PHYSIOLOGY

- Sheet No. 2
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بالتوفيق💚

Excretion → whatever left of filtered fluid after filtration, absorption and secretion processes

Secretion → an active selective process that removes some of the waste products from the Peritubular capillaries that will be eliminated from filtered fluid

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how our kidney handles different substances ?

- We have three processes , **<filtration , reabsorption and secretion >** and the result of these processes **is (excretion) ,,,, you have to differentiate between secretion and excretion .**

If we look at Na^+ as an important electrolytes in the extra-cellular fluid compartment → only 150 mm will be excreted

Renal Handling of Water and Solutes

	Filtration	reabsorption	excretion
L/day Water	180	179	1
+Na mmol/day	25,560	25,410	150
Glucose gm/day	180	180	0
Creatinine gm/day	1.8	0 Poorly absorbed	1.8

Majority

- Note how our kidneys handle **the water** , we've filtration 180 , absorption 179 ,, so the net excretion is one liter per day , (as urine)
  the doctor reads the rest of the table reading .
- Note that the kidney handle the **glucose** in different way , the same amount of filtering is reabsorbed , **leaving NOTHING to be excreted in the urine** . so we don't expect to have any glucose in urine , < except you have disease such as diabetes >
- **Creatinine** is example on waste product in our body , 1.8 gram per day will be filtered , this amount comes from the muscles as a result of the muscular activity as a by product , and there **will be nothing to be reabsorbed** , and all amount will be excreted .and actually the excretion is more than the filtered because of the secretion , the numbers isn't so accurate .

Waste product

- We conclude that the kidney deal in different ways with the substances it doesn't deal with all in the same way .**and this is the function of the kidney , to get away the waste product and keep the needed things < nutrients >**

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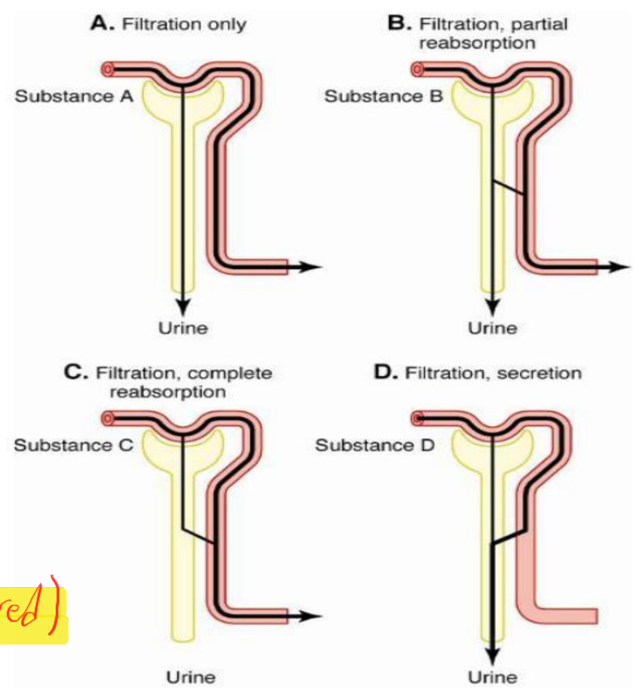
renal handling of different substances :



we have four different choices for how kidney deal with substances :

A. **Filtration only** : the substance will be filtered without any reabsorption or secretion "look at the graph you can't see any arrows between the blood and tubule " it's **very rare** to have substance like that from inside the body , maybe it's expected to give a patient substance like that and get through this pathway . you have to note that not all the blood will be filtered , just 20% . (and just 20% of A will be filtered)

filtration fraction

B. **Filtration and partial reabsorption , part** of the filtered substance will be reabsorped , but part of it stay in urine , this what we called partial reabsorption , in this way we will have some excretion in urine .(**excretion = filtration – reabsorption**) this scenario happen for water and most of electrolytes in our body (Na^+ , Cl^-)

Filtered at the same rate of filtration in substance A → 20%

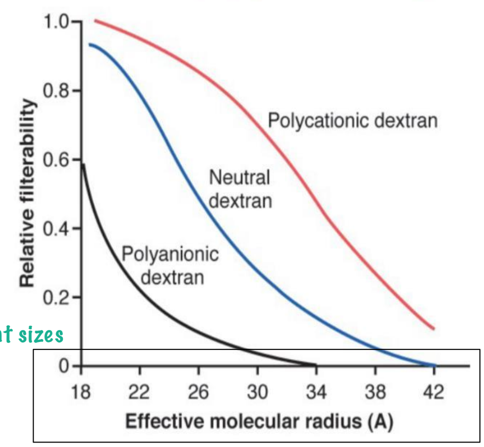
C. **Filtration , complete reabsorption :** we don't have any excretion , complete reabsorption for filtered substances , this is an example of all nutrients in our body such as glucose , amino acids , the reabsorption for this substances is so fast , with no excretion of any valuable substances "to avoid the loss of amino acids and glucose" .

D. **Filtration , secretion :** we have no reabsorption , the body don't want this substance , and it want to get it away from the body by secretion , **(excretion = filtration + secretion),** this is an example of waste products , metabolites of drugs and organic acids and bases that the body excrete to maintain normal PH .

Urinary excretion is very high

Factors that affect filtration process :

Effects of size and electrical charge of dextran on filterability by glomerular capillaries.



Different sizes

- Filtration is a passive process , not selective ,and by this experiment enabled us to know the exact factors that affect the filtration .
- This experiment was designed by giving the animal or the patient three kinds of solutions that they know its components: **polycationic dextran , neutral dextran and polyanionic dextran .**
- Dextran is a kind of sugar (Sugar polymers) designed to be either highly negatively charge (anionic) , or neutral (consist of positive and negative) , or highly positively charge (cationic)
- They designed the same dextran **in different sizes** , in each kind it is designed in several radius according to the difference in molecular weight.
- So in conclusion **they change the charges of the dextrin and the sizes** , then they plotted this graph which represents the type of the solution with the different relative filterability (ratio of filtration)
- By looking at the Y axis , when Y=1 , it will be the best filtration with the highest filtration rate .
- Y= 0.5 the half of filtration ,, and by going down it will be less and less .

- As you can see from the figure, the **polycationic dextran** has the highest rate of filterability , it achieved the highest filterability for each size .
- example : for size 22 the **polycationic dextran is the highest** , then going down the neutral dextran is lower , **and the lowest rate is for the polyanionic dextran** (draw a perpendicular line from size 22 and observe the values of the filterability)

• the highst filtration rate ⟶ when the substanse is positivly charge & as much as small in size .

- So if you fix the molecular radius in certain number , you will find that the **polycationic has the highest filterability , then neutral , lastly is polyanionic**
- That's actually make sense , because we know the composition of the filtration membrane , and we know that one of the barriers **is highly negatively charge** < the basement membrane > so any negative molecule will be so hard to pass through , so the filterability of it will be very low **(polyanionic dextran)** So, the larger size the less filtrability The lower molecular radius the higher filterability
- The **neutral dextran** depends mainly on size , the smaller the size , the more the filterability
- The **polycationic dextran is the best filterability in all different sizes**
- The other factor that affect the filterability is the size , **the smaller the molecule the easier and higher the filterability**
- In some solutions " **anionic** " when it reached too large size , **the filtration stops** , and that because of the charge .and some solution the filtration continues but in low manner .
- **From the previous experiment we can conclude that even if the filtration process is a passive process , it's also depends on the size and charge of the molecule .so different molecules has different rate of filterability**

Glomerular Filtration: it's the same process that we have talked about lately .

- To consider if the glomerular filtration is normal or abnormal , scientists measure a rate which is called **<glomerular filtration rate > GFR**
- They found that if we collect all of the solutions that are filtered in both kidneys per day (**total amount of filtered fluid in each day will be equal to 180 liters/day**)and this is according to the ability of the kidney to filtering.
- GFR = 125 ml/min = 180 liters/day (normal rate) there are differences between male and females in this value , depends on age , body weight .
- If you ask yourself : how I can have 180 liters filtered from my body and I have only 5 liters of fluid in the body and sometimes less ! .... the answer :
  1. Plasma volume filtered 60 times per day :
     a) this is very important for our body health , to rapidly get away from the waste products to prevent them staying long in our body .
     b) it's good for monitoring the changes that happens inside the fluid and blood in very efficient way **<osmolarity , electrolytes balance , blood pressure >**

- Glomerular filtrate composition is about the same as plasma, except for large proteins because they won't pass due to the charge of them and the size .
- **Filtration fraction** (GFR / Renal Plasma Flow)= 0.2 (i.e. 20% of plasma is filtered)
- Filtration fraction is the ratio between filtration rate to plasma flow rate
- **Plasma flow rate** , that entre the kidney , represent how much ml of plasma enters the two kidneys <perfuse the nephron> per minute
- Normally the filtration fraction is 20% , which means that **20% of renal plasma flow filtrates**

Clinical Significance of Proteinuria

- Sometimes when proteins leaks outside the barriers that we talked about previously , in this case we will have proteins in the urine we called this case protein urea, and it's important to do early detection for this case , it helps us to detect any renal disease in early times before any symptoms

  - Early detection of renal disease in at-risk patients

a) hypertension: hypertensive renal disease (such as eclampsia in pregnant females)
b) diabetes: diabetic nephropathy , there will be damage in the membranes , podocytes or basement membrane
c) pregnancy: gestational proteinuric hypertension (pre-eclampsia) it helps the proteins to filter because of the high pressure
d) annual "check-up": renal disease can be silent

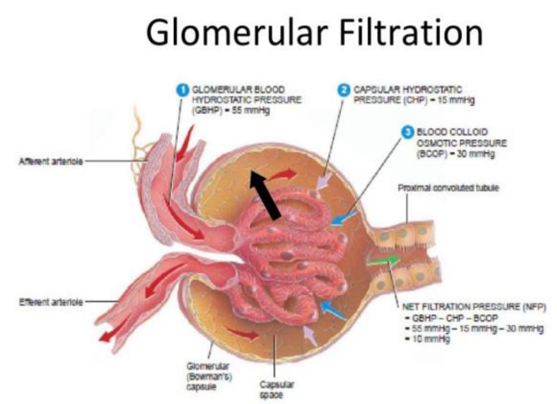
  - Assessment and monitoring of known renal disease

Forces that govern filtration

1. Glomerular filtration

Passive process , depends on hemodynamics processes that regulate the filtration process

Blood is coming through the afferent arteriole having hydrostatic pressure that its origin is from the heart (the blood pressure).



- 3 types of pressure in the nephron:-

Systolic pressure is 120, and the diastolic is 70 or 80, so the mean arteriolic pressure is 100 mmhg. This pressure is decreasing while moving from the heart to other part in the body and when reaching to the afferent arterioles it's gonna be 55 mmhg that is called glomerular blood hydrostatic pressure. (these capillaries have the highst pressure in all capillaries in the body)

When that pressure entering the glomerulus it gonna push the fluid that is located inside the glomerulus in a pressure equal to 55 to the outside of the glomerulus into the bowman's capsule .- black arrow-

The fluid that has been filtered to the bowman's has hydrostatic pressure (any fluid in container has a hydrostatic pressure) it's called capsular hydrostatic pressure, its opposite in direction to the capillaries pressure (its opposite to glomerular hydrostatic pressure) and its low (15 mmhg)

We have another type of pressure that is called colloid osmatic pressure (oncotic pressure) it exist in a place where there is protein that can't pass the barrier (endothelial cells membrane) it exist in the capillaries (glomerulus) in a high value

Related to presence of large protein inside the glomeruli → that can't leave the capillaries due to it's large size

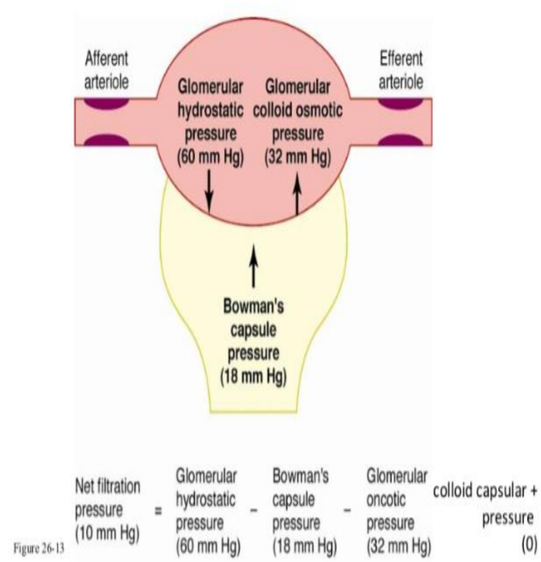
What happen is that because that protein can't cross the membrane it will build a pressure that is trying to draw the fluid back to the glomerulus in order to make osmatic balance (the direction is from bowman's to glomerulus) and its equal to 30 mmhg

The direction is against filtration

** there is no protein in bowman's capsule, so the osmatic pressure (oncotic) is zero, some books says that it has but the value is very low

Net pressure (the doctor leave this part to Lec.3)

1. Net filtration pressure :will give every force with filtration positive sign, and the opposite negative sign.
   -Glomerular hydrostatic pressure : +55
   -Capsular hydrostatic pressure : -15
   -Capillary(glomerular) pressure: -30



So the net = +10 mmhg. Which mean that 10 mmhg favoring filtration from the glomerular into the bowman's capsule , and if we take the colloid capsular pressure in consideration it gonna have positive sign because it is favoring filtration

- In the pic that in the previous paper u can see some differences but that isn't problem

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- Filtration fraction: the blood plasma in the afferent arterioles that becomes filtrate (16- 20 %) that we got it by dividing the GFR over the renal plasma flow (RPF)

  ≈ constant

  GFR: The volume (ml) of fluid filtered through all the corpuscles of both kidneys per minute.
  The volume of fluid filtered daily through all the corpuscles of both kidneys per day = 180 L
  GFR= 180 L/24hours * (1000 ml/ L)*(1hour/60 min)= 125 ml/min (Males)
  In females it's a little bit different, but we will consider that the 125 is the normal GFR

- If we know the FF (20%) and the normal GFR (125), we can know how much renal plasma flow should be in order to have normal GFR

  20% = GFR/ RPF = 125/ RPF, RPF = 625

SO there must be entering of plasma flow rate =625 the nephron (both kidney) to have normal GFR, any change (decreasing) in the flow rate will affect the GFR, because the kidney effectiveness in the filtration process will decrease and the waste product in our bodies will stay longer .

- Renal plasma flow is not the same as blood flow
  55% of blood is plasma, so blood flow rate = 1140ml/min
  How to get it? –> 55% * BF= PF; BF= 625ml/min/ (55%)=1140 ml/min
  SO that mean that 1140 ml/min blood should enter the kidney

Renal Blood Flow of 1140 ml/min = 22.8 % of 5 liters (cardiac output) is required to have GFR of 125ml/min. if it decreased the GFR will be affected.

* Good luck