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Magnesium

Genes that Impact Magnesium Deficiency

Genetic Lifehacks

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What does magnesium do in the body?

Magnesium is a cofactor for more than 600 different enzymatic reactions, which means that many biochemical reactions in the body need both a specific enzyme plus magnesium for the reaction to occur at the proper rate.[ref]

Without enough magnesium (or without the required enzymes), some cellular reactions just won't happen. Research shows that about half of us don't get enough magnesium on a daily basis.[ref]

Which reactions is magnesium a cofactor for?

Importantly, magnesium is crucial for the synthesis of DNA and RNA, as well as the metabolism of ATP.[ref] As you can imagine, magnesium is essential for life and the proper functioning of the body.

In addition to ATP production and DNA synthesis, magnesium is also a cofactor for:

- enzymes involved in glucose metabolism
- enzymes involve in neuromuscular transmission
- mitochondrial function and oxidative phosphorylation
- cardiac excitability and contraction

- pyruvate dehydrogenase (check your genes here)

What are the signs of low magnesium?

Low magnesium levels are referred to as **hypomagnesemia,** which is usually defined as under 1.5 mg/dL on a lab test.[ref]

Research shows that common problems associated with hypomagnesemia include:[ref] [ref]

- migraines
- ADHD
- strokes
- high blood pressure
- insulin resistance
- neurodegenerative diseases.
- muscle weakness
- twitches
- tremors
- heart arrhythmia or palpitations
- seizures

In a nutshell, low magnesium shows up in physiological issues with the brain, heart, or skeletal muscles.

Magnesium is essential for muscle contractions, blood pressure, insulin metabolism, heart rate, and nerve transmission. An imbalance can show up as a heart rhythm problem or a nervous system disorder.[ref]

Should everyone take a magnesium supplement? Just because social media health gurus say that everyone needs to take magnesium (especially the type that they sell), doesn't mean that you necessarily are deficient. A meta-analysis of supplemental magnesium clinical trials showed that elderly people and alcoholics were likely to benefit from magnesium, but that healthy adults and athletes don't show a statistical benefit, on average.[ref]

How do we maintain normal magnesium levels?

The recommended intake of magnesium ranges from:[ref]

- 280 – 360 mg/day for women
- 350-420 mg/day for men

Your body stores magnesium in the bones (53%), muscles (27%), and soft tissues (19%). That leaves only about 1% of your total magnesium circulating in the blood.[ref]

The body tightly controls serum magnesium levels. While lab ranges can vary a little bit, the normal range for an adult is around 1.3 to 2.1 mEq/L (0.65 to 1.05 mmol/L or 1.5 to 2.6 mg/dL).[ref] We take in magnesium from food and mineral-rich drinks. Chlorophyll from green vegetables is a major dietary source of magnesium.

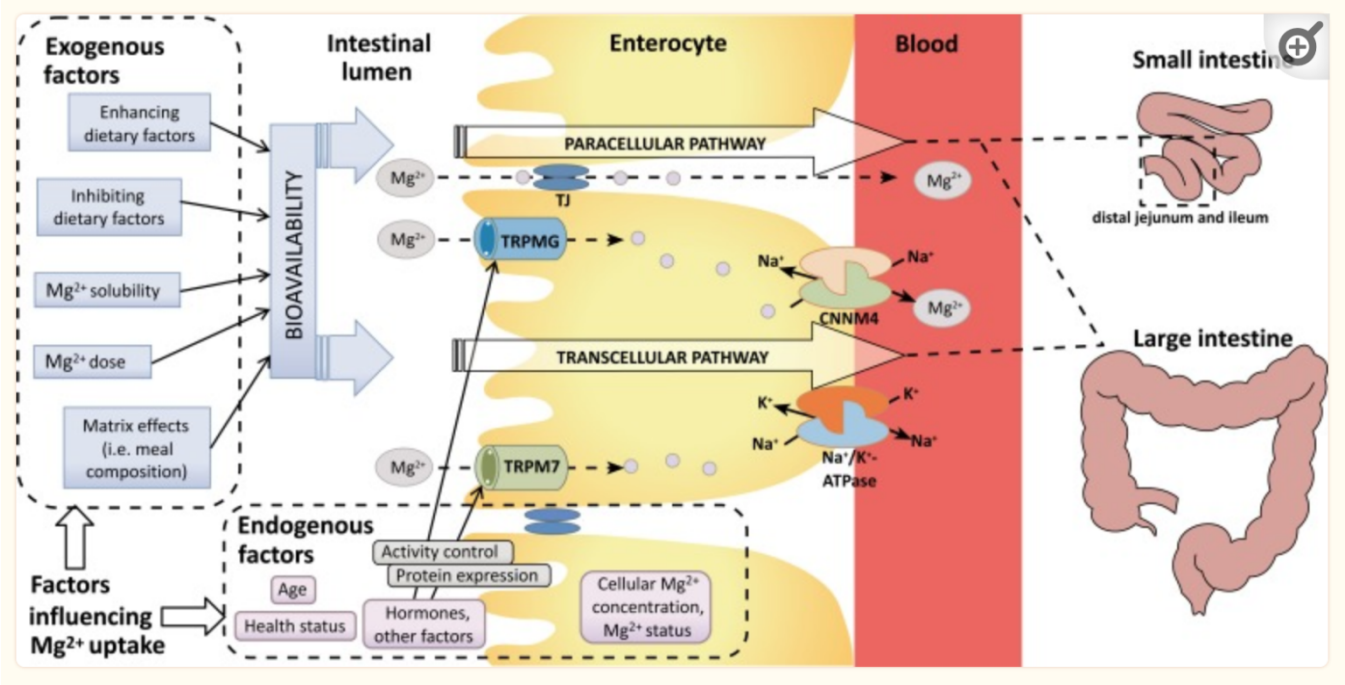
Magnesium is absorbed in the intestines. It circulates in the bloodstream and is taken up by cells as needed. The kidneys reabsorb serum magnesium so that only a small percentage is lost in the urine.[ref]

Low magnesium levels can be caused by:[ref]

- losing too much magnesium in the urine (e.g., uncontrolled diabetes)
- chronic diarrhea
- malabsorption disorders (e.g., celiac, IBD)
- bones taking up too much magnesium (e.g., following thyroid removal)
- alcoholism and chronic pancreatitis

Both diet and genetics play a role in your magnesium levels. Everyone needs to consume enough magnesium, but **the exact amount you need depends, in part, on your genes.**

Below is a diagram showing some of the factors in magnesium absorption. We'll first dig into the genetic factors and then return to the 'exogenous' factors in detail in the lifehacks section.



Absorption of magnesium in the intestines. Creative Commons PMC5652077 (good overview article)

TRPM6 and TRPM7: Magnesium uptake

The **TRPM6 and TRPM7 genes** encode ion channels that transport magnesium ions across cell membranes. These ion channels can also transport calcium or other ions, but they primarily involve magnesium uptake.

Magnesium absorption occurs in the body in two ways:

- Passive absorption in the intestines using an ion gradient to diffuse into intestinal cells
- **Active transport** into intestinal cells using **TRPM6** ion channels

The majority of magnesium uptake is via passive absorption in the small intestines. When the body's magnesium levels aren't met by passive transport, the TRPM6 ion channel is used to fine-tune the absorption.[ref]

Within the body, magnesium can be taken into cells and utilized as needed. The ion channel TRPM7 regulates the cellular uptake of magnesium. TRPM7 is found in tissues throughout the body and is essential for life. When magnesium levels drop within a cell, it activates the TRPM7 channel to take in more magnesium via this ion channel.[ref][ref][ref]

The TRPM6 ion channel is found in the cells lining the intestines, kidneys, and placenta. This ion channel is thought to dial in the right amount of magnesium absorption in the intestines and may play a role in the reabsorption of magnesium in the kidneys.[ref] Magnesium, via the TRPM6 ion channel, affects blood pressure regulation in the kidneys. [ref]

The **TRPM7 ion channel** is found in multiple tissues, including the heart and brain. In the heart, TRPM7 is integral in maintaining the heart's rhythm, along with other ion channels. [ref][ref] Oxidative stress caused by higher intracellular levels of hydrogen peroxide can inhibit the TRPM7 channel.[ref]

CNNM2 and Magnesium Reabsorption:

The body tightly controls magnesium through both the amount absorbed in the intestines and the reabsorption of magnesium in the kidneys. The cyclin M2 (CNNM2) gene encodes a magnesium transporter in the kidneys. When magnesium levels are high in the body, more magnesium is transported out via the urine. Similarly, when magnesium levels are trending lower, more magnesium is reabsorbed. This process is controlled, in part, by the availability of the CNNM2 magnesium transporter.

Rare mutations that cause a deficiency of CNNM2 result in too much magnesium being excreted in the kidneys, which is linked to a loss of circadian rhythm in blood pressure control.[ref] Rare mutations in CNNM2 are also linked to brain development disorders due to the dysregulation of magnesium.[ref]

Magnesium and calcium levels interact through several regulatory mechanisms. Mutations in CNNM2 can show up as calcium dysregulation along with the effect on magnesium.[ref]

SLC41A1 and magnesium movement:

Within cells, magnesium levels are also tightly regulated. The SLC41A1 gene encodes an ion transporter that can move magnesium across cell membranes including in and out of organelles. SLC41A1 acts as an ion exchanger, and when magnesium is moved out, sodium is moved in. One area where SLC41A1 is important is in magnesium reabsorption and excretion in the kidney and in heart function. [ref]

Magnesium Genotype Report

Click here to view your genotype report

Lifehacks:

The RDA for magnesium is 320 mg for women and 420 mg for men.

How can you know how much magnesium you're getting? Cronometer.com is a free web app to track your daily food intake. Keep track for a few days and see what you average for magnesium as a baseline from foods.

Also keep in mind that water accounts for about 10% of magnesium intake in a day, which won't be accounted for if you are tracking on cronometer.com.

If you are drinking water with the minerals filtered out, you may need to increase the amount of magnesium you get from other sources. Drinking too much water can lead to low magnesium levels due to excessive urination. Excessive sweating, such as exercising in the heat or using a sauna, can also lead to low magnesium levels, but it is usually temporary.

Medications can cause you to have low magnesium levels:[ref]

- diuretics
- proton pump inhibitors
- aminoglycoside antibiotics
- digitalis
- calcineurin inhibitors
- certain chemo drugs

Talk with your doctor or pharmacist if you have questions about whether medications could decrease your magnesium levels.

Food sources of magnesium:

Taken from the NIH Health Information fact sheet:

Food	Mg/serving	% RDA
Pumpkin seeds, roasted, 1 ounce	156	37
Chia seeds, 1 ounce	111	26
Almonds, dry roasted, 1 ounce	80	19
Spinach, boiled, ½ cup	78	19
Cashews, dry roasted, 1 ounce	74	18
Peanuts, oil roasted, ¼ cup	63	15
Cereal, shredded wheat, 2 large biscuits	61	15
Soymilk, plain or vanilla, 1 cup	61	15
Black beans, cooked, ½ cup	60	14
Edamame, shelled, cooked, ½ cup	50	12
Peanut butter, smooth, 2 tablespoons	49	12
Potato, baked with skin, 3.5 ounces	43	10
Rice, brown, cooked, ½ cup	42	10
Yogurt, plain, low fat, 8 ounces	42	10
Breakfast cereals, fortified with 10% of the DV for magnesium, 1 serving	42	10
Oatmeal, instant, 1 packet	36	9
Kidney beans, canned, ½ cup	35	8
Banana, 1 medium	32	8
Salmon, Atlantic, farmed, cooked, 3 ounces	26	6
Milk, 1 cup	24–27	6
Halibut, cooked, 3 ounces	24	6

What are the different types of supplemental magnesium?

Magnesium comes bound to other molecules. When you go to the supplement shelf in the store, you'll find magnesium in lots of forms:

- magnesium oxide
- magnesium citrate
- magnesium malate
- magnesium threonate
- magnesium glycinate
- magnesium gluconate
- magnesium taurate

So which is best?

This question can be hard to answer.

First, as you will see in the clinical trial data below, it seems like all types of magnesium supplements will help a bit if your magnesium levels are low.

Magnesium oxide:
This inexpensive form of magnesium has very little absorption (~4%).[ref][ref][ref]

Many studies compare different forms of magnesium to magnesium oxide... and mag oxide always is the worst for boosting magnesium levels. However, this doesn't really tell us much about their absorption compared to each other. So when you read marketing

that says a certain form is 'better absorbed', keep in mind that they may have tested it against magnesium oxide.

Magnesium citrate:
A study compared the magnesium bioavailability of mag citrate, mag oxide, and an amino acid magnesium chelate. The trial lasted 60 days and was conducted on healthy adults. The results showed that magnesium citrate and the amino-acid chelate had greater absorption than magnesium oxide. Magnesium citrate led to the greatest serum magnesium levels both acutely and chronically.[ref]

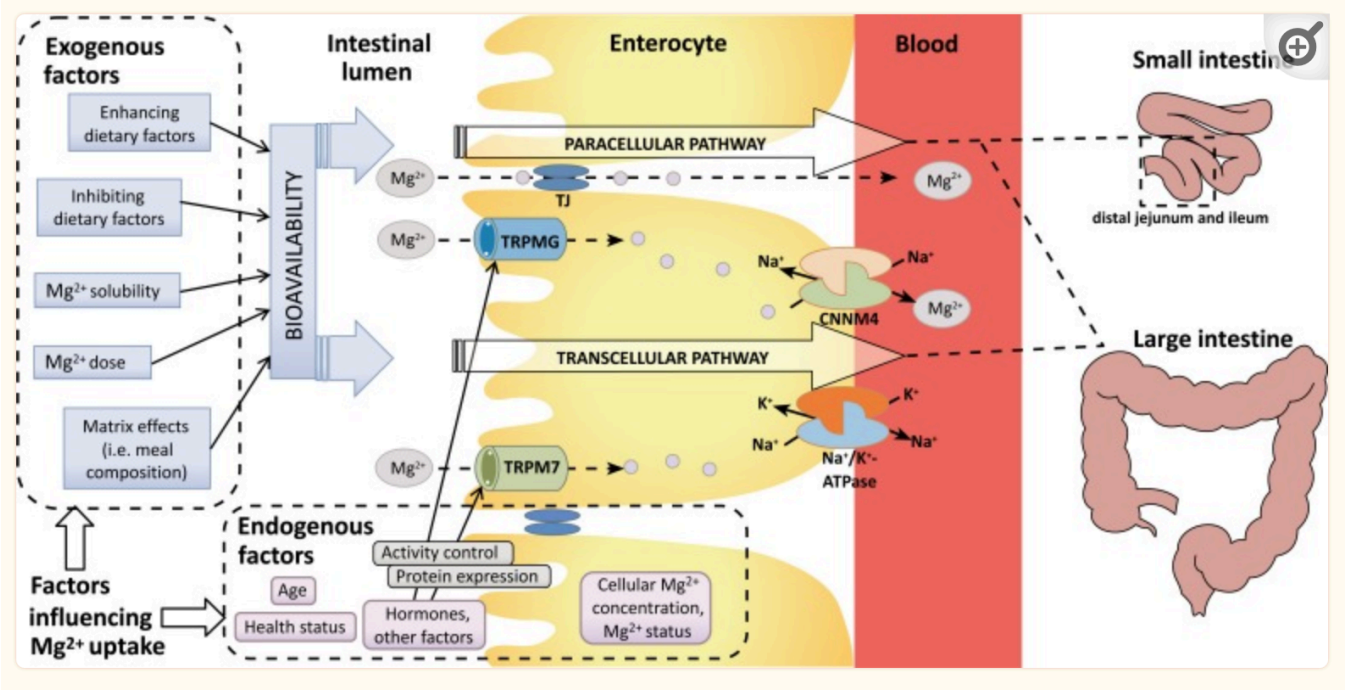
Magnesium threonate for the brain:
Animal studies and human trials show that magnesium threonate is the better form for memory and mood. It is thought that the threonate form of magnesium crosses the blood-brain barrier better than other forms.[ref][ref][ref]

Magnesium acetate > magnesium chloride:
An older study found magnesium acetate absorbs better than magnesium chloride.[ref]

Magnesium malate:
In rats, magnesium malate tops the list for absorption.[ref]

Magnesium taurate:
Research shows that magnesium taruate (magnesium with taurine) may be beneficial for heart health and reducing blood pressure. It is readily absorbed and also may help in anxiety disorders.[ref] [ref]

Let's look again at this diagram on factors influencing Mg uptake:



Absorption of magnesium in the intestines. Creative Commons PMC5652077 (good overview article)

The solubility of magnesium is affected by the type of supplemental magnesium. But as you can see, other factors impact absorption as well.

Taking magnesium with food:
Studies show that magnesium is absorbed a little bit better when taken with food.[ref]
But **less magnesium absorption** has been shown when taken with foods containing **oxalic acid or phytic acid**.[ref]

Better absorbed with fiber:
Non-digestible fiber, such as inulin or chicory, may increase magnesium absorption by around 12%.[ref][ref]

Clinical trials on supplemental magnesium:

Insomnia:
In a clinical trial with older adults, 250 mg of magnesium twice a day increased sleep time, sleep efficiency, and melatonin levels. The study used magnesium oxide as a supplement.[ref]

Diabetes:
A three-month study using 250mg elemental magnesium (combo of oxide, gluconate, and lactate) found improved insulin resistance and decreased HbA1C levels.[ref]

Migraines:
When compared to migraine rescue medications, magnesium showed similar efficacy. The trial used magnesium sulfate (2g) compared to metoclopramide 10 mg or prochlorperazine 10 mg.[ref]

Stress reduction:
In people with low magnesium levels, 300 mg daily of magnesium reduced stress scores by over 40%. The study used magnesium lactate dihydrate.[ref]

Pregnancy leg cramps:
A study using magnesium bisglycinate chelate (300 mg per day) for pregnancy leg cramps showed that it was a little better than a placebo.[ref]

PCOS:
Magnesium supplementation (250 mg magnesium oxide) for eight weeks in women with PCOS was associated with slightly lower testosterone levels and higher DHEA concentrations.[ref]

Insulin resistance:
A study using magnesium-enriched seawater reduced fasting insulin and HOMA-IR values after eight weeks.[ref]

Vitamin D deficiency:
In healthy postmenopausal women, 500 mg/day of magnesium increased vitamin D levels. At the beginning of the trial, all the women had low magnesium status, and 80% were deficient in vitamin D.[ref]

Diabetic wound healing:
A study of 250 mg of magnesium oxide showed improved diabetic wound healing and reduced fasting plasma glucose levels after 12 weeks.[ref]

Blood pressure:
A meta-analysis combining 34 trials using magnesium for blood pressure reduction shows that 300mg/day for a month can modestly reduce blood pressure by a couple of points.[ref]

Examine.com has a good article that covers more clinical trials on magnesium.

Side effects:

Too much supplemental magnesium will clean you out! Absorption of magnesium is tightly controlled in the intestines, and high concentrations there will trigger diarrhea to move it on out. High doses of magnesium citrate are sometimes used for colonoscopy prep...