ELECTROLYTES and Acid Base Imbalance

Dr. Robin Paudel

The Buffering System

- **Acid-base buffers** confer resistance to a change in the pH of a solution when hydrogen ions (protons) or hydroxide ions are added or removed.
- An acid-base buffer typically consists of a **weak acid**, and its **conjugate base** (salt).
- Buffers work because the concentrations of the weak acid and its salt are large compared to the amount of protons or hydroxide ions added or removed.
- When protons are added to the solution from an external source, some of the base component of the buffer is converted to the weak-acid component (thus using up most of the protons added); when hydroxide ions are added to the solution (or, equivalently, protons are removed from the solution, protons are dissociated from some of the weak-acid molecules of the buffer, converting them to the base of the buffer (and thus replenishing most of the protons removed).
- However, the change in acid and base concentrations is small relative to the amounts of these species present in solution. Hence, the **ratio** of acid to base changes only slightly. Thus, the effect on the pH of the solution is small, within certain limitations on the amount of H^+ or OH^- added or removed.

The Carbonic-Acid-Bicarbonate Buffer in the Blood

- By far the most important buffer for maintaining acid-base balance in the blood is the carbonic-acid-bicarbonate buffer.

$$H^+(aq) + HCO_3^-(aq) \rightleftharpoons H_2CO_3(aq) \rightleftharpoons H_2O(l) + CO_2(g)$$

- Metabolic problems : left side
- Respiratory problems : right side
- Normal blood arterial values:
  - pH = 7.35-7.45
  - pCO_2 = 40 mm Hg
  - HCO_3^- = 22- 24 mmol/ L

Acid Base Imbalance

- Four primary disturbances in the system are recognized, each of which results in an altered concentration of H+. The basic deviations from normal can be either an acidosis (excess H+) or an alkalosis (deficiency of H+), which in either case may be caused by either a respiratory or a metabolic problem.
- RespiratoryProblems
- Respiratory Acidosis
  - Caused by a decrease in alveolar ventilation relative to the total body production of CO_2 (hypoventilation). The result is an increase in PCO_2 which causes an increase in H+ (or decrease in pH) and an increase in HCO_3^-.
  - Note that for every H+ produced during the development of respiratory acidosis, one HCO_3^- is also produced. Some rise in HCO_3^- will always occur in uncompensated respiratory acidosis. But in most cases, the HCO_3^- will not rise out of its normal range.
  - cause: increase in $PaCO_2$
  - result: decrease in pH
  - slight increase in HCO_3^-

- Respiratory Alkalosis
  - Caused by an increase in alveolar ventilation relative to body production of CO_2 (hyperventilation). The decrease in CO_2 causes a decrease in H+ (increased pH) and a decrease in HCO_3^-.
  - Note that for every H+ consumed, one HCO_3^- is also consumed. Some decrease in HCO_3 – will alwaysoccur in uncompensated respiratory alkalosis.
  - Summary
    - cause: decrease in $PaCO_2$
    - result: decrease in H+ (increased pH)
    - slight decrease in HCO_3^-

- Metabolic Problems
  - A gain in H+ as fixed acid (i.e., one not due to a respiratory effect) is equivalent to the direct loss of HCO_3^-
  - Either change will produce the same overall effect on H+ (or pH).
  - Also, there is a greater change in HCO_3^- in an uncompensated metabolic disturbance than in an uncompensated respiratory disturbance.
- MetabolicAcidosis
  - Caused by a gain in fixed acid.
  - The increased H+ forces the reaction to the right, decreasing HCO_3^-.
  - Forcing the reaction to the right will produce some CO_2,but, by convention, if there is no respiratory compensation for the metabolic problem, no significant change in arterial PCO_2 is considered to have taken place.
  - cause: gain in H+ as fixed acid (or a loss in HCO_3^- via GI tract or kidney)
  - result: decrease in HCO_3^-

Metabolic Alkalosis

- Caused by a loss of fixed acid. The decreased H+ forces the reaction to the left, increasing HCO_3-.
- cause: loss in H+ as fIxed acid (or a gain in HCO_3-)
- result: increase in HCO_3-

Dr. Robin Paudel

Summary of the Changes in the Uncompensated State

	CO_2	pH	HCO_3^-
1. Respiratory acidosis	↑	↓	↑
2. Respiratory alkalosis	↓	↑	↓
3. Metabolic acidosis	no change	↓	↓↓
4. Metabolic alkalosis	no change	↑	↑↑

Dr. Robin Paudel

- **Acidosis**
  - If the pH is depressed, it is an acidosis.
  - If the CO_2 is elevated, there is a respiratory component to the acidosis (but it could also include a metabolic component).
  - If there is an acidosis and the $CO_2$is not elevated, the only possible explanation is the presence of a metabolic acidosis (bicarbonate must be reduced).
  - If the CO_2 is elevated and the bicarbonate is depressed, it is a combined respiratory and metabolic acidosis.
- **Alkalosis**
  - If the pH is elevated, it is an alkalosis.
  - If the $CO_2$is depressed, there is a respiratory component to the alkalosis (but it could also include a metabolic component).
  - If there is an alkalosis and the CO_2 is not depressed, the only possible explanation is the presence of a metabolic alkalosis (bicarbonate must be elevated).
  - If the $CO_2$is depressed and the bicarbonate is elevated, it is a combined respiratory and metabolic alkalosis.

Dr. Robin Paudel

Combined Disturbances

- If the CO_2 and HCO_3- change in opposite directions, it is a combined disturbance. It is either a combined respiratory and metabolic acidosis or a combined respiratory and metabolic alkalosis.

Dr. Robin Paudel

Compensations

- **Respiratory Compensation**
  - This will occur only in a metabolic disturbance and can begin almost immediately.
  - Metabolic acidosis-compensation is a hyperventilation. The hyperventilation reduces CO_2 ,shifting the reaction to the right and consuming H+.
  - Metabolic alkalosis-compensation is a hypoventilation. The hypoventilation increases CO_2, shifting the reaction to the left and producing H+.

Dr. Robin Paudel

Renal Compensation

- This can occur in a respiratory and/or metabolic disturbance. However, if the kidney is the source of the metabolic disturbance, only respiratory compensation will be significant.
- The kidney has the ability to change plasma bicarbonate. To lower plasma bicarbonate, the kidney excretes HCO_3- in the urine. To raise plasma bicarbonate, the kidney has the capability to generate new HCO_3- (distal tubule collecting duct) and secrete it into the general circulation.
- Renal compensation is slower than respiratory compensation, taking days to fully develop.
- Acidosis-compensation is HCO_3- production by the kidney and its secretion into the circulation.
- This will shift the reaction to the right and consume H+. During renal compensation, plasma HCO_3- should slowly increase.
- For every HCO_3- produced by the kidney, one H+ will be excreted in the urine (acid urine).
- Alkalosis-compensation is HCO_3- excretion (alkaline urine). This will shift the reaction to the left and generate H+. During renal compensation, plasma HCO_3- should slowly decrease.

Dr. Robin Paudel

Electrolyte Imbalance

- Hyponatremia
- Hypernatremia
- Hypokalemia
- Hyperkalemia
- Hypercalcemia
- Hypocalcemia

Dr. Robin Paudel

Hyponatremia

- Normal level : 135 – 145/150 mEq/L
- The imbalance between sodium and water in your blood may occur in three primary ways:
  - **In hypervolemic hyponatremia,** excess water dilutes the sodium concentration, causing low sodium levels. Hypervolemic hyponatremia is commonly the result of kidney failure, heart failure or liver failure.
  - **In euvolemic hyponatremia,** normal water levels are combined with low sodium levels. This condition is commonly due to chronic health conditions, cancer or certain medications.
  - **In hypovolemic hyponatremia,** your water and sodium levels are both low. This may occur, for example, when exercising in the heat without replenishing your fluid electrolytes or with marked blood loss.

Dr. Robin Paudel

- **Causes of hyponatremia**
  Many possible conditions and lifestyle factors can lead to hyponatremia, including:
  - **Consuming excessive water during exercise (exertional hyponatremia).** Because you lose sodium through sweat, drinking too much water during endurance activities, such as marathons can dilute the sodium content of your blood.
  - **Hormonal changes due to adrenal gland insufficiency (Addison's disease).** Your adrenal glands produce hormones that help maintain your body's balance of sodium, potassium and water.
  - **Hormonal changes due to an underactive thyroid (hypothyroidism).** Hypothyroidism may result in a low blood-sodium level.
  - **Water pills (diuretics) — especially thiazide diuretics.** Diuretics work by making your body excrete more sodium in urine.
  - **Syndrome of inappropriate anti-diuretic hormone (SIADH).**In this condition, high levels of the anti-diuretic hormone (ADH) are produced, causing your body to retain water instead of excreting it in your urine.

Dr. Robin Paudel

- **Primary polydipsia.** In this condition, your thirst increases significantly, causing you to drink excessive amounts of fluid.
- **Certain medications.** Some medications, such as some antidepressants can cause you to urinate or perspire more than normal.
- **The recreational drug Ecstasy.** This amphetamine causes a ripple effect on the body's ADH and water levels that — especially when combined with heavy drinking — increases the risk of severe and even fatal cases of hyponatremia.
- **Chronic, severe vomiting or diarrhea.** This causes your body to lose fluids and electrolytes, such as sodium.
- **Diet.** A low-sodium, high-water diet can disturb the proper balance between sodium and fluids in your blood. Excessive intake of diuretics, including beer, can have the same effect.
- **Cirrhosis.** Liver disease can cause fluids to accumulate in your body.
- **Kidney problems.** Kidney failure and other kidney disease may render your body unable to efficiently remove excess fluids from your body.
- **Congestive heart failure.** This condition causes your abdomen and lower extremities to retain fluids.

Dr. Robin Paudel

- ***Hyponatremia in AIDS:*** Hyponatremia has been reported in > 50% of hospitalized patients with AIDS. Among the many potential contributing factors are
  - Administration of hypotonic fluids
  - Impaired renal function
  - Nonosmotic ADH release due to intravascular volume depletion
  - Administration of drugs that impair renal water excretion
  - In addition, adrenal insufficiency has become increasingly common in AIDS patients as the result of cytomegalovirus adrenalitis, mycobacterial infection, or interference with adrenal glucocorticoid and mineralocorticoid synthesis by ketoconazole

  . SIADH may be present because of coexistent pulmonary or CNS infections.

Dr. Robin Paudel

- Hyponatremia: signs and symptoms may include:
  - Nausea and vomiting
  - Headache
  - Confusion
  - Lethargy
  - Fatigue
  - Appetite loss
  - Restlessness and irritability
  - Muscle weakness, spasms or cramps
  - Seizures
  - Decreased consciousness or coma
- As the serum Na falls to < 115 mEq/L, stupor, neuromuscular hyperexcitability, hyperreflexia, seizures, coma, and death can result.

Dr. Robin Paudel

Treatment of Hyponatremia:

- When hypovolemic, 0.9% saline
- When hypervolemic, fluid restriction and sometimes a diuretic
- When euvolemic, treatment of cause
- Rarely, cautious correction with hypertonic (3%) saline

- Rapid correction of hyponatremia, even mild hyponatremia, risks neurologic complications (Osmotic demyelination syndrome). Except possibly in the first few hours of treatment of severe hyponatremia, Na+ should be corrected no faster than 0.5 mEq/L/h. Even with severe hyponatremia, increase in serum Na concentration should not exceed 10 mEq/L over the first 24 h. Any identified cause of hyponatremia is treated concurrently.
- ***Mild hyponatremia:*** Mild, asymptomatic hyponatremia (ie, serum Na > 120 mEq/L) requires restraint because small adjustments are generally sufficient. In diuretic-induced hyponatremia, elimination of the diuretic may be enough; some patients need some Na or K replacement. Similarly, when mild hyponatremia results from inappropriate hypotonic parenteral fluid administration in patients with impaired water excretion, merely altering fluid therapy may suffice.
  - A. With **hypovolemia** and normal adrenal function, administration of 0.9% saline usually corrects both hyponatremia and hypovolemia. When the serum Na is < 120 mEq/L, hyponatremia may not completely correct upon restoration of intravascular volume; restriction of free water ingestion to ≤ 500 to 1000 mL/24 h may be needed.

Dr. Robin Paudel

- B. In ~~hypervolemic patients~~, in whom hyponatremia is due to renal Na retention (eg, heart failure, cirrhosis, nephrotic syndrome) and dilution, water restriction combined with treatment of the underlying disorder is required. In patients with heart failure, an ACE inhibitor, in conjunction with a loop diuretic, can correct refractory hyponatremia. In other patients in whom simple fluid restriction is ineffective, a loop diuretic in escalating doses can be used, sometimes in conjunction with IV 0.9% normal saline. K and other electrolytes lost in the urine must be replaced. When hyponatremia is more severe and unresponsive to diuretics, intermittent or continuous hemofiltration may be needed to control ECF volume while hyponatremia is corrected with IV 0.9% normal saline.

- C. In **euvolemia,** treatment is directed at the cause (eg, hypothyroidism, adrenal insufficiency, diuretic use). When SIADH is present, severe water restriction (eg, 250 to 500 mL/24 h) is generally required. Additionally, a loop diuretic may be combined with IV 0.9% saline as in hypervolemic hyponatremia. Lasting correction depends on successful treatment of the underlying disorder. When the underlying disorder is not correctable, as in metastatic cancer, and patients find severe water restriction unacceptable, demeclocycline (300 to 600 mg q 12 h) may be helpful by inducing a concentrating defect in the kidneys; however, demeclocycline may cause acute renal failure. Renal failure is usually reversible when the drug is stopped. IV conivaptan, an ADH receptor antagonist, causes effective water diuresis without significant loss of electrolytes in the urine and can be used in hospitalized patients for treatment of resistant hyponatremia.

Dr. Robin Paudel

- ***Severe hyponatremia:***
  - Severe hyponatremia (serum Na < 109 mEq/L; effective osmolality< 238 mOsm/kg) in asymptomatic patients can be treated safely with stringent restriction of water intake. Treatment is more controversial when neurologic symptoms (eg, confusion, lethargy, seizures, coma) are present. The debate primarily concerns the pace and degree of hyponatremia correction. Many experts recommend that serum Na be raised no faster than 1 mEq/L/h, but replacement rates of up to 2mEq/L/h for the first 2 to 3 h have been suggested for patients with seizures. Regardless, the rise should be ≤ 10 mEq/L over the first 24 h. More vigorous correction risks precipitation of osmotic demyelination syndrome.

Dr. Robin Paudel

Osmotic demyelination syndrome:

- Osmotic demyelination syndrome (previously called central pontine myelinolysis)
- too-rapid correction of hyponatremia.
- Demyelination may affect the pons and other areas of the brain. Lesions are more common in patients with alcoholism, undernutrition, or other chronic debilitating illness.
- Flaccid paralysis, dysarthria, and dysphagia can evolve over a few days or weeks. The lesion may extend dorsally to involve sensory tracts and leave patients with a locked-in syndrome (an awake and sentient state in which patients, because of generalized motor paralysis, cannot communicate, except possibly by coded eye movements).
- Damage often is permanent. When Na is replaced too rapidly (eg, > 14 mEq/L/8 h) and neurologic symptoms start to develop, it is critical to prevent further serum Na increases by stopping hypertonic fluids. In such cases, inducing hyponatremia with hypotonic fluid may mitigate the development of permanent neurologic damage.

Dr. Robin Paudel

Hypernatremia

- Several risk factors exist for hypernatremia. The greatest risk factor is age older than 65 years. In addition, mental or physical disability may result in impaired thirst sensation, an impaired ability to express thirst, and/or decreased access to water.
- Types:
  - Hypotonic fluid deficits (loss of water and electrolytes)
  - Nearly pure-water deficits
  - Hypertonic sodium gain (gain of electrolytes in excess of water).

Dr. Robin Paudel

- **A. Loss of hypotonic fluid (loss of water in excess of electrolytes)**
  - Patients who lose hypotonic fluid have a deficit in free water and electrolytes (low total body sodium and potassium) and have decreased extracellular volume. In these patients, hypovolemia may be more life threatening than hypertonicity. When physical evidence of hypovolemia is present, fluid resuscitation with normal saline is the first step in therapy.
  - Renal hypotonic fluid loss - Results from anything that will interfere with the ability of the kidney to concentrate the urine or osmotic diuresisDiuretic drugs (loop and thiazide diuretics)
  - Osmotic diuresis (hyperglycemia, mannitol, urea [tube feeding])
  - Renal salt wasting
  - Postobstructive diuresis
  - Diuretic phase of acute tubular necrosis
  - Nonrenal hypotonic fluid lossGastrointestinal - Vomiting, diarrhea, lactulose, cathartics, nasogastric suction, gastrointestinal fluid drains, and fistulas
  - Cutaneous - Sweating (extreme sports, marathon runs), burn

Dr. Robin Paudel

- **B. Pure-water deficits**
  - Patients with pure-water deficits in the majority of cases have a normal extracellular volume with normal total body sodium and potassium. This condition most commonly develops when impaired intake is combined with increased insensible (eg, respiratory) or renal water losses.
  - Free-water loss will also result from an inability of the kidney to concentrate the urine. The cause of that can be either from failure of the hypothalamic-pituitary axis to synthesize or release adequate amounts of AVP (central diabetes insipidus) or a lack of responsiveness of the kidney to AVP (nephrogenic diabetes insipidus). Patients with diabetes insipidus and intact thirst mechanisms most often present with normal plasma osmolality and serum NA +, but with symptoms of polyuria and polydipsia.
  - Water intake less than insensible lossesLack of access to water (through incarceration, restraints, intubation, immobilization)
  - Altered mental status (through medications, disease)
  - Neurologic disease (dementia, impaired motor function)
  - Abnormal thirst
    - Geriatric hypodipsia
    - "Essential" hypernatremia with osmoreceptor dysfunction (reset of the osmotic threshold).
    - Injury to the thirst centers by any lesions to the hypothalamus, including from metastasis, granulomatous diseases, vascular abnormalities, and trauma.
  - Loss of pure water through the respiratory tract

Dr. Robin Paudel

- **Vasopressin (AVP) deficiency (diabetes insipidus)**
  - Central diabetes insipidus can be caused by any pathologic process that destroys the anatomic structures of the hypothalamic-pituitary axis involved in AVP production and secretion. Such processes include the following:
  - Pituitary injury - Posttraumatic, neurosurgical, hemorrhage, ischemia (Sheehan' s), idiopathic-autoimmune
  - Tumors - Craniopharyngioma, pinealoma, meningioma, germinoma, lymphoma, metastatic disease, cysts
  - Aneurysms - Particularly anterior communicating
  - Inflammatory states and granulomatous disease - Acute meningitis/ encephalitis, Langerhans cell histiocytosis, neurosarcoidosis, tuberculosis
  - Drugs - Ethanol (transient), phenytoin
  - Genetic - Neurophysin-AVP gene defect
  - **Nephrogenic diabetes insipidus (decreased responsiveness of the kidney to vasopressin)**
  - Genetic - V2-receptor defects, aquaporin defects (AQP2 and AQP1)
  - Structural - Urinary tract obstruction, papillary necrosis, sickle-cell nephropathy
  - Tubulointerstitial disease - Medullary cystic disease, polycystic kidney disease, nephrocalcinosis, Sj ö gren' s syndrome, lupus, analgesic-abuse nephropathy, sarcoidosis, M-protein disease
  - Electrolyte disorders -Hypercalcemia, hypokalemia
  - Any prolonged state of severe polyuria - By washing out the renal medullary-intramedullary concentration gradient needed for urinary concentration, and by down-regulating kidney AQP2 water channels

Dr. Robin Paudel

- Medications that induce nephrogenic diabetes insipidus
  - Lithium
  - Amphotericin B
  - Demeclocycline
  - Dopamine
  - Ofloxacin
  - Orlistat
  - Ifosfamide
- Medications that possibly cause nephrogenic diabetes insipidus
  - Contrast agents
  - Cyclophosphamide
  - Cidofovir
  - Ethanol
  - Foscarnet
  - Indinavir
  - Libenzapril
  - Mesalazine
  - Methoxyflurane
  - Pimozide
  - Rifampin
  - Streptozocin
  - Tenofir
  - Triamterene hydrochloride
  - Cholchicine

Dr. Robin Paudel

- **Gestational diabetes insipidus**
  - In this form of diabetes insipidus, AVP (Arginine Vasopressin Peptide) is rapidly degraded by a high circulating level of oxytocinase/vasopressinase. It is a rare condition, because increased AVP secretion will compensate for the increased rate of degradation. Gestational diabetes insipidus occurs only in combination with impaired AVP production.
- **C. Hypertonic sodium gain**
  - Patients with hypertonic sodium gain have a high total-body sodium and an extracellular volume overload (rare, mostly iatrogenic). When thirst and renal function are intact, this condition is transient.
  - Administration of hypertonic electrolyte solutions - Eg, sodium bicarbonate solutions, hypertonic alimentation solutions
  - Sodium ingestion - NaCl tablets, seawater ingestion
  - Sodium modeling in hemodialysis

Dr. Robin Paudel

- Diagnosis of hypernatremia is based on an elevated serum sodium concentration (Na^+ >145 mEq/L). It is necessary to obtain the following lab studies:
  - Serum electrolytes (Na^+, K^+, Ca^{2+})
  - Glucose level
  - Urea
  - Creatinine
  - Urine electrolytes (Na^+, K^+)
  - Urine and plasma osmolality
  - 24-hour urine volume
  - Plasma AVP level (if indicated)

Dr. Robin Paudel

- **Treatment guidelines of symptomatic hypernatremia**
  - Correct the serum sodium at an initial rate of 1-2 mEq/L/hr
  - Replace 50% of the calculated water deficit over the first 12-24 hours
  - Replace the remaining deficit over the next 24 hours
  - Perform measurements of serum and urine electrolytes every 1-2 hours
  - Perform serial neurologic examinations and decrease the rate of correction with improvement in symptoms
  - Chronic hypernatremia with no or mild symptoms should be corrected at a rate not to exceed 0.5 mEq/L/h and/or a total of 10 mEq/d (eg, 160 mEq/L to 150 mEq/L in 24 h).
  - If a volume deficit and hypernatremia are present, intravascular volume should be restored with isotonic sodium chloride prior to free-water administration.

Dr. Robin Paudel

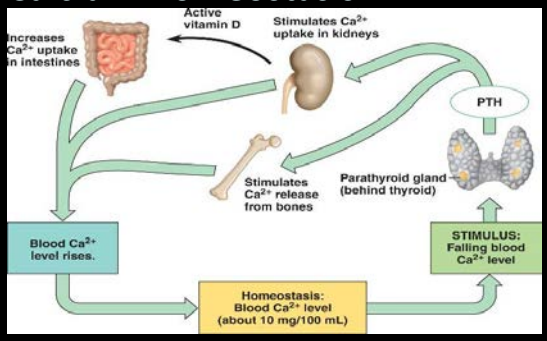
- **Other treatment considerations**
  - If hypernatremia is accompanied by hyperglycemia with diabetes, take care when using a glucose-containing replacement fluid. However, the appropriate use of insulin will help during correction.
  - Hypernatremia in the setting of volume overload may require dialysis for correction.
  - Although water can be replaced by oral and parenteral routes, an obtunded patient requires parenteral treatment. If the deficit is small and the patient is alert and oriented, oral correction may be substituted.
  - Once hypernatremia is corrected, efforts are directed at treating the underlying cause of the condition. Such efforts may include free access to water and better control of diabetes mellitus. In addition, correction of hypokalemia and hypercalcemia as etiologies for nephrogenic diabetes insipidus may be required. Vasopressin (AVP, DDAVP) should be used for the treatment of central diabetes insipidus.

Dr. Robin Paudel

- Surgical treatment may be required in the setting of severe central nervous system trauma and associated central diabetes insipidus.

Dr. Robin Paudel

Calcium Homeostasis



Dr. Robin Paudel

- PTH :
  - Stimulates osteoclasts
  - Increase distal tubular reabsorption of Calcium
  - Decrease Distal tubular reabsorption of Phosphate
  - Increase production of 1,25 hydroxy Vit. D
- Vit. D :
  - Increase Calcium Phosphate intestinal absorption
  - Increase Proximal Tubular Reabsorption of Phosphate
- Calcitonin :
  - Inhibition of bone reabsorption
  - Secreted by parafollicular cells of thyroid gland
  - Physiologic role incompletely understood
- Normal Calcium Level:
  - 8.5 – 10.5 mg/dL

Dr. Robin Paudel

Hypercalcemia

- Causes of hypercalcemia :
  - **Overactivity of parathyroid glands.**
    - The primary cause of hypercalcemia is overactivity in one or more of your four parathyroid glands (primary hyperparathyroidism).
  - **Cancer.**
    - Certain types of cancer, particularly lung cancer and breast cancer, as well as some cancers of the blood, such as multiple myeloma, increase your risk of hypercalcemia. Some cancerous (malignant) tumors produce a protein that acts like parathyroid hormone, stimulating the release of calcium from your bones into your blood. This is considered a paraneoplastic syndrome, your body's response to the presence of cancer or a substance the cancer produces. Spread of cancer (metastasis) to your bones also increases your risk of hypercalcemia.
    - Hyperparathyroidism and cancer are responsible for more than 90 percent of sustained hypercalcemia

Dr. Robin Paudel

- **Other diseases.**
  - Some diseases that produce areas of inflammation due to tissue injury (granulomas) may raise blood levels of vitamin D (calcitriol). Granulomatous diseases include tuberculosis, an infectious lung disease, and sarcoidosis, an inflammatory disease that usually begins in your lungs. Elevated levels of calcitriol stimulate your digestive tract to absorb more calcium, which raises the level of calcium in your blood. Also, a rare genetic disorder known as familial hypocalciuric hypercalcemia causes an increase of calcium in your blood because of faulty calcium receptors in your body.
- **Disease effects.**
  - People with cancer or other diseases that cause them to spend a great deal of time sitting or lying down may develop hypercalcemia because over time, bones that don't bear weight release calcium into the blood.
- **Medications.**
  - Certain drugs, such as lithium, which is used to treat bipolar disorder, may increase the release of parathyroid hormone and cause hypercalcemia. Thiazide diuretics can cause elevated calcium levels in your blood by decreasing the amount of calcium lost in your urine.
- **Supplements.**
  - Excessive intake of calcium or vitamin D supplements over time can raise calcium levels in your blood above normal.
- **Dehydration.**
  - A common cause of mild or transient hypercalcemia is dehydration, because when there is less fluid in your blood, calcium concentrations rise.

Dr. Robin Paudel

- **Symptoms**
  - Abdominal:
    - Constipation
    - Nausea
    - Pain
    - Poor appetite
    - Vomiting
  - Kidney:
    - Flank pain
    - Frequent thirst
    - Frequent urination
  - Muscular:
    - Muscle twitches
    - Weakness
  - Psychological:
    - Apathy
    - Dementia
    - Depression
    - Irritability
    - Memory loss
  - Skeletal:
    - Bone pain
    - Bowing of the shoulders
    - Fractures due to disease (pathological fractures)
    - Loss of height
    - Spinal column curvature

Dr. Robin Paudel

- **Signs and tests**
  - Serum calcium
  - Serum PTH
  - Serum PTHrP (PTH-related protein)
  - Serum vitamin D level
  - Urine calcium
- **Treatment**
  - Treatment is directed at the cause of hypercalcemia whenever possible. In more severe cases of primary hyperparathyroidism, surgery may be needed to remove the abnormal parathyroid gland and cure the hypercalcemia.
  - However, if hypercalcemia is mild and caused by primary hyperparathyroidism, need not go for surgery, but need to monitor y condition closely over time.
- Severe hypercalcemia that causes symptoms and requires a hospital stay is treated with the following:
  - Calcitonin
  - Dialysis
  - Diuretic medication, such as furosemide
  - Drugs that stop bone breakdown and absorption by the body, such as pamidronate or etidronate (bisphosphonates)
  - Fluids through a vein (intravenous fluids)
  - Glucocorticoids (steroids)

Dr. Robin Paudel

- **Prognosis**
  - depends on the cause of hypercalcemia. Patients with mild hyperparathyroidism or hypercalcemia with a treatable cause do well and do not have complications.
  - Patients with hypercalcemia due to conditions such as cancer or granulomatous disease may not do well, but this is usually due to the disease itself, rather than the hypercalcemia.
- **Complications**
  - Gastrointestinal
    - Pancreatitis
    - Peptic ulcer disease
  - Kidney
    - Calcium deposits in the kidney (nephrocalcinosis)
    - Dehydration
    - High blood pressure
    - Kidney failure
    - Kidney stones
  - Psychological
    - Depression
    - Difficulty concentrating or thinking
  - Skeletal
    - Bone cysts
    - Fractures
    - Osteoporosis

Dr. Robin Paudel

How many causes of hypercalcemia can u think about!!??????!!

- Hyperparathyroidism
- Bone breakdown
- Paget's disease of bone
- Bone cancer
- Vitamin A overdose
- Vitamin D overdose
- Aluminium antacid overuse
- Cushing's syndrome
- Brown-Sequard Syndrome - hypercalcemia
- Familial hypocalciuric hypercalcaemia
- Adult T cell leukemia - hypercalcemia
- Berylliosis
- Vitamin D
- Hyperthyroidism
- Hypophosphataemia
- Infantile hypophosphatasia - hypercalcemia
- Acute adult T-Cell leukemia - hypercalcemia
- Parathyroid hormone related peptide
- VIPoma
- Multiple endocrine neoplasia type 1 - hypercalcemia
- Multiple Myeloma - hypercalcemia

Dr. Robin Paudel

- Parathyroid hormone
- Pseudophosphatasia - hypercalcemia
- Adult T-Cell lymphoma - hypercalcemia
- Lithium
- Phosphoethanolaminuria
- Chronic adult T-Cell leukemia - hypercalcemia
- Hyperparathyroidism, primary
- Mycobacterium tuberculosis
- Paricalcitol
- Hypophosphatasia - hypercalcemia
- Jansen type metaphyseal chondrodysplasia - hypercalcemia
- Milk-alkali syndrome
- Adrenal cortex insufficiency
- Myeloma
- Pituitary tumour (growth hormone secreting)
- Hyperparathyroidism, tertiary

Dr. Robin Paudel

- Danazol
- Gestrinone
- Hypokalaemic distal renal tubular acidosis
- Bartter Syndrome - hypercalcemia
- Parathyroid carcinoma
- Tryptophan malabsorption syndrome
- Chlortalidone
- Metastatic neoplasm
- Cuffed blood sample
- Subcutaneous fat necrosis of newborn
- Williams syndrome - hypercalcemia
- Smoldering adult T-Cell leukemia - hypercalcemia
- Hodgkin's lymphoma
- Sarcoidosis
- Vitamin A
- Paraneoplastic syndrome

Dr. Robin Paudel

Hypocalcemia

- The most common cause of hypocalcemia is hypoparathyroidism. Some other causes of blood calcium deficiency are:
  - sepsis
  - chelation
  - alcoholism
  - renal failure
  - pancreatitis
  - chemotherapy
  - kidney disease
  - rhabdomyolysis
  - phosphate enemas
  - hyperphosphatemia
  - malnutrition ~ calcium, vitamin D, magnesium deficiency

Dr. Robin Paudel

Symptoms of Hypocalcemia:

- myalgia
- hypotension
- paresthesias
- memory loss
- hallucinations
- anxiety, depression
- muscle stiffness, cramps, spasms, twitching
- respiratory and laryngeal muscle contractions that can result in stridor and cyanosis. Chronic calcium deficiency can also cause cataracts.

Dr. Robin Paudel

Treatment of Hypocalcemia:

- Calcium Supplements
- Vitamin D
- Magnesium

Dr. Robin Paudel

Hypokalemia

- Normal Level: 3.5 – 5.0 mEq/L
- Causes:
  - Deficient intake
    - Poor potassium intake alone is an uncommon cause of hypokalemia but occasionally can be seen in very elderly individuals unable to cook for themselves or unable to chew or swallow well
    - Total parenteral nutrition (TPN)
  - Increased excretion.
    - Increased Excretion + with poor intake → most common cause
    - Diuretics
    - Mineralocorticoid excess : primary or secondary hyperaldosteronism
    - increased urine flow, as with an osmotic diuresis
    - Gastrointestinal losses:
      - Diarrhoea
      - Vomiting
    - Adrenocortical carcinoma
    - Congenital disorders - Congenital adrenal hyperplasia (11-beta hydroxylase or 17-alpha hydroxylase deficiency)
    - Hyperreninism due to renal artery stenosis
    - Exogenous mineralocorticoid excess
    - Osmotic diuresis: Mannitol and hyperglycemia

Dr. Robin Paudel

Symptoms:

- Symptoms are nonspecific and predominantly are related to muscular or cardiac function.
  - Weakness and fatigue are the most common complaints
    - Can range from mild weakness to severe symptoms like dyspnea, constipation or abdominal distention, or exercise intolerance.
    - Rarely, muscle weakness progresses to frank paralysis.
  - Occasionally, a patient may complain of worsening diabetes control or polyuria due to a recent onset of hyperglycemia or nephrogenic diabetes insipidus
  - Palpitations
  - With severe hypokalemia or total body potassium deficits, muscle cramps and pain can occur with rhabdomyolysis.

Dr. Robin Paudel

- Investigate about:
  - Poor intake :
    - Eating disorders
    - Dental problems
    - Poverty
  - Increased excretion :
    - Medications, including diuretics, AIDS therapy, or antibiotics
    - Polyuria
    - Vomiting or diarrhea
  - Shift of potassium into the intracellular space:
    - Use of high doses of insulin
    - High-dose beta agonist therapy (eg, for chronic obstructive pulmonary disease)

Dr. Robin Paudel

Treatment of Hypokalemia:

- In treating hypokalemia, the first step is to identify and stop ongoing losses of potassium.
  - Discontinue diuretics/laxatives.
  - Use potassium-sparing diuretics if diuretic therapy is required (eg, severe heart failure).
  - Treat diarrhea or vomiting.
  - Control hyperglycemia if glycosuria is present.
- Repletion of potassium losses is the second step.
- Monitor for toxicity of hypokalemia.
  - Cardiac
    - Monitor the patient if evidence of cardiac arrhythmias is observed, and institute very aggressive replacement parenterally under monitored conditions.
- Determine the underlying cause to treat and prevent further episodes
  - Look for clues to the etiology.
    - Urine potassium concentration
    - Presence of hypertension or hypotension
    - Acid-base disturbances
    - Family history
    - Tooth erosion; melanosis coli; obsession with body image; high-risk behaviors such as cheerleading, wrestling, or modeling; or evidence of alcohol abuse

Dr. Robin Paudel

- Surgical intervention is required only after determining that the etiology requires it. Etiologies that may require surgery include the following:
  - Renal artery stenosis
  - Adrenal adenoma
  - Intestinal obstruction producing massive vomiting
  - Villous adenoma

Dr. Robin Paudel

Hyperkalemia

- The incidence of hyperkalemia in the general population is unknown. In hospitalized patients, the incidence ranges from 1.3% to 10%
- Causes: 3 categories:
  - (1) increase in potassium load,
  - (2) decrease in kidney potassium excretion, and
  - (3) transcellular potassium shifts

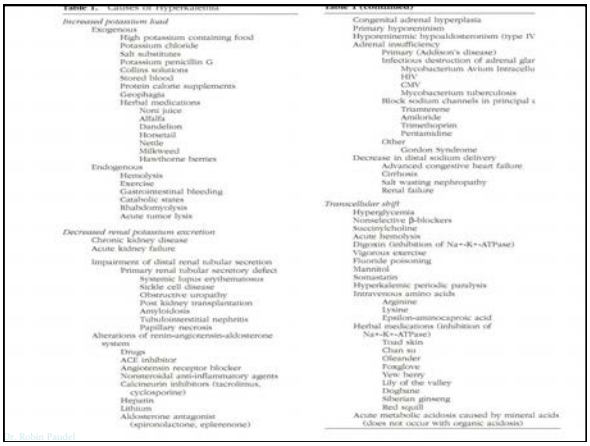
Dr. Robin Paudel

- Hyperkalemia can be difficult to diagnose clinically because complaints may be vague.
- The history is most valuable in identifying conditions that may predispose to hyperkalemia.
- Hyperkalemia frequently is discovered as an incidental laboratory finding.
- Cardiac and neurologic symptoms predominate.
- Patients may be asymptomatic or report the following:
  - Generalized fatigue
  - Weakness
  - Paresthesias
  - Paralysis
  - Palpitations

Dr. Robin Paudel

- Hyperkalemia is suggested in any patient with a predisposition toward elevated potassium level. Potential potassium level elevation is observed in the following:
- Acute or chronic renal failure, especially in patients who are on dialysis
- Trauma, including crush injuries (rhabdomyolysis), or burns
- Ingestion of foods high in potassium (eg, bananas, oranges, high-protein diets, tomatoes, salt substitutes). This alone is not likely to cause clinically significant hyperkalemia in most people; it is often a contributing factor to an acute potassium elevation.
- Medications - Potassium supplements, potassium-sparing diuretics, nonsteroidal anti-inflammatory drugs (NSAIDs), beta-blockers, digoxin, succinylcholine, and digitalis glycoside
- Medication combinations (ie, spironolactone, ACE inhibitors)
- Redistribution - Metabolic acidosis (diabetic ketoacidosis [DKA]), catabolic states

Dr. Robin Paudel



Dr. Robin Paudel

- Evaluation of vital signs is essential to determine hemodynamic stability and presence of cardiac arrhythmias related to the hyperkalemia.
- Cardiac examination may reveal extrasystoles, pauses, or bradycardia.
- Neurologic examination may reveal diminished deep tendon reflexes or decreased motor strength.
- In rare cases, muscular paralysis and hypoventilation may be observed.
- Search for the stigmata of renal failure, such as edema, skin changes, and dialysis sites.
- Look for signs of trauma that could put the patient at risk for rhabdomyolysis.

Dr. Robin Paudel

TABLE 5

Medications Used in Acute Treatment of Hyperkalemia

*Medication**	*Dosage*	*Onset*	*Length of effect*	*Mechanism of action*	*Cautions*
Calcium gluconate	10 to 20 mL of 10 percent solution IV over two to three minutes	Immediate	30 minutes	Protects myocardium from toxic effects of calcium; no effect on serum potassium level	Can worsen digoxin toxicity
Insulin	Regular insulin 10 units IV with 50 mL of 50 percent glucose	15 to 30 minutes	Two to six hours	Shifts potassium out of the vascular space and into the cells; no effect on total body potassium	Consider 5 percent dextrose solution infusion at 100 mL per hour to prevent hypoglycemia with repeated doses. Glucose unnecessary if blood sugar elevated above 250 mg per dL (13.9 mmol per L)
Albuterol (Ventolin)	10 to 20 mg by nebulizer over 10 minutes (use concentrated form, 5 mg per mL)	15 to 30 minutes	Two to three hours	Shifts potassium into the cells, additive to the effect of insulin; no effect on total body potassium	May cause a brief initial rise in serum potassium
Furosemide (Lasix)	20 to 40 mg IV, give with saline if volume depletion is a concern	15 minutes to one hour	Four hours	Increases renal excretion of potassium	Only effective if adequate renal response to loop diuretic
Sodium polystyrene sulfonate (Kayexalate)	Oral: 50 g in 30 mL of sorbitol solution Rectal: 50 g in a retention enema	One to two hours (rectal route is faster)	Four to six hours	Removes potassium from the gut in exchange for sodium	Sorbitol may be associated with bowel necrosis. May lead to sodium retention

Dr. Robin Paudel

IV = intravenously.
**Medications listed in order of use from most to least urgent.*
Information from references 2 and 3.