

Lithium

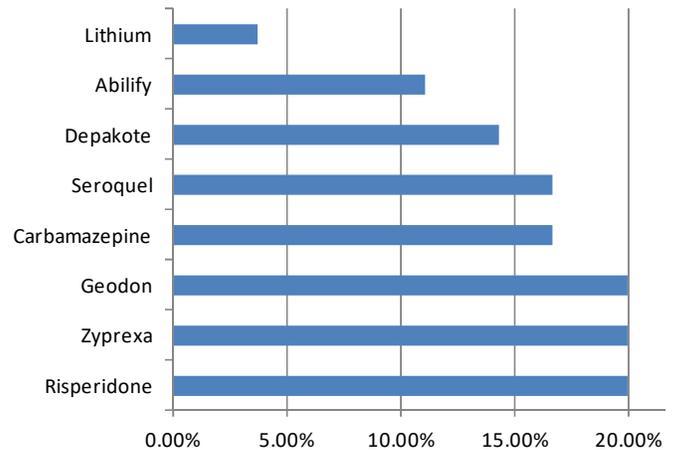
Lithium is natural salt that is found in the earth and, in trace amounts, in the human body. Lithium's healing properties have been known for centuries and has been used in the form of mineral spring water to treat headaches, physical pains and nerve problems. It was advertised as a healthy ingredient in early versions of 7-Up and Coca Cola.

In 1949, doctors discovered that higher doses of lithium could help depression and states of agitation (called mania). Lithium remains one of the most effective treatments available for these conditions, and is the oldest psychiatric treatment still in use. To this day, lithium continues to offer unique benefits for mental health, include:

- It enhances brain growth more than any other medicine.
- It prevent depression and suicide better than most medications.
- It has been called “the closest thing to a cure” for classic bipolar¹.
- It is the only psychiatric medicine that prevent dementia.
- It can allow people with bipolar disorder to safely reduce the number of medicines they take.

Despite these benefits, lithium has been underutilized in the United States because it is natural, so the pharmaceutical industry could never copyright it and had no motive to promote its use among doctors or patients. Lithium is more popular in countries where commercial forces do not play as strong a role on medical practice.

One myth about lithium is that it is difficult to tolerate. All mood stabilizers have problems with tolerability, but the chart at right shows that lithium's tolerability is far greater than that of other options:



Fatigue on mood stabilizers (%)²

Not only does lithium have less fatigue than other options, it also has less weight gain than most mood stabilizers.

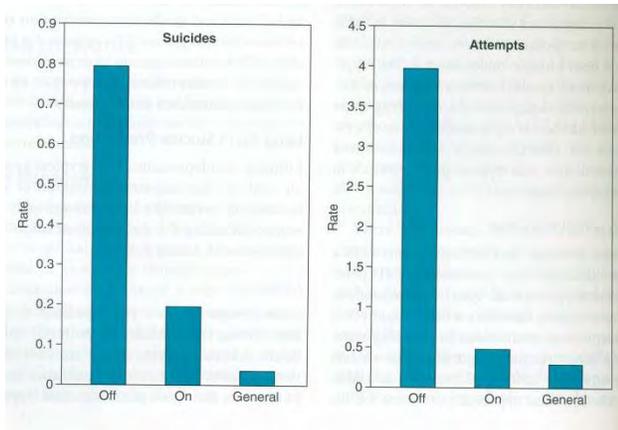
Key Points

1. Very effective for bipolar and non-bipolar depression
2. Helps brain growth, prevents suicide and dementia
3. Most side effects improve with lower dose
4. We will check labs regularly for lithium levels and to prevent thyroid and kidney problems.
5. High lithium levels are dangerous. Don't double up on doses. Stick to aspirin/tylenol for pain (avoid NSAID pain meds like ibuprofen/naproxen); be aware of other drug interactions (especially blood pressure meds).
6. Mood can worsen if lithium is stopped suddenly.

Lithium acts as three different medications, depending on the blood level:

| LEVEL | BENEFITS | SIDE EFFECTS |
|------------------|--|--------------|
| Low (0.2-0.6) | Enhances brain health, promotes immunity and partially prevents depression, bipolar, and dementia. | Rare |
| Medium (0.6-0.8) | Treats & prevents depression | Few |
| High (0.9-1.2) | Treats & prevents depression and mania | Common |

Lithium is often thought of as a treatment for bipolar disorder, but it is actually one of the most effective treatments for non-bipolar depression, and is particularly good at preventing depression. Lithium can prevent many serious mental problems, including violence, suicide and dementia. Sadly, 10-20% of people with chronic mood problems die by suicide. As the chart shows below, lithium brings this risk close to that of the general population:



Rate of completed and attempted suicide in mood disorders on vs. off lithium, and in the general population³

This finding is remarkable when one considers that nearly every other psychiatric medication has a warning that it can increase suicidal thoughts. Tendencies towards suicide and violence have a strong genetic and biological nature, and lithium seems to address this problem in ways that other medications don't. Many people who have struggled with thoughts of death their whole lives find that their mind shifts towards hope and life after starting lithium.

Medical benefits

Lithium improves the body's immune system by increasing the production of the white blood cells that fight infection. People who take lithium have fewer colds, and lithium can reduce specific viral infections such as herpes and possibly HIV. A few psychiatric medications can lower white blood counts, and adding lithium can reverse that

problem (e.g. with carbamazepine, valproate and clozapine).

Lithium has also been used to relieve cluster headaches, menstrual cramps and seborrheic dermatitis.

How it works

No other medicine works quite like lithium, which may explain why its benefits are so unique. It does not simply have a chemical effect; it improves the structure of the brain gradually over time. The brain contains natural healers within it, with names like BDNF and bcl-2, and lithium turns on the genetic pathways which produce more of these. This is how it enhances the growth and protection of brain cells:



Before treatment: the effects of depression and stress have caused this nerve cell to shrink back like a tree with few branches.



After treatment: lithium has strengthened the roots and connections of the brain cell. The result is better communication within the brain and better stress management.

When brain cells grow like this it helps people manage stress better and prevents mood problems for the long-term. Of all psychiatric medications, lithium and depakote have the most benefits on brain growth.

Lithium also modulates serotonin, which may explain how it reduces depression, suicide and violence. Lithium regulates inositol, a B-vitamin which is involved in depression (inositol itself

produces mild benefits in bipolar depression when taken as a supplement).

Lithium helps stabilize daily rhythms of sleep and energy, called circadian rhythms, which are usually disrupted in mood disorders.

How should I take it?

Lithium is better tolerated if taken all at night. This allows you to sleep through any side effects, while its benefits build up gradually over time. Higher doses might need to be split part in morning, part in evening.

Lithium is available as an immediate release form (lithium carbonate) or a stomach-coated, extended release (lithobid or eskalith). The immediate release is a little safer for the kidneys, and may be a better choice if you have side effects that linger in the morning (like tremor). On the other hand, the extended release is preferable if you have stomach problems on it, such as nausea. You should first try to relieve nausea by taking the lithium with milk, food or ginger products (note, regular ginger ale does not contain ginger). If the nausea persists, call us and we can change the formulation.

What if I forget a dose?

Take the missed dose as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule. Do not take a double dose to make up for a missed one. Do not take more than the prescribed daily amount in 24 hours.

How long do I need to take it?

Whether or not you can safely come off lithium depends on your diagnosis and which other medications you are taking. Most people with bipolar disorder need to stay on at least one mood stabilizer for the long term in order to prevent mood swings. If lithium helped, it is best to stay on it for at least 6 months before considering going off it. That gives the brain time to build up habits of stability.

What happens if I stop it?

If you try lithium for less than a month and do not tolerate it, you can stop it without any withdrawal problems. However, if you have been on lithium longer you should talk to us about how to come off. In some people, the original problems can return quickly if lithium is stopped too quickly, and lowering the dose slowly over 3 months can reduce that risk.



Lithium salt crystals. Most lithium was originally mined from Kings Mountain near Charlotte, NC.

Checking labs

You will need to have labs checked 1-2 times per year while on lithium to monitor the level of the medicine and ensure it is not impacting your thyroid or kidneys. If you take the medicine during the day, make sure to get the labs drawn before taking your daytime dose.

Your labs will also help us figure out why lithium isn't working fully. Not only does lithium need to be at the right level to work (see chart on page 1), it also works better when your thyroid levels are optimized (e.g. TSH level between 1.5-3).

We may check labs more often if you have a change in medicines that interact with lithium. After age 65, people may need lower doses of lithium to achieve safe levels.

Side effects

Most side effects occur early in treatment and improve with time or by lowering the dose.

| SIDE EFFECT | DESCRIPTION | TREATMENT |
|-------------------------------------|--|---|
| Thirst, increased urine, dry mouth. | Lithium increases urination and thirst. | Keep hydrated by drinking water. Avoid water in the 2-3 hours before bed if the urination wakes you up. |
| Tremor | A fine tremor, usually of the hands. If the tremor is severe, such as one that prevents you from using a fork, it may be an early sign of toxicity (see below). | Reduce caffeine. Lower the dose or use high-dose vitamin B6 (600-1000 mg/day). Medicines may help tremor (propranolol, primidone, gabapentin). |
| Weight | Weight gain can be due increased calories from drinking beverages, and changes in appetite and metabolism. In some studies lithium caused weight loss, though with long-term use their can be mild weigh gain. | Drink water rather than sodas or high-calorie beverages. Exercise (walk 30 minutes a day). Diet. Check and optimize thyroid levels. Medications (e.g. topiramate) may help. |
| Nausea, stomach discomfort | This is more common in the first months of treatment, occurring in 30% of people, and may go away. "Bloating" feelings can be due to a full bladder. | Take with food; use an extended release form of lithium; try antacids. |
| Tiredness | Lithium usually improves energy when it treats depression, but rarely can cause fatigue (5%). | Check and optimize thyroid levels. Change to immediate release and take at night. |
| Concentration | Some people report trouble with concentration and memory on lithium. Lithium will sometimes help concentration and memory when it treats depression. | Check and optimize thyroid levels. Talk to us about options. |
| Skin changes | <i>Rare:</i> acne, rash, irritation of hair follicles, mild swelling (edema), psoriasis (patches of dry/thick skin). | Antibiotic treatment usually clears the acne. Over-the-counter creams for dry skin. Omega-3 and inositol may help psoriasis and depression. |
| Headaches | Lithium improves <i>cluster headaches</i> , but headaches can also occur as a side effect. | Tylenol, aspirin and clinoril are safe; other NSAIDs (ibuprofen, etc) are not. |
| Diarrhea | Loose stools are common in the beginning of treatment and may continue throughout treatment. | Antidiarrheals such as Imodium are safe to take. |
| Hair loss | This rare (5% of people) effect often improves over time. | Try biotin 10mg/d, or a multivitamin with selenium/zinc (Centrum silver). |
| Sexual function | Little is known about this with lithium; it does not seem to affect sexual function as much as serotonin antidepressants. | Aspirin 240 mg/day helped men who experienced E.D. on lithium. Caution with aspirin if you take blood-thinners or have stomach ulcers. |
| Taste changes | A decrease in taste for food. | Ask us about treatments for dry mouth. |
| Coordination | Occasional periods of feeling faint, weak or uncoordinated. | Ask us about lowering lithium dose. |

Medical risks

Lithium has a few medical risks. Some of these can be prevented by stopping lithium if warning signs appear in your labs. Unlike most of the above side effects, these changes are more likely to happen the longer lithium is taken, and they may persist after stopping lithium.

| CHANGE | DESCRIPTION |
|-------------------------------|--|
| Low thyroid | Symptoms of decreased thyroid hormone (hypothyroidism) include lethargy, weight gain, dry skin, depression, and sensitivity to cold. This effect is common, occurring in 15-25% of people on long-term lithium treatment, and is usually resolves when lithium is stopped or is easily treatable with hormone replacement. |
| Kidney changes | Rare impairment of kidney function, usually caused by an overdose of lithium. Symptoms include increased urination, especially at night. |
| Heart changes | Changes in heart rhythms are rare; cardiac exams (EKG) should be followed if you are at risk. |
| Elevated calcium | Rarely, calcium levels can increase due to overactive parathyroid. Symptoms of high calcium include nausea, loss of appetite, and increased urination. |
| Changes in white blood cells. | Lithium can cause increases in white blood cells; this change is not a problem and may help fight infection. |
| Pregnancy | There is a small risk of heart defects in the child, especially if lithium is taken during the first trimester. Ask us about strategies to manage lithium safely during pregnancy if you need to take it. Lithium poses no known risks to the ovaries when it is taken before pregnancy. |
| Breast-feeding | Although children who are exposed to lithium during breast-feeding appear to develop normally, it is probably best to avoid this exposure. You can also minimize the exposure by breastfeeding when lithium levels are low, such as in the morning or at least 4-6 hours after your dose. Breast milk can also be pumped and stored during these safer times |

Interactions (partial list)

Many medicines can raise lithium levels, including over-the-counter remedies, so consult your physician before trying new medicines. Sometimes these medicines can be taken with careful monitoring of lithium levels.

Alcohol, Caffeine & Recreational Drugs

Alcohol can increase the dizziness and dyscoordination of lithium. Excessive alcohol use can lead to dehydration and high lithium levels. Marijuana can increase lithium's absorption and may lead to high blood levels. Caffeine, tea and coffee can lower lithium levels (slightly), so be careful if you are a regular user of these and then stop (that could raise your level).

Alcohol and recreational drugs can also prevent lithium from working.

Pain Medicines

Many pain medications, including ibuprofen (Motrin, Advil), rofecoxib (Vioxx), celecoxib (Celebrex) and naproxen (Aleve, Naprosyn) can increase lithium levels. Tylenol (acetaminophen), aspirin, clinoril, and opioid pain medicines are safe with lithium.

Diuretics, Heart and Blood Pressure Medicine

Diuretics (e.g. lasix, hydrochlorothiazide), which are often used to treat high blood pressure or edema/swelling, can increase lithium levels, as can ACE (angiotensin-converting enzymes) inhibitors (e.g. enalapril, captopril), and calcium-channel blockers (e.g. verapamil, diltiazem, nifedipine). These medicines should be taken only under close medical supervision.

Other Psychiatric Medicines

Lithium may slightly increase the risk of two very rare conditions that can occur with psychiatric medicines. One is *Serotonin Syndrome*, which causes diarrhea, fever, muscle twitching and confusion, and can happen with antidepressants that affect serotonin (e.g. SSRIs, Effexor, Cymbalta). The other is *Neuroleptic Malignant Syndrome*, which can rarely occur with

antipsychotics. Lithium may prevent a serious side effect of antipsychotics: *Tardive Dyskinesia*.

Other medicines that can raise lithium levels:

Tetracycline, doxycycline, metronidazole, eplerenone. Anti-parkinson medicines can interact with lithium.

Medicines that can lower lithium levels:

Antacids, caffeine, coffee, tea, acetazolamide, urea, and theophylline.

If you stop these after regularly taking them, your lithium level may rise.

For more information on drug interactions:

reference.medscape.com/drug-interactionchecker

Overdose

An overdose of lithium should be assessed and treated in the emergency room. A toxic overdose can cause confusion, imbalance while walking, slurred speech, nausea and vomiting, diarrhea, tremor.

A high level can be dangerous to the kidneys and the brain. If you think your level is too high, stop lithium and drink fluids (especially Gatorade or normal saline, which can be made by dissolving ¼ teaspoon of salt in 1 cup of warm water).

How to store and dispose of medication

- Keep out of the reach of children.
- Store away from heat, direct light and damp places.
- To safely dispose of unwanted pills: Do not pour in the toilet or sink (it will enter the water supply). To prevent children or pets from eating it, mix unwanted pills in a bag with a little water and inedible trash (such as coffee grounds or kitty litter) and throw in the trash.



Before 1950, people flocked to resorts such as the one above in Georgia to drink lithium spring water. Lithium's benefits on health were widely appreciated, and two U.S. presidents had it shipped in bulk to the White House. After 1950, lithium became regulated so that it could only be prescribed by physicians, putting an end to its use as a health-spa treatment and ingredient in popular beverages like 7-up:



Quick facts

| | |
|--------------|--|
| Brand names | Lithobid, Eskalith |
| Dose range | Dosing is based on your blood level, which can range from 0.6-1.2 (see page 1). Typical dosages are 900-1800mg/day. |
| Sizes | <ul style="list-style-type: none"> > Caps: 150, 300, 600mg; Tabs: 300mg > CR (Eskalith)*: 450mg > SR (Lithobid)*: 300mg > Liquid (Citrate): 8 mEq/5 mL <p>*do not crush or chew CR/SR tabs</p> |
| Peak dose | <ul style="list-style-type: none"> > Regular release: 1-1.5 hours after taking it > CR/SR form: 3-4 hours after taking it |
| Release date | 1949 |
| FDA-approval | Bipolar disorder |

References

- [1] Ghaemi SN, Hippocratic psychopharmacology for Bipolar Disorder, *Psychiatry* 2006; 3(6): 30-39.
- [2] Srivastava S, Ketter TA. Clinical relevance of treatments for acute bipolar disorder. *Clin Ther.* 2011(33):B40-8.
- [3] Goodwin FK, Jamison KR. *Manic-Depressive Illness* (p 968). Oxford, 2007.