Renal Anatomy and Physiology

Dr. Robin Paudel

- 7/8 of all nephrons are cortical nephrons
- 1/8 of all nephrons are juxtamedullary nephrons
- Nephron structures in the medulla consist of the long loops of Henle and the terminal regions of the collecting ducts.
- All other structures, including the first section of the collecting ducts, are in the cortex.

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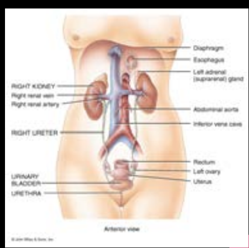
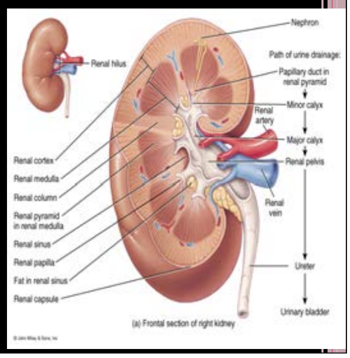
Major Functions of the Kidneys and the Urinary System

1. Regulation of blood ionic composition
2. Maintenance of blood osmolarity
3. Regulation of blood volume
4. Regulation of blood pressure
5. Regulation of blood pH



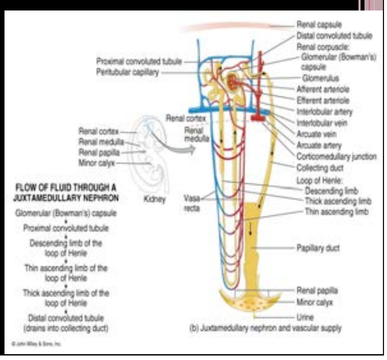
Major Functions of the Kidneys and the Urinary System

6. Release of hormones
   - calcitriol – active form of Vitamin D, helps control calcium homeostasis.
   - erythropoietin – stimulates RBC production
7. Regulation of blood glucose levels via gluconeogenesis



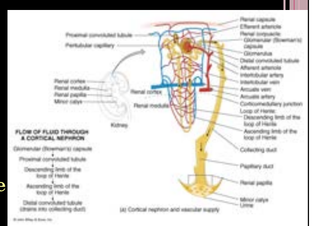
Major Functions of the Kidneys and the Urinary System

8. Excretion of wastes and foreign substances



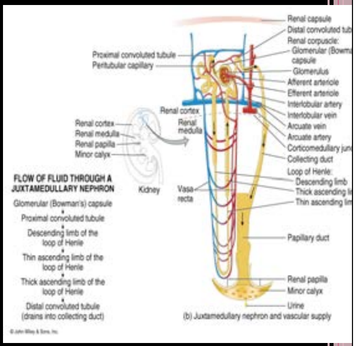
Nephron- The Functional Unit of the Kidneys

- **Cortical Nephrons:**
  80 to 85% of nephrons.
  Have short Loops of Henle that lay mainly in the cortex
- **Juxtamedullary Nephrons:**
  15 to 20% of nephrons.
  Have long Loops of Henle that extend into the deepest regions of the medulla. Produce the most concentrated urine.



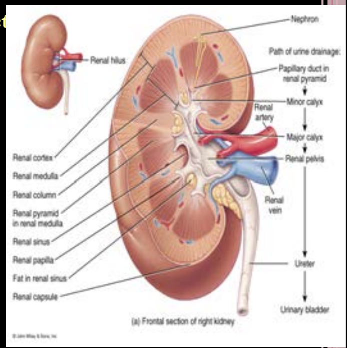
The Anatomy of a Nephron

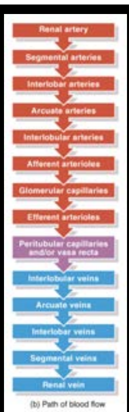
- Subdivision of a Nephron:
1. Renal Corpuscle
2. Proximal Convoluted tubule
3. Descending limb of Loop of Henle
4. Ascending limb of Loop of Henle
5. Distal Convoluted tubule
6. Collecting duct
7. Papillary duct



Urine Drainage through the Kidney and Body

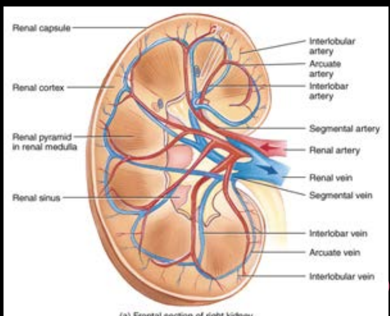
- From papillary duct
- Minor Calyx
- Major Calyx
- Ureter
- Urinary Bladder
- Urethra:
  - prostatic
  - membranous
  - penile





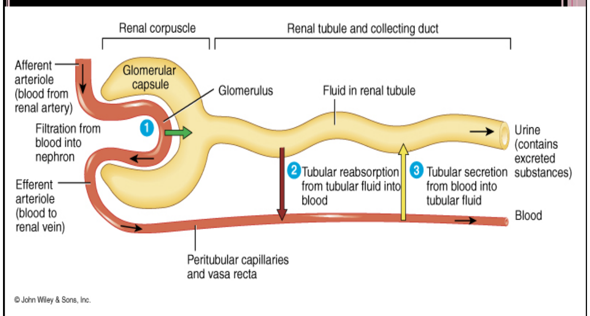
(b) Path of blood flow

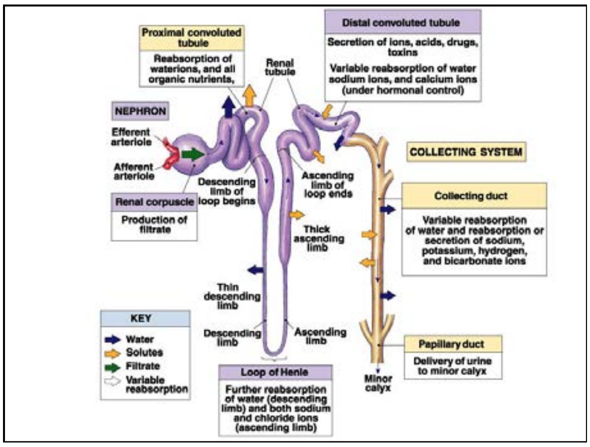
Blood flow through the Kidney



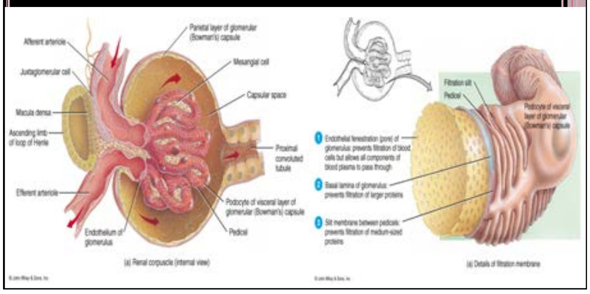
(a) Frontal section of right kidney

Basic Functions of a Nephron





The Glomerular Filtration Membrane



Filtration Pressures and Glomerular Filtration Rate

- Filtration Pressure is the force that drives the fluid and its dissolved substances through the glomerular filter

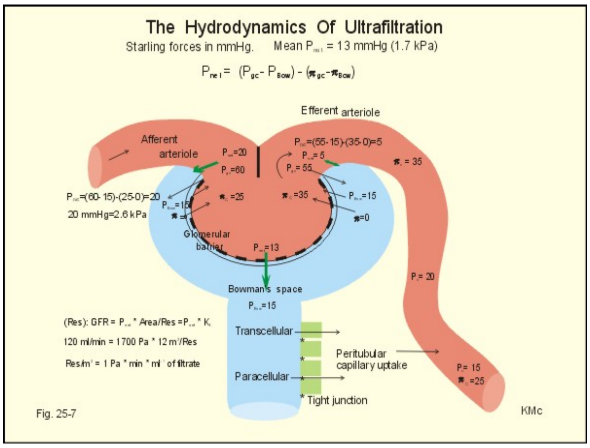
Net Filtration pressure NPF (or Net Hydrostatic Pressure NHP) is the difference between three pressures:

1. Glomerular (blood) hydrostatic pressure GHP or GBHP
2. Capsular Hydrostatic Pressure (CHP)
3. (Blood) Colloid Osmotic Pressure (BCOP)

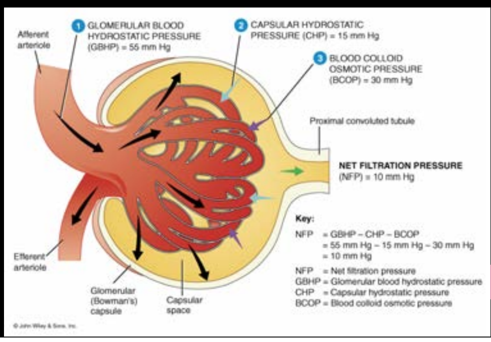
The relationship can be expressed by

NPF = GBHP – (CHP + BCOP)

Glomerular Filtration Rate: amount of filtrate the kidneys produce each minute. (about 125 ml per minute)



Factors affecting filtration rate in the kidney



Regulation of Glomerular Filtration Rate
Neural Regulation

Regulation	Major Stimulus	Mechanism	Effect on GFR
Sympathetic Nerves (Autonomic)	Acute fall in systematic blood pressure. Release of norepinephrine	Constriction of afferent arterioles	Decrease GFR and filtrate volume to maintain blood volume

Regulation of Glomerular Filtration Rate
Hormonal Regulation (see page 1014-1015)

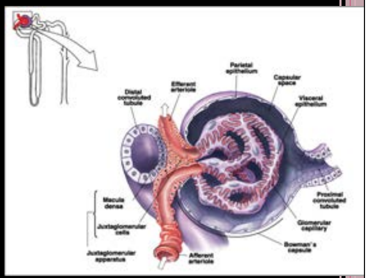
Regulation	Major Stimulus	Mechanism	Effect on GFR
Angiotensin II	Decreased blood volume or decreased blood pressure	Constriction of both afferent and efferent arterioles	Decreases GFR
Atrial natriuretic peptide	Stretching of the arterial walls due to increased blood volume	Relaxation of the mesangial cells increasing filtration surface	Increases GFR

Rate
Hormonal Regulation (see page 1014)

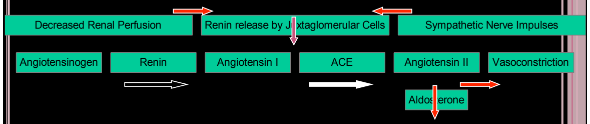
Regulation	Major Stimulus	Mechanism	Effect on GFR
Antidiuretic hormone ADH	Increased Angiotensin II(??) or decreased vol./ osmolality of extracellular fluid	Stimulate insertion of aquaporin-2 (water channels) In apical membrane or principal cells	Increases blood volume to return GFR to normal
Aldosterone	Secreted from adrenal cortex because of increased Angiotensin II levels	Increases reabsorption of Na + and water by principal cells of the DCT collecting duct	Increases blood volume to return GFR to normal

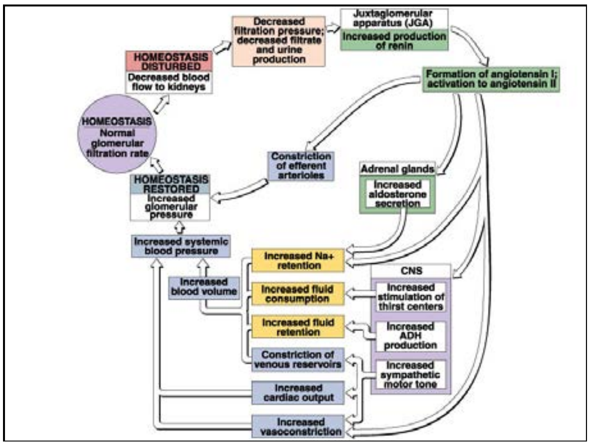
Angiotensin II Pathway

1. Renin is released to the blood by JGA cells due to decreased renal blood flow or perfusion.
2. Renin converts a plasma protein (angiotensinogen) into angiotensin I
3. Angiotensin-Converting Enzyme (ACE) in the lungs convertes Angiotensin I into Angiotensin II



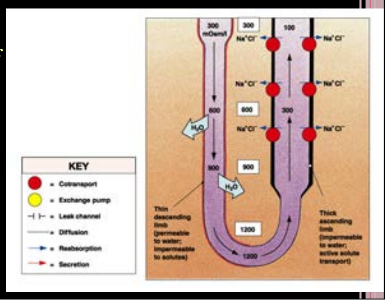
Renin – Angiotensin - Aldosterone System





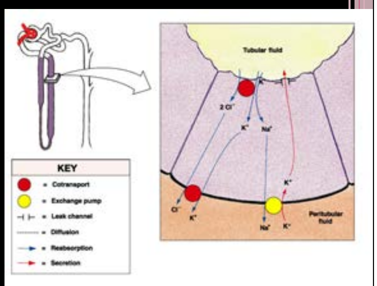
Urine Concentration via Countercurrent Multiplication

- Thin descending limb of Henle is permeable to water but not solutes
- Thick ascending limb of Henle is impermeable to water and solutes. Contains active transport mechanisms for sodium and chloride.

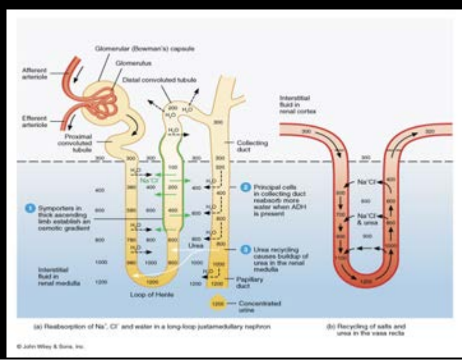


Urine Concentration via Countercurrent Multiplication

- Sodium and Chloride are reabsorbed by thick ascending limb into the peritubular fluid
- These ions elevate the medulla osmotic pressure
- This increases osmotic flow of water out of the thin descending limb
- Increased osmotic potential of tubular filtrate increases active transport in the



Urine Concentration via Countercurrent Multiplication



Roles of the Different Nephron Regions in Urine Formation

Proximal Convoluted tubule

Reabsorption:

60%-70% of water (108 to 116 L/D)

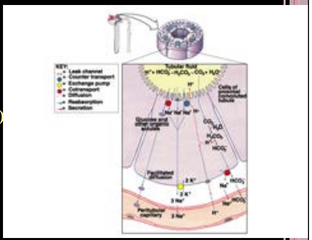
(obligatory water reabsorption)

100% of glucose and other sugars, amino acids, and some vitamins

60%-70% sodium and chloride, along with calcium, magnesium, phosphate, and bicarbonate

Secretion:

Hydrogen ions, ammonium



Roles of the Different Nephron Regions in Urine Formation

Loop of Henle

Reabsorption:

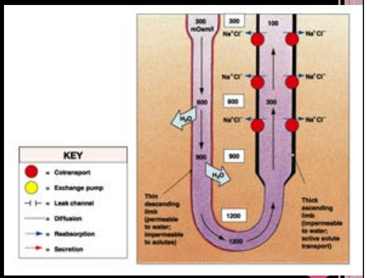
Descending limb

25% of the water

(obligatory water reabsorption)

Thick Ascending limb

20-25% of the sodium and chloride to help maintain the countercurrent system



Roles of the Different Nephron Regions in Urine Formation

Distal Convoluted Tubule

Reabsorption:

Up to 5% of water under ADH control (principle cells)

(Facultative water reabsorption)

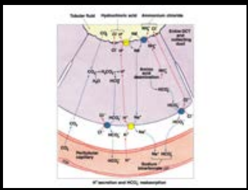
Variable amounts of sodium and chloride under Aldosterone control (principle cells)

Variable amounts of Calcium

Secretion:

Hydrogen ions, ammonium ions,

Creatinine, drugs , toxins



Roles of the Different Nephron Regions in Urine Formation

Collecting Duct

Reabsorption:

Variable amounts of water under ADH control (principle cells)

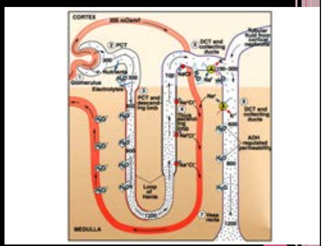
Variable amounts of sodium and chloride under Aldosterone control (principle cells)

Variable amounts of bicarbonate

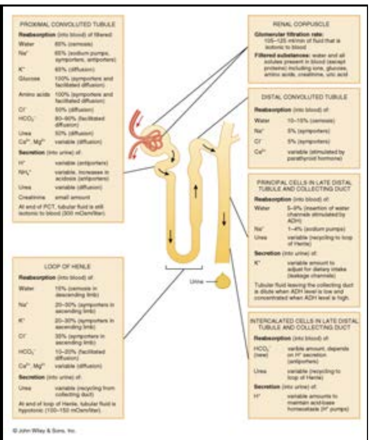
(intercalated cells)

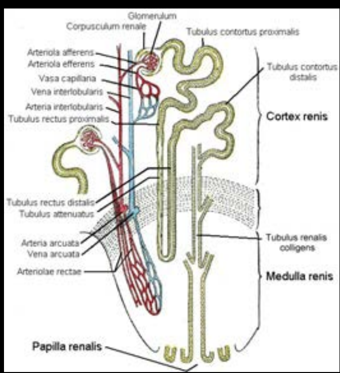
Secretion:

Potassium and hydrogen ions



Summary of the Roles of the Different Nephron Regions in Urine Formation





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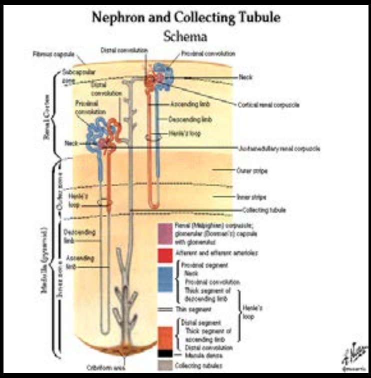

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NEPHRON HEMODYNAMICS

- **Series Hemodynamics and Parallel Hemodynamics**
- The individual nephrons that make up both kidneys are connected in parallel.
- However, the flow through a single nephron represents two arterioles and two capillary beds connected in series.

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HEMODYNAMICS OF A SINGLE NEPHRON

- Connected in series are the high-pressure filtering capillaries of the glomerulus and the low-pressure reabsorbing peritubular capillaries.

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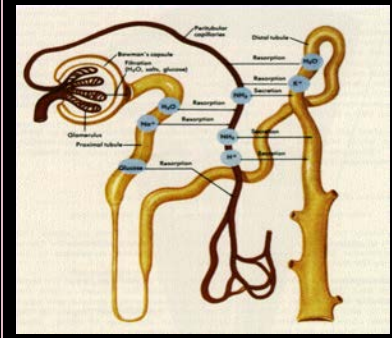

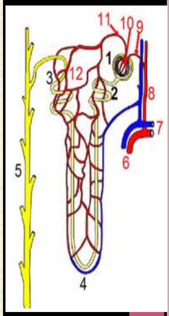

MATERIALS FILTERED

- Freely Filtered
  - Major electrolytes
    - Sodium
    - Chloride
    - Potassium
    - Bicarbonate
  - Metabolic waste products
    - Urea
    - Creatinine
  - Metabolites
    - Glucose
    - Amino acids
    - Organic acids (ketone bodies)
  - Nonnatural substance
    - Inulin
    - PAR (p-aminohippuric acid)
  - Lower-weight proteins and peptides
    - Insulin
    - Myoglobin

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- **Not Freely Filtered**
  - Albumin and other plasma proteins
  - Lipid-soluble substances transported in the plasma attached to proteins
  - Lipid-soluble bilirubin
  - T4 (thyroxine)
  - Other lipid-soluble hormones

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- **Negative Charge on the Filtering Membrane**
  - There is a negative charge on the filtering membrane that inhibits the filtering of protein anions. If this negative charge is not present, significant protein filtration takes place. This simply points out that the glomerular capillaries are very permeable.
- **Fluid Entering Bowman's Capsule**
  - The fluid entering Bowman's capsule is an ultra filtrate of plasma; that is, the filtrate has the same concentration of dissolved substances as plasma, except proteins.
  - The osmolarity of the filtrate is 300 mOsm/L. The criteria for effective osmolarity are the same as those previously stated for extracellular fluid .
  - If a substance is freely filtered by the kidney, the ratio of the filtrate concentration/plasma concentration =1.0. This means the concentrations in Bowman's capsule and the plasma will be the same.

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- **Factors Affecting GFR and Filtration Fraction(FF)**
- FF= fraction of the material that enters the kidney that is filtered
  - For a freely filtered substance, it is 20 %
  - GFR/ RPF = 120/600= 0.2=20%

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DETERMINANTS OF GFR

- Except for an unusual situation when plasma protein concentration changes dramatically or renal obstruction develops, the main factor determining GFR is glomerular capillary pressure.
- An increase in capillary pressure increases GFR, and a decrease in capillary pressure decreases GFR.
- Flow does have a small effect on GFR; an increase in flow will independently increase GFR.
- Factors affecting FF
  - In many circumstances, the main factor affecting FF is renal plasma flow. The longer the fluid remains in the glomerular capillaries, the greater the percentage of the fluid that tends to be filtered.
  - Therefore, as flow decreases, FF will always have a tendency to increase.

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	Afferent Constriction	Efferent Constriction
Glomerular Filtration Pressure	Decrease	Increase
GFR	Decrease	Increase
Renal Plasma Flow	Decrease	Decrease
Filtration Fraction		Increase

FILTERED LOAD

- Filtered load is the rate at which a substance filters into Bowman's capsule.
  - Units are an amount per unit time, e.g., mg/min.
- Filtered load = GFR X Px
  - GFR = glomerular filtration rate
    - units = volume/time, e.g., ml/min, L/day
  - Px= concentration of the substance in the plasma
    - units = amount/volume,e.g.,mg/ml

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TUBULAR REABSORPTION

- Active Mechanisms
  - There are two types of active reabsorption based on system dynamics: TM and gradient-time.
- Transport Maximum(TM) Systems
  - For example, proximal tubular reabsorption of glucose.
  - General Characteristics of TM Systems
  - Carriers are easily saturated.
  - Carriers have a high affinity for the substrate.
  - Low back leak.
  - Back leak refers to the back diffusion of the substance into the tubule after it is reabsorbed into the interstitium. Minimal back leak of glucose occurs because the proximal tubule is not permeable to glucose.
  - The entire filtered load is reabsorbed until the carriers are saturated; then the excess is excreted.

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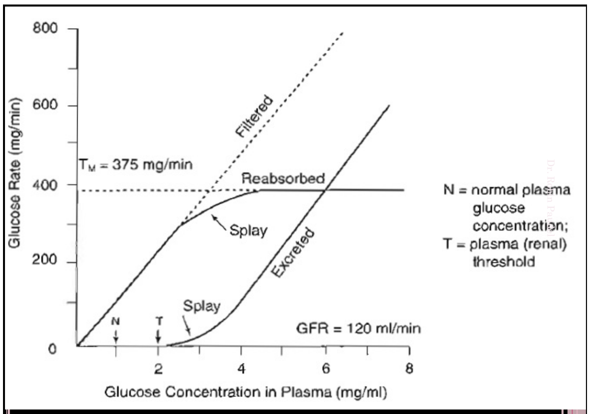


- Substances Reabsorbed by Tm System
  - Almost all natural organic and some inorganic substances that are reabsorbed by the nephron are reabsorbed by a TM system.
  - These substances include
    - Glucose
    - amino acids
    - small peptides and proteins
    - ketone bodies
    - Calcium
    - phosphate.
    - An exception with respect to natural organic substances is urea. Urea is freely filtered and partially reabsorbed, mainly by passive mechanisms.

GRADIENT-TIME SYSTEM

- For example, the proximal tubular reabsorption of sodium
- General Characteristics
  - Carriers appear to be never saturated.
  - Carriers have a low affinity for the substrate.
  - High back leak.
  - High back leak means that some of the sodium that is actively reabsorbed back diffuses into the proximal tubule. The proximal tubule has leaky tight junctions to sodium and also to a few other substances, such as potassium, chloride,and water.

- Approximately a constant percentage of the filtered sodium is reabsorbed in the proximal tubule.
- Under normal conditions it is close to 66%, which means about two-thirds of the filtered sodium is reabsorbed in the proximal tubule.
- Also, the active reabsorption of sodium by the proximal tubule is the main metabolic process going on in the kidney. Thus, oxygen consumption of the kidney is directly proportional to sodium reabsorption and GFR.

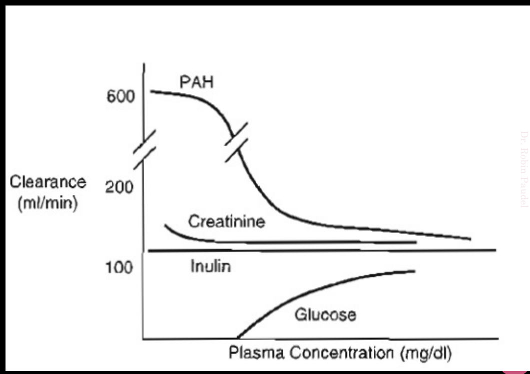
TUBULAR SECRETION

- **Transport Maximum System**
  - **p-Amino hippuric Acid(PAH)Secretion**
    - PAH secretion from the peritubular capillaries into the proximal tubule is an example of a transport maximum system. It has the general characteristics discussed for the reabsorption of glucose except for the direction of transport.
    - At low plasma levels, 20% of the PAR entering the kidney is filtered, and 80% is actively secreted.

- **Net Reabsorption**
  - Filtration> Excretion
- **Net Secretion**
  - Filtration < Excretion

CLEARANCE

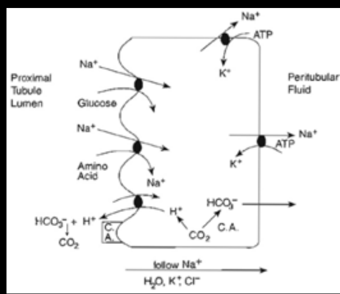
- *Definition: theoretical volume of plasma from which a substance is removed over a* period of time.
- Give some examples !!
- Formula:
  - Clearance of substance x = excretion rate/ plamsa conc.
  - Excretion rate= urine concentration * urine flow rate
- **CLEARANCE OF INULIN AS AN INDEX OF GFR AND RENAL FUNCTION**
- The concentration of inulin in the nephron tubule is an index of water reabsorption.
- The segment of the nephron with the highest concentration of inulin is the terminal collecting duct.
- The segment of the nephron with the lowest concentration of inulin is Bowman's capsule.



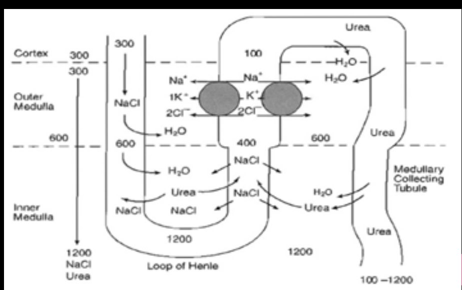
RENAL PLASMA FLOW(RPF)

- The clearance of PAH is generally regarded as the standard estimate of the RPF.
- **Renal Blood Flow:**
  - **Renal Plasma Flow/ (1 – hematocrit)**
- **Concept of Free water Clearance**

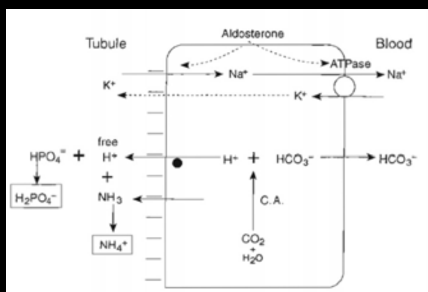
PCT



LOOP OF HENLE



DISTAL TUBULE AND COLLECTING DUCTS

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