Electrolyte Disorders

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Osmolality

- Number of **particles** (osmoles, Osm) dissolved in solution.
- Water moves between body compartments along osmolal gradients from an area of **lower osmolality** to an area of **higher osmolality**
- Only **effective osmoles** (substances that do not freely cross cell membranes) induce a water shift
- Predominant effective osmole: **sodium**
- Ineffective osmole (does not induce fluid shift): **urea**
- The body attempts to regulate osmolality primarily via **retention or excretion of water**, not osmoles (i.e., sodium, Na+)

Sodium and Water Balance

- **Sodium:**
  - As the **major extracellular cation**, Na+ is the predominant solute contributing to osmolality
  - Na+ is actively pumped from the intracellular to the extracellular space
  - Na+ leaves the body primarily through **urinary excretion**, which is tightly regulated
  - Serum osmolality may be estimated using the following equation:
  - Serum osmolality =

[2×serum Na (mEq/L)]+[blood urea nitrogen (mg/dL)/2.8]+[glucose (mg/dL)/18]

Sodium and Water Balance

- **Water:**
  - Total body water (TBW) represents **60% of body weight in men and 50% in women**
  - TBW is distributed:
    - Intracellular 2/3
    - Extracellular 1/3
    - Interstitial ¾ of extracellular
    - Intravascular ¼ of extracellular
  - Water losses occur via the **kidney**, **GI tract**, **skin**, and **respiratory tract**
  - Renal water excretion is tightly regulated via concentration or dilution of urine
  - 500 to 1000 mL/day lost through skin and respiratory tract (“insensible losses”)
  - **Thirst** is an essential mechanism for preventing and correcting a water deficit
  - Stimulated by hypovolemia and an elevated serum osmolality

Sodium and Water Balance

- **Aldosterone:**
  - Mineralocorticoid produced in the **zona glomerulosa** of the adrenal glands
  - Major actions are to stimulate Na+ reabsorption and potassium (K+) secretion in the renal collecting tubule.
  - Hydrogen (H+) secretion is increased due to the electronegative lumen generated by Na+ reabsorption.
  - Aldosterone release is stimulated by:
    - Hyperkalemia
    - Angiotensin II
  - The renin-angiotensin-aldosterone axis modulates Na+ retention and excretion to regulate **total body volume** (and hence blood pressure)

Sodium and Water Balance

- **Antidiuretic Hormone (ADH, Vasopressin):**
  - ADH is the principal hormone regulating **osmolality**
  - ADH increases water reabsorption from the collecting duct lumen back into the circulation
  - **ADH present:** concentrated urine; smaller urine volume
  - **ADH absent:** dilute urine; larger urine volume
  - ADH release from the posterior pituitary is stimulated by:
    - Increases in plasma osmolality as small as 1%
    - Pain, nausea, multiple medications
    - Greater than or equal to 10% decrease in effective circulating volume

Sodium Disorders

HYPONATREMIA

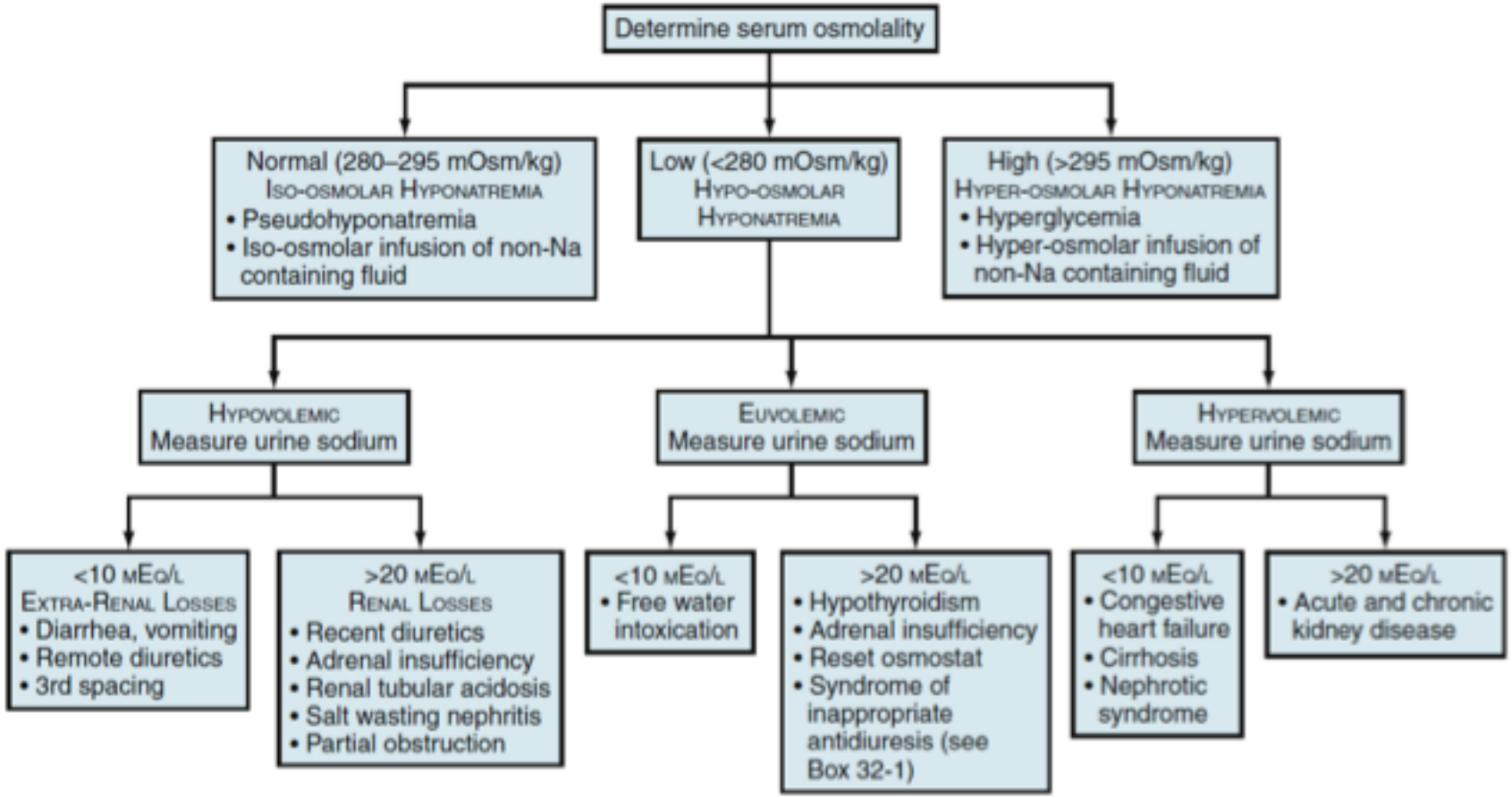
HYPONATREMIA

- Serum Na+ concentration less than **135 mEq/L**
- **Most common electrolyte disturbance in hospitalized patients**
- Can occur with **low**, **normal**, or **high** total body Na+
- hyponatremia requires the **presence of too much water** relative to the quantity of total body Na+
- Clinical Presentation:
  - Not all hyponatremia is symptomatic
  - Signs and symptoms are due to swelling of the central nervous system (CNS)
- As serum osmolality falls, water shifts intracellularly to an area of higher osmolality until an osmolal gradient no longer exists

HYPONATREMIA | Clinical Presentation

Signs and Symptoms of Hyponatremia		
Mild	**Moderate**	**Severe**
[Na+] = 125–135 mEq/L	[Na+] = 120–125 mEq/L	[Na+] <120 mEq/L
• Anorexia • Apathy • Restlessness • Nausea • Lethargy • Muscle cramps	• Agitation • Disorientation • Headache	• Seizures • Coma • Areflexia • Cheyne-Stokes respirations • Incontinence • Death

HYPONATREMIA



HYPONATREMIA | Diagnosis and Evaluation

- Determine osmolality
  - **Normal**
    - Pseudohyponatremia: Hyperlipidemia and hyperproteinemia
    - can cause an artifactual decrease in measured serum Na+.
    - The true serum Na+ concentration is normal.
    - Asymptomatic; exclude before pursuing evaluation of hyponatremia
  - **High**
    - Osmotically active particles may pull water into the extracellular space, creating a dilutional hyponatremia
    - Examples: glucose, mannitol, maltose
    - For every 100-mg/dL increase in glucose above 100, serum Na+ decreases around 1.6 to 2.4 mEq/L
  - **Low**
    - Characteristic of most cases of hyponatremia

HYPONATREMIA | Diagnosis and Evaluation

- Determine volume status
  - **Findings suggestive of hypovolemia**
    - Hypotension, tachycardia, dry mucous membranes, skin tenting, absence of edema
  - **Findings suggestive of hypervolemia**
    - Edema, elevated jugular venous pressure, crackles, S3 heart sound, pulmonary edema

HYPONATREMIA | Diagnosis and Evaluation

- Evaluate urine indices
  - Can be seen in hypovolemia or hypervolemia (congestive heart failure, cirrhosis)
    - Urine Na+ less than 10 mEq/L
    - Fractional excretion of sodium (FENa) less than 1%: [(Urine Na + × serum creatinine) / (Serum Na + × urine creatinine)] × 100
    - Urine osmolality greater than serum osmolality
  - Suggestive of euvolemia or recent diuretic use
    - Urine Na+ greater than 20 mEq/L
  - Special consideration: Syndrome of inappropriate antidiuresis (SIADH)
    - Must exclude known stimuli of ADH release before labeling idiopathic
    - Must be clinically euvolemic
    - Urine sodium greater than 20 mEq/L
    - Urine osmolality greater than serum osmolality

HYPONATREMIA | Diagnosis and Evaluation

Causes of Syndrome of Inappropriate Antidiuresis

- Idiopathic
- Pulmonary disease
- Ectopic ADH production (e.g., small cell carcinoma of lung)
- Infections: meningitis, encephalitis, abscess, VZV
- Vascular: subarachnoid hemorrhage, CVA, temporal arteritis
- Severe nausea/vomiting
- Drugs: SSRIs, narcotics, cyclophosphamide, chlorpropamide
- Ecstasy ingestion (aggravated by
- HIV
- Prolactinoma
- Waldenström macroglobulinemia
- Shy-Drager syndrome
- Delirium tremens
- Oxytocin
- Marathon runner

HYPONATREMIA | Treatment

- **Treat underlying cause**
- **Hypovolemic hypo-osmolar:** Isotonic saline
- **Hypervolemic hypo-osmolar:** Fluid restriction, diuresis, dialysis
- **Euvolemic hypo-osmolar:** Fluid restriction, consider use of V2 receptor antagonists, address any contributing medical condition
  - V2 receptor antagonists (“vaptans”)
  - Block the V2 ADH receptor in collecting duct
  - Only for use in euvolemic (SIADH) and potentially hypervolemic disorders
  - Results in aquaresis without significant natriuresis
  - Hyponatremia will reoccur with discontinuation of drug if underlying cause not addressed
  - Demeclocycline is an older therapy to antagonize ADH action that is rarely used

HYPONATREMIA | Treatment

- **Severe CNS symptoms (e.g., seizure, obtundation):**
  - Raise Na+ concentration **1 to 2 mEq/L/hr** with **3% saline** until symptoms abate
- Rate of correction is usually proportional to rate at which hyponatremia developed
- **Chronic hyponatremia (>24-48 hours):**
  - Raise Na+ concentration **0.5 to 1 mEq/L/hr** and **no more than 8 to 10 mEq/L in 24 hours**
- **Acute hyponatremia (<24-36 hours):**
  - Can raise **1 to 2 mEq/L/hr** usually without the need for 3% saline unless severe CNS symptoms are present
- Rapid correction can result in prompt cerebral dehydration and irreversible osmotic demyelination of the CNS (i.e., central pontine myelinolysis)

HYPERNATREMIA

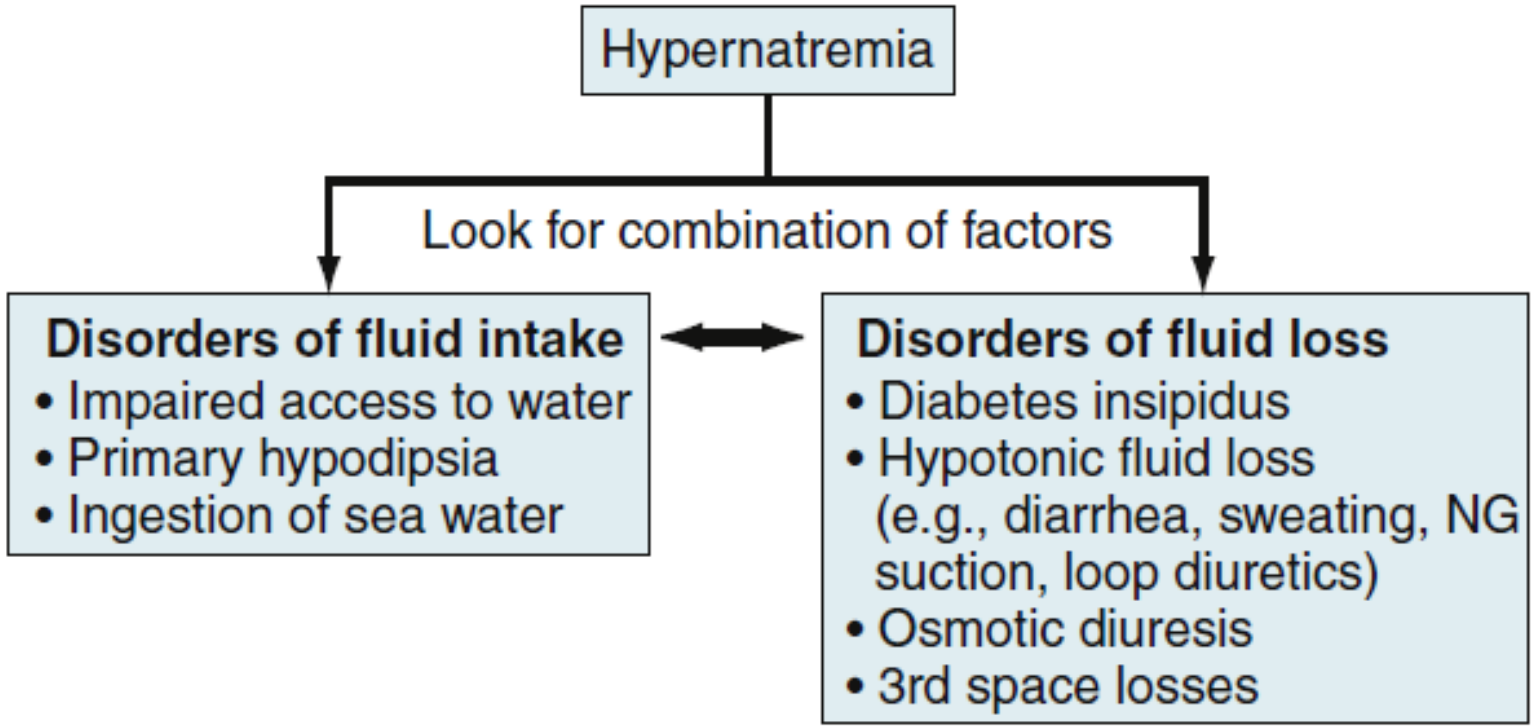
HYPERNATREMIA

- Serum Na+ concentration greater than **145 mEq/L**
- **Thirst** is the major defense against the development of hypernatremia
- Usually requires **impaired access to water** If free access to water is present, consider **impaired thirst mechanism**
- Most cases occur in **hospitalized** patients
- **Classic outpatient presentation:** Elderly nursing home resident with underlying infection

HYPERNATREMIA | Clinical Presentation

- Signs and symptoms are due to **dehydration** of the CNS
- As serum osmolality rises, water flows from inside cells of the CNS into the extracellular space along the osmolal gradient
- Patients may experience:
  - restlessness, irritability, lethargy
  - muscle twitching, hyperreflexia, spasticity
  - in severe cases, intracranial hemorrhage

HYPERNATREMIA



HYPERNATREMIA | Diagnosis and Evaluation

- Special consideration: **Diabetes insipidus (DI)**
  - **Insufficient ADH** action leads to polyuria and free water loss
  - **Central:** Lack of pituitary ADH production
  - **Nephrogenic:** Renal resistance to ADH action
  - High-normal to high serum Na+ concentration with
  - low urine osmolality (<300 mOsm/kg)
  - Differential diagnosis—Rule out polyuria due to:
    - Primary polydipsia
    - Diuretics
    - Osmotic diuresis (e.g., hyperglycemia)
    - Major causes of DI include pituitary tumor or apoplexy, lithium, hypercalcemia, hyperkalemia, and pregnancy

HYPERNATREMIA | Treatment

- **Address underlying cause**
- Overly rapid correction can result in cerebral edema
- If evidence of circulatory collapse, first correct hypovolemia with isotonic saline
- To calculate free water deficit:
- **Free water deficit = TBW × [(Serum sodium concentration / 140) − 1]**
- Decrease serum Na+ concentration approximately **0.5 mEq/L/hr** and **no more than 8 to 10 mEq/L in 24 hours**

Potassium Disorders

POTASSIUM BALANCE

- K+ is the **major intracellular** cation
- Intracellular K+ is maintained at a high concentration by the **3Na,2K-ATPase pump**
- 95% to 98% of total body K+ is stored **intracellularly**
- 80% of K+ excretion occurs via the **kidney**, with the remainder in the **stool** and **sweat**
- Renal K+ excretion increased by aldosterone
- Increased Na+ and water delivery to the distal nephron increases K+ excretion
- **Disorders of K+ concentration occur via:**
  - Gain or loss in total body K+ stores
  - Shifts between intracellular and extracellular compartments
- Changes in the electrical potential of cellular membranes lead to the major signs and symptoms

HYPOKALEMIA

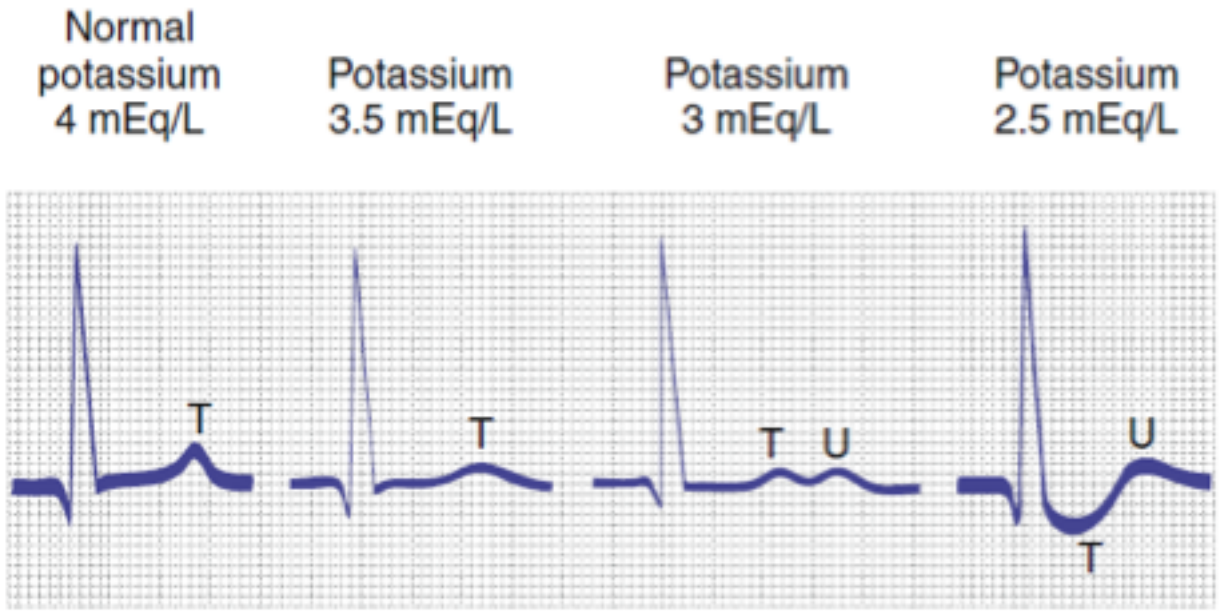
HYPOKALEMIA

- Serum K+ concentration **less than 3.5 mEq/L**
- In the absence of intracellular shifting, hypokalemia implies **low total body K+** Most commonly results when **K+ losses exceed intake**
- More rarely may result simply from **inadequate daily intake**

HYPOKALEMIA | Clinical Presentation

- May result in **fatigue** progressing to **muscle weakness** and **arrhythmia**, followed by **tetany** or **rhabdomyolysis** at K+ less than 2.5 mEq/L and then **paralysis** when less than 2 mEq/L
- Cardiac conduction is affected, resulting in **T-wave flattening**, the development of **U waves**, and **arrhythmias** (e.g., atrial tachycardia, atrioventricular dissociation, ventricular tachycardia, and ventricular fibrillation)
- Risk of arrhythmia is increased in the presence of high concentrations of digoxin
- Hypokalemia may **increase the risk of osmotic demyelination** when correcting hyponatremia
- If neurologically stable, **correct hypokalemia before correcting hyponatremia**

HYPOKALEMIA



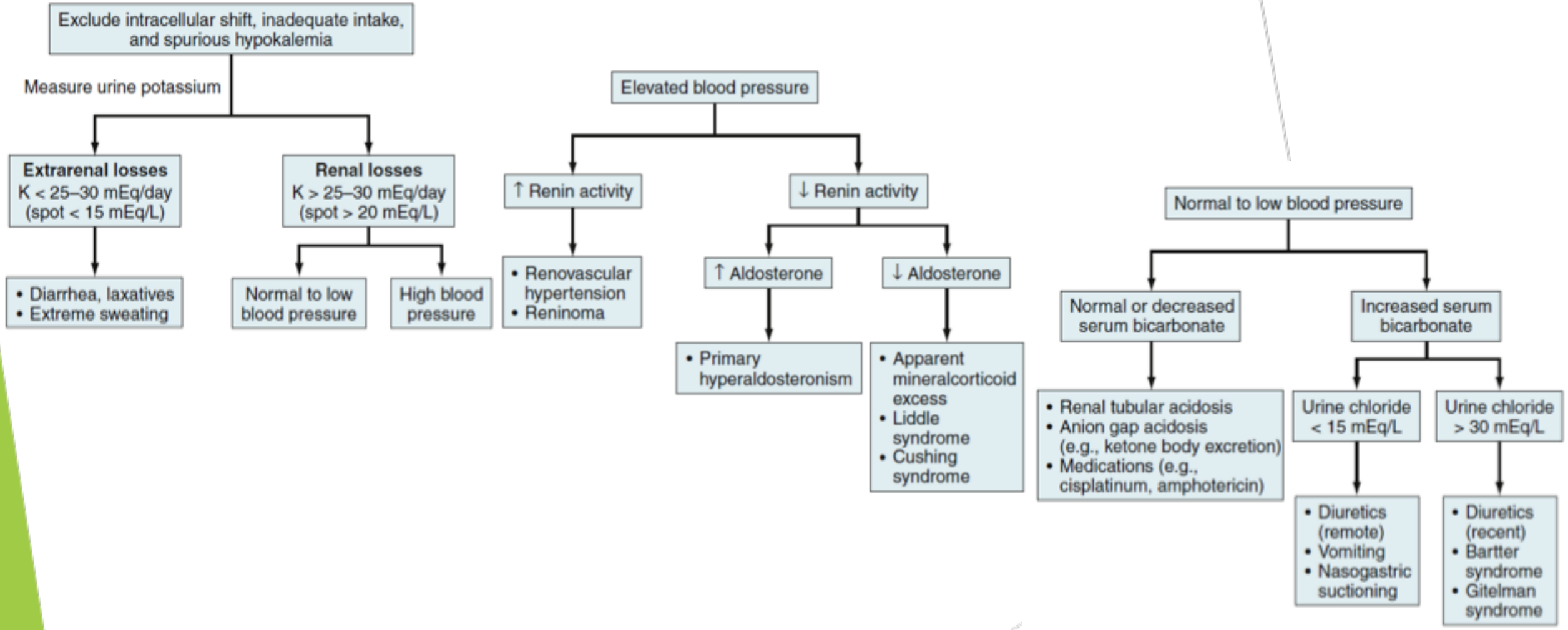
HYPOKALEMIA | Diagnosis and Evaluation

- Evaluate for **spurious hypokalemia**, **intracellular shift**, and **inadequate intake**
- **Spurious hypokalemia** due to increased uptake after venipuncture when leukocytosis greater than 100,000 cells/mm3 is present
- **Intracellular shift** due to insulin, ß-receptor stimulation, or alkalosis
- Classic example of intracellular shifting is **hypokalemic periodic paralysis**
  - Autosomal dominant inheritance—mutations in **CACNA1S** (Ca2+ channel) or **SCN4A** (Na+ channel)
  - Onset in childhood to adolescence
  - Attacks last for minutes to days and are of longer duration than in hyperkalemic periodic paralysis
  - Acquired form may be seen in **thyrotoxicosis**

HYPOKALEMIA | Diagnosis and Evaluation

- **Renal K+ wasting**
  - Urine K+ concentration greater than **25 to 30 mEq/day** or spot greater than **20 mEq/L** in the presence of normal urine output
- **Extrarenal K+ wasting**
  - Urine K+ concentration less than **25 to 30 mEq/day** or spot less than **15 mEq/L** in the presence of normal urine output

HYPOKALEMIA



HYPOKALEMIA | Treatment

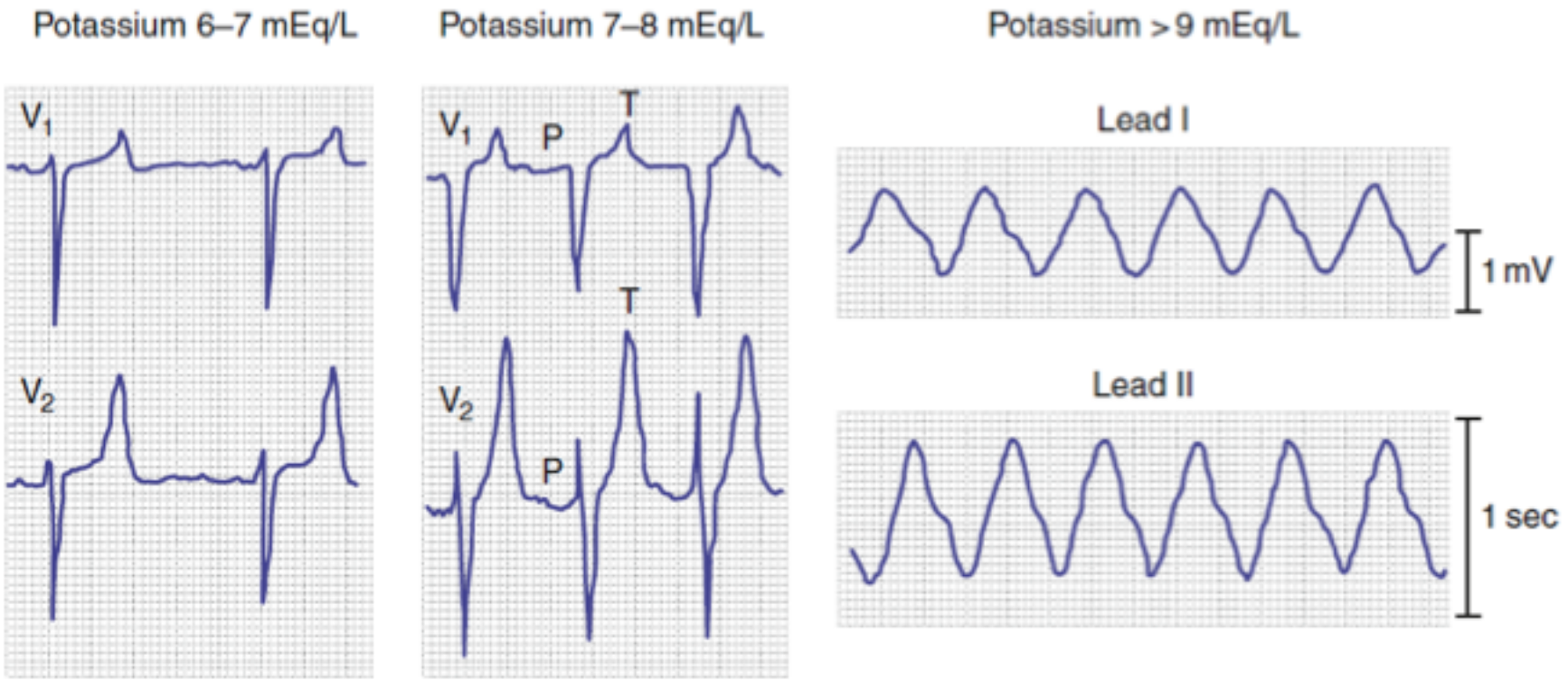
- **Investigate and treat underlying cause**
- Nature of treatment determined by degree of hypokalemia and presence or absence of symptoms
- Patients at increased risk of arrhythmia (e.g., digoxin therapy, coronary artery disease) merit more aggressive treatment
- In patients with total body depletion, serum K+ concentration of 3 mEq/L represents loss of approximately 200 to 300 mEq of K+
  - **K+ concentration 3 to 3.5 mEq/L:** Prevent further K+ loss and consider oral repletion
  - **K+ concentration less than 3 mEq/L:** Intravenous K+ repletion with cardiac monitoring should be considered
- **Hypomagnesemia** and **hypocalcemia** may render correction of hypokalemia more difficult and should be addressed prior to K+ repletion
- In patients with impaired renal function, intravenous K+ repletion can lead to

HYPERKALEMIA

HYPERKALEMIA | Clinical Presentation

- Serum K+ concentration **greater than 5.5 mEq/L**
- Rarely caused by excess intake alone, as normally functioning
- kidneys have a substantial excretory capacity
- **Mild elevations (5.5-6 mEq/L):** Usually asymptomatic
- **Greater than 6.5 mEq/L:** Progressive weakness, muscle aches, areflexia, paresthesia's, electrocardiogram (ECG) Changes
- **Greater than 7 mEq/L:** Paralysis, respiratory failure, life threatening arrhythmias
- ECG changes are not a sensitive marker for presence or severity of hyperkalemia
  - **6 to 7 mEq/L:** Peaked T waves (height >5 mm)
  - **7 to 8 mEq/L:** Widening of QRS complex, prolonged P-R interval with flattening of P wave

HYPERKALEMIA



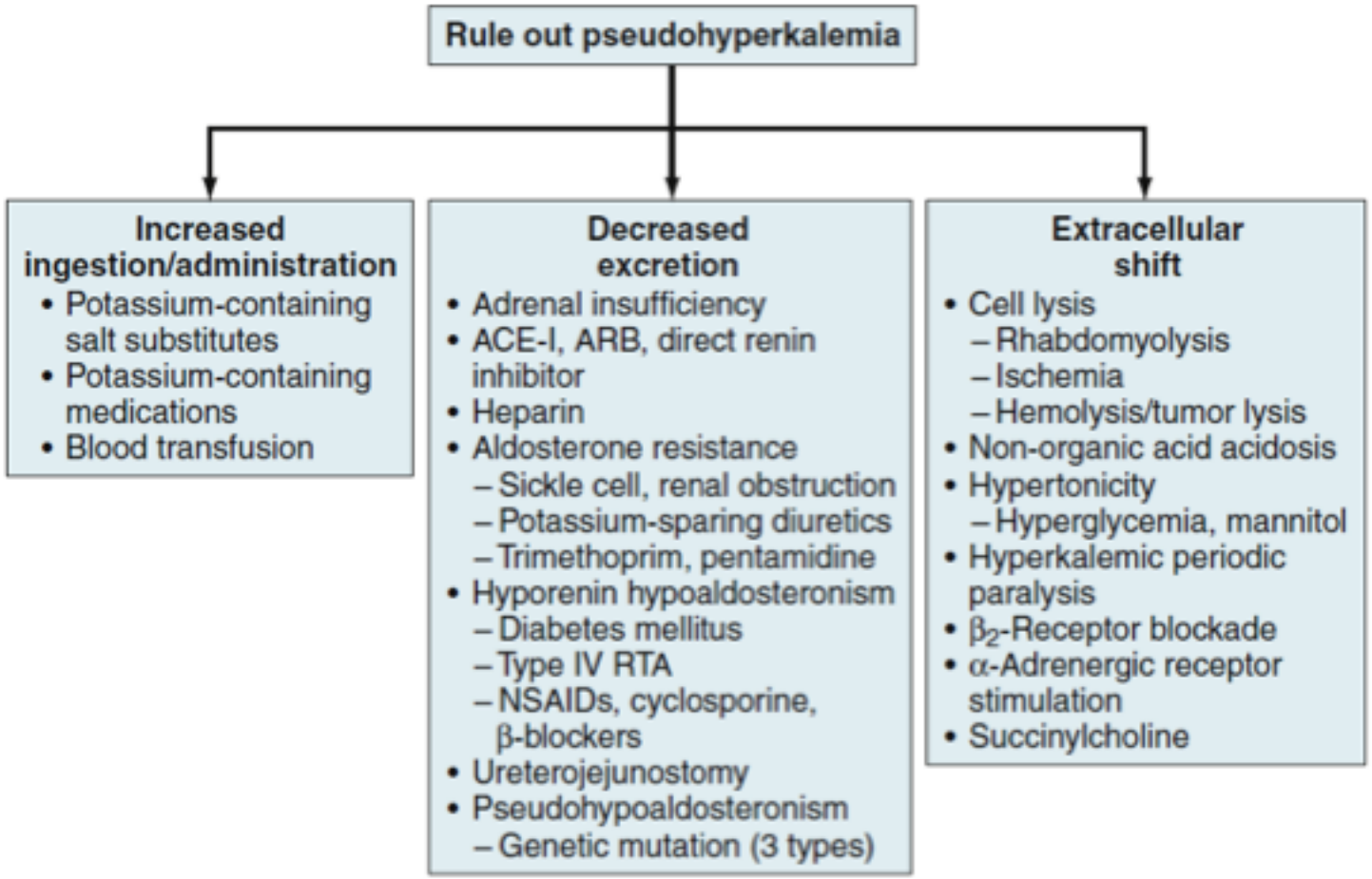
HYPERKALEMIA | Diagnosis and Evaluation

- Evaluate for extracellular shift and **pseudohyperkalemia**
- **Pseudohyperkalemia** may occur with:
  - Hemolysis during venipuncture
  - Leukocytosis greater than 100,000 cells/mm3 or
  - thrombocytosis greater than 500,000 cells/mm3. Plasma (as compared to serum) K+ should be normal.
- Classic example of extracellular shifting is hyperkalemic periodic paralysis
  - Autosomal dominant inheritance—mutation in SCN4A Na+ channel
  - Onset early in life
  - Attacks more frequent and of shorter duration than with hypokalemic periodic paralysis

HYPERKALEMIA | Diagnosis and Evaluation

- Evaluate for mechanisms of impaired renal excretion
- Calculate transtubular potassium gradient (TTKG):
- **TTKG = (Urine K / Plasma K) / (Urine Osm / Plasma Osm)**
- Value less than 5 suggests hypoaldosteronism or K+ secretory defect in setting of urine Na+ greater than 25 mEq/L and urine osmolality greater than plasma osmolality
- True utility of TTKG, however, is often quite limited

HYPERKALEMIA



HYPERKALEMIA | Treatment

- For K+ greater than 6.5 mEq/L or in the presence of ECG changes, administer **IV calcium** to decrease myocardial excitability
- **Decrease intake of K+**
  - Examine medications and dietary factors high in K+
  - Avoid medications that inhibit K+ secretion
- **Shift K+ intracellularly**
  - Correct hyperglycemia, if present
  - 10 units of regular insulin administered intravenously with an ampule of 50% dextrose in water (D50W) to prevent hypoglycemia
  - Consider IV bicarbonate, although effectiveness is marginal

HYPERKALEMIA | Treatment

- **Increase K+ elimination from the body**
  - Oral or rectal administration of a K+ exchange resin, sodium polystyrene sulfonate (SPS). One gram binds approximately 1 mEq K+ in vivo.
  - SPS is ineffective in patients with prior colectomy
  - Loop diuretics may be of utility in a stable patient with mild hyperkalemia
  - Dialysis if severe and life-threatening

Thank You