Fluids, Electrolytes, Management

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Introduction

- Multiple physical principles
- Non-intuitive concepts
- Clear definition of issues is key
- No single assay, no foolproof tests
- Need to utilize a combination of history, clinical exam, lab tests, monitoring, algorithms
- In practice these are “fluid” issues

Objectives

-Definitions in the discussion of fluids
-Distinguishing between water and volume
-Clinical determination of volume status
-Body fluid compartments in normal physiology
-Components and differences between fluid compartments
-Routine IV fluids

-Sodium and water pathophysiology
    -Hypernatremia
    -Hyponatremia
-Potassium Balance
    -Hyperkalemia
    -Hypokalemia

Definitions

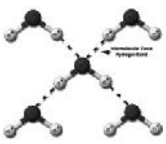
- **flu·id** (flo͞o) *n.* A continuous, amorphous substance whose molecules move freely past one another and that has the tendency to assume the shape of its container; a liquid or gas.
- **volume** (vŏl'yoom, -yəm) ***n.*** The amount of space occupied by a three-dimensional object or region of space, expressed in cubic units.

Definitions (2)

- **Dehydration** = free water deficit, may lead to hypernatremia
- **Hypovolemia = volume depletion =**extracellular fluid volume (ECFV) depletion
- **Hypervolemia** = volume excess =ECFV increase over baseline

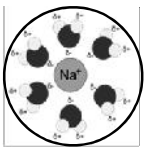
Water vs. Volume… a dip into the waters of physical chemistry

Water



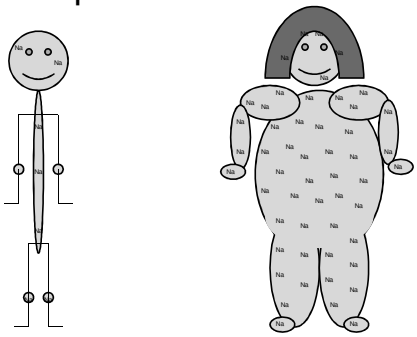
Water Lattice Structure
- -weak intermolecular bonds
- -easily broken, reformed
- -small enough to pass through membranes

Volume



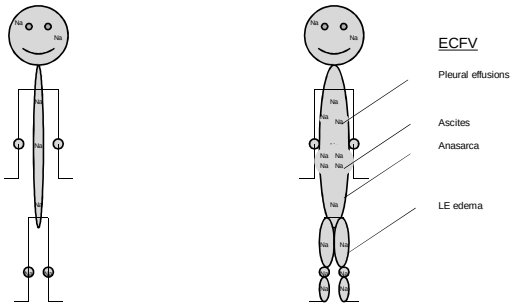
Sodium Ion Hydration Shell
- -Na^+ does not move without the shell
- -water molecules in relatively locked structure
- -fundamentally alters character of fluid
- -does not pass through membranes

Jack Spratt and his wife



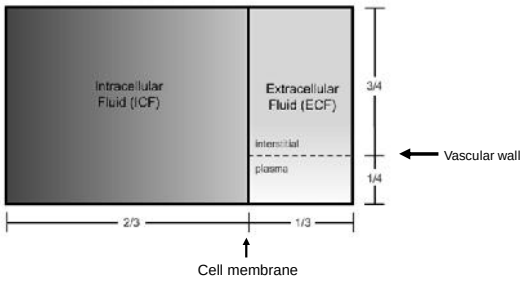
Who has more volume?
Who is hypervolemic?

Jack Spratt and his CHF



Where does he have more volume?
Where does he have more total Na?

Fluid Compartments



Clinical Signs of ECFV Status

-ECFV overload = hypervolemia = too much Na in extracellular space: LE edema, sacral edema, ascites, pulmonary edema, pleural effusions

-ECFV depletion = hypovolemia = too little sodium in extracellular space: poor skin turgor, tachycardia, orthostatic blood pressure, (history is major clue: n/v/d, trauma, diaphoresis, etc.)

-balancing these two extremes to maintain homeostasis = euvolemia and is determined by renal sodium regulation = intake vs. excretion

Percent Volume Depletion Clinical Symptom

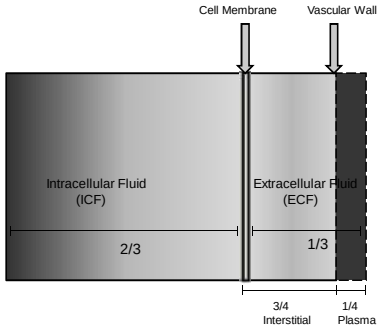
<5%	• Rapid heart rate • Dry mucous membranes	• Concentration of urine • Poor tear production*
5-8%	• Increased severity • Decreased skin turgor	• Sunken eyes • Oliguria
>9%	• Pronounced severity of above signs • Supine Hypotension	• Delayed capillary refill • Acidosis (large base deficit)

Question: how many liters does 5% of 70kg indicate?

FeNa and FeUrea

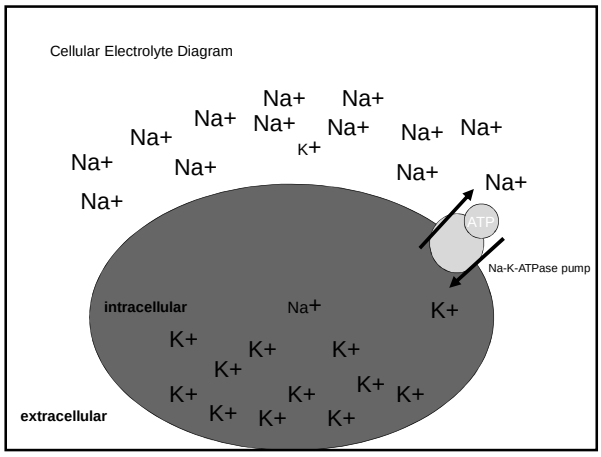
- Fractional Excretion of Sodium (FENa) = $(P_{Cr} * U_{Na}) / (P_{Na} \times U_{Cr})$ %
  - <1% consistent with prerenal azotemia (often hypovolemia)
  - May not give reliable result in setting of diuretics, in which case can send:
  - Fractional Excretion of Urea (FEUrea) = $(Serum_{Cr} * U_{Urea}) / (Serum_{Urea} \times U_{Cr})$ %
    - <30-35% consistent with prerenal

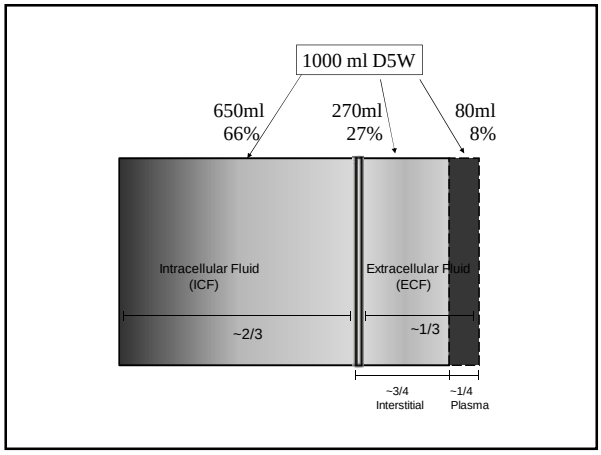
Aqueous Fluid Compartments

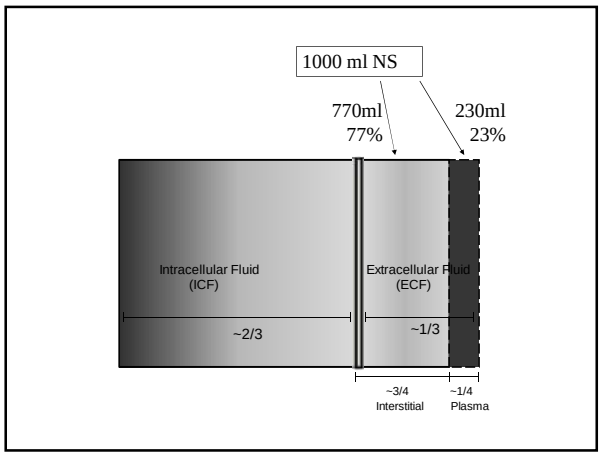


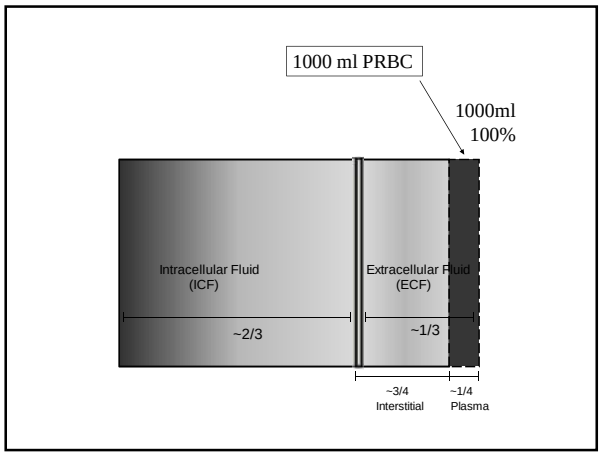
Composition of fluid compartments

	plasma	*interstitial*	*intracellular*
Cations			
Na	**140**	**146**	**12**
K	**4**	**4**	**150**
Ca	**5**	**3**	**10**
Mg	**2**	**1**	**7**
Anions			
Cl	**103**	**104**	**3**
HCO3	**24**	**27**	**10**
SO4	**1**	**1**	**-**
HPO4	**2**	**2**	**116**
Protein	**16**	**5**	**40**




1000 ml D5W
650ml
66%
270ml
27%
80ml
8%
Intracellular Fluid
(ICF)
Extracellular Fluid
(ECF)
~2/3
~1/3
~3/4
Interstitial
~1/4
Plasma


1000 ml NS
770ml
77%
230ml
23%
Intracellular Fluid
(ICF)
Extracellular Fluid
(ECF)
~2/3
~1/3
~3/4
Interstitial
~1/4
Plasma


1000 ml PRBC
1000ml
100%
Intracellular Fluid
(ICF)
Extracellular Fluid
(ECF)
~2/3
~1/3
~3/4
Interstitial
~1/4
Plasma

Fluid Bolus

- Who needs it?
  - Pt's who are under-resuscitated/hypovolemic
- How Much?
  - 10-20 ml/kg to start, then reassess
  - 500ml-1000ml, then reassess
- How Fast?
  - Healthy vs Premorbid Illness
- Which one to give?

NS *vs.* LR

Normal Saline	*Lactated Ringer's*
• 154 meq Na, Cl • Often has 20 meq KCl/L added • pH 5.7; 308 mOsm/L • $7 / L	• 130 meq Na • 109 meq Cl • 4 meq K • 3 meq Ca • 28 meq lactate • pH 6.4; 273 mOsm/L • $22 / L • Can't use with blood

Note: NEVER bolus fluid with KCl added

Maintenance IV Fluids

- Who Needs Maintenance Fluids?
  - -euvolemic patients who can't maintain fluid status otherwise
    - N/V/D, other ongoing fluid losses
    - NPO
- What's Maintenance?
  - How much volume?
  - Two options: 1. 4:2:1 rule or 2. 100:50:20 rule
    - 4ml/kg/hr or 100 ml/kg/d (for 1st 10 Kg)
    - 2ml/kg/hr or 50 ml/kg/d (for 2nd 10 Kg)
    - 1ml/kg/hr or 20 ml/kg/d (for every Kg > 20 Kg)
  - Na?
  - K?
  - Dextrose?

Maintenance IV Fluids

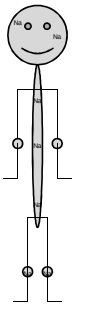
- For a 70 Kg person
  - 1000ml+ 500ml + 1000ml = 2500ml=105ml/hr. Now try 4:2:1…
  - Daily Na losses = 2-4meq/kg/d
    =140-280 meq/d ~ 200 meq/2.5L = 80meq/L
    Note: 1/2NS =77 meq/L
  - Daily K losses: 1-2mEq K/kg/d. ~70 meq/d
    ~70 meq/2.5L = 28meq/L.
    - + 20 meq KCl/L
  - Therefore typical maintenance fluids:
    D5 1/2NS + 20 meq KCL/L @ 100 cc/hr
    Why D5? – prevent catabolism, gives small amount of energy, reduces hunger.

Sodium Physiology

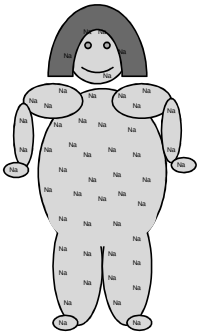
- Sodium is the major extracellular cation
  - Responsible for most of the osmotic driving force (tonicity)
  - Since sodium is main tonicity determinant, it is the main ECFV determinant
  - Therefore, total sodium content in the extracellular fluid is the major determinant of the ECFV **size**
  - This is not the sodium concentration! This is total sodium cation load.
  - Since sodium is mainly extracellular and determines ECFV, the total amount of body sodium can be assessed qualitatively by body volume i.e. euvolemia, hypervolemia, hypovolemia

Important:
-Plasma is small component of ECFV.
* Do not confuse plasma sodium concentration with total body sodium content.

Jack Spratt and his wife

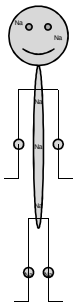


[Na]: 140

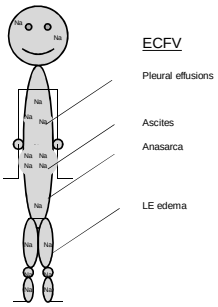


[Na]: 140

Jack Spratt and his CHF



[Na]: 140



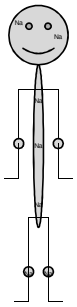
[Na]: 140

Dehydration: loss of total body water

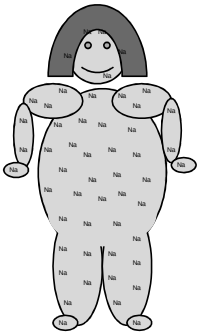
- Loss of intracellular water causing cellular desiccation.
- May cause elevated plasma sodium concentration and osmolality
- Example:
  - Elderly pt with fluid losses in heat and poor access to water

-Remember dehydration is not the same as hypovolemia, water and volume are not the same

Dehydrated Jack Spratt and his wife

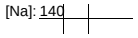


[Na]: 150



[Na]: 150

Sodium *Concentration*



⇨ Not a measure of total body sodium
Not a measure of total body volume

=The number we see on the labs

- Hyponatremia = sodium concentration <135 mEq/l
- Hypernatremia = sodium concentration > 145 mEq/l

This is an independent issue from the volume status.

SO: to change sodium *concentration* either the amount of sodium changes or the amount of water changes.

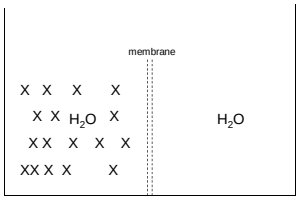
Definitions (3)

- **Osmosis**= movement of water across a membrane
- **Osmolality** = total solute concentration in a fluid compartment
- **Tonicity =** net movement of water across a membrane -due to the combined effect of all solutes in a compartment (osmolality)
- **Isotonic =** the same solute concentration as plasma
  = no net movement of water
- **Hypotonic** = lesser solute concentration than plasma
  = net movement of water into cell
- **Hypertonic** = higher solute concentration than plasma
  =net movement of water out of cell

Water Metabolism

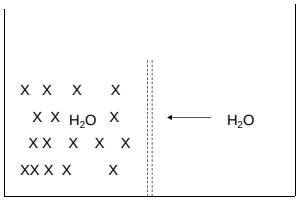
- -Water comprises 50-60% of mass
  - Women TBW (total body water) = 0.5 x body wt (kg)
  - Men TBW = 0.6 x body wt (kg)
- -Most cell membranes have free water permeability
- -Therefore, osmolality is typically the same among diffferent compartments…but the contributors to that osmolality are different in different compartments

Simple physics



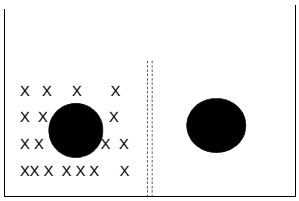
X = solute that cannot cross membrane

Osmosis:



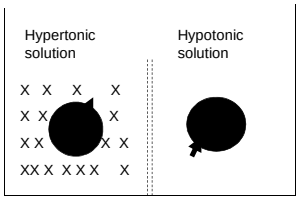
Osmosis is a special kind of diffusion; the diffusion of water molecules across a membrane, typically the membrane of a living cell.

Tonicity

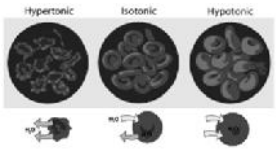


If a cell is in a surrounding environment that is:
isotonic: no net movement of water between cell and environment
hypertonic: a higher concentration of solute
hypotonic: a lower concentration of solute

Tonicity

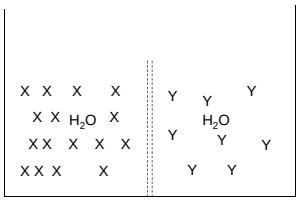


Shrinkage and Swelling



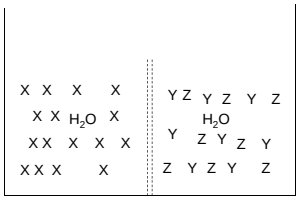
www.absoluteastronomy.com/topics/Red_blood_cell

Osmotic Balance



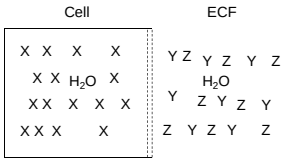
No net movement of water if osmotic potential of Y=2X

Osmotic Balance

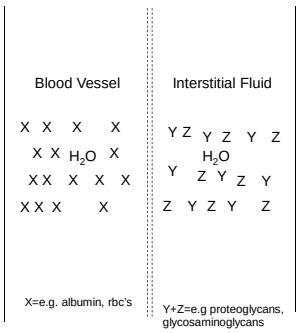


…Or if Y+Z=X

Theory Applied #1



Theory Applied #2



Osmolality

- Normal serum osmolality:
- Calculated = 2 x [Na] + [glucose]/18 + [BUN]/2.8

- Sodium greatest single contributor
- Maintained in ECF by Na-K-ATPase
- Only solutes incapable of crossing membrane can cause tonicity. Tonicity is the result of osmolar content/osmolality.
- Solutes incapable of crossing membrane- effective osmoles
- Glucose *typically* does not factor strongly into tonicity, due to being taken in by cells. Generally not effective osmoles
- Urea can cross membranes and distributes freely in TBW – also *typically* not an effective osmole.
- Iatrogenic effective osmoles: mannitol, sorbitol

Osmolal Gap

- Osm gap = measured Osm – Calc Osm
- Serum Osmolality (US) = (2 * (Na) + (BUN / 2.8) + (glucose / 18) + (ethanol/4.6)
- Gap >10 is abnormal
- Abnormal gap indicates presence of other osmolal acting substances
- Since glucose, BUN, Na are calculated do not contribute to gap
- Methanol, ethylene glycol will contribute

Tonicity

- Determined by ECF sodium concentration
- Necessary to keep cellular hydration and size constant – critical for cellular function
- Very carefully regulated by body – a few mOsm/l increase will lead to mechanisms to increase water balance: thirst, ADH
- Conversely, decreased tonicity will lead to kidney excretion of dilute urine

The Nephron! Dang, do I really have to see that again?!!

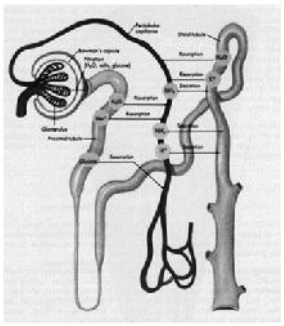
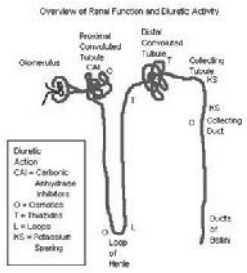


Figure 4. Diagram showing the steps in urine formation in successive parts of a nephron: filtration, reabsorption, and secretion (dissection view for illustrative purposes). In this figure, the term "resorption" is equivalent to "reabsorption" used here.
Stolen from: home.bway.net/rjnoonan/humans_in_space/fluid.html

Another nephron?! What the??



Stolen from: faculty.swosu.edu/scott.long/phcl/diuretic.htm

Requirements for Water Excretion

- 1. Adequate glomerular filtration rate
- 2. Adequate delivery of filtrate to distal tubule
- 3. Intact concentrating/diluting mechanisms
- 4. ADH regulation and responsiveness

Hyponatremia and Hypernatremia disorders depend on the existence of abnormalities in the above mechanisms.

1. GFR

- -Critical in delivering fluid and electrolytes to the kidney
- -Neither possible to dilute urine (excrete water) nor to concentrate electrolytes by reabsorption if filtration is impaired.
- -At 20% normal function kidney loses ability to concentrate or dilute urine effectively

2.. Delivery to Distal Nephron

- -Absorption of all glomerular filtrate proximal to distal nephron prevents concentration and dilution
- -Without water excretion, hyponatremia may result
- -e.g. in severe volume depletion from vomiting or diarrhea
- -e.g. in edema seen in CHF, cirrhosis, nephrotic syndrome (impaired GFR impairs distal delivery of fluid)

3. Renal Concentration

- -Ascending limb of loop of Henle
  - Reabsorbs 20-30% of filtered sodium
  - Generates medullary concentration gradient
  - Water follows concentration gradient
  - ADH allows water reabsorption in collecting tubule
  - Loop diuretics block sodium reabsorption, reduce medullary concentration gradient. (As a result relatively neutral Na and volume loss.)

4. Renal Dilution

- -Sodium-Chloride cotransporter
  - Removes Na and Cl from lumen into interstitium –dilute urine results
  - Blocked by thiazide diuretics
    - Often leads to more Na loss than water loss
- -ADH (anti-diuretic hormone = reduces diuresis)
  - Most important factor in dilute vs. concentrated urine
  - Allows regulation to generate urine 50-1200mOsm/l range
  - Allows water to flow down concentration gradient into medullary interstitium
    - Leads to water gain not Na gain

Osmoregulation vs. Volume Regulation

	Osmoregulation	Volume Regulation
What is sensed?	Plasma osmolality	Effective circulating volume
How assessed?	Plasma $[Na^+]$, P_{osm}	History, physical exam, urine $[Na^+]$
Sensors	Hypothalamic osmoreceptors	Carotid sinus Atria Afferent arteriole (JGA)
Effectors	ADH Thirst mechanism	Sympathetic nervous system Renin-angiotensin-aldo system Natriuretic peptides ADH
What is affected?	Water excretion (via ADH), Water intake (thirst)	Sodium excretion

Hypernatremia

- Hypernatremia usually indicates that rates of water loss have exceeded rates of water intake
  ($H_2O_{OUT} > H_2O_{IN}$)
- Increase in plasma osmolality should stimulate ADH secretion and thirst with decreased water excretion and increased water intake => THUS persistent hypernatremia does not occur in normal subjects
  - Must have defect in thirst mechanism (e.g., hypothalamic lesion), OR
  - Limited access to free water (e.g., infants or adults with impaired mental status) OR
  - Excessive sodium gain without compensatory free water

Consequences of Hypertonicity: Cellular Dehydration

- ECF hypertonicity causes water to shift from the ICF to the ECF resulting in cellular dehydration (ICF contraction).
- Brain cells respond to cellular dehydration by generating organic osmolytes ("idiogenic osmoles") to raise intracellular osmolality, reshift water intracellularly and re-establish normal cell volume.
- These idiogenic osmoles serve a protective role, but removal of them is slow when isotonicity is re-established => rapid correction of hypertonicity can cause cerebral edema.

Symptoms of Hypertonicity: Neurologic

Adults: (P_{Na} > 170 mEq/L)
- Lethargy, weakness, twitching, confusion, mental obtundation, seizures and coma
- Less common with chronic hypernatremia

Infants: severe neurological sequelae
- Cellular dehydration → rupture of cerebral veins resulting in focal intracerebral & subarachnoid hemorrhages

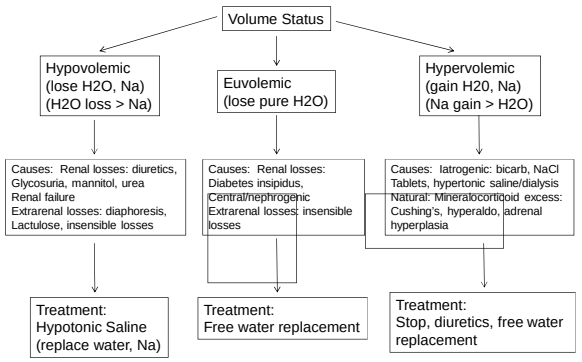
Pathogenesis of Hypernatremia

Normal-Volume Hypernatremia
- Conditions associated with a loss of "electrolyte free" fluids (loss of pure water)

Low-Volume Hypernatremia
- Conditions associated with the loss of hypotonic fluids (fluids containing more water than sodium)

High-Volume Hypernatremia
- Conditions associated with ingestion or administration of sodium containing hypertonic solutions

Hypernatremia



Normal-Volume Hypernatremia
Pure Water Loss: Pathogenesis

- Renal Loss*
  - Central diabetes insipidus
  - Nephrogenic diabetes insipidus
- Insensible Losses (skin or lungs)*
  - Fever
  - Hot Room
  - Hyperventilation

** In association with deficit in water intake*

Normal-Volume Hypernatremia
Treatment (pure water loss)

- Replace water deficits with p.o. water or i.v. electrolyte-free fluids
- Replace only half of water deficit in first 24-48°
- Free water deficit is estimated by taking into account patient's estimated total body water and the plasma Na^+
- FWD= (pt's Na – 140) /140* weight * 0.6

Central Diabetes Insipidus - Causes

- Idiopathic (?autoimmune)
- Neurosurgery or trauma
- Primary or secondary CNS tumors
- Infiltrative disorders (e.g., CNS sarcoidosis)
- Others (e.g., hypoxic encephalopathy, bleeding, infection)

Nephrogenic Diabetes Insipidus - Causes

- Chronic lithium treatment
- Hypercalcemia
- Hereditary nephrogenic DI (children)
  - X-linked: defects in V_2 receptor gene
  - Autosomal recessive: defects in AQP-2 water channel
- Persistent severe hypokalemia
- Other (e.g., sickle cell Dz, amyloidosis, Sjogren's)

Distinguishing CDI from NDI

- History, chronicity (central often more acute)
- Administration of dDAVP 10 mcg intranasally or vasopressin 5 units SQ

Chronic Treatment

- CDI: dDAVP, correct underlying disorder if possible
- NDI: thiazides, dietary solute (salt, protein) restriction, NSAIDs, amiloride (lithium-induced NDI), correct underlying disorder if possible

High-Volume Hypernatremia - Pure Solute Addition

- Causes: exogenous solute administration
  - $NaHCO_3$ administration (1786 mOsm/Kg H_2O)
  - Hypertonic NaCl
  - Salt poisoning, salt tablets
  - Sea water ingestion

High-Volume Hypernatremia - Treatment

- Diuretics
  - remove Na^+ and water
- Replacement of water losses from diuretic
- Dialysis if concurrent renal failure

Low-Volume Hypernatremia - Loss of Hypotonic Fluid

- Most common fluid loss causing hypernatremia:
  - loss of both osmotic solutes and water in hypotonic proportion (H_2O > Na)
  - =>both ECF volume depletion and free water deficit

Loss of Hypotonic Fluid: Two Major Causes

- Renal Losses
  - Osmotic diuresis
    - urea 2° to tube feedings, post-obstructive diuresis
    - glucosuria
  - Diuretics
- GI Losses
  - Diarrhea, vomiting, sweating etc.

Low-Volume Hypernatremia - Treatment

- Always resuscitate first
- If hypotensive especially: bolus.
- Then give free H_2O (D5W or p.o. water to correct hypernatremia - only after plasma (and ECF) volume is re-expanded

Case Presentation

- A 78 year old diabetic female nursing home resident is admitted for decreased mental status following a febrile upper respiratory tract infection treated with p.o. antibiotics. Her caregiver had been withholding insulin because she had stopped eating.
- Physical Exam: Obtunded, wt. 50 kg. (previous normal wt. 60 kg.), BP 85/45 supine, T 38.5°C, P 125; poor skin turgor, dry mucous membranes, foul-smelling urine
- Lab Values: Plasma: Na^+ 170, K^+ 3.9, Cl^- 134, total CO_2 23, BUN 45, Cr 1.6, glucose 1000

Diagnoses

- Hyperosmolar Hyperglycemic Non-Ketosis (diabetes +/- infection)
- Effective Circulating Blood Volume Depletion (loss of total-body Na^+ from glucose-induced osmotic diuresis, poor po, insensible losses)
- Hypernatremia/Dehydration (hypotonic fluid losses from osmotic diuresis + pure water losses from fever/insensible losses w/ no free water intake, and probable UTI)

Management

- Volume resuscitation with isotonic fluids ~ bolus.
- Correction of hyperglycemia – some insulin; monitor K^+ and Phos, Mg
- Calculate free water deficit using corrected P_{Na} (= 170 + ((1000-100)/100) x 1.6 = 184)
- Correction of free water deficit - SLOWLY => avoid cerebral edema caused by adaptive intracellular accumulation of osmolytes (e.g., myo-inositol)
- Free water deficit = 0.6(wt.)(Pt[Na]-Nrl[Na])/Nrl[Na]

Summary: Therapy

- If free water deficit, correct with H_2O slowly over days
- If pure solute gain, use diuretics (in combination with free H_2O slowly)
- If evidence for hypotonic losses (water > Na^+ loss): give isotonic saline or colloid expanders until BP is stable and pt. is euvolemic, then correct free H_2O deficit slowly over several days

Hyponatremia: Clinical Manifestations

- Depend on magnitude of the hyponatremia and rapidity of its development.
  - Acute (< 48 hrs): Symptoms at $[Na^+]$ of ≤ 125 mEq/L. Seizures and coma at ≤ 115 mEq/L.
  - Chronic**:** often asymptomatic until $[Na^+]$ drops to ≤ 115 mEq/L; adaptation through loss of intracellular solutes (osmolytes)
- Symptoms - mainly CNS
  - Early: nausea, malaise, headache, muscle twitching, lethargy
  - Late/Severe: obtundation, seizures, coma, respiratory arrest

Hyponatremia

- **Hypertonic** - hyperglycemia or mannitol therapy => osmotic shift of water from ICF to ECF, diluting ECF $[Na^+]$; $[Na^+]$ decreases ~1.6 mEq/L for every 100 mg/dL [glucose] is above its normal value (100 mg/dL).
- **Isotonic** - lab artifact w/ marked elevation of plasma lipids or protein - no longer encountered in most clinical labs due to use of ion-specific electrodes. aka Pseudohyponatremia
  -No treatment necessary.
- **Hypotonic** - most common and important clinically; from this point on, we will consider only hypotonic hyponatremia

Hypotonic Hyponatremia

At its core: Water intake > Water excretion

– Normally, osmolality is maintained constant at ~285 mOsm by matching water excretion and intake. If water intake exceeds water excretion, then hypotonicity ensues.

– Renal water excretory capacity is normally very large (up to 20 L/day) => enormous amounts of water intake are required to cause hypotonic hyponatremia under normal conditions.

– …unless renal water handling is impaired, then only modest amounts of water intake can cause hypotonicity

–Finding out why the kidney cannot clear water is the key to diagnosing the cause of hyponatremia

Causes of Impaired Water Excretion

- -Renal Failure (Impaired GFR)
- -ECFV depletion (vomiting with water drinking)
- -Edema states: CHF, cirrhosis, nephrotic syndrome
  - Kidney abnormally absorbing Na and water
- -Thiazide diuretics – excrete more sodium than volume and decrease ECFV.
- -SIADH: malignancy, lung disease, pneumonia
- -Endocrine abnormalities: Hypothyroidism, adrenal insufficiency
- -Decreased solute intake compared to fluid intake
  - "Tea and toast" diet
  - Beer potomania
  - Psychogenic polydipsia

as a resultt…

HYPOTONIC HYPONATREMIA

has

3 subtypes

-Hypovolemic
-Euvolemic
-Hypervolemic

Step 1: what is patient's volume status?

Approach to Diagnosis: Hypovolemic (Low-Volume) Hyponatremia

- **Physiology**
  - Caused by impaired free-water excretion
    - $\Downarrow$ ECFV $\Rightarrow$ limited distal delivery of fluid
    - high ADH
      - Low ECFV and low BP stimulates ADH release via volume receptors (left atrium and aortic arch) and baroreceptors (carotid sinus) $\Rightarrow$ hold on to free water, dilute Na.

Approach to Diagnosis: Low-Volume Hyponatremia

aka Hypovolemic Hyponatremia

- Probably most commonly seen clinically

- Clinical**:** Orthostasis, low JVP, etc. Patient's history
- Laboratory**:** low urine Na^+ (extrarenal causes)
- Etiology**:** Low ECF volume along with low effective circulating blood volume and enhanced water intake
  - Extrarenal: Na^+ loss through GI tract, skin, 3rd spacing (e.g., vomiting, diarrhea, profuse sweating, post-op)
  - Renal: Na^+ loss via kidneys (e.g., diuretics, renal failure)

Composition of Body Fluids (mEq/L)

Source	Daily loss	Na+	K+	Cl-	HCO3-
Saliva	1000	30-80	20	70	30
Gastric	1000-2000	60-80	15	100	0
Panc	1000	140	5-10	60-90	40-100
Bile	1000	140	5-10	100	40
SB	2000-5000	140	20	100	25-50
LB	200-1500	75	30	30	0
Sweat	200-1000	20-70	5-10	40-60	0

Approach to Diagnosis: High-Volume Hyponatremia

aka Hypervolemic Hyponatremia

- Clinical**:** Edema, JVD $\pm$ pulm. edema
- Laboratory**:** Low urine Na^+
- Etiology**:** High ECF volume, with enhanced thirst and water intake
  - CHF- poor pump function, so poor renal perfusion
  - Liver disease- hypotension and low effective circulating blood volume (ECBV), so poor renal perfusion (low albumin)
  - Nephrotic syndrome- low intravascular oncotic pressure (low albumin), low ECBV so poor renal perfusion

Approach to Diagnosis: High-Volume Hyponatremia (cont.)

- **Physiology**
  - Caused by impaired free water excretion
  - ⇓ ECBV or ⇓ renal perfusion ⇒ limited distal delivery of fluid to nephron
    - high ADH (kidney "thinks" there is not enough volume because of reduced lood flow
      - low ECBV stimulates ADH release via volume receptors
      - low BP stimulates ADH release via baroreceptors

Approach to Diagnosis: Euvolumic Hyponatremia

- Clinical: Not orthostatic and not edematous (± 10%); Patient's history, current meds, and labs will help establish Dx.
- Etiology/Physiology
  - psychogenic polydipsia- water intake >15-20 L/day; urine maximally dilute (<100 mOsm)
  - diuretic-induced- subclinically hypovolemic (⇓ECBV, ⇑ADH)
  - mineralocorticoid deficiency- (⇓'d Na reuptake, ⇑ADH)
  - hypothyroidism- poor effective circulating volume due to poor pump function & ⇑ADH; ?renal tubular effects?
  - SIADH (syndrome of inappropriate ADH)- too much ADH

Causes of SIADH

- **Tumors** - esp. lung (e.g., small cell) CA, other carcinomas, lymphoma, leukemia
- **Pulmonary Disease** - infectious (e.g., pneumonia, abscess, empyema, TB, etc.)
- **CNS Disorders** - cerebral tumors, infections (e.g., abscess, meningitis, encephalitis), bleeds
- **Drugs** - e.g., carbamazepine, cyclophosphamide, SSRIs, phenothiazines, narcotics, nicotine

Table 3-1. CAUSES OF SIADH

CNS disorders	Acute intermittent porphyria Infectious diseases Systemic lupus erythematosus Trauma Tumor Vascular diseases
Malignancy with ectopic hormone production	Hodgkin's disease Lymphosarcoma Pancreatic carcinoma Reticulum cell sarcoma Small cell carcinoma of lung Thymoma
Pulmonary disease	Lung abscess Pneumonia Tuberculosis
Drugs	Carbamazepine Chlorpropamide Cyclophosphamide General anesthetics Narcotics Oxytocin

Approach to Treatment for Hyponatremia

- **Volume Problem**
  - Correct underlying condition impairing renal perfusion first if possible:
    - If hypovolemic, resuscitate
    - If hypervolemic, diurese
    - If hypervolemic but intravascularly dry, reverse third spacing
- **ĕADH**
  - Correct underlying disorder if possible: pneumonia, lung disease, malignancy, drug effect)
  - Restrict free-water intake if unable to correct underlying problem
  - Consider increasing solute intake (high-salt, high-protein diet)
    - Rarely necessary. Usually the wrong thing to do.
  - Salt (hypertonic saline - emergent therapy (reserved for seizing pts); salt tablets - chronic therapy)
  - Use drugs to block ADH effect (e.g., demeclocycline, loop diuretics, V_2 receptor antagonists)

Cellular Adaptation to Hyponatremia

- Brain most affected
- Cell swelling causes a rise in intracranial pressure
- Adaptations
  - increased outflow of CSF (acute)
  - loss of intracellular K and anions (starts within 3-4 hrs after fall in tonicity and maximal in less than 24 hrs => acute cell volume regulation)
  - loss of other intracellular organic osmolytes (occurs over several days => chronic cell volume regulation)
    - AAs (e.g., gutamlne, taurine), polyols (e.g., myo-inositol), methylamines

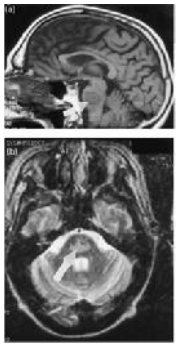
Safe Correction of Hyponatremia

- **General principle**: correct osmolality of plasma at a rate that reflects the rate of creation of hyponatremia
  - Do not exceed 10-12 mEq/L rise in P_{Na} in first 24°; and 20 mEq/L rise in P_{Na} after 48°
  - If seizures or severe neurological abnormalities present, then correct more rapidly initially (e.g., 1.5 - 2 mEq/L/hr for 3-4 hrs with hypertonic saline), but still limit total rise in P_{Na} to 10-12 mEq/L in first 24°.
- **Danger of rapid correction**
  - Central Pontine Myelinolysis (osmotic demyelination syndrome)

Central Pontine Myelinolysis

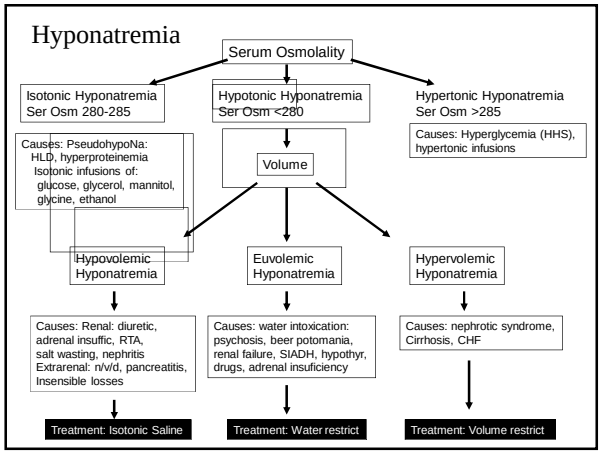
- **-**overly rapid correction of chronic hyponatremia; most common if P_{Na} rises by >15-20 mEq/L/day
- **-**osmotic shrinkage of axons => demyelination; direct injury due to rapid increases in cellular cations?
- -neurologic (early: dysarthria, dysphagia, paraparesis; late: lethargy, coma); generally delayed 2-6 days after correction; irreversible with poor prognosis
- -no proven therapy, prevention is crucial => avoid rapid correction; if overly rapid correction occurs, immediately stop any further rise in P_{Na} and consider re-lowering P_{Na} (dDAVP or free water)

Central Pontine Myelinolysis



Radiographic evidence may not appear until up to 4 weeks later.

Smith, DM, et al., *Clin Endocrinol* 52: 667, 2000



Fluids

- Crystalloid
  - D5W, D5NS, D5 ½ NS
  - D10W
  - ½ NS, ¼ NS
  - NS, 3%, (5%, 10%)
  - LR
- Colloid
  - PRBC
  - Plasma
  - Albumin
  - Synthetic (Hetastarch)

Isotonic: LR, NS
Hypotonic: ½ NS, D5 1/2NS, "D5W", "D10W"
Hypertonic: 3% saline, 5% saline, 10% saline
Note: free water leads to hemolysis- no clinical application

Example Cases

- 77yo anasarca. Na 128
- 56yo h/o schizophrenia, Na 115
- 69yo small cell lung Ca, Na 119
- 89yo osteoporosis, HTN, Na 127, K2.5
- 93yo dementia, fever, Na 170
- 23yo diabetes, Na 151, K 6.9

Composition of Parenteral Fluids

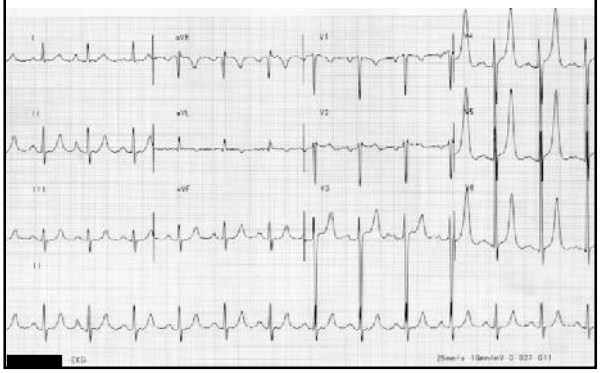
Fluid	Na+	K+	Ca2+	Cl-	HCO3-	pH
ECF	142	4	5	103	27	7.4
LR	130	4	2.7	109	28	6.5
.9% NaCl	154			154		4.5-5.7
.45% NaCl	77			77		4.5
.2% NaCl	30			30		4.5
3% NaCl	513			513		4.5
5% NaCl	855			855		4.5
5% Albumin	145					7.4

Na bicarb:~1,000 mEQ Na/liter

Thank You

Changing Gears… about time

Diagnosis?

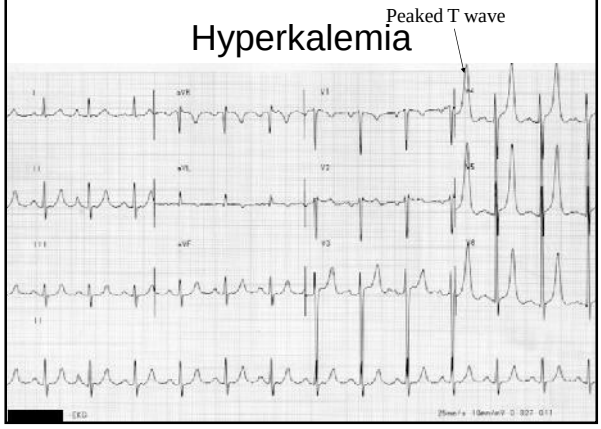


Hyperkalemia

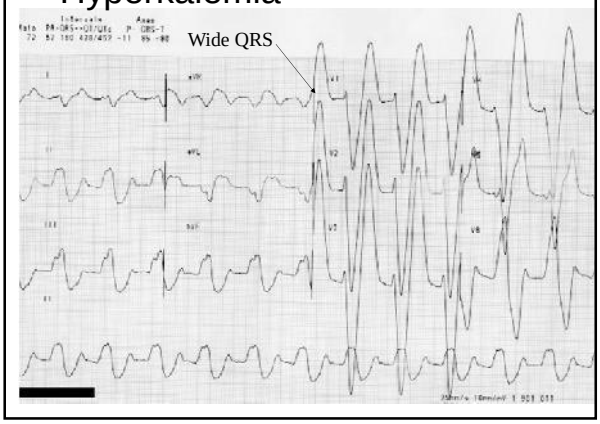
Hyperkalemia:
Causes

- Decreased excretion
  - Drugs, renal failure, hypoaldosteronism
- Increased production
  - Trauma, tumor lysis, “microwave”
- Volume contraction
- Hypertonic states
- Acidosis

Hyperkalemia

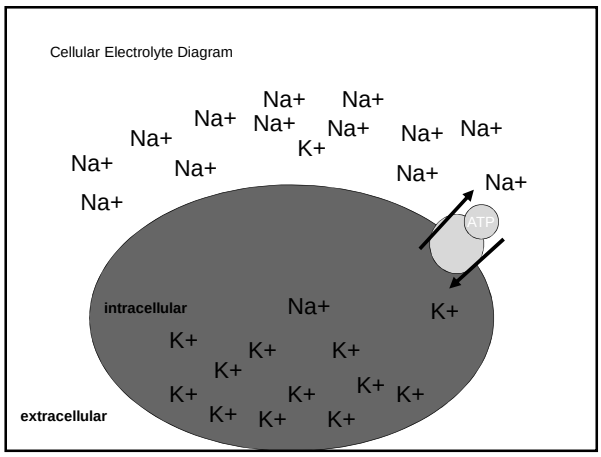


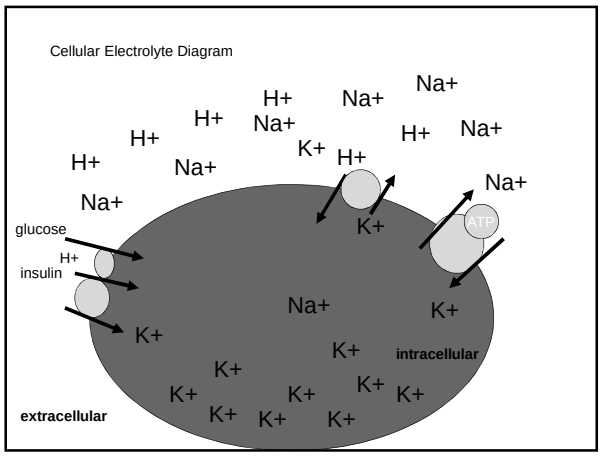
Hyperkalemia



Hyperkalemia

- Changes in cellular transmembrane potentials can lead to lethal cardiac arrhythmias
- Transcellular shifts – acidosis, succinylcholine, “insulin deficiency”, massive tissue destruction
- Often associated with renal impairment coupled with exogenous K+ administration or drugs that increase K+
- Massive blood transfusions
- Pseudohyperkalemia - Thrombocytosis, hemolysis, leukocytosis
- Urine K+ excretion rate can be used to help determine exact cause of hyperkalemia: TTKG





Hyperkalemia (cont.)

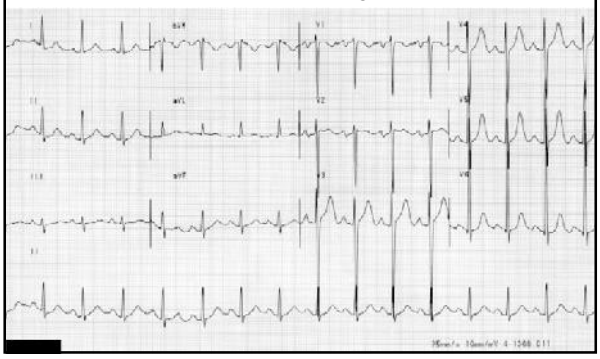
- Drugs causing hyperkalemia – K+ sparing diuretics, ACEI, NSAIDs, heparin, spironolactone, cyclosporin, tacrolimus, tmp/smx
- EKG Changes
  - 5.5 – 6.5 mEq/L – peaked T-waves
  - 6.5 – 7.5 mEq/L – loss of P-waves
  - > 8.0 mEq/L – widened QRS

Treatment of Hyperkalemia

- C BIG K Drop
- Calcium - If EKG changes administer 10 mL of 10% Calcium Gluconate
  - Does not correct K but stabilizes cardiac membrane, muscle
- Bicarbonate, beta agonists
  - 1 amp sodium bicarbonate
  - Albuterol 10-20 mg (onset 3-5 min, duration 2-4 hours)
- Insulin - 10 units IV insulin (onset 10-20 minutes, duration 2-3 hours) with:
- Glucose- 1 amp D50
- Kayexalate - 15-30 g (oral onset 4-5 hours, enema onset 1 hour)
- Diuretics- furosemide usually
- Dialysis

Hyperkalemia

After CaGluc, $NaHCO_3$, Insulin/D50



Hypokalemia

- Defined as serum [K+] less than 3.6 mEq/L
- Marker of whole body depletion of K+
- Occurs in up to 20% of hospitalized patients or more
- 2.5 mEq/L – muscular weakness, myalgia
- <2.5 mEq/L – cramps, paresthesias, ileus, tetany, rhabdomyolysis, PVCs, A-V block, V-tach, V-fib

Hypokalemia

- Usually asymptomatic
- Symptoms usually secondary to whatever causing the hypokalemia

Hypokalemia-causes

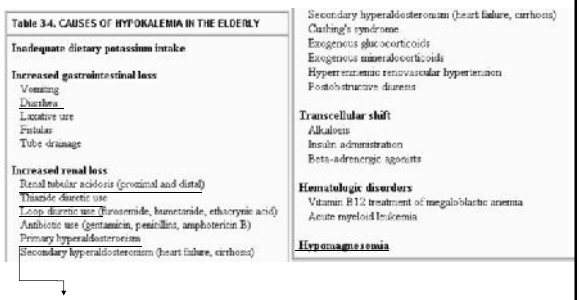


Table 34. CAUSES OF HYPOKALEMIA IN THE ELDERLY

Inadequate dietary potassium intake

Increased gastrointestinal loss
- Vomiting
- Diarrhea
- Laxative use
- Fistulas
- Tube drainage

Increased renal loss
- Renal tubular acidosis (proximal and distal)
- Thiazide diuretic use
- Loop diuretic use (furosemide, bumetanide, ethacrynic acid)
- Antibiotic use (gentamicin, penicillins, amphotericin B)
- Primary hyperaldosteronism
- Secondary hyperaldosteronism (heart failure, cirrhosis)
- Secondary hyperaldosteronism (heart failure, cirrhosis)
- Cushing's syndrome
- Exogenous glucocorticoids
- Exogenous mineralocorticoids
- Hypertensive renovascular hypertension
- Postobstructive diuresis

Transcellular shift
- Alkalosis
- Insulin administration
- Beta-adrenergic agonists

Hematologic disorders
- Vitamin B12 treatment of megaloblastic anemia
- Acute myeloid leukemia

Hypomagnesemia

Hypertension and Hypokalemia: Think Hyperaldosteronism

Hypokalemia: causes

- Inadequate intake
- Increased excretion – diarrhea, diuretics, alkalosis, glucocorticoids, RTA
- Transcellular shifts – beta-agonists, theophylline, insulin, hyperthyroidism, barium

Hypokalemia -Treatment

- Correct K to 4.0. Even lower normal may represent whole body depletion
- For every 10mEq, serum K will rise 0.1mEQ/l
- If K 2.8, nrl is 4.0. Will require 120mEq K
- Replace no faster than 20 mEq/h peripherally and 40 mEq/h centrally
- Bananas: 1mEq K/inch. 10inch banana will raise K 0.1mEq/l
- K will not be corrected if hypomagnesemic. Correct Mg to 2.0
- If marginally low K with alkalosis, consider contraction alkalosis. Replace K to 4.5 to replace whole body deficit

Example Cases

- 77yo anasarca. Na 128
- 56yo h/o schizophrenia, Na 115
- 69yo small cell lung Ca, Na 119
- 89yo osteoporosis, HTN, Na 127, K2.5
- 93yo dementia, fever, Na 170
- 23yo diabetes, Na 151, K 6.9

Thank You