The Most Common Adverse Effects of Testosterone Therapy

Authored by

mohammad looti

November 14, 2025

The Most Common Adverse Effects of Testosterone Therapy

Primary Disciplinary Field(s): Endocrinology, Pharmacology, Men's Health

1. Core Definition

Testosterone Replacement Therapy (TRT) involves the exogenous administration of testosterone or its synthetic derivatives, primarily prescribed to men diagnosed with hypogonadism--a condition characterized by abnormally low levels of endogenous testosterone. While effective in alleviating the debilitating symptoms associated with testosterone deficiency, such as erectile dysfunction, profound fatigue, sleep disturbances, and clinical depression, TRT is not without significant risk. The introduction of supra-physiological or even replacement-level dosages of the hormone into the body systemically triggers a cascade of physiological adjustments and adverse reactions. These effects range in severity from minor, cosmetic issues to serious, life-threatening cardiovascular and oncological risks, necessitating careful patient selection and rigorous medical monitoring throughout the course of treatment.

The decision to initiate testosterone supplementation requires a comprehensive risk-benefit analysis, particularly for individuals who may present with pre-existing conditions that are known to be exacerbated by hormonal changes. Since testosterone is a powerful steroid hormone, its supplementation mimics, and in some cases amplifies, the side effects commonly associated with anabolic steroid use. Therefore, understanding and mitigating the adverse effects associated with TRT is central to its safe clinical application, prompting regulatory bodies and medical associations to issue strict guidelines regarding appropriate use and patient monitoring protocols.

2. Range and Classification of Adverse Effects

Adverse effects of testosterone therapy can be broadly classified into three categories based on their detection method and clinical significance: those detected primarily through laboratory testing (metabolic and hematological changes), those involving severe, life-threatening complications (cardiovascular and oncological risks), and those involving localized or systemic unpleasant, though often non-lethal, reactions (dermatological, behavioral, and reproductive changes). The intensity and prevalence of these effects are highly individualized, depending on the dosage, route of administration, duration of therapy, and the patient's underlying health status.

The most critical concern for clinicians is the potential for severe adverse events, especially in older male populations who are already at elevated baseline risk for cardiovascular disease. However, even the less severe side effects often contribute significantly to the patient's quality of life and compliance with treatment. Effective clinical management requires routine laboratory assessment, including full blood counts, lipid panels, and regular monitoring of prostate health markers to catch potentially dangerous trends early, allowing for timely dose adjustment or

cessation of therapy.

3. Cardiovascular and Life-Threatening Risks

A primary concern when prescribing TRT is the potentially increased risk of serious cardiovascular events, including myocardial infarction (heart attack) and stroke (cerebrovascular accident). While the precise mechanisms remain subject to ongoing debate and research, several studies suggest a correlation between TRT initiation, particularly in elderly or high-risk patients, and elevated cardiovascular morbidity and mortality. This increased risk may stem from several factors, including changes in blood viscosity and direct effects on the vascular endothelium.

Crucially, testosterone therapy significantly increases the risk of thromboembolic events (blood clots). This is primarily driven by a rise in the hematocrit level--the volume percentage of red blood cells (RBCs) in the blood. When RBC counts increase too dramatically, the blood becomes thicker, leading to a state of hyperviscosity. This condition predisposes the patient to the formation of blood clots, which can result in life-threatening complications such as deep vein thrombosis (DVT) or pulmonary embolism (PE). Patients undergoing TRT who experience symptoms indicative of clotting, such as leg swelling or shortness of breath, require immediate medical intervention and often necessitate the use of anticoagulant medications or cessation of hormone treatment.

Furthermore, testosterone supplementation can exacerbate pre-existing sleep disorders, most notably obstructive sleep apnea (OSA). OSA is a serious condition where breathing repeatedly stops and starts during sleep. Exogenous testosterone can worsen the severity of these apneic episodes, leading to increased risk, especially when combined with depressants like alcohol. In severe cases of untreated or aggravated sleep apnea, the increased risk of dying in one's sleep becomes a major clinical consideration, requiring mandatory screening and treatment for OSA before and during TRT. Finally, an increased, though statistically varied, chance of developing or accelerating the growth of existing **prostate cancer** is a fundamental life-threatening risk associated with TRT.

4. Alterations in Clinical Laboratory Parameters

Many of the initial adverse effects of TRT are not clinically noticeable to the patient but are readily apparent through routine blood analyses. These changes necessitate frequent monitoring to ensure the patient remains within safe physiological ranges. A significant effect is the increase in **red blood cell counts** (polycythemia), reflected by an elevated hematocrit, which, as noted above, drives the risk of hyperviscosity and thromboembolism. If the hematocrit level exceeds 50% or 52% (depending on clinical protocol), the dosage must often be reduced or the patient may require therapeutic phlebotomy (blood removal) to lower the risk of clotting.

Another critical laboratory alteration is the increase in Prostate Specific Antigen (PSA) levels. PSA

is a protein marker used primarily for the screening of prostate cancer. While an increase in PSA is common and expected upon initiating TRT, a sudden or disproportionately large elevation can signal the presence or progression of prostate malignancy. Therefore, all men considering TRT must undergo thorough prostate cancer screening prior to starting therapy, and PSA levels must be diligently tracked throughout treatment.

Metabolic parameters also shift under the influence of TRT. Although not universally consistent, many patients experience changes in their **blood lipid levels**, specifically an increase in triglycerides and total cholesterol, which can contribute negatively to overall cardiovascular risk profiles. Additionally, in men of reproductive age, exogenous testosterone suppresses the hypothalamic-pituitary-gonadal axis, leading to a significant decrease in endogenous testosterone production and, most critically, a decline in **sperm count**. This suppression can result in temporary or persistent infertility, posing a major consideration for men who wish to conceive children during therapy.

5. Reproductive and Endocrine System Changes

The introduction of synthetic testosterone triggers a negative feedback loop within the endocrine system, resulting in distinct adverse effects on the testes and associated hormonal balances. The suppression of Luteinizing Hormone (LH) and Follicle-Stimulating Hormone (FSH) production by the pituitary gland leads directly to the shutdown of natural testicular function. Clinically, this manifests as **testicular atrophy** (shrinkage) due to the reduction in size and function of the germ cells responsible for sperm production, leading directly to the aforementioned infertility risk.

A seemingly counter-intuitive, yet common, endocrine side effect is **breast enlargement**, known medically as gynecomastia. This occurs because the exogenous testosterone is metabolized by the enzyme aromatase into estradiol (a potent form of estrogen). If the conversion rate is high, the resulting elevated estrogen levels can stimulate breast tissue growth. This condition is often highly distressing and embarrassing for male patients, sometimes requiring co-administration of aromatase inhibitors or selective estrogen receptor modulators (SERMs) to manage estrogenic activity.

6. Dermatological and Behavioral Side Effects

Many of the non-life-threatening side effects of TRT are related to the potent androgenic nature of testosterone, which influences peripheral tissues such as the skin and central nervous system activity. Dermatological symptoms are frequent and include increased activity of the sebaceous glands, resulting in **oily skin** and the development or worsening of acne. These symptoms are often dose-dependent and can usually be managed with topical treatments, though they contribute to patient discomfort.

Behavioral and psychological changes represent a complex array of potential side effects. While TRT is often used to treat depression associated with low T, it can also lead to mood instability. Some individuals experience increased irritability, impatience, and aggressive tendencies, sometimes referred to colloquially as mood swings or heightened "androgenic effect." Conversely, other patients may experience persistent **moodiness and depression** despite the hormone replacement. Furthermore, systemic effects often include **fluid retention** (edema or bloat) in body tissues, which can be managed but requires attention. Urinary changes, often involving difficulty or frequency in urination, may also arise due to mild prostate enlargement, separate from cancerous changes (Benign Prostatic Hyperplasia, or BPH).

7. Contraindications and Risk Assessment

The determination of whether the therapeutic benefits of TRT outweigh the risks is the most important clinical step. Patients who fall into a high-risk category regarding life-threatening adverse effects are generally considered medically disqualified from receiving the therapy. Absolute contraindications include, but are not limited to, a known history or confirmed diagnosis of **prostate cancer** or **male breast cancer**, as these hormone-sensitive malignancies can be stimulated by exogenous testosterone.

Additionally, individuals with severe, uncontrolled cardiovascular conditions, a history of blood clots, or untreated severe obstructive sleep apnea are typically excluded from TRT. In cases where less life-threatening side effects--such as dermatological issues, mood changes, or infertility--are the primary concern, the decision becomes a personalized negotiation between the patient and the clinician, weighing the severity of the original hypogonadism symptoms against the discomfort and management burden imposed by the adverse effects. The therapeutic goal is always to improve quality of life safely, and if the side effects compromise this objective, alternative treatments or cessation of TRT is warranted.

Further Reading

U.S. Food and Drug Administration (FDA) Safety Information on Testosterone Products
Risks of Testosterone Replacement Therapy in Men
Testosterone Replacement Therapy (Wikipedia)