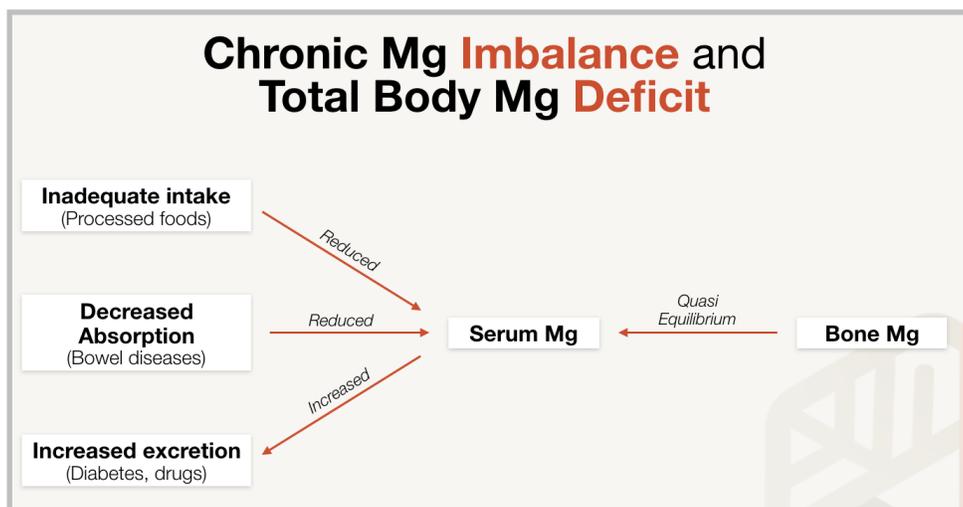


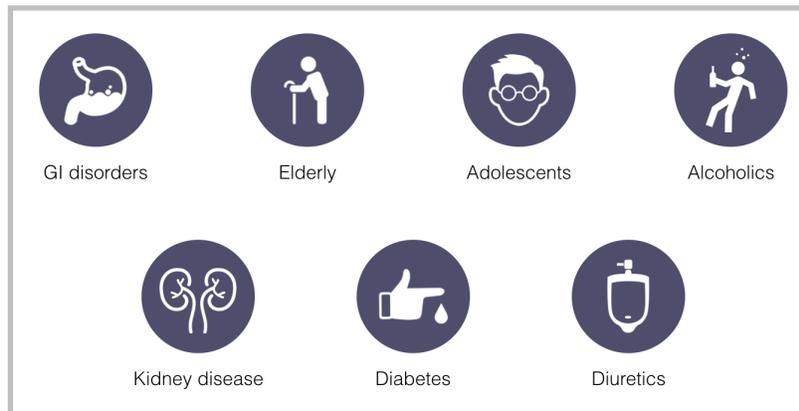
# Blood Chem Magnesium Deficiency and Thyroid Hypofunction Part I Review

## MAGNESIUM

- Magnesium (Mg) is an essential mineral and cofactor for hundreds of enzymes. It's involved in many physiological pathways, including the examples below.
- It's the fourth most abundant mineral in the body after calcium, potassium, and sodium. It's necessary for phosphorylation.
- Magnesium deficiency is one of the most common nutrient deficiencies in the U.S. and likely in the industrialized world
- Primary causes of magnesium deficiency are increased excretion, decreased absorption or inadequate intake.
  - Increased excretion of magnesium occurs primarily with diabetes and diuretic drugs that cause increased urination.
  - Magnesium absorption may be decreased by GI pathologies such as IBD, celiac, and SIBO. Very high-dose zinc, very high-fiber intake, and low-protein diets below 30 g per day also decrease magnesium absorption. Magnesium absorption is decreased in alcoholics.
  - Inadequate intake, in part due to soil depletion, but also due to a reduction in the consumption of nutrient-dense wild plant foods. The cultivated plants that we eat today don't contain as much magnesium as the wild plants that our ancestors ate.



## POPULATIONS AT RISK FOR MAGNESIUM DEFICIENCY



## FACTORS THAT DECREASE MAGNESIUM STATUS

GI pathologies
High-dose zinc
High fiber intake
Low-protein diets
Alcoholism
High calcium intake

Magnesium deficiency is associated with a wide variety of pathologies and diseases from type 2 diabetes and metabolic syndrome to elevated C-reactive protein, hypertension, atherosclerotic vascular disease, sudden cardiac death, osteoporosis, migraine headache, asthma, and colon cancer.

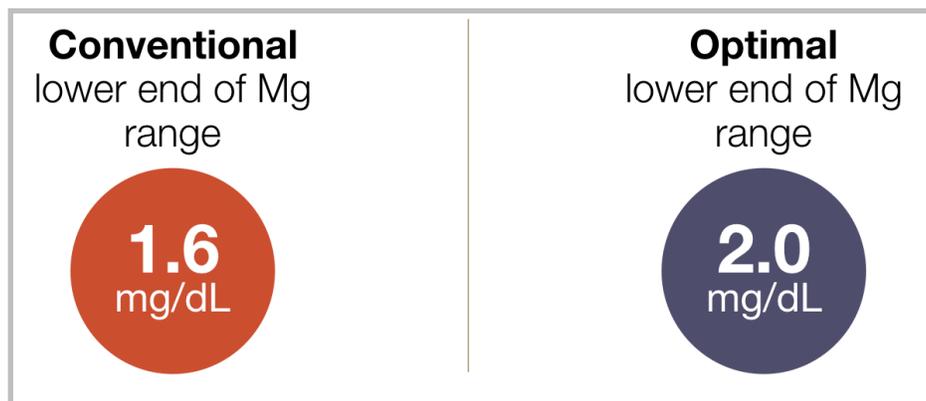
## SIGNS AND SYMPTOMS OF MAGNESIUM DEFICIENCY

Early	Late	
Loss of appetite	Hypomagnesia	Hypertension
Headache	Hypocalcemia	CVD
Nausea	Hypokalemia	Pregnancy complications
Fatigue	Sodium retention	Infertility
Weakness	Low serum PTH	Neurological/muscular
	Osteoporosis	Personality changes
	Diabetes	Vomiting

Over 60 percent of the magnesium in the body is found in the skeleton, about 27 percent is found in the muscle, 6 to 7 percent is found in other cells, and less than 1 percent of magnesium is found in serum. Therefore, serum magnesium is not necessarily an accurate representation of what is in the soft tissue and inside of the cells where it is used and needed.

The lab reference range of 1.8 to 2.3 was determined by the NHANES I cohort study.

Studies support the lower end of the functional magnesium range should be 2.0.



## CLINICAL MAGNESIUM DEFICIENCY AT VARIOUS SERUM MAGNESIUM LEVELS

Serum Mg level (mg/dL)	% with clinical Mg deficiency
<b>1.7</b>	90
<b>1.85</b>	50
<b>1.95</b>	10
<b>2.2</b>	1

### TESTING FOR MAGNESIUM

- I recommend using the serum magnesium cutoffs discussed above and do therapeutic trials of magnesium supplementation.
- This is because other options for testing for magnesium are either not widely available or cost prohibitive.

### MAGNESIUM REPLETION

- Recommend about 500 mg per day for adult males and 400 mg per day for adult females and increasing the other minimums by a 20 percent safety margin.
- Even people on a nutrient-dense, healthy diet may need to supplement magnesium.
- If serum levels are low, you can give your patients a list of foods that are high in magnesium, but you should probably also give them supplements.
- People with kidney damage are at the greatest risk of toxicity such as lethargy, confusion, disturbances in normal cardiac rhythm, and deterioration of kidney function. This is mostly related to severe hypotension caused by excess magnesium.
- I suggest retesting serum magnesium after 60 to 90 days, and you should see an
- increase in the serum magnesium concentration. Then you can drop to a maintenance dose of 200 to 250 mg per day.

**Highest dietary sources of magnesium**

<b>Food</b>	<b>Amount (mg per 200cal)</b>
<b>Canned clams</b>	1,100
<b>Swiss chard, cooked</b>	860
<b>Purslane</b>	850
<b>Spinach, cooked &amp; raw</b>	756
<b>Beet greens, cooked &amp; raw</b>	636
<b>Kelp</b>	563
<b>Basil, fresh</b>	556
<b>Kale</b>	407
<b>Arugula</b>	376
<b>Okra, cooked</b>	327
<b>Chives, raw</b>	280
<b>Coconut water</b>	263

**MAGNESIUM FORMS AND INDICATIONS**

<b>Form</b>	<b>Indication</b>
<b>Orotate</b>	Cardiovascular
<b>Glycinate</b>	Sleep and constipation
<b>Malate</b>	Energy and pain relief
<b>Taurate</b>	Blood sugar imbalances and anxiety
<b>Citrate</b>	Sleep and hard stools
<b>Oxide</b>	Poor bioavailability; causes loose stools
<b>Sulfate</b>	Not generally used in oral supplements; little evidence on topical absorption

For magnesium, different forms are best for different purposes. Refer to the chart above for some specifics. In addition, L-threonate improves brain and memory function, and it is highly absorbable.

## THYROID HYPOFUNCTION

- More than one in 10 individuals will develop a thyroid condition in their lifetime and most will be unaware of their condition.
- Women are five to eight times more likely than men to have thyroid problems.
- Pregnant women with undiagnosed or inadequately treated hypothyroidism have an increased risk of miscarriage, preterm delivery, and severe developmental problems in their children
- Thyroid dysfunction is often a symptom or result of a deeper underlying problem.
- Free T4 and free T3 are better indicators of what's happening at the cellular level than total T4 and total T3.
- Low T4-to-T3 conversion, high reverse T3, or a high RT3-to-free T3 or -total T3 ratio, can be a sign of inflammation, HPA axis dysfunction, or nutrient imbalance.
- Antibody production
  - Precedes the development of clinical thyroid disease by many years.
  - Identifying patients with positive antibodies and normal TSH and thyroid hormones can prevent future problems.
- Our functional reference range for TSH as 0.5 to 2.0.
  - That does not mean that everyone with a TSH above 2.0 requires treatment, but we should start looking more carefully when you see TSH above that level to decrease the chance of developing into clinical hypothyroidism in the future

## SUBCLINICAL HYPOTHYROIDISM

- Defined by elevated TSH but normal thyroid hormone levels.
- Prevalence of subclinical hypothyroidism increases with age and is approximately 10 percent in women over 60 years old and somewhat lower in men.
- Many studies have found that subjects with subclinical hypothyroidism have higher total cholesterol, LDL, and C-reactive protein than euthyroid subjects.
- May increase the risk of cardiovascular disease by 60 percent.
- Treatment of subclinical hypothyroidism has been shown to improve cardiovascular markers.
- There is a risk of overtreatment.

## SECONDARY HYPOTHYROIDISM

- Low TSH due to low pituitary output and low T4 or T3.

- Caused by a dysfunction of the hypothalamus or pituitary gland, leading to decreased activity of the thyroid gland.
- Also will have low growth hormone, LH, FSH, and ACTH.
- Rare, 46 cases out of 100,000 people, so less likely to see it in clinical practice.

## CENTRAL HYPOTHYROIDISM

- Due to insufficient stimulation by TSH of an otherwise normal thyroid gland.
- Can be secondary to hypothyroidism caused by pituitary malfunction or tertiary hypothyroidism caused by hypothalamic malfunction.
- Usually due to pituitary macroadenomas, pituitary surgeries, or post-radiation.
- This presentation can also occur in Hashimoto's, especially in the early stages when the immune attack is relapsing and remitting.
- Confirmed by a TSH stimulation test.

## HASHIMOTO'S THYROIDITIS

- High TSH, low T3 and T4, and high TPO antibodies as seen in the example below is textbook Hashimoto's.
- Is the cause of hypothyroidism in up to 90 percent of cases.
- Patients with elevated thyroid antibodies are far more likely to develop hypothyroidism, whether overt, clinical, or subclinical.
- However, the presence of thyroid antibodies alone does not guarantee progression to clinical disease.
- 70 percent of the risk of developing Hashimoto's is genetic
- Most common time of onset in women is after childbirth.
- Up to 20 percent of patients with autoimmune thyroid disease don't produce antibodies, and 13 percent have only low levels of antibodies.
- If only clinical and serum findings were used to diagnose Hashimoto's, the diagnosis would be missed in at least half of patients.
- Antibodies can vary from high to normal.
  - Low levels of antibody production may not be abnormal as autoantibodies often occur in healthy individuals and play an important role in the homeostasis of the immune system.
- Thyroid ultrasound can be performed to confirm a suspected Hashimoto's diagnosis.
- Prevalence of celiac disease is much higher in patients with autoimmune thyroid disease.
- Antigliadin antibodies are more likely to be present in patients with autoimmune thyroid disease.

## NUTRIENTS FOR THYROID HEALTH

- The thyroid needs several nutrients to function properly, including iodine, selenium, iron, zinc, vitamin B12, vitamin B2, vitamin C, vitamin A, vitamin D, and magnesium.
- **Iodine**
  - An essential nutrient required for reproduction and growth; its only known function is the synthesis of thyroid hormone.
  - Iodine supplementation can be helpful to normalize TSH and improve thyroid symptoms.
  - Serum iodine is not considered to be a very accurate indicator of iodine levels
  - If you have a patient with hypothyroidism, two to three negative antibody tests, and a negative thyroid ultrasound, consider iodine deficiency
  - Some studies have shown that increased iodine intake, especially in supplement form, can increase the autoimmune attack on the thyroid. Iodine reduces the activity of thyroid peroxidase, and TPO is required for proper thyroid hormone production.
  - Selenium may protect against the harmful effects of iodine. Other studies have shown that selenium prevents the triggering and flaring of autoimmune disease that excess iodine without selenium can cause.
  - You can begin iodine supplementation with or without testing.
- **Selenium**
  - Long-term high dose selenium supplementation can lead to complications such as gastrointestinal upset, hair loss, white blotchy nails, garlic breath odor, fatigue, irritability, and mild nerve damage.
  - I usually recommend that patients obtain adequate selenium intake through their diet and possibly to use testing for selenium levels at baseline to determine whether selenium supplementation is warranted.
- **Iron**
  - Deficiency reduces heme-dependent thyroid peroxidase activity in the thyroid, resulting in impaired production of thyroid hormone.
- **Magnesium, B12 and zinc**
  - Required for synthesis of TSH
- **Riboflavin and vitamin C**
  - Required for iodine symporter
- **Vitamins A & D**
  - Required to activate the nuclear thyroid receptor