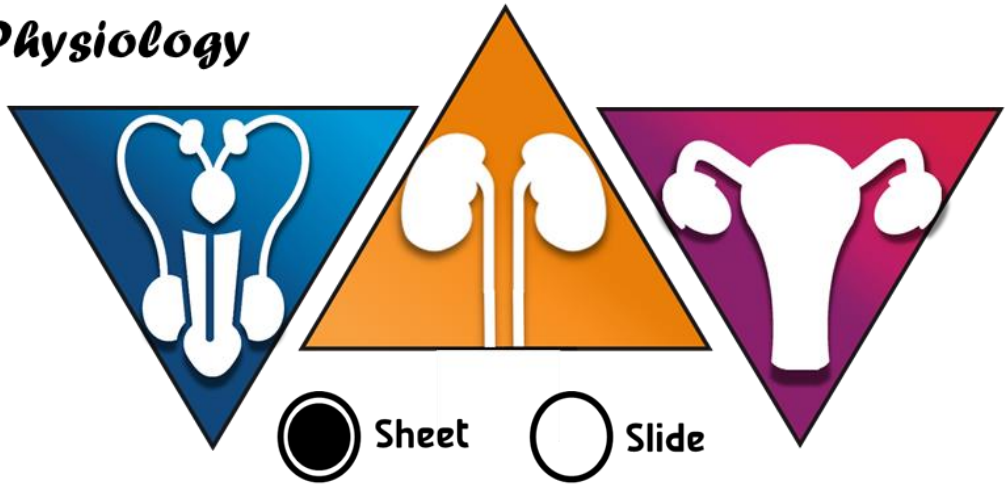
Urogenital system

Physiology



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GFR (glomerular filtration rate)

GFR is a tool used to tell us whether the kidney is functioning normally or it's damaged, and if it was damaged GFR helps us know the stage of damage, is it stage 1, 2, 3 ,4 …. etc.
GFR is the 'most' important kidney function test (KFT). It's not the only one but it's the most important of them.

The normal value of GFR is 125 ml/min, but it is not the same in all individuals, as it differs by:
1- Sex (males have higher GFR)
2- Age (after age 40 it starts decreasing gradually 1% each year, so you wouldn't expect the GFR of an 80-year-old person to be 125ml/min, it may be 70 or 60)

The doctor listed different categories for staging renal diseases (decreased renal reserve). There are many, and not all of them are categorized on a medical basis. That's why the doctor said it's not required to know these classifications and the only thing he wanted us to know is that **GFR is a tool used to classify kidney diseases.**

Blood enters through the afferent arteriole and the blood carries plasma with it, and the renal plasma flow **RPF** is 650ml/min, after that in the capillaries 20% are filtered (125ml) and we called that the **filtration fraction**, which is the same as GFR (125ml). What remains then (525ml) continues through the efferent arterioles to the peritubular capillaries where secretion and reabsorption take place and we finally end in the renal vein.

What we want to learn in this lecture is how are we going to measure RPF and GFR, and if we measured RPF we can use it to measure RBF (renal blood flow) using the following equation:

$$\boldsymbol{RBF = \frac{RPF}{1 - hematocrit}}$$

For example, if the hematocrit was 50% then:

$$RBF = \frac{650}{1 - 0.5} = 1300 ml/min$$

So, we measure RPF then take a drop of blood from the patient to know his/her hematocrit and then we measure RBF.

Now to measure RPF we use a substance that is **completely removed from the blood and completely excreted in the urine once it enters the kidney.**
Note: 1) this substance is not produced by the kidney and not accumulated in the kidney or metabolized by it.
2) we need a substance that doesn't appear in the renal vein once it enters through the renal artery.

Excretion comes from 2 routes:
1- Filtration
2- Secretion

Filtration is constant under normal conditions and it's 20% so we guarantee that 20% of this substance is filtered on the condition that it's not reabsorbed, that leaves 80% of this substance that flowed through the efferent and reached the peritubular capillaries, so we want this substance to be completely secreted and not reabsorbed.

Eventually in the urine 100% concentration of this substance appear, 20% coming from filtration and 80% from secretion (provided that the substance is not reabsorbed as we said before)

Again, as we said we are going to use a substance that is completely removed, or we can say that the plasma is completely **cleared** from this substance (none of it returns through the renal vein).

To measure the amount of a substance excreted through the urine per minute we are going to need to know the **concentration of this substance in the urine and the urine flow rate.**
And to know its amount in the plasma that flows per minute we need to know its **concentration in the plasma and the renal plasma flow (RPF).**
Because once this substance enters the kidney all of it is going to be excreted in the urine and none will appear in the renal vein (zero concentration in the renal vein) we can apply **the law of conservation of mass** and say that the:

Amount excreted in the urine mg/min = Amount provided to the kidney (by the renal artery) for excretion mg/min

U_{PAH} x V_{PAH} = RPF x P_{PAH}

U_{PAH}: concentration of PAH in the urine (measured)

V_{PAH}: urine output/min (measured)

RPF: renal plasma flow (unknown, found using the above formula)

P_{PAH}: concentration of PAH in the plasma (measured)

$$RPF = \frac{\text{U PAH } x\, V\, PAH}{P\, PAH}$$

Another characteristic of this substance is that it's **freely filtered,** which means that its concentration in the plasma= its concentration in bowman's capsule after filtration.

Note: substances can also be partially filtered, or not filtered (if their concentration in bowman's capsule is zero like proteins 'normally')

The substance the we've been talking about is **PAH** (para-aminohippuric acid) which is synthetic and not found in our bodies.

Note: no substance produced by our body meets this criterion.

Since PAH is completely secreted it must be secreted against a gradient, that's why secretion is **active.** while filtration is **passive.**

Active transport has a transport maximum or T_{max} which is the point at which further increase in the concentration of the substance will not result in increased Secretion (plateau) .

In passive diffusion there's no plateau and as we increase the concentration diffusion will increase.

So, another criterion that must be met is to ensure that the amount of PAH provided to the kidney is below T_{max}, to guarantee that the amount of plasma entering the kidney/min(RPF) was exited through the renal vein completely cleared from PAH.

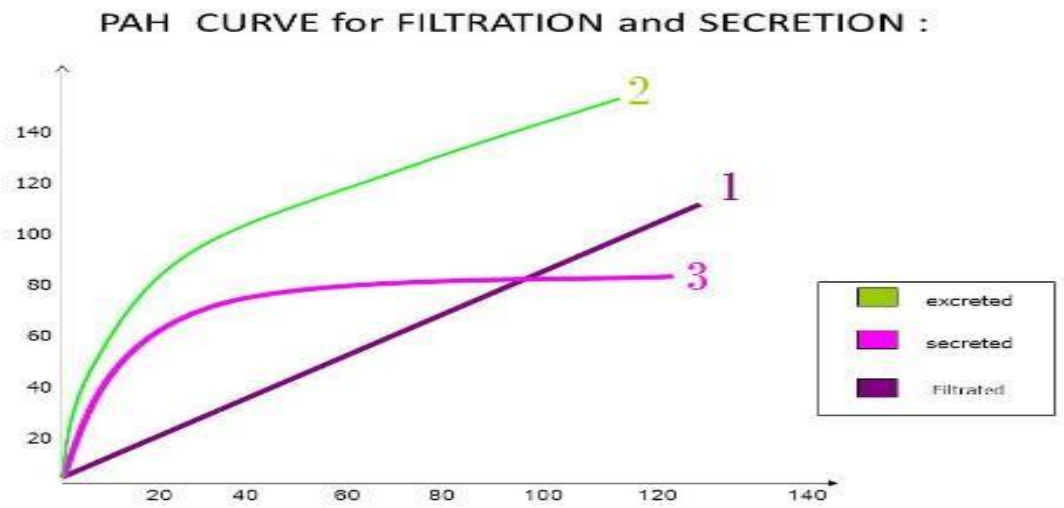
If you provide a concentration if PAH above T_{max} the plasma will not be completely cleared and its concentration in the renal vein will be more than zero.

The characteristics of RPF marker or PAH are:

1- Freely filtered

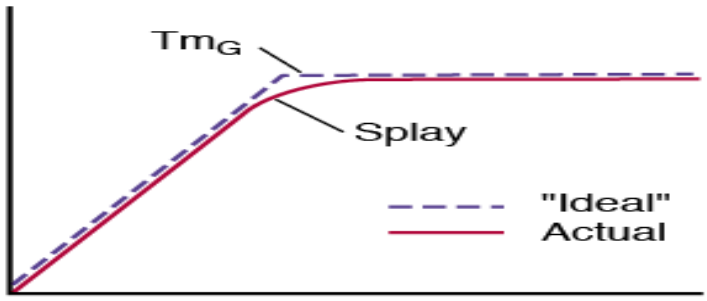
2- Not reabsorbed

3- Completely secreted, under one condition, **which is ensuring the amount provided to the kidney is below T_{max}.**



Notice how filtration is linear while secretion plateaus at T_{max}.
Excreted = secreted + filtered.

Now let's suppose that the T_{max} of the receptor is 200mg/min, so if we provide 1000mg/min it will transport 200mg and leave 800mg and if you provide 60mg it will transport 60mg and leave nothing, but if we provide 150mg (which is close to the T_{max}) it may transport 140mg and leave 10mg , if we provide 200mg it may transport 180 and leave 20mg .
So, for the receptor to fully express itself the concentration must be supersaturated, but concentrations that are around T_{max} will not allow the receptor to express itself fully and that's why the **splay** appears, which is the difference between what is expected and what is observed. And the reason behind this is that the affinity of receptors towards their ligands is not infinity, it is limited.



clearance

Clearance is the volume of plasma that provides X for excretion per minute. (it's volume/min and not amount)
ex: protein in urine is zero, plasma that entered is 650ml and carries protein. how much volume of plasma that provide protein for excretion?
Clearance of proteins is zero because none of it gets cleaned from the plasma.

Clearance of PAH (C_{PAH}) = Volume of plasma cleaned from PAH / min

C_{PAH} = RPF because all the plasma that entered through the renal artery has been cleared from PAH.
Let's suppose that the T_{max}=80mg/min and you provided 100 mg of PAH then 80mg will be transported and 20mg will continue through the renal vein, that means that the plasma will not be completely cleared from PAH and the clearance in this case **underestimates RPF**.
(RPF will not equal clearance because not all the plasma was cleared)
If you greatly increased the concentration of PAH provided to 8000mg for example, then the amount secreted will be 80mg which is negligible compared to the 8000mg provided and what appears in the urine will be what was coming through filtration (20%) in this case this substance becomes GFR marker rather than RPF marker.
The clearance of PAH will equal 650ml/min until it reaches the T_{max} it will start decreasing gradually but it will never decrease below 125ml/min because filtration is passive, and it is guaranteed.
so basically
1) below Tmax works as RPF marker
2) above Tmax works as GFR marker