Sheet #30 (physiology)

We finish talking about Glomerular Filtration as the first process of urine formation.

The second process is Tubular Reabsorption &secretion.

Let's start with clearness because if you measure the clearness you can know the GFR which is a measure of kidney's functions:

If GFR is low that’s mean there is kidney failure.

The clearness describes the rate in which the plasma is cleared completely.

Renal clearance of a substance: is the volume of plasma completely cleared of a substance per min by the kidneys.

Definition: The volume of plasma completely cleared of a substance (x) per minute.

Units are ml/min

s.

\* Renal clearness isn’t something that you feel it; it's something that you calculate it.

\* First thing you calculate what's excreted & what's filtered so (clearness= what's excreted /plasma concentration of the substance).

(What's excreted): mainly we care about urine collection.

We collect the urine in a whole day then we divide it on 1440 “60 minutes \* 24 hours” and the answer will be in ml/min

\*(Ux \*v) is what is been excreted from a substance (how much is excreted).

\* From what is excreted we want to see how much is coming from the plasma.

To know from how much plasma is coming we have to divide it by plasma concentration of that substance & this is called clearness.

If we have urine we have to know how much is coming from plasma then we divide it by plasma concentration of that substance.

Substance like Inulin that’s not reabsorbed, freely filtered, not degraded so the clearness of this substance is how much is going to be filtered. So all what's filtered (they loss there substances) & those who is filtered they are also reabsorbed (99%).

This substance its clearness is a measure of GFR (what's filtered per minute is equal to GFR).





**CInulin – is equal to the GFR.(Glomerular Marker) Inulin is a Fructose polymer ; freely filtered across the membrane and neither reabsorbed nor secreted.**

**General equation:**

**Urine flow rate (ml/min)….if we give it to you in mg/100ml of urine you have to be careful to units.**

**Glucose is completely reabsorbed so the clearness is equal to zero,because nothing from plasma is lost there.**

**Albumin clearness is zero because it is not filtered at all.**

**Clearness of sodium is 0.9 so its less than GFR so it is must be reabsorbed.**

**Clearness of urea is 70 because it is really reabsorbed.**

**Clearness of Inuline is 125 which is equal to GFR**

**Clearness of creatine is 140 so its secreted.**

**ClearnessofPAH(Paraminohippuric acid )is 600 so its completely secreted.**

**This substance is exogenous (this substance is excreted ,filtered&whats left is secreted completely so there will be no substance in plasma ,so all the plasma flow to the kidney has lost their PAH &its clerness is a measure of plasma flow.)**

**So use of clearness to measure GFR :**

**1-Substance that’s completely filtered, not reabsorbed ,not secreted(Inulin,iodine creatinine,but Creatinine is a little bit secreted………….(renal clearness=GFR)**

**2-Theoretically, if a substance is completely cleared from the plasma(completely secreted), its clearance rate would equal renal plasma flow**

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

**(RPF=Renal plasma flow)\*plasma concentration**

But if it wasn’t completely cleared (only 90%) you have to do correction.

How you can calculate renal blood flow?

Using PCV value, if it was 50%...So blood flow =1200(600\*2)

If the PCV was 45% this plasma flow constitutes 55% of the blood flow. We multiply by (100/55).

PAH some of it may not be secreted (some of it still in the efferent arteriole) so we have to do correction.

**Calculation of Tubular Reabsorption:**

**\*Reabsorption = Filtration –Excretion**

**\*Filt s = GFR x Ps**

**Ps (plasma concentration)**

**\*Excret s = Us x V**

**(Concentration Of the substance in urine\*flow rate).**

**Calculation of Tubular Secretion:**

**Secretion = Excretion – Filtration**

**\*you can know if there is net secretion or net Reabsorption.**

**\*Secreted>reabsorbed (there is net secretion)**

**\* Excretion= Filtration+secretion**

**Use of Clearance to Estimate Renal Plasma Flow:**

**Theoretically, if a substance is completely cleared from the plasma, its clearance rate would equal renal plasma flow.**

**Cx = renal plasma flow.**

**Substance Clearance (ml/min**

**inulin 125**

**PAH 600**

**glucose 0**

**sodium 0.9**

**urea 70**

**\*Clearance of inulin (Cin) = GFR**

**if Cx < Cin : indicates net reabsorption of x\***

**if Cx > Cin : indicates net secretion of x**

**if Cx=0 :completely reabsorbed or no filtration.\***

**Clearance creatinine \*(Ccreat) ~ 140 (used to estimate GFR) because cretinine is endogenous substance(we take blood sample but still we need the volume so we collect a sample of urine for 24 hours &then we divide it by 1440 the answer(flow) will be in ml/min .we take the sample of this &measure the creatinine concentration in the urine.**

**Clearness of Inulin we use renal plasma flow.\***

**\*If the GFR decreases (50%) so Plasma concentration creatinine increases double. (This is a sign of renal failure).**

**\*When we want to see if this person has renal failure we should see the creatinine concentration in plasma. (This gives us indication about GFR.**

**\*creatinine production it decreases at the beginning but then it will remain constant.**

**\*CRETININE concentration as a function of Glomerular filtration.(the creatinine concentration is about 1mg/100ml plasma).**

**\*when the GFR decreases ..Creatinine increases**

**Curvy linear not exactly linear so as if the GFR is 125 the plasma creatinine concentration is very high.**

**\*people that have a high creatinine plasma concentration (there is a problem in kidney, impaired filtration, so filtration is decreases.**

**\* Example: Given the following data, calculate the rate of Na+ filtration, excretion, reabsorption, and secretion:**

**GFR =100 ml/min (0.1 L/min)**

**PNa = 140 mEq/L .**

**urine flow = 1 ml/min (.001 L/min)**

**urine Na conc = 100 mEq/L**

**\*Reabsorption=filtration-excretion.**

**\*Example: Given the following data, calculate the rate of Na+ filtration, excretion, reabsorption, and secretion:**

**GFR =100 ml/min;**

 **PNa = 140 mEq/L**

 **urine flow = 1 ml/min;**

 **urine Na conc = 100 mEq/L**

**Filtration Na = 0.1 L/min x 140 mEq/L = 14 mEq/min**

**Excretion Na = .001 L/min x 100 mEq/L = 0.1 mEq/min**

**Reabsorption Na =Filtration Na - Excretion Na**

**Reabs Na = 14.0 - 0.1 = 13.9 mEq/min**

**Secretion Na =There is no net secretion of Na since excret Na < Filt Na**

**\*\*mechanisms of Reabsorption:**

**\*for water Reabsorption one of the most important mechanisms is bulk flow.**

**\*bulk flow: is the flow of all the contents of plasma through intercellular junctions (pores).**

**\*Like the water that moves through a valley &it take all the contents with it.**

**\*bulk flow is where the water & contents coming from the peritubular .**

**Intercellular junctions differ between one part of the tubule from the other parts.**

**\*proximal convoluted tubules: the intercellular junction is open, that’s why it's very permeable to ions.**

**\*it's much tighter in the distal convoluted tubules so the permeability will be less.**

**\*if it was very permeable no gradient or no net flow (no difference between inside &outside)**

**\*if it was tight, the gradient between tubule &paratubule is more.**

**\*this is what we will talk about when we will talk about acid-base balance.**

**\*in acid –bas balance the difference between ph of the tubular lumen &the ph of the peritubular cells.(the junction is impermeable )**

**\*the proximal convoluted tubule the tight junction is not really tight. But they are tight in the distal convoluted tubules.**

**\*there is paracellular path / Transcellular path/passive osmosis.**

**\*most of the water is reabsorbed secondary to sodium Reabsorption.**

**\*sodium Reabsorption is the primary factor that determines how much oxygen been used.**

\*Primary active transport uses ATP directly by Na-K pump, which removes Na from intracellular to interstitial, so it keeps Na intracellular low, so there is always gradient between tubular fluid and intracellular.

\*Na-K pump removes Na down its concentration gradient. At intercellular junction, it makes osmotic pressure. This moves water and sodium (but the junction is not so tight)

\*At the lumen, there is brush border contains enzymes, carriers for glucose and amino acids, that’s called glucose-sodium co transport, amino acid-sodium co transport and sodium-hydrogen counter transport… they are all at the brush border and all called primary active co transport of Na through Na-K pump.

\*Secondary active co transport like glucose-Na co transport, glucose here does not go passively

\*What makes glucose to go from one side of cell to another? Na inside the cell is kept low by Na-K pump

Luminal Na= plasma Na= 140…….so filtrate is kept high (140)\*

Glucose goes from one cell to another passively\*

If we block Na-K pump, there will be no secondary active co transport\*

Counter transport is driven by concentration of Na\*

\*Glucose is absorbed completely in proximal convoluted tubule, once it passes the proximal convoluted tubule, it will appear in urine, because no process to transport glucose anywhere except in this area (proximal tubule).

\*Proximal tubule is a carrier mediated, has binding sites , if these binding sites are completely saturated, we call this Tmax , transport maximum, or Vmax. We cannot exceed this.

\*Km is for affinity, Vmax or Tmax are for capacity.

\*If concentration of glucose in filtrate < Vmax, then all glucose is reabsorbed.

If concentration of glucose in filtrate > Vmax. Then what's extra of Vmax will appear in urine.

\*Glucose might appear in urine before Vmax, that’s called threshold. Means that not all nephrons have the same (general) Tmax

\*If Tmax of nephrone < Tmax general, then what's going to pass through the proximal tubule, will be excreted in urine, so its Tmax=180, all above 180 will be in urine because the Tmax general is 200, e.g. if Tmax of nephrone is 180, if it reached 200 the 20 (200-180) will be in urine--> this is called threshold--> saturated carriers for substances… that’s all because of that every nephrone works independently

\*So when Glu appear in urine before Tmax, this is due to not all nephrons have the general Tmax, they might have a less one

\*So glucose might appear in urine, and its normal, because we consider Tmax=180, and all above this is in the urine.

So Tmax is the saturation of carriers, threshold is the tubular road to transport in nephrons, and not all nephrons have the same Tmax.

Glucose-amino acids---> have carriers.

\*\*An Example to calculate what's excreted of glucose:--

GFR=90 ml/min in plasma, Glu=2mg/ml plasma, Tmax=150 ml/min

So, what's filtered=GFR\*2=90\*2=180

What's reabsorbed=Tmax=150

So what's excreted is what's filtered**-**what'sreabsorbed=180-150=30 ml/min

It's possible to be more than this in case of threshold

Reabsorption of glucose and other solutes is coupled with Na Reabsorption like Glu/aa co transport

Reabsorption of water= Reabsorption of sodium

Water will go through by osmosis (osmotic pressure traps water), after water, bulk flow of all contents occurs…what drives this mechanism? Na-K pump

Luminal Cl- and urea --> bulk flow passively by –ve potential

Proximal tubule is freely permeable to almost all substances beside glucose and amino acids

What's going to be reabsorbed is 2/3 of the filtrate, that’s passively by what's called obligatory Reabsorption (u like it)

If u have 120 ml filtrate…so u have 2/3 of this reabsorbed…80

Osmolarity of plasma of filter is 300…its isotonic solution

What's reabsorbed in proximal tubule is called isotonic Reabsorption

What's the osmolarity in the terminal of the proximal tubule? 300 because its isotonic, its constant, like if u have a cup of tea when u remove its 2/3 content, the concentration stays the same

So 2/3 is the Reabsorption

When u reach loop of Henley, then 1/3 of filtrate remains, and osmolarity of filtrate is 300 because it's isotonic

Osmolarity of tubule/osmolarity of plasma=1….isotonic solution

From the beginning of the proximal tubule to its terminal, osmolarity doesn’t change..Na,Cl concentrations are the same. But glucose and amino acid concentrations will change, creatinine and urea will increase (secreted). Water is the same; it remains as 1/3 of filtrate. HCO3- is not reabsorbed completely we need it in acid base balance.

Good luck☺

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**\*** **Clearance of PAH (CPAH) ~ effective renal plasma flow**

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