The Collagen Crisis: Why Most Adults May Be Running a Deficit They Don't Know About

Analysis by Dr. Joseph Mercola | June 11, 2026

STORY AT-A-GLANCE

- Your body needs about 12 grams of glycine daily just for collagen synthesis, but can only make about 3 grams and gets 2 to 4 grams from a typical diet, leaving a notable 10-gram daily deficit in many adults
- This deficit isn't a disease. It's an evolutionary constraint built into human biochemistry. Our glycine synthesis pathway has a hard stoichiometric bottleneck that can never be overcome, regardless of how healthy you are
- Collagen makes up 25% to 30% of your total body protein, but its production is limited by glycine, which occupies every third position in the collagen chain. The procollagen quality control cycle destroys 30% to 50% of newly synthesized collagen, and some amino acids lost in this process cannot be fully recycled
- Over time, chronic glycine deficiency may contribute to changes in skin, joints, bones, gut lining, blood vessels, and sleep quality. Glycine deficiency has been observed across a range of conditions, including Type 2 diabetes, insulin resistance, pregnancy, and xenobiotic exposure
- A 2025 meta-analysis reported that collagen peptide supplementation was associated with improvements in bone and muscle health markers in the populations studied, consistent with the idea that glycine availability may have functional implications

Collagen is the most abundant protein in your body. It constitutes roughly 25% to 30% of your total protein mass, forming the structural framework of your skin, bones, tendons, ligaments, blood vessels, gut lining, and the cornea of your eyes. You have more collagen than any other single protein, and it is woven into virtually every tissue you have.

But here is something the vast majority of people — and most of the medical establishment — do not know. You are not making enough of it. The reason for this has to do with a fundamental limitation in human biochemistry that has existed throughout human evolution.

The Stoichiometric Bottleneck

In 2009, Spanish biochemist Enrique Meléndez-Hevia, Ph.D., published a landmark paper demonstrating something remarkable. The metabolic capacity for glycine biosynthesis does not satisfy the need for collagen synthesis in humans.[1]

- **Glycine production falls short of collagen requirements —** The paper showed that glycine — the amino acid that occupies every third position in the collagen triple helix — has a production bottleneck that cannot be solved by the human body, no matter how well you eat or how healthy your metabolism is.
- **The bottleneck is stoichiometric —** This means it's built into the chemistry of the pathway itself. Glycine is synthesized primarily from serine via the enzyme serine hydroxymethyltransferase. But this reaction produces glycine in a fixed 1-to-1 ratio with a one-carbon fragment called THF-C1.
- **The body can only use so much THF-C1 —** Once that demand is saturated, the glycine production pathway stalls. It doesn't matter how much serine you have or how active the enzyme is — the bottleneck is structural.

The Glycine-Serine Metabolic Coupling

What makes this even more notable is the tight metabolic coupling between glycine and serine. A 2025 review in Metabolism: Clinical and Experimental laid out the full picture — because serine hydroxymethyltransferase mediates the interconversion of both amino acids, a deficiency in one tends to drag down the other.[2]

- **Depletion in one amino acid may disrupt the broader system —** When glycine is depleted, serine levels often fall with it, and both depend on adequate one-carbon metabolism to function properly. This can create a cascading metabolic vulnerability that extends beyond collagen production.

- **The review also highlighted a subtlety that earlier analyses had missed —** When you supplement large amounts of glycine alone, a portion of it is shunted back toward serine synthesis via serine hydroxymethyltransferase, consuming methylenetetrahydrofolate in the process. This means high-dose glycine supplementation can potentially deplete the one-carbon pool needed for methylation reactions.

The author argued that co-administering glycine with L-serine may be more appropriate in glycine-deficient conditions, though no head-to-head studies comparing the two approaches currently exist.

The Widespread 10-Gram Deficit

Meléndez-Hevia calculated the numbers. A 70-kilogram human needs roughly 12 grams of glycine per day just for collagen synthesis. Add another 1.5 grams for glutathione production, plus additional amounts for creatine, heme, purines, and bile salts. Total daily glycine demand: about 14.5 grams or more.

- **Daily glycine requirements exceed supply —** The body's own synthesis produces about 3 grams. A typical diet contributes 1.5 to 3 grams. That leaves a deficit of approximately 10 grams per day.

- **The deficit appears to be widespread —** It affects most adult humans and is not conditional on illness, age, or diet. Meléndez-Hevia argued that glycine should be reclassified from “non-essential” to “essential” because the body’s synthesis capacity is fundamentally inadequate.

- **Deficit increases in specific conditions —** A 2022 study confirmed that glycine becomes conditionally indispensable during late pregnancy, when the deficit becomes especially acute.[3]

The 2025 Metabolism review further established that glycine deficiency occurs across a wide range of conditions, including diabetes, insulin resistance, metabolic syndrome, and xenobiotic exposure, and that endogenous synthesis consistently falls short of meeting the body's needs.[4]

This finding is important because it suggests the deficit is not merely theoretical. Blood glycine levels are measurably reduced in patients with Type 2 diabetes and metabolic syndrome, suggesting the deficit may have clinical relevance that extends beyond collagen.

Why We've Survived — But Not Optimally

You might wonder — if humans have always had this deficit, how have we survived? The answer is that we have survived, but not optimally. Collagen turnover slows with age, and one likely contributor is that the raw materials to maintain it are insufficient.

- **Collagen turnover is slow when glycine availability is limited —** Skin collagen has a half-life of about 15 years; cartilage collagen, 117 years; intervertebral disc collagen, 95 years.[5] These are not rapid turnover rates. They are consistent with chronic substrate limitation — the body cannot replace collagen quickly when glycine availability is constrained.

- **What this means in practical terms —** A 2022 narrative review on musculoskeletal connective tissue remodeling noted that even the relatively fast-turnover collagen in tendons, ligaments, and fascia only cycles at approximately 0.5% to 2% per day — giving a half-life measured in months, not weeks.[6]

- **Injury repair is constrained by the speed of collagen synthesis —** This means that when you sustain a tendon injury, the repair process is inherently limited by how fast you can synthesize new collagen. Because collagen synthesis depends on glycine availability, every tendon tear, ligament sprain, or surgical wound may heal more slowly than it biologically could when glycine supply is limited.

The Procollagen Quality Control Furnace

But there's a deeper problem still. When your body synthesizes collagen, it doesn't just build it and install it. Fibroblasts degrade 30% to 40% of newly synthesized collagen within minutes of making it, before it even leaves the cell.[7]

- **This is a quality-control mechanism called the procollagen cycle —** The cell checks whether the triple helix folded correctly. If it didn't, the molecule is destroyed.

- **In some tissues, this wastage rate reaches 50% or more —** A study in adult rat tissues found that the proportion of newly synthesized collagen rapidly degraded ranged from 8.8% in skin to 53% in heart tissue.[8]

- **Not all collagen components can be recycled —** The amino acids released should be recycled — and most are — with one important exception. Hydroxyproline and hydroxylysine, created by post-translational modification after they're already incorporated into the collagen chain, cannot be recycled back into new collagen. They need to be remade from scratch.

This means the procollagen cycle behaves like a glycine-burning furnace. Every failed collagen molecule consumes glycine that can never be recovered.

The Skeletal and Cardiovascular Consequences

The consequences of this chronic deficit extend to the skeletal system. A 2025 meta-analysis in Frontiers in Nutrition pooled data from multiple randomized trials and found that collagen peptide supplementation was associated with increased bone mineral density at both the femoral neck and spine in the populations studied.[9]

- **Researchers examined the link between collagen peptides and bone density —** When collagen peptides were combined with vitamin D and calcium, the trials reported additional improvements in bone turnover markers and muscle performance compared with collagen alone.

  This suggests that providing amino acids and peptides implicated in collagen synthesis may, in the populations studied, be linked with measurable changes in bone-related markers.

- **The cardiovascular system may also be affected by the collagen deficit —** Arterial walls rely on collagen for structural integrity and elasticity. As collagen degrades and is not adequately replaced, blood vessels can stiffen.

- **The effect of collagen peptides on cardiovascular markers —** A 2022 systematic review and meta-analysis of randomized placebo-controlled trials reported that collagen peptide supplementation was associated with an average reduction in systolic blood pressure of approximately 5 mmHg and with lower low-density lipoprotein (LDL) cholesterol in the study populations examined.[10]

  Taken together, these pooled randomized-trial findings point to potential cardiovascular-related effects of collagen peptides that warrant further investigation.

The Metabolic Connection

Beyond the structural consequences, there is mounting evidence that the collagen deficit intersects with metabolic health.

- **Collagen peptides improved metabolic markers in high-calorie animal models —** A 2025 meta-analysis of animal studies found that collagen peptide administration exerts significant antiobesity effects in rodents on high-caloric diets, reducing body mass, adipose tissue, LDL, and triglycerides while increasing HDL and adiponectin.[11]

  While these are animal findings, they suggest that collagen-derived peptides may influence metabolic signaling pathways beyond their structural role. Whether the same effects extend to humans remains to be tested in controlled trials.

- **Chronic glycine deficiency may contribute to gradual systemic changes over time —** The consequences could accumulate quietly in humans. Over decades, connective tissues and the vasculature undergo gradual changes.

  These include loss of skin elasticity, joint stiffness, reduced bone density, thinning of the gut lining, reduced vascular compliance, greater injury susceptibility, and slower wound-healing. Emerging research suggests that chronic glycine deficiency may be one contributing factor among many.

Glycine, Glutathione, and the Aging Connection

And the deficit doesn't just affect collagen. Glycine is the rate-limiting substrate for glutathione, your body's master intracellular antioxidant.

- **Researchers examined whether supplementing key glutathione precursors could address measured glutathione deficiency in older adults —** A 2023 randomized clinical trial at Baylor College of Medicine found that supplementing glycine and N-acetylcysteine in older adults was associated with corrected glutathione deficiency, reduced oxidative stress and inflammation, better mitochondrial function, and improvements in several biomarkers related to aging over a 16-week study period.[12]

- **Physical and metabolic health improved alongside cellular repair —** The trial reported that gait speed improved, muscle strength increased, waist circumference decreased, and molecular markers of genomic damage were reduced. All from supplementing the two rate-limiting precursors for glutathione synthesis — glycine and cysteine.

- **Earlier trial findings reported broad systemic effects —** An earlier pilot trial from the same group reported broader effects over a 24-week supplementation period — corrected intracellular glutathione deficiency, improved mitochondrial fuel oxidation, reduced inflammation and endothelial dysfunction, better insulin resistance and cognition, and enhanced muscle strength and exercise capacity.[13]

  Importantly, when glycine and N-acetylcysteine (GlyNAC) supplementation was stopped for 12 weeks, the benefits declined, suggesting that an ongoing glycine deficiency may require ongoing correction.

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

Independent Validation

A 2022 randomized controlled clinical trial conducted by Nestlé researchers attempted to independently validate the GlyNAC effect in 114 healthy older adults. While they found that GlyNAC supplementation was safe and well-tolerated, the primary endpoint — increased total glutathione — was not reached in the overall population.[14]

However, a post-hoc analysis revealed something notable — subjects who started with both high oxidative stress and low baseline glutathione showed significant increases in glutathione after receiving the medium and high doses. This suggests the response may be most pronounced in those who are most depleted, which is consistent with what the underlying biochemistry would predict.

In mice, GlyNAC was reported to extend lifespan by 24%.[15] A follow-up study reported that it improved brain glutathione, reduced brain oxidative stress, and enhanced cognitive function in aging mice.[16] Again, these findings are from laboratory or animal research and may not directly apply to human health.

The Bottom Line

The peer-reviewed, placebo-controlled trials I explored in this article have reported that GlyNAC supplementation was associated with measurable improvements in several aging-related biomarkers in the populations studied. Researchers have identified potential nutritional strategies — centered on glycine and collagen-peptide intake — worth exploring further. It begins with understanding that an underlying biochemical limitation exists — and that it is built into how the body produces glycine.

Frequently Asked Questions (FAQs) About Glycine and Collagen

Q: How do I know if I'm deficient in glycine?

A: There isn't a definitive symptom checklist for glycine deficiency, and changes like reduced skin elasticity, joint stiffness, slower recovery from injury, or declining sleep quality have many possible contributors. Some emerging research suggests chronic glycine deficiency may be one of them. The biochemical analysis explored in this article suggests a glycine gap exists in most adults, even without obvious symptoms.

Q: Why can't my body just make enough glycine on its own?

A: Your body produces glycine through a pathway that is chemically rate-limited. It depends on a reaction tied to one-carbon metabolism, and that reaction can only run at a fixed rate. Once that limit is reached, production effectively plateaus, regardless of how healthy you are or how much protein you eat. This isn't a lifestyle issue — it's a built-in feature of human biochemistry.

Q: How much glycine do I actually need each day?

A: Your body uses roughly 12 grams of glycine daily for collagen alone, plus additional amounts for other functions. You typically produce about 3 grams and get a few more from diet, leaving a gap of around 10 grams.

Q: Why is glycine essential for building collagen?

A: Glycine is required at every third position in the collagen chain, allowing the triple helix to form correctly. Without sufficient glycine, collagen assembly is constrained, which can, in turn, limit how much new connective tissue your body produces.

Q: Does this affect more than just my skin and joints?

A: Yes. Collagen supports your blood vessels, gut lining, bones, and parts of your eyes. Glycine also plays a central role in glutathione production, which has been linked to oxidative stress, inflammation, and cellular health. When glycine availability is constrained, multiple systems may be affected together.

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

Sources and References

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