



Male Hypogonadism

Almost every error happens before treatment is considered · a single convenience-timed level is not a diagnosis

Morning, fasting, repeated
then interpret against SHBG

△ THE THREE TESTING RULES THAT PREVENT MOST MISDIAGNOSIS

△ HOW TO DRAW IT

(1) **MORNING and FASTING** -testosterone has a diurnal rhythm peaking early, and an afternoon sample can be substantially lower in the same man; food also lowers it. (2) **REPEAT an abnormal result on a separate day BEFORE diagnosing** -biological and assay variability is considerable and many initially low levels are normal on repeat. (3) **NEVER test during acute illness**, which transiently suppresses the axis. **Total testosterone is the initial test; free testosterone is a second step, not a screen.**

WHO TO TEST

Not asymptomatic men -screening is not recommended, and the complaints driving most requests (fatigue, low mood, weight gain) have a long differential in which hypogonadism is uncommon. **SPECIFIC features that justify testing:** reduced morning erections, low libido, erectile dysfunction, small or shrinking testes, gynecomastia, loss of body hair, infertility, fragility fracture. **Case-find** in T2DM, obesity, chronic opioids or glucocorticoids, HIV with weight loss, unexplained osteoporosis, pituitary or testicular disease.

PRIMARY vs SECONDARY

Measure LH and FSH once low T is confirmed -this single step determines the whole workup. **HIGH = PRIMARY** (testicular): Klinefelter, mumps orchitis, trauma, cryptorchidism, chemo/radiation; fertility usually **not** recoverable. **LOW or INAPPROPRIATELY NORMAL = SECONDARY** (pituitary/hypothalamic); fertility often **is** recoverable with gonadotropins. **△ A normal LH against a low testosterone is the ABNORMALITY, not reassurance.**

△ THE SHBG TRAP *the commonest reason a man is mislabeled hypogonadal*

Direction	Causes	What it does to the numbers
SHBG LOWERED	Obesity, insulin resistance and T2DM , nephrotic syndrome, hypothyroidism, glucocorticoids, androgen use	Lower SHBG drags TOTAL testosterone down , so an obese diabetic man can have a low total with a NORMAL free testosterone and no true deficiency . This is the classic overdiagnosis
SHBG RAISED	Aging , hyperthyroidism, liver disease, HIV, anticonvulsants, estrogens	Higher SHBG lifts the TOTAL , so an older man can look reassuring while his free testosterone is genuinely low . The missed diagnosis
What to measure	Free or bioavailable testosterone when the total is borderline, or whenever an SHBG-altering condition is present. Use equilibrium dialysis or a CALCULATED free testosterone (from total T, SHBG and albumin). △ Direct analog free-testosterone immunoassays are unreliable and must not drive this decision	

FIND THE CAUSE BEFORE REACHING FOR THE GEL

Step	Detail
△ Functional / reversible causes come first	The commonest reason for a low level, and treated by fixing the cause rather than prescribing. OBESITY leads (lower SHBG plus aromatization of testosterone to estradiol in fat; weight loss genuinely raises testosterone). OPIOIDS are a major and widely missed cause, suppressing the axis dose-dependently, as are glucocorticoids . Also OSA, alcohol, poor glycemic control, acute illness, anabolic steroid use
Secondary workup	Prolactin (and review meds -antipsychotics, metoclopramide), iron studies for hemochromatosis , and the other pituitary axes. Obtain pituitary MRI if testosterone is severely low, prolactin raised, other pituitary hormones abnormal, or mass-effect features (headache, visual field loss). Do not skip this in a young man with markedly low T and low gonadotropins
Primary workup	Send a KARYOTYPE for Klinefelter (47,XXY) with small firm testes, tall stature, gynecomastia and infertility -substantially underdiagnosed into adulthood, with cardiometabolic and malignancy implications. Raise sperm banking before gonadotoxic treatment , and semen analysis before any therapy if fertility matters

TREATMENT: THE TWO THINGS THAT CAUSE LASTING HARM

△ NEVER TREAT A MAN WHO WANTS CHILDREN

The error with the most permanent consequences. **Exogenous testosterone suppresses LH and FSH by negative feedback**, shutting down intratesticular production and **suppressing spermatogenesis, frequently to AZOOSPERMIA**. It is an effective male contraceptive -that is exactly the problem. **Recovery takes months and is NOT guaranteed. Ask every man about fertility intentions before prescribing.** Where fertility is desired, raise endogenous production instead: **hCG** (acts like LH on the testis), gonadotropins, or a **SERM such as clomiphene**, with specialist input.

△ ERYTHROCYTOSIS: THE HEMATOCRIT RULE

Testosterone stimulates erythropoiesis and **erythrocytosis is the commonest adverse effect**. Check hematocrit at **BASELINE, 3-6 MONTHS, then ANNUALLY**. If it exceeds **54%: STOP** until it falls, evaluate for hypoxia and sleep apnea, restart at a **REDUCED dose** -the concern is hyperviscosity and thromboembolic risk. **Baseline above 50% is a relative contraindication**, since many of those men will cross 54% on treatment.

MONITORING, CONTRAINDICATIONS & CARDIOVASCULAR SAFETY

Item	Detail
Response & level	Reassess symptoms and check the level at 3-6 months , targeting the mid-normal range (sample timing depends on formulation). △ If there is no symptomatic benefit, STOP -a normalized number in a man who feels no different is not a treatment success
Contraindications	Known or suspected prostate or breast cancer , a man actively seeking fertility, an unevaluated prostate nodule or raised PSA , baseline Hct > 50% (relative). Caution in untreated severe OSA, severe lower urinary tract symptoms, uncontrolled heart failure, thrombophilia or prior VTE
Formulations	Gels give steady levels but risk skin-to-skin transfer to partners and children causing virilization -counsel on covering the site and washing hands. Injections are cheap and effective; shorter-acting esters cause peak-and-trough swings felt as fluctuating energy and mood
Cardiovascular TRAVERSE 2023	5,246 men aged 45-80 with hypogonadism plus CV disease or high risk. PRIMARY endpoint (MACE: CV death, nonfatal MI, nonfatal stroke) was NONINFERIOR to placebo , largely settling a decade-old question. △ But not a clean bill of health: more atrial fibrillation (3.5% vs 2.4%), acute kidney injury (2.3% vs 1.5%) and pulmonary embolism (0.9% vs 0.5%) . AF and AKI were unexpected; caution with prior thromboembolism . It studied CONFIRMED hypogonadism at replacement doses and licenses nothing beyond that

PEARLS & PITFALLS

- **A low testosterone with a normal LH is a reason to image the pituitary**, not a reason to hand out a gel. Treating the level without asking why can mean treating the symptom of a prolactinoma.
- **Hypogonadism is a clinical syndrome, not a laboratory value** -it needs consistent symptoms AND repeatedly low testosterone. Diagnosing it from one borderline level in a tired man commits him to therapy that suppresses his own production and fertility.

References: Endocrine Society clinical practice guideline on testosterone therapy in men with hypogonadism (diagnostic confirmation, hematocrit thresholds and

monitoring intervals) · TRAVERSE,

N Engl J Med

2023 (cardiovascular safety of testosterone-replacement therapy).

Educational aid; verify against current guidance, local formulary and patient factors.

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