Breaking the Seal…

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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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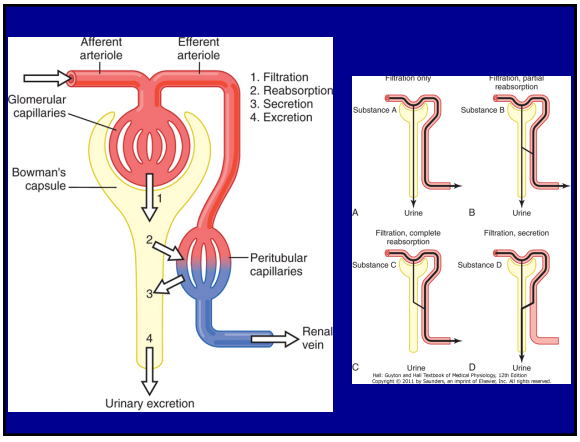

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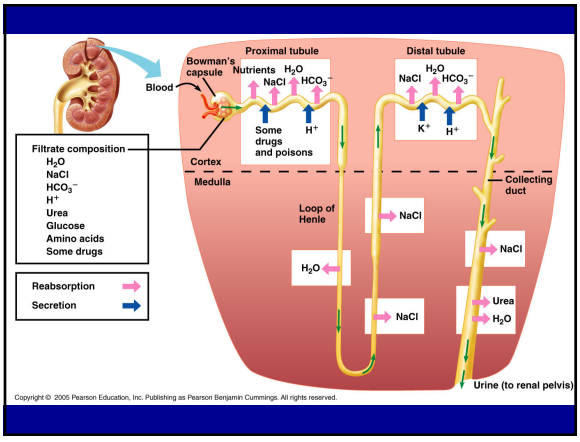

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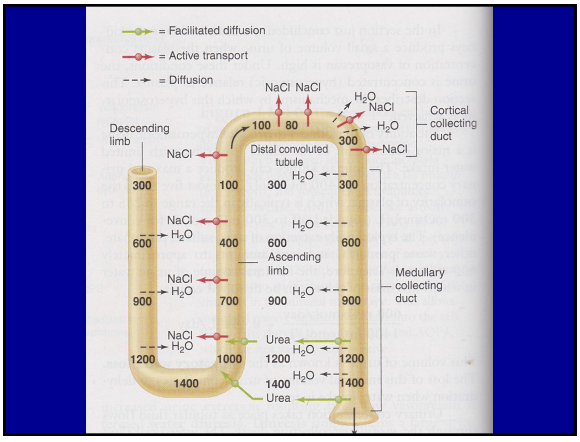

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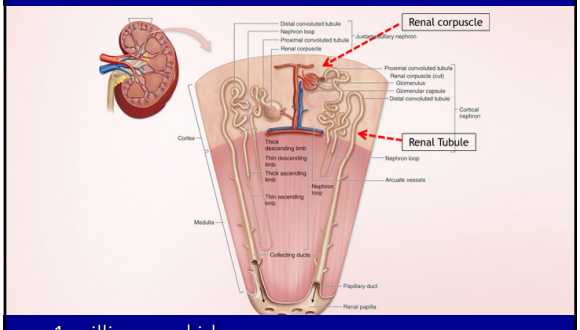
Nephrons



~1 million per kidney

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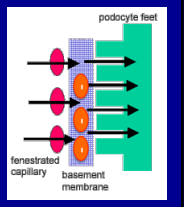
Glomerular Filtration

- 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[a] (mL/min per 1.73 m²)
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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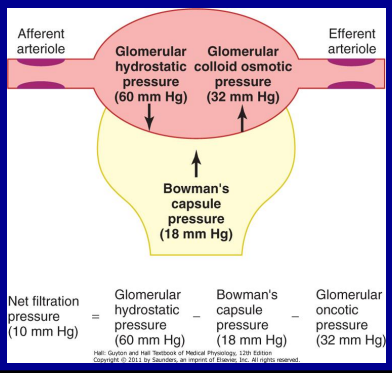
Glomerular Filtration



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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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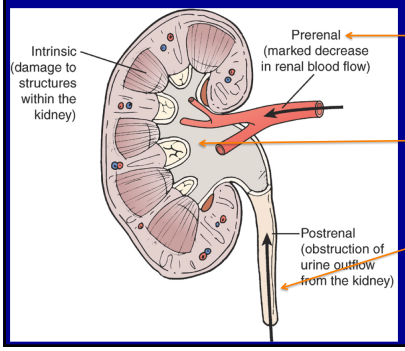
BUN:Creatinine ratio

(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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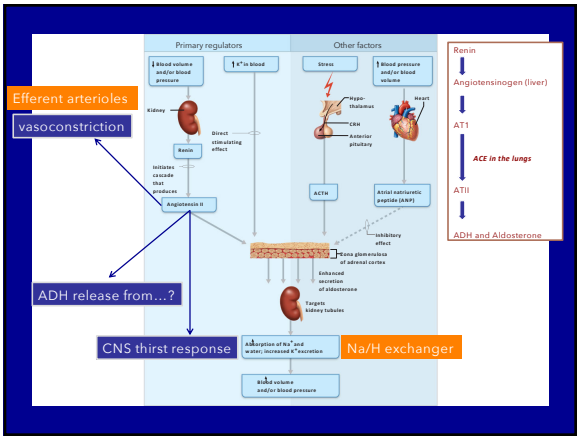

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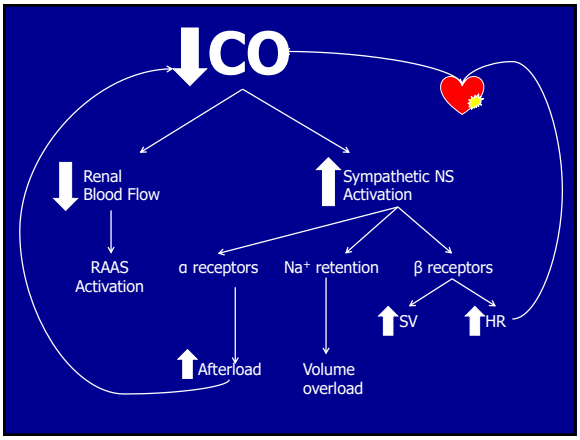

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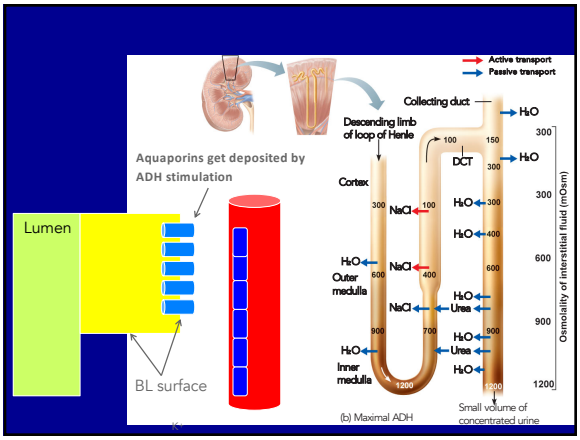

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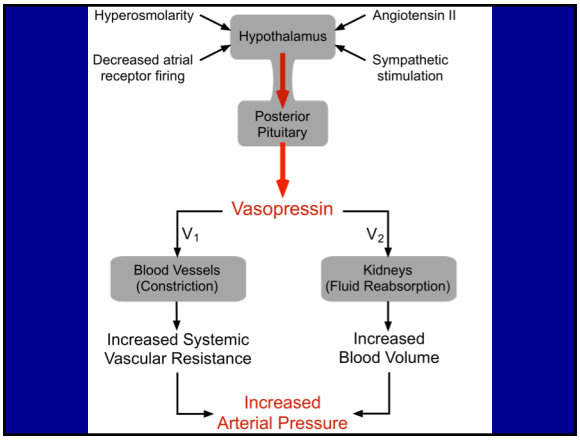

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Major causes of Kidney Failure

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

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Prerenal Disease

- Reduced renal perfusion due to volume depletion and/or decreased perfusion
- Caused by:
  - Dehydration
  - Volume loss (bleeding)
  - Heart failure
  - Shock
  - Liver disease

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Vascular Disease

- Acute
  - Vasculitis – Wegener's granulomatosis
  - Thromboembolic disease
  - TTP/HUS
  - Malignant hypertension
  - Scleroderma renal crisis
- Chronic
  - Benign hypertensive nephrosclerosis
    - Intimal thickening and luminal narrowing of the large and small renal arteries and the glomerular arterioles usually due to hypertension.
    - Most common in African Americans
    - Treatment:
      - Hypertension control
  - Bilateral renal artery stenosis
    - should be suspected in patients with acute, severe, or refractory hypertension who also have otherwise unexplained renal insufficiency
    - Treatment:
      - Medical therapy, surgery, stents.

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Glomerular Disease

- Nephritis
  - Inflammation seen on histologic exam
  - Active sediment: Red cells, white cells, granular casts, red cell casts
  - Variable degree of proteinuria (< 3g/day)
- Nephrotic
  - No inflammation
  - Bland sediment: No cells, fatty casts
  - Nephrotic range proteinuria (>3.5 g/day)
  - Nephrotic syndrome = proteinuria + hyperlipidemia + edema

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AKI: Medication Induced

- Diuretics
- NSAIDS
- Contrast media
- ACE inhibitors
- Antibiotics
  - Vancomycin, Gentamicin, Quinolones, Nitrofurantoin, Cephalosporins

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Chronic Renal Failure

- Is a gradual & irreversible deterioration
- Usually not diagnosed until 75% of function is lost
- Causes
  - Diabetes mellitus 43%
  - Hypertension 26%
  - Inflammatory, immunological, or hereditary diseases
  - May follow acute failure

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Consequences

- Nephrons enlarge to compensate
- Overburdened nephrons degenerate
- End-stage renal disease occurs

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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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Steroids

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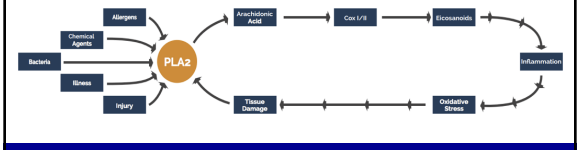

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Steroids

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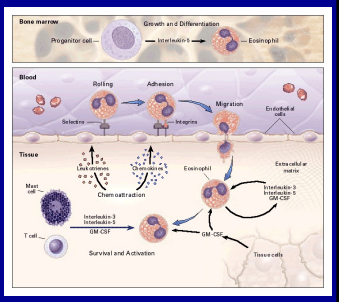

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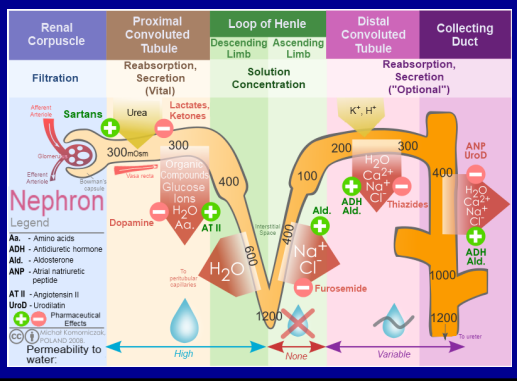
Renal drugs



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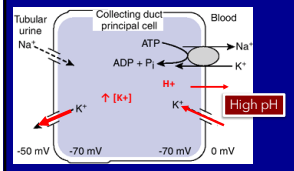
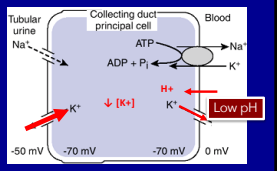
EFFECTS OF ACID-BASE DISTURBANCES on K+

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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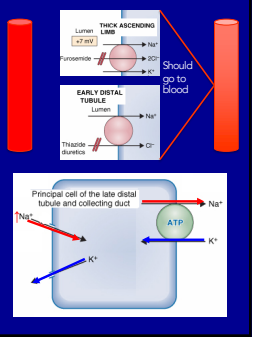
Effects of loop & thiazide diuretics on K+

- 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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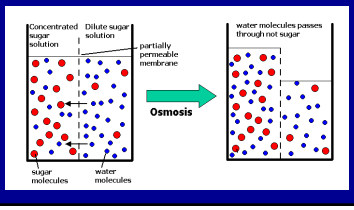
Renal Pharmacology

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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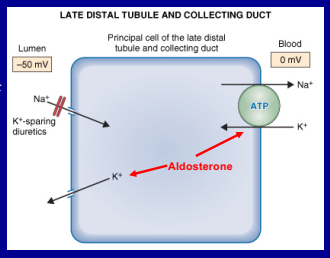
EFFECTS OF K-SPARING DIURETICS ON K+ EXCRETION

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



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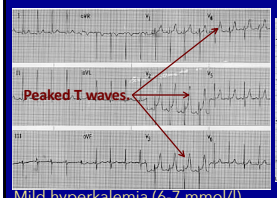
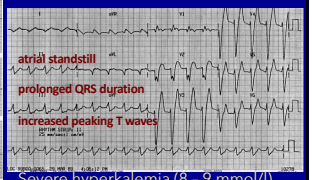
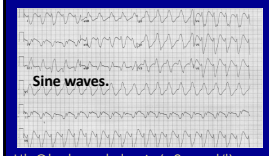
Hyper K -Cardiac Arrhythmia's – ECG changes



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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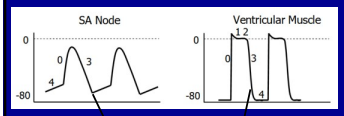
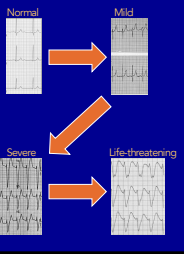
Hyper K- Cardiac Arrhythmia's

- Ventricular dysrhythmias
- Asystole

K+ is the problem…

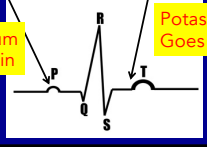
High levels of K^+ will cause the heart to become more positive and closer to threshold and ultimately prolong repolarization leading to a long QT





Calcium Goes in

Potassium Goes out



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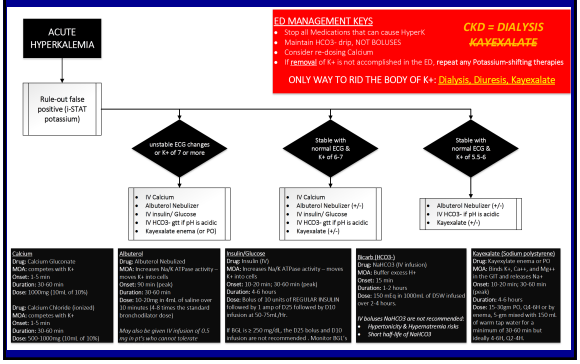
ACUTE management



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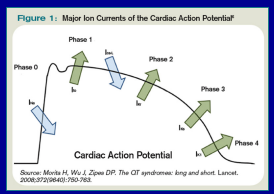
ACUTE management

- 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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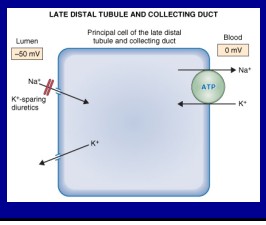
ACUTE management

- 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 attempt 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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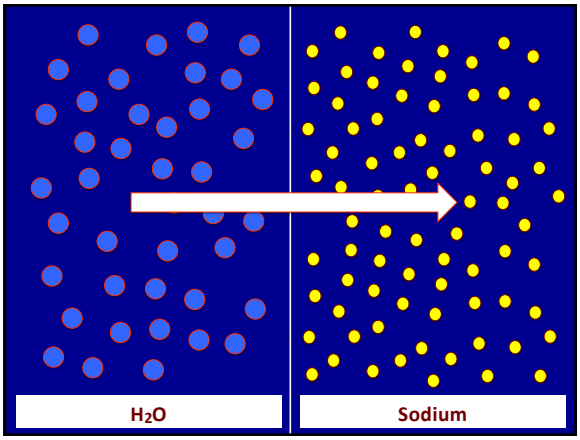

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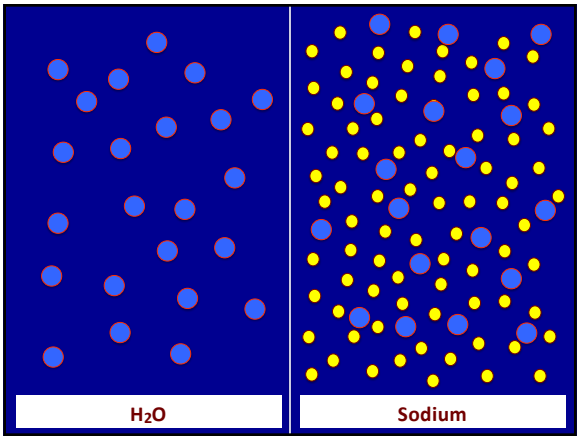

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What if I correct too fast

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BUN (Blood Urea Nitrogen)

- Consume Protein
- Amino Acids get liberated
- Ammonia is Created
- Urea is released
- Urea is excreted through kidneys

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BUN (Blood Urea Nitrogen)

- Consume Protein
- Amino Acids get liberated
- Ammonia is Created
- Urea is released
- Urea is excreted through kidneys

Kidney's Fail

BUN goes up

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Cardiac Physiology

α_1	↑TPR = ↑ preload	↑ Venous Return = ↑ afterload
β_1	↑ HR, conduction	↑ contraction, automaticity
α_2	↓ NE Synthesis	↓ NE release
β_2	↓ TPR = ↓ preload	↓ Venous Return = ↓ afterload

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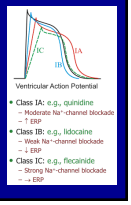
Cardiac Pharmacology

Class I – Na^+ Channel Blockers

- Class 1A
  - Procainamide, Disopyrimide, Quinidine
- Class 1B
  - Mexiletene, Lidocaine, Tocainide, Phenytoin
- Class 1C
  - Encainide, Flecainide, Propafenone



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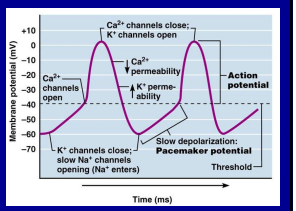
Cardiac Pharmacology

Class II – Beta Blockers

- **Cardioselective:**
  - Diltiazem (Cardizem)
  - Verapamil
- **Vasoselective**
  - "Pines"
  - Nicardipine
  - Nimodipine



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Cardiac Pharmacology

Class III – Potassium Channel Blockers

- **Amiodarone**
  - Contains elements of all class
  - Class I, II, III, IV
- **Sotalol**
  - Contains Class II and III

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Cardiac Pharmacology

Class IV – Calcium Channel Blockers

- **Cardioselective:**
  - Diltiazem (Cardizem)
  - Verapamil
- **Vasoselective**
  - "Pines"
  - Nicardipine
  - Nimodipine

- Decreases Action Potentials in the atria and thalamus
- Increases PR Interval
- Decreases smooth muscle tone

Absence seizures?
Where do they originate

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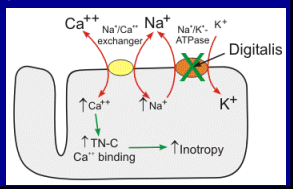
Cardiac Pharmacology

Other Anti- Arrhythmics

- **Digoxin**
  - Inhibits Na/K ATPase
    - **Indirectly Inhibits Na^+/Ca^{2+} Exchange**
  - **Clinical Use:**
    - CHF
    - Atrial Fibrillation



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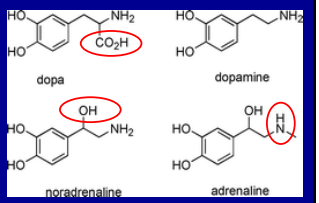
Cardiac Pharmacology

Vasopressors

Phenylalamine
↓
Tyrosine
↓
L-Dopa
↓
Dopamine
↓
Norepinephrine
↓
Epinephrine



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Cardiac Pharmacology

Vasopressors

- **Norepinephrine**
  - Septic Shock
  - Distributive shock after volume replacement
- **Dobutamine**
  - Cardiogenic shock
- **Dopamine**
  - Refractory Sepsis or cardiogenic shock
- **Epinephrine**
  - Refractory Shock or cardiogenic shock

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Cardiac Pharmacology

Vasopressors

- Norepinephrine
  - α_1 ++++
  - B_1 +++

α_1	↑TPR = ↑ preload	↑ Venous Return = ↑ afterload
β_1	↑ HR, conduction	↑ contraction, automaticity
α_2	↓ NE Synthesis	↓ NE release
β_2	↓ TPR = ↓ preload	↓ Venous Return = ↓ afterload

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Cardiac Pharmacology

Vasopressors

- Dobutamine
  - β_1 +++
  - β_2 +

Lower HR effect then Dopamine

α_1	↑TPR = ↑ preload	↑ Venous Return = ↑ afterload
β_1	↑ HR, conduction	↑ contraction, automaticity
α_2	↓ NE Synthesis	↓ NE release
β_2	↓ TPR = ↓ preload	↓ Venous Return = ↓ afterload

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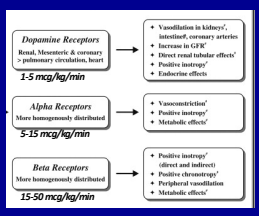
Cardiac Pharmacology

Vasopressors

- Dopamine
  - α_1 ++ (10-20 µ/Kg/Min)
  - β_1 +++ (5-10 µ/Kg/Min)
  - β_2 +
  - DA ++ (0.5-5 µ/Kg/Min)



α_1	↑TPR = ↑ preload	↑ Venous Return = ↑ afterload
β_1	↑ HR, conduction	↑ contraction, automaticity
α_2	↓ NE Synthesis	↓ NE release
β_2	↓ TPR = ↓ preload	↓ Venous Return = ↓ afterload

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Cardiac Pharmacology

Vasopressors

- Epinephrine
  - α_1 ++
  - β_1 +++
  - β_2 +

Inject the full 1 mg into a 1,000 mL normal saline bag (final concentration 1 mcg/mL).

Push-dose or dirty gtt is a great interim strategy

α_1	↑TPR = ↑ preload	↑ Venous Return = ↑ afterload
β_1	↑ HR, conduction	↑ contraction, automaticity
α_2	↓ NE Synthesis	↓ NE release
β_2	↓ TPR = ↓ preload	↓ Venous Return = ↓ afterload

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THANK YOU!!

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