

Reducing Unnecessary HFE Gene Analysis for the Diagnosis of Hereditary Hemochromatosis

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Hereditary hemochromatosis (HH) is an autosomal recessive disorder of iron metabolism. For individuals with clinical symptoms consistent with HH or biochemical evidence of iron overload, an HH diagnosis is typically based on the results of transferrin-iron saturation and serum ferritin concentration. Molecular testing (HFE gene analysis) can be done to confirm the diagnosis.

Transferrin saturation is the ratio of serum iron to total iron-binding capacity (TIBC). If transferrin saturation is greater than 45%, Hemochromatosis HFE gene analysis may be performed to detect the presence of C282Y or H63D mutations to confirm the diagnosis of hereditary hemochromatosis.

HFE gene analysis is useful in the following circumstances:

1. Establishing or confirming the clinical diagnosis of HH in adults.
 2. Testing for individuals with increased serum transferrin-iron saturation and ferritin.
 3. With appropriate genetic counseling, predictive testing of individuals with a family history of HH.
- HFE genetic testing is NOT recommended for population screening.

We performed a recent retrospective audit of request for HFE Gene Analysis. This audit showed that HFE gene analysis was frequently ordered on patients without any evidence of iron overload (i.e., no serum iron and TIBC previously ordered or transferrin saturation $\leq 45\%$).

Beginning in January 2014, clinicians who order Hemochromatosis HFE gene analysis on patients whose transferrin saturation is $\leq 45\%$ within the past month or on whom no prior transferrin saturation testing results are available will be called by the laboratory to determine if HFE gene analysis is necessary.

Optimum Timing of Blood Draws for Serum Testosterone Measurements

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Testosterone is the major androgenic hormone. It is responsible for the development of genitalia and secondary sexual characteristics in men and serves as an estrogen precursor in women and men. Men who are deficient in testosterone can have a variety of signs and symptoms including decreased libido, loss of body hair and muscle mass, decreased bone density, decreased energy and depressed mood. None of these are specific for androgen deficiency and other causes must be considered in the differential diagnosis.

Measuring levels of total testosterone in serum is the first step in the diagnosis of androgen deficiency. Timing of blood draws is critical for proper interpretation of test results because testosterone exhibits a significant circadian variation. A 20-40% increase in serum testosterone occurs during the night and levels decrease during the day. In young males, early-morning testosterone levels are, on average, 50% higher than p.m. levels. This circadian rhythm is **not** blunted with aging. Because laboratory reference values for serum testosterone are established from a.m. samples, ***blood for testosterone measurements for diagnosing androgen deficiency should always be collected in the morning between 8 and 10 am.*** Testosterone levels can also fluctuate substantially between days; therefore, assessment of androgen status should be based on at least two measurements.

Timing of blood draws is also important when monitoring testosterone in men receiving supplemental therapy with transdermal testosterone patches or gels. Current guidelines recommend that samples be drawn 3-12 hours after application of the patch or gel.

Recommended Blood Sampling Times for Serum Testosterone Measurements

Purpose of testing	Recommended Draw Time
Diagnosis of androgen deficiency	Morning: 8 am to 10 am
Monitoring testosterone therapy: Transdermal patches and gels	3-12 hours after application of patch or gel

Please advise your patients on the appropriate blood draw time when ordering serum testosterone measurements. The above information is being incorporated into the Order Instructions and Patient Instructions sections of the Allscripts system. For morning samples, we strongly recommend that patients make an appointment at one of our Patient Service Centers by calling 203-739-4999 to insure that blood is drawn at the correct time.

Questions? Contact Dr. Sena at 203-739-7622.

References

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3. Testosterone, Total, Serum. Mayo Clinic-Mayo Medical Laboratories. www.mayomedicallaboratories.com/test-catalog/print/8533. Accessed 12/4/13.