Understanding Intracrinology and Testosterone Pellet Therapy

A Patient-Friendly Guide to How Your Body Uses Hormones

Based on: Glaser R. "Intracrinology and Testosterone Pellet Therapy: An Enzyme-Aware, Symptom-Driven Approach to Hormone Optimization in Aging." Cureus 18(4): e106377. Published April 3, 2026.
doi.org/10.7759/cureus.106377

Section 1: The Mechanism

Intracrinology: Local Hormone Production in Tissues

Peripheral tissues convert circulating precursors (DHEA, androstenedione, testosterone) into active hormones on demand via local intracrine enzymes — independent of blood levels.

The intracrinology concept, introduced by Labrie, explains that the majority of active sex steroids in adults are synthesized within target tissues from adrenal precursors rather than delivered by the bloodstream.

Testosterone is the most abundant biologically active sex steroid in both men and women. It exerts a dual role by directly activating androgen receptors throughout the body and, equally importantly, serving as the primary substrate for local intracrine conversion to estradiol via the enzyme aromatase.

Aromatase is widely expressed across multiple tissues, enabling cells to produce estradiol on demand through intracrine mechanisms — where both the enzymatic conversion of testosterone to estradiol and the subsequent receptor activation occur within the same cell — without substantially raising systemic estradiol levels.

Key Insight: Serum testosterone levels do not accurately reflect total androgenic activity in peripheral tissues. Most bioactive androgens acting at the androgen receptor are generated locally through intracrine conversion of adrenal pro-androgens such as DHEA and androstenedione. These adrenal precursors account for approximately 50% of total androgenic activity in adult men and over 80% in postmenopausal women. Their profound age-related decline leads to substrate deficiency in peripheral tissues, even when serum testosterone concentrations appear normal.

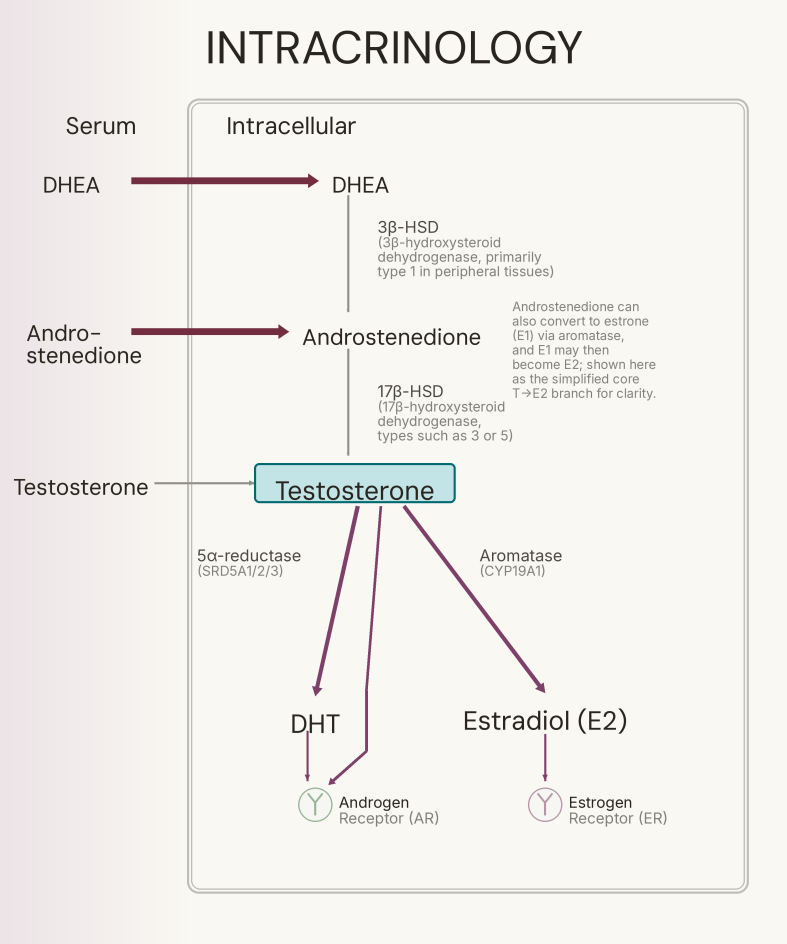

Figure 1. Intracrinology: how serum precursors (DHEA, androstenedione, and testosterone) enter peripheral cells and are converted by local enzymes into active hormones. With aging, all three circulating building blocks decline significantly, reducing the substrates available for intracellular hormone production.

Section 2: The Problem

Age-Related Decline of All Hormones

With aging, circulating levels of all major androgen precursors decline dramatically. This deprives tissues of the raw material needed for local intracrine hormone production.

Hormone	What Happens With Age
DHEA	Drops by 60–95%
Androstenedione	Falls by ~50%
Testosterone	↓ 1–2% per year, often starting before age 40

When these building blocks run low, your tissues cannot make enough of the active hormones they need. This leads to common symptoms of aging:

- Decline in mental and physical health
- Loss of muscle mass & bone density
- Reduced libido & energy
- Mood disturbances & brain fog
- Increased body fat
- Hot flashes (women)

Tissue-Level Deficits

- Cells starved of substrate for local hormone production
- Serum levels mask true tissue-level deficiency
- Women: >80% of active sex steroids from intracrinology post-menopause
- Men: 20–50% of androgenic activity from adrenal precursors

The decline in precursors is the root cause — not simply a drop in circulating testosterone. Without adequate substrate, intracrine enzymes cannot produce sufficient DHT, estradiol, or other active metabolites at the tissue level, regardless of serum values.

Clinical Insight: Standard serum hormone panels fail to capture intracrine production. Symptom assessment is essential for detecting tissue-level deficiency.

Section 3: The Solution

Testosterone Delivered by Pellet Implant

Testosterone pellet therapy restores organ-level hormonal control by supplying sufficient testosterone for direct androgen receptor activation and as substrate for local intracrine enzymes, often without mandatory systemic estradiol supplementation.

Outcomes demonstrate clear dose dependency, with best results achieved by titrating to symptom resolution and adverse effect surveillance (e.g., erythrocytosis, symptoms of excess estrogen, and skin and body hair changes) rather than mid-range serum targets.

Adjunctive Therapy

When selectively employed, adjunctive low-dose aromatase or 5α-reductase inhibitors (often combined in the pellet implant) correct conversion imbalances while preserving stable substrate delivery.

Judicious integration of enzyme modulators and lifestyle interventions yields durable symptom relief in both sexes with acceptable safety under appropriate monitoring.

The Paradigm Shift

Old Approach	New Approach
Serum targets	Symptom-driven dosing
Fixed reference ranges	Individual enzyme profiles
Universal protocols	Adjunctive AI/5ARI when needed
Mandatory E2 targets	Clinical symptom monitoring

Best results achieved by titrating to symptom resolution and adverse effect surveillance.

Future Direction: Large, long-term randomized trials are needed to definitively establish this enzyme-aware approach in clinical practice.

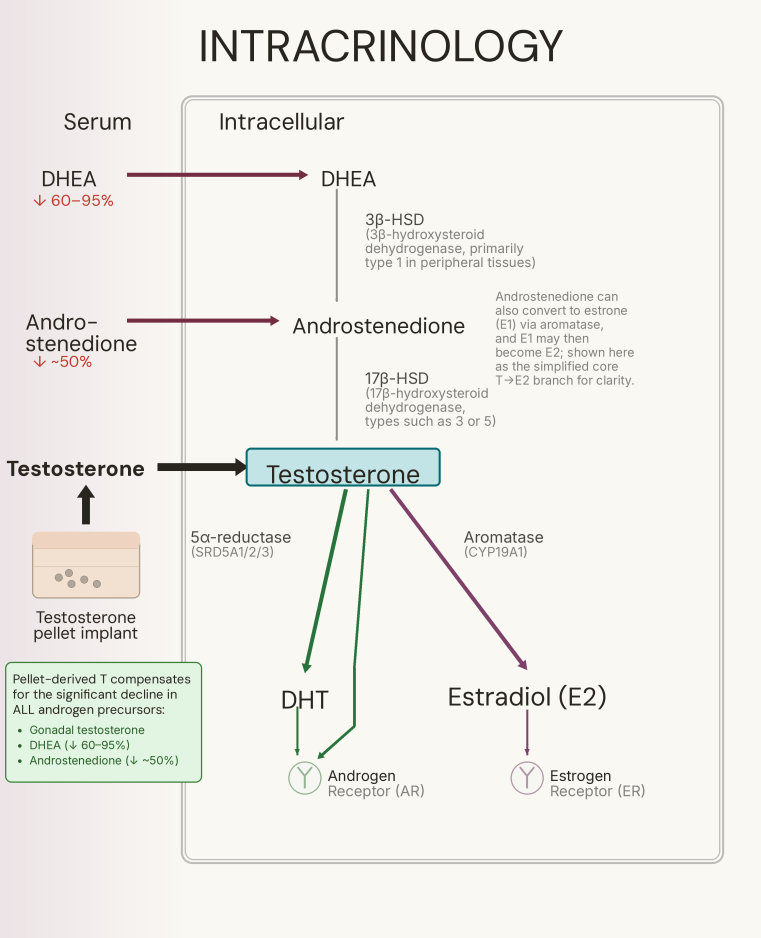

Figure 2. Testosterone pellet therapy and intracrinology. The subcutaneous pellet implant delivers a steady supply of testosterone into the serum. This testosterone enters peripheral cells where it replaces both declining gonadal testosterone and the significant contribution from declining adrenal androgen precursors (DHEA and androstenedione), restoring substrate for local conversion to DHT and estradiol via intracrine enzymes.

What These Hormones Do Throughout the Body

Testosterone and the hormones made from it (estradiol and DHT) affect nearly every organ system. Here are some of the key benefits:

Body System	How These Hormones Help
Bones	Build and maintain bone density; prevent osteoporosis
Muscles	Increase strength and mass; reverse age-related muscle loss
Brain	Support memory, mood, and mental clarity; provide neuroprotection
Heart	Improve cholesterol; reduce metabolic syndrome risk; protect blood vessels
Body fat	Reduce belly fat; improve body composition
Sexual health	Restore sex drive, function, and satisfaction

Energy	Improve overall vitality and reduce fatigue
Skin/Hair	Maintain skin health (DHT supports sebaceous gland function)
Immune system	Help regulate inflammation throughout the body
Lungs	Improve breathing capacity; reduce inflammation

Why Blood Levels May Not Tell the Whole Story

Standard medical guidelines recommend keeping blood testosterone levels within a "normal" range based on healthy young adults. But there is an important catch:

In a healthy young person, the adrenal glands produce abundant DHEA and androstenedione, which supply the tissues with additional building blocks independent of blood testosterone. So the "normal" blood testosterone level in a young person represents only a fraction of the total hormone activity happening inside the body.

In an older person receiving testosterone therapy, those adrenal building blocks have declined dramatically. The testosterone from pellets must now do double duty — serving as both the direct hormone and the primary building block for tissue conversion. This is why older patients often need blood testosterone levels higher than the "normal" young-adult range to achieve the same tissue-level effects.

> This concept is called "pharmacologic dosing for physiologic effect" — meaning a higher-than-normal blood level is needed to produce a normal, healthy level of hormone activity inside the tissues.

What About Estradiol Monitoring?

Estradiol (the main form of estrogen) is produced primarily inside your tissues during testosterone pellet therapy. The estradiol made locally in your cells is used and broken down right there — it only "spills over" into the blood when production exceeds what the tissue can use.

This means that blood estradiol levels may not accurately reflect what is happening inside your tissues. Your provider will monitor you based on:

- How you feel — symptoms like breast tenderness, bloating, mood changes, hot flashes, libido
- Physical signs — changes in body composition, skin, hair
- Objective measures — bone density scans, quality-of-life assessments
- Side effects — any unwanted changes that suggest enzyme imbalance

> This is called a symptom-driven approach: treating the person, not just the numbers.

Safety and Monitoring

Testosterone pellet therapy has been used for decades with a strong safety profile when properly monitored. Your provider will track:

- Blood counts — testosterone can stimulate red blood cell production (important to watch in men)
- Symptoms of excess estradiol — breast tenderness, bloating, mood swings
- Symptoms of excess DHT — acne, unwanted hair growth, scalp hair thinning
- Overall well-being — energy, mood, sexual function, sleep quality
- Breast health — research suggests testosterone may be protective; monitoring continues per standard guidelines

If side effects arise, your provider can adjust the dose or add enzyme-balancing medications (aromatase inhibitors or 5-alpha reductase inhibitors) at the time of the next pellet insertion.

The Bottom Line

Your body is designed to make hormones where it needs them, using building blocks from the blood. As we age, those building blocks decline, and tissues can no longer make enough of the active hormones they need. Testosterone pellet therapy provides a steady supply of testosterone that your tissues can convert into estradiol and DHT on demand — restoring the natural intracrine process.

This approach treats you as a whole person — focusing on how you feel, how your body responds, and your individual enzyme profile — rather than chasing a single number on a blood test. It represents a shift toward personalized, enzyme-aware hormone optimization.

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