Osmotic effects on reabsorption

• Water is reabsorbed only by osmosis through the paracellular route or through aquaporin channels

• Increasing the amount of unreabsorbed solutes in the tubule decreases water reabsorption due to the high osmotic pressure and thus lower osmosis rate

Examples:

- diabetes mellitus: unreabsorbed glucose because of excretion of glucose in tubules and this increase the osmotic pressure in the tubular fluid causes diuresis and water loss

- osmotic diuretics (mannitol): taking mannitol to reduce the pressure through diuresis : mannitol's concentration increases in the tubular fluid which increases the osmotic pressure and induce diuresis.

Ways to assess kidney function

• Plasma concentration of waste products (e.g. BUN, creatinine)

• Urine specific gravity, urine concentrating ability

• Urinalysis test reagent strips (protein, glucose, etc)

• Biopsy

• Albumin excretion (microalbuminuria)

• Isotope renal scans

• Imaging methods (e.g. MRI, PET, arteriograms, iv pyelography, ultrasound etc)

• Clearance methods (e.g. 24-hr creatinine clearance)

"Clearance" describes the rate at which substances are removed (cleared) from the plasma.

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

We can get the clearance from this equation .

$$Cs \times Ps = Us \times V$$

$$Cs = \frac{Us \times V}{Ps} = \frac{\text{urine excretion rate}}{\text{Plasma conc. s}}$$

Where : Cs = clearance of substance S
Ps = plasma conc. of substance S
Us = urine conc. of substance S
V = urine flow rate

Substance	Clearance (ml/min)
glucose	0
albumin	0
sodium	0.9
urea	70
inulin	125
creatinine	140
PAH	600

The renal clearance of different substances is different. glucose and albumin have zero clearance because their excretion is zero . The clearance rate of the exogenous substances, such as inulin and PAH and the endogenous like creatinine is very high because these substances are toxic and thus the body works to get rid of them

For a substance that is freely filtered, but not reabsorbed or secreted (inulin, ^{125}I-iothalamate, creatinine), renal clearance is equal to GFR. Thus, the clearance of these substances can give estimation of GFR

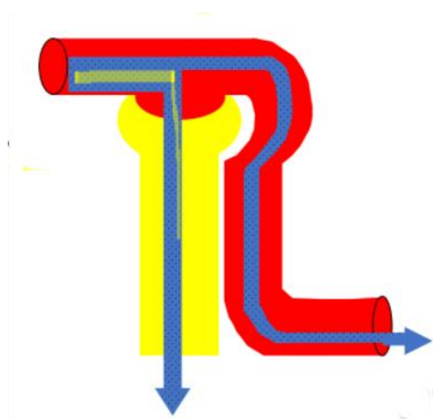
amount filtered = amount excreted

$$GFR \times Pin = Uin \times V$$

$$GFR = \frac{Uin \times V}{Pin}$$

P_{in} → Plasma concentration of inulin

U_{in} →Urine concentration of inulin



Calculate the GFR from the following data:

$P_{inulin} = 1.0$ mg / 100ml
$U_{inulin} = 125$ mg/100 ml
Urine flow rate = 1.0 ml/min

$$GFR = C_{inulin} = \frac{U_{in} \times V}{P_{in}}$$

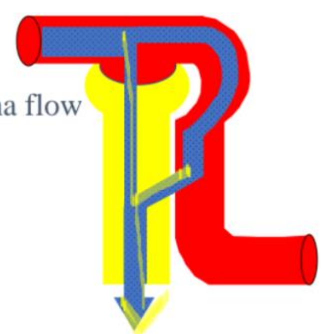
$$GFR = \frac{125 \times 1.0}{1.0} = 125 \text{ ml/min}$$

Once we take the plasma concentration for inulin from a blood sample and taking the urine concentration for inulin and the urine flow rate after 24 hours collection of urine from the patient then we apply the equation we will have the clearance of inulin which equals the GFR and equals 125 ml/min.

Theoretically, if a substance is completely cleared from the plasma, its clearance rate would equal renal plasma flow.
These substances give an estimation of renal plasma flow

Cx = renal plasma flow

Cx = renal plasma flow



Paraminohippuric acid (PAH) is freely filtered and secreted and is almost completely cleared from the renal plasma. Since almost 90% of this substance is cleared from the plasma and only 10% remains in the plasma concentration, it can be used to estimate the renal plasma flow.

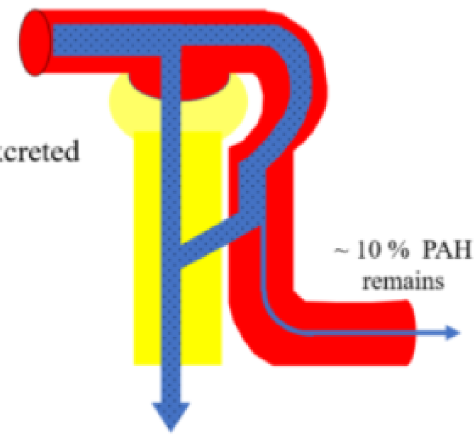
1. amount enter kidney = $RPF \times P_{PAH}$

2. amount entered ≅ amount excreted

3. $ERPF \times P_{pah} = U_{PAH} \times V$

$$ERPF = \frac{U_{PAH} \times V}{P_{PAH}}$$

$$ERPF = \text{Clearance PAH}$$



Since 10% of PAH remains in the plasma and is not completely cleared, the ERPF value obtained from the clearance rate of PAH must be corrected to get the actual renal plasma flow level.

(We are not required to know the correction calculations)….

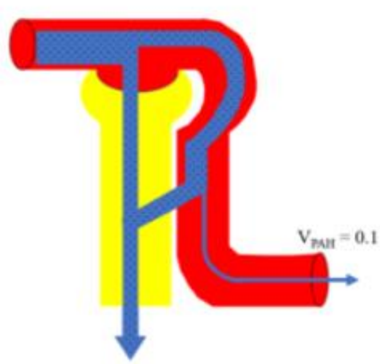
$A_{PAH} = 1.0$

$$E_{PAH} = \frac{A_{PAH} - V_{PAH}}{A_{PAH}} = \frac{1.0 - 0.1}{1.0} = 0.9$$

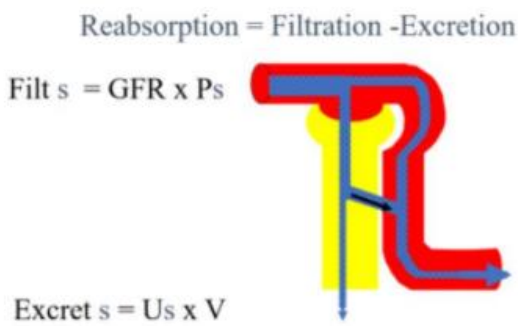
normally, $E_{PAH} = 0.9$

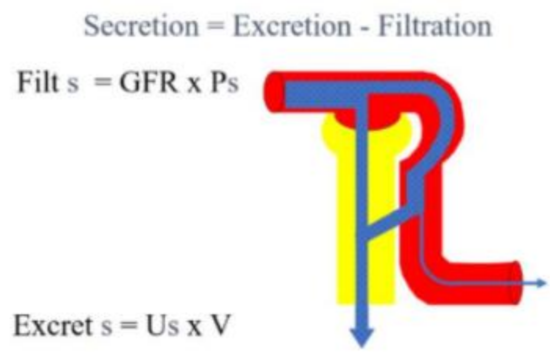
i.e PAH is 90 % extracted

$$RPF = \frac{ERPF}{E_{PAH}}$$



We should know these two important equations





Q: The maximum possible clearance rate of a substance that is completely cleared from the plasma by the kidneys would be equal to

1. glomerular filtration rate
2. the filtered load of the substance
3. urine excretion rate of the substance
4. renal plasma flow
5. none of the above

Substance	Clearance (ml/min
inulin	125
PAH	600
glucose	0
sodium	0.9
urea	70

Clearance of inulin (C_{in}) = GFR

if Cx < Cin : indicates reabsorption of x

if Cx > Cin : indicates secretion of x

Clearance creatinine (C_{creat}) ~ 140 (used to estimate GFR)

Clearance of PAH (C_{pah}) ~ effective renal plasma flow

The clearance of PAH was used to estimated the renal plasma flow while the

clearance of inulin was used to estimate the GFR.

If the clearance rate of a substance was less than the clearance rate for inulin or less then GFR, it means that reabsorption of that substance took place.

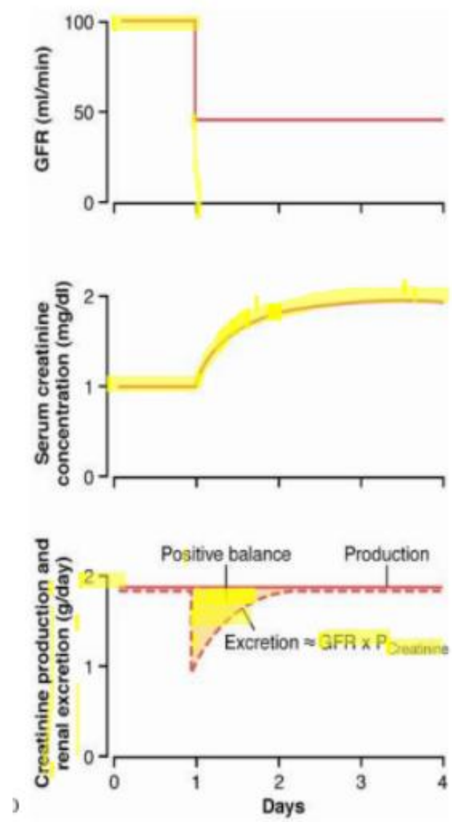
If the clearance rate of substance x is more than the clearance rate of inulin or more than GFR, it means that secretion of that substance to the filtrate took place.

The clearance rate of creatinine is close to the clearance rate of inulin but is slightly

higher (also higher than GFR); due to some level of secretion of creatinin. Although

only a freely filtered substance that doesn't undergo secretion or reabsorption is used to estimate GFR, creatinine is clinically used to estimate GFR because it is easier to track.

Effect of reducing GFR by 50 % on serum creatinine concentration and creatinine excretion rate



Since creatinine clearance rate can be clinically used to estimate GFR, how will serum creatinine concentration be affected if GFR was reduced by

50% ?

1-The first graph depicts the level of GFR. GFR was originally 100 mL/min in day 1 but was reduced to 50 mL/min in day 2

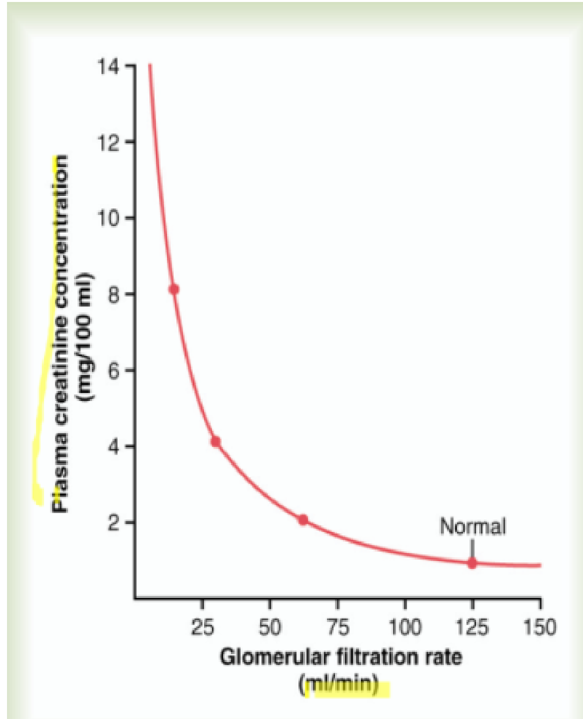
The second graph depicts serum creatinine concentration in mg/dL. Creatinine serum concentration was normal in day 1. However, as the GFR level was dropped by half, creatinine serum concentration was doubled to 2 mg/dL .

The third figure depicts creatinine production and renal excretion in g/day. Creatinine production is constant at 2 g/day as shown by the solid line on the graph. The renal excretion, as shown by the dashed line, was superimposed to the solid line that represent creatinine production during day 1 when the GFR was normal and serum creatinine concentration was also normal. However, when the GFR was reduced to half and creatinine serum concentration was doubled in response on day 2, creatinine excretion is reduced to half. This is the acute effect of reduced GFR level. However, creatinine excretion start to increase gradually. This is because, according to this equation:

$$\text{Excretion} = \text{GFR} \times P_{\text{creatinine}}$$

As GFR level was reduced by half, plasma creatinine concentration was doubled; thus creatinine excretion was able to gradually increase to be equal to creatinine production during the next day. Thus, as plasma creatinine concentration increases even though GFR level decreases, creatinine excretion increases to bring, creatinine levels in the blood back to normal. This relationship maintains constant levels of serum creatinine concentration and prevent the plasma creatinine concentration to exceed 2 mg/dL.

Plasma creatinine can be used to estimate changes in GFR



This plot shows the relationship between the GFR (mL/min) and plasma creatinine concentration (mg/100mL). Using this plot, the plasma creatinine concentration can be measured by matching it with the corresponding estimated GFR.

This plot differs according to

different body weights, body mass index (BMI), age and gender.

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