

Appropriate testosterone testing for male hypogonadism

By [Dr. Breay Paty](https://thischangedmypractice.com/author/brpaty/) on January 21, 2020

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Breay W. Paty, MD ([biography and disclosures](https://thischangedmypractice.com/bios/#breaypaty))

Disclosures: Dr. Paty has received speaking fees and/or sat on advisory boards for Abbott, Astrazeneca, BI/Lilly Alliance and Novo Nordisk related to diabetes monitoring and treatment. No conflict of interest involving testosterone testing or products. Recommendations in this article are consistent with current practice patterns. Treatments or recommendations in this article are unrelated to products/services/treatments involved in disclosure statements.

What have I have noticed

The therapeutic use of testosterone has increased dramatically in the last two decades. The reasons for this increase appear to be due to the frequency of testing and marketing of testosterone replacement for middle-aged and older men. While men with unequivocally low testosterone levels usually benefit from hormone replacement, the risk/benefit ratio for men with equivocal (“borderline”) levels is not clear, especially in men who desire fertility. Testosterone therapy suppresses endogenous hormone production and reduces fertility. Also, once men start treatment, they may find it difficult to stop because of prolonged hypogonadism during recovery of the hypothalamic-pituitary-testicular axis. For these reasons, it is particularly important to have a rational approach to testing and diagnosis of hypogonadism in men.

What I recommend (practice tips)

When assessing for male hypogonadism, consider the following: (see [Figure 1](https://med-fom-tcmp.sites.olt.ubc.ca/files/2020/01/Figure1-Male-Hypogonadism-Algorithm.pdf))

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1. Do not order a testosterone level in men who express only non-specific symptoms.

The clinical diagnosis of hypogonadism is made in men who have low total testosterone levels combined with symptoms and/or signs suggesting hypogonadism. Evidence suggests that sexual symptoms, such as reduced libido, decreased sexual thoughts, and fewer morning erections are more specifically associated with male hypogonadism. Non-specific symptoms, such as fatigue, low mood, weight gain, or generalized weakness have many potential causes. For men who express non-specific symptoms, but not sexual symptoms, investigations should focus on other potential diagnoses. A testosterone level should not be ordered until and unless other diagnoses have been thoroughly explored.

2. Start with total testosterone (TT).

Total testosterone (TT) is the most direct measure of testosterone in men. Sensitivity and specificity vary depending on the reference range. While calculated bioavailable (bT) or free testosterone (fT) measurements theoretically reflect physiological levels, standard methods for measuring these values have not been well established. Consequently, TT is recommended as the first choice for evaluating male hypogonadism. If TT is unequivocally normal or low, no further testing is needed. If the TT is repeatedly equivocal (“borderline”), the measurement of calculated fT or bT may be helpful to clarify the diagnosis.

3. Measure testosterone at 8 am, fasting.

Testosterone exhibits diurnal variation, peaking in the morning (between 8-10 am) with a nadir in the evening (about 8 pm). The morning, fasting testosterone level (8 am) has been validated for assessment of hypogonadism. Measuring testosterone at any other time of day is not a valid indicator of endogenous testosterone production. Also, food intake can suppress testosterone levels, so fasting is recommended.

4. Confirm unequivocally low testosterone levels on at least 2 -3 occasions before making a diagnosis.

Testosterone level should be repeated at least twice (or 3 times in the case of equivocal results) over weeks or months, to confirm a consistently low value in the absence of any other external cause. Because hypothalamic and pituitary hormones are prone to variation, testosterone fluctuates over hours, days, and weeks. For this reason, it is important to repeat the testosterone test on several occasions, especially if there is an external factor that may be suppressing hypothalamic or pituitary function.

For men under the age of 50, repeated TT levels below 8.0 nmol/L (or below 7.0 nmol/L for men over the age of 50) on 2-3 occasions are considered unequivocally low. Total testosterone levels between 8.0-11.0 nmol/L (7.0-11.0 nmol/L for men over age 50) are considered equivocal and the test should be repeated and external causes should be examined (see 5 below). Total testosterone values above 11.0 nmol/L are considered normal and do not require further testing.

Total Testosterone (TT) levels measured at 8 AM, fasting (repeated)

| Hypogonadism | Equivocal | Normal |
|-------------------------------|----------------------------------|---------------|
| < 8.0 mmol/L (men < 50 years) | 8.0-11.0 mmol/L (men < 50 years) | > 11.0 mmol/L |
| < 7.0 mmol/L (men > 50 years) | 7.0-11.0 mmol/L (men > 50 years) | |

5. If hypogonadism is diagnosed, determine if it is primary (testes) or secondary (brain)

If an unequivocally low testosterone is identified, luteinizing hormone (LH) and follicular stimulating hormone (FSH) should be ordered (along with a repeat morning testosterone). An elevated LH or FSH suggests a primary (testicular) cause, while a low or inappropriately “normal” LH and FSH suggests that the problem may be hypothalamic or pituitary (brain) in origin. This will help guide further investigation and treatment.

6. In cases of secondary hypogonadism, look for a treatable cause.

In cases of secondary (brain) hypogonadism, prolactin should be ordered to rule out hyperprolactinemia and ferritin to rule out hemochromatosis. If these tests are normal, then other factors should be considered. Hypothalamic/ pituitary hormones can be influenced by a variety of external factors (so-called “functional” hypogonadism), including obesity, stress, depression, systemic illness, extreme exercise or diet, medication, alcohol, marijuana and other causes. These factors may often be transient and treatable. If any external factors are identified, they should be addressed before considering testosterone therapy. In cases of primary hypogonadism (low testosterone, elevated LH/FSH), including congenital conditions, such as Klinefelter syndrome, or acquired conditions, such as mumps or testicular trauma, testosterone treatment is often the best option. In cases where the cause is uncertain, consider a referral to an endocrinologist or other specialist familiar with the evaluation and treatment of male hypogonadism.

General characteristics of Primary, Secondary, and “Functional” hypogonadism

| Type of Hypogonadism | Testosterone | LH/FSH | Duration |
|---------------------------------|--------------|---------|--------------------------------|
| Primary (testes) | ↓↓ to ↓↓↓ | ↑ to ↑↑ | Usually permanent |
| Secondary (brain) | ↓ to ↓↓ | ↓ or ↔ | May be Persistent or Transient |
| “Functional” (external factors) | ↔ to ↓ | ↔ | Often Transient |

Symbols: ↓ reduced, ↑ elevated, ↔ normal or no change

7. Is fertility a consideration?

If a man with hypogonadism desires fertility (either immediately or in the future), testosterone therapy is not generally recommended (except for unequivocal primary hypogonadism), since it tends to suppress fertility. For men with secondary (hypothalamic/pituitary) hypogonadism, in whom no cause is identified and who desire fertility, a semen analysis should be obtained and if it is low, consider referring the patient to a fertility clinic.

This is not a complete review of the investigation of male hypogonadism, but addresses some of the common issues that arise in the primary care setting. Having a sound approach to testosterone testing is critical to good clinical decision making, especially for men with equivocal testosterone levels and other factors which may be

causing their symptoms. Understanding what symptoms to look for and how to undertake investigation will allow for appropriate choices for therapy and help to avoid unnecessary or inappropriate use of testosterone.

References

1. Lawrence KL, Stewart F, Larson BM. Approaches to male hypogonadism in primary care. Nurse Pract. 2017;42(2):32–37. [View](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5278890/pdf/npr-42-32.pdf) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5278890/pdf/npr-42-32.pdf).
2. Grossmann M, Matsumoto AM. A Perspective on Middle-Aged and Older Men With Functional Hypogonadism: Focus on Holistic Management. J Clin Endocrinol Metab. 2017 Mar 1; 102(3): 1067-1075. [View](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5477803/) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5477803/).

Resource:

BC Guidelines: Testosterone Testing – Protocol. Effective Date: September 19, 2018.

<https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/testosterone-testing>
(<https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/testosterone-testing>).

Please indicate how this article will change your practice:

Appropriate Testosterone Testing for Male Hypogonadism

- I disagree with this approach
- I will consider changing my practice, but need more information/time
- I will likely change my practice
- I will definitely change my practice
- I already do this

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11 responses to “Appropriate testosterone testing for male hypogonadism”

Simon Pimstone

[Permalink](#)

January 22, 2020 (Wednesday, January 22nd, 2020, 12:51 pm) at 12:51 pm (Wednesday, January 22nd, 2020, 12:51 pm)

Excellent summary

When in cycle ideally should TT be measured in men already taking replacement to determine biochemical response?

Mid-cycle or at trough pre next dose ?

Gail R Dodek Wenner

[Permalink](#)

January 22, 2020 (Wednesday, January 22nd, 2020, 1:23 pm) at 1:23 pm (Wednesday, January 22nd, 2020, 1:23 pm)

This is a succinct article that will help Physicians educate men with minor complaints. Often a total testosterone is really not necessary.

Duncan Etches

[Permalink](#)

January 22, 2020 (Wednesday, January 22nd, 2020, 5:38 pm) at 5:38 pm (Wednesday, January 22nd, 2020, 5:38 pm)

Clear & comprehensive article. Thank you.

Herbert L Domke

[Permalink](#)

January 22, 2020 (Wednesday, January 22nd, 2020, 7:33 pm) at 7:33 pm (Wednesday, January 22nd, 2020, 7:33 pm)

Good outline to follow.

Dennis Boettger

[Permalink](#)

January 23, 2020 (Thursday, January 23rd, 2020, 7:20 am) at 7:20 am (Thursday, January 23rd, 2020, 7:20 am)

Succinct,rational. Is there a particular pattern that would indicate the recovery phase or the withdrawal phase of someone who had used illicit androgens?

Riffat Nagra

[Permalink](#)

January 23, 2020 (Thursday, January 23rd, 2020, 12:13 pm) at 12:13 pm (Thursday, January 23rd, 2020, 12:13 pm)

Great article

Brice Nouthé

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January 25, 2020 (Saturday, January 25th, 2020, 8:38 pm) at 8:38 pm (Saturday, January 25th, 2020, 8:38 pm)

Excellent! Thank you!

Judith Hammond

[Permalink](#)

January 26, 2020 (Sunday, January 26th, 2020, 10:32 pm) at 10:32 pm (Sunday, January 26th, 2020, 10:32 pm)

Nice article! Perhaps a dumb question...but is there a patient age above which you would suggest to a man that it is not pathological age-related hypogonadism that would benefit from treatment, but rather is normal aging?

Breay Paty

[Permalink](#)

February 1, 2020 (Saturday, February 1st, 2020, 3:18 pm) at 3:18 pm (Saturday, February 1st, 2020, 3:18 pm)

Thanks for your questions. I'll address each one briefly below:

1. For men who are taking testosterone by injection, I usually recommend a peak and trough level after 2-3 months. This allows for adjustment of the dose (based on the peak level) and frequency (based on the trough level). Once the dose and frequency have been determined, I usually monitor a mid-cycle testosterone annually to ensure no change in the dosing. For testosterone patch or gel, a single testosterone measurement while on therapy is adequate.

2. Recovery of endogenous testosterone after use of androgens can be highly variable depending upon the dose and duration of therapy and the age and underlying health status of the patient. I usually quote a recovery time of 3-6 months in men under the age of 50 years with no other reasons for hypogonadism. Of course, this assumes that the patient abstains from all supplements that may contain androgenic properties. If there is no significant recovery in that time, it's unlikely that full recovery will take place.

3. There is no age limit for testosterone therapy. Even men in their 70s and 80s may benefit, if they have unequivocally low testosterone levels and symptoms associated with hypogonadism. However, I recommend having a detailed discussion with the patient about the goals of therapy and possible adverse effects and if these goals are not being met within 3-6 months, consider stopping treatment.

I plan to discuss testosterone therapy in a future article.

Robert Thompson

[Permalink](#)

February 2, 2020 (Sunday, February 2nd, 2020, 8:38 pm) at 8:38 pm (Sunday, February 2nd, 2020, 8:38 pm)

The reminder about hemochromatosis was useful.

I have been to two lectures where suppression of testosterone in diabetic men was discussed. Narcotic use has also been mentioned- where would you advise UDS?

I am interested in the cost of this iterative method for establishing a diagnosis. We never see the costs of the laboratory testing, and the patients never see the cost of the repeat visits.

Carole Billington

[Permalink](#)

[July 2, 2022 \(Saturday, July 2nd, 2022, 12:15 pm\) at 12:15 pm \(Saturday, July 2nd, 2022, 12:15 pm\)](#)

My husband has testosterone levels at 52, six weeks later it is 29. He is 52 years old. Any thought on what is happening?