Biochemistry assignment

Toxicity and deficiency manifestation of

**Potassium**

This is called hyperkalemia, or high **potassium**. According to the Mayo Clinic, a normal **range of potassium** is between 3.6 and 5.2 millimoles per liter (mmol/L) of blood. A **potassium** level higher than 5.5 mmol/L is critically high, and a **potassium** level over 6 mmol/L can be life-threatening.

**Calcium**

Because of the large amount of calcium in bones, deficiency is rare. **Hypocalcemia** (low serum calcium levels in blood) can result in tetany (involuntary muscle contractions). In addition, calcium deficiency in children can lead to [rickets](https://med.libretexts.org/Bookshelves/Nutrition/Book%3A_Intermediate_Nutrition_%28Lindshield%29/12%3A_Blood%2C_Bones%2C_and_Teeth_Micronutrients/12.1%3A_Vitamin_D/12.1F%3A_Vitamin_D_Deficiency%2C_Toxicity_and_Insufficiency), which is a vitamin D deficiency. While not a deficiency, low calcium intake can lead to decreased bone mineral density and the conditions **osteopenia** and **osteoporosis**. How these differ from osteomalacia and normal bone is illustrated and described below. There are two different bone components that we will consider to understand what is happening in the bone. Matrix is the scaffolding onto which mineral is deposited. Mineral is at it sounds, the mineral that is deposited on the matrix.

* **Osteomalacia** - Bone mass is normal, but the matrix to mineral ratio is increased, meaning there is less mineral in bone.
* **Osteopenia** - Bone mass is decreased, but the matrix to mineral ratio is not altered from normal bone. This condition is intermediate in between normal and osteoporosis.
* **Osteoporosis** - Bone mass is further decreased from osteopenia, but the matrix to mineral ratio is not altered from normal bone.

**Magnesium**

Magnesium is a mineral that is naturally found in your body and in the food you consume daily. It is responsible for many processes within your body that includes, but not limited to, protein synthesis, bone formation, blood pressure regulation, nerve function, and electrical conduction in the heart. However, too much magnesium, whether it’s due to over-consumption or under-excretion, can result in serious health issues for the patient. This activity will cover the causes, as well as the early symptomatic presentation of magnesium toxicity. Additionally, it will highlight the importance of diagnosing and treating magnesium toxicity early on and how a strong interprofessional effort is important to prevent fatal complications.

**Etiology**

While magnesium toxicity is rare in the general population, there is a subset of patients who are at risk of developing this pathology. Magnesium is excreted in the kidneys, and so those with chronic kidney disease are particularly at risk. However, magnesium excretion is only impaired when the creatinine clearance falls below 30 ml/minute. Patients on dialysis can also experience a quick rise in magnesium levels if their treatments are missed. Additionally, the magnesium concentration in cells is much higher than that in plasma. Therefore, patients undergoing cancer treatment, who have high rates of cellular hemolysis, are also at risk. Lastly, women who are being treated for preeclampsia are also at risk for magnesium toxicity due to the high dosage needed to prevent seizures. Identifying the causes of magnesium toxicity, whether it is through over-absorption or under-secretion, is vital to not only identify patients at risk for magnesium toxicity but also to prevent future toxicities.

**Epidemiology**

Magnesium toxicity occurs in both sexes as this condition is indirectly developed due to underlying pathology or excessive exogenous intake. However, women are more likely to develop magnesium toxicity as magnesium is universally used for the treatment of pre-eclampsia, which complicates about 3% of pregnancies nationwide. Additionally, magnesium toxicity occurs at a higher rate in the U.S. versus worldwide, likely due to the wider availability of magnesium-containing over-the-counter supplements. The prevalence of hypermagnesemia among hospitalized patients in the U.S. was also found to be 9.3%.

**Pathophysiology**

Magnesium serves as a co-factor for over 300 biochemical reactions within the body. The importance of magnesium is found in protein synthesis, nerve and muscle functioning, bone growth, regulation of blood pressure and glucose, and normal cardiac rhythm. An average adult has approximately 22 to 26 grams of magnesium. 60% of total levels is stored in bone, 39% is stored intracellularly, and only 1% is found in its free or ionized active form in blood vessels. Magnesium is also involved in sodium, potassium, and calcium channels. The homeostasis of magnesium is dependent on kidney and small bowel function, as well as storage in bone and cells. When these processes are affected, whether it is due to under-excretion by the kidneys, over-absorbance by the small bowel, or displacement of stored magnesium into the serum, hypermagnesemia occurs and leads to magnesium toxicity. The most common findings of early-onset toxicity are diarrhea, nausea and vomiting, muscle weakness, and low blood pressure. However, as levels continue to rise, patients experience loss of deep tendon reflexes, sinoatrial (SA) or atrioventricular (AV) node blocks, respiratory paralysis, and eventually cardiac arrest

**Toxicokinetics**

The toxic effects of magnesium are inherently linked to the levels (mEq/liters) found in the serum. As the levels of magnesium rise, different symptoms start to manifest, and the fatality of those symptoms is proportional to the levels of magnesium found. Starting at 5 to 10 mEq/L, patients will begin to develop ECG changes (prolonged PR interval, widened QRS). At 10 mEq/L, there will be a loss of deep tendon reflexes and muscle weakness. At 15 mEq/L, signs of abnormal conductivity surface as SA/AV node block. Additionally, patients begin to experience respiratory paralysis. At 20 mEq/L or higher, the patient is likely to experience cardiac arrest.

**History and Physical**

Obtaining a thorough history is paramount when diagnosing magnesium toxicity as magnesium levels are not checked in a routine workup, and the symptoms that patients can present with tend to be nonspecific. As previously discussed, magnesium toxicity results from under-excretion, over-consumption, and storage displacement. The history should be focused on their etiology, such as history of chronic kidney disease, use of magnesium-containing medications such as antacids and laxatives, and recent chemotherapy treatment. Patients on dialysis who may have missed their treatments are also especially at risk. A physical exam is difficult as patients may present with nonspecific findings such as visual changes, flushing, muscle paralysis, and somnolence. However, loss of patellar reflexes should raise suspicion for magnesium toxicity. Patients who are receiving a magnesium infusion, such as those with preeclampsia, require a continuous reassessment of patellar reflexes.

**Evaluation**

Hypermagnesemia can be diagnosed relatively quickly if there is a high index of suspicion. This can be done by obtaining a measurement of the concentration of magnesium in the blood. Levels that are greater than 2.2 mEq/L (or greater than 1.1 mmol/L) are diagnostic for hypermagnesemia. When suspicion for magnesium toxicity is high, workup including an initial ECG as this can be readily done and can identify lethal dysrhythmias that may require emergent treatments. In addition to an ECG, a clinician should also order a complete metabolic panel, including magnesium and phosphorus, to rule out additional electrolyte abnormalities as well as evaluate the patient's renal function as magnesium is excreted by the kidneys.

**Treatment / Management**

The treatment of magnesium toxicity begins with the discontinuation of all magnesium-containing supplements and medication. In severe cases, intravenous calcium gluconate can be used to displace and neutralize the effects of magnesium. However, definitive treatment requires a reduction of magnesium levels within the body. In patients with normal kidney function, this is achievable through intravenous diuretics. For patients with impaired kidney function, dialysis treatment is necessary.

**Differential Diagnosis**

Due to the indistinct symptomatic presentation of magnesium toxicity, the differential diagnosis is wide. However, electrolyte imbalances, such as hypokalemia and hypercalcemia, should always be included within the list. Therefore, a provider’s workup should include other electrolytes such as potassium, calcium, and phosphorus, in addition to magnesium levels.

* Lithium
* Depression
* Hypothyroidism
* Addison disease
* Familial hypocalciuric hypercalcemia
* Milk alkali syndrome

**Prognosis**

The prognosis of magnesium toxicity can include a complete resolution of symptoms without residual effects if diagnosed and treated early. Quality of life, long-term complications, and life expectancy are unaffected if toxic levels of magnesium are stabilized early on using calcium gluconate and subsequently lowered using diuretics or dialysis. However, if left untreated, magnesium toxicity has a high rate of mortality due to respiratory paralysis and cardiac arrest.

**Complications**

Complications of magnesium toxicity can be both systemic and organ-specific, depending on the levels of magnesium concentration in the blood. Minor side effects seen early on in hypermagnesemia include flushed skin, nausea or vomiting, and generalized muscle weakness. However, as the levels of magnesium increase, the muscle weakness progresses to loss of deep tendon reflexes and eventually, flaccid paralysis that can cause respiratory compromise. Further complications include those in the cardiovascular system, beginning with hypotension and bradycardia. If magnesium levels remain uncorrected, this can lead to a complete heart block and, subsequently, cardiac arrest.

**Chloride**

Chlorine gas is a pulmonary irritant with intermediate water solubility that causes acute damage in the upper and lower respiratory tract. Occupational exposures constitute the highest risk for serious toxicity from high-concentration chlorine (see the image below). Mixing of chlorine bleach (sodium hypochlorite) with ammonia or acidic cleaning agents is a common source of household exposure. As with all poisons, the dose determines the toxicity. Exposure to low concentrations of chlorine for prolonged periods may have destructive effects, as might very short-term exposure to high concentrations.

**Iron**

Iron overdose has been one of the leading causes of poisoning deaths in children younger than 6 years. Iron is used in pediatric or prenatal vitamin and mineral supplements and for treatment of anemia. Iron tablets are particularly tempting to young children because they look like candy. Iron overdose in adults is typically a suicide attempt. [14]

Iron overload may develop chronically as well, especially in patients requiring multiple transfusions of red blood cells. This condition develops in patients with sickle cell disease, thalassemia, and hematologic malignancies such as myelodysplastic syndromes