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The Uric Acid Paradox: Why Too Little May Hurt Your Brain and Too Much Hurts Your Joints

Analysis by Dr. Joseph Mercola | November 26, 2026

STORY AT-A-GLANCE

- A new study found that people with Alzheimer's-related brain plaques and memory problems had depleted blood levels of uric acid and allantoin, a compound formed when uric acid neutralizes free radicals. Lower levels tracked with heavier plaque burden and worse cognitive scores
- Uric acid is one of your body's most important antioxidants and supplies roughly half of the antioxidant capacity in your blood. Yet it is also the compound that crystallizes in your joints and causes gout
- Whether uric acid helps or harms depends on where it sits, how your body makes it, and whether it crystallizes. Concentration alone does not tell the whole story
- Temperature, sodium, calcium, acidity, hydration, and repeated impact all influence when uric acid crystallizes. This helps explain why gout so often strikes the big toe in the middle of the night
- Raising uric acid with supplements failed to slow Parkinson's disease in a major clinical trial and increased kidney stones. The smarter goal is to keep your level in a moderate middle range through hydration, whole foods, warmth, and a healthy metabolism

Uric acid has a terrible reputation. Most people know it only as the cause of gout, the excruciating joint disease that once earned the nickname "disease of kings." Doctors routinely flag high uric acid on blood work and prescribe drugs to push it down.

But uric acid has a second identity that rarely makes headlines. It is one of the most powerful antioxidants circulating in your blood. A new study published in JCI Insight suggests that when uric acid levels fall too low, your brain may lose part of its defense against Alzheimer's disease.[1]

So which is it: villain or protector? The answer is both, and the reason why reveals something important about how your body manages oxidative stress. Understanding the variables that tip uric acid one way or the other gives you practical control over which side of the paradox you land on.

Low Uric Acid Linked to Plaques and Cognitive Impairment

Researchers at Ruijin Hospital in Shanghai combined a mouse model of Alzheimer's disease with a human clinical study. Their goal was to understand how purine metabolism relates to the buildup of amyloid-beta, the sticky protein fragments that form Alzheimer's plaques.[2] Purines are building blocks of DNA and of adenosine triphosphate (ATP), your cells' energy currency. Uric acid is the end product of purine breakdown in humans.

- **Purine metabolism was the most disrupted pathway in the mice —** Broad metabolic profiling of blood from Alzheimer's-model mice identified purine metabolism as the most significantly altered pathway. Levels of compounds such as adenine and adenosine shifted as plaque burden increased across disease stages.

- **People with plaques and cognitive impairment had depleted uric acid —** In the human cohort of 103 people, participants were classified by brain amyloid status and cognitive function. Those with confirmed plaques and cognitive impairment had specifically lower blood levels of uric acid and allantoin. Lower levels correlated with heavier amyloid load, more brain inflammation, and poorer cognitive scores.

- **Plaques appeared to be the link —** Statistical modeling suggested that low uric acid and allantoin did not impair cognition directly. Instead, their association with cognitive decline ran through amyloid buildup.

- **Changes may predict future decline —** Over two years of follow-up in a subgroup of 26 people, changes in guanosine, a purine metabolite appeared to forecast how quickly cognition would worsen.

- **Allantoin helped the brain's cleanup crew in mice —** When the researchers gave allantoin to Alzheimer's-model mice, plaque buildup decreased in a small group of mice. The researchers attributed this to microglia, the brain's resident immune cells, which appeared to become better at engulfing and removing amyloid.*

Why You Shouldn't Rush to Raise Your Uric Acid

These findings are intriguing, but several important caveats keep them from being a green light to push uric acid higher.

- **Low uric acid may be a result of decline, not a cause —** People developing cognitive impairment often eat less, lose weight, and become frail. Uric acid naturally falls with weight loss and reduced protein intake. Low levels may simply reflect a body in decline.

- **The mouse results may not translate to people —** This point is easy to miss. Mice have an enzyme called uricase that converts uric acid into allantoin as a routine metabolic step. Humans lost that enzyme millions of years ago.

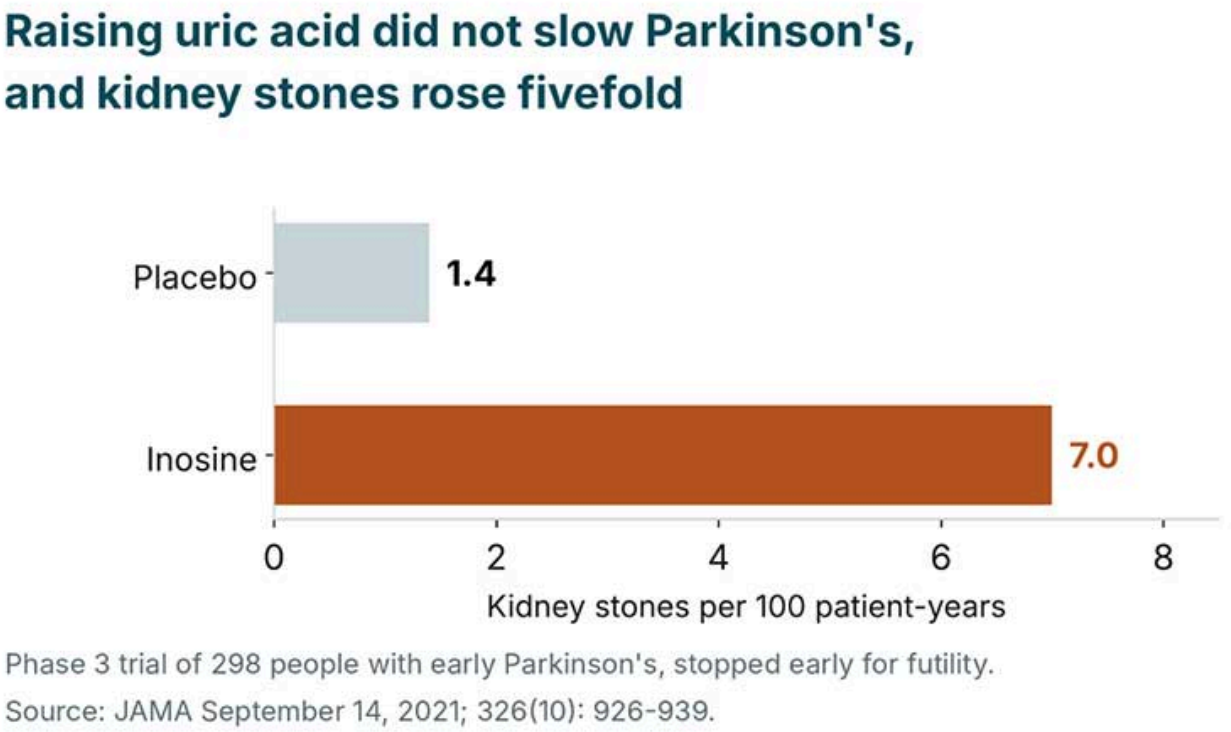
  In your body, allantoin forms only when uric acid is burned up neutralizing free radicals. In fact, allantoin is so closely tied to oxidation that researchers use it as a marker of oxidative stress. In one study, plasma allantoin rose about 200% above baseline after just 10 minutes of intense running, while uric acid rose only 20%.[3] That's why giving allantoin to a mouse is a very different intervention from anything that happens naturally in a human.

- **Genetic evidence does not show cause and effect —** Researchers can study gene variants that set a person's lifelong uric acid level, a kind of natural experiment. A large analysis of this type found no clear causal effect of uric acid on Alzheimer's,

Parkinson's, amyotrophic lateral sclerosis (ALS), or multiple sclerosis.[4]

- **Raising uric acid has already been tested and failed —** The strongest evidence comes from Parkinson's disease, where low uric acid also predicts faster progression. In a phase 3 trial, 298 people with early Parkinson's received either inosine, a compound that raises uric acid, or a placebo for up to two years.[5]

  Inosine raised uric acid by about 2 milligrams per deciliter (mg/dL), from an average of 4.6 mg/dL. Disease progression did not slow, and the trial was stopped early for futility. The inosine group did have fewer serious adverse events, but it developed kidney stones five times as often: 7.0 versus 1.4 per 100 patient-years.



  On the other side of the ledger, the observational signal keeps showing up. In a United Kingdom study of nearly 300,000 people, those diagnosed with gout had about a 24% lower risk of developing Alzheimer's disease, even after matching for age, sex, and body weight.[6]

Gout Is a Crystal Problem, Not Just a Uric Acid Problem

To reconcile these findings, it helps to understand what actually happens in gout. Gout is driven by physical chemistry. In your body fluids, uric acid circulates as a salt called monosodium urate. When its concentration rises above about 6.8 mg/dL at normal body temperature, it can come out of solution and form needle-shaped crystals.

Your immune system treats those crystals as a threat. It triggers an intense inflammatory response that produces the swelling, heat, and severe pain of a gout attack. Below that threshold, dissolved uric acid behaves very differently.

Large population studies show that both extremes carry risk. Data from the U.S. National Health and Nutrition Examination Survey show a U-shaped relationship between uric acid and death risk.[7] Among adults with cardiovascular disease, the risk of dying was lowest at about 5.7 mg/dL and rose on either side.[8] In other words, there appears to be a sweet spot.

How Uric Acid Switches from Protector to Troublemaker

Here is how I see the paradox resolving. Some of these points are well established, and others are my interpretation of how the pieces fit together.

- **Location matters —** In your blood, outside your cells, uric acid is a potent antioxidant. Bruce Ames proposed decades ago that humans retained high uric acid levels partly to compensate for losing the ability to make vitamin C.[9] Uric acid is particularly good at neutralizing peroxynitrite, one of the most damaging oxidants in your body.

  Inside your cells, uric acid behaves differently. It can activate enzymes that generate oxidants, stress your mitochondria, and reduce nitric oxide, the molecule that keeps blood vessels flexible.

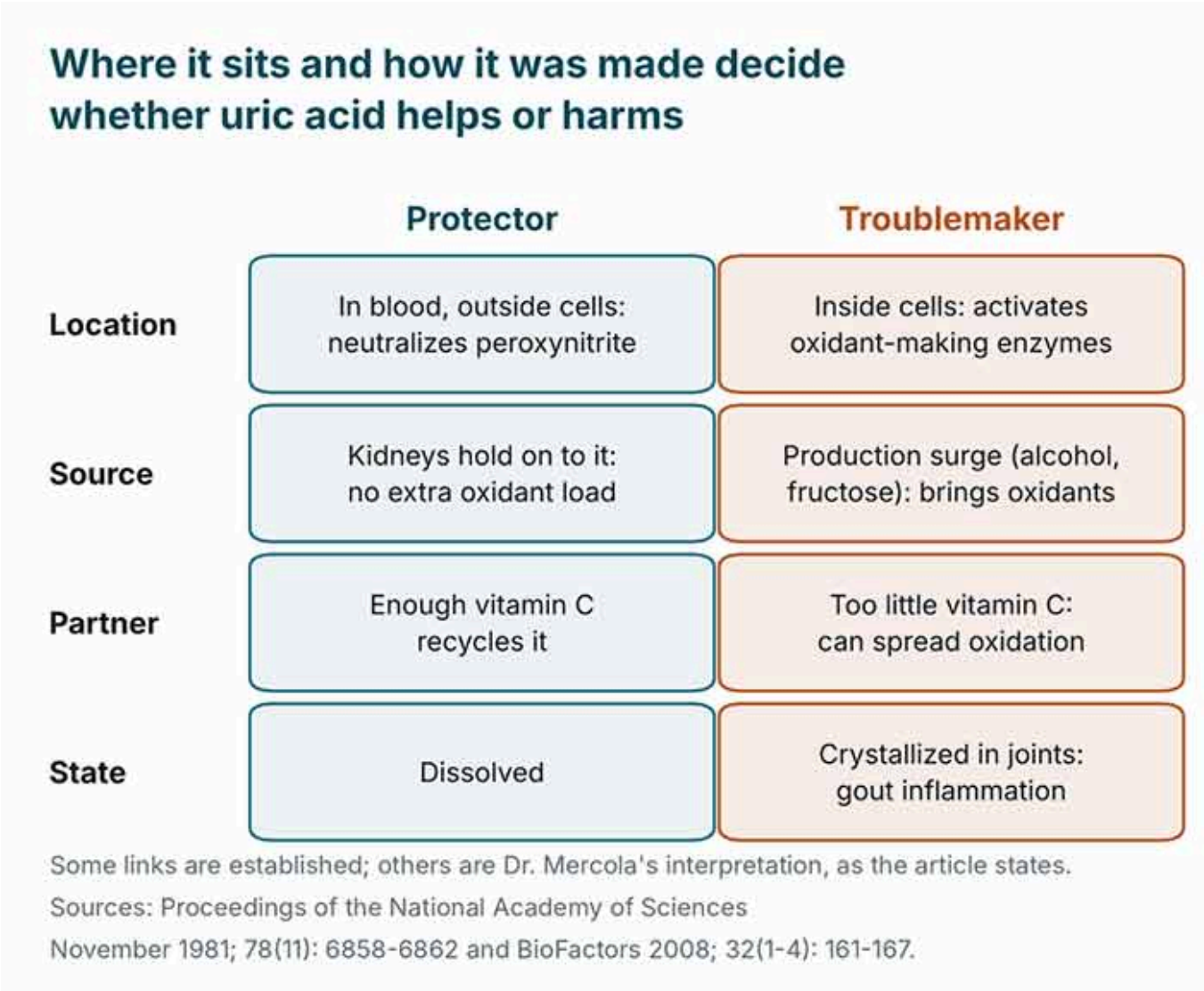
- **How your body makes it matters even more —** This is the variable a blood test cannot see. The enzyme that produces uric acid, xanthine oxidase, releases superoxide and hydrogen peroxide as it works. When uric acid rises because

production is surging, such as after heavy alcohol intake or large amounts of fructose from sodas and processed foods, it arrives with its own load of oxidants.

When uric acid is moderately elevated simply because your kidneys hold on to it, that oxidant burden is not there. Children with Down syndrome illustrate this split. They have high uric acid and higher total antioxidant capacity, yet they also show elevated allantoin, a sign of ongoing oxidative damage.[10]

- **Antioxidant partners matter —** When uric acid neutralizes a free radical, it becomes a mild radical itself. Vitamin C helps recycle it. Without enough vitamin C, particularly in fatty environments like cell membranes, uric acid can spread oxidation rather than stop it.

- **Metabolic health matters —** Insulin signals your kidneys to retain uric acid. Much of the research linking high uric acid to heart disease and metabolic problems may actually be measuring insulin resistance, with uric acid serving as a convenient marker.



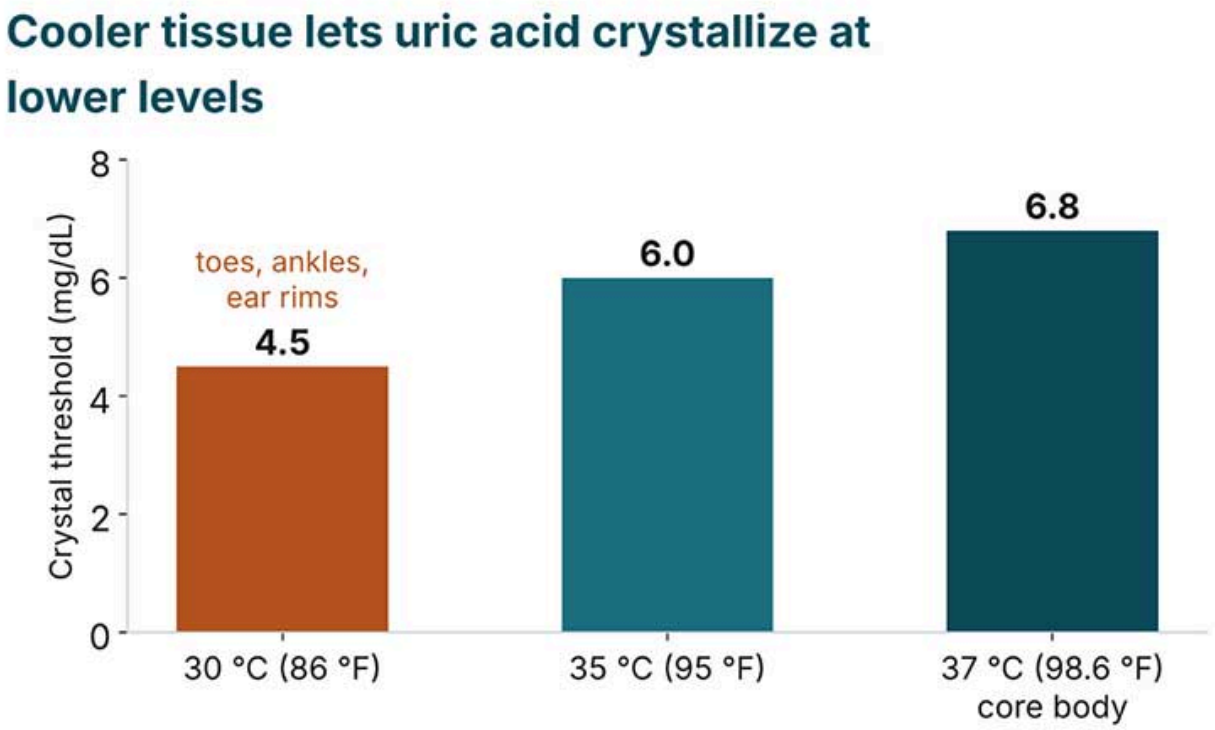
For the brain, one plausible explanation ties these points together. Microglia need energy and intact cell membranes to clear amyloid, and peroxynitrite damages both. Falling uric acid may weaken your defense against peroxynitrite at the blood-brain barrier and in the tiny blood vessels of the brain, leaving microglia less effective.

It is equally possible that low uric acid is simply a readout of disrupted energy metabolism upstream. If that's the case, raising uric acid would be like adjusting a gauge rather than fixing the engine, which would explain the failed Parkinson's trial.

The Variables That Control Uric Acid Crystals

If gout comes down to crystals, the next question is what makes uric acid more or less likely to crystallize. Several factors play a role.

- **Temperature —** This is the factor most people overlook. Uric acid becomes less soluble as tissue cools. Laboratory measurements show the crystallization threshold falling from about 6.8 mg/dL at 37 degrees Celsius (98.6 degrees F) to roughly 6.0 at 35 C (95 F) and about 4.5 at 30 C (86 F).[11] Your toes, ankles, and the rims of your ears run cooler than your core, which helps explain why gout so often strikes the big toe and why uric acid deposits can form on the ears.



Laboratory measurements. Source: Arthritis & Rheumatism 1972; 15(2): 189-192.

- **Acidity —** Acid speeds up crystal formation both directly and by freeing up calcium, which strongly promotes urate crystals.[12] An inflamed joint can become more acidic, which may help a gout attack feed on itself.

- **Calcium and sodium —** Calcium greatly accelerates both the formation and growth of urate crystals.[13] Because the crystal is a sodium salt, higher sodium in body fluids also reduces how much urate can stay dissolved.

- **Dehydration and the nighttime effect —** One explanation is that at night, your joints reabsorb water faster than they clear uric acid, so its concentration in joint fluid rises. Combine that with cooler feet and some overnight dehydration, and you have

the classic gout attack that wakes someone at 3 a.m.

- **Mechanical shock —** Physical impact greatly increased crystal formation in laboratory studies.[14] Impact can also dislodge crystals already sitting in a joint. The big toe joint takes heavy repeated loading with every step, which adds to its vulnerability.

- **Cartilage condition —** Worn or damaged cartilage provides surfaces where crystals can take hold. This may be why gout tends to settle in joints already affected by arthritis.

- **Rapid swings in uric acid —** Sudden drops, such as when starting uric acid-lowering drugs, can trigger attacks by loosening existing deposits. So can sudden rises after heavy drinking.

- **Lactate and ketones —** Heavy alcohol use, intense exercise, and extended fasting raise these acids, which compete with uric acid for removal by your kidneys and push blood levels higher.

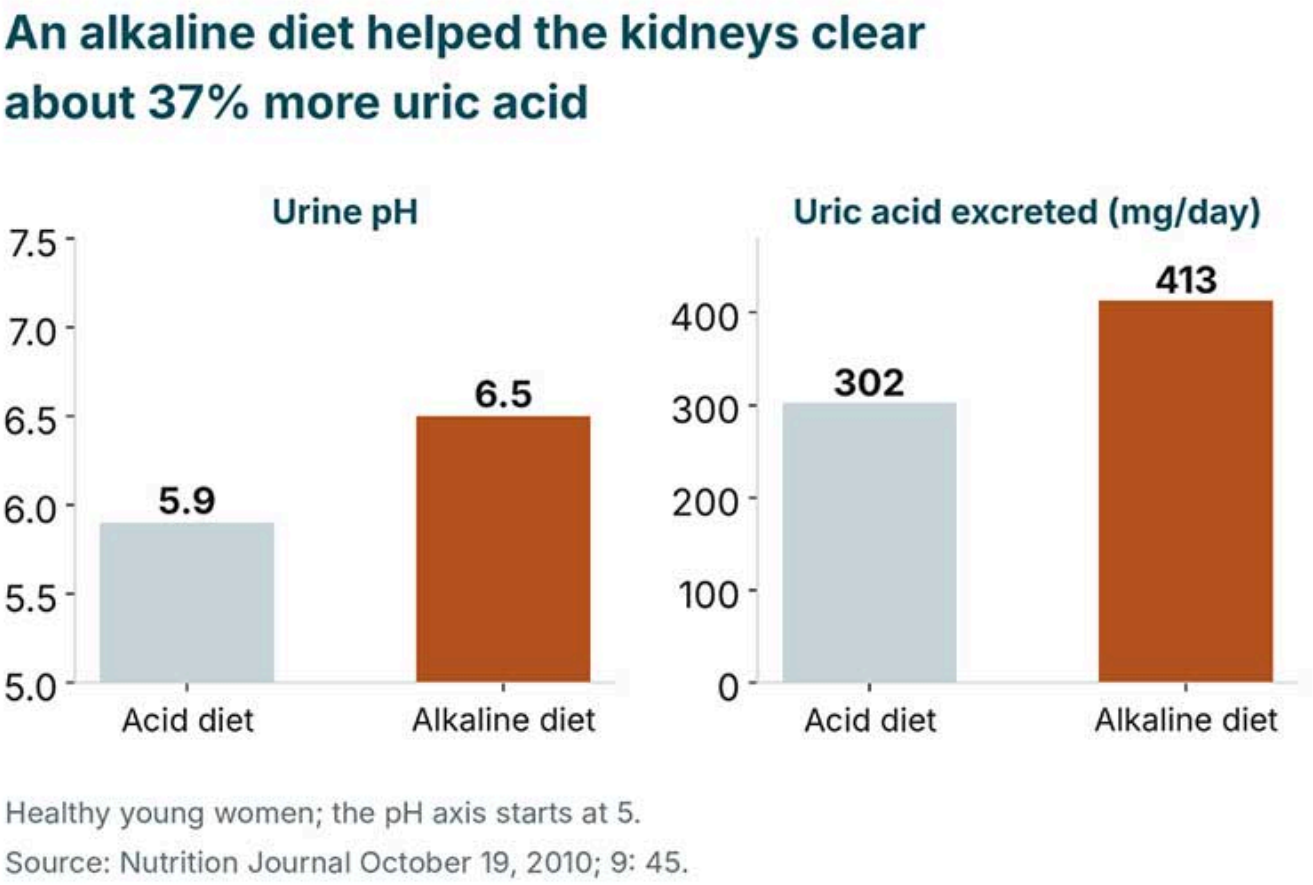
Would Being More Alkaline Help?

Many people assume that eating a more alkaline diet raises the level at which uric acid crystallizes in the blood. It doesn't, because your blood pH is held tightly between 7.35 and 7.45. At that pH, about 98% of uric acid is already in its dissolved salt form, so there is little room for improvement.

Where pH makes a large difference is in your urine. Urine pH ranges from about 5 to 7.5. In acidic urine, uric acid is poorly soluble and can form kidney stones. In more alkaline urine, it is many times more soluble.

That shift also helps you excrete more uric acid. In a study of 26 healthy young women, a vegetable- and fruit-rich alkaline diet raised urine pH to 6.5, compared with 5.9 on a protein-rich acid diet.[15] Daily uric acid excretion was 413 mg on the alkaline diet versus

302 mg on the acid diet, about 37% higher, even though the alkaline diet contained fewer purines.



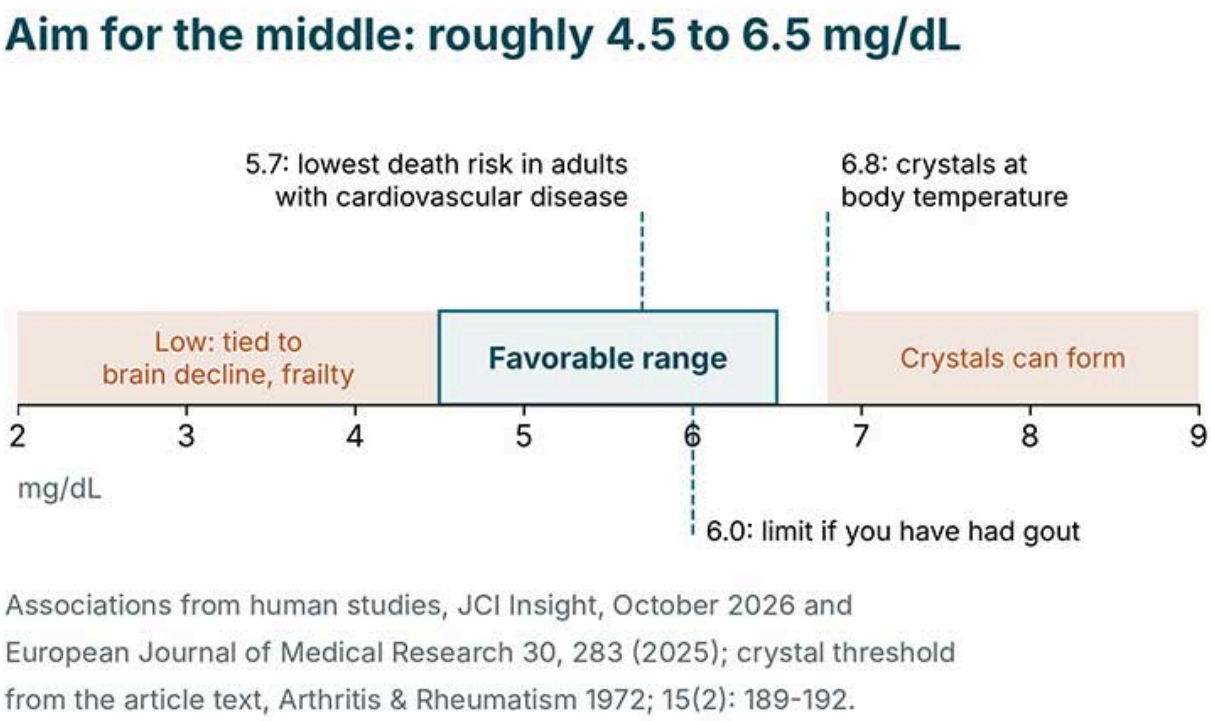
So an alkaline diet won't let you safely carry more uric acid in your blood. It does help your kidneys clear the excess and helps protect you from uric acid stones.

How to Keep Uric Acid in the Healthy Middle

The goal is not to drive uric acid as low as possible or to push it higher. It is to keep it in a moderate range while reducing the factors that turn it harmful.

- **Know your number —** Uric acid is not part of a standard metabolic panel, so you'll need to ask for it. Talk to your healthcare provider about whether this testing is appropriate for you. Based on the current evidence, a range of roughly 4.5 to 6.5 mg/dL looks reasonable to me.

That is above the low levels associated with brain decline and frailty, and below the point where crystals form at core body temperature. If you've ever had gout, aim to stay under 6 mg/dL, since cooler joints crystallize at lower levels.



Associations from human studies, JCI Insight, October 2026 and European Journal of Medical Research 30, 283 (2025); crystal threshold from the article text, Arthritis & Rheumatism 1972; 15(2): 189-192.

- **Cut the sources that produce uric acid along with oxidants —** Eliminate sodas, sweetened drinks, and processed foods containing high-fructose corn syrup. Avoid alcohol, especially beer, which delivers purines and alcohol together. Whole fruit is a different matter. Its fiber, potassium, and vitamin C help buffer its fructose, and vitamin C helps your kidneys excrete uric acid.

- **Eat to alkalinize your urine —** Build meals around whole fruit and well-cooked vegetables. This raises urine pH, increases uric acid excretion, and may help lower your risk of uric acid kidney stones.

- **Stay hydrated, especially in the evening —** Steady water intake keeps uric acid diluted in your blood, urine, and joint fluid. Drinking enough in the evening helps counter the overnight concentration effect.

- **Keep your feet warm —** If you're prone to gout, wear socks at night and avoid letting your feet get cold. A few degrees can meaningfully change whether uric acid stays dissolved.

- **Avoid crash diets and extreme fasting —** Ketones compete with uric acid for removal by your kidneys and can trigger attacks. Most adults do well with roughly 250 grams of carbohydrates daily from whole fruit, white rice, and root vegetables, which also support healthy metabolism.

- **Protect your joints from repeated impact —** Walking patterns that slam the heel and roll inward concentrate stress on the big toe joint with every step. Softer, more controlled walking may help reduce that mechanical load.

- **Don't take inosine or allantoin supplements to raise uric acid —** The inosine trial showed no benefit for Parkinson's and a fivefold rise in kidney stones. Allantoin supplementation has only been tested in mice, which handle uric acid very differently than humans.

- **Pay attention to unexpectedly low levels as you age —** A falling uric acid level in an older adult, especially alongside weight loss, can be an early sign of frailty. Protect muscle with resistance training and adequate protein, about 0.8 grams per pound of ideal body weight daily, with about one-third from collagen.

If you take uric acid-lowering medication or have a history of kidney stones or kidney disease, don't change your treatment without talking to your doctor.

**These findings are from laboratory or animal research and may not directly apply to human health.*

Frequently Asked Questions

Q: Is uric acid good or bad for you?

A: Both. In your blood, uric acid is a powerful antioxidant that supplies roughly half of your blood's antioxidant capacity. Above about 6.8 mg/dL, it can crystallize in your joints and cause gout. Large population studies show the lowest risk of death in the moderate middle range, with higher risk at both extremes.

Q: What did the new Alzheimer's study find?

A: People with Alzheimer's-related brain plaques and cognitive impairment had lower blood levels of uric acid and allantoin, and lower levels tracked with more plaque and worse cognition.[16] In mice, allantoin supplementation helped the brain's immune cells clear amyloid. Because mice process uric acid differently than humans, the supplementation results may not apply to people.

Q: Should I try to raise my uric acid to protect my brain?

A: No. A major clinical trial that raised uric acid with inosine failed to slow Parkinson's disease and increased kidney stones fivefold.[17] Genetic studies also do not show that higher uric acid prevents Alzheimer's.[18] Focus instead on keeping it in a healthy middle range.

Q: Why does gout usually affect the big toe?

A: Uric acid becomes less soluble as temperature drops, and the big toe is one of the coolest joints in your body. It also absorbs heavy repeated impact with every step, and both cool temperatures and mechanical shock promote crystal formation.

Q: Does an alkaline diet raise the level of uric acid I can tolerate?

A: Not in your blood, because your body holds blood pH within a narrow range. An alkaline diet does raise urine pH, which helps your kidneys excrete more uric acid and can reduce your risk of uric acid kidney stones.[19]

This article is for informational purposes only and does not constitute medical advice. Consult a qualified healthcare provider before making changes to your health regimen.

Sources and References

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