

**Fluid and Electrolyte Disorders**

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**Objectives**

- Sodium and free water metabolism
- Potassium metabolism

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**First principles**

- How does the electrolyte enter the body?
  - Oral, intravenous, absorption from another site
- Where is it found in the body?
  - Intra- vs extracellular space; depot locations
- How is it lost from the body?
  - GI, renal, skin
  - Don't forget insensible losses through the lungs for water!
- What factors (endocrine, electrical charges, etc) influence the preceding?

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## Sodium and Water Metabolism

- Two are intertwined
  - Na<sup>+</sup> major extracellular, osmotically active cation
  - But Na<sup>+</sup> level is simply a ratio of Na<sup>+</sup> to free H<sub>2</sub>O
- Separating out disorders of Na<sup>+</sup> requires considering both Na<sup>+</sup> and H<sub>2</sub>O

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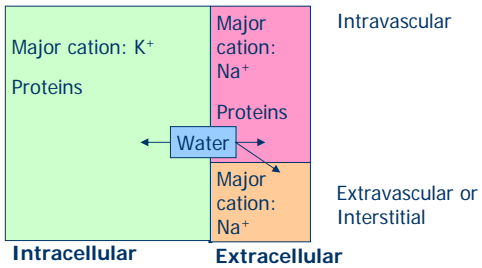
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## Sodium and Free Water



\*Gradient between Na<sup>+</sup> and K<sup>+</sup> maintained by Na,K ATPase

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## What influences distribution of H<sub>2</sub>O?

- Osmolality
  - Serum osm =  $2(\text{Na}^+) + \text{glucose}/18 + \text{BUN}/2.8$
  - Other solutes which are (typically) unmeasured:
    - Alcohols, other sugars, etc.
    - Osmolar gap: difference between measure and calculated of >10
    - Normal osmolality (275-300 mOsm/kg)
- Movement of fluid across cell membranes:
  - Effective osmoles (Na<sup>+</sup>, etc.)
  - Ineffective osmoles (EtOH, ethylene glycol, methanol, urea)

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## Systems involved in Na<sup>+</sup> metabolism

- Entry into the body
  - Gut: generally not major issue
  - Intravenous: generally not an issue (as long as no hypertonic saline use or renal dysfunction)
- Egress from the body
  - Skin: usually hypotonic losses
  - GI: usually iso-osmolar losses
  - Renal

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## Renal Handling of Na<sup>+</sup>

- GFR
- Tubular reabsorption
  - Concentrating gradient
    - Lesions: osmotic diuresis, tubulointerstitial disease or effects on specific transporters, changes in blood flow in vasa recta
- Na,K ATPase

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## Na-K ATPase

- Decreased renal perfusion triggers release of renin from the JGA
- Renin activates angiotensinogen
- Angiotensin II stimulates aldosterone release from the adrenal glands
- Aldosterone stimulates Na,K ATPase in proximal convoluted tubule
- Net reabsorption of Na<sup>+</sup>

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## Na<sup>+</sup> Re-cap

- Major factors affecting Na<sup>+</sup> handling:
  - Na, K-ATPase and aldosterone
  - GFR
  - Concentrating gradient and specific transporters in the kidney
- Infrequently related to losses from other sites or intake
- BUT Na<sup>+</sup> level may appear to be altered related to changes in total body water

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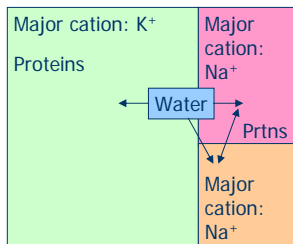
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## Total body water



- Distribution
- Consider:
  - Cell volumes and effects/constrains upon same
  - Rate of change of volume and effects

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## Free Water Homeostasis

- Entry into body
  - Oral intake may be a problem (drive or access)
- Exit from the body
  - Skin: generally requires massive losses
  - Gut: protracted emesis, diarrhea
  - Insensible: may be a contributor in ill patients
  - Renal handling: delivery of solute to the distal tubule, and ADH

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## Renal handling of water

- GFR
- Coupled to Na<sup>+</sup> early in glomerulus
- Distal tubule: dependent upon delivery of solute
- ADH in CD as uncoupling mechanism
  - But may not be enough to overcome a heavy solute load

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## ADH and renal handling of H<sub>2</sub>O

- Released by pituitary
- Stimuli
  - Osmolality (hypothalamic receptors)
  - Intravascular volume (baroreceptors)
- Effects
  - Stimulate thirst
  - Increased reabsorption of H<sub>2</sub>O in CD

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## Disorders of Na<sup>+</sup> and H<sub>2</sub>O

- Variety of permutations of total body Na<sup>+</sup> and total body water levels
- But all LOOK like hyponatremia or hypernatremia

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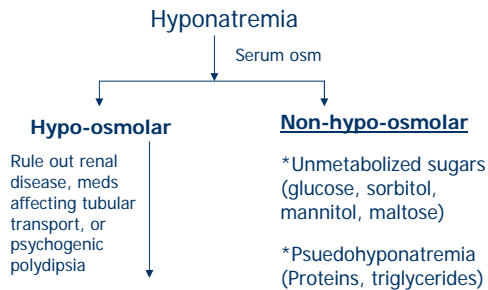
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## So what causes hyponatremia?




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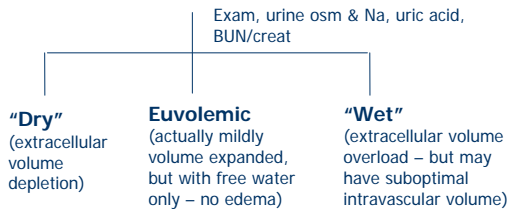
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## Hypo-osmolar hyponatremia

- Determine clinical volume status



- What's the homeostatic response for each?

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## Euvolemic hypo-osmolar hyponatremia

- Can be a **reset osmostat** in response to pregnancy, chronic disease, etc.
- Could be **SIADH**
  - Causes: CNS disease or CNS-active drugs, malignancy, pulmonary disease; acutely, stress
  - Differential diagnosis:
    - Adrenal insufficiency** (cortisol, aldosterone)
    - Hypothyroidism**

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## Signs and symptoms of hypo-osmolar hyponatremia

- Largely related to water distribution
  - CNS symptoms, emesis, weakness
- Varies based on acuity
  - Ability to preserve CNS intracellular volume
  - Typically won't get seizure until  $\text{Na}^+ < 117$ ; even lower if develops slowly
- Look for neurologic signs

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## Treatment

- **Based on acuity and underlying cause**
- Rules of thumb:
  - Don't correct more quickly than you got there
  - No more than 12 meq/L change in first day, more slowly thereafter
  - If severe symptoms, goal to increase by 4-6 meq/L quickly, then more slowly thereafter
    - Eg, 3% NaCl at 1-2 cc/kg/hr initially for seizures

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## Treatment by cause

- Med induced: stop the med!
- Hypovolemia: replace intravascular volume with an isotonic solution
- Volume overload: mobilize interstitial fluid, improve cardiac contractility, etc.
- Euvolemic: fluid restrict to reset tubular concentrating gradient

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## SIADH treatment

- Why would a patient with SIADH get worse when given normal saline IV?
  - Retain all of the free water
  - Excrete all of the sodium
- Other potential treatments:
  - Loop diuretic (water > Na<sup>+</sup> excretion)
  - Demeclocycline (inhibits ADH action)

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## Hypernatremia

- Causes
  - Poor water intake (debilitated, restricted access to fluids, with ongoing fluid losses)
  - Excessive salt intake (oral or IV)
  - Increased losses
    - Skin
    - GI
    - Insensible
    - Renal

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## Signs and symptoms of hypernatremia

- If also has Na<sup>+</sup> loss, will have evidence of intravascular volume depletion
- Otherwise primarily CNS symptoms due to intracellular volume depletion
  - Intracranial hemorrhage
  - Mental status changes
  - Seizure
  - Hyperventilation
  - Increased tone and reflexes
  - Fever

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## Treatment of hypernatremia

- Differs based on cause
  - Hypotonic fluid losses with intravascular volume depletion
    - Replace volume first, then free water
  - Free water losses
    - Depends on cause – look at renal mechanism

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## Water deficit

- $= (\text{nl body water})[1 - (\text{meas. Na}^+/140)]$
- Where nl body water is 0.5-0.6 of adult body weight

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## Mechanisms of renal loss of H<sub>2</sub>O

- Lack of ADH production
  - Central diabetes insipidus
- Lack of ADH action
  - Nephrogenic diabetes insipidus
- Osmotic pull limiting effects of ADH
  - Diuretics (loops especially)
  - Sugars
  - Increased urea excretion

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### Hallmarks of diabetes insipidus

- Polyuria
- Polydipsia

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### Central diabetes insipidus

- Lesion or process affecting hypothalamus or posterior pituitary
- Pregnancy
- Genetic

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### Nephrogenic diabetes insipidus

- Chronic renal disease affecting tubules
- Medications
  - Demeclocycline
  - Lithium
  - Foscarnet, etc etc
- Electrolyte abnormalities
  - Hypokalemia
  - Hypocalcemia
- Genetic

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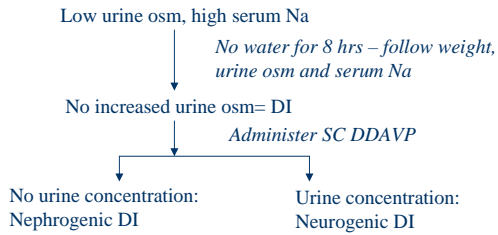
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## Differentiating causes

### Water deprivation test for diabetes insipidus



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## Treatment of diabetes insipidus

- Same rules of thumb as for hyponatremia regarding rates
- Central DI:
  - DDAVP
  - limit salt and protein intake, push oral free water
- Nephrogenic DI:
  - Thiazides
  - NSAIDs
  - supportive measures

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## Questions?

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## Potassium Disorders

- What influences intra- vs extracellular distribution of  $K^+$
- Effects of hypo- or hyperkalemia
- Treatments of each

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## Pseudohypo- & -hyperkalemia

- Hemolysis
- Leukocytosis, thrombocytosis

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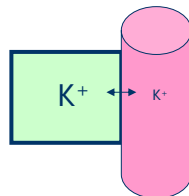
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## Factors influencing $K^+$ distribution

- **Cell membrane integrity**
  - Production or destruction
- **Shifts across membrane**
  - Insulin, Beta-2 receptors
  - Acid base abnormalities
  - Misc: thyroid dz, charged substances



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## Potassium Handling

- Non-renal losses
  - Skin
  - GI: colonic losses
- Rarely related to intake alone

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## Renal handling of K<sup>+</sup>

- GFR
- Tubular handling
  - Mix of reabsorption and secretion
  - Coupled with Na<sup>+</sup> and Cl<sup>-</sup> reabsorption in thick ascending limb (loop-sensitive)
  - Principal cell K<sup>+</sup> secretion in response to aldosterone, solute delivery, etc.
  - Intercalated cell reabsorption in response to hypokalemia

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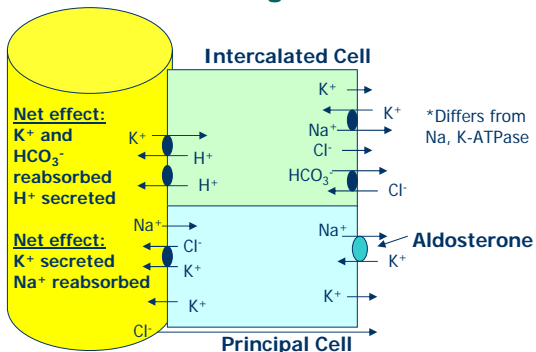
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## Cortical Collecting Duct



Adapted from Renal and Electrolyte Disorders, p. 205-206

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## “Stumper”

- Why does protracted vomiting cause hypokalemia?
- Loss of H+ in emesis results in metabolic alkalosis
- Metabolic alkalosis stimulates principal cells to increase K+ secretion

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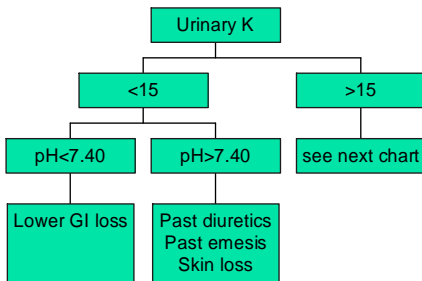
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## Hypokalemia work up



Adapted from The Washington Manual of Medical Therapeutics

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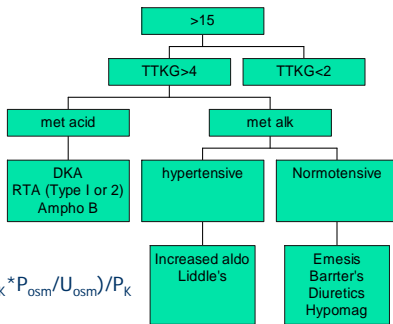
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## Hypokalemia work up, cont'd



$$TTKG = (U_K * P_{osm} / U_{osm}) / P_K$$

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## Effects

- **Hypokalemia**
  - **Cardiac:**
    - Arrhythmias, ST-T segment changes
  - **NMSK:**
    - weakness, cramps, paresthesias
  - **Renal:**
    - DI, volume loss (decreased Na<sup>+</sup> and Cl<sup>-</sup> reabsorption)
- **Hyperkalemia**
  - **Cardiac:**
    - Shortened PR to peaked Ts to widened QRS to sinus waves
  - **Neuro:**
    - Weakness, paresthesias

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## Treatment of Hypokalemia

- Preferred route
  - Maximum IV 20 mmol/hr (requires telemetry)
- Address underlying cause

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## Treatment of Hyperkalemia

- Are there any cardiac changes?
  - Yes: Calcium IV
    - Exception: dig toxicity
  - No: Proceed with other treatment
- Shift into cells (insulin, glc; beta agonists, NaHCO<sub>3</sub>)
- Increase elimination (gut, renal, dialysis)
- Address underlying cause

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## Questions?

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## References

- The Washington Manual of Medical Therapeutics. 30<sup>th</sup> ed. Editors, SN Ahya et al. Lippincott Williams & Wilkins, Philadelphia. 2001.
- Renal and Electrolyte Disorders. 5<sup>th</sup> ed. Editor RW Schrier. Lippincott-Raven, Philadelphia. 1997.

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