Hyponatremia

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Background: Hyponatremia is defined as a serum sodium concentration of less than 130 mEq/L. This is the most common electrolyte abnormality encountered in clinical practice, with an incidence of 1.5% of all pediatric hospital admissions. Symptoms and signs of hyponatremia are related to the absolute level and rate

of fall of serum sodium from baseline. Symptoms do not correlate with specific sodium levels. However, symptoms may appear when the serum sodium concentration is less than 125 mEq/L. Understanding the pathophysiology and treatment options is important because the morbidity and mortality of untreated hyponatremia are significant.

Pathophysiology:

Causes

Three general mechanisms are as follows:

1. Deficiency in sodium intake

2. Excessive loss of sodium (renal or extrarenal)

3. Excessive water retention

Risk factors

Because the human body protects itself from hyponatremia through an intact thirst mechanism, conditions associated with alteration in thirst mechanism are more prone to induce hyponatremia. For specific conditions, see History.

Hyponatremia rarely is caused by a deficient intake, except in infants fed with hypotonic fluids. The most common cause of hyponatremia in children is loss of sodium from the gastrointestinal (GI) tract. Diarrhea is responsible for most incidents of hyponatremia in children. Sodium loss also occurs via the kidneys. Diuretics are the most common culprit, followed by less common causes (eg, salt-losing nephritis, mineralocorticoid deficiency, cerebral salt-wasting syndrome).

Excessive antidiuretic hormone (ADH) secretion causes water retention and subsequent dilutional hyponatremia. Excessive secretion of ADH occurs in response to pain, nausea, vomiting, and morphine intake in postoperative patients and in children following spinal fusion. Excessive secretion of ADH can occur without physiologic stimuli (eg, increased serum osmolality, decreased intravascular volume); hence, the condition is named syndrome of inappropriate secretion of ADH (SIADH). Some drugs (eg, vincristine) also can cause SIADH. In patients with cirrhosis, cardiac failure, or renal failure, hyponatremia may be caused by one of many mechanisms.

Clinical manifestations vary from asymptomatic to severe neurologic dysfunction. CNS symptoms predominate in hyponatremia, although cardiovascular and musculoskeletal findings also are present. Three factors contribute to CNS symptoms as follows:

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1. Rate of change in serum sodium

2. Level of serum sodium

3. Duration of the abnormal serum sodium level

The gradual change in serum sodium, such as that observed with chronic hyponatremia, may not result in neurologic dysfunction even at serum sodium levels less than 100 mEq/L.

Central nervous system

When serum sodium declines, the decrease in serum osmolality results in an osmotic gradient across the blood-brain barrier causing water to move into the brain intracellular space. The resultant edema is responsible for symptoms such as headache, nausea, vomiting, irritability, and seizures. Animal studies have demonstrated that the brain swells only as much as 46% of the predicted level for a particular level of serum sodium when compared to other tissues after 6 hours of hyponatremia. This discrepancy becomes greater with time. This response of brain tissue indicates a significant degree of adaptation to hypo-osmolality. Thus, the subsequent amount of brain swelling is less than expected when considering osmotic gradient alone. The brain's adaptation to hyponatremia is accomplished by 2 mechanisms as follows:

1. Loss of interstitial fluid into the cerebrospinal fluid

2. Loss of cellular solute and organic osmolytes

When water moves into the brain, increasing hydrostatic pressure shifts interstitial fluid into cerebrospinal fluid, which subsequently is absorbed through the arachnoid villi. The interstitial fluid is rich in sodium, and, by removing this fluid, the brain equilibrates the osmolal gradient. In addition, intracellular solutes (eg, potassium) act similarly with a maximal response occurring in 24 hours. If hyponatremia lasts longer, intracellular amino acids extrude to maintain the osmolar gradient. This shifting of solutes and organic osmolytes plays an important role in protecting the brain from cerebral edema. The resultant hypo-osmolar state makes the brain vulnerable to dehydration secondary to rapid correction of hyponatremia. The optimum speed of correction is not known; however, rapid correction in fully compensated chronic hyponatremia results in a demyelinating lesion in the pons known as central pontine myelinosis (CPM). However, rapid correction in acute hyponatremia is well tolerated.

Cardiovascular response

Arterial blood volume may be increased, decreased, or normal depending on the underlying clinical condition. Intravascular volume is determined by distribution of water and solute in the intracellular

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space and extracellular space. Fluid shifts from extracellular space into intracellular space with a subsequent decrease in arterial blood volume. This may result in hypotension. Because of this fluid shift, hyponatremia causes more pronounced hemodynamic disturbance for a particular degree of dehydration.

Frequency:

- **In the US:** Frequency is 1.5% of hospitalized pediatric patients.

Sex: Incidence of hyponatremia is equal in both sexes; however, CNS complications are more likely among females who are menstruating.

History:

- Infants fed with hypotonic formula or free water
- Conditions causing GI fluid loss, such as through the following:
  - Diarrhea
  - Vomiting
  - Fistulas
- Renal disorders, including the following:
  - Salt-losing nephropathy
  - Acute renal failure
  - Chronic renal failure
- Postoperative states
- Psychiatric conditions
- Coma
- Drug use
- CNS and pulmonary diseases
- Hypothyroidism

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- Adrenal insufficiency
- Cirrhosis
- Congestive heart failure
- Acquired immune deficiency syndrome

Physical:

- Central nervous system
  - Early signs include the following:
    - Anorexia
    - Headache
    - Nausea
    - Emesis
  - Advanced signs include the following:
    - Impaired response to verbal stimuli
    - Impaired response to painful stimuli
    - Bizarre behavior
    - Hallucinations
    - Obtundation
    - Incontinence
    - Respiratory insufficiency
  - Far-advanced signs include the following:
    - Decorticate or decerebrate posturing
    - Bradycardia
    - Hypertension or hypotension
    - Altered temperature regulation
    - Dilated pupils
    - Seizure activity

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        - Respiratory arrest
        - Coma
- Cardiovascular
    - Hypotension
    - Renal failure as consequence of hypotension
    - Tachycardia
- Musculoskeletal
    - Weakness
    - Muscular cramps

Causes:

- Hypervolemic hyponatremia
    - Congestive heart failure
    - Cirrhosis
    - Nephrotic syndrome
    - Acute or chronic renal failure
- Hypovolemic hyponatremia due to renal loss
    - Diuretic excess
    - Osmotic diuresis
    - Salt-wasting diuresis
    - Adrenal insufficiency
    - Proximal renal tubular acidosis
    - Metabolic alkalosis
    - Pseudohypoaldosteronism
- Hypovolemic hyponatremia due to extrarenal loss
    - GI conditions, such as the following:
        - Vomiting

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        - Diarrhea
        - Tubes
        - Fistula
    - Sweat
    - Third-spacing conditions, such as the following:
        - Pancreatitis
        - Burns
        - Muscle trauma
        - Peritonitis
        - Effusions
        - Ascites
- Normovolemic hyponatremia
    - SIADH
        - Tumors (ie, adenocarcinoma of duodenum, adenocarcinoma of pancreas, carcinoma of ureter, carcinoma of prostate, Hodgkin disease, thymoma, acute leukemia, lymphosarcoma, histiocytic lymphoma)
        - Chest disorders (ie, infection [tuberculosis, bacterial, mycoplasmal, viral, fungal]), positive pressure ventilation, decreased left atrial pressure [pneumothorax, atelectasis, asthma, cystic fibrosis, mitral valve commissurotomy, patent ductus arteriosus ligation], malignancy)
        - Central nervous system disorders (ie, infection [tuberculous meningitis, bacterial meningitis, encephalitis], trauma, hypoxia-ischemia, psychosis, brain tumor, miscellaneous [Guillain-Barré syndrome, ventriculoatrial shunt obstruction, acute intermittent porphyria, cavernous sinus thrombosis, multiple sclerosis, anatomic abnormalities, vasculitis, stress, idiopathic])
        - Drugs (ie, chlorpropamide, vincristine, vinblastine, diuretics, clofibrate, carbamazepine, fluphenazine, amitriptyline, morphine, isoproterenol, nicotine, adenine arabinoside, colchicine, barbiturates)

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- Reset osmostat
- Glucocorticoid deficiency
- Hypothyroidism
- Water intoxication due to intravenous (IV) therapy, tap water enema, or psychogenic water drinking

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Lab Studies:

- Verify accuracy of laboratory results.
- Exclude pseudohyponatremia.
  - Flame emission spectrophotometry
    - If the sodium measurement is performed using flame emission spectrophotometry, hyponatremia is falsely low in patients with hyperproteinemia and hypertriglyceridemia.
    - Raised proteins and lipids increase the nonaqueous portion of plasma, which normally comprises 7% of the plasma.
    - Flame photometry measures the concentration of sodium present only in the aqueous portion of plasma.
    - However, newer ion-specific sodium electrodes measure sodium from the aqueous phase only, which reduces the likelihood of pseudohyponatremia.

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  - Correction factors for raised proteins and lipids

    Triglycerides (mg/dL) X .002 = mEq/L decrease in plasma sodium

    (Plasma protein level [g/dL] - 8) X 0.25 = mEq decrease in plasma

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sodium

Each 100-mg/dL rise in glucose greater than the serum glucose level of 100 mg/dL = 1.6 mEq/L decrease in sodium

- Exclude distributive hyponatremia: This condition occurs when plasma glucose concentration exceeds 100 mg/dL.
- Obtain routine laboratory studies.
    - Serum sodium
    - Serum osmolality
    - BUN and creatinine
    - Urine osmolality
    - Urine sodium
- Urine sodium level changes according to the type of hyponatremia as follows:
    - Hypovolemic hyponatremia
        - Renal losses caused by diuretic excess, osmotic diuresis, salt-wasting nephropathy, adrenal insufficiency, proximal renal tubular acidosis, metabolic alkalosis, and pseudohypoaldosteronism result in a urine sodium concentration greater than 20 mEq/L.
        - Extrarenal losses caused by vomiting, diarrhea, sweat, and third spacing result in a urine sodium concentration less than 20 mEq/L.
    - Normovolemic hyponatremia: When hyponatremia is caused by SIADH, reset osmostat, glucocorticoid deficiency, hypothyroidism, or water intoxication, urine sodium concentration is greater than 20 mEq/L.
    - Hypervolemic hyponatremia
        - If hyponatremia is caused by an edema-forming state (eg, congestive heart failure, cirrhosis, nephrotic syndrome), urine sodium concentration is less than 20 mEq/L.
        - If hyponatremia is caused by acute or chronic renal failure, urine sodium concentration is greater than 40 mEq/L.
- Special laboratory studies include the following:
    - Aldosterone
    - Cortisol
    - Thyroid function tests

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- Adrenocorticotropic hormone
- ADH

Imaging Studies:

- Neuroimaging
  - Skull radiographs: These images reveal intracranial pathology (eg, calcification, sutural diastasis, bone defects).
  - CT scan
    - CT scan is much more sensitive and specific than skull radiographs in delineating intracranial pathology.
    - CT scan is superior to MRI in delineating hemorrhage and calcifications.
    - Intracranial calcifications, intracranial tumor, hydrocephalus, and intracranial hemorrhage may be observed.
  - MRI: MRI is more sensitive than CT scan in detecting tumors.
- Abdominal imaging
  - Ultrasound: Ultrasound may reveal an abdominal mass in individuals with bilateral adrenal hyperplasia and adrenal tumor.
  - CT scan and MRI: These tests further delineate the tumor.

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Medical Care:

- Principles of treatment
  - The most common and devastating effects of hyponatremia are of CNS origin. Therefore, being aware of the risk factors that lead to hyponatremia is very important; recognizing and treating the condition appropriately is also very important.
  - Although it occurs slowly, an adaptation mechanism in the brain prevents deleterious effects of hypo-osmolality. However, this protective mechanism leaves the brain susceptible to dehydration during treatment, especially in persons with chronic hyponatremia, if the correction is rapid.
  - In children who present with acute hyponatremic seizures due to water intoxication from dilute formulas or excessive free water intake, obtaining a history of such intake is important. Once the diagnosis is reasonably certain, and even before laboratory data are available, correct hyponatremia with IV

bolus of 3% sodium chloride. Generally, seizures resulting from acute water intoxication are not responsive to antiepileptic drugs; however, such seizures respond very well to 3% sodium chloride. Consider IV furosemide to increase water excretion.

- In patients with chronic hyponatremia, correcting the sodium slowly is important to prevent potential demyelinating lesions. Optimal rate of correction is 0.5 mEq/h, not to exceed serum sodium of 125 mEq/L.

- Correction of sodium deficit
  - When using 3% sodium chloride to correct sodium deficit, use the following calculation:

    Sodium deficit = Weight in kg X 0.6 X (125 - observed sodium)

  - Each milliliter of 3% sodium chloride contains approximately 0.5 mEq Na/L. Administering 1 mL/kg of 3% sodium chloride raises the serum sodium by 1.6 mEq.

- Symptomatic hyponatremia
  - In individuals with hypovolemic hyponatremia, administer 3% sodium chloride to correct hyponatremia and 0.9% sodium chloride for intravascular volume expansion.
  - In persons with normovolemic hyponatremia, administer 3% sodium chloride to correct hyponatremia.
  - In persons with hypervolemic hyponatremia, administer 3% sodium chloride to raise the sodium level.

- Asymptomatic hyponatremia
  - In individuals with hypovolemic hyponatremia, use 0.9% sodium chloride for replacement and maintenance therapy.
  - In persons with normovolemic hyponatremia, restrict fluids (two-thirds maintenance or more) and administer diuretics (furosemide is preferred).
  - In persons with hypervolemic hyponatremia, restrict fluids (two-thirds maintenance or more).

Consultations:

- Transfer patients with symptomatic hyponatremia to a pediatric intensive care unit for appropriate treatment and close monitoring.
- Order an endocrinology consultation for patients with hypothyroidism or adrenal insufficiency.
- Order a nephrology consultation for patients with salt-losing nephropathies or renal

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failure.

Diet:

- Patients with salt-wasting disorders (eg, salt-losing nephropathies) need sodium supplementation throughout continued loss of excessive sodium.
- Patients with SIADH and renal failure require fluid restriction.

Medications include 3% sodium chloride (513 mEq/L sodium), normal saline (154 mEq/L sodium), diuretics, and other drugs used in persons with SIADH (eg, lithium carbonate, demeclocycline, ethanol, phenytoin, vasopressin analogs).

Drug Category: *Diuretics* -- Promote excretion of water and electrolytes by kidneys. Used to treat heart failure or hepatic, renal, or pulmonary disease when sodium and water retention has resulted in edema or ascites. May be used as monotherapy or combination to treat hypertension.

Drug Name	Furosemide (Lasix) -- Potent loop diuretic. Inhibits reabsorption of sodium and chloride in proximal and distal tubules and loop of Henle. High efficacy largely due to unique site of action. Action on distal tubule is independent of any possible inhibitory effect on either carbonic anhydrase or aldosterone.
Adult Dose	20-80 mg PO qd; may repeat dose after 6-8h; titrate not to exceed 600 mg/d if necessary Parenteral: 20-40 mg IV/IM, increasing by 20 mg q2h until desired response is achieved Administer IV doses slowly; infusion rate not to exceed 4 mg/min is recommended for patients receiving IV doses >120 mg or for patients with cardiac or renal failure
Pediatric Dose	0.5-2 mg/kg/d PO divided q6-12h, not to exceed 6 mg/kg/d Premature neonates: Oral bioavailability is poor; 1-4 mg/kg PO q12-24h has been used Parenteral: 1-2 mg/kg IV/IM q6-12h, not to exceed 6 mg/kg/d Premature neonates: 1-2 mg/kg IV/IM q12-24h
Contraindications	Documented hypersensitivity; hepatic coma; severe preexisting electrolyte imbalance (eg, hyponatremia, hypokalemia, hypocalcemia, hypochloremia, hypomagnesemia)

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Interactions	Furosemide-induced electrolyte disturbances (eg, hypokalemia, hypomagnesemia) can predispose patients to digitalis toxicity Mineralocorticoid activity (eg, cortisone, fludrocortisone, hydrocortisone) can cause additive hypokalemia Because amphotericin B, cisplatin, and other loop or thiazide diuretics can cause hypokalemia and hypomagnesemia, concomitant administration with any of these agents can lead to significant hypokalemia and/or hypomagnesemia Indomethacin may reduce diuretic and antihypertensive effects; use cautiously with other ototoxic agents (eg, capreomycin, carboplatin, chloroquine, cisplatin, deferoxamine, erythromycin, hydroxychloroquine, NSAIDs, quinine, salicylates, vancomycin)
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Caution in diabetes mellitus, ventricular arrhythmias, heart failure, potassium-losing nephropathy, aldosterone excess, diarrhea, severe renal impairment (dosage adjustment), and hyperuricemia Adverse effects include hyponatremia, hypokalemia, hypocalcemia, hypochloremia, hypomagnesemia, allergic interstitial nephritis, hyperuricemia, ototoxicity, glycosuria, hyperglycemia, hemolytic anemia, aplastic anemia, pancytopenia, leukopenia, neutropenia, thrombocytopenia, agranulocytosis, and pancreatitis Administer oral dose with food or milk to decrease stomach upset

Drug Category: *Antidiuretic hormone inhibitors* -- Produce diuresis by inhibition of ADH water reabsorption.

Drug Name	Lithium (Eskalith, Lithobid) -- Inhibits renal response to ADH.
Adult Dose	900-1200 mg PO divided tid/qid, not to exceed 2400 mg/d
Pediatric Dose	15-20 mg/kg/d PO divided tid/qid, not to exceed 2400 mg/d
Contraindications	Documented hypersensitivity; severe cardiovascular disease, renal impairment, or dehydration
	Potentiates effects of nondepolarizing neuromuscular blockers ACE inhibitors increase risk of lithium toxicity

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Interactions	Alkalinizing agents, particularly those that affect urinary pH, can increase renal clearance (eg, potassium acetate, potassium bicarbonate, potassium citrate, sodium bicarbonate, sodium citrate, sodium lactate, tromethamine); hypernatremia increases clearance Carbamazepine and fluoxetine may potentiate CNS effects Calcium-channel blockers may precipitate lithium neurotoxicity; this has been reported for both diltiazem and verapamil Lithium serum concentrations decrease during administration of caffeine, osmotic diuretics, and carbonic anhydrase inhibitors; concentrations increase during administration of thiazides and other distal tubule diuretics; concentrations may not change during administration of loop diuretics NSAIDs reduce excretion Concomitant use of chlorpromazine appears to affect kinetics of each drug; concomitant use of potassium iodide can increase likelihood of this adverse reaction
Pregnancy	D - Unsafe in pregnancy
Precautions	Although classified as pregnancy category D, sometimes lithium therapy may be warranted during pregnancy; however, warn patients about possible damage to fetus; if possible, withhold during first trimester Adverse effects include anorexia, ataxia, coma, confusion, diarrhea, drowsiness, dysgeusia, goitre, hypotension, hypothyroidism, leukemia, leukocytosis, myoclonia, nausea, vomiting, nephrotic syndrome, polydipsia, polyuria, seizures, sinus bradycardia, ST-T wave changes, tremor, visual impairment, weight gain, and xerostomia; administer with food to decrease GI adverse reactions Caution in women who are breastfeeding, hypothyroidism, hyponatremia, renal impairment, cardiac disease, sinus syndrome, psoriasis, preexisting seizure disorder, parkinsonism, organic brain syndrome, CNS impairment, attempted suicide, or history of alcohol or substance abuse
	Demeclocycline (Declomycin) -- Only tetracycline used in treatment of SIADH. Diuresis is produced by inhibition of ADH-induced water reabsorption in distal portion

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Drug Name	of convoluted tubules and collecting ducts of kidneys. Effects are observed within 5 d and are reversed within 2-6 d following cessation of therapy.
Adult Dose	600-1200 mg PO divided tid/qid
Pediatric Dose	>8 years: 7-13 mg/kg PO divided bid/qid
Contraindications	Documented hypersensitivity; do not use in children <8 y
Interactions	Antacids reduce absorption; calcium salts and magnesium salts present in foods and dairy products can form chelates with tetracyclines and impair absorption Ferrous sulfate and other iron salts can affect absorption of either demeclocycline or iron product Do not use sodium bicarbonate concurrently because of increased gastric pH unless administration of each agent can be separated by 1-3 h May increase action of warfarin Concomitant use of oral contraceptives containing estrogen may reduce their protection and increase incidence of breakthrough bleeding Methoxyflurane can increase potential for demeclocycline-induced nephrotoxicity Potentiates neuromuscular effects of nondepolarizing neuromuscular blockers
Pregnancy	D - Unsafe in pregnancy
Precautions	Caution in women who are breastfeeding Adverse effects include increased intracranial pressure, diarrhea, nausea, vomiting, epigastric distress and anorexia, hepatotoxicity, candidiasis (oral, rectal, or vaginal), photosensitivity, rashes, discolored nails, erythema multiforme, tooth discoloration, enamel hypoplasia, teratogenesis, neutropenia, eosinophilia, and Fanconi syndrome Administer 1 h before or 2-3 h after ingestion of milk or food

Drug Name	Phenytoin (Dilantin) -- Inhibits secretion of ADH.
Adult Dose	Loading: 15-20 mg/kg PO/IV Maintenance: 5-8 mg/kg PO/IV q8h
Pediatric Dose	Administer as in adults
Contraindications	Documented hypersensitivity; sinoatrial block, second-degree and third-degree AV block, sinus bradycardia, or Adams-Stokes

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	syndrome (unless pacemaker is present)
Interactions	Amiodarone, benzodiazepines, chloramphenicol, cimetidine, fluconazole, isoniazid, metronidazole, miconazole, phenylbutazone, succinimides, sulfonamides, omeprazole, phenacemide, disulfiram, ethanol (acute ingestion), trimethoprim, and valproic acid may increase toxicity Effects may decrease when taken concurrently with barbiturates, diazoxide, ethanol (long-term ingestion), rifampin, antacids, charcoal, carbamazepine, theophylline, and sucralfate May decrease effects of acetaminophen, corticosteroids, dicumarol, disopyramide, doxycycline, estrogens, haloperidol, amiodarone, carbamazepine, cardiac glycosides, quinidine, theophylline, methadone, metyrapone, mexiletine, oral contraceptives, and valproic acid
Pregnancy	D - Unsafe in pregnancy
Precautions	Caution in hematologic disease, dental disease, intermittent porphyria, hepatic disease, renal failure, radiation therapy, hypothyroidism, and systemic lupus erythematosus Rapid IV infusion can result in arrhythmias, marked hypotension, and cardiac arrest; infusion not to exceed 1 mg/kg/min CNS reactions include dizziness, drowsiness, nystagmus, ataxia, lethargy, coma, seizures, choreoathetosis, and dystonic reaction; severity increases as serum concentrations increase; while lethargy, dizziness, and drowsiness may occur at therapeutic serum concentrations, ataxia, coma, and drug-induced seizures usually occur at supratherapeutic concentrations GI effects include nausea, vomiting, constipation, abdominal pain, and gingival hyperplasia Dermatologic reactions include maculopapular rash and more serious responses (eg, bullous rash, exfoliative dermatitis, purpura, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis); can produce hypertrichosis or hirsutism (unusual growth of hair) in some patients Lupuslike symptoms have been described with use Lymph node reactions include lymphoid

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	hyperplasia, pseudolymphoma, pseudo-pseudolymphoma, and lymphoma Blood dyscrasias (eg, thrombocytopenia, leukopenia, granulocytopenia, agranulocytosis, pancytopenia, macrocytosis, megaloblastic anemia) Long-term therapy can lead to osteomalacia secondary to interference with vitamin D metabolism Has been associated with sexual dysfunction (eg, libido decrease, impotence, priapism) Injection contains 40% propylene glycol, which has caused cardiac arrhythmias when infused into dogs; never administer IM because phenytoin precipitates at injection site, producing delayed and erratic absorption Teratogenic agent, fetal hydantoin syndrome and manifestations include craniofacial features (eg, strabismus, broad and/or depressed nasal bridge, high-arched palate, smaller head circumference)

Deterrence/Prevention:

- Avoid administering hypotonic fluids when the patient is experiencing diarrhea.
- Carefully monitor patients receiving medications.
- Monitor serum electrolytes regularly in patients with brain tumors, intracranial infections, pulmonary infections, head trauma, and in patients following surgery, especially in those undergoing spinal fusion.
- Pay careful attention to fluid management in children with coma and other critical illnesses.

Complications:

- CPM in patients with chronic hyponatremia
  - This condition most commonly is observed in prepubescent children and women who are menstruating.
  - During chronic hyponatremia, the CNS undergoes significant adaptation by losing intracellular osmolytes in order to maintain the equilibrium between the intracellular and extracellular compartment. This change prevents the development of hyponatremia and makes cells susceptible to dehydration during treatment, especially if significant osmolar change in the extracellular environment exists. The resultant dehydration predominantly affects pontine

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regions where gray and white matter fibers are mixed together, resulting in CPM.

- A number of studies have demonstrated that cerebral demyelinating lesions develop only when patients with chronic hyponatremia have the following:
  - Inadvertent hyponatremia during treatment
  - An absolute increase in plasma sodium that exceeds 25 mmol/L in the first 24-48 hours of therapy
  - Hypoxic event
  - Severe liver disease
- Clinical features of CPM include the following:
  - Motor abnormalities that slowly progress to flaccid paralysis
  - Cranial nerve abnormalities manifested as dysphagia or pseudobulbar palsy
  - Alteration of mental status (eg, behavioral changes, depression of sensorium, lethargy, coma)
  - Seizures (uncommon)
  - Condition usually fatal in 3-5 weeks (however, survival increasingly reported, frequently with residual disability)
- MRI is superior to CT scan in CPM because MRI permits visualization of the brain stem and is sensitive to alterations in white matter. Lesions become apparent 1-2 weeks later.

Patient Education:

- Advise parents not to replace diarrheal fluid loss with hypotonic fluids such as tea and soda.

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Medical/Legal Pitfalls:

- Avoid rapid correction of chronic hyponatremia.
  - In persons with asymptomatic chronic hyponatremia, rapid correction may result in the severe neurologic impairment of CPM.
  - In individuals with acute symptomatic hyponatremia, initiate therapy with intravenous 3% sodium chloride, using an intravenous pump with the infusion

designed to raise plasma sodium at a rate of approximately 1 mmol/L per hour until 125 mEq/L is reached. Following resolution of symptoms, correction can proceed at a slower rate.

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