Renal Physiology

By Hamza – Year 2

GKTeach 23/24

Learning Objectives

- To recap the anatomy and structure of the nephron
- To understand the basic renal processes of the nephron
- To explain factors affecting basic renal processes
- To explain how acid-base regulation occurs in the kidney
- To read pH, bicarbonate and CO_2 readings

Functions of the Kidney

- Excreting of metabolites and ingested substances
- Control of body fluid composition:
  - Volume regulation
  - Osmoregulation
  - pH regulation
- Endocrine functions
  - ADH, Aldosterone, Natriuretic peptides, PTH, FGF23 -> Kidney
  - Kidney -> Renin, Activated VitD$_3$ (calcitriol), Erythropoietin, PG

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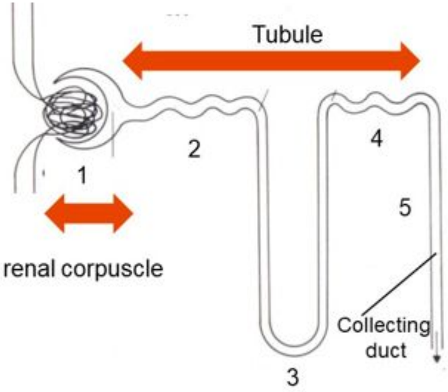
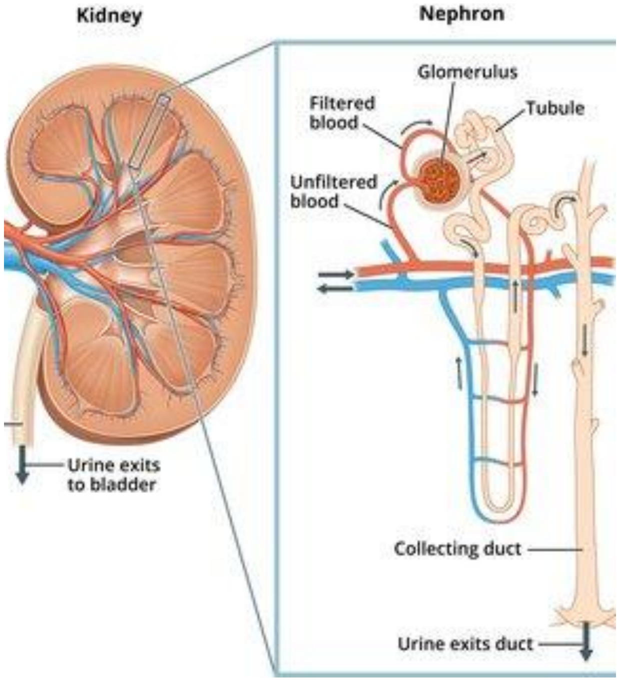
Structures in the Nephron

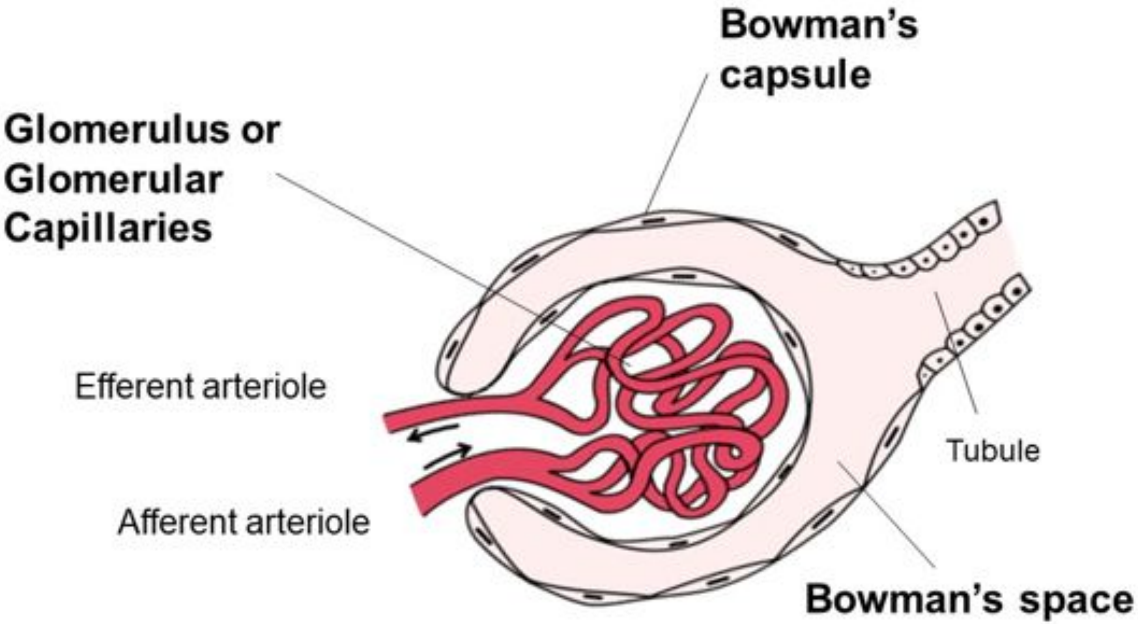
Anatomy of the Nephron

- Kidney has > 1 million nephrons
- Each nephron:
  - Renal corpuscle
  - Tubule





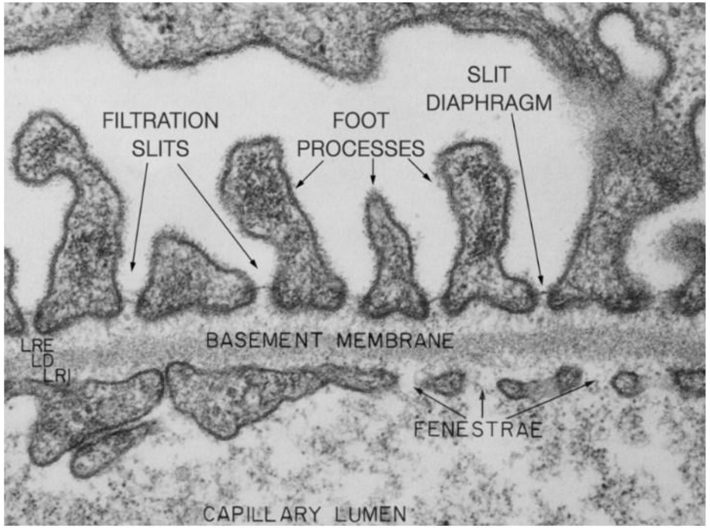
Renal Corpuscle



- 20% of plasma is filtrated across the filtration space

Filtration interface

- 3 components:
  - Fenestrated capillary endothelium (pores max size 15nm)
  - Basement membrane (fixed polyanions)
  - Tubular epithelium / podocytes) (filtration slits ~ 8nm)

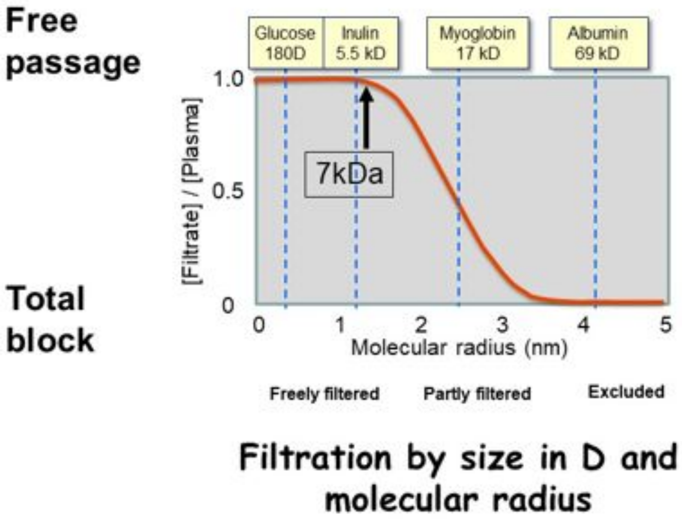


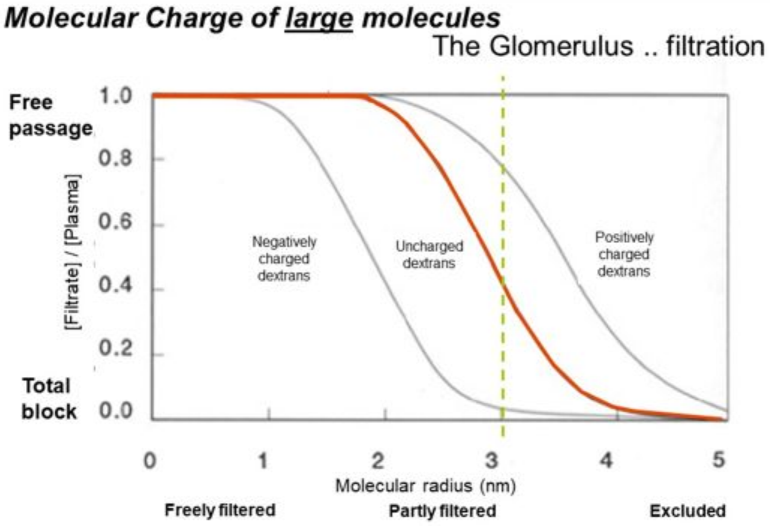
Podocytes have foot processes and branching pedicles
Between these foot processes are filtration slits
Nephrin and podocin are important for making filtration slits

What can pass through the filtration barrier?

- Most plasma constituents can be freely filtered except proteins
- Filtration properties depend on:
  - Molecular size – Filtration slits
  - Charge – Basement membrane
  - Possibly shape

What can pass through the filtration barrier?

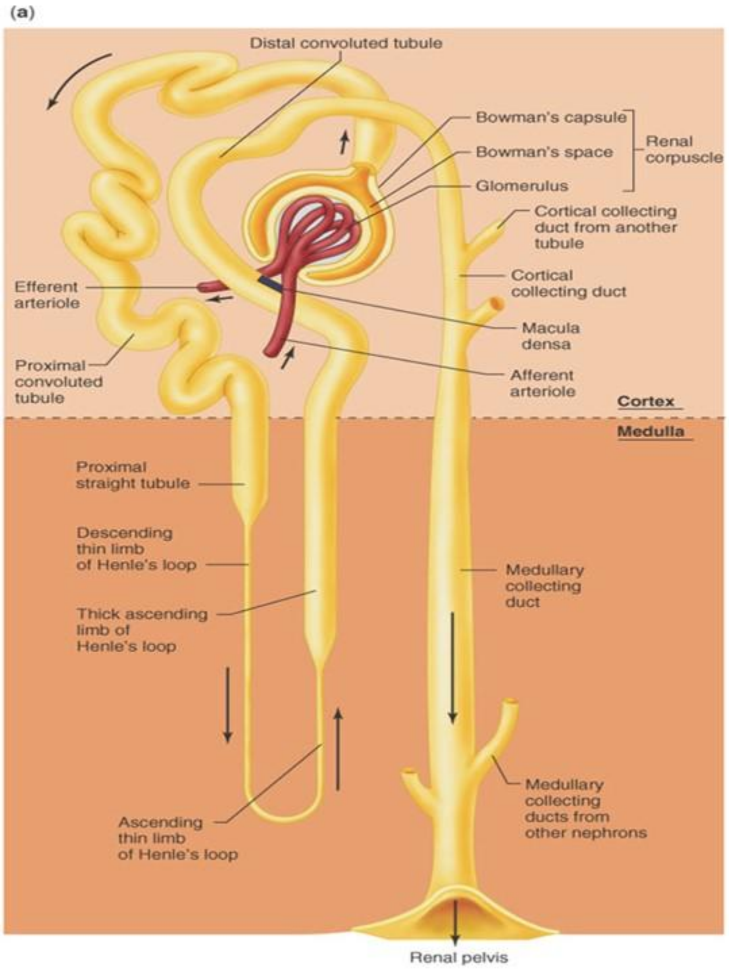


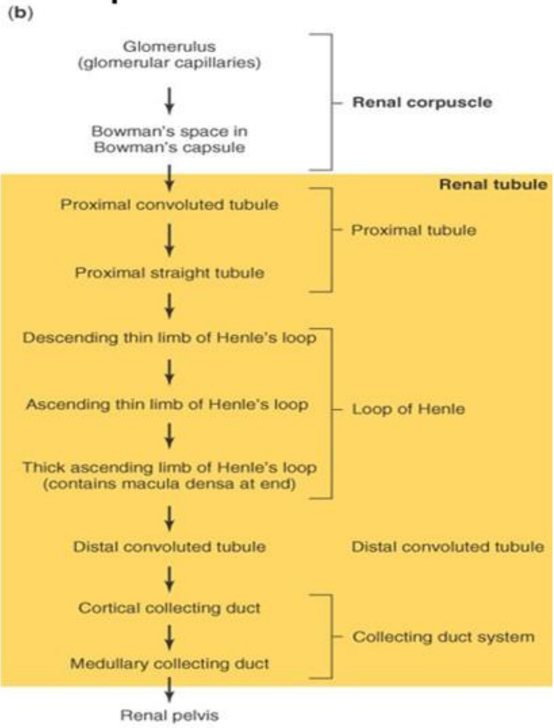


Smaller molecules are more permeable

Anionic (negatively charged) dextrans are more permeable

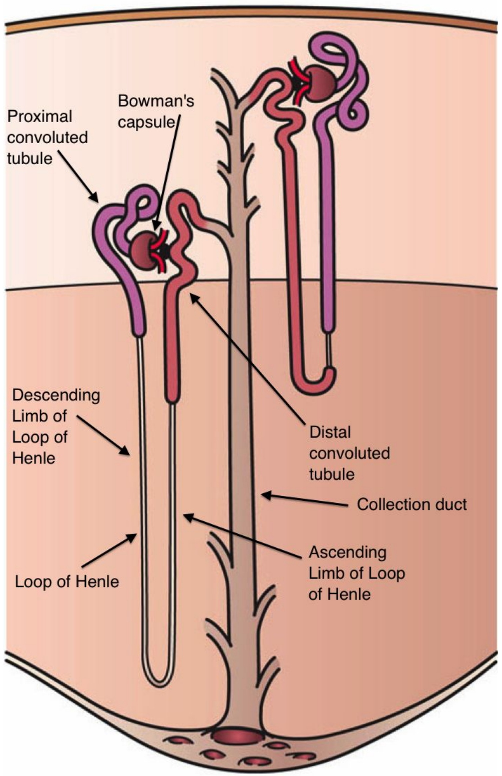
NEPHRON
Important features:

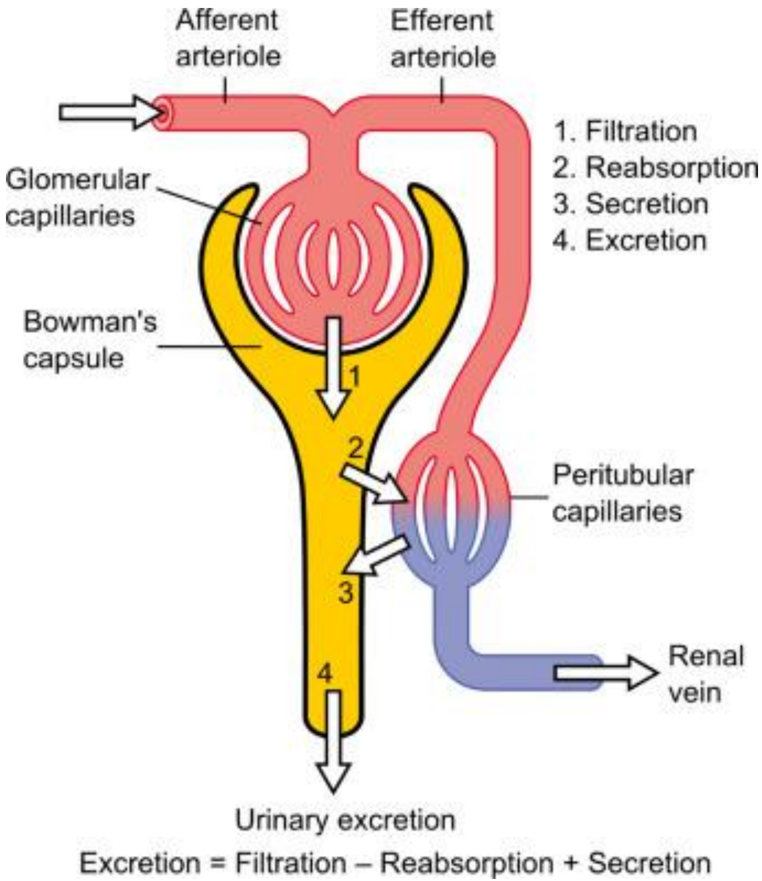


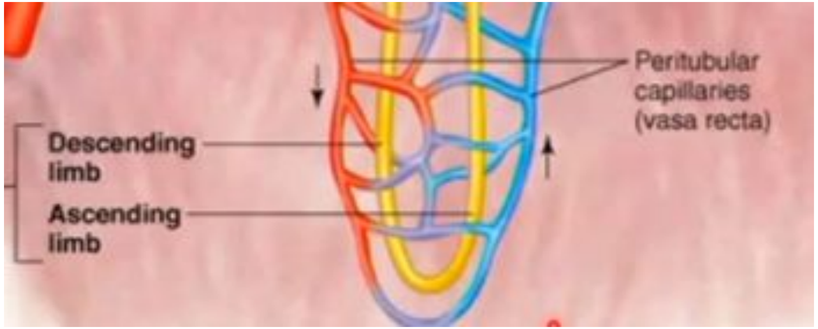


2 Types of Nephron

	Cortical	Juxtamedullary
Proportion	85%	15%
Location	Outer 2/3 of cortex	Inner 1/3 of cortex
Features	Short loop of Henle	Long loop of Henle







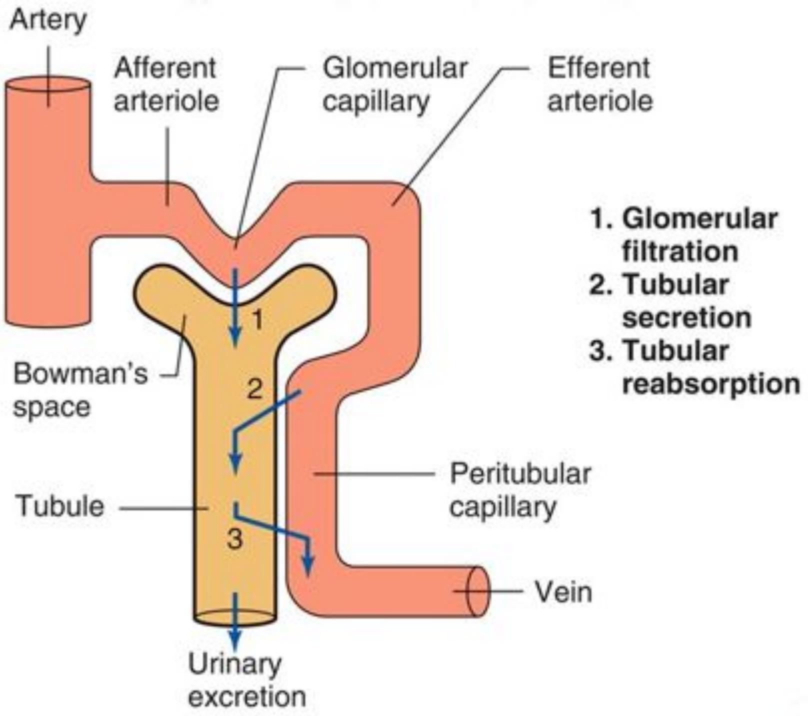
^ In the loop of Henle peritubular capillaries have a special name (Vasa recta)

Questions?

Basic Renal Processes

Renal Processes

- Glomerular filtration
- Tubular Reabsorption
- Tubular secretion



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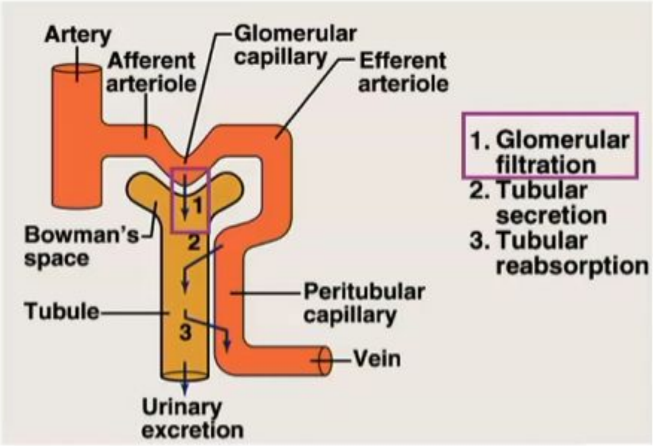
Glomerular filtration

- Movement of both fluid and solutes from glomerulus to the bowman's space – occurs only in renal corpuscle



2 Factors which affect filtration:

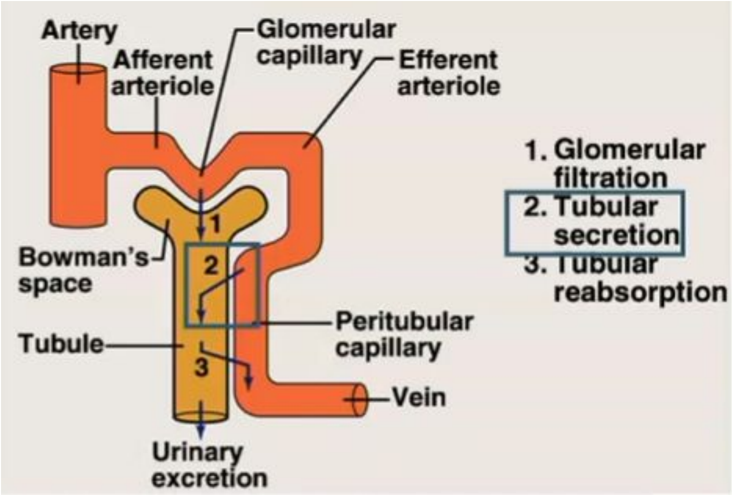
- Hydrostatic pressure
- Colloid osmotic pressure

Things to note (From lectures)

- Certain drugs and ions can bind to proteins and so will also not be freely filtered:
  - Acidic drugs – bind to albumin
  - Basic drugs – bind to alpha-1-acid glycoprotein
- Calcium is a divalent ion (Ca^{2+})
  - 40% is bound to proteins so only 60% (unbound ions) can be filtered
- Damage to glomerulus or high BP can cause:
  - Protein in urine – proteinuria
  - Haemoglobin in urine – haemoglobinuria
  - Red cells in urine - haematuria

Tubular secretion

- Secretion of solutes from the peritubular capillaries into the tubules
- Occurs in proximal tubule + collecting duct



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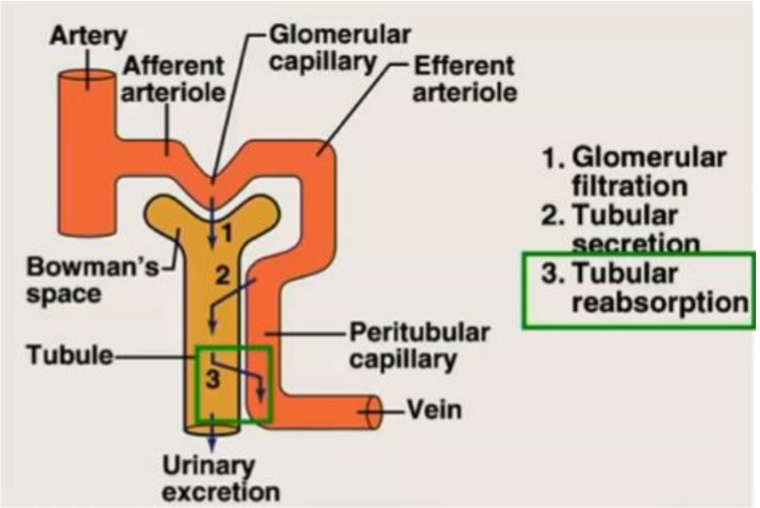
Tubular reabsorption

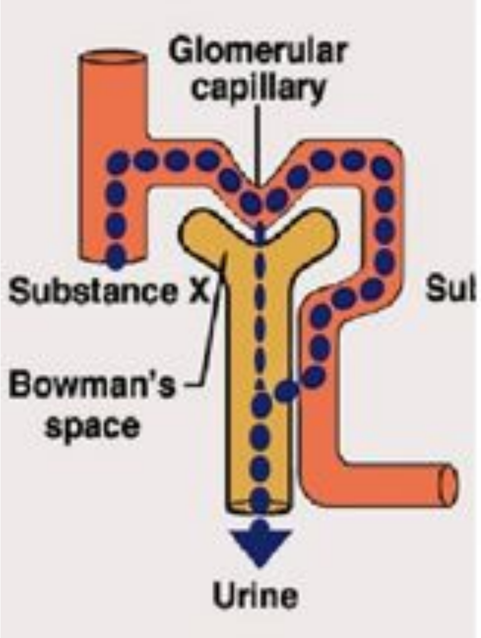
- Movement of materials from the filtrate in the tubules into the peritubular capillaries
- Can occur anywhere but predominantly in proximal tubule



Formula for excretion

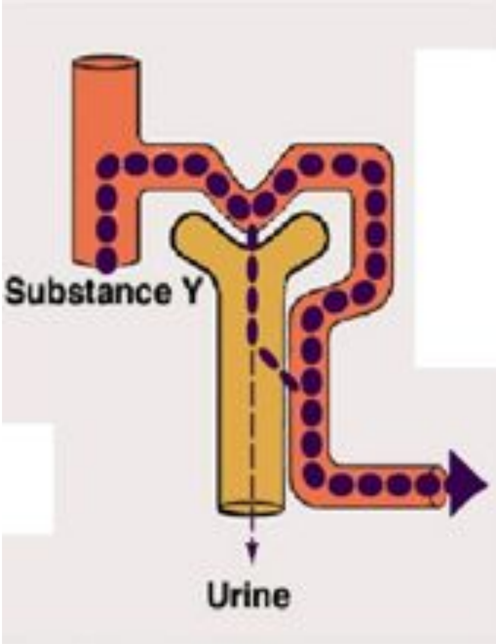
Amount excreted in urine = Amount filtered + Amount secreted − Amount reabsorbed

Substance X



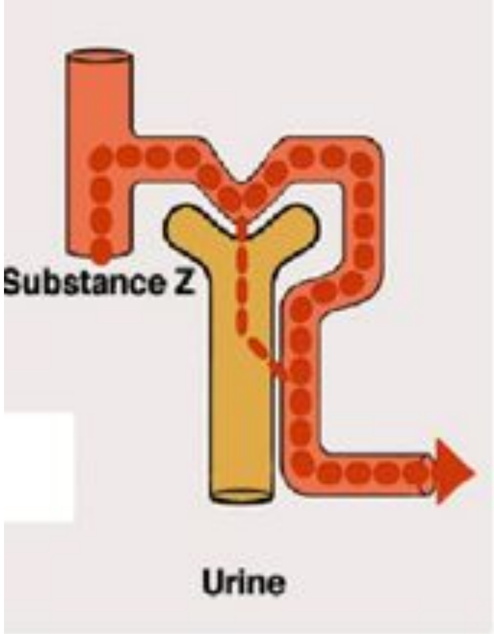
- Filtered, excreted but not reabsorbed
- All of PAH exits into the urine
- Para-aminohippiuric acid (PAH)
- Used as a marker of blood flow

Substance Y



- Filtered
- Not all is reabsorbed – some present in the urine
- E.g. water and most electrolytes

Substance Z



- Filtered
- Completely reabsorbed
- Should not be present in the urine
- E.g. Glucose

Metabolism

- 4th Process that occurs in the nephron
- Glutamine is metabolised
- Will go over in acid-base balance slides

SBA 1

How is para-aminohippuric acid excreted in the kidney?

1. Filtered, completely reabsorbed
2. Filtered, secreted completely, not absorbed
3. Filtered partially, reabsorbed partially

SBA 1

How is para-aminohippuric acid excreted in the kidney?

1. Filtered, completely reabsorbed
2. **Filtered, secreted completely, not absorbed**
3. Filtered partially, reabsorbed partially

SBA 2

What percentage of calcium can be freely filtered?

1. 100%
2. 90%
3. 60%
4. 40%
5. 0%

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SBA 2

What percentage of calcium can be freely filtered?

1. 100%
2. 90%
3. **<u>60%</u>**
4. 40%
5. 0%

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Questions?

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Filtration

Glomerular filtration rate

- Volume of fluid filtered from glomeruli per minute
- Depends on:
  - Net filtration pressure
  - Permeability characteristics
  - Surface area
- Regulated by neural and hormonal input
- High GFR - greater secretion of salt and water

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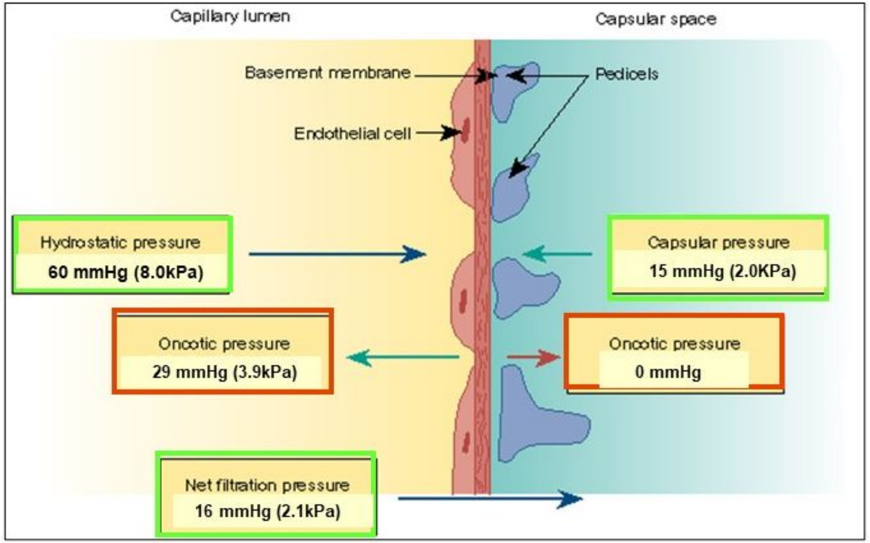
Net filtration pressure

- Plasma flows across a capillary wall from:
  - High to Low hydrostatic pressure
  - Low to high colloid osmotic pressure



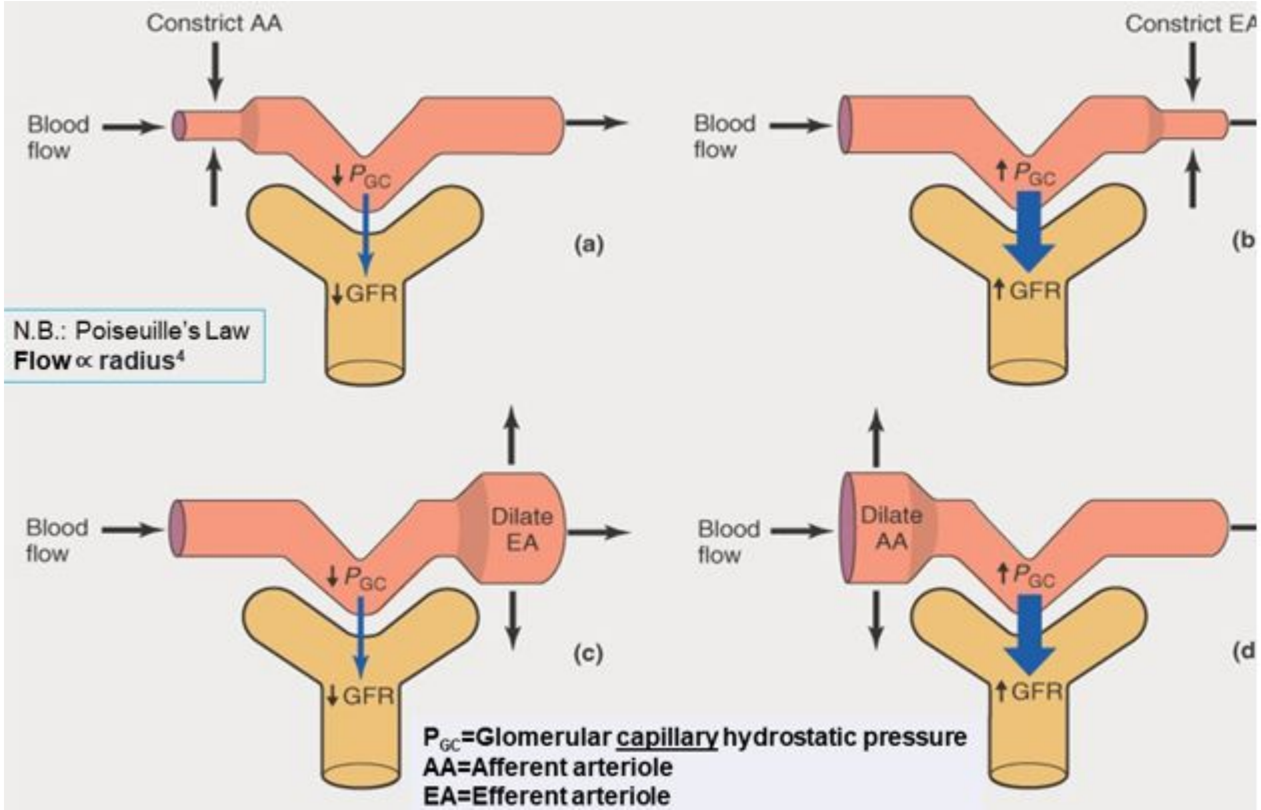
To calculate net filtration pressure, we need to find:

- Hydrostatic pressure gradient (60-15): 45mmHg
- Oncotic pressure gradient (29-0): 29mmHg

Net filtration pressure is 16mmHg

No protein is filtered across into bowman's space
-> Therefore, oncotic pressure in bowman's space is 0

Hydrostatic Pressure

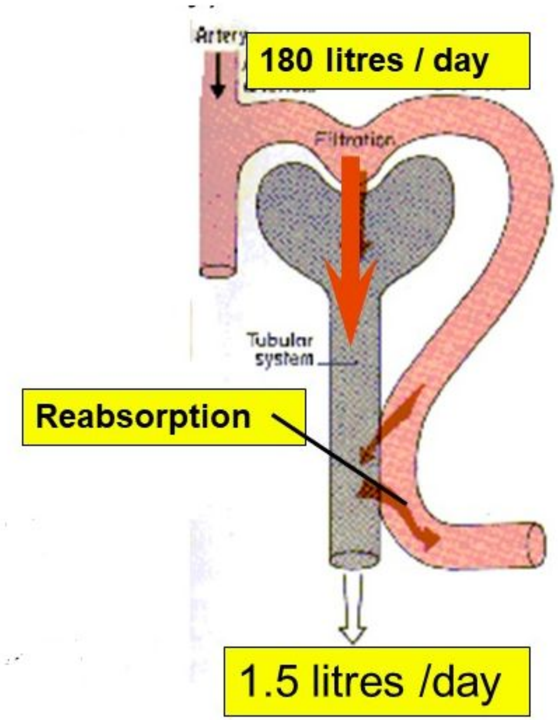


Surface area of filtration interface

- Can be altered by glomerular mesangial cells on glomerulus – contain smooth muscle actin
- When there is increase in sympathetic tone then muscle contracts -> less surface area -> filtration reduces

GFR – Values to know

- GFR is around 180 litres per day (125ml/min)
- Urine output is typically only 1.5 litres
Why? - 99% of water is reabsorbed



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Acid-Base Balance

Why does pH matter?

- Influences protein stability and function
- Affects nerve and muscle excitability
- Influences electrolyte distribution

Respiratory H+ mechanism

- $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$
- Generation of H^+ occurs from CO2
- Decreased ventilation (less CO_2 being removed) can cause an increase in H^+ ions -> causes Acidosis
- Opposite is true for increased ventilation

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Metabolic H+ mechanism

- Production of nonvolatile acids such as sulfuric acid, lactic acid and phosphoric acid can increase the amount of H^+

- (If someone is on high protein -> causes gain in hydrogen ions in the body)
- Metabolic reactions utilise H^+ ions for metabolism of various organic anions

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Gastrointestinal H+ mechanism

- You can lose H+ due to vomiting -> Acid produced in stomach is being lost

$$CO_2 + H_2O \Leftrightarrow H_2CO_3 \Rightarrow HCO_3^- + \cancel{H^+}$$

- You gain H+ (Sort of) as you lose bicarbonate in diarrhoea or other nongastric GI fluids

$$CO_2 + H_2O \Leftrightarrow H_2CO_3 \Rightarrow \cancel{HCO_3^-} + H^+$$

Renal H+ mechanism

- Acids other than respiratory acid (due to CO_2) can be excreted by the kidneys
- Kidneys can maintain pH by:
    - Reabsorbing bicarbonate
    - Getting rid of excess H^+

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Bicarbonate reabsorption 1

- Occurs in PT, Ascending loop of Henle and Cortical collecting ducts (intercalated cells type A)
- Occurs in the tubular epithelial cells
- Key equation H_2CO_3 -> $HCO_3^- + H^+$
- HCO_3^+ is excreted into blood (increasing pH by reducing H^+)
- And H^+ is excreted into tubular lumen to be excreted (decreasing pH as H^+ is lost)

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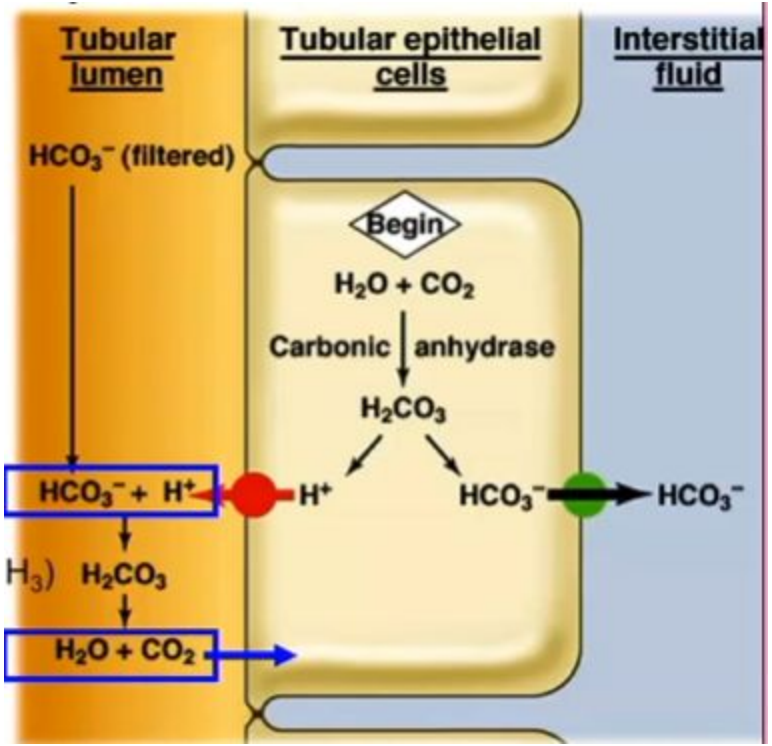
Bicarbonate reabsorption 2

- Channels involved:
- Na^+-H^+ countertransporters (NH3)
- H^+-ATPase pumps
- H^+-K^+-ATPase pumps

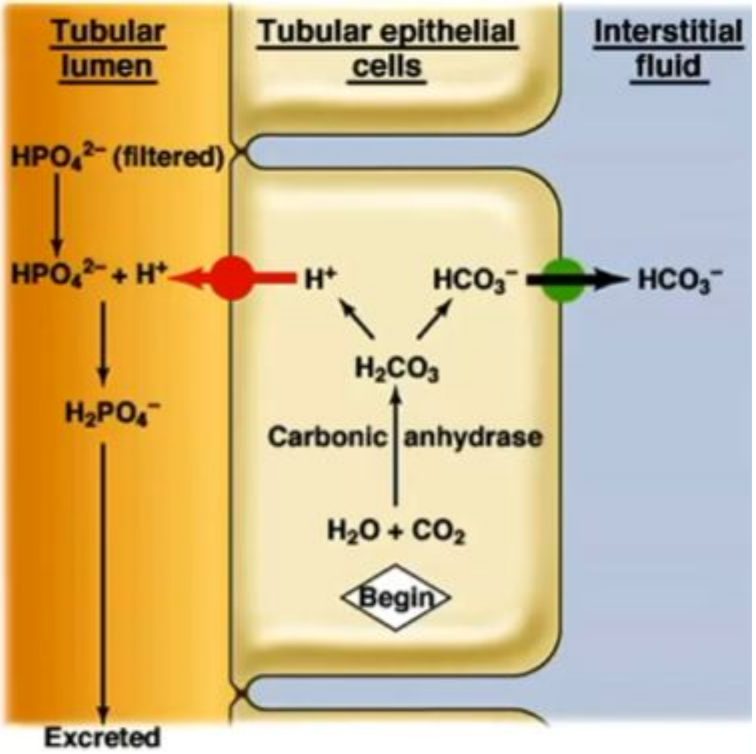
- Key enzyme:
  - Carbonic Anhydrase



H+ excretion

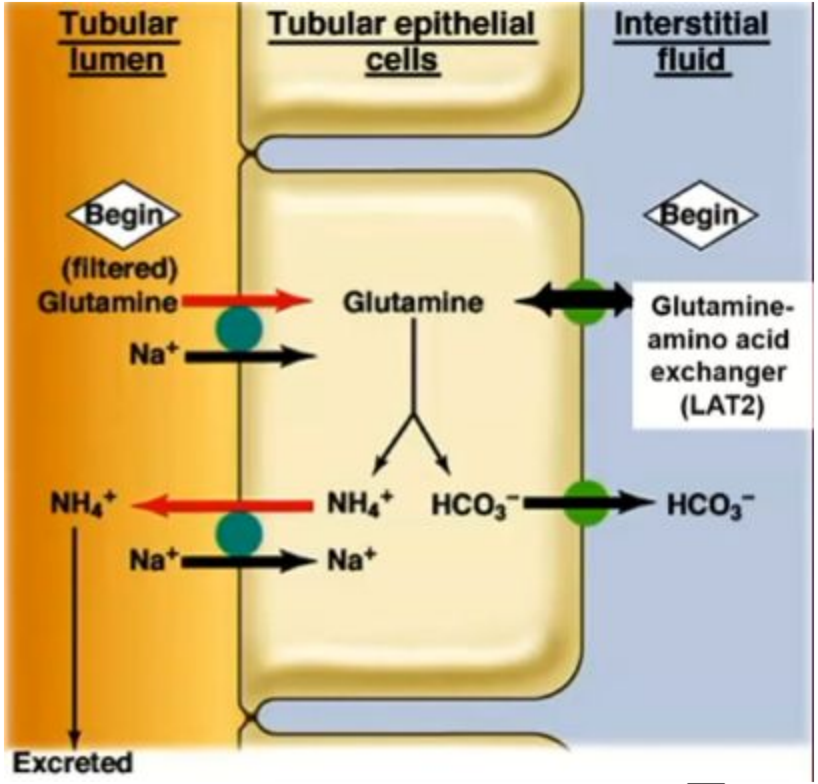
- Occurs in combination of HPO_4^{2-} (Monohydrogen phosphate)
- Without this the unbuffered H+ would cause urine pH to be below <5

- Results in addition of new HCO_3^- to plasma (H^+ is lost)



Glutamine metabolism

- Filtered glutamine is transported into the cell
- Glutamine is metabolised into NH_4^+ and Bicarbonate
- Ammonia is transported out in exchange for sodium and is excreted (H^+ is lost)
- Bicarbonate is transported into the interstitial fluid



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Three ways pH is buffered

- Chemical buffers:

  Work in seconds
- Brain stem respiratory centre:

  Works in minutes
- Renal mechanisms:

  Works in hours to days

Acid base disturbances

- Acidosis is plasma pH of below 7.35
- Alkalosis is plasma pH of above 7.45

- Respiratory acidosis/alkalosis is caused by a respiratory issue
- Metabolic acidosis/alkalosis is caused by a non-respiratory issue

Metabolic or Respiratory?

- Number 1 tip – look for at pH, bicarbonate and CO_2 and identify which out of bicarbonate and CO_2 can cause the pH
- E.g. pH is acidotic, bicarbonate is raised, CO_2 is raised

- E.g. pH is alkalotic, bicarbonate is high, CO_2 is high

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Metabolic or Respiratory?

- Number 1 tip – look for at pH, bicarbonate and CO_2 and identify which out of bicarbonate and CO_2 can cause the pH
- E.g. pH is acidotic, bicarbonate is raised, CO_2 is raised
- -> Respiratory acidosis

- E.g. pH is alkalotic, bicarbonate is high, CO_2 is high
- -> Metabolic alkalosis

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Is there compensation?

- Identify pH, bicarbonate and CO_2
- After finding out whether pH is due to CO_2 or bicarbonate, look at the other value. If it is normal then there is no compensation
- If the change in the other value is paradoxical to pH then there is compensation, if value remains normal then there is no compensation
- E.g. pH is acidotic, bicarbonate is raised, CO_2 is raised
- -> Respiratory acidosis with partial metabolic compensation
- E.g. pH is alkalotic, bicarbonate is high, CO_2 is high
- -> Metabolic alkalosis with partial respiratory compensation

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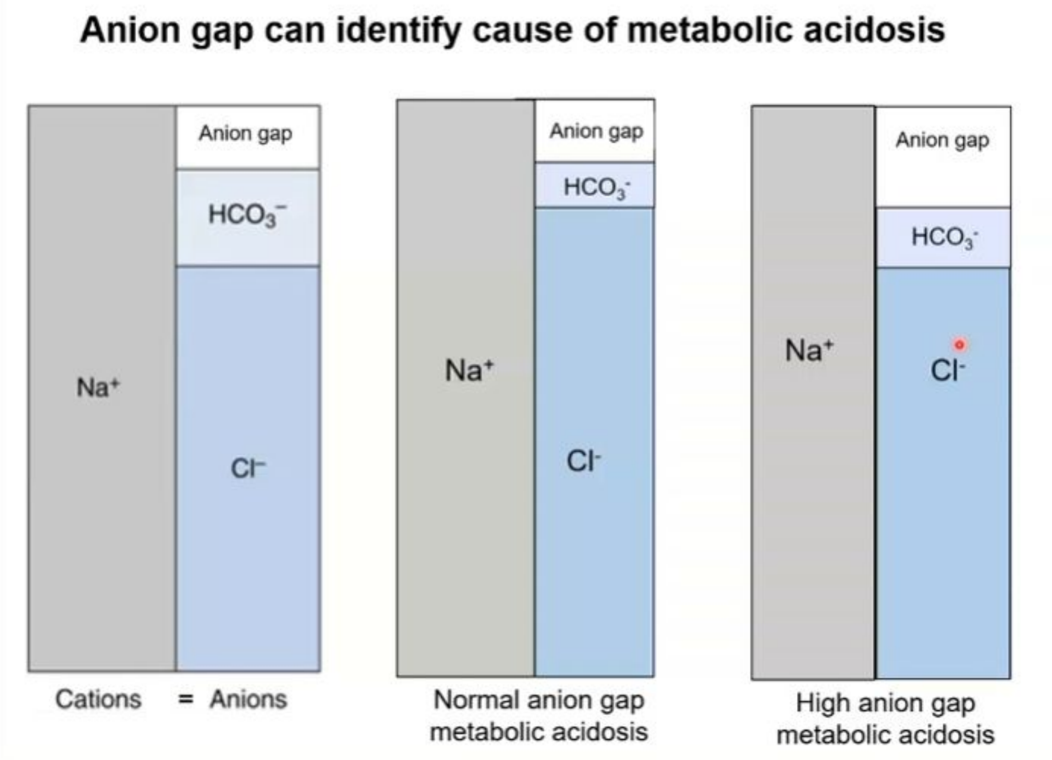
Acid base disturbances



- Anion gap helps rule out causes
- Normal anion gap should be 8-12mM and is normally due to problems with the kidney or GI tract (bicarbonate lost but replaced with chloride)
- Increased anion gap is caused by excess H^+ (due to loss of bicarbonate without increase in chloride) (e.g. lactic acidosis, diabetic ketoacidosis)

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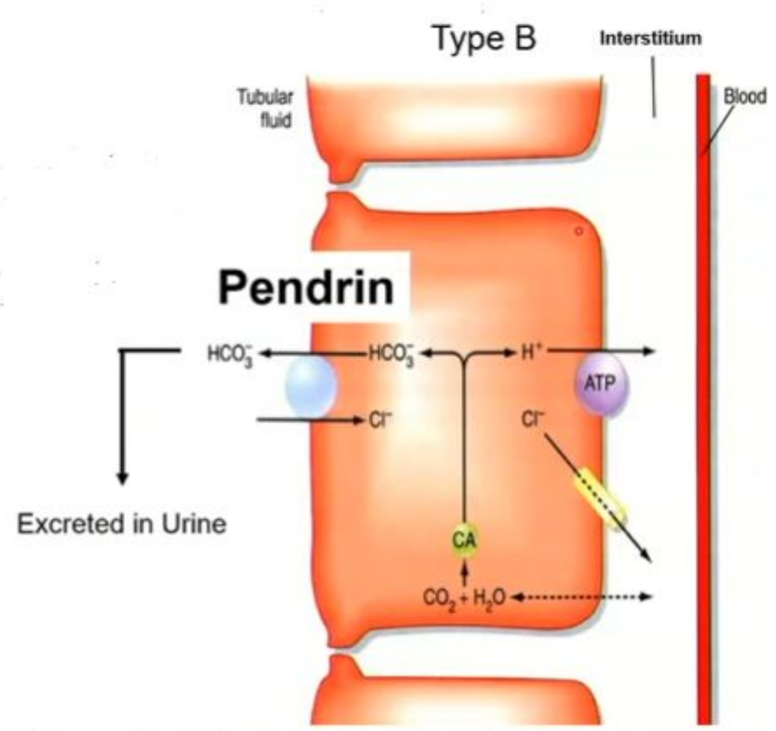
Renal compensation in metabolic acidosis

- Type B intercalated cells of collecting duct remove bicarbonate into the urine AND acidify the plasma by pumping H^+ out to the interstitium and into the blood



Questions?

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