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Vitamin B3 Reversed Body-Wide Damage from NAD Loss in Mice; Why Niacinamide Is the Preferred Form

Analysis by Dr. Joseph Mercola | November 16, 2026

STORY AT-A-GLANCE

- NAD is a coenzyme every cell needs to turn food into energy, repair DNA, and run its repair and renewal programs
- A new Mayo Clinic study starved young mice of NAD for months. The result was frailty, bone and muscle loss, cataracts and an early death. Six weeks of ordinary vitamin B3 reversed most of it
- The researchers rescued the mice with nicotinic acid, the form in standard lab diets. That doesn't make it the best form for you, though. The way your body actually builds NAD points to niacinamide
- Taken by mouth, the expensive precursors nicotinamide riboside (NR) and nicotinamide mononucleotide (NMN) are largely converted to plain niacinamide in your liver. A 2026 phase 3 trial of NR in Parkinson's patients found they did worse than on placebo
- Niacinamide is the fuel. The enzyme NAMPT is the bottleneck that turns it into NAD, and exercise and fasting turn NAMPT up

Why NAD Is One of the Most Important Molecules in Your Body

If you had to pick one molecule that touches nearly every process keeping you alive, NAD (nicotinamide adenine dinucleotide) would be near the top of the list. It does two very different jobs.

First, it carries electrons. Inside your mitochondria, NAD picks up electrons from the food you burn and hands them to the energy chain that makes ATP, your cells' fuel. Second, it is consumed as raw material. Enzymes that repair DNA (PARPs), the sirtuins that govern cellular maintenance, and the immune enzyme CD38 all break NAD apart to do their work.[1]

Table 1. Major jobs of NAD in your body

System	What NAD Does
Energy	Carries electrons to the mitochondrial energy chain to make ATP
DNA repair	Fuels PARP enzymes that fix damaged DNA
Repair and renewal	Powers sirtuins that regulate metabolism and stress resistance
Immunity	Consumed by CD38, which rises with inflammation
Daily rhythm	NAD production cycles with your internal clock[2]
Reproduction	Placental NAD helps set the timing of labor[3]
Eyes and brain	Low NAD is linked to retinal degeneration and proposed as a risk factor for late-onset Alzheimer's[4,5]

Researchers increasingly see falling NAD as a common thread linking aging and chronic disease.[6] That is why efforts to keep it high deserve attention. The question is, what's the best way to do it?

What Happens When NAD Runs Low

Mice are hard to make NAD-deficient because, unlike us, they efficiently make NAD from the amino acid tryptophan. Researchers at Mayo Clinic and Utah State University got around this with "acquired niacin dependency" mice. These mice carry a human enzyme that diverts tryptophan away from NAD, making them depend on dietary B3 the way humans do.[7,8]

When these young mice were fed a B3-free diet, NAD fell in all nine tissues tested.[9] What followed reads like accelerated decline.

Table 2. What the 2026 study found[10]

Finding	Detail
NAD	Fell in spleen, liver, heart, brain, kidney, lung, fat, muscle, and pancreas
Frailty	Higher frailty scores, kyphosis (hunched spine), cataracts, and loss of fur color
Bone	Fewer and thinner trabeculae; bone formation fell and breakdown rose
Muscle	About 55% worse grip test within four weeks; less lean mass and endurance
Metabolism	Fat stores depleted; blood sugar crashed during fasting because the liver couldn't make glucose

Finding	Detail
Inflammation	Rising inflammatory signals, immune cells invading the liver, more senescent “zombie” cells
Survival	Deficient mice died early; 40% of deficient females died, with no deaths among controls
Reversal	After 15 weeks of deficiency, six weeks of B3 restored NAD and reversed most damage. Of 3,695 liver genes thrown off, 3,409 returned to normal

A drug that clears senescent cells helped somewhat without restoring NAD. Restoring B3 did far more. The takeaway is simple and powerful: In these mice, the damage from chronic NAD loss was largely reversible, and plain dietary B3 at an ordinary dose reversed most of it. No exotic precursor was needed. These findings are from laboratory or animal research and may not directly apply to human health.

How to Read This Study Like a Scientist

Studies are only as useful as your ability to read them correctly. This one is a great teaching example.

Table 3. Questions to ask of any study, applied to this one

Question	What this study shows
What exactly was tested?	NAD deficiency and its reversal, not supplementing healthy animals

Question	What this study shows
Which form of the nutrient?	Nicotinic acid, the standard B3 in this lab's diets[11]
Was that form compared to others?	No. Niacinamide, nicotinamide riboside (NR), and nicotinamide mononucleotide (NMN) were never tested
Is it a model of aging?	The authors say no. Epigenetic age didn't change, and most aging-related gene changes were nonexistent. There was also no rise in lipid peroxidation
What was not measured?	The mouse dose doesn't translate to a human dose

The most important lesson is this: Just because researchers used nicotinic acid doesn't mean it's the best choice. Scientists usually pick the form that is standard in lab chow, not the form that is optimal for people. To decide which form is best, you need to look at how your body handles each one, and at the human evidence.

Why Niacinamide Beats Nicotinic Acid

- **It's the form your body actually moves around —** Isotope-tracing work from Princeton shows how the system really runs. Your liver makes NAD from tryptophan and then releases niacinamide into your blood. Your other tissues build their NAD from that circulating niacinamide.[12]

  In other words, niacinamide is your body's own NAD currency. Nicotinic acid enters through a different enzyme that is most active in the liver, kidney, and gut. Much of its benefit to the rest of your body is routed back through niacinamide anyway.

- **Your muscles depend on the niacinamide route —** In skeletal muscle, NAD is made mainly through the salvage pathway, where NAMPT converts niacinamide into NAD.[13]

- **Nicotinic acid brings baggage at high doses —** Nicotinic acid triggers the well-known skin flush. In the 25,673-person HPS2-THRIVE trial, 2 grams a day of extended-release nicotinic acid (with a flush-blocking drug) did not reduce heart attacks or strokes, while increasing serious diabetes complications, new diabetes, infections and bleeding.[14]

- **Niacinamide has the stronger human outcome record —** In a phase 3 randomized trial, 500 mg of niacinamide twice daily reduced the rate of new nonmelanoma skin cancers by 23% over 12 months in 386 high-risk patients, with no notable side effects.[15] In a 2026 analysis of 2,920 matched patients with high eye pressure, niacinamide users were 66% less likely to develop glaucoma over about four years.[16]

  That glaucoma study is observational. It shows an association, not proof of cause, and it didn't report doses.

To be fair, nicotinic acid can raise NAD well. In a small Finnish study, 750 to 1,000 mg a day raised blood NAD up to eightfold and improved muscle strength in people with mitochondrial myopathy.[17] It works. It just carries side effects that niacinamide avoids, and it isn't the form your tissues ultimately use.

These findings are from research conducted in clinical settings. Results may not apply to all individuals.

The Expensive Precursors: What the Evidence Really Shows

NR and NMN are marketed as smarter ways to raise NAD because they skip the NAMPT step. That argument works in a test tube, but it mostly falls apart in your gut.

When given intravenously, both reach tissues intact. When swallowed, both are largely broken down to niacinamide in the liver.[18] So most of what you pay for becomes the same niacinamide you could buy for pennies, and it still has to pass through NAMPT.

The clinical results are sobering. In the NOPARK trial, an independent phase 3 study published in JAMA in October 2026, 410 people with early Parkinson's disease took 1,000 mg of NR a day or a placebo for a year.[19] Those on NR did worse. Their disease rating scores worsened by 2.72 points more than placebo, and their nonmotor symptoms also worsened more.

In fairness, serious adverse events were actually less common in the NR group (8.3% vs 14.1%). Still, a year of the most heavily studied NAD precursor failed to help, and the treated group declined faster.

That leads to another lesson in reading studies: Check who paid. The widely cited mouse study claiming NR has "superior" bioavailability to niacinamide and nicotinic acid included co-authors from the company that sells NR.[20] Industry funding doesn't make a study wrong, but it is a reason to look harder.

Then there's the cost. Niacinamide costs about 72 cents a month at my recommended dose. That is roughly 30 times cheaper than a typical NMN product and nearly 70 times cheaper than branded NR (Figure 2).[21,22]

No one is going to run ad campaigns for a vitamin that costs pennies. That is exactly why you rarely hear about it.

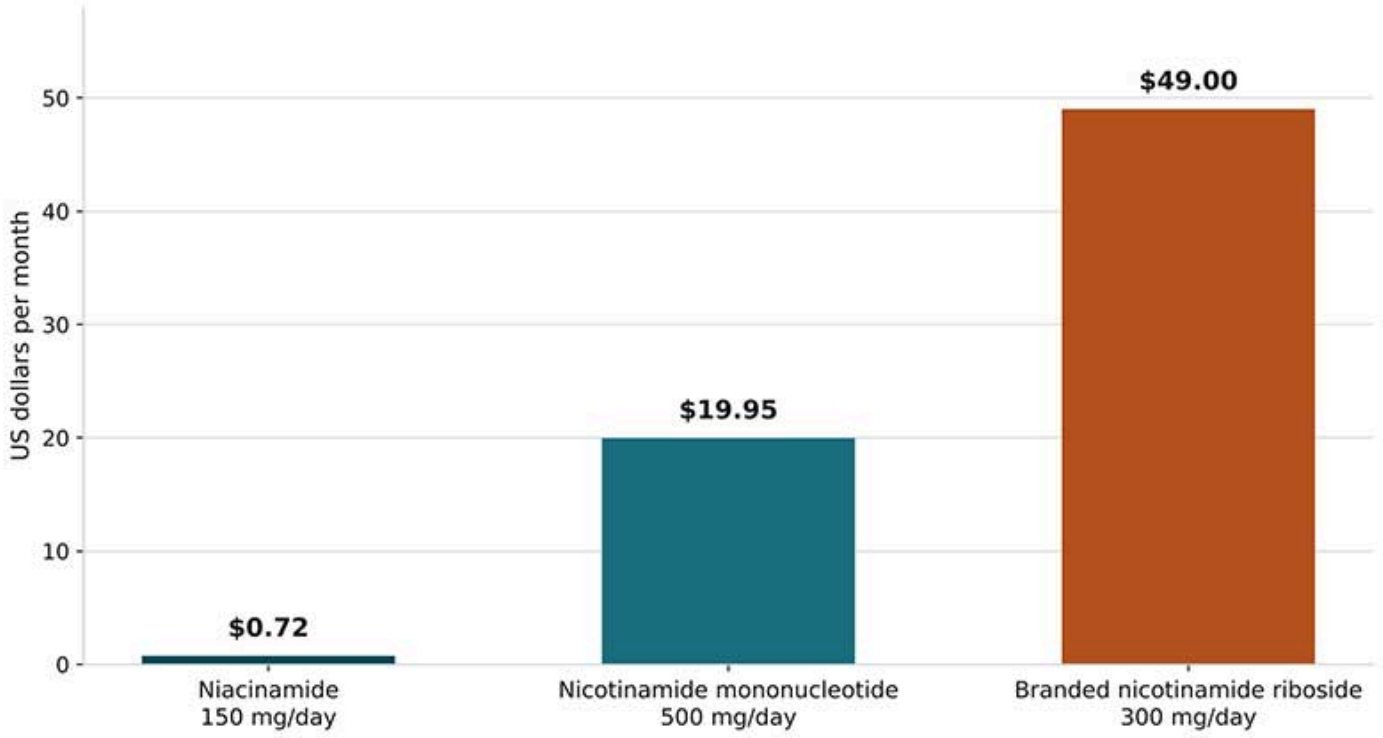


Figure 2. Monthly cost of common NAD precursors at typical doses. Niacinamide is priced per milligram from a 500 mg, 100-capsule bottle; nicotinamide mononucleotide from a 500 mg, 30-day bottle; nicotinamide riboside from the branded 300 mg, 30-capsule list price.[23,24]

Table 4. B3 forms compared

Form	Route to NAD	Flush	Key Human Evidence	Monthly Cost
Niacinamide	NAMPT salvage, used by most tissues	No	Skin cancer trial benefit; glaucoma association	Under $1
Nicotinic acid	Preiss-Handler route in liver, kidney, gut	Yes	Mitochondrial myopathy benefit; harms at 2 g/day	Under $1

Form	Route to NAD	Flush	Key Human Evidence	Monthly Cost
NR (nicotinamide riboside)	Mostly converted to niacinamide when swallowed	No	Parkinson's trial: worse than placebo	About $39 to $49
NMN (nicotinamide mononucleotide)	Mostly converted to niacinamide when swallowed	No	Small open-label platelet trial	About $20 to $60

NAMPT: Feed It, Then Turn It Up

Look at Figure 1. Niacinamide is the fuel, and NAMPT is the engine that turns it into NAD. NAMPT is the rate-limiting step, the bottleneck that determines how fast your cells can rebuild NAD.[25,26] And NAMPT doesn't sit at a fixed level. You can raise it.

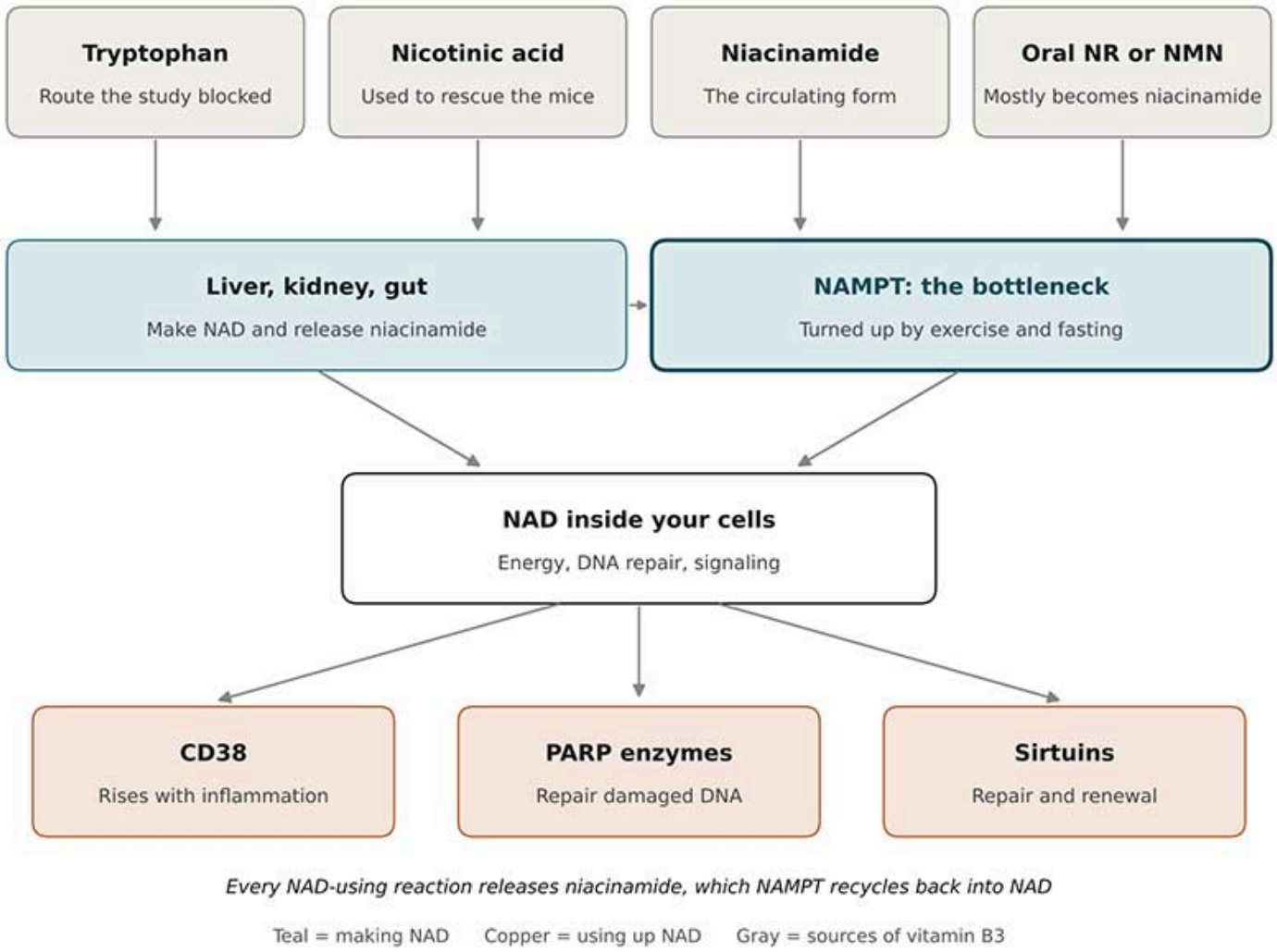


Figure 1. How your body makes and spends NAD. Four sources of vitamin B3 feed two production routes. Both fill the NAD pool in your cells, which is used up by CD38, PARP enzymes, and sirtuins. Each of those reactions releases niacinamide, which NAMPT recycles.

- **Exercise —** Athletes carry about twice as much NAMPT in their muscles as sedentary people. Just three weeks of training raised muscle NAMPT by 127% in previously sedentary adults.[27]

  In a separate study, 12 weeks of aerobic or resistance training raised NAMPT by 12% to 30%. It reversed the age-related decline, with the biggest gains in people 55 and older.[28]

- **Fasting —** Rodents fasted for 48 hours showed higher NAMPT and more NAD inside their mitochondria, which protected their cells from dying.[29] The energy sensor AMPK, switched on by both fasting and exercise, is the shared trigger.[30] Activating AMPK raised NAMPT gene activity 3.4-fold in human muscle cells.[31]

- **Your daily rhythm —** Your internal clock directly controls NAMPT production, so NAD rises and falls across the day.[32] That's another reason a regular sleep schedule and morning daylight matter.

New 2026 research, mostly in animals, points to how central NAMPT is:

- Drugs that activate NAMPT improved strength and muscle fiber size in 2-year-old mice.[33] Another raised endurance and muscle energy.[34]

- Activating NAMPT helped protect heart tissue after blocked blood flow through a coenzyme Q10-dependent defense.[35]

- NAMPT activation reduced lung scarring in idiopathic pulmonary fibrosis models.[36]

- Obese mice engineered with extra NAMPT in their fat had less fatty liver and better glucose control.[37]

- A compound from aged garlic raised circulating NAMPT in old mice and in humans, and improved frailty in the mice.[38] The study was funded by an aged garlic extract maker.

Table 5. What turns NAMPT up, and what holds it down

Raises NAMPT or NAD	Lowers NAMPT or NAD
Regular aerobic and resistance exercise[39,40]	Sedentary living[41]
Fasting, in animal studies[42,43]	Chronic inflammation, which raises NAD-consuming CD38[44]

Raises NAMPT or NAD	Lowers NAMPT or NAD
A steady daily rhythm with morning light[45]	Disrupted sleep and clock
Adequate niacinamide as raw material	Quaternary ammonium disinfectants, which directly inhibit NAMPT[46]

Stop the Drains

Making more NAD only helps if you aren't pouring it out faster. In the deficient mice, the NAD-destroying enzyme CD38 rose along with inflammation.[47]

A 2026 study found that quaternary ammonium compounds, common in disinfecting wipes and sprays, bind and block NAMPT in placental cells at nanomolar levels.[48] That is one more reason to choose simple soap and water.

Excess linoleic acid from seed oils is, in my view, one of the biggest drains. In my published reviews, I've described how excess linoleic acid oxidizes into harmful compounds, including oxidized linoleic acid metabolites and 4-hydroxynonenal. These can impair mitochondrial function, damage cell membranes and switch on inflammatory signaling.[49,50,51]

Oxidative damage of that kind is exactly what calls PARP repair enzymes into action, and every repair job spends NAD. A diet rich in omega-6 fats also floods your mitochondria with electron donors, piling up NADH relative to NAD. I've described this state as reductive stress, and restoring NAD is one of the ways to correct it.[52]

Linoleic acid has a half-life in your body of roughly two years, so cutting seed oils takes time to pay off.[53] That is another reason to start now. This mechanism was not tested in the new study, which found no rise in lipid peroxidation in the deficient mice.

Counterpoints Worth Considering

A fair look at the evidence includes what cuts the other way:

- **No head-to-head human trial exists** comparing niacinamide with NR or NMN on health outcomes. My case rests on physiology, safety, and the human outcome data above.
- **NMN showed a modest signal** in an open-label trial. At 450 mg twice daily for two weeks, 20% of 25 patients with immune thrombocytopenia met the main platelet target.[54]
- **NR was associated with slower muscle epigenetic aging** in a 2026 analysis, though it measured clock markers rather than how people functioned.[55]
- **Blood NAD may not tell the whole story —** A 2026 Nature Metabolism study across seven cohorts found whole-blood NAD did not change with age or lifestyle changes, though it rose with NR.[56] Exercise works at the level of muscle NAMPT, not necessarily blood levels.
- **Precursors raise NAD markers, but proof of disease prevention is limited** for heart disease and other conditions, including for niacinamide.[57]

My Recommendations

I've recommended niacinamide over the expensive precursors for about eight years. My preferred dose is 50 mg three times a day. The low dose is deliberate:

- **NAMPT is the bottleneck, not your niacinamide supply —** Flooding the system doesn't push more through, and splitting the dose keeps a steady supply for a vitamin that clears quickly.
- **More can backfire —** In mice, higher-dose niacinamide suppressed the liver's own salvage machinery.[58] In heart cells and fruit flies, low doses protected against age-related arrhythmia while high doses caused arrhythmias.[59]

- **Excess B3 has to be disposed of —** Excess B3 is cleared as waste products called 2PY and 4PY. In 2024, higher 4PY was linked to vascular inflammation and greater cardiovascular risk.[60]

The gram-level doses used in some glaucoma and skin cancer research are a different therapeutic question, and you should take them only with your doctor's guidance. Most stores sell 500 mg capsules, which is 10 times my per-dose recommendation. Look for lower-dose tablets or a pure powder you can measure. Then turn up the engine:

- Exercise regularly, combining aerobic and resistance training.
- Eat within a compressed daily window.
- Get morning daylight and keep a steady sleep schedule.
- Eliminate seed oils. In my cardiovascular review, I describe restricting linoleic acid under 5 grams a day.[61] Aim for 2 to 5 grams a day, since a small amount of linoleic acid is still essential.
- Skip quaternary ammonium disinfectants.

As the new mouse study suggests, the damage from low NAD is not destiny. Restoring NAD doesn't appear to require an expensive patented molecule. It requires the right fuel and an engine you keep running.

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.

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