

TESTOSTERONE REPLACEMENT THERAPY

RESTORING PHYSIOLOGY RATHER THAN PURSUING EXCESS

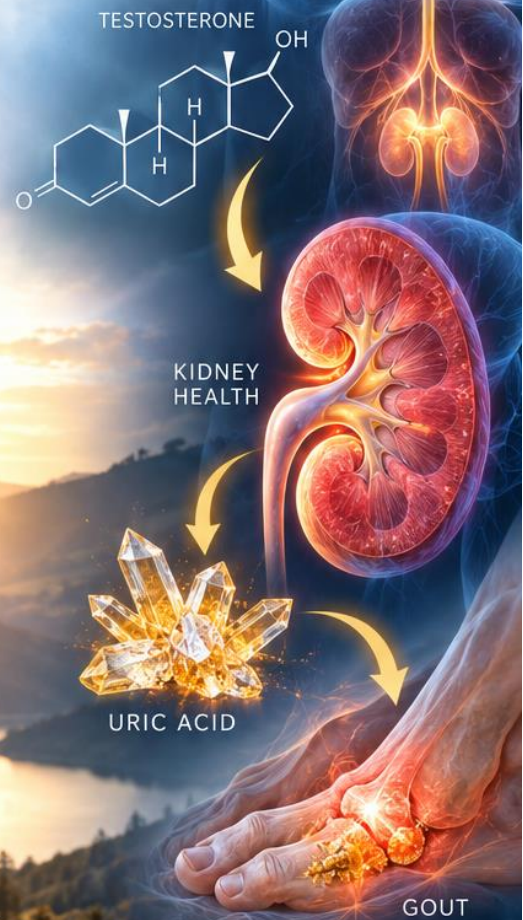
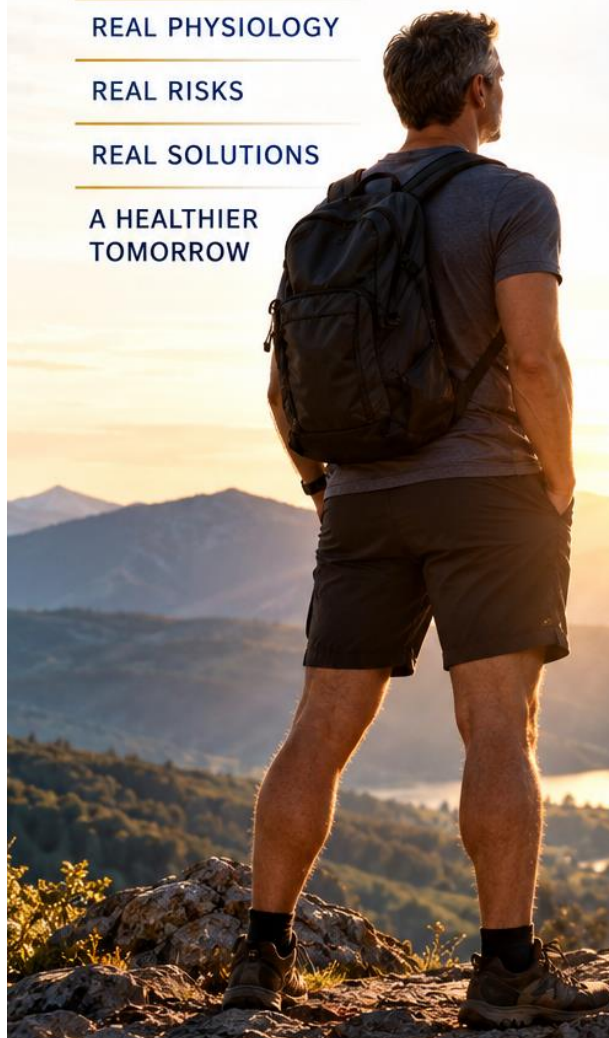
*Understanding the Relationship Between
Excessive Testosterone, Uric Acid, and Kidney Health*

REAL PHYSIOLOGY

REAL RISKS

REAL SOLUTIONS

A HEALTHIER
TOMORROW



A CLINICAL PERSPECTIVE BY

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Addressing Health One Neuron at a Time.



When Testosterone Is Too High: Understanding Uric Acid, Kidney Health, and the Risks of Excessive Testosterone

An Educational Guide for Men Receiving Supraphysiological Testosterone Therapy

Preamble - My Opinion.

Over my 46 years of practicing medicine, I have devoted nearly 35 years to understanding the complexities of human hormones through the science of endocrinology, with the past 22 years focused particularly on neuroendocrinology. During this journey, one of the most important lessons I have learned is that the practice of hormone replacement therapy is too often influenced by aspirations rather than an understanding of human physiology.

In some corners of testosterone replacement medicine, the philosophy seems to be driven by dreams of extraordinary physical performance: bench-pressing 500 pounds or approaching the remarkable 264-kilogram clean-and-jerk record of Olympic weightlifter Lasha Talakhadze. While such achievements may inspire competitive athletes, they rarely reflect the goals of the average man seeking medical care.

Most men who visit a men's health or sports medicine clinic are not aspiring to become professional bodybuilders. They are looking for something far more meaningful: improved mental clarity and emotional stability, restoration of physical strength, recovery following surgery or injury, renewed sexual health, better sleep, and an improved quality of life, all while minimizing the potential adverse effects of treatment.

Their goal is not to become superhuman. Their goal is to feel human again.

Unfortunately, during my nearly 35 years of examining testosterone replacement practices, I have repeatedly encountered treatment approaches that appear more focused on achieving impressive laboratory numbers and promoting muscle development than on restoring normal physiological function.

Why do I make such a strong statement?

Consider a simple physiological fact. A healthy young adult male typically produces approximately 4–10 milligrams of testosterone daily, equivalent to roughly 28–70 milligrams per week.

If this is the amount the healthy male body naturally produces, why are some patients routinely prescribed 200 milligrams of testosterone cypionate every ten days, or even every seven days, without sufficient attention to their individual physiological responses?

To be clear, the milligrams of testosterone naturally produced by the testes cannot be directly equated with the milligrams of injectable testosterone cypionate. The injectable preparation contains an ester, has different absorption and release characteristics, and does not deliver its entire dose immediately. Nevertheless, this comparison raises an important clinical question: **Are we replacing what the body needs, or are we administering more testosterone than the patient's physiology requires?**

The answer should never be determined by an arbitrary injection schedule or the belief that higher testosterone concentrations must produce better outcomes. Instead, it should be guided by the patient's symptoms, laboratory findings, treatment response, and potential adverse effects.

My motivation for writing this paper arose from a recent consultation with a kind gentleman, a military veteran, and his wife. Together, they described a series of medical problems that had developed during approximately eight years of treatment with 200 milligrams of testosterone cypionate every ten days.

Among the concerns was the development of gout, a painful inflammatory condition associated with elevated uric acid concentrations in the blood, known as *hyperuricemia*.

Their experience prompted me to revisit an important but often overlooked relationship between testosterone exposure and uric acid metabolism.

Testosterone can influence uric acid through several biological pathways, including changes in purine metabolism and the kidneys' ability to eliminate uric acid. Purines are natural components of our cells that, when broken down, can generate uric acid. Research has demonstrated that testosterone administration can increase serum uric acid in some individuals, although the magnitude of this effect varies and the precise mechanisms remain under investigation.

It would be scientifically inappropriate to suggest that elevated testosterone invariably causes gout or that every case of hyperuricemia in a patient receiving testosterone is caused by excessive androgen exposure. Nevertheless, the biological relationship is sufficiently important to warrant attention, particularly when testosterone concentrations exceed physiological requirements.

This brings us to the central purpose of this paper.

Testosterone replacement therapy should be guided by the restoration of physiological balance, not by the pursuit of supraphysiological hormone concentrations.

I hope this discussion encourages healthcare professionals who prescribe testosterone to reconsider the assumption that more is necessarily better. A treatment protocol should not be judged solely by the amount of testosterone administered or the highest laboratory concentration achieved. It should be evaluated by how effectively it restores function while minimizing avoidable harm.

For some patients, smaller and more frequent injections may provide a more stable hormonal environment than larger, less frequent doses. A regimen such as 20 milligrams every 72 hours may be appropriate for certain individuals, while others will require different doses or schedules. No single regimen should be considered universally optimal, and any adjustment must be guided by clinical evaluation and properly timed laboratory monitoring.

Ultimately, successful hormone replacement requires understanding the individual rather than forcing the individual into a standardized protocol.

After decades of studying the interconnected relationships among hormones, I remain convinced that the greatest benefit of testosterone therapy comes not from maximizing a single hormone, but from restoring the physiological balance that allows the entire endocrine and neuroendocrine systems to function together.

The objective of medicine should never be to create the highest testosterone level possible. It should be to restore the healthiest physiological state achievable for the individual patient.

Introduction: More Testosterone Is Not Always Better

Testosterone is an important hormone that helps maintain muscle strength, energy, sexual function, bone health, and overall well-being. When testosterone levels are abnormally low, appropriately prescribed testosterone replacement therapy (TRT) can improve symptoms and quality of life.

However, there is an important difference between **replacing testosterone to achieve healthy levels** and **prescribing testosterone at doses that raise blood concentrations above the normal physiological range**.

The second approach is called *supraphysiological testosterone therapy*.

Some men receiving testosterone injections, pellets, creams, or other preparations may develop testosterone levels substantially higher than those normally produced by the body. Although higher levels may initially be associated with increased muscle mass, strength, or sexual desire, they can also produce unwanted changes in blood chemistry and organ function.

One potentially overlooked change is an increase in **uric acid**, a substance produced naturally when the body breaks down certain cellular compounds.

Understanding the relationship between excessive testosterone, uric acid, and kidney function is important for men receiving high-dose testosterone therapy.

1. What Is Uric Acid, and Why Does It Matter?

Every day, the body breaks down old cells and processes substances called *purines*. Purines are natural components of DNA, RNA, and many foods.

When purines are broken down, the body produces uric acid.

Normally, uric acid enters the bloodstream, travels to the kidneys, and is removed primarily through urine. A smaller amount is eliminated through the intestines.

Problems can develop when the body produces more uric acid than it can eliminate, or when the kidneys do not remove enough.

This condition is called **hyperuricemia**, meaning too much uric acid in the blood.

High uric acid can contribute to:

- **Gout:** Painful inflammation of joints caused by uric acid crystals.
- **Kidney stones:** Crystals can form stones within the urinary system.
- **Kidney complications:** Particularly when uric acid stones, obstruction, or other kidney problems are present.

High uric acid is also associated with hypertension, cardiovascular disease, and chronic kidney disease. However, an association does not necessarily mean uric acid is directly causing these conditions.

Many individuals with elevated uric acid have no symptoms.

2. How Can Excessive Testosterone Increase Uric Acid?

Researchers have identified several possible connections between testosterone and uric acid metabolism.

A. Testosterone may reduce the kidneys' ability to eliminate uric acid.

Think of the kidneys as filters that clean the blood.

After uric acid is filtered, the kidneys can either allow it to leave through urine or return some of it to the bloodstream.

Special transport proteins help control this process.

One important protein is called **URAT1**. It helps the kidneys reabsorb uric acid.

Testosterone may influence how the kidneys handle uric acid. Human studies of testosterone treatment have found increases in blood uric acid and, in some patients, decreases in the amount of uric acid eliminated relative to what is filtered.

In simple terms, **more uric acid may remain in the bloodstream instead of leaving through urine.**

B. Testosterone may increase uric acid production.

Testosterone stimulates muscle development and other anabolic processes.

During tissue growth and normal cellular activity, the body processes compounds containing purines.

Purines can ultimately be converted into uric acid.

Researchers have proposed that increased muscle mass and changes in purine metabolism contribute to the uric acid elevations observed during testosterone treatment.

However, this mechanism is not fully established, and muscle growth does not automatically mean that uric acid will increase.

C. Testosterone increases red blood cell production.

Testosterone stimulates the bone marrow to produce red blood cells.

This can be beneficial when correcting certain forms of anemia, but excessive testosterone exposure may cause the body to produce too many red blood cells.

This condition is called *erythrocytosis*.

An increased red blood cell count may be accompanied by changes in cellular metabolism. Although increased purine turnover has been proposed as a possible contributor to uric acid production, it has not been established that testosterone-induced erythrocytosis is a major direct cause of hyperuricemia.

Importantly, erythrocytosis is itself a recognized complication of testosterone therapy and requires monitoring.

3. Why Are Supraphysiological Testosterone Levels a Concern?

The objective of conventional testosterone replacement therapy is to restore testosterone to an appropriate physiological range, not to maintain concentrations above the body's normal requirements.

Men exposed to excessive testosterone may experience:

- Increased hematocrit, meaning a greater proportion of the blood consists of red blood cells.
- Acne and oily skin.
- Breast tenderness or enlargement in some patients.
- Suppression of natural testosterone and sperm production.
- Reduced fertility and testicular size.
- Worsening of obstructive sleep apnea in susceptible men.
- Changes in blood pressure and cholesterol.
- Potential cardiovascular and kidney complications, particularly with prolonged anabolic-androgenic steroid exposure.

Higher testosterone does not necessarily mean better health or better sexual performance.

A laboratory value above the normal range should not automatically be interpreted as a therapeutic success.

The risks depend on the dose, duration, testosterone formulation, other medications, and the patient's underlying health.

4. What Uric Acid Levels Should Concern You?

Uric acid is measured through a routine blood test.

Serum uric acid	General interpretation
Below 6.8 mg/dL	Below the approximate concentration at which urate crystals can form under typical physiological conditions
6.8–7.9 mg/dL	Elevated or borderline, depending on laboratory range and clinical circumstances
8.0–8.9 mg/dL	More pronounced elevation requiring assessment of contributing factors
9.0 mg/dL or higher	Significant hyperuricemia; warrants closer evaluation, particularly with gout, kidney stones, or renal impairment

These are educational categories, not universal treatment thresholds. Laboratory reference ranges vary, and a single uric acid result does not determine whether medication is needed.

For patients receiving treatment for gout, the usual serum uric acid target is **below 6.0 mg/dL**.

5. What Can Be Done When Uric Acid Becomes Elevated?

The first step is to identify why uric acid is increasing.

In a man receiving high-dose testosterone, the healthcare provider should review testosterone exposure, kidney function, hydration, dietary habits, alcohol consumption, other medications, and any history of gout or kidney stones.

There are two principal ways medications can lower uric acid.

Approach One: Help the kidneys eliminate more uric acid.

Medications called *uricosuric agents* encourage the kidneys to release more uric acid into urine.

Probenecid is an established example.

It works by reducing the amount of uric acid that the kidneys reabsorb into the bloodstream.

Imagine the kidneys are recycling too much uric acid back into the blood. Probenecid reduces that recycling, allowing more uric acid to leave through urine.

However, probenecid is not appropriate for everyone. It can increase the risk of uric acid kidney stones and may be less effective in people with impaired kidney function.

Other medications, such as losartan for high blood pressure and fenofibrate for certain cholesterol disorders, can also modestly lower uric acid through effects on renal elimination.

These are not automatically substitutes for established gout treatment.

Approach Two: Reduce the amount of uric acid the body produces.

Medications such as allopurinol and febuxostat reduce uric acid production by blocking an enzyme called xanthine oxidase.

Rather than encouraging the kidneys to eliminate more uric acid, they reduce how much is produced in the first place.

Allopurinol is generally the preferred first-line urate-lowering medication for patients with gout who require long-term treatment.

Importantly, **not every patient with high uric acid needs medication.** For people who have never experienced gout or uric acid stones, urate-lowering drugs are generally not recommended solely because a blood test shows elevated uric acid.

6. Why Correcting Excessive Testosterone May Be the Most Important Step

If uric acid rises after testosterone doses are increased, the testosterone regimen deserves careful review.

For example, consider a man whose testosterone concentration increases substantially above the laboratory's normal range after receiving a higher injection dose.

Several months later, his uric acid rises from 5.5 to 8.8 mg/dL.

This pattern raises the possibility that testosterone exposure contributed to the increase.

It does not prove testosterone was the only cause.

Rather than immediately adding another medication, his healthcare provider should consider whether testosterone dosing can be adjusted to achieve an appropriate physiological concentration.

Correcting excessive testosterone exposure may improve the underlying metabolic environment while also reducing the risk of erythrocytosis and other adverse effects.

Patients should not independently change prescribed doses without discussing the findings with their clinician.

7. Final Message: Hormonal Optimization Is Not Hormonal Excess

Testosterone is essential for male health, but the benefits of testosterone therapy depend on appropriate dosing, careful monitoring, and attention to the body's overall physiology.

Excessive testosterone can alter red blood cell production, reproductive hormone signaling, cardiovascular risk factors, and potentially uric acid metabolism.

Studies have demonstrated that testosterone administration can increase serum uric acid in some populations. However, research has not established that every man receiving supraphysiological testosterone will develop hyperuricemia, or that testosterone is always the cause when uric acid rises.

When uric acid becomes elevated, the solution is not necessarily to add another medication.

The more important question may be whether the testosterone regimen itself is appropriate.

The goal of testosterone replacement therapy should be restoration of healthy hormonal function, not the pursuit of the highest possible testosterone number.

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Medical Disclaimer

This document is provided for general educational purposes and is not a substitute for individualized medical care. Decisions concerning testosterone dosage, uric acid management, kidney function, and prescription medications should be made with a qualified healthcare professional. Patients should not start, stop, or adjust testosterone or urate-lowering medication without medical supervision.

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