephrons
- It related to Renin secretion

JGA plays a role in the control of :

- blood pressure
- renal blood flow
- electrolytes balance
- ereythropoiesis

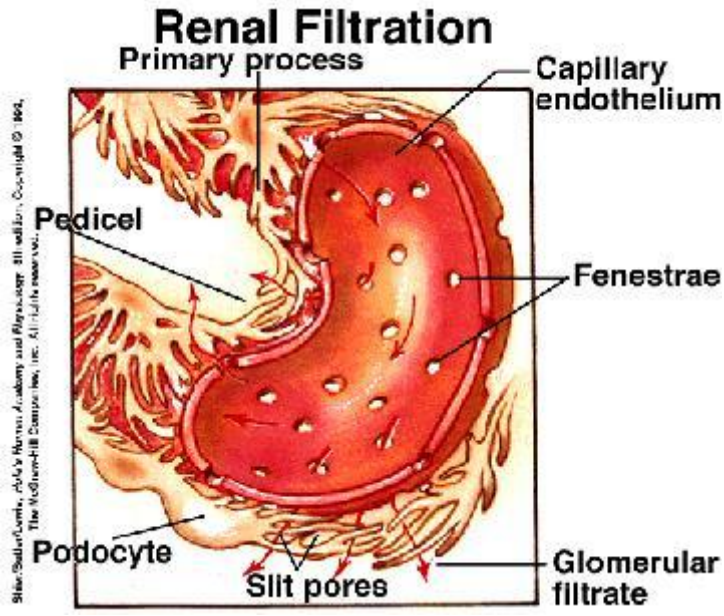
Glomerular membrane

Ordinary capillary membrane has **2** layers , but Glomerular membrane has **3** layers :

- 1st layer : **endothelial** , has a fenestrae
- middle layer : **the basement membrane** : -ve charged associated with protoglycans
- outer layer : **epithelial cells** (podocytes) on the surface which have pores

Fanestrea : small pores (holes) that perforate the capillary endothelial cells , there are thousands of them .

Slit : fingerlike projections that cover the basement membrane



ℰ.ℓ The differences between filtration and osmosis is :

- **filtration**: solid and liquids are both move in kidney
- **osmosis**: only solid moves.

Glomerular permeability

Filtration passes through **3** layers as we mentioned before ,each of them is several hundred times as porous as usual capillary membrane .

It has extremely high degree of selectivity . it's permeability is about **50** times more than the capillaries in skeletal muscles .

Depends on:

Size of the pores : 8 nm . the pore can easily allow molecule up to 8 nm to pass through

- Less than 4 : freely filtered
- More than 8 : no chance

↑ Diameter = ↓ filtration

Electrical charge (more than size) : basement membrane are lined with proteoglyacans that have very strong **–ve** charge .

It keeps virtually all protein molecules less than **69,000** molecular weight from passing through .

e.g. Albumen (plasma protein) is only about **6** nm , but it doesn't pass through the membrane , **why ?**

Because of it's charge !

- The amount of protein in the urine is normally less than **100** mg/d
- The presence of albumen in urine called **: abuminurea**
- **In Nephritis** : **-ve** charges in Glomerular wall are dissipated , then , albumen will shows up in the urine causing abuminurea without changing the size of the pores !

Q Low molecular weight substances such as **Calcium** and **fatty acid** are not freely filtered , **why** ?

Because they are partially Bound to plasma protein

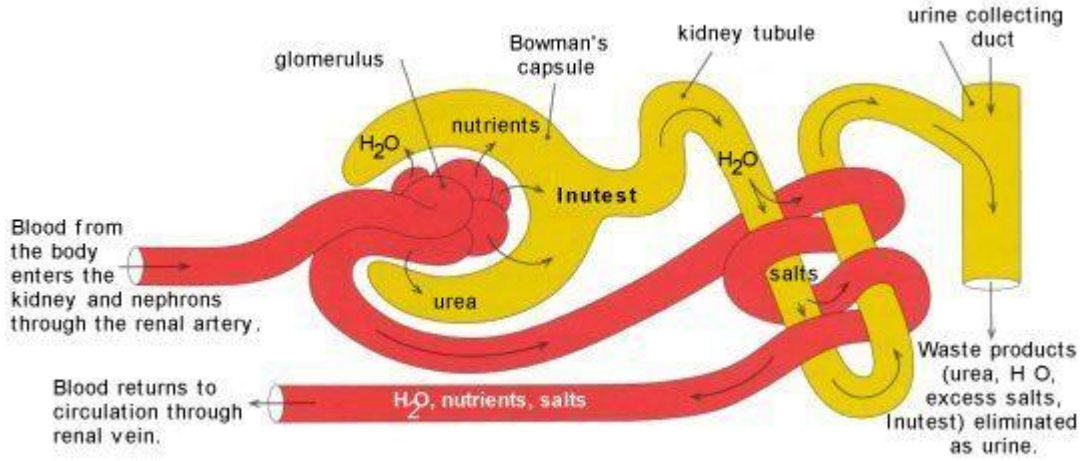
Urine formation begins with filtration of large amounts of fluid through the glomerular capillaries into Bowman's capsule.

- The glomerular filtrate is essentially **protein-free** , cellular element (red blood cells) are also not found
- Blood flow to kidney is 22% of Cardiac Output (1100 ml/min)

The urine formation steps :

1. Filtration : between glomerular and bowman's space.
2. Reabsorbtion : from nephron to blood capillary
3. Secretion : from capillary to nephron
4. Excretion

Urinary excretion rate = filtration rate – reabsorbtion rate + secretion rate



Glomerular Filtration Rate GFR

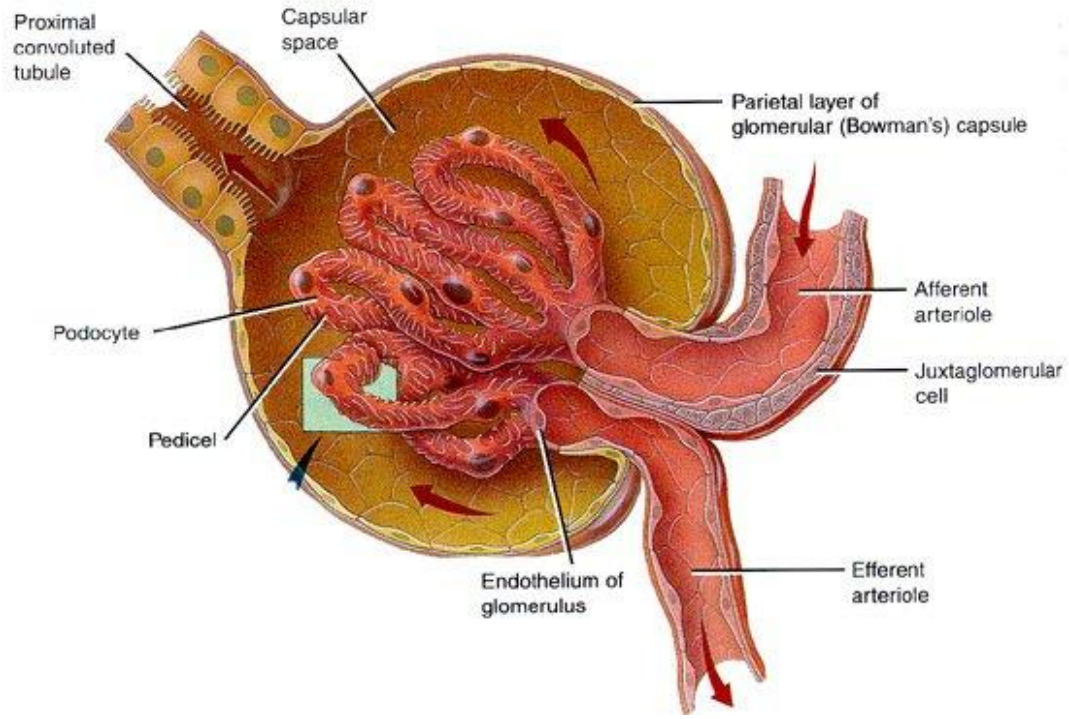
Is the fluid filtered through the glomerulas into bowman's capsule per minute

◥Normal value : **120** ml/min or **180** L/day , but the normal urine volume is : **1** L/ day

.. that's mean : **99%** of glomerular filtrate is normally reabsorbed in the renal tubules .

◥In females , GFR is **10%** **lower** than males even after correction for surface area.

◥ Every **5** minutes the kidneys clear the whole blood.



Determinates of the GFR:

◥Any disease leads to increase the plasma protein will decrease GFR

◥Afferent arteriole constriction = ↓ GFR

◥Efferent arteriole constriction:

- if it is mild or moderate = ↑ GFR
- if it is severe constriction = ↓ GFR , due to accumulation of plasma protein (Biphasic effect)

◥Stone in proximal tubule = ↓ GFR

Note : **Angiotensin II** has effect (constriction) on efferent more than afferent arteriole.

Filtration Fraction FF :

It's the fraction of the renal plasma flow that becomes glomerular filtrate .

- plasma flow = **650** ml/min
- the ratio of : $\frac{GFR\ (\ Glomerular\ \ Filtration\ \ Rate\ )}{RPF\ (\ Renal\ \ Plasma\ \ Flow\ )}$ = **16 –20 %**

Q when there is a fall in systemic blood pressure : the GFR become less then RPF , **why ?**

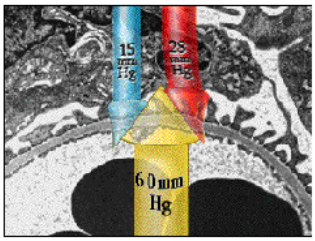
because of efferent arteriolar constriction , and consequently the FF ↑

Pressure role in Glomerular Filtration

It's the force that drives the fluid and it's dissolved substances through the glomerular filter.

There are **4** pressures affecting glomerular filtration:

1. Glomerular hydrostatic pressure = 60 mm Hg →
2. Bowman's capsule colloid osmotic pressure = 0 mm Hg →
3. Bowman's capsule hydrostatic pressure = 18 mm Hg ←
4. Glomerular capillary colloid osmotic pressure = 32 mm Hg ←



Net filtration pressure NFP :

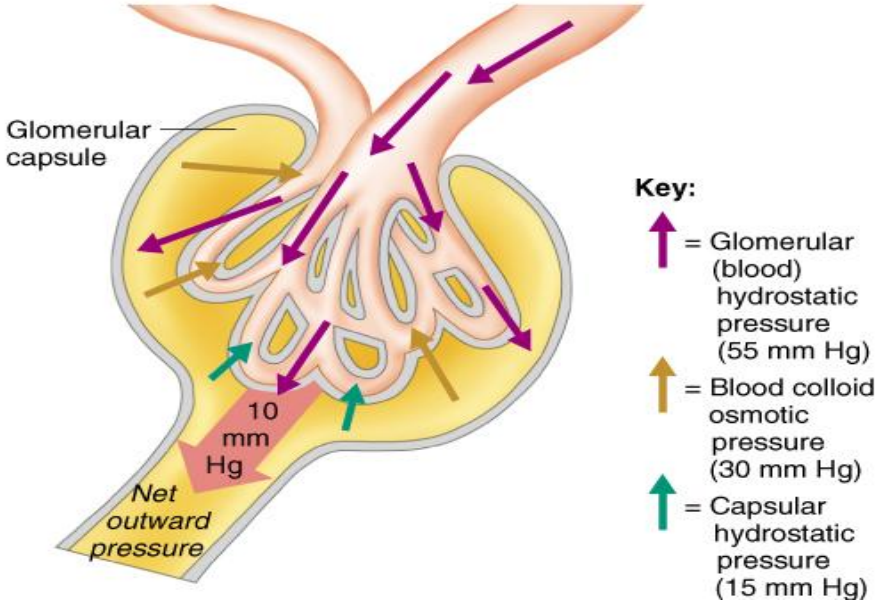
Is the different between three pressures :

- Glomerular Hydrostatic pressure GHP , GBHP = **60**
- Bowman's Capsular pressure CHP = **18**
- Blood Osmotic pressure = **32**

NPF = GBHP – (CHP + BCOP)

= 60 – (18 + 32)

= 19 mmHg



GFR regulation

There are **3** mechanisms control GFR :

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

↑ arterial pressure = ↑ GFR

if the mean arterial pressure between **75 – 160** = GFR remains constant

if the mean arterial pressure below **75** = ↓ GFR

$$\mathbf{GFR = K_f \{ P_{GC} - P_t) - (\pi_{GC} - \pi_T) \}}$$

✱ K_f : is the glomerular ultrafiltration coefficient , is the product of the glomerular capillary wall

K_f depends on :

- Permeability : affected by negative charge & size of particle
- surface area : affected by mesangial cell & loss of nephrons

K_f ↓ by :

- ↓ Capillary filtration
- ↑ Thickness

✱**P_{GC}** : hydrostatic pressure in the glomerular capillaries

✱**P_t** : hydrostatic pressure in the tubule

✱**π_{GC}** : osmotic pressure of the plasma in the glomerular capillaries

✱**π_T** : osmotic pressure of the filtrate in the tubule

Renal Autoregulation

❶intrinsic factors:

- myogenic : change pressure in renal blood vessels
- tubuloglomerular feedback : senses change in the Jaxtaglomerular apparatus

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

❷extrinsic factors :

sympathetic innervations. Angiotensin II and nitric oxide “NO”

Neural regulation

Sympathetic :

When SNS (sympathetic nervous system) is at rest :

- renal blood vessels maximally dilated
- Autoregulation mechanism prevails

Under stress :

- Norepinephrine is released by SNS
- 2-Epinephrine is released by adrenal medulla
- 3-afferent arterioles constrict and filtrate is inhibited

Note : SNS also stimulates **renin-angiotensin** mechanism

Hormonal

Renin angiotensin mechanism :

- angiotensin is triggered when JG cells release renin
- renin acts on Angiotensinogen , that will release **angiotensin I**
- **angiotensin I** → **angiotensin II**

angiotensin II increase arterial blood pressure and release **aldosterone** →

aldosterone increase systemic and hydrostatic glomerular pressure

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
- Endothelin
- Angiotensin II

↗Hormonal factors **Increase** GFR :

- Endothelial-derived nitric oxide
- Prostaglandins

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

Measuring GFR

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

The ideal substance used for measuring GFR should be :

1. Must be freely filtered and not reabsorbed or secreted
2. Non-toxic and not metabolized by the body

Note : the benefit of secretion is may be there are substances not filtered, so they are secreted instead

Urea in reabsorbed 50%

Inulin is the substance that meet the criteria so it is used for measuring GFR . plasma and urine Inulin concentration are determined and the clearance is calculated

Plasma Clearance:

- 20% of plasma filtered
- plasma flow = 650 ml/min

3 things are important in plasma clearance :

1. plasma concentration
2. urine concentration
3. urinary flow rate

Clearance formula:

Volume of plasma to be cleared × plasma concentration = volume of urine × urine concentration

Ps × Cs = Us × V

$$Cs = Us \times \frac{v}{ps}$$

- Note : volume of plasma to be cleared = GFR.
- plasma clearance is done in 24 hrs of urine.

Inuline clearance:

$$P_{Inuline} \times GFR = U_{inuline} \times V$$

Filtered inuline = excreted inuline

↓ GFR = ↓ Clearance of inuline

NUMB3RS :

- U_{IN} (Inulin in urine) = 35 mg/ml
- V (urine flow per unit of time) = 0.9 ml/min
- P_{IN} (Inulin arterial plasma level) = 0.25 mg/ml
- C_{IN} (clearance of Inulin) = 126 ml/min

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.

That's all :)