Physiology Team 431

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Renal Blood flow and Renal Clearance

- ## Renal Blood flow:

  - The kidney receives extremely high blood flow compared with other organs, to supply the kidneys with enough plasma for the high rates of glomerular filtration.
  - In average adult RBF =1.1L/min = 22% of Cardiac output
  - PAH (para-aminohippuric acid) an organic acid used for measurement of RBF.
  - In one renal circulation/min PAH is almost completely removed(90%) from the plasma & excreted in urine.
  - PAH clearance = volume of plasma cleared from PAH/min = RPF/min
  - RPF= the amount of a PAH excreted per unit **time**

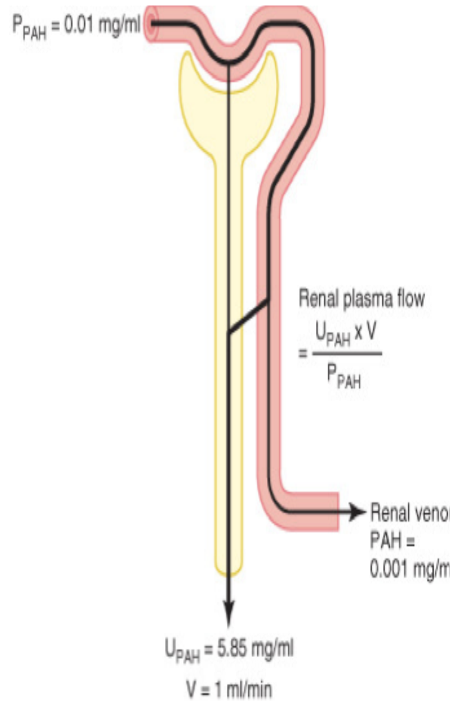
> Theoretically, if a substance is completely cleared from the plasma, the clearance rate of that substance is equal to the total renal plasma flow

<u>Calculation of renal blood flow:</u>

<u>To calculate the RBF we have to follow a number of steps:</u>

1- **Calculate the renal plasma flow by finding the clearance of PAH**

$C_{PAH=}$ $(U_{PAH}$ x V)/P_{PAH} = 585ml/min = effective renal plasma flow (ERPF)



1- $C_{PAH=}$ Clearance of PAH
2- $U_{PAH=}$ Urine PAH concentration= 5.85mg/ml
3- V= urine flow rate, it can be measured by 24hrs collecting urine.
Supposing = 1440 ml/24 hrs   1440÷24÷60= 1ml/min
4- P_{PAH}= arterial plasma PAH concentration

2- **But because only 90% of PAH in arterial blood is removed by the kidney we have to calculate the Actual renal plasma flow (ARPF)**

ARPF= ERPF/extraction ratio = 585/0.9= 650ml/min

Extraction ratio=(P_{PAH}-Renal venous $_{PAH}$)/P_{PAH} =

(0.01-0.001)/0.01)= 0.9

3- **Now we have to Calculate the renal blood flow (RBF)**

RBF= RPF/(1-hematocrit)

= 650/(1-0.45)=1182 ml/min

Or

RBF = <u>Renal artery pressure – Renal vein pressure</u>

Total Renal vascular pressure

Hematocrit= The hematocrit (is the volume percentage (%) of red blood cells in blood. It is normally about 45% for men and 40% for women

****PAH is used to measure the RBF**
****CERATININE is used to measure the GFR**

Auto regulation:

- It's a Feedback mechanism to keep RBF and GFR relatively constant despite marked changes in ABP
- Range of auto regulation is between 75-160 mmHg ABP
- If the ABP became lower than 60, GFR decreases tremendously leading to kidney shutdown.
- When it exceeds 160 mmHg, damage to kidney will occur

Auto regulation of GFR:

- Auto regulation largely occurs by the regulation of renal vascular resistance

- Changes diameters of afferent, efferent arteriole, and glomerular capillaries.
- Drop pressure results in dilation of afferent arteriole, dilation of glomerular capillaries and constriction of efferent arteriole.
- Rises in pressure results in constriction of afferent arteriole
- In severe cases of increased ABP efferent dilatation will occur along with afferent vasoconstriction.

Three processes controlling GFR:

1. Myogenic auto regulation
2. Hormonal regulation (tubuloglomerular & renin-angiotensin)
3. Autonomic regulation (extrinsic)
4. Nitric Oxide (NO):
    - Causes arteriolar vasodilation
    - Elevated NO may result in hyperfiltration of early Diabetes Mellitus
    - Reduced NO after salt intake may lead to hypertension

1. Myogenic auto regulation:

The ability of blood vessels to resist Stretching

• ↑ Hydrostatic Pressure → stretching Vessels wall → reflex contraction

2. Hormonal Regulation:

I. Tubuloglomerular feedback
II. Renin-angiotensin Aldosterone
III. Other Hormones

3. Autonomic Regulation of GFR:

• In normal condition Sympathetic NS has little influence on GFR

• ↓ BP (hemorrhage) → ↑ sympathetic → Vasoconstriction of renal artery → ↓ RBF →

vasoconstriction of afferent → ↓ GFR

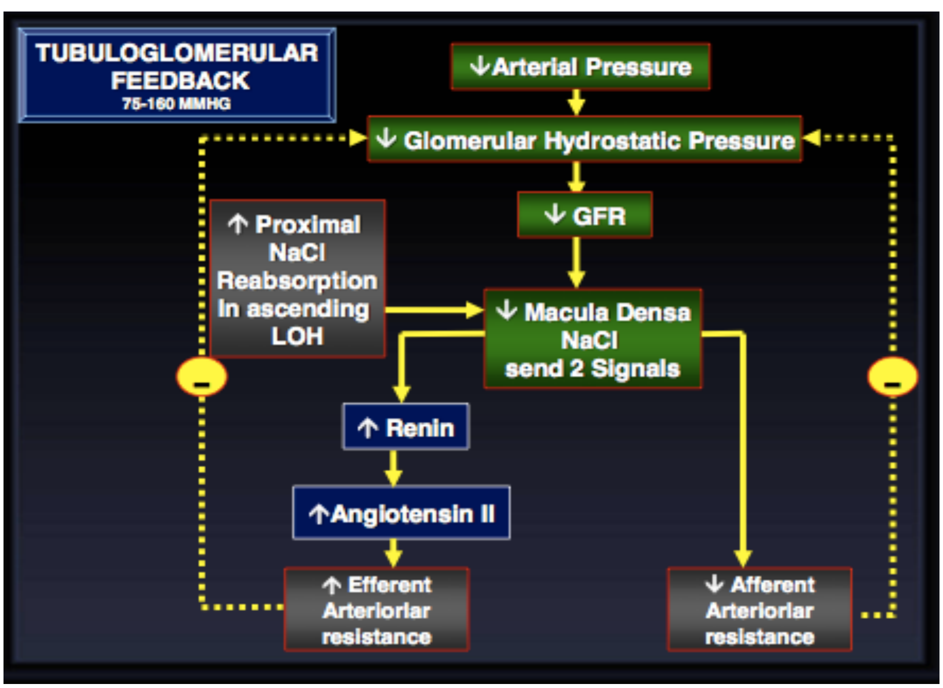
TO DIVERT BLOOD TO VITAL ORGANS

I. Tubuloglomerular feedback:

- ↓ GFR ⟶ slow flow ⟶ Nacl reabsorption to the circulation due to hypotension ⟶ ↓ Nacl at macula densa leading to:

1. ↑ renin ⟶ ↑angiotensin II ⟶ efferent vasoconstriction ⟶ ↑GFR
2. Afferent dilation ⟶ ↑GFR

To perform the function of auto regulation, the kidneys have a feedback mechanism that links changes in sodium chloride concentration at the macula densa with the control of renal arteriolar resistance. The tubuloglomerular feedback mechanism has 2 components that act together to control GFR: 1st an afferent arteriolar feedback mechanism and 2nd an efferent arteriolar feedback mechanism. These feed back mechanisms depend on special anatomical arrangements of the juxtaglomerular complex. The juxtaglomerular complex consists of macula densa cells in the initial portion of the distal tubule and juxtaglomerular cells in the walls of the afferent and efferent arterioles. The macula densa cells sense changes in volume delivery to the distal tubule by way of signals that are not completely understood. Experimental studies suggest that decreased GFR may slow the flow rate in the loop of henle causing an increase in reabsorption of sodium and chloride ions in the ascending loop of henle and thereby reducing concentration of sodium and chloride concentration in turn initiates a signal from the macula densa that has 2 effects: (1) it decreases resistance of the afferent arteriole, which raises glomerular hydrostatic pressure and helps to return GFR toward normal and (2) it increases renin release from the juxtaglomerular cells of the afferent and efferent arterioles, which are major storage sites for renin. Renin released from these cells then functions as an enzyme to increase the formation of AngII. Finally, the AngII constricts the efferent arterioles, thereby increasing glomerular hydrostatic pressure and returning GFR toward normal



II. Renin-angiotensin Aldosterone:

- **Renin is released into plasma due to:**
  - **low ECF Na or low ECV**
  - **↑ sympathetic (due to hypotension)**
  - **↓ afferent pressure (hypotension)**

- **Renin acts on angiotensinogen → Angiotensin I**
- **Angiotensin converting enzyme (ACE): Angiotensin I → angiotensin II**
- **Angiotensin II act on adrenal cortex → aldosterone secretion → ↑ Na reabsorption in distal & collecting duct of nephron**
- **↑ H and K secretion in exchange for Na**

III. Other Hormonal Regulator of GFR:

1. **Adrenaline, noradrenaline → afferent vasoconstriction → ↓ GFR**
2. **Angiotensin II → Vasoconstriction of efferent → ↑ GFR**
3. **Prostaglandins, bradykinin → afferent vasodilator → ↑ GFR**

Renal Clearance:

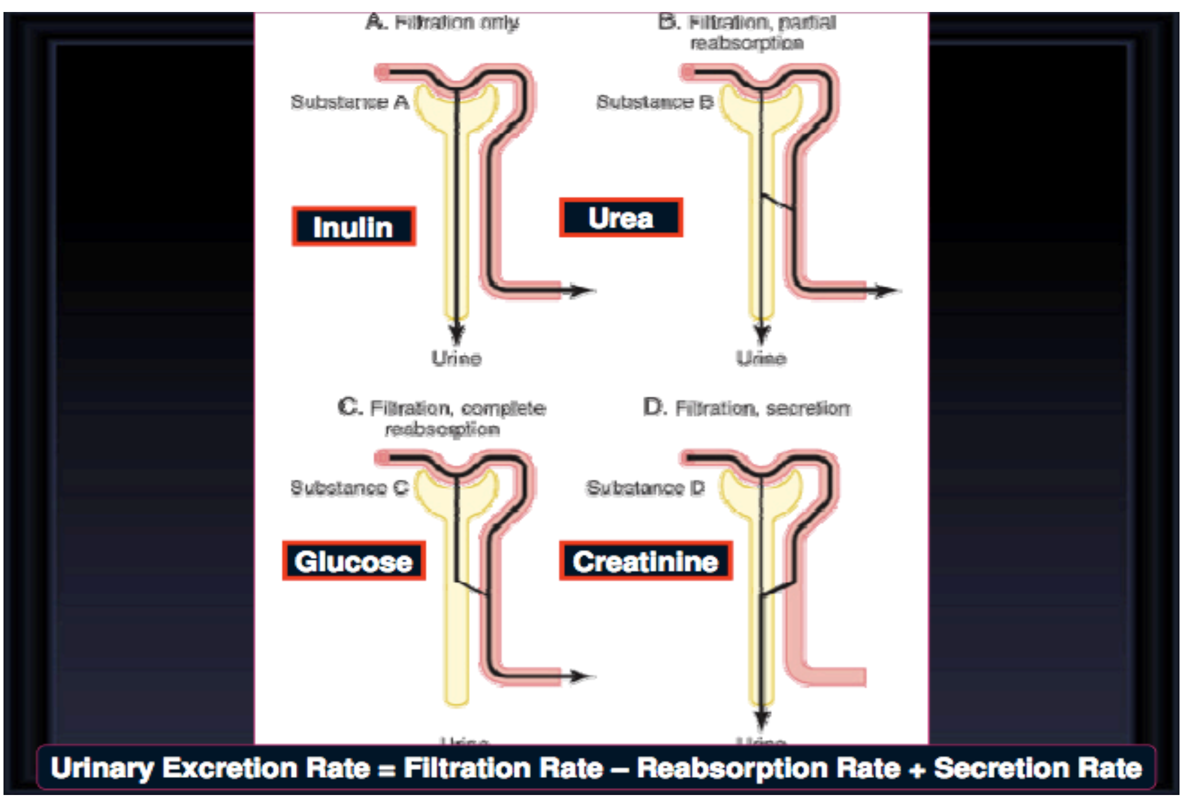
- The Volume of Plasma that is completely cleared of any substance by the Kidneys per minute is called the clearance of that particular substance
  - Clearance equation
    - Cs = ([U]s x V)/[P]s = ml/min

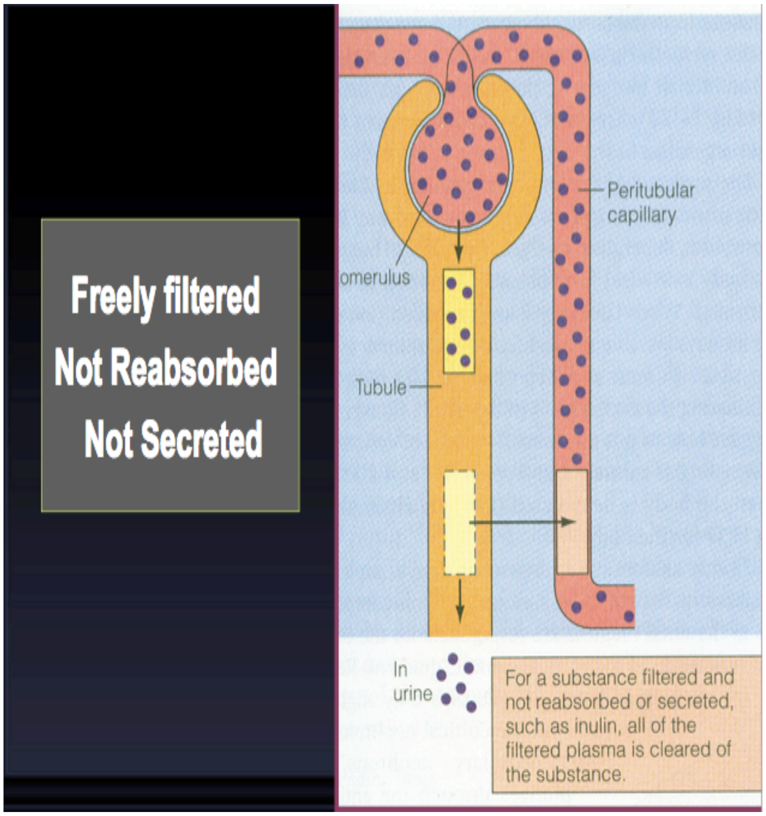
Cs=clearance rate of any substance
Us=urine concentration of that substance
Ps=plasma concentration of that substance
V= Urine flow rate per minute

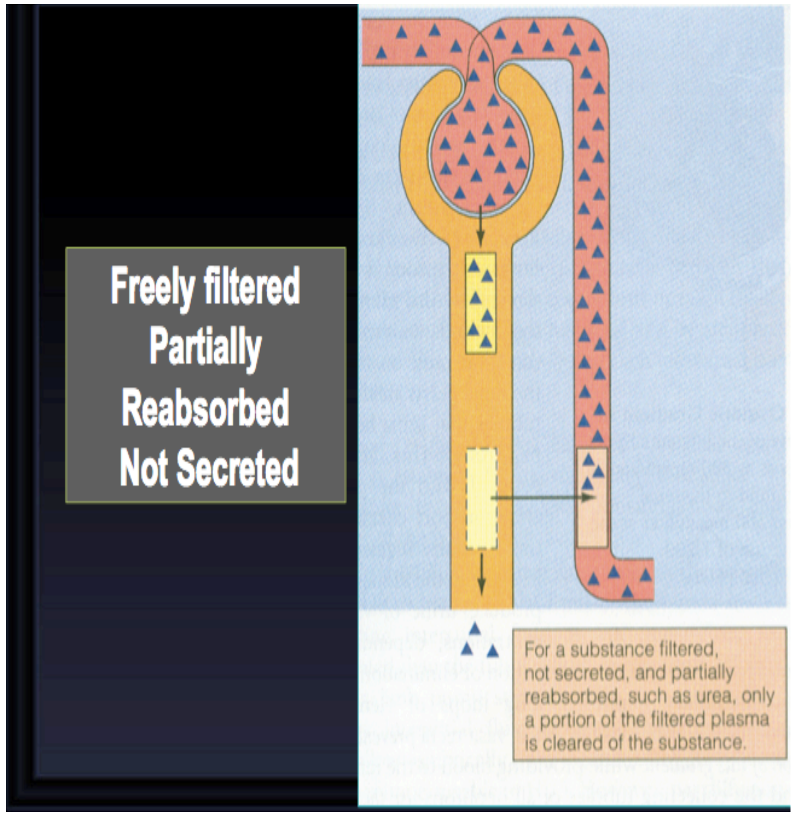
- Renal clearance for different substances various between 0-600ml/min

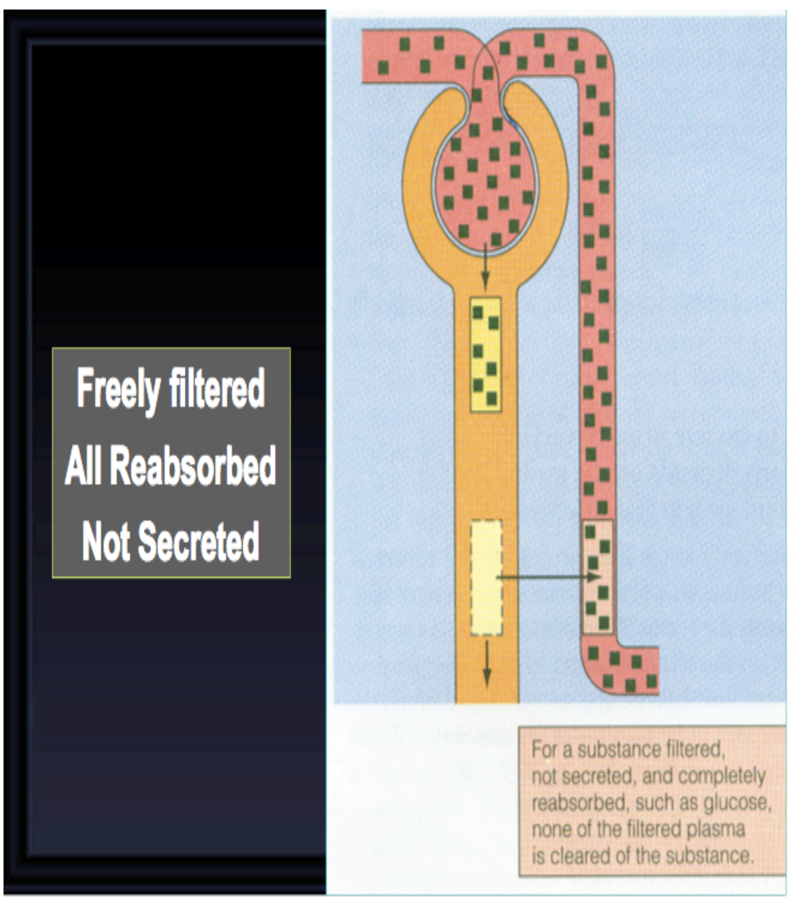
AFTER A SUBSTANCE IS FREELY FILTERED THERE ARE FOUR POSSIBILITIES:

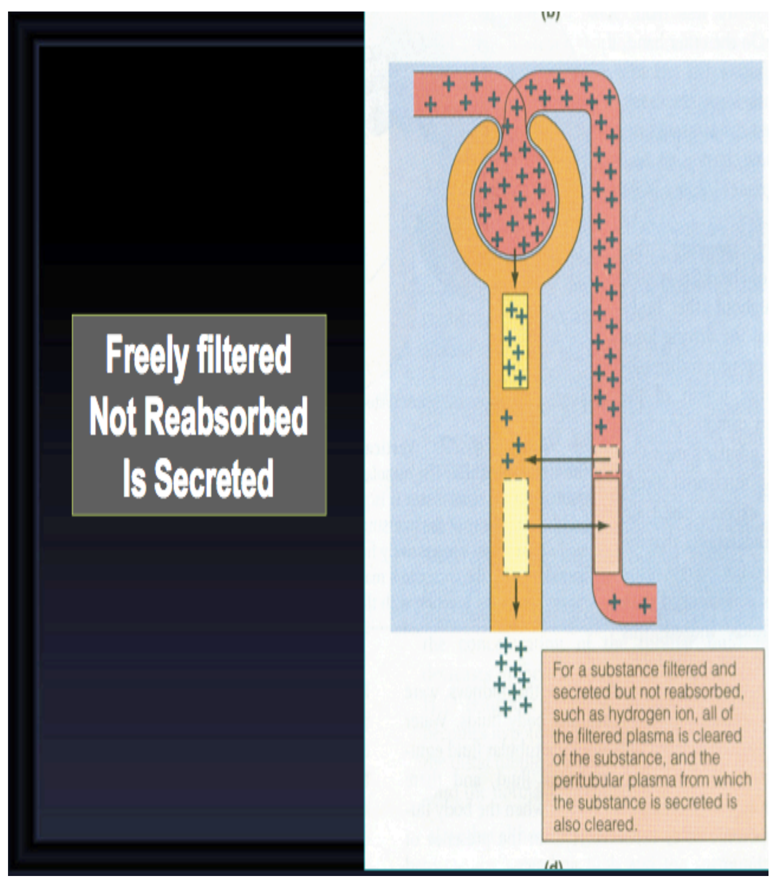
1. Neither reabsorbed nor secreted (e.g. Inulin)
   - All the substance will go into urine. Whatever is filtered is excreted
2. All is reabsorbed but is not secreted (e.g. Glucose)
   - This substance will not be found in urine
3. Partially reabsorbed and is not secreted (e.g. urea)
   - Part of this substance will be excreted to the urine and the rest (about 50%) will be reabsorbed
   - The only waste product which is reabsorbed is urea
4. Not reabsorbed but it is secreted (e.g. creatinine)
   - More concentrated in urine that it is in filtrate



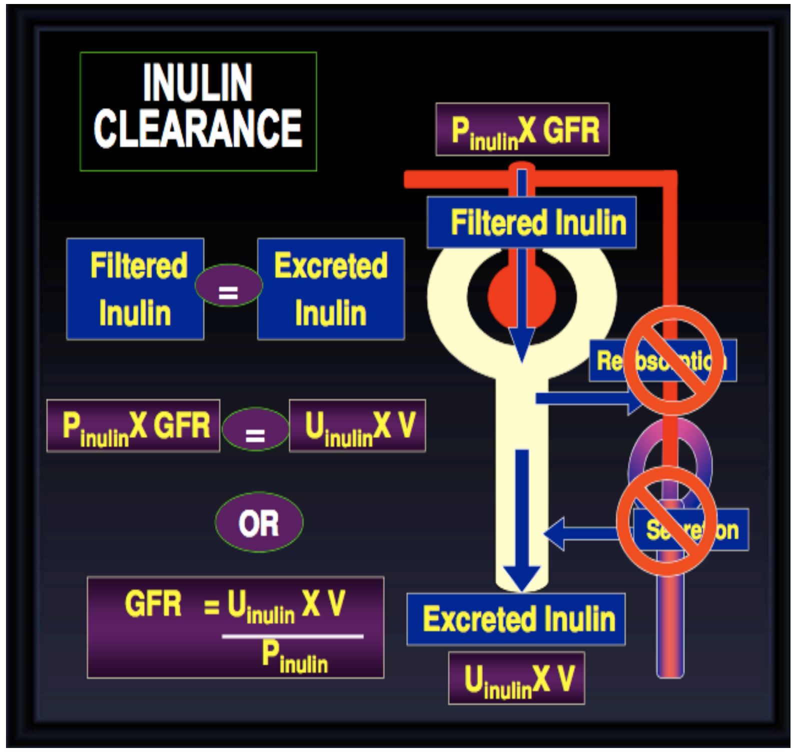

Freely filtered
Not Reabsorbed
Not Secreted
Peritubular capillary
omerulus
Tubule
In urine
For a substance filtered and not reabsorbed or secreted, such as inulin, all of the filtered plasma is cleared of the substance.


Freely filtered
Partially
Reabsorbed
Not Secreted
For a substance filtered, not secreted, and partially reabsorbed, such as urea, only a portion of the filtered plasma is cleared of the substance.


Freely filtered
All Reabsorbed
Not Secreted
For a substance filtered, not secreted, and completely reabsorbed, such as glucose, none of the filtered plasma is cleared of the substance.


Freely filtered
Not Reabsorbed
Is Secreted
For a substance filtered and secreted but not reabsorbed, such as hydrogen ion, all of the filtered plasma is cleared of the substance, and the peritubular plasma from which the substance is secreted is also cleared.

Inulin clearance & GFR:



- 120 ml/min

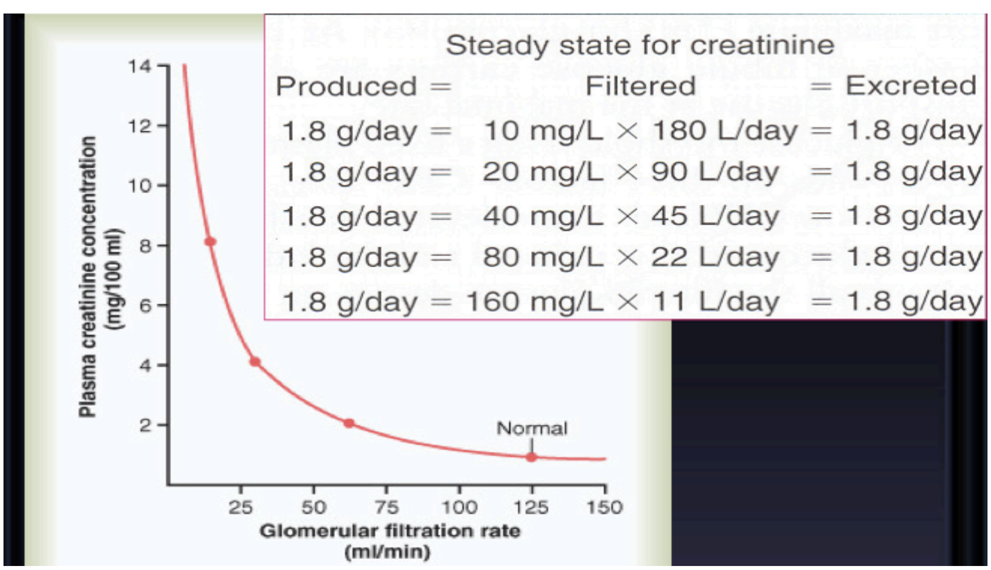
  As inulin is freely filtered not secreted or

  Reabsorbed

  Inulin clearance = GFR

Creatinine clearance &GFR:

- Creatinine is an endogenous substance used routinely to measure GFR
- Completely filtered, but secreted in small quantity
- Inverse relationship between GFR & plasma creatinine
- For example: when the GFR increase the plasma creatinine is decreased and vies versa.



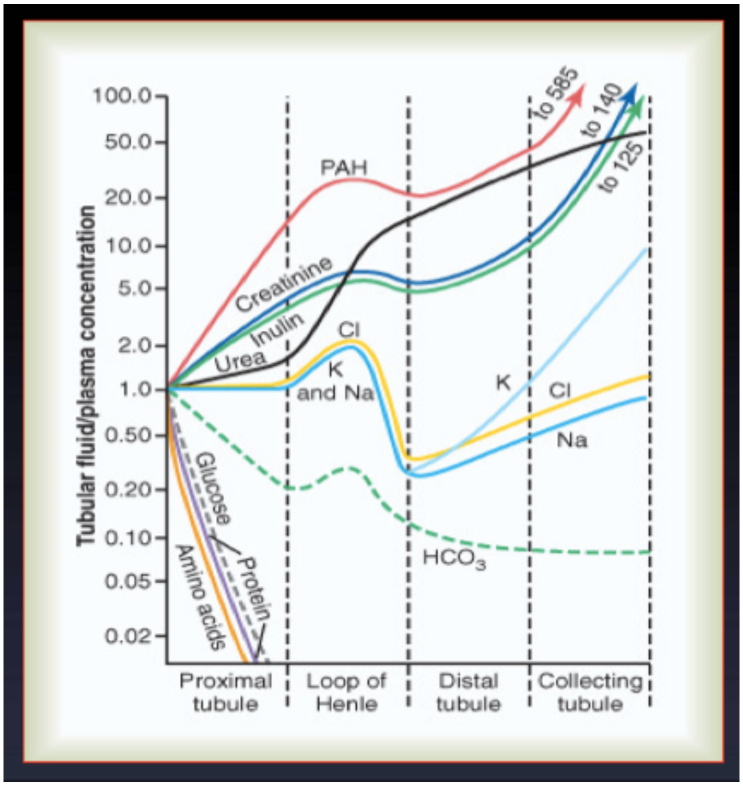
Produced =	Filtered	= Excreted
1.8 g/day =	10 mg/L × 180 L/day	= 1.8 g/day
1.8 g/day =	20 mg/L × 90 L/day	= 1.8 g/day
1.8 g/day =	40 mg/L × 45 L/day	= 1.8 g/day
1.8 g/day =	80 mg/L × 22 L/day	= 1.8 g/day
1.8 g/day =	160 mg/L × 11 L/day	= 1.8 g/day

Glucose & urea clearance:

- Renal clearance of glucose=zero
- Filtered, completely absorbed, no glucose in urine
- [U]g x V = zero
- Urea clearance = 60 ml/min, urea filtered, partially reabsorbed

Inulin clearance vs. clearance of other substance

- Cx = inulin clearance (GFR) → Substance x is filtered but not absorbed or secreted=GFR
- Cy < inulin clearance (GFR) → Substance y is filtered and partially absorbed < GFR
- Cz > inulin clearance (GFR) → Substance z is filtered and secreted >GFR



Changes in average concentration of different substances at different points in the tubular system relative to the concentration of each substance in the glomerular filtrate. A value 1.0 indicates that concentration of the substance in the tubular fluid is the same as the concentration of that substance in the glomerular filtrate. Values below 1.0 indicate that the substance is reabsorbed more avidly than water, whereas values above 1.0 indicate that the substance is reabsorbed to a lesser extent that water.

FILTRATE HANDLING

Relative Concentrations of Substances in the Plasma, Glomerular Filtrate, and Urine

Substance	Plasma	Glomerular filtrate	Urine
Concentrations (mEq/1)			
Sodium (Na^+)	142	142	128
Potassium (K^+)	5	5	60
Calcium (Ca^{+2})	4	4	5
Magnesium (Mg^{+2})	3	3	15
Chloride (Cl^-)	103	103	134
Bicarbonate (HCO_3^-)	27	27	14
Sulfate (SO_4^{-2})	1	1	33
Phosphate (PO_4^{-3})	2	2	40
Concentrations (mg/100ml)			
Glucose	100	100	0
Urea	26	26	1820
Uric acid	4	4	53

It demonstrates the concentration of different substances at different levels, e.g. Glucose is absent in the urine= 0.

Substance	Clearance rate ml/min
Glucose	0
Sodium	0.9
Chloride	1.3
Potassium	12.0
Phosphate	25.0
Inulin	125.0
Creatinine	140.0

CREATININE CLEARANCE IS A TEST OF RENAL FUNCTION TO ESTIMATE GFR

	Amount Filtered	Amount Reabsorbed	Amount Excreted	% of Filtered Load Reabsorbed
Glucose (g/day)	180	180	0	100
Bicarbonate (mEq/day)	4,320	4,318	2	>99.9
Sodium (mEq/day)	25,560	25,410	150	99.4
Chloride (mEq/day)	19,440	19,260	180	99.1
Potassium (mEq/day)	756	664	92	87.8
Urea (g/day)	46.8	23.4	23.4	50
Creatinine (g/day)	1.8	0	1.8	0

Indicate wither in of the following factors would (A) increase (B) decrease the GFR:

__1.Tubuloglomerular feedback response to decreased salt delivery to the distal tubule

__2.Affernt arteriole vasoconctriction

__3.A dramatic fall in arterial pressure following sever hemorrhage (<80 mmHg)

__4.A fall in plasma protien concentration resulting from loss of these proteins from a large burned surface of skin

__5.Contraction of podocyte

__6.Contraction of mesangial cells

__7.A rise in bowman's capsule pressure resulting from ureteral obstruction by kidney stone

__8.Myogenic response of an afferent arteriole stretched as a result of an increased driving blood pressure

__9.Increase in sympathatic actvity to the afferent arterioles.

the answers:
1)a
2)b
3)b
4)a
5)b
6)b
7)b
8)b
9)b