Testosterone Prescribing Issues

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Alabama Board of Medical Examiners

Continuing Medical Education

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The Testosterone Prescribing Surge

11M+	1/3	25%	50%
Rx in 2024 (up from 7.3M in 2019)	of patients never diagnosed with deficiency	never had baseline serum T checked	never had follow-up T level checked

Source: IQVIA 2024 | American Urologic Association 2024 | New York Times, Jan 25 2025

The market is growing faster than clinical standards are being applied.

Up to one-third of men receiving testosterone have never been formally diagnosed with deficiency, and half have no follow-up monitoring.

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A Controlled Substance — Not a Lifestyle Drug

Schedule III Controlled Substance

- Significant adverse effects
- Risk of abuse and dependence
- Requires documented medical indication
- Appropriate monitoring is mandatory

The Goal

Serve patients with genuine deficiency — not market demand.

Inappropriate prescribing harms patients and undermines legitimate therapy.

Fueled by direct-to-consumer marketing and unregulated clinics

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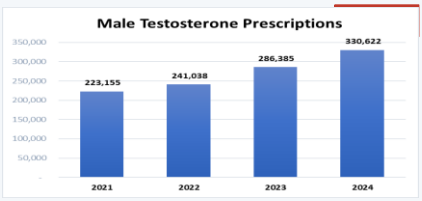
Alabama: Male Testosterone Prescriptions — 48% Rise Since 2021



Source: Alabama Department of Public Health

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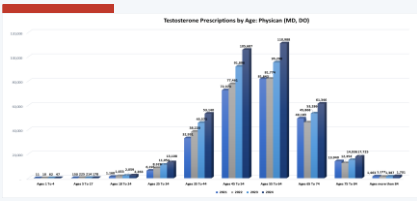
Prescriptions by Age: Physicians (MD/DO) — Notable Surge in Ages 25–34



Source: Alabama Department of Public Health

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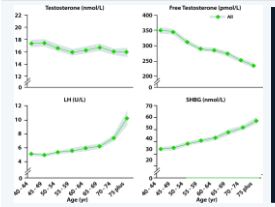
The Biology: Testosterone Declines with Age



Key Insight

- Total T declines modestly with age
- Free T declines significantly due to rising SHBG
- LH rises — compensatory signal from pituitary
- Functional hypogonadism (obesity, metabolic disease) is distinct from age-related decline

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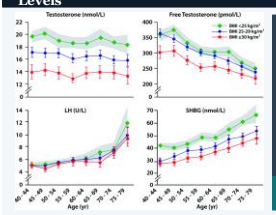
Obesity Compounds the Effect: Age, BMI & Hormone Levels



Clinical Take-Away

- BMI ≥30 reduces total & free T by 25–30% vs. lean men
- Obesity-related hypogonadism is often reversible with weight loss
- Always address lifestyle before or concurrent with TRT in obese men

Ask: Have we tried lifestyle optimization first?

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Who Is a Candidate for Androgen Supplementation?

1 Confirmed Biochemical Deficiency

Total testosterone < 300 ng/dL on two fasting early-morning samples

2 Valid Symptoms Present

Fatigue, decreased libido, ED, muscle loss, mood change, osteopenia

3 Adequate Evaluation Completed

History, physical exam, confirmatory labs including LH, PSA, CBC, prolactin

4 No Contraindications

Fertility not desired; no active prostate/breast cancer; no uncontrolled OSA or erythrocytosis

AUA Guideline 2024 | Endocrine Society 2018

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Pre-Treatment Evaluation

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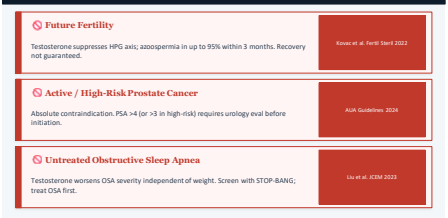
Contraindications to TRT — Part 1



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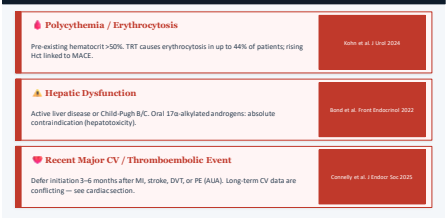
Contraindications to TRT — Part 2



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Counseling Patients: Key Risks to Disclose

Testicular atrophy & impaired fertility
Up to 95% azoospermia within 3 months

Erythrocytosis
Hct >50% in 44% of patients; independently raises MACE risk

Cardiovascular & thrombotic events
RCT (TRAVERSE) neutral; long-term observational data conflicting

Cardiac arrhythmia
Small increased risk with supraphysiologic levels

Estrogen elevation / gynecomastia
Via aromatization; mood effects possible

Prostate growth / LUTS
Monitor PSA; avoid in active prostate cancer

Informed consent must be documented. Kohn et al. J Urol 2024; Bond et al. Endocr Connect 2026

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Counseling Patients: Potential Benefits of TRT

❤️ Libido

⚡ Erectile Function

💪 Body Composition

🩸 Insulin Sensitivity

🧠 Mood & Energy

🦴 Bone Density

Benefits are most reliable when testosterone is genuinely deficient (<300 ng/dL) and symptoms are present.

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Additional Counseling: Lifestyle First

Before initiating TRT, optimize:

- Weight management — obesity is the single largest modifiable driver of functional hypogonadism
- Sleep quality — untreated OSA independently suppresses testosterone
- Stress reduction — cortisol antagonizes HPG axis
- Alcohol — heavy use reduces testosterone significantly
- General medical evaluation — rule out systemic illness, medications (opioids, glucocorticoids)

Often overlooked

These variables will often help normalize testosterone levels without needing replacement therapy.

Optimizing lifestyle variables is not optional counseling — it is standard of care.

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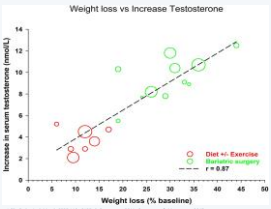
Weight Loss Significantly Raises Testosterone



r = 0.87

Strong correlation between % weight lost and testosterone rise — across both diet/exercise and bariatric surgery.

Bariatric surgery can normalize testosterone in the majority of obese hypogonadal men without TRT.

J Clin Endocrinol Metab 2025;110:e3125. | Grossmann 2011; Grossmann & Matsumoto 2017

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Treatment Options: Formulations Compared

Transdermal Gel — Daily	Intramuscular Injection — 1–2x/week
✓ Steady levels; easy dosing	✓ Reliable delivery; inexpensive
✗ Skin transfer risk; daily application	✗ Peak/trough fluctuations; injection site
Testosterone Pellets — 3–6 months	**Oral (Jatenzo/Tlando) — Twice daily**
✓ Convenient; consistent levels	✓ No injection/skin contact
✗ Insertion procedure; dose adjustment difficult	✗ GI absorption variability; cost

Choice should be driven by patient preference, compliance, cost, and safety profile. Lowest effective dose principle applies.

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3-Month Follow-Up: The First Assessment Gate

Required at 3 Months	Decision Points
• Serum total testosterone • Hemoglobin and hematocrit • PSA level • Physical exam by physician • Evaluate symptomatic response	• No benefit confirmed → discontinue • Target range: 450–600 ng/dL (AUA); avoid >800 • Lowest effective dose principle • Check PDMP for potential abuse • Consider referral: urologist or endocrinologist if uncertain

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Ongoing Monitoring: Every 6 Months

Labs	Thresholds	Standards
• Serum testosterone • Hemoglobin / hematocrit; blood pressure • PSA (annually after year 1)	• T >800 ng/dL: reduce dose • Hct >54%: hold; consider phlebotomy • PSA rise >1.4/yr: refer. Monitor BP (FDA 2025)	• Physician exam at least annually • Telehealth alone is not acceptable • Check PDMP at initiation + annually • Refer complex cases to specialist

Steady-state levels may not be achieved until 3–6 months after dose changes.

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Testosterone in Women

HSDD, Menopause, and Off-Label Use

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The Cultural Moment: Media Normalizing Testosterone for Women

NY Times, Oct 22, 2025

Media coverage and online communities are driving demand that may outpace clinical evidence.

No FDA-approved testosterone formulation for women exists in the US. All use is off-label.

Our role: separate evidence-based benefit (HSDD) from unproven claims (mood, cognition, energy).

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Hypoactive Sexual Desire Disorder (HSDD)

DEFINED: Persistent absence of sexual desire or fantasies causing personal distress or relationship difficulty for ≥6 months — not explained by another condition or relationship problem.

Neurobiological	Pharmacological	Psychological	Cultural/Social
Neuroendocrine imbalance, dopamine/serotonin dysregulation, hypogonadism	SSRIs/SNRIs, antipsychotics, opioids, hormonal contraceptives	Depression, anxiety, trauma, self-esteem, relationship distress	Religious or cultural norms around sexuality; partner dynamics

Impact: Significant effects on mood, self-esteem, relationships, and quality of life.

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HSDD Diagnosis and Evaluation

Validated Screening Tool

- Decreased Sexual Desire Screener (DSDS)
- 5-question validated instrument
- Distinguishes generalized acquired HSDD from other sexual dysfunction

Panay N. Post Reprod Health 2022;28(3):158

Free testosterone may explain non-response in women with elevated SHBG — consider if symptoms persist on therapy.

Lab Evaluation

- Total serum testosterone — mid-to-high normal premenopausal range may not need supplementation
- Sex Hormone Binding Globulin (SHBG) — elevated SHBG reduces bioavailability; less likely to benefit from testosterone therapy
- Free testosterone — especially if SHBG elevated or poor response to therapy

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When Testosterone Therapy Is NOT Recommended in Women

The evidence supports testosterone ONLY for HSDD in postmenopausal women. Other uses lack RCT evidence.

- ✗ Infertility treatment
- ✗ Depression or general wellbeing
- ✗ Sexual dysfunction other than HSDD
- ✗ Cognitive performance or delay of cognitive decline
- ✗ Cardiovascular, metabolic, or bone health
- ✗ Low androgens due to hypopituitarism, adrenal insufficiency, surgical menopause, or pharmacologic glucocorticoid use

Global Consensus 2019 (Davis et al. ICEM 504:86400) | Islam et al. Lancet Diab Endocrinol 2019

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Contraindications in Women — Part 1

Pregnancy / Fertility

Testosterone is teratogenic. Absolute contraindication if pregnant or attempting conception. Effective contraception required during therapy.

Global Consensus 2019 (Davis et al. JCEM)

Androgen-Sensitive Cancer (Breast, Endometrial, Ovarian)

Insufficient long-term safety data. Islam et al. 2019 meta-analysis found no significant increase in breast cancer at physiologic doses, but caution required pending longer RCT data.

Islam et al. Lancet Diab Endocrinol 2019

Polycythemia / Erythrocytosis

Less common at physiologic female doses, but baseline hematocrit >48% warrants risk-benefit discussion before initiating.

AUA/Endocrine Society 2024

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Treatment Options for Women: Off-Label Transdermal

No FDA-approved formulation for women in the US. Use male-formulation gels at approximately 1/10 the male dose.

Compounded Transdermal Gel — Preferred

Custom-compounded at 1/10 male dose. Most widely used. Monitor serum T every 6 weeks until stable.

Male-Formulation Gel (off-label) — Acceptable

Available commercially. Requires careful dose management. Document off-label use and monitoring.

Testosterone Pellets — NOT RECOMMENDED

FDA warning re: adverse event under-reporting (BioTE case). Risk of irreversible virilization. No major society endorsement.

Oral / Injectable — Not used

Not appropriate for women at physiologic doses. No safety or efficacy data in this context.

Dutcmoor-Su R. Ob Gyn 2021 | Global Consensus 2019

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Testosterone Pellets: A Warning

FDA Warning: BioTE Medical (Irving, TX) failed to report >4,200 adverse events including endometrial cancers.

No Society Endorsement

The Global Consensus Statement on testosterone use in women explicitly states pellets DO NOT represent appropriate care.

Irreversible Virilization

Mustache, voice deepening, clitoromegaly — some patients discover these effects are permanent.

Dose Cannot Be Adjusted

Once implanted, pellets cannot be removed. Supraphysiologic levels persist until they dissolve. No ability to titrate down.

Regulatory & Liability Risk

Prescribers face significant liability. Adverse events underreported by manufacturers.

Dutcmoor-Su R. Ob Gyn 2021;136309

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Duration and Monitoring: Women on Testosterone Therapy

Before 1st dose	6 weeks	3–6 months	Every 6 months
• Baseline T, SHBG, free T • Hematocrit, LFTs • Symptom score (DSDS) • Contraindications excluded	• Serum testosterone • Check for virilization signs • Symptom response?	• T, SHBG, free T • Assess symptom benefit • Adjust dose if T out of range • Evaluate for virilization	• Repeat T monitoring • Ongoing symptom scoring • Annual mammography • Reassess indication

Global Consensus 2019 | Islam et al. Lancet Diab Endocrinol 2019

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Safety Data: Prostate and Liver

Prostate Safety

- Large meta-analyses: TRT does not increase prostate cancer risk in men without pre-existing disease
- Monitor PSA at 3 months, 12 months, then annually
- PSA rise >1.4 ng/mL above baseline in any 12-month period → urology referral

Morgentaler et al. NEJM 2023

Liver Function

- Obtain baseline LFTs before initiation
- Oral 17α-alkylated androgens (methyltestosterone): risk of peliosis hepatis, cholestasis, hepatocellular carcinoma — AVOID
- Injectable and transdermal formulations: minimal hepatic risk at therapeutic doses

Bond et al. Front Endocrinol 2022

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Androgen Abuse in Clinical Practice: A Growing Challenge

6.4%	1.6%	>20%
Global lifetime prevalence in men	Global lifetime prevalence in women	Gym-goers in Netherlands used androgens (2023)

Intermittent Cycling	Self-Initiated TRT	Blast-and-Cruise
8–16 week supraphysiologic cycles with 'off' periods	150–300 mg/wk vs. appropriate 75–100 mg/wk; no documented deficiency	Cycles followed by lower-dose maintenance — prolonged HPG suppression

Clinical Alert: Suppressed gonadotropins in a healthy young man who has completed puberty strongly suggest exogenous androgen exposure. Total testosterone can appear normal or low — do NOT rely on T level alone to exclude abuse.

Lee SL, et al. J Clin Endocrinol Metab 2006;91:4450

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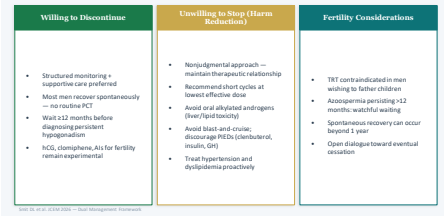
Managing Androgen Abuse: Harm Reduction Framework



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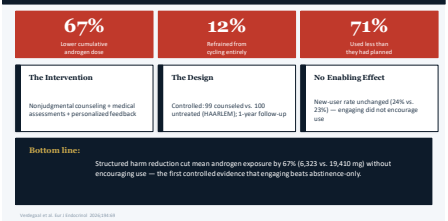
HARNAS Trial: Does Harm Reduction Actually Work?



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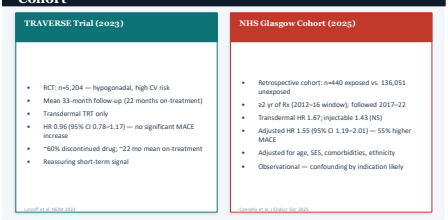
Long-Term CV Risk: TRAVERSE RCT vs. NHS Glasgow Cohort



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NHS Glasgow Data: Key Findings & What They Mean

Primary Outcome: 12.7% MACE events (TRT-exposed) vs. 8.6% (unexposed) | Adjusted HR 1.55 (CI 1.19–2.01; p=0.001)

Formulation Subgroup	Transdermal HR 1.67 (CI 1.13–2.48; p=0.010); injectable HR 1.43 (CI 0.99–2.06; p=0.055, NS). Note: transdermal is the exact formulation TRAVERSE found neutral — arguing against a true dose effect and toward confounding.
Context vs. TRAVERSE	TRAVERSE is a randomized trial (~22 mo on-treatment); NHS is observational over a longer window. Duration differs — but so does design, and only the observational study shows harm.
Study Limitations	Only 440 exposed men; prescription-based exposure proxy; residual confounding (BMI, smoking not fully captured); TRT group had higher baseline comorbidity burden. Cannot establish causation.

Bottom line: one observational cohort, weighed against a neutral RCT and the FDA's Feb 2025 removal of the CV boxed warning. Not proof of harm — but grounds to individualize, monitor, and document informed consent.

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Reconciling the CV Evidence: Why They Differ & How to Counsel

The disagreement is about study design and duration — not a settled fact. One RCT and most real-world cohorts reassure; a single cohort does not.

RCT vs. Real-World	TRAVERSE randomizes, balancing sick and healthy men; observational cohorts cannot. Sicker men get testosterone (confounding by indication), which can create a false signal. The transdermal subgroup — TRAVERSE's own formulation — drove the NHS signal.
The Fuller Picture	The FDA removed the CV boxed warning (Feb 2025), adding a blood-pressure warning instead. Competing 2025 cohorts — Lin (US EHR) and a Canadian claims study — found no increase, or reduced risk. NHS Glasgow is the outlier.
What Is Actually Solid	Rising hematocrit independently predicts MACE, and supraphysiologic dosing is genuinely risky. Keep total T mid-normal, monitor hematocrit and blood pressure, and never chase high-normal levels.

How to counsel: testosterone is reasonable for confirmed deficiency with symptoms. Disclose that long-term (>2 yr) CV data conflict, keep dosing physiologic, monitor Hct and BP, and document the shared decision.

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Conclusions

1 — Rapidly Rising Prescriptions Demand Rigor

11M+ Rx in 2024. Up to 1/3 of patients were never formally diagnosed. Rigorous evaluation, confirmed biochemical deficiency, and documented indication are required before initiation.

2 — Male TRT: Contraindications Must Be Systematically Screened

Fertility desire, active prostate cancer, uncontrolled OSA, pre-existing erythrocytosis, hepatic dysfunction, and recent major CV events are all contraindications.

3 — Long-Term CV Risk Is Unsettled — Individualize

TRAVERSE (RCT) found no MACE increase, and the FDA removed the CV boxed warning in Feb 2025. One observational cohort (NHS Glasgow) shows a 55% signal; other real-world cohorts show none. Beyond ~2 years the data conflict — individualize, monitor, and document informed consent.

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Conclusions (continued)

4 Women: Evidence Supports HSDD Only

The Islam et al. 2019 meta-analysis and 2019 Global Consensus confirm physiologic testosterone is safe and effective specifically for HSDD in postmenopausal women. Not for mood, cognition, or bone health.

5 Androgen Abuse Is a Public Health Problem

Particularly among young men in strength training. Harm reduction (nonjudgmental engagement, dose reduction, CV risk management) is medically and ethically defensible when abstinence is not immediately achievable.

6 Ongoing Monitoring Is Non-Negotiable

Serum T, CBC (erythrocytosis), PSA, lipids, LFTs, blood pressure (FDA 2025 warning), OSA reassessment. Telehealth alone is inadequate. Physician exam at least annually. Check FOMP.

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Case Studies

Applying the principles — three clinical scenarios

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Case Study 1: The Motivated 34-Year-Old

THE CASE · Would you prescribe testosterone?

- 34-year-old male presents requesting testosterone therapy
- Complaints: fatigue, reduced motivation at the gym, slightly reduced libido
- BMI 31, works long hours, sleeps 5–6 hours per night, drinks 3–4 drinks/night
- Total T: 285 ng/dL (single morning lab, non-fasting)
- LH: 5.2 IU/L (normal); FSH normal; PSA 0.6; Hct 44%; no OSA diagnosis

Discussion

- Single non-fasting lab is insufficient — two fasting AM levels required
- Functional hypogonadism likely: obesity, sleep deprivation, alcohol use, stress
- Optimize lifestyle first: weight loss, sleep hygiene, alcohol reduction
- OSA screen indicated (STOP-BANG): untreated OSA suppresses T independently
- Defer TRT; reassess in 3–6 months after lifestyle changes

Take-home: Obesity + alcohol + sleep debt = functional hypogonadism. Screen lifestyle before prescribing. Single non-fasting T is not sufficient evidence.

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Case Study 2: "I Want Testosterone — But Also Want Kids"

THE CASE · Start testosterone — or not?

- 29-year-old male referred for fatigue, low libido, difficulty concentrating
- Two fasting AM total T: 218 and 231 ng/dL. LH: 2.1 IU/L (low). FSH: 1.8 IU/L (low)
- Diagnosis: secondary (hypogonadotropic) hypogonadism confirmed
- Married 6 months; actively trying to conceive with his wife
- Prolactin normal; MRI pituitary unremarkable; BMI 24, no medications

Discussion

- TRT absolutely contraindicated — azoospermia develops in up to 95% within 3 months; recovery not guaranteed
- Correct pivot: clomiphene citrate 25–50 mg/day (SERM) stimulates endogenous LH/FSH, raises T, and preserves spermatogenesis
- Semen analysis at baseline and 3 months; target T 400–600 ng/dL; if E2 >50 pg/mL add anastrozole 0.5 mg
- Counsel on off-label clomiphene use, limited long-term male data, and visual symptom monitoring
- Revisit TRT only after fertility goals are complete and clomiphene is discontinued

Take-home: Fertility desire = absolute contraindication to TRT. Secondary hypogonadism + fertility goal = clomiphene/SERM first, not testosterone.

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Case Study 3: The Gym-Goer with a "Normal" Testosterone Level

THE CASE · His T reads "normal." Treat?

- 26-year-old competitive bodybuilder: fatigue, low libido, depressed mood — 3 months after stopping "a cycle"
- Total T: 310 ng/dL (borderline). LH: 0.4 IU/L. FSH: 0.3 IU/L — profoundly suppressed
- Hematocrit 51%; HDL 28 mg/dL (severely low); LFTs mildly elevated
- Admits to 16-week testosterone enanthate 400 mg/week + oral stanozolol
- Insists he needs TRT because "my levels are low" — will continue cycling regardless

Discussion

- Suppressed LH/FSH in a young post-pubertal male = exogenous androgen exposure until proven otherwise — do NOT initiate TRT
- Diagnosis: PFAAH (Prolonged Post-Androgen Abuse Hypogonadism) — most recover spontaneously but may take >12 months
- Oral alkylated androgens (stanozolol): serious hepatic + severe lipid toxicity — HDL 28 and elevated LFTs confirm exposure
- Patient refuses abstinence → nonjudgmental harm reduction: shortest cycles, eliminate oral androgens, avoid blast-and-cruise, treat dyslipidemia and HTN, monitor CBC/lipids/LFTs/echo
- TRT only after ≥12 months abstinence with confirmed persistent biochemical + symptomatic hypogonadism

Take-home: Suppressed LH in a young man = androgen abuse until proven otherwise. T level alone is unreliable. Harm reduction is medically defensible when abstinence is refused.

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