Electrolyte Disorders

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Overview and Objectives
- Topics
  - Hyponatremia
  - Hypernatremia
  - Hypokalemia
  - Hyperkalemia
  - Understand the basic physiology, diagnosis and treatment

Case #1: Hyponatremia
- A 62 y/o woman w/ PMH of asthma underwent laparoscopic surgery for acute cholecystitis.
- Develops persistent nausea post-op, and her pain was poorly controlled despite the use of IV toradol.
- She was permitted ice chips, and D2 0.45 NS was given at 70 cc/hr. On post-op day 3 her serum sodium was 125 mEq/L and the pt was complaining of a headache.

Hyponatremia
- REMEMBER
  - Dysnatremias are a WATER problem
  - The RAAS system is intact to maintain euvolemia
  - Aside from psychogenic polydipsia, beer potomania, and tea/toast, HYPONATREXIA is ALWAYS an ADH issue
    - Appropriate ADH vs Inappropriate ADH
    - Even with volume depletion (or low EACV), hyponatremia is caused by elevated ADH response

Case #1: Hyponatremia
- What do you do first?
  - Vitals/Exam
  - No orthostasis (ie euvolemic)
  - Next?
  - Labs

<table>
<thead>
<tr>
<th>Serum Chemistries</th>
<th>Urine Chemistries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium 125 mM</td>
<td>Sodium 100 mM</td>
</tr>
<tr>
<td>Potassium 3.0 mM</td>
<td>Potassium 40 mM</td>
</tr>
<tr>
<td>BUN 4 mg/dL</td>
<td>Osmolality 600 mOsm/L</td>
</tr>
<tr>
<td>Creatinine 0.7 mg/dL</td>
<td></td>
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<tr>
<td>Uric Acid 1.0 mM</td>
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<tr>
<td>Osmolality 260 mOsm/L</td>
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Hyponatremia

<table>
<thead>
<tr>
<th>Osmoregulation</th>
<th>Volume Regulation</th>
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<tbody>
<tr>
<td>Senses</td>
<td>Serum osmolality</td>
</tr>
<tr>
<td>Effects</td>
<td>Vasopressin (ADH)</td>
</tr>
<tr>
<td>Affects</td>
<td>Urine osmolality</td>
</tr>
<tr>
<td>ADH release</td>
<td>Osmotic</td>
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</tbody>
</table>
Hyponatremia

What does our patient have?
- Hypotonic (serum osms 260)
- Euvolemic

Inappropriately high urine osms and urine sodium

SIADH from nausea/pain induced ADH release and receipt of more free water than she could effectively excrete

What if this patient were to receive NS? Would the Na rise?
- Initially yes, but ultimately Na would decrease
  - You must give a solution that is HYPERTONIC to the urine (in this case 600 mosm/L to make the Na rise)

SIADH: Causes

<table>
<thead>
<tr>
<th>Malignancy</th>
<th>Pulmonary Disorders</th>
<th>CNS Disorders</th>
<th>Drugs</th>
<th>Other</th>
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<tbody>
<tr>
<td>Lung CA</td>
<td>Infections</td>
<td>Infections</td>
<td>Chlorpropramide</td>
<td>Hereditary</td>
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<tr>
<td>Oropharynx</td>
<td>Asthma</td>
<td>Bleeding and Masses</td>
<td>SSRIs</td>
<td>Idiopathic</td>
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<tr>
<td>GI – Stomach Pancreas</td>
<td>Cystic fibrosis</td>
<td>Multiple sclerosis</td>
<td>Captopril</td>
<td>Endurance</td>
</tr>
<tr>
<td>GU – Bladder Prostate</td>
<td>Respiratory failure (PEEP)</td>
<td>Guillain-Barre Syndrome</td>
<td>Nicotine</td>
<td>General Anesthesia</td>
</tr>
<tr>
<td>Endocrine Thymoma</td>
<td>Acute int. Purpura</td>
<td>MDMA (&quot;ecstasy&quot;)</td>
<td>Narcotics</td>
<td>Nausea</td>
</tr>
<tr>
<td>Lymphomas</td>
<td>Debrilin tremens</td>
<td>NSAIDS</td>
<td>Pain</td>
<td></td>
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<tr>
<td>Sarcomas</td>
<td>Acute int. Purpura</td>
<td>MDDA</td>
<td>AVP Analogues</td>
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SIADH: Diagnosis

- Essential Features
  - Decreased effective osmolality (< 275 mOsm/L of water)
  - Urinary osmolality > 100 mOsm/L of water during hypotonicity
  - Clinical euvolemia: No orthostasis; No volume overload
  - Urinary sodium > 40 mmol/L with normal dietary salt intake
  - Normal thyroid and adrenal function
  - No recent use of diuretic agents

ADH: Physiology

Hyponatremia: Work Up

Serum Osmolality
- Not Low
- Low

Pseudohyponatremia
- Hyperglycemia
- Low Aldo
- Diuretics, loop defect
- Vomiting
- SIADH
- Reset Osmostat
- Low Cortisol
- Hypothyroid
- CHF
- Low albumin
- Urine K
- Urine Na
- ECF Volume
- Not Low
- Low (Primary Na low)
- Effective Circulatory Volume
- Not Low (Primary water gain)
- Urine Na ≤ 10 mM
- > 20 mM Urine K
- SIADH
- Resect Osmostat

Hyponatremia: Diagnosis

- Supplemental Features
  - Plasma uric acid < 4 mg/dL
  - Blood urea nitrogen < 10 mg/dL
  - Fractional excretion Na > 1%; fractional urea excretion > 55%
  - Failure to correct hyponatremia after 0.9% saline infusion
  - Correction of hyponatremia through fluid restriction
  - Elevated plasma AVP levels
Treatment: Asymptomatic Hyponatremia

- Free water restriction
- Increase of dietary osm intake to obligate free water excretion
  - Ex: If one consumes 600 mOsm of food and you urine osmolality is fixed at 600 mOsm/L, you will make 1L of urine
- Dilute urine with loop diuretics
- Induce Nephrogenic DI with medications
  - Demeclocycline, ADH antagonists

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<tbody>
<tr>
<td>Conivaptan</td>
<td>20-40 mg daily</td>
<td>V2 &amp; V1</td>
<td>IV</td>
<td>↑</td>
<td>↓</td>
<td>No Change</td>
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<tr>
<td>Tolvaptan</td>
<td>15-60 mg daily</td>
<td>V2</td>
<td>Oral</td>
<td>↑</td>
<td>No Change</td>
<td></td>
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<tr>
<td>Lixivaptan</td>
<td>100-200 mg daily</td>
<td>V2</td>
<td>Oral</td>
<td>↑</td>
<td>No Change</td>
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<tr>
<td>Satavaptan</td>
<td>12.5-50 mg daily</td>
<td>V2</td>
<td>Oral</td>
<td>↑</td>
<td>No Change</td>
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Symptomatic Hyponatremia

- Who is at risk?
  - Children
  - Menstruating women
  - Hypoxic patients

Case #2: Hypernatremia

- A 55 year old man presents with a serum sodium of 160. He is asymptomatic and has no complaints. What can you conclude?
  - One can conclude that the patient has a hypothalamic lesion involving the detection of thirst. Hypertonicity should stimulate thirst.
  - As a general rule, a patient with hypernatremia either has altered mental status or the patient has been denied access to free water.

Symptomatic Hyponatremia

- Take Home Points
  - Hyponatremic encephalopathy should be recognized promptly and treated with 3% hypertonic saline.
  - A bolus of 100cc of 3% NaCl for active seizures and respiratory failure recommended.
  - Repeat 1-2 more times at 10 minute intervals to raise Na 4-6 mmol/L acutely to alleviate symptoms.
  - What if Na is corrected too rapidly?
    - Administration of D5W and/or ddAVP to lower Na has been shown to decrease morbidity and mortality

Symptomatic Hyponatremia

- Severe Hyponatremia < 125 mmol/L
  - Acute (duration < 48 hours) or coma, seizure
  - Moderate symptoms: And unknown duration
  - Asymptomatic

  - Begin diagnostic evaluation
  - Rule out or address Correctable factors
  - Start 3% saline bolus
  - Begin saline infusion alone
  - Begin saline and furosemide
  - Step when serum sodium level rises 8-10 mEq within first 24 hours
  - Consider Vaptans

  - Urine osmolality must be fixed at 600 mOsm/L, you will make 1L of urine
  - Dilute urine with loop diuretics

Take Home Points

- Hyponatremic encephalopathy should be recognized promptly and treated with 3% hypertonic saline.
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Hypernatremia
- ICF volume is contracted in all patients
- Na gain is rarely responsible
- Almost always due to water loss
- Major responses should be increased thirst and excretion of minimal volume of maximally concentrated urine
- Major causes
  - DI: maximally dilute urine, very high volume
  - Renal losses (osmotic diuresis): relatively high urine osms, fairly high volume
  - Non renal losses: very high urine osms, low volume

Case #3: Hypernatremia
- Diabetes Insipidus?
  - Unlikely
- Urine osmolality is quite high at 450 mOsm/L
- Osmotic Diuresis?
  - The presentation is more consistent with an OSMOTIC diuresis secondary to glucosuria or a urea load from tissue breakdown

Hypernatremia
- Water Loss
- Burns
- Fever
- Respiratory Infection
- Renal Loss
  - Central DI
  - Nephrogenic DI
  - Osmotic Diuresis
- GI Loss
  - Osmotic Diarrhea
- Sodium Retention
  - Administration of Hypertonic NaCl or Na HCO3

Central Diabetes Insipidus: Causes
- Head Trauma
- Post Hypophysectomy
- Tumors
  - Meningioma
  - Glioma
  - Benign Cysts
  - Leukemia / Lymphoma
  - Metastatic tumors
  - Pinocytosis
  - Cerebral palsy
- Idiopathic
  - Familial
  - Idiopathic thymosins
- Sheehan's Syndrome
- Infections
  - TB
  - Syphilis
  - Mycoses
  - Toxoplasmosis
  - Encephalitis
- Granulomatous DZ
  - Sarcoidosis
  - Histiocytosis X
  - Wegner’s
- CVA
- Aneurysms
- Cavernous sinus
Nephrogenic Diabetes Insipidus: Causes

**Congenital**
- Vasopressin V2-receptor mutation
- Aquaporin-2 water channel mutations

**Chronic tubulointerstitial diseases**
- Analgesic abuse
- Sickle cell nephropathy
- Multiple myeloma
- Sarcoidosis
- Sjogren’s
- PCKD
- Medullary cystic diseases

**Electrolyte abnormality**
- Hypokalemia
- Hypercalcemia

**Medications**
- Lithium
- Amphotericin B
- Demeclocycline
- Methoxyflurane
- Obstructive Uropathy

Diabetes Insipidus: Diagnosis

- Begin Water Deprivation
- Give AVP

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<thead>
<tr>
<th>Plasma Osmolality</th>
<th>Urine Osmolality</th>
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<tbody>
<tr>
<td>280</td>
<td></td>
</tr>
<tr>
<td>295</td>
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Complete Central DI
- ddAVP: nasal or IM replaces deficiency

Partial Central DI
- Chlorpropamide: increases renal response to ADH
- Carbamaepine: increases renal response to ADH
- Clofibrate: may increase ADH secretion

Nephrogenic DI
- Thiazide Diuretics (volume deplete → raise ADH)
- Amiloride (especially in the setting of lithium toxicity)

Case #4: Hypokalemia
- A 53 year old female presents to her doctor after being initiated on hydrochlorothiazide about a week ago. She is found to have a serum potassium level of 3.2 mEq/dL.

Hypokalemia

- Teaching point
  - The development of hypokalemia in the setting of diuretic initiation should alert the physician to look for secondary causes of hypertension

Hypokalemia

- Sources of transcellular shift?
  - Nonrenal loss?
    - Profuse diarrhea, severe burns
  - Diuretic induced loss?
    - (especially thiazide or loop diuretic)

- Plasma Mg
  - Normal or High
  - K ≥ 1.5 after Mg Repletion

- Urine K+
  - Low
  - High

- Recheck plasma K Hypokalemia Resolved?
  - Yes
  - No

- Pseudohypokalemia
  - No

- Hypomagnesemia
  - Yes
Hypokalemia

- **Urine K**
  - > 20 mmol/day (Renal Loss)
  - < 20 mmol/day (Non-renal loss)

- TTKG
  - < 2
  - > 4

- Increased Tubular Flow
  - Osmotic Diuresis
  - Previous vomiting
  - Previous diuretic use
  - Poor dietary intake

- Mineralocorticoid Excess
  - Bartter Syndrome
  - Gitleman Syndrome

- Acid Base Status
  - Alkalosis
  - Blood Pressure
    - High
  - Low or Normal

- Alkalosis
  - Mineralocorticoid Excess
  - Liddle’s Syndrome

- Low or Normal
  - Loop/Thiazide Diuretics
  - Vomiting, Gastric Suction
  - Bartter Syndrome
  - Gitleman Syndrome

- High
  - Mineralocorticoid Excess
  - Liddle’s Syndrome
  - Bartter Syndrome
  - Gitleman Syndrome

- Previous vomiting
  - Previous diuretic use
  - Poor dietary intake

- DKA
  - Amphotericin B
  - Acetazolamide

- High
  - Renal loss; excess aldosterone effect

- Low or Normal
  - Non-renal cause, nl aldosterone effect

- With hypokalemia
  - < 2 = GI loss
  - > 4 = Renal loss; excess aldosterone effect

- With hyperkalemia
  - < 6 = Renal; Decreased aldosterone effect
  - > 10 = non-renal cause, nl aldosterone effect

Hypokalemia: The Aldosterone Effect

- **Urine potassium Excretion**
  - Less than 30 mEq/day
  - Greater than 30 mEq/day

- **Plasma renin activity**
  - Low
  - High or Normal

- **Plasma aldosterone**
  - High
  - Low

- Primary hyperaldosteronism
  - Conn’s syndrome
  - Bilateral Adrenal Hyperplasia
  - Glucocorticoid Remediable HTN

- **Adrenal vein aldosterone levels and/or CT scan**
  - Lateralizing
    - Licorice/Other mineralocorticoid
  - Nonlateralizing

- **Continued diuretic usage**
  - Renovascular HTN
  - Malignant HTN
  - Salt-wasting Renal Disease
  - Cushing’s Syndrome

- **Increased diuretic usage**

- Hyperaldosteronism

- High Aldosterone/Renin ratio
  - Higher the ratio the higher the specificity for primary hyperaldosterone (ie a ratio of 30 is more specific, but less sensitive than a ratio of 20)
  - Aldosterone level itself must be elevated (ie > 12.15)

- Three causes
  - Conn’s syndrome
  - Bilateral Adrenal Hyperplasia
  - Glucocorticoid Remediable HTN

- Hyperkalemia: Other Etiologies

- **Decreased net intake**

- **Increased entry into cells, leading to transient hypokalemia**
  - (pH, insulin, β-adrenergic activity, Periodic paralysis, Anemia, hyperthermia)

- **Increased gastrointestinal losses**

- **Increased urinary losses**
  - Diuretics, mineralocorticoid excess, salt wasting, Nephropathies, Vomiting, Metabolic Acidosis, Amphotericin B, Hypomagnesemia, Polyuria, P-Dopa, Liddle’s syndrome, Licorice

- **Increased sweat losses**
Case #5: Hyperkalemia

A 63 year old man presents to the emergency room following initiation of an ACE Inhibitor complaining of weakness. He is found to have a serum potassium value of 6.4.

Hyperkalemia

- Taking in too much
  - Oral/IV
  - Normally not an issue with higher GFR
- Shifts
  - Pseudohyperkalemia
  - Metabolite acidosis
  - Insulin deficiency
  - Tonic catalepsy
  - β-blockers
  - Diuretics
  - Metabolic acidosis
  - Tissue catabolism
  - β-blockers
  - Severe exercise
  - Digitalis overdose
  - Periodic paralysis hyperkalemic form ( BOARD trivia question usually for HYPOKALEMIC form... Asian male with thyrotoxicosis and unremarkable urine potassium)
- Not getting rid of enough
  - AKI, CKD
  - Effective circulating volume depletion
  - Hyperaldosteronism
  - Type 1 renal tubular acidosis - hyperkalemic
  - Type 5 renal tubular acidosis
  - Renovascular

Hyperkalemia in the setting of ACEI occurs almost always with low renal blood flow and ultimately low urine output.

Four basic etiologies of hyperkalemia

- Pseudohyperkalemia (mitigated by checking plasma NOT serum labs)
- Taking in too much
- Not getting rid of enough
- Shifts (tonicity, pH, etc)

K > 5.5 mmol/L

- Hemolysis
  - Leukocytes > 70,000
  - Platelets > 500,000
- Recheck K plasma after rapid separation of non-hemolyzed sample. K normalized
- Pseudohyperkalemia
- Sources of trans-cellular shift (Especially rhabdomyolysis, necrosis, tumor lysis, DKA, HHS)

Ongoing IV or PO sources of excess potassium?

Medications associated with hyperkalemia?

(ACE, ARB, NSAIDS, K+ sparing diuretics)

Acute Kidney Injury, Oliguria, or GFR < 20 ml/min/1.73m²?

TTKG

Hyperkalemia: Hypoaldosteronism

- Associated with decreased activity of the renin-angiotensin system
  - Hyporeninemic hypoaldosteronism with mild to moderate renal insufficiency (COMMON)
  - NSAIDS
  - ACE-I
  - Cyclosporine
  - AIDS
  - Metastatic CA (due to infarction)
  - Histoplasma (infiltration, glands normally enlarged)
Hyperkalemia: Hypoaldosteronism

- Primary decrease in adrenal synthesis
  - Normal cortisol levels
  - Heparin (decreased synthesis of aldosterone only)
  - Isolated hypoaldosteronism
  - Post removal of adrenal adenoma
- Low cortisol levels
  - Primary adrenal insufficiency
  - Congenital adrenal hyperplasia – primarily 21-hydroxylase deficiency

Hyperkalemia: Hypoaldosteronism

- Aldosterone resistance
- Potassium-sparing diuretics
- Cyclosporine
- Pseudohypoaldosteronism (Gordon’s syndrome)