Critical Care Chemistry

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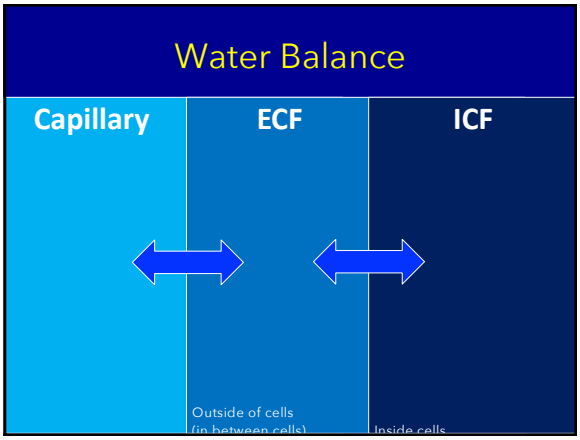
Water Balance



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Body Fluid Compartments

Intracellular fluid	Extracellular fluid	Transcellular fluid*
2/3 of TBW 28 L 40% of BW	1/3 of TBW 14 L 20% of BW	15 ml/kg of the BW; Small amounts

Interstitial fluid	Plasma
10.5 L 75% of ECF	3.5 L 20% of ECF

*Pericardial, pleural, peritoneal, & synovial fluids, intraocular fluid, CSF, endolymph

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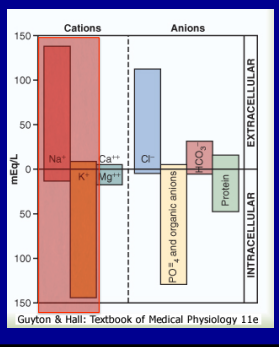
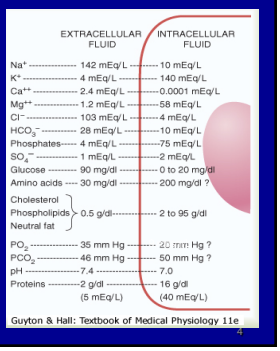
Ionic composition of body fluids





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Kidney Functions

- Removal of toxins, metabolic wastes, and excess ions from the blood
- Regulation of blood volume, chemical composition, and pH
- Gluconeogenesis during prolonged fasting
- Endocrine functions
  - Renin: regulation of blood pressure and kidney function
  - Erythropoietin: regulation of RBC production
- Activation of vitamin D

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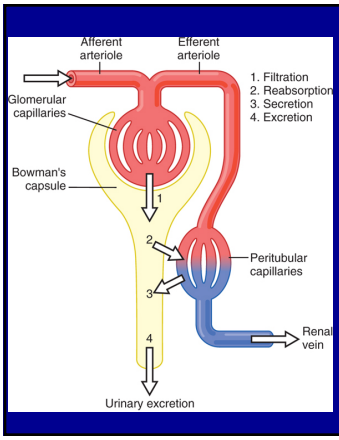

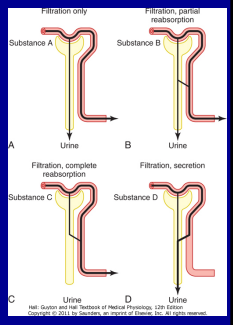

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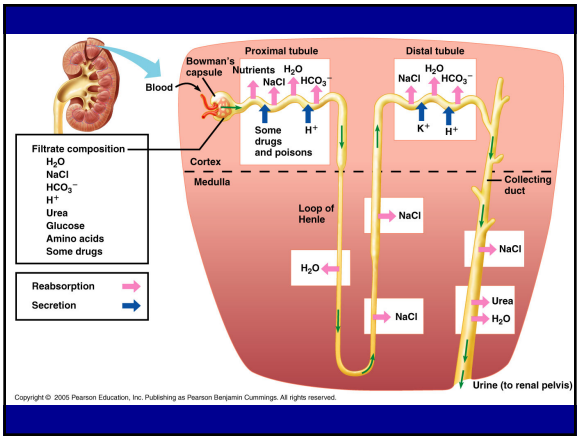

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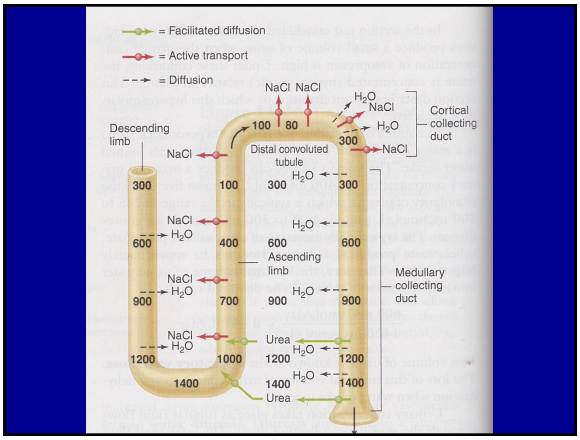

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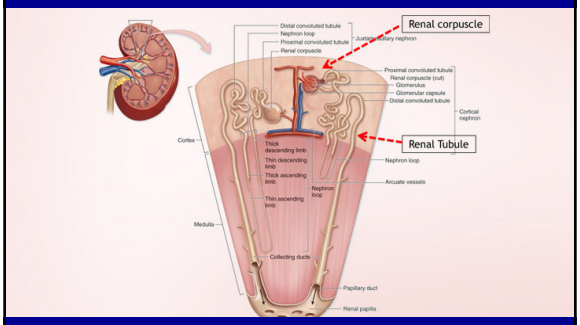
Nephrons



~1 million per kidney

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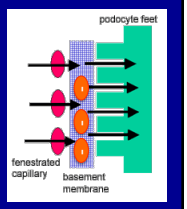
Glomerular Filtration

- Passive mechanical process driven by hydrostatic pressure
- Governed by (and directly proportional to)
  - Total surface area available for filtration
  - Filtration membrane permeability
  - Net filtration pressure
  - Particle size
  - Charge on the particle



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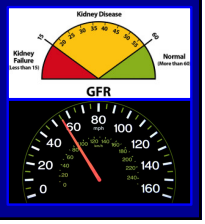
Glomerular Filtration

- Passive mechanical process driven by hydrostatic pressure – primarily
- Indirectly measured by creatinine and creatinine clearance calculation

Stage of Disease	Description	GFR* (mL/min per 1.73 m^2)
1	Kidney damage with normal or increased GFR	≥90
2	Kidney damage with mildly decreased GFR	60–89
3	Moderately decreased GFR	30–59
4	Severely decreased GFR	15–29
5	Kidney failure	<15 (or undergoing dialysis)



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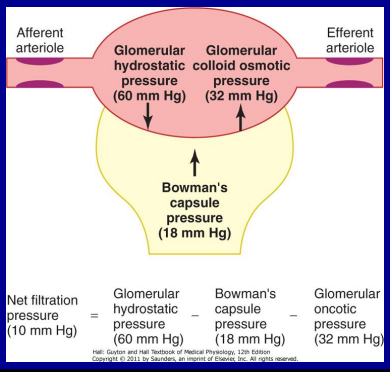
Glomerular Filtration



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Opposite forces affecting GFR

- Prostaglandin E_2
  - Vasodilator that counteracts vasoconstriction by norepinephrine and angiotensin II
  - Prevents renal damage when peripheral resistance is increased

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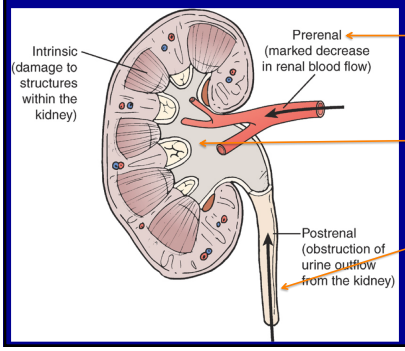
BUN:Creatinine ratio

(in the setting of renal failure / elevated creatinine)



Pre-renal
- >20:1
- Heart failure
- Shock
- Blood loss

Renal
- <10:1
- Infections
- Toxins/Drugs
- Direct trauma

Post-renal
- 10-20:1
- Urinary tract obstructions

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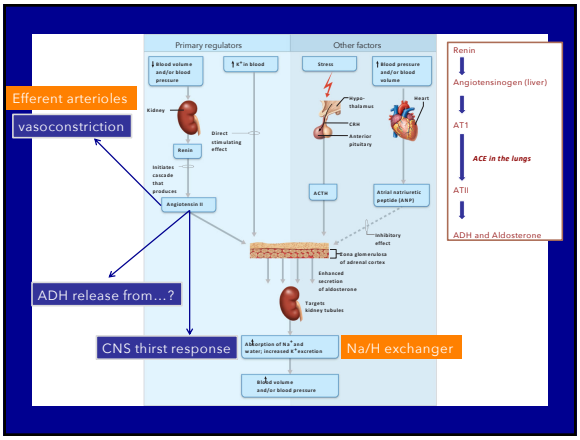

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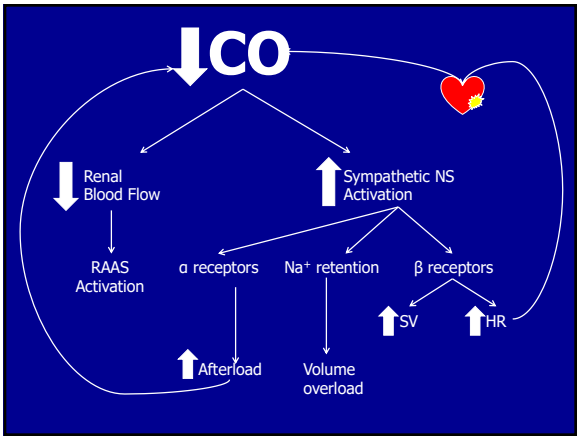

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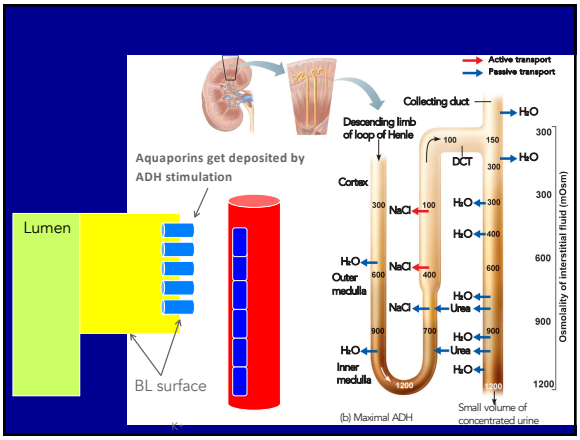

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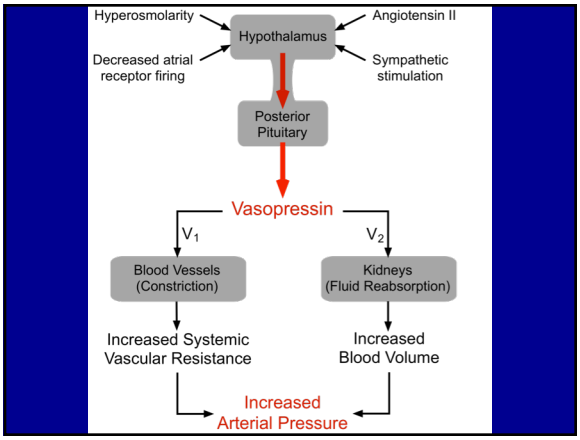

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Major causes of Kidney Failure

- Prerenal Disease
- Vascular Disease
- Glomerular Disease
- Interstitial/Tubular Disease
- Obstructive Uropathy

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Remember this…

- Fat (lipid) soluble
  - Basic pH (NH3+ to NH2)
  - Can cross membranes
  - Uncharged (neutral)
  - Non-polar
  - Lipophilic
  - Processed by liver
  - Nuclear or cytoplasmic receptors
  - Requires carrier protein
  - Long half-life
  - High volume of distribution
  - Small molecule
- Water soluble
  - Acidic pH (COOH to COO-)
  - Does not cross membranes
  - Charged
  - Polar
  - Hydrophilic
  - Processed by kidneys
  - Cell surface receptors
  - Has no carrier protein
  - Short half-life
  - Low volume of distribution
  - Large molecule

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Steroids

- Mechanism of Action "I-KISS"
  - I – Inhibits Phospholipase A_2
  - K – Kills T Cells and Eosinophils
  - I – Inhibits Macrophage Migration
  - S – Stabilizes Mast Cells
  - S – Stabilizes Endothelium

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30

Steroids

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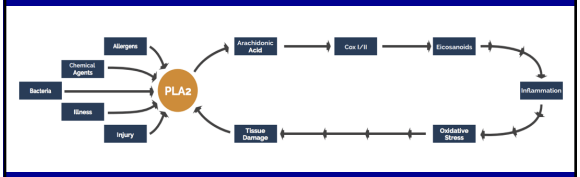

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Steroids

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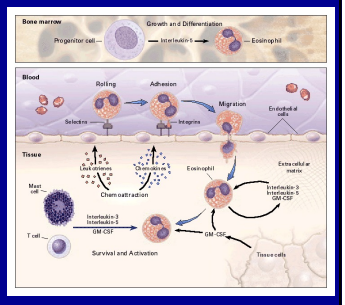

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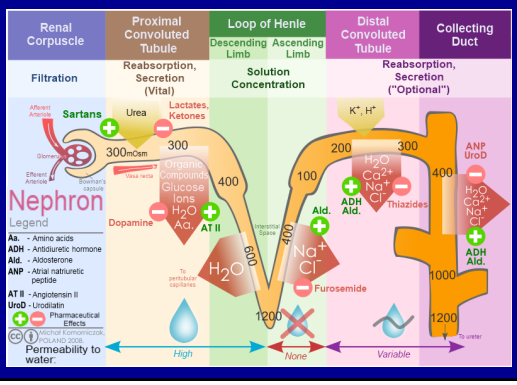
Renal drugs



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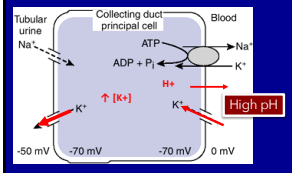
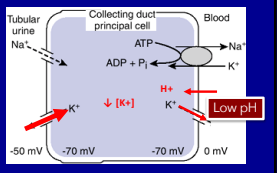
EFFECTS OF ACID-BASE DISTURBANCES on K+

Alkalosis = HypoK



H+ leaves the cells and enters the blood
K+ enters the cells and leaves the blood

Acidosis = HyperK



H+ leaves the blood and enters the cells
K+ leaves the cell and enters the blood

+ for +

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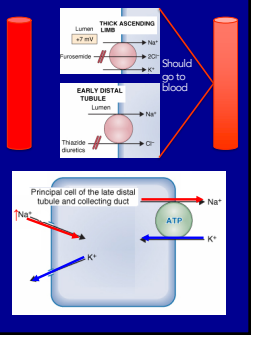
Effects of loop & thiazide diuretics on K+

- Net effect: ↑K excretion → **hypokalemia**
- **Loop diuretics block Na-K-2Cl co-transporters**
- **Thiazide diuretics block Na-Cl co-transporter**
  - ↑Na^+ delivery to the principal cells in the CD → ↑ Na^+ diffusion into the cells via luminal membrane → ↑ **Na^+ pumping out of the cell by Na-K ATPase → ↑ K^+ influx into the cell & K^+ into urine**



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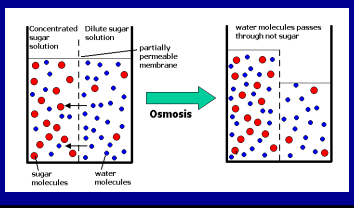
Renal Pharmacology

Osmotic Diuretics

- Mannitol (Osmitrol)
  - Increases Urine Output
  - Increases Fluid Osmolarity in Tubules



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Renal Pharmacology

Loop Diuretics

- Furosemide (Lasix)/ Ethycrynic Acid/ Bumex
  - Inhibit Na/K/2Cl in the Thick Ascending limb of the Loop of Henle
    - Stimulates the Release of PGE
      - Action of PGE Inhibited by NSAIDS
    - **Ethycrynic Acid- Does NOT have Sulfur**

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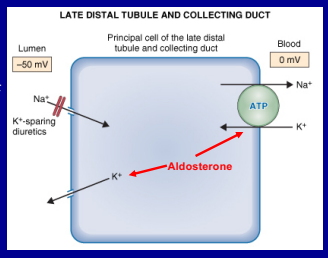
EFFECTS OF K-SPARING DIURETICS ON K+ EXCRETION

- **Do not cause K+ loss via urine**
- **Mechanism**: inhibition of stimulatory effect of aldosterone on Na^+ reabsorption and K^+ secretion



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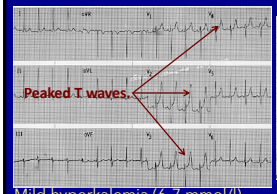
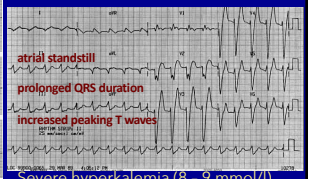
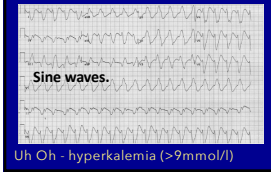
Hyper K -Cardiac Arrhythmia's - ECG changes



Mild hyperkalemia (6-7 mmol/l)



Severe hyperkalemia (8 – 9 mmol/l)



Uh Oh - hyperkalemia (>9mmol/l)

TREAT THE HYPER-K^+ and Resuscitate per ACLS if pulseless

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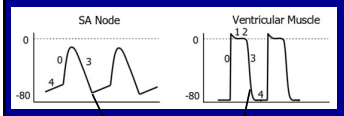
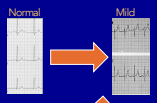
Hyper K- Cardiac Arrhythmia's

- Ventricular dysrhythmias
- Asystole

K+ is the problem...

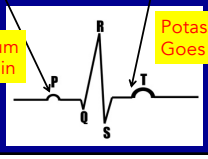
High levels of K+ will cause the heart to become more positive and closer to threshold and ultimately prolong repolarization leading to a long QT

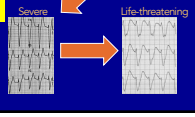




Calcium Goes in

Potassium Goes out





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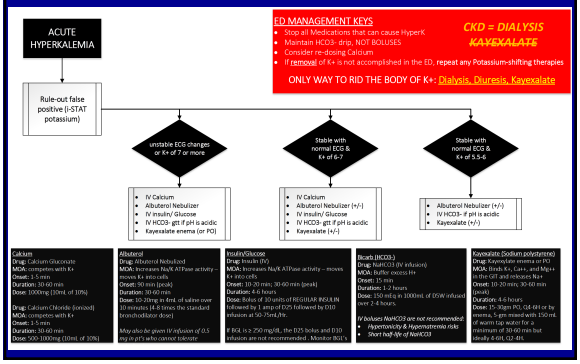
ACUTE management



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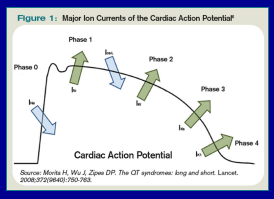
ACUTE management

- Calcium for HyperK
  - Interferes with the excessive excitation caused by K+
  - Blocks the K+ channels
  - CaCl in adults,
  - CaGluconate in peds

Only use Ca^{++} if the QRS is wide!



$$V_m = \frac{RT}{F}\ln\left(\frac{p_K[K^+]_o + p_{Na}[Na^+]_o + p_{Cl}[Cl^-]_i}{p_K[K^+]_i + p_{Na}[Na^+]_i + p_{Cl}[Cl^-]_o}\right)$$

Goldman Hodgkin Katz equation

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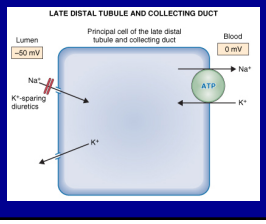
ACUTE management

- Insulin/Glucose
  - Insulin stimulates the Na/K pump and increases it's activity. Moving K+ into the cell.
  - Glucose will correct any hypoglycemia associated with the insulin administration

Check BGL levels – Glucose is not necessary in a hyperglycemic patient

- Albuterol
  - The Beta 2 properties increase activity of the Na/K pump and move K+ into the cell.



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ACUTE management

- Bicarbonate
  - Works on the H+/K+ exchange mechanism
    - As HCO3- is added to the blood, H+ will leave the cell in an atempt to buffer the alkaline load and force K+ to move into the cell to balance the ICF charge.

- 3 D's
  - The ONLY ways to REMOVE excess K+
    - Dialysis
    - Diarrhea (induced)
      - Kayexalate
    - Diuresis
      - Bolus with NaCl and administer a diuretic simultaneously

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Hypernatremia

- Etiology
  - Dehydration
  - Water deprivation
  - Dietary intake

- Pathophysiology
  - net water loss or a sodium gain
- S/Sx
  - Intense thirst
  - HTN
  - Edema
  - Agitation
  - Convulsions

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Hyponatremia

- Etiology
  - Excessive water intake
  - chronic vomiting or diarrhea,
  - Aldosterone deficiency
  - Dietary is rare
  - Diuretics
- Pathophysiology
  - Cellular edema
- S/Sx
  - Muscle weakness
  - dizziness
  - Hypotension
  - tachycardia
  - Altered mentation

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ACUTE management

- **Hypernatremia**
- Acute Change in Na (occurred within 24 hours)
  - correct the serum sodium at rate of 2-3 mEq/L/h (maximum total, 12 mEq/L/d)
- Progressive change in Na – chronic sodium imbalance
  - corrected at a rate not to exceed 0.5 mEq/L/h and a total of 8-10 mEq/day
- If HYPERvolemic, salt and water restriction plus diuretics and V2 antagonists (ADH blockers)

- **Hyponatremia**
- Acute Change in Na (occurred within 48 hours)
  - Overtly symptomatic pt (Sz) will be treated with 3% (hypertonic saline).
- Progressive change in Na – chronic sodium imbalance
  - Free water restriction (<1 L/day)
- If HYPERvolemic, salt and water restriction plus diuretics and V2 antagonists (ADH blockers)

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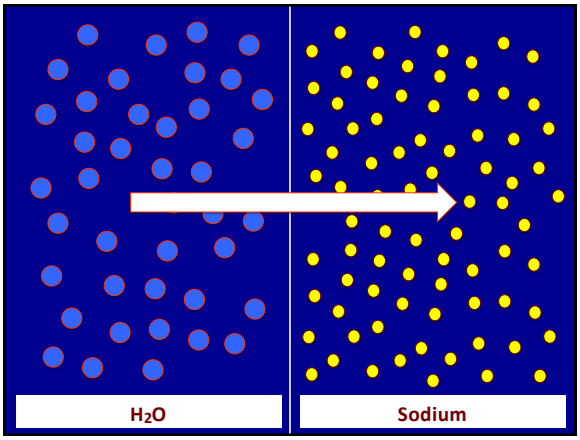

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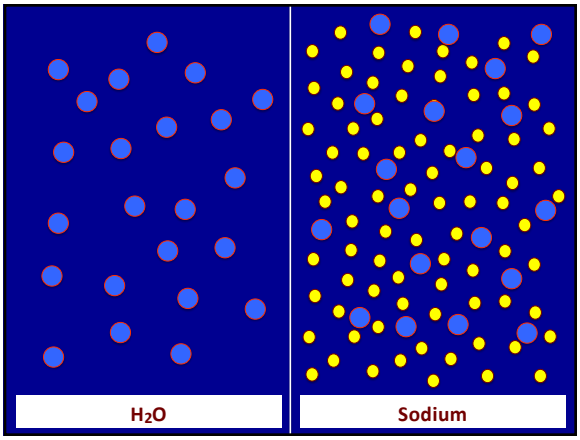

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What if I correct too fast

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Sodium case

27-year-old male presents with lightheadedness and hypotension after spending the day drinking alcohol at a local music festival.

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Sodium case

Pt states that he has not been urinating despite significant alcohol intake.

- REMEMBER – Alcohol blocks ADH – He should be peeing like crazy!!!
- ADH Should cause people to retain fluids – preventing urination and therefore decreases plasma osmolality (increased plasma volume).

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Sodium case

Summary of findings thus far:

Causation	Physiology	Outcome
Ingested ETOH	Blocks ADH	Water loss
Decreased H2O	Vasodilated	Hypotension
Decreased urine output	ADH should cause water retention – or dehydration	Retain water
Hot temperature	Sweating	Water loss

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Sodium case

Pt taken to the ED and iSTAT demonstrates the following:

- Na+ is 118mEq/L (normal is 135-145)
- BUN and Creatinine indicate some dehydration

What's the problem here?

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Sodium case

- Na+ is 118mEq/L (normal is 135-145)
- BUN and Creatinine are slightly elevated (disproportionate to the Na+)

The sodium indicates the pt's plasma should be concentrated (hyperosmolar) but the minimalistic changes to the BUN/Creatinine indicate that the plasma volume is not reduced enough to give a Na+ of 118. In other words, he is NOT that dehydrated.

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Sodium case

15 minutes after arrival in the ED, the iSTAT was repeated:

- Na+ is 146mEq/L (normal is 135-145)
- BUN and Creatinine are unchanged, and no new fluids have been given

Who can explain this?

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Sodium case

- Upon further questioning:
  - The pt had a history of bed wetting that could not be controlled so he was prescribed DDAVP (desmopressin).
  - DDAVP is a nasal spray that works like ADH (vasopressin)
  - Extrinsic administration supersedes the intrinsic production…

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Sodium case

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Ingested ETOH	Blocks ADH	Water loss
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Decreased urine output	ADH should cause water retention – or dehydration	Retain water
Hot temperature	Sweating ADH release to compensate -	Water loss Retain water
DDVAP	Acts like ADH	Retain water

NET RESULT SHOULD BE WATER RETENTION WHICH MEANS HIS SODIUM SHOULD HAVE BEEN DILUTE (LOW)

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Sodium case

The Pt decided that he didn't want to use the porta-potties and as a result, took his DDAVP throughout the day. He continued to drink in the hot environment. As his body temp increased, he vasodilated. Because the DDAVP potentiated his ADH, his cells were dehydrated but his blood volume remained sufficient… His Na+ level was artificially low and once the DDAVP wore off, the pt stopped reabsorbing his sodium.

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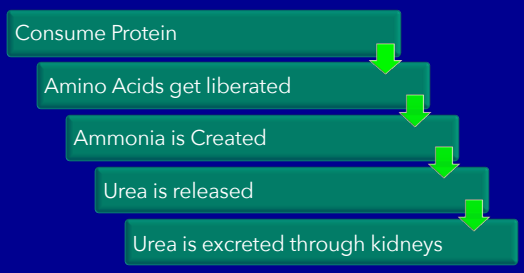
BUN (Blood **Urea** Nitrogen)



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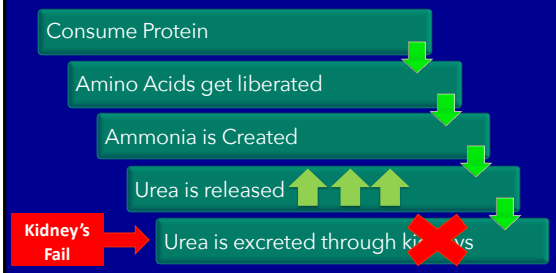
BUN (Blood **Urea** Nitrogen)



BUN goes up

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Acid Base Balance

Buffering Component - Instant

$H^+ + HCO_3 \longleftrightarrow H_2CO_3 \longleftrightarrow H_2O + CO_2$

Respiratory Component – Quick; minutes.

↑ Respirations = ↓ CO_2 ↓ H^+ ↑ pH

↓ Respirations = ↑ CO_2 ↑ H^+ ↓ pH

Renal (metabolic) component

– slow; days.

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Anion Gap Acidosis

- **CAT MUDPILES**
  - **C**O, cyanide, CHF
  - **A**minoglycosides
  - **T**heophyline/Toluene
  - **M**ethanol
  - **U**remia
  - **D**KA (any ketoacidosis)
  - **P**aracetamol/Acetaminophen
  - **I**ron/INH/Inborn errors of Metabolism
  - **L**actic acidosis
  - **E**thanol/Ethylene Glycol
  - **S**alicylates

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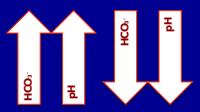
Acid-Base

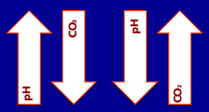
- **Algorithm**
  1. Calculate AG
  2. If AG is present, calculate the delta AG with corrected HCO3-
  3. pH/PCO2

AG = 12
pH = 7.4
HCO_3^- = 24

Metabolic etiology



Respiratory etiology



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Case 1

Anion gap acidosis

pH	7.2
HCO_3^-	18
PCO_2	24
Na^+	140
Cl^-	77

1. AG: 140- (18+104) = 18
2. △ AG: 18-12 = 6
3. Corrected HCO_3^-: 18+6 = 24
4. pH = 7.23 (low) = Acidosis
5. pCO_2: 24 (low) = not resp

Normal

- **Algorithm**
  1. Calculate AG
  2. If AG is present, calculate the delta AG with corrected HCO3-
  3. pH/PCO2

AG = 12
pH = 7.4
HCO3- = 24

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Case 2

Anion gap acidosis

pH	7.23
HCO_3^-	9
PCO_2	22
Na^+	140
Cl^-	77

1. AG: 140- (9+77) = 54
2. △ AG: 54-12 = 42
3. Corrected HCO_3^-: 9+42 = 51
4. pH = 7.23 (low) = Acidosis
5. pCO_2: 22 (low) = not resp

Metabolic Alkalosis

Corrected HCO3- is much higher than the normal HCO3- of 24 = High HCO3- means a metabolic alkalosis was present before the AG acidosis suggesting a mixed imbalance

89 female with HX N/V/D x 3 days

AG = 12
pH = 7.4
HCO3- = 24

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Case 3

Anion gap acidosis

pH	7.12
HCO_3^-	4
PCO_2	13
Na^+	140
Cl^-	115

1. AG: 140- (4+115) = 21
2. △ AG: 21-12 = 9
3. Corrected HCO_3^-: 9+4 = 13
4. pH = 7.12 (low) = Acidosis
5. pCO_2: 13 (low) = not resp

Non-gap acidosis

- **Algorithm**
  1. Calculate AG
  2. If AG is present, calculate the delta AG with corrected HCO3-
  3. pH/PCO2

AG = 12
pH = 7.4
HCO3- = 24

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THANK YOU!!

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