Week One SAQs

Anatomy of the Kidney:

<table>
<tr><td>Location of kidney</td><td colspan="4">• Lie behind the peritoneum on the posterior abdominal wall on either side of the vertebral column. (From T 12 to L3)
• Retroperitoneal. (Retro = behind)</td></tr>
<tr><td>Characteristic</td><td colspan="4">- Reddish brown.
- Right kidney lies slightly lower than the left due to the large size of the right lobe of the liver.
- The upper border of the right kidney is at the level of 11th intercostal space
- The upper border of the left kidney is at the level of 11th rib.</td></tr>
<tr><td>Function</td><td colspan="4">• Excretion of the wastes.
• Synthesis of hormones (erythropoietin) and enzyme (renin)
• Regulation of water and electrolytes balance
• Convert Vitamin D to its active form.</td></tr>
<tr><td>Covering (layers) From inner to outer</td><td colspan="4">- Fibrous capsule
- Perirenal (perinephric) fat
- Renal fascia
- Pararenal (paranephric) fat</td></tr>
<tr><td>Blood supply (Arteries)</td><td colspan="4">Aorta (at the level of L2) → renal artery → five segmental artery (4 in front and 1 behind the renal pelvis) → lobar artery (arises from each segmental artery, one for each renal pyramid) → 2 or 3 interlobar artery (run toward the cortex on each side of the renal pyramid) →arcuate arteries (at the junction of the cortex and medulla) → interlobular arteries. → afferent glomerular arterioles.</td></tr>
<tr><td>Veins</td><td colspan="4">• Vein drains into IVC.
• The left renal vein receives the left gonadal and the left suprarenal veins.</td></tr>
<tr><td>Nerve supply</td><td colspan="4">Renal sympathetic plexus (no parasympathetic)</td></tr>
<tr><td>Two capillary beds</td><td colspan="4">• The glomerulus
• The peritubular capillary</td></tr>
<tr><td>Hilum transmits (Anterior to posterior) VAUA</td><td colspan="4">- Renal vein
- Renal artery
- Ureter
- Third branch of renal artery.</td></tr>
<tr><td rowspan="2">Relations
Very important</td><td colspan="2">Anterior Relations</td><td colspan="3">Posterior Relations
(for both right and left)</td></tr>
<tr><td>Right Kidney</td><td>Left Kidney</td><td>Muscles (4)</td><td>Nerves (3)</td><td>Others</td></tr>
<tr><td>• Right suprarenal gland
• Liver
• Second part of the duodenum
• Right colic flexure
• Colic of small intestine</td><td>• Left suprarenal gland
• Stomach
• Spleen
• Pancreas
• Left colic flexure
• Descending colon
• Colic of jejunum</td><td>- Diaphragm
- Psoas major
- Quadratus lamborum
- Transvers abdominis</td><td>• Subcostal nerve (T12)
• Iliohypogastric nerve (L1)
• Ilioinguinal nerve (L1)</td><td>12th ribs
Costodiaphragmatic pleural recess.</td></tr>
</table>

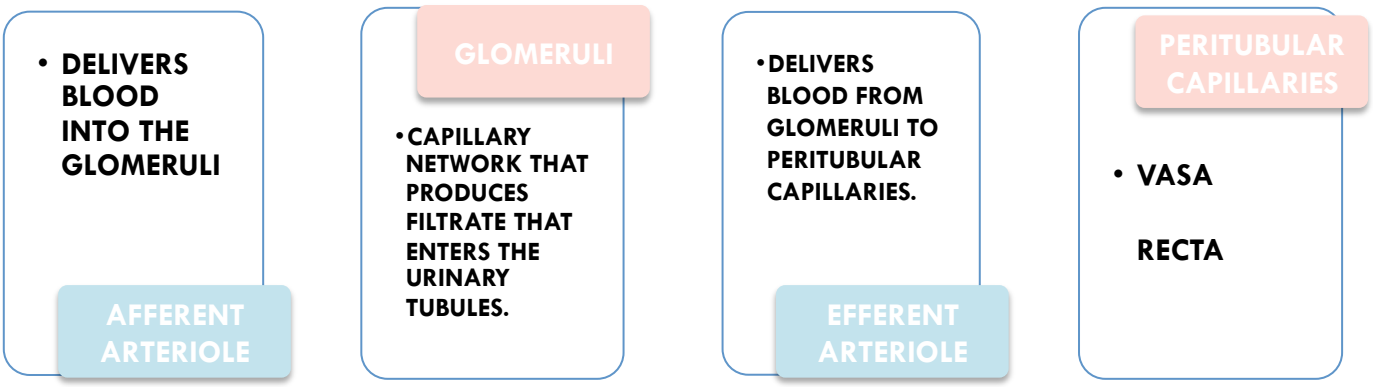
* Done by Afnan Almalki

Physiology of the Kidney:

Homeostatic functions of the kidney are:

- Regulation of water and electrolyte balances
- Regulation of body fluid osmolality and electrolyte concentrations.
- Excretion of metabolic waste products and foreign chemicals (UREA, CREATININE, URIC ACID)
- Regulation of arterial blood pressure (RAS, excretion of excess salt and water)
- Regulation of acid-base balance.
- Detoxification and excretion of drug.
- Synthesizing function:
    - Active form of vit. D (D3) = 1,25 dihydroxycholicalciferol.
    - Erythropoietin production.
    - Renin formation
    - Gluconeogenesis (synthesis of glucose from amino acid during prolonged fasting)

Renal Blood Vessels:



Features of renal circulation:

- High blood flow rate (1200 ml/min). "Range: 1018-1200"
- Presence of two capillary beds: ***glomerular and peritubular.***
- Efferent and afferent arterioles are major sites of renal resistance.

Urine Formation:

The primary function of the kidney is to 'clear' unneeded substances from the blood to be excreted in urine.

Steps of urine formation (basic renal processes):

1- Glomerular filtration:

Filtration of fluid from glomerular capillaries into the renal tubules.

2- Tubular reabsorption

3- Tubular secretion.

4- Excretion.

Urinary excretion rate = Filtration rate - reabsorption + secretion

GFR:

The FIRST step in urine formation is glomerular filtration.

- It is the filtration of fluid from the glomerular capillaries into the renal tubules.
- It contains all substances present in plasma except proteins.
- GFR is normally 125 ml/min = 20% renal plasma flow.

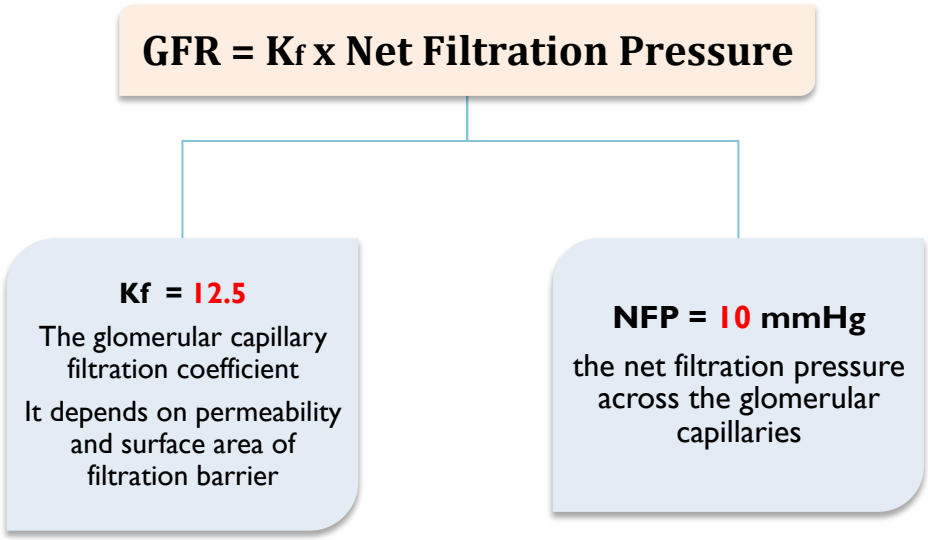
Blood in the glomerulus is separated from the fluid in the Bowman's space by a filtration barrier (glomerular membrane) consisting of three layers:

1. Single layer of capillary endothelium.
2. Single epithelial lining of Bowman's capsule (Podocytes)
3. During filtration the fluid moves between their foot processes (pseudopodia).
4. Basement membrane between endothelium and epithelium.

Characteristics of glomerular membrane

- **Albumin** does not normally pass as they are repelled by the negative charge of the glycoproteins material of basement membrane.

- **Blood cells** do not normally pass through the membrane.



Glomerular Filtration Rate (GFR) is directly proportional to the net filtration pressure (NFP) :

- When NFP increase → GFR increase
- When NFP decrease → GFR decrease

Changes in GFR normally result from changes in glomerular blood pressure.

Forces controlling GFR : Starling's forces

Hydrostatic pressure inside glomerular capillaries (PG) = **60** mmHg
Promotes filtration

Hydrostatic pressure in Bowman's capsule (PB) = **18** mmHg
Opposes filtration

Colloid osmotic pressure of glomerular plasma proteins (Πg) = **32** mmHg
Opposes filtration

Colloid Osmotic Pressure of Bowman's proteins (Πb) = **0** mmHg
Promotes filtration

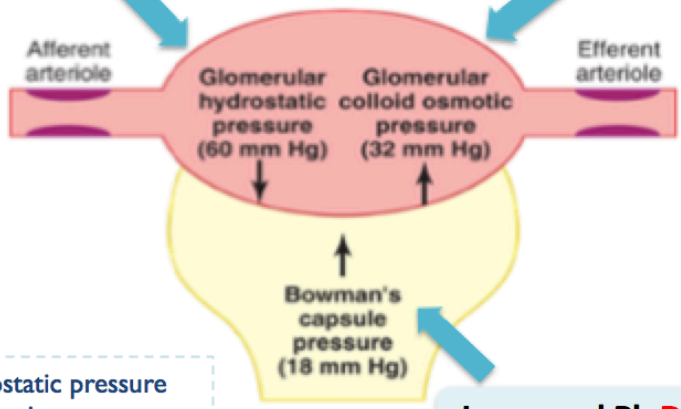
So, NFP = 60 – 32 – 18 = +10 mmHg

$$GFR = Kf \times [(Pg - Pb) - (\pi g - \pi b)]$$
$$GFR = Kf \times [(60 - 18) - (32 - 0)]$$

How do changes in forces determining GFR affect GFR?

Increased Pg Increases GFR.
This pressure is affected by:
- ABP.(arterial blood pressure)
- Afferent & Efferent arteriolar resistance

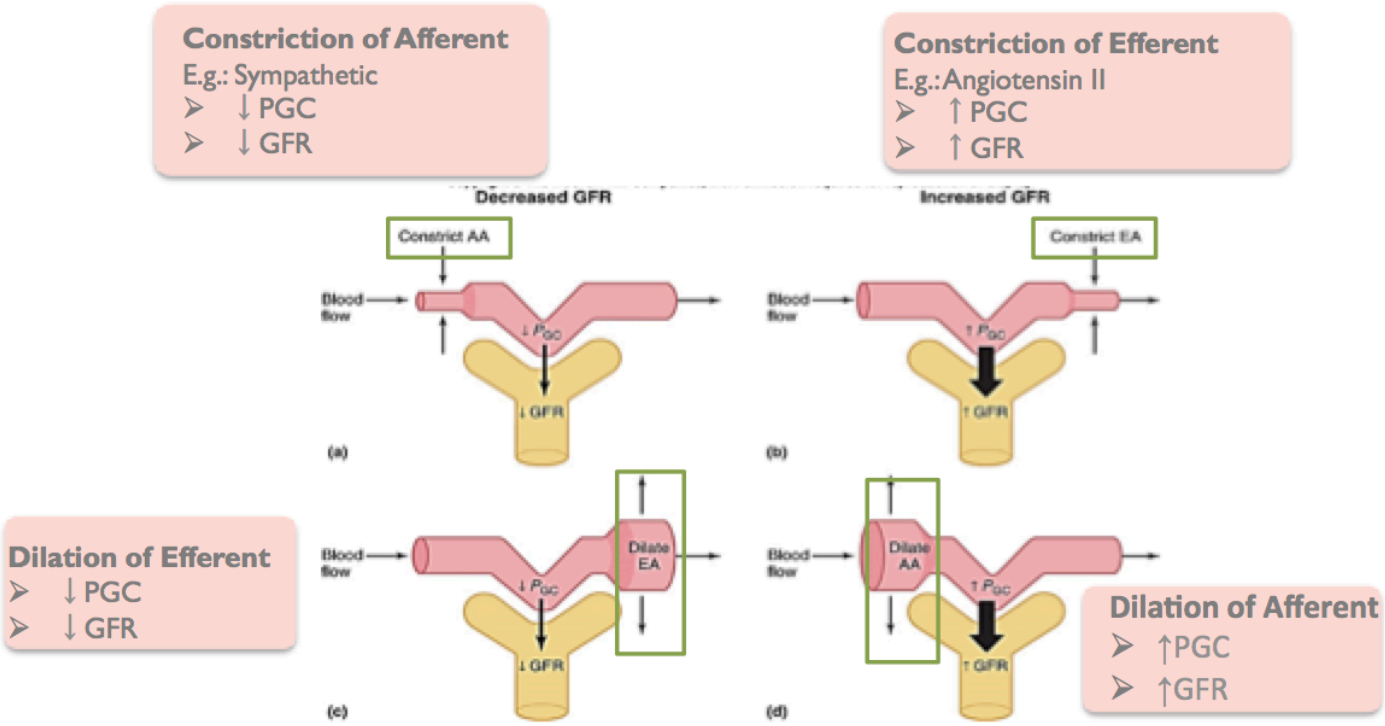
Increased π g Decreases GFR



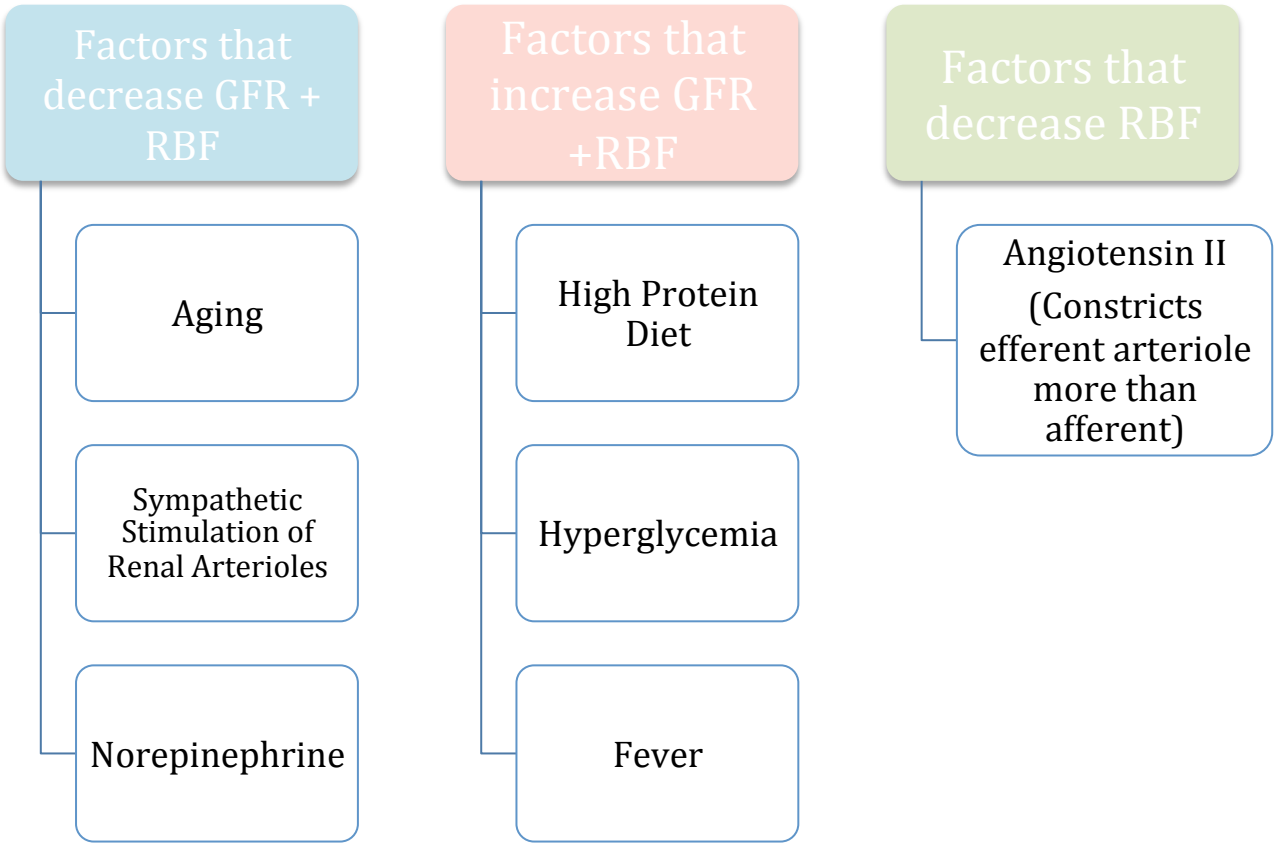
Pg = Glomerular hydrostatic pressure
Pb = Bowman's hydrostatic pressure
π g = Colloid osmotic pressure of glomerular plasma proteins

Increased Pb Decreases GFR
In urinary obstruction
e.g. stones or tumors.

As vasodilation and vasoconstriction of the afferent and efferent arterioles alter the blood flow through the glomerular capillaries, there are corresponding alterations in the glomerular filtration rate **(GFR).**



Factors Affecting Renal Blood Flow and GFR:



Regulation of GFR

If the GFR is too high :

Fluid flows through tubules too rapidly to be absorbed.
↓
Urine output rises.
↓
Creates threat of **dehydration** and electrolyte depletion. (It will lead to Hypo. Cases)

If the GFR is too low :

Fluid flows sluggishly through tubules
↓
Tubules reabsorb wastes that should be eliminated
↓
Azotemia develops (high levels of nitrogen-containing substances in the blood)

Substances Used to Measure GFR

Inulin

- Freely filtered into the Bowman's capsule
- Not reabsorbed, secreted or metabolized by the nephron
- Non-endogenous, has to be infused intravenously
- **Best marker .**

Creatinine

- endogenously released into plasma by skeletal muscle
- Not as accurate as inulin as a small quantity is secreted into the proximal tubule
- amount excreted > amount filtered
- Reasonably accurate measurement of GFR
- **Clinically , Best marker.**

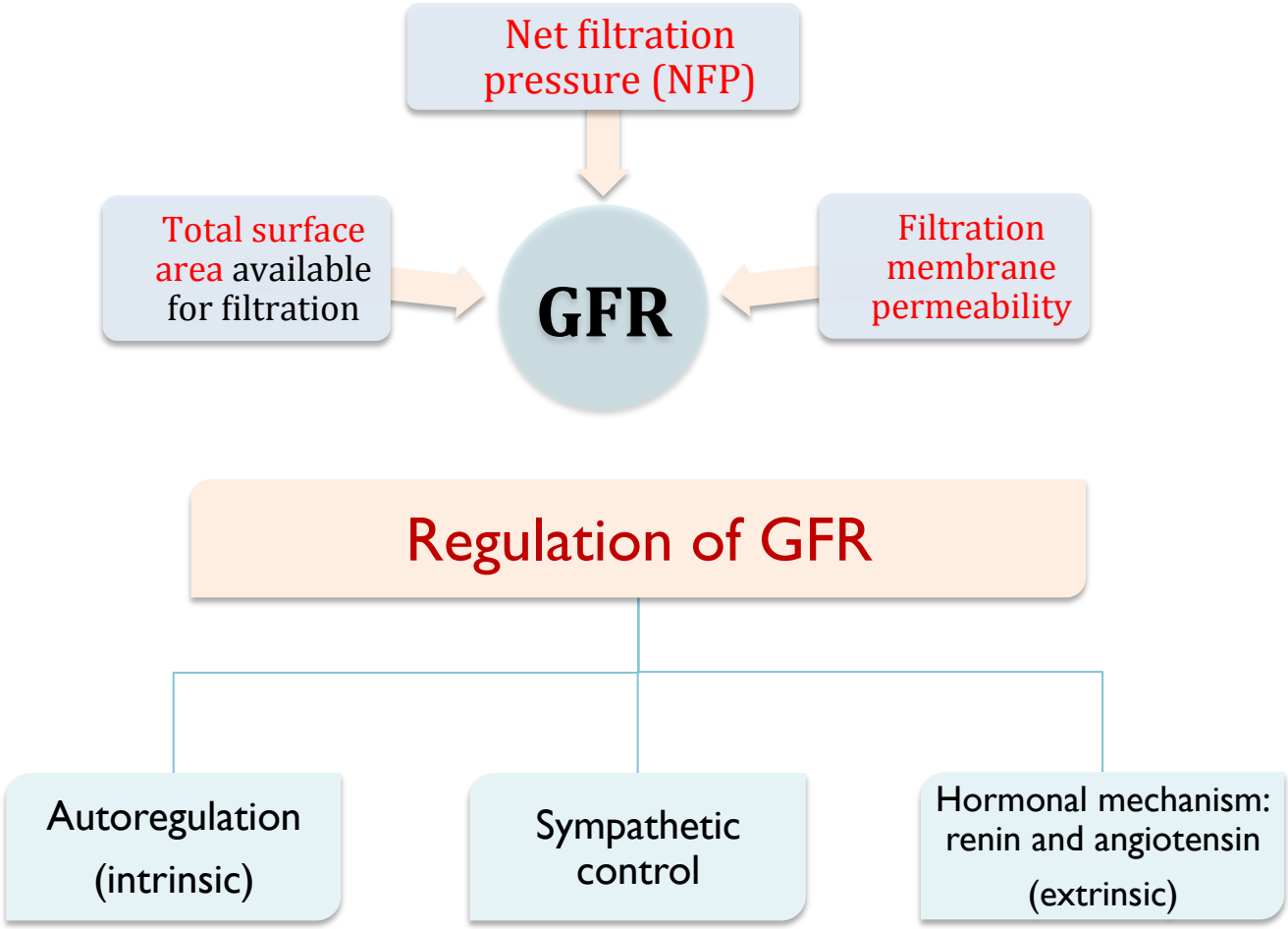
• د.أحمد قال عن الـ inulin انه افضل شي لقياس الـ GFR ولكن ليس في البشر "موضع سؤال في الـ MCQs "
فإذا لم يحدد في السؤال البشر: أنيولين، أما إذا حدد : كرياتينين.

Goals of Glomerular Filtration Rate (GFR)

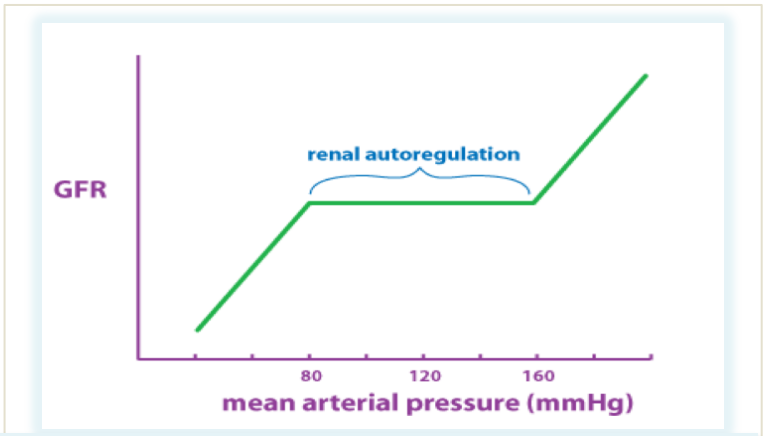
Index of kidney function

Sum of the filtration rates of all functioning nephrons
(indicator for number of functioning nephrons)

Factors governing filtration rate at the capillary bed are:



Effect of arterial blood pressure on GFR:



Normally when ABP increase → GFR increase

But , because of the autoregulation the body maintains constant GFR over an ABP range of 75-160 mmHg.

Filtration stops when > 50 mmHg

1- Autoregulation (intrinsic):

It is the relative constancy of GFR and renal blood flow in response to changes in blood pressure range from 75 to 160 mmHg

However, autoregulation is not perfect but it prevents potentially great changes in GFR , with changes in blood pressure, therefore, kidney continue to excrete waste

That means in a normal kidneys, a decrease in arterial blood pressure as low as 75 mmHg, or an increase as high as 160 mmHg causes a change in GFR by only a few percentage

General information

- Refer to feedback mechanisms intrinsic to the kidney
- keep the renal blood flow and GFR relatively constant despite fluctuations in ABP
- These mechanisms operate over an ABP ranging between 75 -160 mmHg (systolic)

Achieved by 2 major mechanisms

1. Myogenic auto-regulation
2. Tubulo -glomerular feedback

Renal Autoregulation of GFR		
Blood pressure	Afferent arteriole	Efferent arteriole
↑ BP	Constriction	Dilation
↓ BP	Dilation	Constriction

Can not compensate for extreme BP changes.

Stable for BP range of 75 to 160 mmHg (systolic).

Tubuloglomerular Feedback Mechanism:

Increase in ABP

Increase blood flow in renal tubules
→ increase GFR

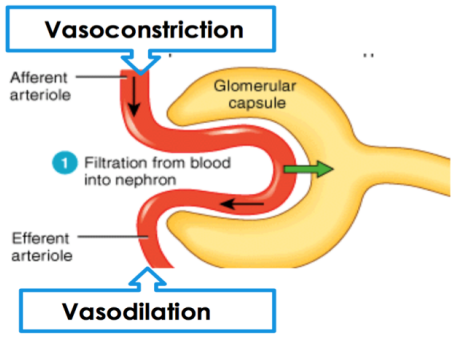
decrease reabsorption by renal tubules (caused by the rapid flow)

increase delivery of NaCl to the macula densa cells, which are capable of sensing this change

Macula densa releases signals which will cause vasoconstriction of Afferent arterioles.

inhibit the release of Renin from the juxtaglomerular cells leading to vasodilation of EFFERNT arterioles.

Net result :
1- Decrease glomerular hydrostatic Pressure.
2- GFR back to its normal rate.



Decrease in ABP

Decrease blood flow in renal tubules
→ Decrease GFR

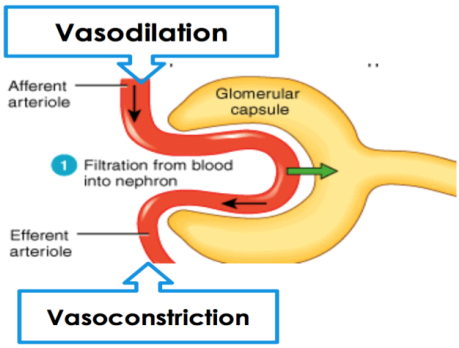
Increase reabsorption by renal tubules

Decrease delivery of NaCl to the macula densa cells, which are capable of sensing this change

Macula densa releases signals which will cause vasodilatation of Afferent arterioles.

Increase in Renin release from the juxtaglomerular cells to → Ang II → cause vasoconstriction of EFFERNT Arteriole.

Net result :
1- Increase glomerular hydrostatic Pressure.
2- GFR back to its normal rate.



Myogenic auto-regulation Mechanism:

It is the intrinsic capability of blood vessels to **constrict** when blood pressure is increased

This constriction prevents excess increase in renal blood flow and GFR when blood pressure rises

When blood pressure decreases , the myogenic mechanism reduces vascular resistance and the vessel **dilates**

2-(Extrinsic): Hormonal Control of GFR:

Hormonal factors:

- Epinephrine, Nor-Epinephrine, Angiotensin II, Prostaglandin (F) and Thromboxane cause renal vasoconstriction and results in decrease in RBF and GFR.

- Acetylcholine, Bradykinin, Prostaglandin (D, E, and I), and bacterial pyogens cause renal vasodilation and results in increase in RBF and GFR.

Physiological Stress:

- Cold, deep anesthesia, fright, sever exercise, hypoxia and ischemia stimulate sympathetic nerve fibers leading to renal vasoconstriction and decrease in RBF.

Posture:

- RBF increase in supine than sitting than standing. Changing the posture from lying to standing leads to a decrease of about 15% in RBF due to the stimulation of sympathetic NF.

3- Sympathetic Control of GFR:

Under stress

- **Norepinephrine** is released by the sympathetic nervous system
- **Epinephrine** is released by the adrenal medulla
- Afferent arteriole constrict and filtration is **inhibited**
- stimulation of renin angiotensin mechanism → This induces vasoconstriction of efferent arteriole

at rest

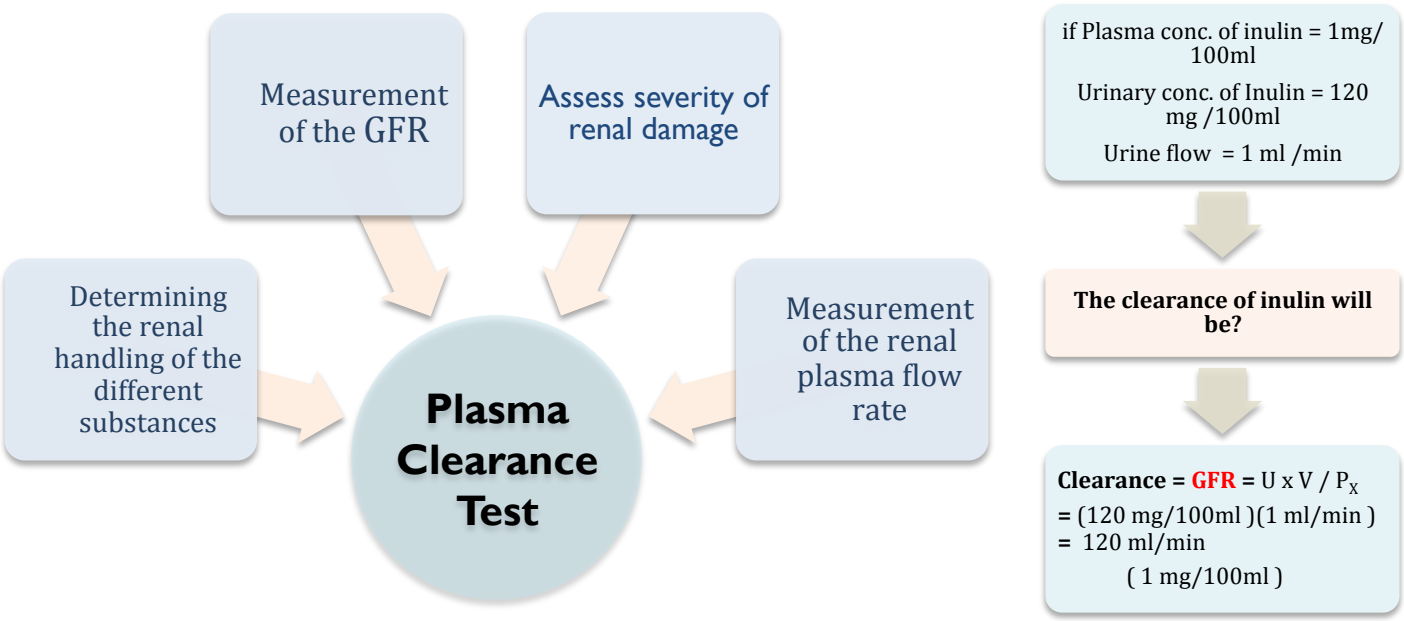
- Renal blood vessels are maximally dilated
- Autoregulation mechanisms prevail

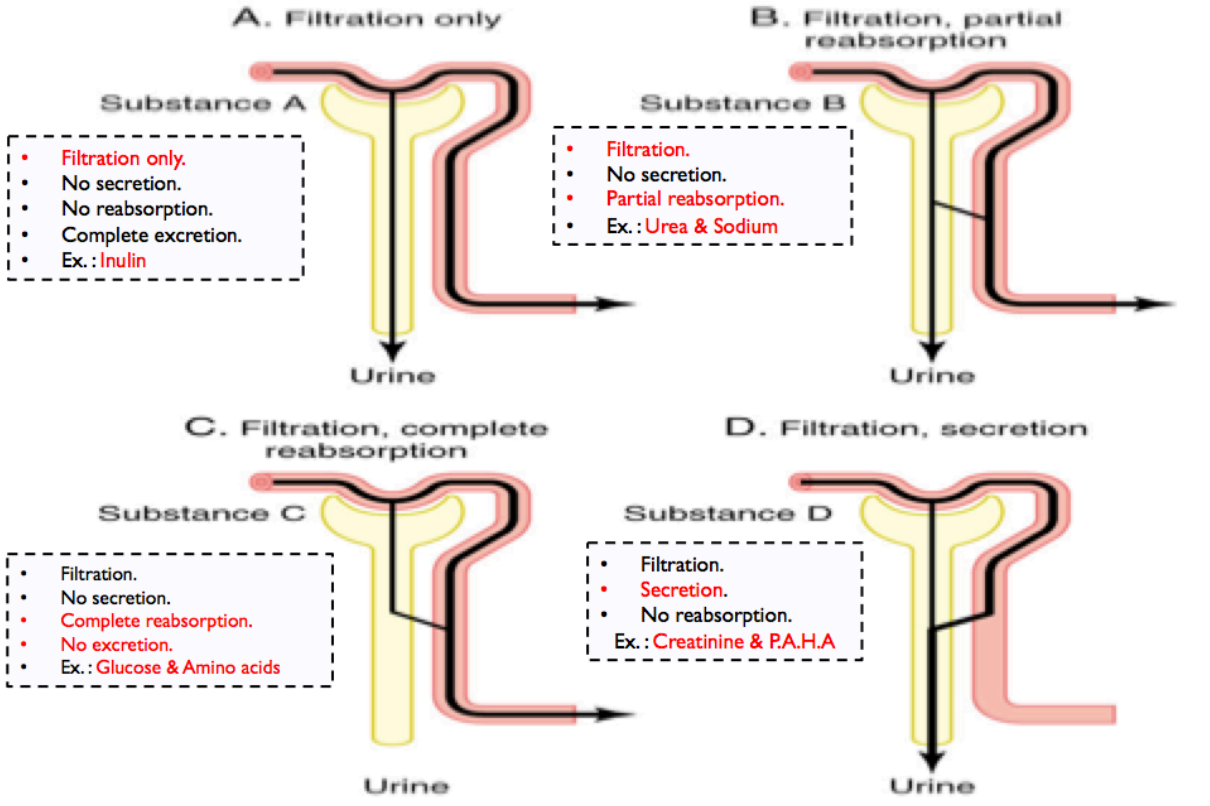
Note: during fight or flight blood is shunted away from kidneys

Definition	**The clearance value of a certain substance :** *[means the volume of plasma which is cleared from this substance in urine each minute].*
Calculation	**The formula is :** C = UXV/P **C =** Renal clearance (ml/min) **(V) =** Volume of urine (ml /min). *(urine flow rate)* **(U) =** Conc. of the substance in urine (mg/ml). **(P) =** Conc. of the substance in plasma/serum (mg/ml). **UXV =** Excretion rate of substance
Plasma Clearance Tests	**The properties of any exogenous substance *used in* plasma *clearance tests* are:** 1. Stays in the plasma (does not enter the RBC's). 2. Does not affect the renal functions. 3. Not metabolized by the kidney. 4. Easily measured in plasma & urine. 5. Non toxic.
Assume	If the substance is freely filtered at the glomeruli and is not reabsorbed, secreted or metabolized in the nephron *(such as Inulin)*, then: Amount filtered per minute = Amount excreted per minute $[sub]_{plasma}$ x GFR = $[sub]_{urine}$ x urine flow rate

Amount of substance excreted = (filtered – reabsorbed + secreted)

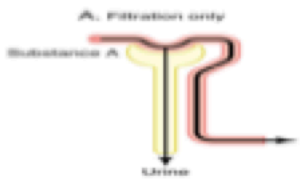
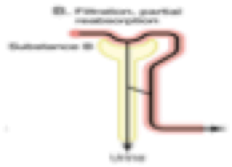
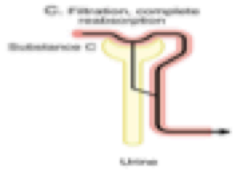
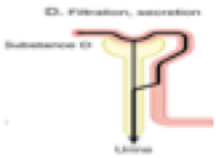
$\{ U_x V = GFR \times P_x \pm T_x \}$





*Every single word in this slide is VERY IMPORTANT !

P.A.H.A (Para-Aminohippuric acid)

	• Filtration only. • No secretion. • No reabsorption. • Complete excretion. • Ex. : Inulin
	• Filtration. • No secretion. • Partial reabsorption. • Ex. : Urea & Sodium
	• Filtration. • No secretion. • Complete reabsorption. • No excretion. • Ex. : Glucose & Amino acids
	• Filtration. • Secretion. • No reabsorption. • Ex. : Creatinine & P.A.H.A

Types of clearance tests	
Endogenous	**Exogenous**
- Creatinine - Urea - Uric acid	- Inulin - Para amino hippuric acid (PAHA) - Diodrast (di-iodo pyridone acetic acid)

Criteria of a substance used for GFR measurement

- ❖ Freely filtered
- ❖ Not secreted by the tubular cells.
- ❖ Not reabsorbed by the tubular cells.
- ❖ Should not be toxic
- ❖ Should not be metabolized
- ❖ Easily measurable.

Examples of such a substance:	
Endogenous	**Exogenous**
Creatinine by-product of skeletal muscle metabolism	**Inulin** It is a polysaccharide with a molecular weight of about 5200 and it fits all the above requirements.

P.A.H.A
(Para - Aminohippuric Acid)

Paraminohippuric acid (PAH) is *freely filtered* and *secreted* and is almost *completely cleared* from the renal plasma.

*** Uses :**

Used to measure the RBF

(Renal Blood Flow)

*** Special Properties :**

When it presents below a certain conc. in the blood ; They are completely cleared from the renal plasma by a single circulation through the kidney , due to :

Easily filtered - Secreted by renal tubules - Not reabsorbed after filtration

*** Other Properties :**

- Not enter RBC's or other tissue cells.
- Not metabolized by tissues.
- Not toxic.
- Not adsorbed to the unfiltrated plasma proteins.

1. **Amount enter kidney =** RPF x PPAH
2. **Amount entered = Amount excreted**
3. **ERPF x PPAH=** UPAH x V
4. **ERPF =**
5. **ERPF = Clearance of PAH**

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

- Conc. of PAH in urine=25.2 mg/ml
- Conc. of PAH in arterial blood=0.05 mg/ml

And the Urine flow =1.1 ml/min

Then CPAH or Renal Plasma Flow =
(25.2 x 1.1)/0.05 = 560 ML/ min

Lets say the hematocrit is 45%

Then renal blood flow will be:
(560 x 100)/(100-45)= 1018 ml/min
"Range = 1018-1200 ml/min"

Comparison of clearance of a substance with clearance of inulin		
= inulin clearance	< inulin clearance	> Inulin clearance
Only filtered not reabsorbed or secreted	Reabsorbed by nephron tubules	Secreted by nephron tubules

Calculation of tubular reabsorption or secretion from renal clearance

1. Clearance measurements are also used to *examine renal management of substances absorbed or secreted by the kidney.*

For substances secreted by the kidney:
$([sub]_{plasma} \times GFR) + T = [sub]_{urine} \times V$ *(urine flow rate)*
So, What goes into the nephrons = What leaves the nephrons.
Secretion into nephrons is occurring when: **C sub. > C inulin**

For substances absorbed by the kidney (Nephrons):
$[sub]_{plasma} \times GFR = T + ([sub]_{urine} \times V$ *(urine flow rate)*
So, What goes into the nephrons = What leaves the nephrons.
Absorption from nephrons is occurring when: **C sub. < C inulin**

Conclusion	$T = ([sub]_{plasma} \times GFR) - ([sub]_{urine} \times V)$
Note	$[sub]_{urine} \times V$ = normally zero for glucose & amino acids.

Which means: glucose & amino acids will completely reabsorbed by the renal tubules and there will be no excretion.

T *= Amount Transported*
C sub. *= clearance of substance,*
C inulin *= clearance of inulin*

Calculation of tubular reabsorption	
Substances that are completely reabsorbed from the tubules (amino acids, glucose)	Substances highly reabsorbed (Na+)
clearance = zero because the urinary secretion is zero.	**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*

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

Filtration fraction:
is the ratio of GFR to renal plasma flow.

FF = GFR/RPF = 125/650 = 0.19

Glucose clearance

1. The glucose clearance is **zero** at plasma glucose values *below the threshold and gradually rises as plasma glucose rises.*
2. We can express the excretion of glucose quantitatively at plasma concentrations *beyond the threshold,* where the glucose reabsorption rate **(T_m)** *has reached its maximum:*

Tubular transport maximum

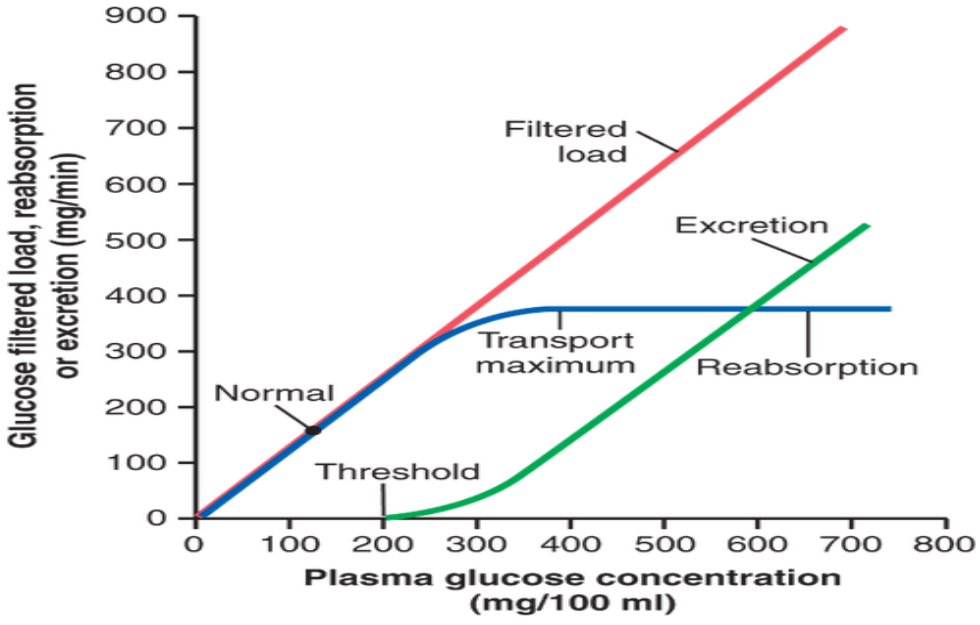
The Maximum limit/rate at which a solute can be transported across the tubular cells of kidneys is called **Tubular Transport Maximum**

Tm for Glucose is 375 mg/min

Glucose reabsorption

FBG = 60-110 mg/dl
RBG = 110-200 mg/dl

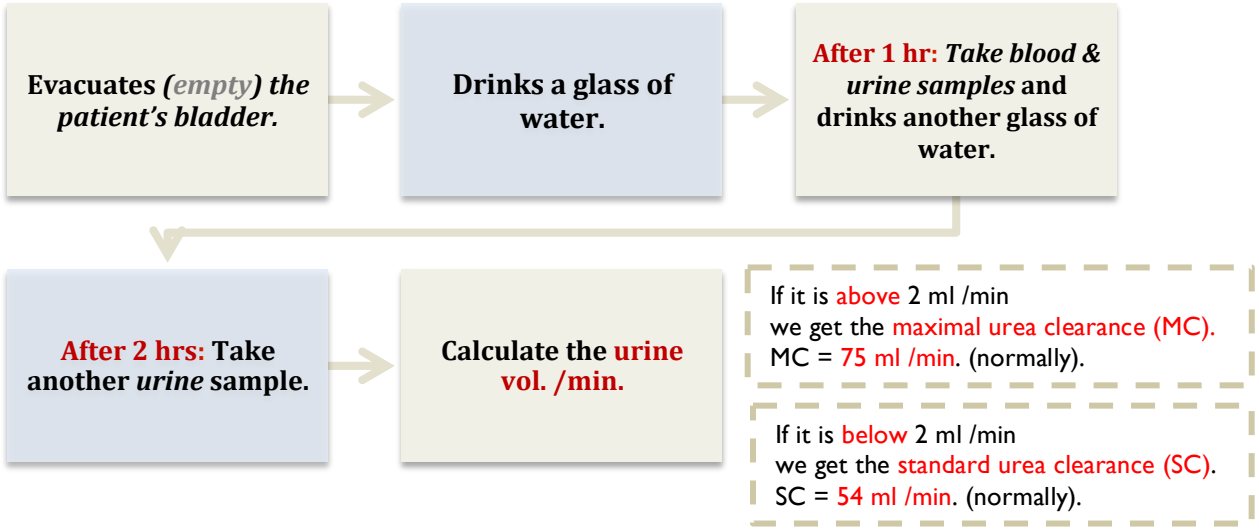
Transport max : 375 mg/min
Renal Threshold : 200mg/dl



Tubular transport maximum for glucose

Filtered load	GFR x $[P]_{glucose}$ ↑ plasma [glucose]= ↑ Filtration
plasma [glucose] < 200	• Filtered load of glucose is *completely reabsorbed.* • clearance = zero
plasma [glucose] > 200	• Filtered load is not completely reabsorbed. • "Threshold" or plasma [glucose] at which glucose is first excreted in urine
plasma [glucose] > 350 or 375	• Filtered load is not completely reabsorbed • Na+ - glucose cotransporters are *completely saturated.* • Maximal glucose reabsorption (Tm)

Urea Clearance Test



Biochemistry:

Routine kidney function test include the measurement of :

- Serum creatinine.
- Creatinine clearance.
- Serum urea.

Both serum creatinine and creatinine clearance are used as kidney function tests to:

- Confirm the diagnosis of renal disease.
- Give an idea about the severity of the disease.
- Follow up the treatment.

1. What is "Clearance"?

it is the volume of plasma cleared from the substance excreted in urine per minute.

In other words, the volume of plasma from which a substance is completely removed by the **kidney** in a given amount of time (usually a minute).

❖ **It could be calculated from the following equation:**

$$\text{Clearance (ml/min)} = \frac{U \times V}{P}$$

علشان ما تلخبط : البسط فقط فيه اشياء متعلقة بالبورين ، حجمه وتركيز الكيراتين فيه

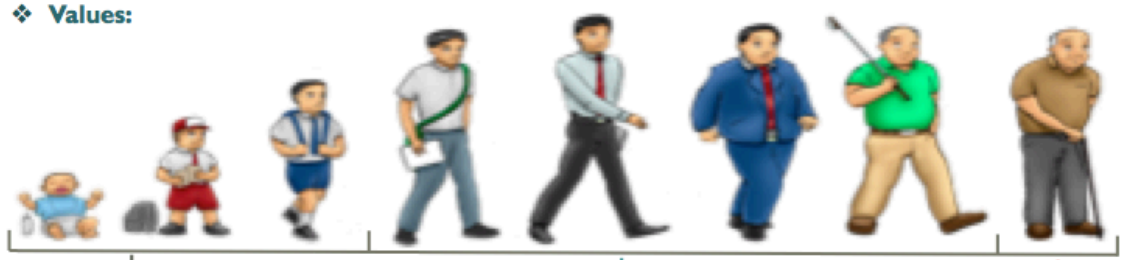
U = Concentration of creatinine in urine µmol/l

V = Volume of urine per min

P = Concentration of creatinine in serum µmol/l

clearance كلما قل
creatinine serum نستنتج من
القانون انه كلما زاد

❖ **Values:**



In children:
the GFR should be related to surface area, when this is done, results are similar to those found in young adults.

in the 20-40 year old adults:
Creatinine clearance is usually about 110 ml/min

in individuals over 80 years of age:
It falls slowly but progressively to about 70 ml/min

1. the creatinine clearance is measured by using **a 24-hour urine collection**, but this does introduce the potential for **errors** in terms of **completion of the collection**

1. An alternative and convenient method is to employ various formulae devised to calculate creatinine clearance using parameters **such as** **serum creatinine level**, **sex**, **age**, and **weight of the subject**.

the creatinine clearance's measurement can be inaccurate due to some mistakes during collecting the urine. that's why we use the cockcroft-gault formula because there's no need for collecting urine.

Cockcroft-Gault Formula for Estimation of GFR

$$GFR = \frac{K \times (140 - age) \times Body\ weight}{Serum\ creatinine\ (\mu mol/L)}$$

From this formula we can conclude that:
- Serum creatinine is inversely proportional to GFR, so high serum creatinine levels mean that the GFR is low.

K is a constant that varies with sex:
- 1.23 for male
- 1.04 for females

The constant K is used as females have a relatively lower muscle mass.

muscle mass = creatinine

It should not be used if:

- Serum creatinine is changing rapidly
- the diet is unusual, e.g., strict vegetarian
- Low muscle mass, e.g., muscle wasting
- Obesity

Obesity will give a normal GFR even if creatinine serum is high.

Serum creatinine is a better kidney function test than creatinine clearance.. Why?

- Serum creatinine is more accurate
- Serum creatinine level is constant throughout adult life

Creatinine clearance is only recommended in:

- Patients with early (minor) renal disease.
- Assessment of possible kidney donors.
- Detection of renal toxicity of some nephrotoxic drugs.

we use creatinine clearance for early renal disease due to its tight range. as for creatinine serum its range is wide and therefore it won't indicate impaired renal function unless its highly raised.

Urinary excretion of creatinine is:	0.5 - 2.0 g per 24 hours in a normal adult, varying according to muscular weight.	
Serum creatinine :	80 – 125 ml/min	
Creatinine clearance:	Males	90 – 140 ml/min
	Females	80 – 125 ml/min

Raised Serum creatinine:
A good indicator of impaired renal function

Normal serum creatinine
Does not necessarily indicate normal renal function, as serum creatinine may not be elevated until GFR has fallen by as much as 50%

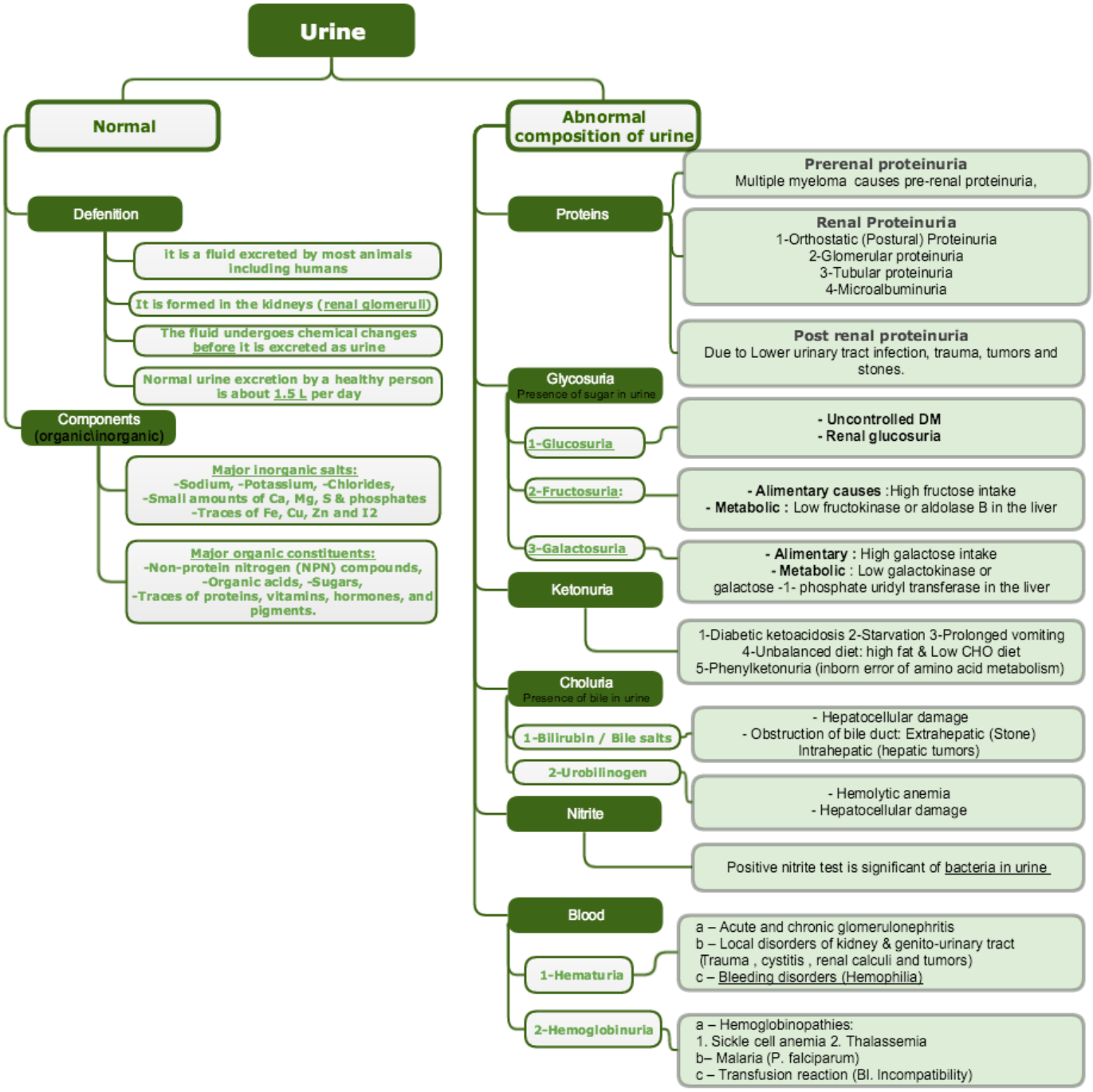
As a kidney function test, serum urea is inferior (secondary) to serum creatinine because:

High protein diet increases urea formation

Any condition of ↑ proteins catabolism *(Cushing syndrome, diabetes mellitus,* starvation, *thyrotoxicosis)* →↑ urea formation.

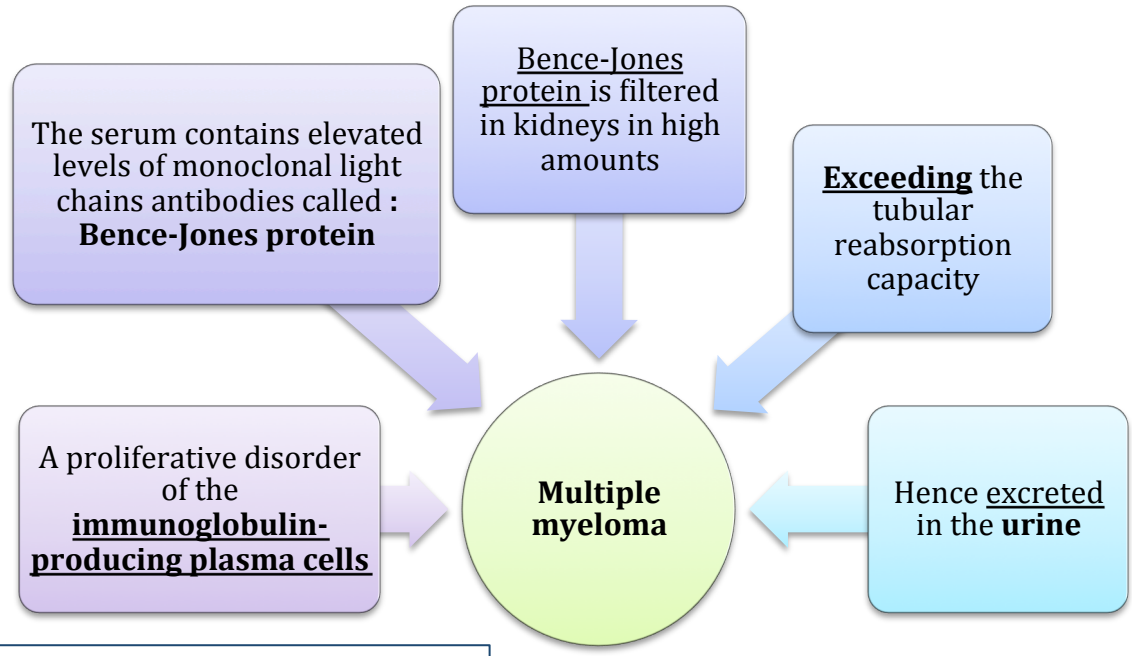
50 % or more of urea filtered at the glomerulus is passively reabsorbed by the renal tubules.

Chemical Examination of Urine

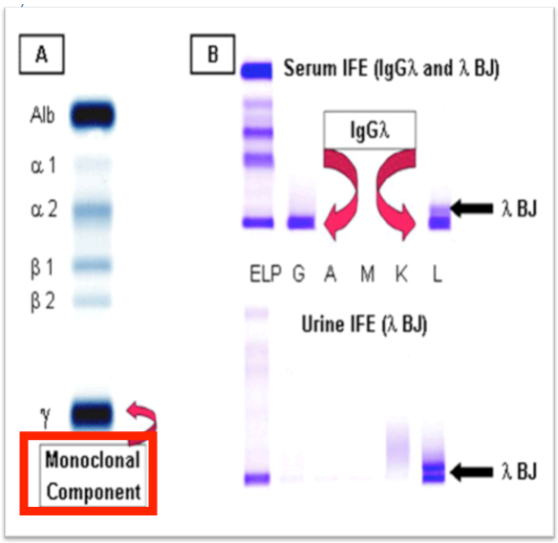


*** Done By: Nouf Alabdulkarim**

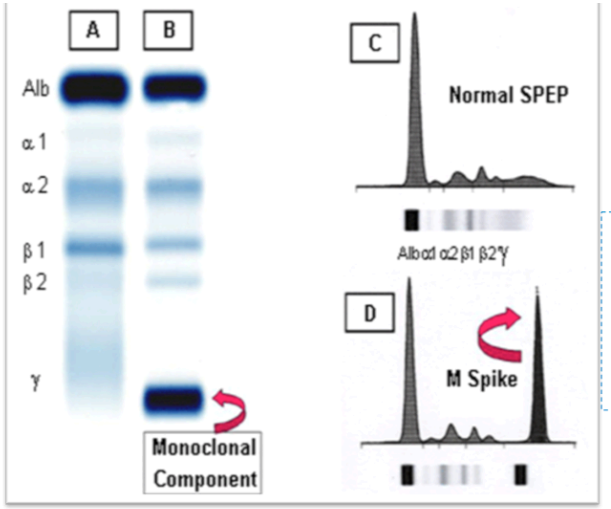
1. **Multiple myeloma cases are diagnosed by using:**
    1. **Serum electrophoresis**
    2. **Immunoelectrophoresis**



1. **The Bence-Jones protein:**
1. **Coagulate at** 40–60 °C
2. **Dissolves at** 100 °C



A: serum protein electrophoresis demonstrating the M component.
B: serum and urine immunofixation electrophoresis



the second spike in D indicate that there is multiple myeloma

A: normal serum.
B: multiple myeloma showing M component in the gamma region.
C: densitometry tracing of A showing the 5 zones of the high resolution agarose electrophoresis.
D: densitometry of the M component of B, termed the M Spike

1- Glomerular Proteinuria:

-**glomerular permeability:** High
- Causes filtration of **high molecular weight** proteins **(e.g. glomerulonephritis)**

2-Tubular proteinuria:

1. **Glomerular permeability:** normal.
2. **Tubular reabsorption:** Low.

- Causes excretion of **low** molecular weight proteins . **(e.g. chronic nephritis)**

3- Orthostatic (Postural) Proteinuria

What is it?

1. A persistent benign proteinuria. (Type of renal proteinuria).

- It affects:

Young adults (teenagers between age 14 and 19).

1. **It happens due:**

Periods spent in a vertical posture (it is found in young teenage boys after playing. they complain of having frothy or white dish in their urine).

1. it's believed that the reason for this condition is **the increase in orthostatic pressure on the renal vein** while the person is in the vertical position, and thus that will cause orthostatic proteinuria (by forcing the proteins to filtrate by the pressure).
2. **It disappears in: horizontal posture**.

How can we diagnose it?

-They diagnose it by exclusion. (Because they didn't find an exact hypothesis for it)

4- Microalbuminuria

What is it?

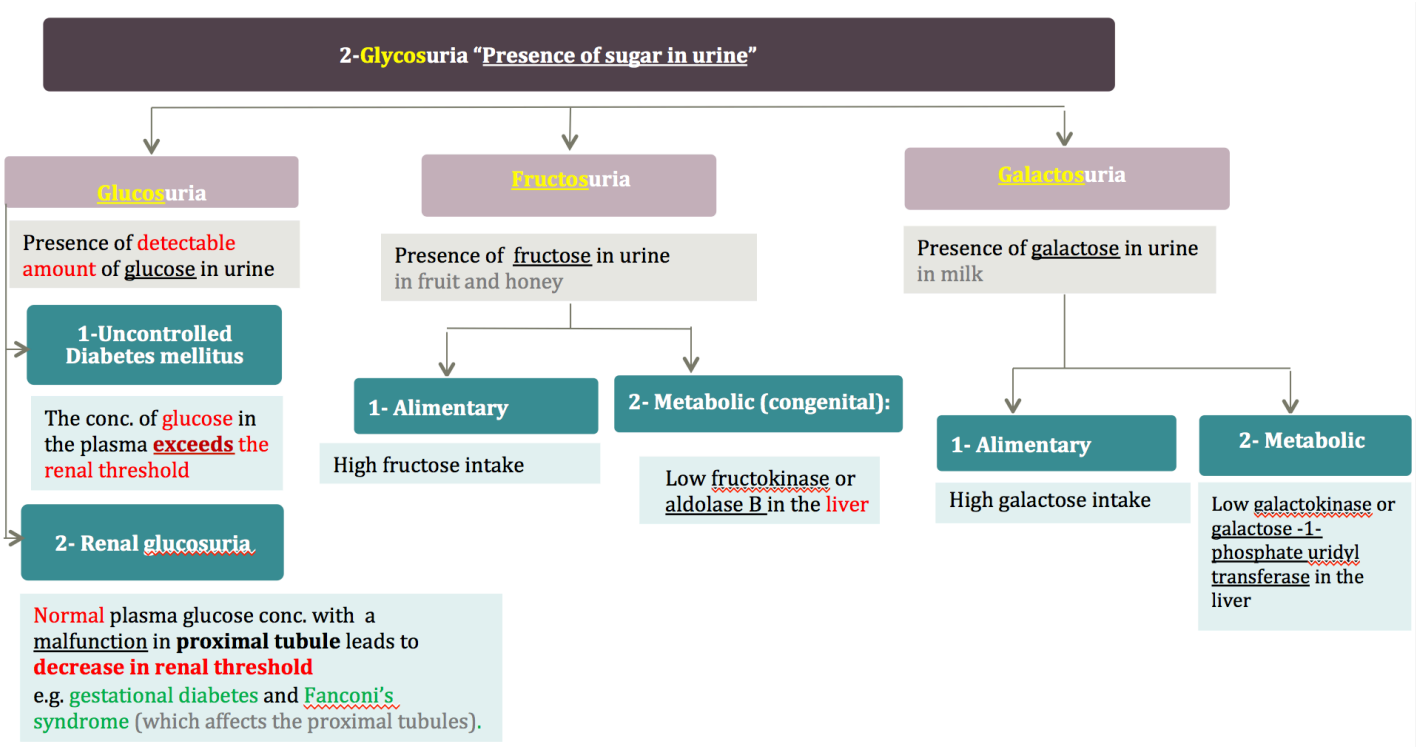
1. Presence of small amounts of albumin in the urine. (Between 20– 200 mg/day)

- How it's detected?

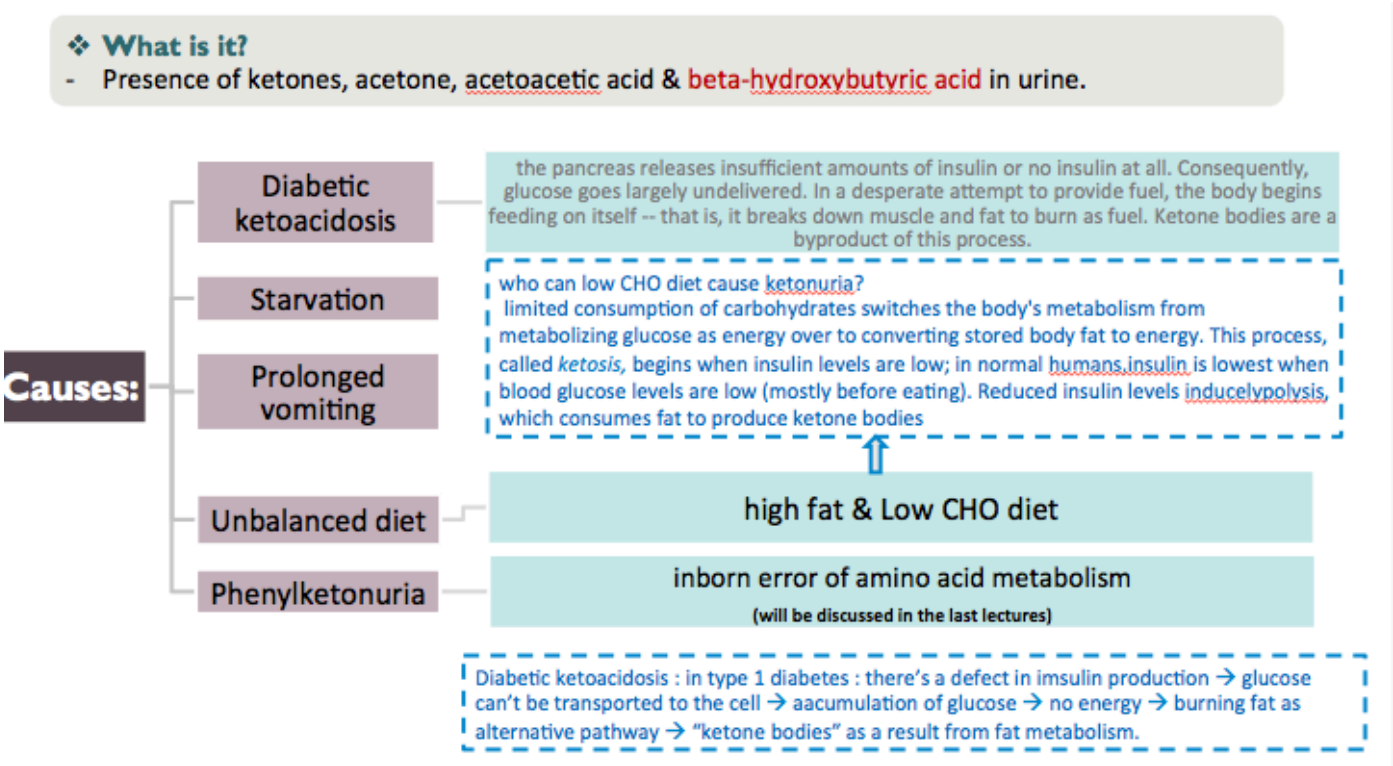
it needs **special tests** for detection, because It cannot be detected by ordinary urine testing.
Ordinary urine test = deep stick test

-What does it detect?

It is an early indicator of glomerular dysfunction (renal impairment), due to uncontrolled **diabetes mellitus** or **hypertension**.


2-Glycosuria "Presence of sugar in urine"
Glucosuria
Presence of detectable amount of glucose in urine
1-Uncontrolled Diabetes mellitus
The conc. of glucose in the plasma exceeds the renal threshold
2- Renal glucosuria
Normal plasma glucose conc. with a malfunction in proximal tubule leads to decrease in renal threshold
e.g. gestational diabetes and Fanconi's syndrome (which affects the proximal tubules).
Fructosuria
Presence of fructose in urine in fruit and honey
1- Alimentary
High fructose intake
2- Metabolic (congenital):
Low fructokinase or aldolase B in the liver
Galactosuria
Presence of galactose in urine in milk
1- Alimentary
High galactose intake
2- Metabolic
Low galactokinase or galactose -1-phosphate uridyl transferase in the liver

3- Ketonuria:


What is it?
- Presence of ketones, acetone, acetoacetic acid & beta-hydroxybutyric acid in urine.
Causes:
Diabetic ketoacidosis
the pancreas releases insufficient amounts of insulin or no insulin at all. Consequently, glucose goes largely undelivered. In a desperate attempt to provide fuel, the body begins feeding on itself -- that is, it breaks down muscle and fat to burn as fuel. Ketone bodies are a byproduct of this process.
Starvation
Prolonged vomiting
who can low CHO diet cause ketonuria?
limited consumption of carbohydrates switches the body's metabolism from metabolizing glucose as energy over to converting stored body fat to energy. This process, called ketosis, begins when insulin levels are low; in normal humans insulin is lowest when blood glucose levels are low (mostly before eating). Reduced insulin levels inducelypolysis, which consumes fat to produce ketone bodies
Unbalanced diet
high fat & Low CHO diet
Phenylketonuria
inborn error of amino acid metabolism
(will be discussed in the last lectures)
Diabetic ketoacidosis : in type 1 diabetes : there's a defect in imsulin production → glucose can't be transported to the cell → aacumulation of glucose → no energy → burning fat as alternative pathway → "ketone bodies" as a result from fat metabolism.

4-Choluria:

❖ What is a Choluria?
Presence of bile in urine

	Bilirubin / Bile salts	Urobilinogen
What is it?	Presence of bilirubin in the urine, which normally (physiologically) not detectable in the urine. Remember: bilirubin resukts from breaking of RBCs	Presence of High amounts of urobilinogen, which is normally (physiologically) present in trace amounts in urine.
Detected in:	1- Hepatocellular damage	1-Hemolytic anemia
	2- Obstruction of bile duct: - Extrahepatic (Stone) - Intrahepatic (hepatic tumors).	2- Hepatocellular damage.

##5-Nitrite (not nitrate):

Positive nitrite test is significant of bacteria in urine

6-Blood :

	Hematuria	Hemoglobinuria
What is it?	presence of detectable amount of blood in urine	Presence of hemolysed blood in urine
Detected in:	1-Acute and chronic glomerulonephritis	1- Hemoglobinopathies: - Sickle cell anemia - Thalassemia
	2- Local disorders of kidney & genito-urinary tract (Trauma , cystitis , renal calculi and tumors)	2- Malaria (P. falciparum), Plasmodium falciparum is a protozoan parasite, one of the species of Plasmodium that cause malaria in humans.
	3- Bleeding disorders (Hemophilia).	3- Transfusion reaction (Bl. Incompatibility).

Pathology of the kidney (AKI):

What is acute kidney injury (acute renal failure)?

Acute kidney injury is defined as a sudden decline in renal function. (Within hours to days)

What constitutes ARF?

- Acid-base disturbance.
- Increased Scr.
- Electrolyte and mineral disorders.
- Derangement of extracellular fluid balance.
- Accumulation of nitrogenous waste products.

Etiology:

A- Outpatients: the most common cause is Prerenal.

B- Inpatients: the most common cause is Intrarenal.

C- Obstruction happens to both with approximately same percentage.

Predictors of Dialysis in AKI:

- Oliguria:
  - Less than 400cc/24hr 85%will require dialysis
  - More than 400cc/24hr 30-40% will require dialysis. (But not as much)
- Mechanical ventilation.
- Acute myocardial infarction.
- Arrhythmia (K+ Level up).
- Hypoalbuminemia.
- ICU stay.
- Multisystem organ failure.

Causes of acute kidney injury:

- **Prerenal ARF:**

  Any condition that ↓ renal blood flow would cause a decrease in (**GFR**) → **azotemia**

  Decreased blood flow could be due to:

- Hypotension: Shock (septic, cardiogenic, hypovolemic)
- Vascular pathology: Renal artery stenosis for example.
- Third spacing.
- Volume depletion: Loss of fluids, for example:
- Drug induced: NSAID, CsA, FK506, ACE, ARB

  - In prerenal azotemia there is decreased renal perfusion with *no damage* to the kidney parenchymal cells (in the beginning).
  - In addition, decreased blood flow → Decrease in GFR → ischemia to the nephrons → necrosis of the kidney's cells after hours.

- **Intrarenal ARF:**

  Happens from the kidney itself, due to one or more of the four elements, which are: tubules, glomeruli, blood vessels and interstitium.

  How is it described based on Clinicopathological entity?

  Pathologically:

  Destruction of tubular epithelial cell (Acute tubular necrosis)

  Clinically:

  Acute suppression of renal function (no urine or below 400 ml/24h)

- Postrenal ARF:
  - Results when urine flow is obstructed.
  - Examples include kidney stones, BPH (Benign Prostatic Hyperplasia), tumors, etc.

Acute tubular injury:

Ischemia: Shock, sepsis, incompatible blood transfusion, thrombotic disease.

Tubular Toxins:

- Antimicrobials: Aminoglycosides, vancomycin, foscarnet, pentamidine, amphotericin B.
- Chemotherapeutics: Cisplatin, mitomycin C, ifosfamide.
- Immunotherapy: IVIG (Intravenous immunoglobulin)
- Complex Sugars: Maltose, sucrose, mannitol
- Heavy metals.
- Sepsis, hypoxia.
- Radiocontrast agents.

We have two types of toxins:

- Endogenous: Produced by our own body, for example:
  - Crush injury: Myoglobin (normally in skeletal muscles)
  - Hemoglobinopathy.
- Exogenous: Drugs, Radiocontrast dye, Metals.

Other causes for acute kidney injury include:

- **RPGN** (Rapidly Progressive Glomerulonephritis):

  A syndrome defined by the loss of renal function over days to weeks due to acute glomerulonephritis.

- Diffuse renal vascular diseases, such as microscopic polyangiitis and thrombotic microangiopathies.
- Acute **drug induced** allergic interstitial nephritis.