

The NAD⁺ Paradox: More Precursor Does Not Necessarily Mean More Repair

Absurd Health Institute · Conceptual research essay · 390 words

Abstract

Increasing a blood or tissue NAD⁺ pool does not establish that an organ has repaired itself. Human evidence for precursor supplementation remains substantially more limited than popular longevity claims suggest. This essay examines compartment-specific NAD metabolism, pathway engagement and the requirement for meaningful functional outcomes rather than biomarker elevation alone.

A compelling molecule, an incomplete prescription

Nicotinamide adenine dinucleotide participates in redox reactions and functions as a substrate for enzymes involved in DNA repair, signaling and cellular regulation. Its prominence in aging research has encouraged efforts to increase NAD⁺ through precursor supplementation. Yet a 2025 review of human clinical evidence concluded that age-related declines in human NAD⁺ have not been consistently established across many tissues and that clinical benefits from precursor trials remain limited. This should shift the question away from whether one can increase a biomarker toward what happens after the molecule enters a particular tissue.

The compartment problem

Cells maintain mitochondrial, nuclear and cytosolic NAD-related pools with distinct local functions. Dietary precursor absorption, conversion pathways, transport, enzyme activity and disease-associated consumption can all affect where a precursor goes and what it changes. A rise in whole-blood NAD⁺ does not necessarily prove improved neuronal metabolism or muscle repair. Likewise, changing an NAD-dependent enzyme's activity can have consequences not captured by measuring the metabolite alone.

The repair hypothesis

The defensible idea is that NAD metabolism may constrain some cellular repair programs under some conditions. But an organism also requires perfusion, nutrient supply, correct cellular identity and tissue-level organization. Excessively broad supplementation claims ignore the possibility that distinct tissues respond differently or that another bottleneck dominates. A successful experimental strategy would link compartment-specific biochemical correction to restoration of a relevant function.

What evidence should decide

A clinical trial should distinguish precursor uptake, changes in NAD pools, pathway engagement, clinical improvement and safety. If circulating NAD⁺ increases without measurable benefit in an appropriately selected outcome, the intervention has achieved a biochemical effect, not demonstrated rejuvenation. That is not a reason to abandon NAD research. It is a reason to replace simplistic replacement narratives with tissue-specific metabolic science.

A clinical thought experiment

A patient may demonstrate elevated NAD-related measurements after supplements while experiencing no improvement in muscle function, sleep or recovery. That observation does not disprove the biochemical pathway, but it is inconsistent with an unqualified therapeutic claim. The opposite pattern—clinical improvement without large circulating changes—would suggest the measured pool is an incomplete proxy.

What would discriminate among explanations

The key experiment links tissue exposure to target engagement and functional outcomes in an appropriate population. Trials limited to small biomarker changes should not be translated into promises about lifespan or organ regeneration. Lack of clear human age-related NAD decline across every tissue is a reason to refine the mechanism, not to insist supplementation must help everyone.

Selected scientific readings

Vinten KT et al. (2025). NAD⁺ precursor supplementation in human ageing: clinical evidence and challenges. *Nature Metabolism*.

<https://www.nature.com/articles/s42255-025-01387-7>

López-Otín C et al. (2023). Hallmarks of aging: An expanding universe. *Cell*.

<https://doi.org/10.1016/j.cell.2022.11.001>

Evidence note: a proposed conceptual synthesis. These papers do not establish a novel clinical diagnosis, validated rejuvenation treatment or human lifespan benefit.