ELECTROLYTE DISTURBANCES

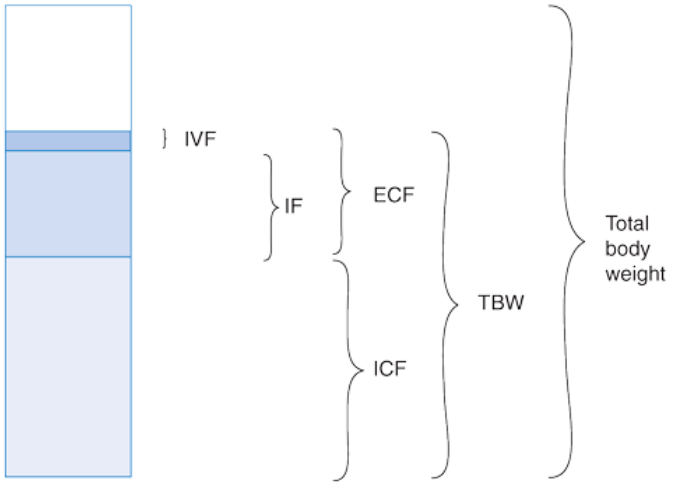
FLUIDS

COMPARTMENTS:

- TBW accounts for 60% of total body weight and is divided into INTRACELLULAR AND EXTRACELLULAR FLUID compartments
    - ECF comprised of intravascular and interstitial (extravascular) fluid

Figure 21-1.

As a function of	TBW	ICF	ECF	IF	IVF
Total weight	60%	40%	20%	15%	5%
TBW		67%	33%	25%	8%
ECF compartment				75%	25%



Relation of fluid compartment to body weight and each other. ECF = extracellular fluid; ICF = intracellular fluid; IF = interstitial (extravascular) fluid; IVF = intravascular fluid; TBW = total body water.

SOLUTES:

- Normal serum osmolarity ranges form 275-295mosm/L
    - The presence of additional osmotically active agents should be suspected when the measured osmolality differs from the calculated osmolality by more than ten → THE OSMOLAR GAP → could be the result of:
        - Lab error
        - Decreased serum water in the setting of high lipid or protein
        - Additional low-molecular eight substances in the serum → ethanol, methanol, ethylene glycol, acetone, lactate

HOMEOSTASIS:

- To maintain fluid balance, an average adult needs 2-3L per day, which accounts for insensible/urinary losses
    - Insensible loss can accelerate in the setting of fever (500mL per 1C), sweating and GI losses

ELECTROLYTES:

- Each electrolyte disorder can be assessed using the same approach
- In general → increased concentration of an electrolye is the result of:
    - EXCESS TOTAL BODY AMOUNT
    - SHIFT BETWEEN COMPARTMENTS
    - RELATIVE FLUID LOSS
- Similarly, decreased concentrations are a result of:
    - DEPLETED TOTAL BODY AMOUNT
    - SHIFT AMONG COMPARTMENTS
    - RELATIVE FLUID GAIN
- The RATE OF CHANGE, rather than the absolute concentrations usually determines the severity of symptoms
    - Correction of the electrolyte disturbance should occur over a time frame similar to the course during which the abnormality developed
- Concentrations of various electrolytes shown below:

Table 21-1 Electrolyte Concentrations of Fluids (mEq/L)

Solution	Plasma	Interstitial	Intracellular	Normal Saline	Lactated Ringer's Solution
Cations					
Sodium	142	144	10	154	130
Potassium	4	4.5	150	—	4
Magnesium	2	1	40	—	—
Calcium	5	2.5	—	—	3
Total cations	153	152	200	154	137
Anions					
Chloride	104	113	—	154	109
Lactate	—	—	—	—	28
Phosphates	2	2	120	—	—
Sulfates	1	1	30	—	—
Bicarbonate	27	30	10	—	—
Protein	13	1	40	—	—
Organic acids	6	5	—	—	—
Total anions	153	152	200	154	137

SODIUM [Na+]:

- Found predominantly in ECF space (98%), with a concentration of 140 meq/L (intracellular concentration is 10-12meq/L)

- Sodium moves passively into cells along its concetration gradient and is actively extruded via Na/K ATPase

HYPONATRAEMIA:

- Strictly defined as measured [Na+] of <135meq/L
- Results form:
    - PRIMARY WATER GAIN and or SODIUM LOSS (greater than that of water)
    - ALTERATION IN THE DISTRIBUTION OF BODY WATER
    - LAB ERROR
- Development of symptoms relates more to the rate of change
- Values <120 are more likely associated with symptoms, event when slowly developing and seizures are likely at levels <113
- PATHOPHYSIOLOGY:
    - CNS → as Na decreases, osmotic gradient develops across BBB, which draws water into the brain and leads to altered consciousness, agitation, headaches, seizures and even coma. Mortality rate in acute, severe hyponatraemia as high as 50%, but patients exhibit fewer symptoms when onset is slower.
        - If correction occurs more rapidly than the brain can recover solute, the higher plasma osmolality may result in a fluid shift out of cells and injury to the brain → OSMOTIC DEMYELINATION OR CENTRAL PONTINE MYELINOLYSIS
    - CARDIOVASCULAR → in volume-depleted patients, hyponatraemia can cause a further decrease in the intravascular volume by allowing movement of water out of the ECF into the ICF space. Thus, SHOCK WILL OCCUR AT LESSER DEGREES OF TBW DEPLETION
        - ADH is increased in almost all hyponatraemic states and this results in increased peripheral resistance
    - MUSCULOSKELETAL → cramps and weakness
    - RENAL → usual response is production of dilute urine, which is often cancelled out by ↑'d ADH
        - A urinary sodium of <10mEq/L usually indicates that the renal handling of sodium is intact. If urinary sodium >20, often indicates intrinsic renal tubular damage or a natriuretic response to hypervolaemia
- DIAGNOSIS:
    - The FIRST STEP in the evaluation of a patient with a low measured [na+] should include a clinical evaluation of ECF volume status and measured and calculated plasma osmolalities
        - In true hyponatraemia, the plasma osmolality is reduced and in factitious hyponatraemic states, the osmolality is normal or increased
- HYPERTONIC HYPONATRAEMIA (OSM >295)
    - Occurs when large quantitites of osmotically active solutes accumulate in the ECF→ net movement of WATER from ICF to ECF, thereby diluting the ECF

    - MOST COMMON CAUSE IS HYPERGLYCAEMIA → rough correction by adding 1/3 glucose level to measured sodium
- ISOTONIC HYPONATRAEMIA (OSM 275-295):
    - Often termed PSEUDOHYPONATRAEMIA and is often caused by high plasma proteins and lipids
    - No treatment required
- HYPOTONIC HYPONATRAEMIA (OSM <275):
    - Results from intracellular volume expansion with consequent derangement of cellular functions and can be further subdivided based on functional ECF volume and urinary [Na+]
    - HYPOVOLAEMIC HYPONATRAEMIA → associated with a disproportionate loss of [Na+] and water often with INADEQUATE water replacement. Manifestations are often due to the volume deficit and treatment is reexpansion of the ECF volume.
    - EUVOLAEMIC HYPONATRAEMIA → normal volume status, resent with symptoms related to CNS hypotonicity. SIADH → diagnosis of exclusion

Table 21-4 Diagnostic Criteria for Syndrome of Inappropriate Secretion of Antidiuretic Hormone
Hypotonic hyponatremia
Inappropriately elevated urinary osmolality (usually >200 mOsm/kg)
Elevated urinary [Na+] (typically >20 mEq/L)
Clinical euvolemia
Normal adrenal, renal, cardiac, hepatic, and thyroid functions
Correctable with water restriction

Table 21-5 Causes of Syndrome of Inappropriate Secretion of Antidiuretic Hormone

Central Nervous System Disease	Pulmonary Disease	Carcinoma
Tumor	Tumor	Lung
Trauma	Pneumonia	Pancreatic
Infection	Chronic obstructive pulmonary disease	Thymoma
Cerebral vascular accident, subarachnoid hemorrhage	Lung abscess	Ovarian
Guillain-Barré syndrome	Tuberculosis	Lymphoma
Delirium tremens	Cystic fibrosis	
Multiple sclerosis		

    - HYPERVOLAEMIC HYPONATRAEMIA → described as TBW in great excess and is characterised by an impaired ability to excrete a water load the results in water retention in excess of sodium retention
        - Management of this group includes optimising treatment for the underlying disorder coupled with salt and water restriction. Diuretics are usually added to aid in management
    - OUTLINE OF CAUSES OF HYPONATRAEMIA SHOWN BELOW:

Table 21-3 Causes of Hyponatremia
Hypertonic hyponatremia (P_{osm} >295)
Hyperglycemia
Mannitol excess
Glycerol therapy
Isotonic (pseudo) hyponatremia (P_{osm} 275–295)
Hyperlipidemia
Hyperproteinemia (e.g., multiple myeloma, Waldenström macroglobulinemia)
Hypotonic hyponatremia (P_{osm} <275)
Hypovolemic
Renal
Diuretic use
Salt-wasting nephropathy (renal tubular acidosis, chronic renal failure, interstitial nephritis)
Osmotic diuresis (glucose, urea, mannitol, hyperproteinemia)
Mineralocorticoid (aldosterone) deficiency
Extrarenal
Volume replacement with hypotonic fluids
GI loss (vomiting, diarrhea, fistula, tube suction)
Third-space loss (e.g., burns, hemorrhagic pancreatitis, peritonitis)
Sweating (e.g., cystic fibrosis)
Hypervolemic
Urinary [Na+] >20 mEq/L
Renal failure (inability to excrete free water)
Urinary [Na+] <20 mEq/L
Congestive heart failure (perceived as low-flow state by kidneys, stimulates ADH)
Nephrotic syndrome (low serum protein secondary to urinary loss)
Cirrhosis (low intravascular oncotic pressure secondary to decreased protein production)
Euvolemic (urine [Na+] usually >20 mEq/L)
Syndrome of inappropriate secretion of antidiuretic hormone (**Tables 21-4** and **21-5**)
Hypothyroidism (possible increased ADH or deceased glomerular filtration rate)
Pain, stress, nausea, psychosis (stimulates ADH)
Drugs: ADH, nicotine, sulfonylureas, morphine, barbiturates, NSAIDs, acetaminophen, carbamazepine, phenothiazines, tricyclic antidepressants, colchicine, clofibrate, cyclophosphamide, isoproterenol, tolbutamide, vincristine, monoamine oxidase inhibitor
Water intoxication (psychogenic polydipsia, lesion in thirst center)
Glucocorticoid deficiency (glucocorticoids required to suppress ADH)
Positive pressure ventilation
Porphyria
Essential (reset osmostat or sick cell syndrome—usually in the elderly)

EMERGENCY TREATMENT OF SEVERE HYPONATRAEMIA:

- There is generally little urgency to address the hyponatraemia immediately when [Na+] is >120
    - Becomes more urgent at levels below 115 or when the patient is symptomatic
- EVALUATION AND TREATMENT:
    - Urine electrolytes are ONLY USEFUL BEFORE BEGINNING TREATMENT AND THEREFORE SHOULD BE COLLECTED IN ED
    - In hypovolaemic patients, the sodium deficit should be calculated and replaced with normal saline
    - CALCULATION OF SODIUM DEFICIT → TOTAL DEFICIT = DESIRED [NA+] – ACTUAL PLASMA [NA+] X T.B.W. (BODY WEIGHT IN KILOGRAMS X 0.6) → this determines the mEq that need to be administered to reverse a sodium deficit
    - **THE RISE IN [NA+] SHOULD BE NO GREATER THAN 0.5-1MEQ/L PER HOUR → in the face of seizures, this can be increased to 1-2 mEq/L per hour**
        - Normal saline has 154 mEq/L, 3% saline has 513 mEq/L of sodium
        - If corrected faster than this, it is faster than the brain can adapt and results in CENTRAL PONTINE MYELINOLYSIS → contributing risk factors include alcoholism, malnutrition, toxins and metabolic imbalance. → typical cases include findings of fluctuating levels of consciousness, behavioural disturbances, dysarthria, dysphagia or convusions progressing to quadriparesis

<u>HYPERNATRAEMIA:</u>

PATHOPHYSIOLOGY:

- Defined as serum [Na+] >150 mEq/L
- Caused most commonly by decrease in total body water (less commonly by decreased Na intake). MOST CASES SEEN IN ED ARE DUE TO VOLUME LOSS
- Main defense against hypernatraemia is THIRST
- Primary causes are outlined below

Table 21-6 Causes of Hypernatremia
Inadequate water intake*
Inability to obtain or swallow water
Impaired thirst drive
Increased insensible loss
Excessive sodium
Iatrogenic sodium administration
Sodium bicarbonate
Hypertonic saline
Accidental/deliberate ingestion of large quantities of sodium
Substitution of salt for sugar in infant formula or tube feedings
Salt water ingestion or drowning
Mineralocorticoid or glucocorticoid excess*
Primary aldosteronism
Cushing syndrome
Ectopic adrenocorticotropic hormone production
Peritoneal dialysis
Loss of water in excess of sodium
GI*
Vomiting, diarrhea, intestinal fistula
Renal loss
Central diabetes insipidus
Impaired renal concentrating ability
Osmotic diuresis (multiple causes)*
Hypercalcemia
Decreased protein intake
Prolonged, excessive water intake
Sickle cell disease
Multiple myeloma
Amyloidosis
Sarcoidosis
Sjögren syndrome
Nephrogenic diabetes insipidus
Congenital
Drugs/medications
Alcohol, lithium, phenytoin, propoxyphene, sulfonylureas, amphotericin, colchicine
Skin loss
Burns, sweating
Essential hypernatremia

- **DIABETES INSIPIDUS:**

- Characterised by the FAILURE OF CENTRAL OR PERIPHERAL ADH RESPONSE
- Urine osmolality is LOW (200-300), with urinary sodium (60-100) resulting in excessive loss of hypotonic urine
- Causes are central (due to failure in secretion of ADH) or nephrogenic (lack of renal responsiveness to ADH) → see below:

Table 21-7 Causes of Diabetes Insipidus

Central	Nephrogenic
Neoplasms	Familial
Pituitary surgery	Hypercalcemia
Trauma	Hypokalemia
Granulomas	Renal disease
Idiopathic	Drug induced
	Hematologic disorders
	Malnutrition

- **Symptoms of DI** → rate of change is important. Symptoms usually seen above [Na+] 158. Neurologic symptoms predominate → irritability, increased muscle tone, seizures, coma, and death.
  - If plasma osmolality above 350, incidence of severe morbidity and mortality is >50%
  - Enough cellular fluid loss and resultant brain shrinkage can occur to cause tearing of cerebral blood vessels leading to brain haemorrhage
- DIAGNOSIS → note serum and urine osmolality and the response to 5 units of DESMOPRESSIN → patients with nephrogenic DI show little or no response to desmopressin, whereas central DI will lead to response in decreasing UO
- TREATMENT OF HYPERNATRAEMIA:
  - Cornerstone of treatment is VOLUME REPLETION → do first with normal saline or Hartmanns → EITHER WILL HAVE A LOWER [NA+] than the patients serum. Most hypernatraemic states have a total body sodium deficit and the use of NS allows a more gradual decrease in serum sodium.
  - Once perfusion has been establish, solution should be converted to 0.45% saline or another hypotonic solution
  - Reduction of sodium should not exceed 10-15mEq/L per day
  - Estimation of water deficit in litres = (measured Na/normal Na) -1

POTASSIUM:

- Elemental potassium is the MAJOR INTRACELLULAR CATION OF THE BODY → intracellular concentration is 100-150 mEq/L and the normal extracellular concentration is 3.5-5.0
- Excreted predominantly by the kidneys → freely filtered and then reabsorbed in the proximal and ascending tubules and is secreted in the distal tubule in exchange for sodium
- A decrease in measured serum [K+] from 4.0 to 3.0 represents a total body deficit of approximately 200-400 mEq as extracellular [K+] represents only about 2% of total body potassium
    - Extracellular K is influenced by total body stores and distribution between the ICF and ECF spaces
    - Significant intracellular to extracellular shifting occurs in response to:
        - Surgical stress
        - Trauma
        - Burns
        - Acid-base imbalance
        - Catabolic states
        - Insulin deficiency

HYPOKALAEMIA:

- PATHOPHYSIOLOGY:
    - The most frequent causes of hypokalaemia are intracellular shifts and increased losses
    - Potassium will also shift into cells as the pH of the ECF rises in exchange for hydrogen ions → a rise in pH of 0.10 generally cause a 0.5mEq/L decreases inserum [K+] levels in metabolic derangements → for unclear reasons, respiratory acid-base disturbance does not change potassium levels
    - SYMPTOMS BELOW:

Table 21-10 Symptoms and Signs of Hypokalemia
Cardiovascular
Hypertension
Orthostatic hypotension
Potentiation of digitalis toxicity
Dysrhythmias (usually tachydysrhythmias)
T-wave flattening, U waves, ST depression
Neuromuscular
Malaise, weakness, fatigue
Hyporeflexia
Cramps
Paresthesias
Paralysis
Rhabdomyolysis
GI
Ileus
Renal
Increased ammonia production
Urinary concentrating defects
Metabolic alkalemia, paradoxical aciduria
Nephrogenic diabetes insipidus
Endocrine
Glucose intolerance

- Causes are outlined below:

Table 21-9 Causes of Hypokalemia
Extracellular to intracellular potassium shifts
Alkalosis*
Increased plasma insulin (treatment of diabetic ketoacidosis)
β-Adrenergics
Hypokalemic periodic paralysis
Decreased intake
Poor dietary intake, geophagia
GI loss*
Vomiting, nasogastric suction, diarrhea (laxative, enema abuse), malabsorption, ureterosigmoidostomy, enteric fistula, villous adenoma
Renal loss
Diuretic therapy*
Primary aldosteronism
Secondary aldosteronism
Licorice ingestion
Excessive use of chewing tobacco
Renal tubular acidosis
Postobstructive diuresis
Osmotic diuresis
Drugs and toxins
Carbenicillin, penicillin, amphotericin B, l-dopa, lithium, thallium, theophylline, dopamine
Sweat loss
Heavy exercise, heat stroke, febrile illness
Other
Hypomagnesemia, acute leukemia, IV hyperalimentation, recovery from megaloblastic anemia

- **TREATMENT OF HYPOKALAEMIA:**
  - **REPLACEMENT OF POTASSIUM**
    - A cumulative dose of 20mEq will raise serum potassium by about 0.25mEq/L
    - CARDIAC MONITORING FOR MORE THAN 20MEQ/L/HOUR

HYPERKALAEMIA:

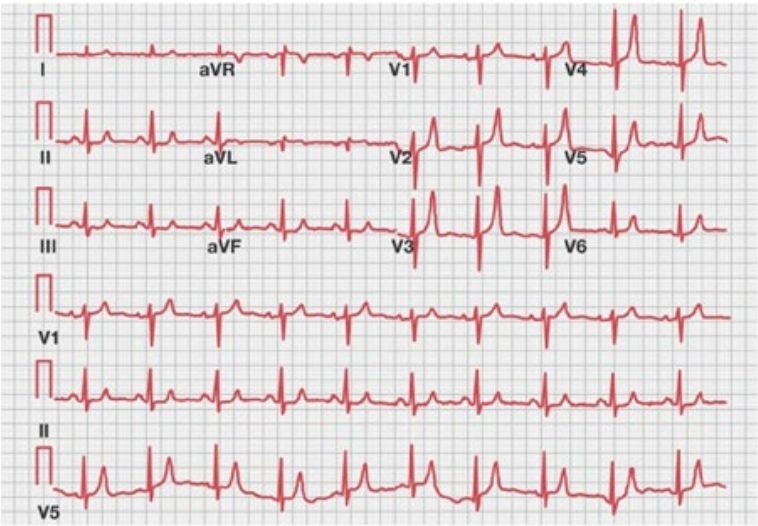
- PATHOPHYSIOLOGY:
  - Hyperkalaemia is defined as measrured serum K >5.5
  - Most common causes is factitious hyperkalaemia due to release of intracellular potassium caused by haemolysis during phlebotomy
  - Other causes are outlined below

Table 21-11 Causes of Hyperkalemia
Pseudohyperkalemia
Tourniquet use
Hemolysis (in vitro)*
Leukocytosis
Thrombocytosis
Intra- to extracellular potassium shift
Acidosis*
Heavy exercise
β-Blockade
Insulin deficiency
Digitalis intoxication
Hyperkalemic periodic paralysis
Potassium load
Potassium supplements
Potassium-rich foods
IV potassium
Potassium-containing drugs
Transfusion of aged blood
Hemolysis (in vivo)
GI bleeding
Cell destruction after chemotherapy
Rhabdomyolysis/crush injury*
Extensive tissue necrosis
Decreased potassium excretion
Renal failure*
Drugs—potassium-sparing diuretics,* β-blockade, NSAIDs, angiotensin-converting enzyme inhibitors
Aldosterone deficiency*
Selective defect in renal potassium excretion
Pseudohypoaldosteronism, systemic lupus erythematosus, sickle cell disease, obstructive uropathy, renal transplantation, type IV renal tubular acidosis

- Clinical manifestations usually result from disordered membrane polarisation with cardiac manifestations being the most common. ECG changes are outlined below. It is important to note that chronic or slowly developing hyperkalaemia will develop ECG changes at higher [K] levels. Cardiac arrhythmia (VF, CHB, asystole) may occur. Other symptoms include neuromuscular weakness, paraesthesie, areflexia, ascending paralysis and GI upset

Table 21-12 ECG Changes Associated with Hyperkalemia

[K+] (mEq/L)	ECG Changes
6.5–7.5	Prolonged PR interval, tall peaked T waves, short QT interval
7.5–8.0	Flattening of the P wave, QRS widening
10–12	QRS complex degradation into a sinusoidal pattern



ECG with peaked T waves in hyperkalaemia

- TREATMENT OF HYPERKALAEMIA:
  - Obtain ECG → if no cardiac derangements, the initial step in treatment of hyperkalaemia is to confirm the presence of nonfactitious hyperkalaemia by a repeat sample
  - Asymptomatic patients with relatively small derangements (K 5-6) require determination and treatment of the underlying cause
  - EMERGENCY TREATMENT DIVIDED INTO THREE PHASES:
    - MEMBRANE STABILISATION (calcium)
    - INTRACELLULAR SHIFT OF POTASSIUM (insulin/dextrose, salbutamol)
    - REMOVAL OR EXCRETION OF POTASSIUM FROM THE BODY (resonium, frusemide, dialysis)
      - SEE TABLE BELOW FOR OUTLINE OF TREATMENT OPTIONS
      - If calcium is to be given to a patient on digoxin, great caution as HYPERCALCAEMIA potentiates the toxic cardiac effects of digoxin

Table 21-13 Emergency Therapy of Hyperkalemia

Therapy	Dose and Route	Onset of Action	Duration of Effect	Mechanism
Albuterol (nebulized)	2.5 milligrams in 4 mL normal saline, nebulized over 20 min	15–30 min	2–4 h	Upregulates cyclic adenosine monophosphate, shifts [K+] into cell
Calcium chloride (10%)*	5–10 mL IV	1–3 min	30–50 min	Membrane stabilization
Calcium gluconate (10%)*	10–20 mL IV	1–3 min	30–50 min	Membrane stabilization
$NaHCO_3$	50–100 mEq IV	5–10 min	1–2 h	Shifts [K+] into cell
Insulin and glucose	5–10 units regular insulin IV	30 min	4–6 h	Shifts [K+] into cell
	1–2 amps D50W IV			
Furosemide	40 milligrams IV	Varies	Varies	Renal [K+] excretion
Sodium polystyrene sulfonate	25–50 grams PO or PR	1–2 h	4–6 h	GI [K+] excretion
Hemodialysis	—	Minutes	Varies	Removes [K+]

CALCIUM:

- Calcium is the most abundant mineral in the body, 99% being bound to bone as phosphate and carbonate, with the remained in the ECF compartment
- Primarily absorbed in the small bowel by active (vitamin D dependent) and passive (concentration-dependent) mechanisms
    - Excretion via stool
- Intravascular calcium exists as 50% bound to plasma proteins, 45% free active ions (ionised) and 5% nonionised
    - THE IONISED FRACTION IS THE PHYSIOLOGICALLY ACTIVE COMPONENT
    - Alkalosis produces a decrease in ionised fraction with no change in serum Ca2+, each 0.1 rise lowers ionised [Ca2+] by 3-8%. Acidosis produces an increased in ionised fraction

HYPOCALCAEMIA:

- PATHOPHYSIOLOGY:
    - Defined as ionised level <1.05-1.13 mmol/L)
    - Common causes are SHOCK, SEPSIS, RENAL FAILURE AND PANCREATITIS (other causes listed below)

Table 21-14 Some Causes of Hypocalcemia
Decreased calcium absorption
Vitamin D deficiency
Malabsorption syndromes
Increased calcium excretion
Alcoholism
Chronic renal insufficiency
Diuretics
Endocrine disorders
Hypoparathyroidism
Pseudohypoparathyroidism
Drugs (**Table 21-15**)
Miscellaneous
Sepsis
Acute pancreatitis
Massive transfusions
Hypomagnesemia
Rhabdomyolysis

    - CELLULAR DYSFUNCTION:
        - Any process that interferes with cellular metabolism will result in net movement of Ca across the cell membrane

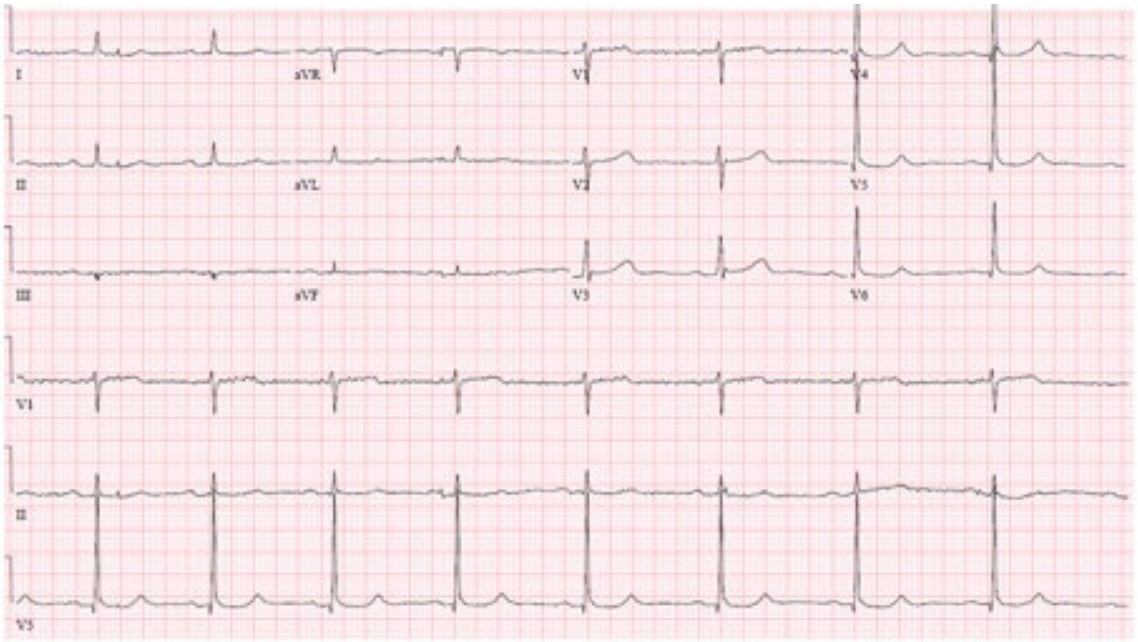
- PANCREATITIS:
  - Pancreatic lipase breaks down fat into fatty acids and glycerol
  - The fatty acids combine with Calcium to form insoluble calcium soaps and lead to reduction in serum Ca
- DRUGS → NUMEROUS IMPLICATED:

Table 21-15 Drugs that Can Cause Hypocalcemia
Phosphates (e.g., enemas, laxatives)
Phenytoin, phenobarbital
Gentamicin, tobramycin, actinomycin
Cisplatin
Heparin
Theophylline
Protamine
Glucagon
Norepinephrine
Citrate
Loop diuretics
Glucocorticoids
Magnesium sulfate
Sodium nitroprusside

- POST-OPERATIVE HYPOCALCAEMIA:
  - Approximately 10% of post-parathyroidectomy patients may have hypoPTH
- RENAL FAILURE:
  - Frequent finding
  - May be due in part to resulting HYPERPHOSPHATAEMIA but also due to decreased production of vitamin D → decreases intestinal absorption of calcium
- PHOSPHATE OVERLOAD → rhabdomyolysis, major trauma

- SYMPTOMS OF HYPOCALCAEMIA:
  - Serious changes usually do not occur until IONISED CALCIUM REACHES 0.7-0.8MMOL/L.
  - Severity of symptoms and signs depends greatly on the rapidity of the decrease, with neurons becoming more permeable to sodium and thus becoming more EXCITABLE
  - Decreased ionised calcium reduces strength of myocardial contractility by inhibiting relaxation
  - CHVOSTEK SIGN → twitch at the corner of the mouth when tapping over the facial nerve
  - TROUSSEAU SIGN → more reliable, positive if carpal spasm is produced when the examiner applies a blood pressure cuff to the upper arm and maintains a pressure above systolic for 3 minutes

Table 21-16 Symptoms and Signs of Hypocalcemia
General
Weakness, fatigue
Neurologic
Tetany
Chvostek sign, Trousseau sign
Circumoral and digital paresthesias
Impaired memory, confusion
Hallucinations, dementia, seizures
Extrapyramidal disorders
Dermatologic
Hyperpigmentation
Coarse, brittle hair
Dry, scaly skin
Cardiovascular
Heart failure
Vasoconstriction
Muscular
Spasms, cramps
Weakness
Skeletal
Osteodystrophy
Rickets
Osteomalacia
Miscellaneous
Dental hypoplasia
Cataracts
Decreased insulin secretion



ECG of patient with hypocalcaemia that demonstrates prolonged QT interval (true QT prolongation)

- TREATMENT OF HYPOCALCAEMIA:
    - Tailored to individual presentation and directed toward the underlying cause
    - If minor deficiency → oral replacement with vitamin D may be sufficient
    - IV calcium recommended only in cases of symptomatic or SEVERE hypocalcaemia (ionised <0.65mmol/L), because IV calcium can cause vasoconstriction and possible ischaemia, especially in patients with low cardiac output
    - 10mL of CaCl2 can be given as a bolus over 10-20 minutes followed by a continuous IV infusion at 0.02-0.08mL/kg/hour (1.2-5.6mL/h in 70kg patient)
    - Be very cautious in patients on digoxin
    - IT IS VERY DIFFICULT TO CORRECT HYPOCALCAEMIA IF THE PATIENT ALSO HAS **HYPOMAGNESAEMIA** → as hypomagnesaemic states reduce PTH and calcium releases from bone → concurrent magnesium replacement is important

HYPERCALCAEMIA:

- PATHOPHYSIOLOGY:
    - Relatively common and is defined as an ionised calcium >1.3mmol/L
    - More than 90% of occurrences are associated with hyperPTH or malignancy, the latter being the most likely underlying presentation in ED
    - See list of causes below:

Table 21-17 Causes of Hypercalcemia
Malignancy*
Lung (squamous cell cancer)
Breast
Kidney
Myeloma
Leukemia
Endocrinopathies
Primary hyperparathyroidism
Hyperthyroidism
Pheochromocytoma
Adrenal insufficiency
Acromegaly
Drugs
Hypervitaminosis D and A
Thiazides
Lithium*
Hormonal therapy for breast cancer
Granulomatous disease*
Sarcoidoses
Tuberculosis
Histoplasmosis
Coccidioidomycosis
Immobilization
Miscellaneous
Paget disease of bone
Postrenal transplantation
Recovery from acute renal failure
Phosphate depletion syndrome

*More likely to be encountered in the ED.

- SYMPTOMS OF HYPERCALCAEMIA:
  - A mneumonic sometimes used for the signs and symptoms of hypercalcaemia is:
    - STONES → RENAL CALCULI
    - BONES → OSTEOLYSIS
    - MOANS → PSYCHIATRIC DISORDERS
    - ABDOMINAL GROANS → PEPTIC ULCER DISEASE, PANCREATITIS, CONSTIPATION
  - See below for list of symptoms and signs of hypercalcaemia:

Table 21-18 Symptoms and Signs of Hypercalcemia

General	Cardiovascular
Malaise, weakness	Hypertension
Polydipsia, dehydration	Dysrhythmias
Neurologic	Vascular calcifications
Confusion	ECG abnormalities
Apathy, depression, stupor	QT shortening
Decreased memory	Coving of ST-T wave
Irritability	Widening of T wave
Hallucinations	Digitalis sensitivity
Headache	GI
Ataxia	Anorexia, weight loss
Hyporeflexia, hypotonia	Nausea, vomiting
Mental retardation (infants)	Constipation
Metastatic calcification	Abdominal pain
Band keratopathy	Peptic ulcer disease
Conjunctivitis	Pancreatitis
Pruritus	Urologic
Skeletal	Polyuria, nocturia
Fractures	Renal insufficiency
Bone pain	Nephrolithiasis
Deformities	

- TREATMENT OF HYPERCALCAEMIA:
  - Should be initiated in ANY SYMPTOMATIC PATIENT and consists of:
    - VOLUME REPLETION (WITH NORMAL SALINE)
    - DECREASING CALCIUM MOBILISATION FROM BONE (PAMIDRONATE, 90MG IV OVER 24 HOURS OR ZOLEDRONIC ACID 4MG IV OVER 15 MINUTES → WORK BY POTENT INHIBITION OF OSTEOCLAST-MEDIATED BONE RESORPTION
    - CORRECTION OF UNDERLYING DISORDER

- USE OF LOOP-DIURETICS NO LONGER ADVOCATED

MAGNESIUM:

- Total body content is 24 grams, 50-70% of which is fixed in bone and only slowly exchangeable, the remained is in the ICF space. It is the secondmost abundant intracellular cation
- Mg promotes enzyme reactions within the cell during metabolism, assists production of ATP and plays many other physiological roles

HYPOMAGNESAEMIA:

- PATHOPHYSIOLOGY:
  - Wide variety of problems can cause hypomagnesaemia (see below)
  - Most frequently seen in adults with those with alcoholism, malnutrition and those with cirrhosis, pancreatitis or excessive GI fluid losses
  - Treatment of DKA without adequate provision of Mg can cause an abrupt fall in plasma magnesium levels

Table 21-19 Causes of Hypomagnesemia
Redistribution
Postparathyroidectomy
IV glucose
Correction of diabetic ketoacidosis
IV hyperalimentation
Refeeding after starvation
Acute pancreatitis
Extrarenal loss
Nasogastric suction (infrequent)
Lactation
Profuse sweating, burns, sepsis
Intestinal or biliary fistula
Diarrhea
Decreased intake
Alcoholism (cirrhosis)
Malnutrition, poor intake
Small-bowel resection
Malabsorption
Increased renal loss
Ketoacidosis
Drugs
Loop diuretics
Aminoglycosides
Amphotericin B
Vitamin D intoxication
Alcohol
Cisplatin
Syndrome of inappropriate antidiuretic hormone
Hyperthyroidism
Hyperparathyroidism
Hypercalcemic states
Primary or secondary aldosteronism
Tubulointerstitial renal disease
Saline or osmotic diuresis
Potassium depletion
Familial hypophosphatemia

- SYMPTOMS:
  - INCREASED NEUROMUSCULAR IRRITABILITY COMMON → hyperreflexia, Chvostek and Trousseau sign
  - ECG changes → ↑PR, QT, widened QRS, ST depression → similar to hypokalaemia, hypocalcaemia

Table 21-20 Symptoms and Signs of Hypomagnesemia
Neuromuscular
Tetany
Muscle weakness
Cerebellar (ataxia, nystagmus, vertigo)
Confusion, obtundation, coma
Seizures
Apathy, depression
Irritability
Paresthesias
GI
Dysphagia
Anorexia, nausea
Cardiovascular
Heart failure
Dysrhythmias
Hypotension
Miscellaneous
Hypokalemia
Hypocalcemia
Anemia

- TREATMENT:
    - Hypokalaemia, hypocalcaemia, and hypophosphataemia often present with severe hypomagnesaemia and must be monitored carefully
    - Approximately half of administered magnesium will be lost in the urine

HYPERMAGNESAEMIA:

- PATHOPHYSIOLOGY:
    - Rarely encountered in ED and a small elevation has little clinical significance
    - Most commonly seen in those with renal impairment who take magnesium-containing drugs

Table 21-21 Causes of Hypermagnesemia
Renal failure
Acute or chronic
Increased magnesium load
Magnesium-containing laxatives, antacids, or enemas*
Treatment of preeclampsia/eclampsia (mothers and neonates)
Diabetic ketoacidosis (untreated)*
Tumor lysis
Rhabdomyolysis*
Increased renal magnesium absorption
Hyperparathyroidism
Familial hypocalciuric hypercalcemia
Hypothyroidism
Mineralocorticoid deficiency, adrenal insufficiency

- SYMPTOMS AND SIGNS (SEE BELOW):

Table 21-22 Symptoms and Signs of Hypermagnesemia	
Level (mEq/L)	**Symptom**
2.0–3.0	Nausea
3.0–4.0	Somnolence
4.0–8.0	Loss of deep tendon reflexes
8.0–12.0	Respiratory depression
12.0–15.0	Hypotension, heart block, cardiac arrest

- EVALUATION AND TREATMENT → IMMEDIATE CESSATION OF MAGNESIUM, DILUTION BY IV FLUIDS, CALCIUM IF SEVERE AND SYMPTOMATIC

CHLORIDE:

- Alteration in serum chloride is seldom a primary disturbance
- Chloride is a major extracellular anion that plays a major role in the maintenance of urinary output, ECF, acid/base and potassium balance
- HYPOCHLORAEMIA:
  - Usually caused by excessive diuresis, vomiting or NG drainage
  - Volume loss leads to alkalosis
  - Treatment is aimed at acute manifestations associated with the underlying cause
    - The treatment of chloride response metabolic alkalosis is saline administration
- HYPERCHLORAEMIA:
  - Usually result of excessive saline administration, volume depletion and treatment aimed at underlying cause

PHOSPHURUS:

- Exists mainly as hydroxyapatite (85%) or as an intracellular constituent (10-15%)
- Only about 1% is in the ECF, so serum measures donot reflect total body stores
- Serum calcium and phosphate are inversely proportional
- Phosphorus absorption is proportion to dieteary intake with excretion being predominantly through the urine → freely filtered in the glomerulus and majority resorbed by the proximal tubules, regulated by PTH
- Phosphate is essential to a wide variety of biochemical reactions → especially energy metabolism

HYPOPHOSPHATAEMIA:

- PATHOPHYSIOLOGY:

- Because phosphorus is abundant in many foods, hypophosphataemia is relatively unusual
- Causes → movement of phosphate into cells (with alkalosis), increased renal excretion and decreased GI absorption. Other causes → prolonged anabolic stress, recovery from starvation or severe burns, partial hepatectomy

- SYMPTOMS:
  - Low levels are well tolerated

Table 21-23 Symptoms and Signs of Hypophosphatemia
Hematologic
Reduced survival of platelets and red and white blood cells
Impaired platelet function
Spherocytosis
Tissue hypoxia secondary to decreased 2,3-diphosphoglycerate
Impaired macrophage function
Neuromuscular
Weakness
Tremors
Circumoral and fingertip paresthesias
Decreased deep tendon reflexes
Decreased mental status
Anorexia
Hyperventilation
Cardiac
Impaired myocardial function

  - Should be sought as a potential complication after initiation of treatment of DKA or alcholic ketoacidosis
- EASILY REVERSIBLE WITH REPLACEMENT

HYPERPHOSPHATAEMIA:

- PATHOPHYSIOLOGY:
  - May be due to reduced renal excretion, increased phosphate movement out of cells or increased phosphorus or vitamin D intake
- SYMPTOMS USUALLY RELATED TO OTHER CONDITIONS
- TREATMENT → with normal renal function, phosphate excretion can be increased with IV saline.
  - Phosphurus absorption can be decreased from the GI tract with administration of PHOSPHATE BINDERS (caltrate, magmin, sevelamer)