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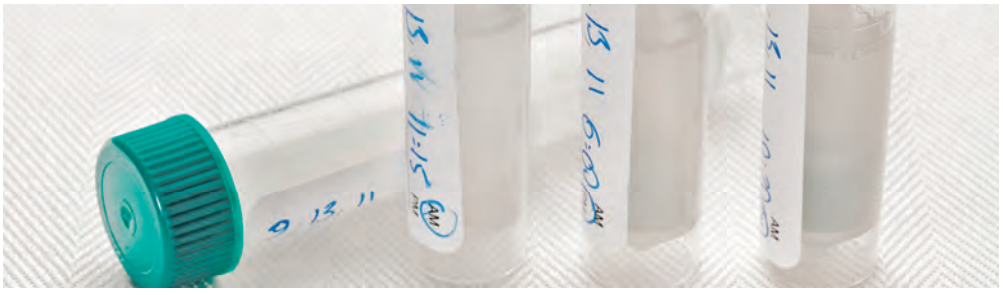
Evaluating Andropause and Low Testosterone in Men

by: Lisa Canar, ND

As men age, natural levels of testosterone decline. This decline is sometimes referred to as late-onset hypogonadism or andropause. Yet unlike menopause in women, the age-related decline in testosterone levels in men generally tends to be modest and gradual. In many cases, however, this gradual decline is associated with numerous clinical signs and symptoms including fatigue, depression, loss of sexual function and interest, memory loss, loss of muscle mass, anemia, and bone loss. Low testosterone levels are also associated with impaired glucose tolerance, abdominal obesity, and increased risk of cardiovascular disease. In fact, low testosterone levels can occur in men at any age and often correlate with these same signs, symptoms, and risk factors.[1,2]

Hypogonadism in men technically refers to a low level of sperm production and/or testosterone production. Testosterone is normally produced by the Leydig cells of the testes as a result of stimulation by luteinizing hormone (LH) from the pituitary gland, and sperm are produced in the seminiferous tubules due to stimulation from testosterone and by follicle-stimulating hormone (FSH) from the pituitary. Testosterone, in turn, inhibits both LH and FSH secretion, both on its own and via conversion to estradiol.[2]

As men age, concentrations of serum total testosterone and, to a greater extent, serum free testosterone, decrease. Salivary testosterone, being directly correlated with serum free testosterone, likewise decreases with age.[3] Studies also show an increase in sex hormone binding globulin (SHBG) levels with age. This carrier protein binds to free testosterone in the blood, making testosterone less available to the cells. Gonadotropin concentrations, both FSH and LH, also tend to increase with age due to the overall loss of negative feedback, however this increase in FSH and LH levels is generally not as great as one would expect from the drop in testosterone levels. In some cases, elevated estrogen levels may provide an ongoing negative feedback effect, preventing a steeper increase in FSH and LH levels. Pituitary and/or hypothalamic causes may also underlie some cases of low or declining testosterone levels.[1]



In this article, we review common laboratory findings regarding hormones and aging, and we assess the numerous potential contributing factors and causes of low testosterone in men. We then discuss comprehensive laboratory evaluation of testosterone and other male hormones, including assessment of the androgen hormone pathway, the adrenal stress response, and related gastrointestinal health markers that may impact hormone levels.

(Continued on page 2)

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Common Laboratory Findings Associated with Aging

Serum total testosterone decline

Several cross-sectional and longitudinal studies show a decline of serum total testosterone concentration with increasing age. As a result, many older men have testosterone values sufficiently low to be considered hypogonadal in young men. In the largest cross-sectional study to date (European Male Aging Study, n=3220, ages 40 to 79 years), serum total testosterone concentrations fell 0.4 percent per year and free testosterone concentrations fell 1.3 percent per year.[4]

Longitudinal studies tend to show even more pronounced decreases in testosterone levels. In the Baltimore Longitudinal Study of Aging (n=890), serum testosterone decreased in healthy males at a fairly constant rate, independent of other variables. The percentage of men with total testosterone concentrations in the hypogonadal range (defined as <325 ng/dL) was 20, 30, and 50 percent for men in their 60s, 70s, and 80s, respectively.[5]

The Massachusetts Male Aging Study also showed a decrease in total testosterone with increasing age and an even greater decrease in serum free testosterone with age. The decrease with age was greater if it was accompanied by obesity, a new illness, or a serious emotional stress.[6]

Serum free testosterone decline

Although serum total testosterone declines with age, serum free testosterone levels fall to an even greater degree. As a result, men who are 80 years old have serum free testosterone values that are only one-half to one-third of those in men who are 20 years old. In the Baltimore Longitudinal Study of Aging, the percentage of men with low estimates of serum free testosterone was 40, 70, and 90 percent for men in their 60s, 70s, and 80s, respectively.[5] In the Massachusetts Male Aging Study, the decline in serum free testosterone was 2.8 percent per year.[7]

Sex hormone binding globulin (SHBG) increase

SHBG concentrations increase slightly and gradually as a function of age. The clinical implication, because SHBG binds testosterone with high affinity, is that with increasing age, less of the total testosterone in the blood is free (i.e., biologically active). Factors in addition to aging which tend to increase SHBG include hyperthyroidism, liver disease, and high estrogen concentrations.[2]

By contrast, obesity tends to decrease the serum concentration of SHBG, which lowers the serum total testosterone concentration. The decrease in SHBG levels is proportional to the degree of obesity and may be reversed by weight loss. Similarly, insulin resistance and type 2 diabetes tend to decrease SHBG levels, as do hypothyroidism, growth hormone excess, androgen therapy, anabolic steroids, and glucocorticoid drugs.[2]

Increase in gonadotropins

As men age, serum FSH and LH concentrations both tend to increase owing to the decrease in normal negative feedback effect of testosterone on the pituitary. In the New Mexico Aging Process Study, the mean serum LH concentration increased over 15 years from 9.4 to 13.7 mIU/mL, and the FSH increased from 14.1 to 27.4 mIU/mL.[8] In the Massachusetts Male Aging Study, the LH increased by 0.9 percent per year and the FSH by 3.1 percent per year.[7] In the European Male Aging Study, the fall in serum total and free testosterone levels with age was associated with an increase in serum LH concentration, yet the fall in testosterone levels with obesity alone (without aging) was not associated with any increase in LH levels.[4] In obese men, high estrogen levels may be contributing to an overall negative feedback effect on pituitary secretion of FSH and LH. Hypothalamic/pituitary dysfunction may also contribute to decreased testosterone levels in obesity.

Contributing Factors and Causes of Low Testosterone in Men

A sizeable portion of the decline in testosterone levels in aging men may be related to the development of obesity and other comorbidities including insulin resistance, metabolic syndrome, and diabetes mellitus.[9] In fact, low testosterone levels are related to a variety of associated hormonal imbalances, including insulin resistance, overproduction of estrogen due to increased aromatase activity, imbalances in cortisol and DHEA production, and low thyroid function. A chronic state of systemic inflammation can also contribute to depressed testosterone levels. Similarly, toxic environmental exposures, autoimmune conditions, chronic stress, digestive disorders, nutrient deficiencies, certain medications, and diseases such as chronic hepatitis can contribute to low testosterone levels and related hormone imbalances.[9-11] From this list, it is clear that numerous dietary and lifestyle factors may contribute significantly to declining testosterone levels.

Obesity

Testosterone deficiency is associated with increased fat mass, and in particular, abdominal adiposity. A bidirectional relationship between low testosterone and obesity is evident in this association. Men who are overweight or obese tend to have lower serum levels of SHBG and, therefore, lower serum concentrations of total testosterone. Obese men also may have low serum free testosterone. By contrast, weight loss can lead to increased testosterone levels. As mentioned above, serum LH concentrations may remain low in obese men, indicating a persistent negative feedback on the pituitary, perhaps due to elevated estrogen levels or other dysregulated feedback mechanisms.[9]

Diabetes mellitus

Men who have type 2 diabetes are more likely to have low serum total testosterone and free testosterone as compared to nondiabetic men. Some studies suggest that prevalence of hypogonadism may be up to 50% in men with type 2 diabetes.[12] In a comprehensive review (43 studies, n=6427), men with type 2 diabetes had serum total testosterone concentrations on average 76 ng/dL lower than nondiabetic men.[13] Low testosterone levels may also play a causative role: men with higher testosterone concentrations have a lower risk of developing type 2 diabetes.

Insulin resistance and metabolic syndrome

Testosterone deficiency is associated with reduced insulin sensitivity, impaired glucose tolerance, elevated triglycerides and cholesterol, and low HDL-cholesterol. These factors are all found in the metabolic syndrome, and together contribute to increased cardiovascular risk.[14] Hypogonadism and metabolic syndrome are thought to share a bidirectional relationship as a result of the complex interplay between adipocytokines, proinflammatory cytokines and hypothalamic hormones that control the pituitary-testicular axis. Therapeutic interventions to improve insulin resistance may help to restore normal testosterone levels. As in type 2 diabetes, low testosterone may also play a causative role: low serum testosterone concentrations have been associated with subsequent development of central obesity, elevated insulin levels, metabolic syndrome, elevated C-reactive protein levels, and increased cardiovascular mortality.[1,12] Interventional studies have noted beneficial effects of testosterone therapy on metabolic syndrome markers, type 2 diabetes, and related cardiovascular risk factors, including insulin resistance, dyslipidemia, endothelial dysfunction, and inflammation.[15,16]

Inflammation and estrogen excess

Low testosterone is associated with increased inflammatory cytokine signaling, a characteristic of chronic low-grade inflammation. Beyond its role in disrupting insulin signaling, chronic inflammation also may contribute to low testosterone via stimulation of aromatase enzyme activity. Aromatase activity is present in all adipose tissue, but is more heavily concentrated in visceral fat, and as such is increased in men with abdominal obesity. Aromatase activity is increased by inflammatory cytokines and may also be stimulated by stress and excess cortisol concentrations. High levels of estrogens (estradiol and estrone) result from excess aromatase activity, which in turn may lead to lower testosterone levels. This pattern is found most particularly in men with central obesity, as visceral fat is a primary site of conversion of androstenedione to estrone and testosterone to estradiol. Elevated estradiol and estrone levels may also feedback to inhibit LH production in the pituitary, the overall effect being a further reduction in testosterone production.[14,15,17]

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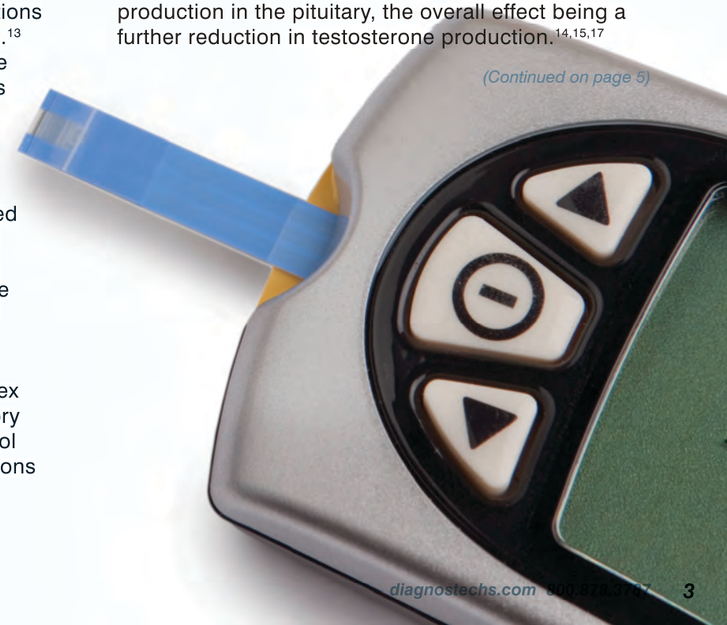

Tech Talk

Quarterly updates from our Diagnos-Techs Research & Development Team

Mass Spectrometry – the gold standard for quantification of a variety of clinically important analytes:

- Tandem mass spectrometry instruments, including both GC-MS/MS and LC-MS/MS, drive our research and development of improved assays for small molecules such as steroid hormones.
- Proteomic analysis using MALDI-TOF mass spectrometry provides unparalleled speed and accuracy in identification of microorganisms in our Microbiology department.
- Our new state-of-the-art ICP-MS/MS will enable Diagnos-Techs to provide testing for heavy metals and other elements in clinical specimens in the near future.

Dr. Dialogue Current Medical topics

Normalization of testosterone levels may reduce cardiovascular risk

This latest study on the possible risks and benefits of testosterone replacement therapy suggests that testosterone supplementation in older men, when used to normalize low serum testosterone, may reduce the risk of myocardial infarction (MI), stroke, and all cause mortality. This was a large retrospective study of national data on 83,010 men with documented low serum total testosterone, age 50 or above, who received care from the Veterans Administration. Follow up ranged from 4.6 to 6.2 years. The men were divided into three groups: 43,931 who were treated and attained normal total testosterone levels, 25,701 who were treated but without reaching normal, and 13,378 who were untreated. Study groups were matched to eliminate any differences in age, BMI, chronic diseases, LDL cholesterol, and the use of aspirin, beta blockers, and statins. The sharpest contrast emerged between the men who were treated and attained normal testosterone levels and those who went untreated. The treated men were 56% less likely to die during the follow up period, 24% less likely to suffer an MI, and 36% less likely to have a stroke. The difference between the men who were treated and attained normal levels and those who were treated but did not attain normal levels was similar but less pronounced — the former were 37% less likely to die, 18% less likely to suffer an MI, and 30% less likely to suffer a stroke. No significant difference emerged between the two groups whose testosterone did not reach normal levels, except that the treated men were 16% less likely to die than the untreated men. The study authors commented that previous studies showing an increased risk of cardiovascular events with testosterone supplementation may have done so because their study populations were not well controlled or because the patients did not attain normal testosterone levels.

Sharma R, Oni OA, Gupta K, et al. Normalization of testosterone level is associated with reduced incidence of myocardial infarction and mortality in men. *Eur Heart J.* 2015;36(40):2706-15. doi: 10.1093/eurheartj/ehv346.

Working long hours can increase risk of stroke and coronary heart disease

A new meta-analysis shows that working 55 or more hours per week is associated with an increased risk for stroke (relative risk [RR] 1.33). Long working hours are also associated with an increased risk for coronary heart disease, but the association is weaker than for stroke (RR 1.13). This analysis, which included 25 studies from the United States, Australia, Finland, Denmark, Sweden, the Netherlands, Belgium, Germany, the United Kingdom, Northern Ireland, and Israel, was larger than any previous report. The meta-analysis of stroke comprised data for 528,908 men and women, and of coronary heart disease for 603,838 men and women. The analysis adjusted for various confounding factors, including age, sex, socioeconomic status, smoking, BMI, physical activity, and alcohol consumption. The study authors conclude that more attention should be paid to the management of vascular risk factors in individuals who work long hours.

Kivimaki M, Jokela M, Nyberg ST, et al, for the IPD-Work Consortium. Long working hours and risk of coronary heart disease and stroke: a systematic review and meta-analysis of published and unpublished data for 603,838 individuals. *Lancet* 2015; published online Aug 20. http://dx.doi.org/10.1016/S0140-6736(15)60295-1.

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Autoimmune disease and low thyroid function

Low testosterone is also associated with increased risk of inflammatory and autoimmune diseases such as rheumatoid arthritis and lupus in men.[18,19] Hypothyroidism also is associated with low testosterone levels.[20,21] Autoimmune polyglandular disease, a relatively uncommon autoimmune condition, is characterized by hypothyroidism, hypoadrenalism (low cortisol levels), and hypogonadism, including low testosterone levels and infertility.[10]

High cortisol states and chronic stress

Cushing's syndrome (whether due to a disease process or to excessive corticosteroid medication) can lead to a decline in testosterone levels. The mechanism of this effect is not clear, but inhibition may occur at both the testes and the pituitary/hypothalamus via negative feedback effects.[10] Likewise, subclinical hypercortisolism (cortisol excess without overt signs or symptoms) and other elevated cortisol states secondary to emotional stress or anxiety may also reduce natural testosterone levels.

Toxins

Many potentially toxic environmental chemicals are known to cause direct testicular damage and decreased spermatogenesis in laboratory animals. Low testosterone levels and/or decreased receptor sensitivity may also be induced by direct environmental toxic damage.[22] In addition, many environmental toxins are known to induce inflammation, insulin resistance, and obesity, which all may contribute to testosterone deficiency.[23]

Digestion and nutrition

Nutrient deficiencies or marginal nutrient status (most notably vitamin D, vitamin E, boron, selenium, and zinc) may impair the production of testosterone or the activity of the hormone at its receptor sites. Nutrients that impact blood sugar levels, insulin sensitivity, inflammation, and adrenal hormone levels (including B vitamins, vitamin C, chromium, magnesium, zinc, flavonoids, fiber, etc.) may also impact testosterone levels.[24] Malabsorption of nutrients, as found in inflammatory bowel disorders and celiac disease, can also lead to lowered testosterone levels. Similarly, any degree of dysbiosis that impairs or disrupts nutrient absorption or hormone metabolism may contribute to declining testosterone levels. Finally, acute alcohol ingestion is known to cause secondary hypogonadism (subnormal serum testosterone concentration levels without increases in either LH or FSH).[2]

Medications and anabolic steroid abuse

Long-term treatment with glucocorticoids, on average, lowers testosterone levels by approximately one-third.[10] Inhibition may occur at both the testes and the pituitary/hypothalamus. Use of anabolic steroids will also lead to suppression of testosterone levels after discontinuation due to the persistence of negative feedback effects.

Certain other medications may impair testosterone production and are associated with low testosterone levels. Cholesterol-lowering drugs (statins) have been found to decrease testosterone (by a slight amount).[25] Beta-blockers may also have a testosterone-lowering effect.[26] Antidepressants also are associated with low testosterone levels, but it is unclear whether they play a causative role.

Chronic opiate administration for pain management may lead to subnormal testosterone concentrations. Also note that the antifungal drug ketoconazole directly inhibits testosterone biosynthesis and may lead to testosterone deficiency. And finally, anti-neoplastic medications can lower sperm counts and impair testosterone production.[10]

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Systemic disease

Certain debilitating chronic and systemic illnesses, including cirrhosis, chronic renal failure, chronic lung disease, and acquired immune deficiency syndrome, may cause hypogonadism via both primary and secondary effects.[10]

Iron deposition in hemochromatosis also leads to testosterone deficiency via pituitary suppression, and sarcoidosis and Langerhans cell histiocytosis (eosinophilic granuloma) may lower testosterone levels via hypothalamic suppression. Phlebotomy treatment to reverse hypogonadism from hemochromatosis is more likely to be successful in men under the age of 40 years.[11]

In addition, hyperprolactinemia of any cause (including stress-induced) can suppress gonadotropin secretion and thereby suppress testicular function. And finally, any kind of pituitary adenoma or cyst can cause sufficient pressure on the pituitary gonadotroph cells to interfere with their function and decrease LH and FSH secretion.[11]

Acute disease

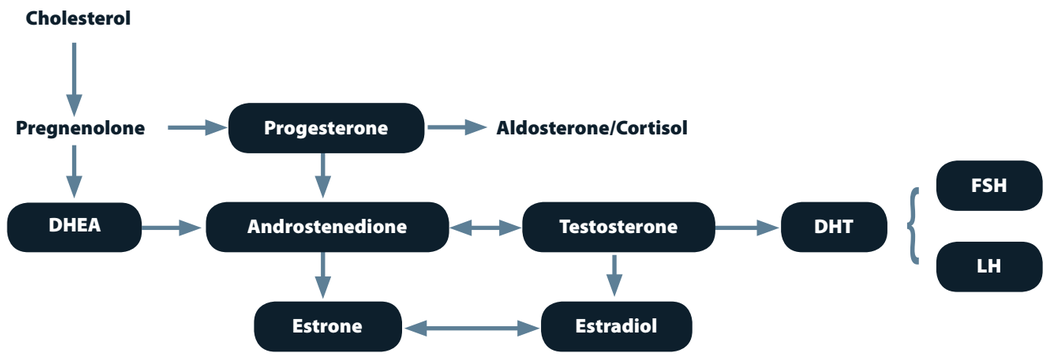
Any critical acute illness or stress, including surgery, myocardial infarction, or head trauma, can also cause hypogonadism and low testosterone levels. Serum LH levels in acute illness are likely to remain low, indicating a pituitary or hypothalamic cause in these cases. Hypogonadism due to acute illness tends to resolve as patients recover.[11]

Comprehensive Male Hormone Evaluation

Evaluation of andropause should not be limited to standard laboratory assessment of serum testosterone levels. In 2007, the Endocrine Society concluded that “the manner in which most [serum] assays for total testosterone and free testosterone are currently performed is decidedly unsatisfactory.”[27] Today it is still the case that most commercially available assays for serum total testosterone and serum free testosterone (including calculated free testosterone values), are prone to error and may not be reliable. If serum free testosterone is measured, this test should be performed via equilibrium dialysis assay in one of the select laboratories that specialize in endocrine testing.[2]

Androgen pathway overview

Diagnos-Techs measures salivary testosterone, the free and active concentration of testosterone found in the tissues and saliva, which has been shown to have a direct correlation with accurate measurements of serum free testosterone.[28] The Diagnos-Techs expanded Male Hormone Panel also includes measurements of the free and active levels of other relevant steroid hormones, including the more potent androgen dihydrotestosterone (DHT), as well as DHEA/DHEA-S, progesterone, androstenedione, estrone, estradiol, and the pituitary hormones FSH and LH. This comprehensive expanded Male Hormone Panel constitutes an accurate and complete assessment of individual hormone levels and relative hormone balance, upon which an informed and specific therapeutic treatment program may be based.



Stress hormone testing

Whether manifesting as cortisol excess or adrenal fatigue, chronic stress may play a significant role in andropause. Insulin response and resistance may also be a significant factor in testosterone decline. For this reason, our Adrenal Stress Index (ASI) panel can add considerable insight into the overall hormonal assessment. The ASI panel includes a profile of the diurnal free cortisol rhythm, an afternoon value for DHEA/DHEA-S, two salivary insulin values (fasting and non fasting), and the level of 17-hydroxyprogesterone, a cortisol hormone precursor. The ASI panel also includes a measure of mucosal immune function – total salivary sIgA – and a specific sIgA test to screen for potential immune reactivity to gliadin, a constituent of gluten.

Digestive function analysis

Gastrointestinal health testing via stool and salivary markers (Diagnos-Techs GI Health Panels) can also be helpful in overall evaluation of hormone balance. As mentioned above, digestive function and nutrient absorption can impact testosterone production and activity, as can the balance of intestinal bacteria and the presence of any intestinal inflammation.

When during the day should testosterone be measured?

Interpretation of testosterone measurements, especially in young men, should take into consideration its diurnal fluctuation, which reaches a maximum at about 8 AM and a minimum (approximately 70 percent of the maximum) at about 8 PM.[2] Even though young men may exhibit this diurnal variation to a greater extent than older men, we suggest following the same collection guidelines regardless of patient age. To measure peak levels of testosterone and other androgen pathway hormones, collection should always be done in the morning, most ideally around 8 AM or earlier, upon arising. Additionally, because food (especially glucose ingestion) tends to decrease testosterone concentrations, specimens should be collected before breakfast and after an overnight fast.[2]

How often should testosterone be measured?

Evaluation of testosterone levels should not be limited to a single testosterone assessment. Testosterone and other hormone concentrations may fluctuate somewhat, even early in the morning, although to a limited degree. If a single 8 AM value is well within the normal range, testosterone production can be assumed to be normal. If a single 8 AM value is low, borderline low, or does not fit with the clinical findings, the measurement should be repeated at least once more. Other steroid hormone concentrations may also fluctuate somewhat, and repeated measurements are warranted whenever values are borderline low or differ from the clinical picture.[2]

Additional testing to consider

Further testing may include a CBC, comprehensive metabolic panel, lipid panel, thyroid panel, SHBG, iron and ferritin, HbA1c, hsCRP, vitamin D, PSA, and related markers. Follow up testing may include additional hormone assays (e.g., serum prolactin, FSH, and LH) and imaging studies as appropriate.

Diagnos-Techs comprehensive hormone evaluation

Beyond a simple testosterone deficiency, andropause reflects a complex interplay of factors affecting individual hormone levels and the balance between these hormones. To accurately assess hormone deficiencies and imbalances, a comprehensive hormone profile is needed. Saliva testing has been validated for numerous steroid hormones, including cortisol, DHEA/DHEA-S, testosterone, estradiol, and progesterone.[3,28-30] Saliva hormone testing is a convenient, noninvasive, and accurate way to measure the adrenal stress response and to assess the relative levels of androgen pathway hormones. The Diagnos-Techs expanded Male Hormone Panel (eMHP) provides a comprehensive look at the entire androgen pathway, including the pituitary hormones FSH and LH. The eMHP constitutes an ideal assessment of a man’s hormone status, upon which an informed and specific treatment program may be based. The eMHP also allows for follow up monitoring of hormone levels to further guide and individualize therapy.

Thank you to Nathan Goodyear, MD for sharing his valuable experience and insight, which helped to shape the research for this article.

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Meet Your Microbiota

Quarterly updates from our Diagnos-Techs Microbiology Team

An Update on Enteric Pathogens, Part 2

All stool specimens received for bacterial stool culture at Diagnos-Techs are screened for the presence of bacterial organisms implicated in causing enteric disease. In our last issue we discussed potential pathogens including *Aeromonas, Salmonella, Shigella, Vibrio,* and *Yersinia.* This issue will focus on *Campylobacter, Clostridium difficile* toxins, Shiga toxin-producing *E. coli*, and other potentially pathogenic *E. coli* strains.

Campylobacter

Campylobacter species *(jejuni and coli)* cause self-limiting gastroenteritis. Autoimmune disorders are a long term complication in about one in 2,000 cases. Occasionally, infection may lead to Guillain-Barré syndrome, reactive arthritis, postinfectious irritable bowel syndrome, and possibly immunoproliferative small intestinal disease. A very small percentage of patients may develop complications such as meningitis, hepatitis, cholecystitis, and pancreatitis. Most cases of campylobacteriosis are self-limiting, and acute infections typically last from two to ten days. Fever, diarrhea (which may be bloody), abdominal cramps, and vomiting are the major symptoms.

Campylobacteriosis is the leading cause of food-borne gastroenteritis worldwide. Outbreaks have been associated with unpasteurized dairy products, contaminated water, poultry, and produce. Most cases are associated with eating raw or undercooked poultry or from cross-contamination of other foods. Animals can also be infected, and some people get infected from contact with the stool of an ill dog or cat. The organism may spread from one person to another (fecal-oral).

Because *Campylobacter* species are fastidious and quickly lose the ability to grow on bacterial stool culture plates, Diagnos-Techs uses antigen testing to check for the presence of this organism in stool specimens.

Clostridium difficile toxins

Clostridium difficile is a gram positive, spore forming bacterium. It is the most common cause of hospital-acquired diarrhea, typically occurring after antibiotic use. It is also found in a growing number of outpatients related to the use of proton pump inhibitors and H_2-blocking medications. *C. difficile* can produce several toxins which cause symptoms, including watery diarrhea, fever, loss of appetite, nausea, and abdominal pain or tenderness. As a complement to our bacterial stool culture, Diagnos-Techs tests for the presence of *C. difficile* toxins in stool specimens.

Shiga toxin-producing Escherichia coli

Shiga toxin-producing *E. coli* (STEC), also referred to as *Enterohemorrhagic E. coli* (EHEC), are biochemically identical to other nontoxigenic strains of *E. coli* except for the production of Shiga toxins. STEC or EHEC organisms are transmitted through contaminated water or food, or through contact with animals or infected persons. Infection with Shiga toxin-producing *E. coli* may cause acute symptoms ranging from mild diarrhea to severe acute abdominal cramping and bloody diarrhea. Severe infections associated with hemorrhagic colitis may progress to life-threatening complications including thrombocytopenia, hemolytic uremic syndrome, and kidney failure. *E. coli* O157 is the predominant disease-causing strain of this type and can be identified directly by culture. All other Shiga toxin-producing *E. coli*, including the less virulent forms, are routinely identified by immunoassay testing to check for the presence of Shiga toxins. PCR-based assays are also used for identification, and Diagnos-Techs is actively working to develop such assays.

In uncomplicated cases, duration of acute symptoms due to Shiga toxin-producing *E. coli* is two to nine days, with an average of eight days. Antibiotic treatment is never indicated in this type of infection as it can increase the patient's likelihood of developing hemolytic uremic syndrome. Treatment is supportive and may require aggressive rehydration therapy.

Other potentially pathogenic E. coli strains

Escherichia coli (E. coli) are commonly found in the intestines of people and animals. The majority of *E. coli* strains are commensal and may provide benefits by preventing more harmful bacteria from overgrowing. However, the various strains of *E. coli* comprise a diverse group of bacteria. Beyond the Shiga toxin-producing *E. coli* strains, other potentially pathogenic forms of *E. coli* include several different types:

- ***Enterotoxigenic E. coli (ETEC)***
  organisms are the leading cause of travelers' diarrhea and a major cause of bacterial diarrheal illness in lower-income countries, especially in children. ETEC strains produce bacterial toxins, and are transmitted by food or water contaminated with animal or human feces. Symptoms from this infection typically include diarrhea without inflammation or fever.

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- ***Enteropathogenic E. coli (EPEC)***
  include moderately invasive and adherent *E. coli* strains that may produce Shiga-like toxins. Symptoms from infection with EPEC organisms typically include diarrhea with blood and inflammation.

- ***Enteroinvasive E. coli (EIEC)***
  are adherent and invasive *E. coli* organisms that can multiply inside intestinal cells, although these strains do not produce toxins. Symptoms from infection with EIEC include diarrhea with mucus and blood, severe inflammation, and fever.

- ***Enteroaggregative E. coli (EAEC)***
  are non-invasive *E. coli* strains that produce ST-like toxins and hemolysin. EAEC strains typically infect children, and symptoms include persistent diarrhea but no inflammation or fever.

- ***Adherent invasive E. coli (AIEC)***
  are adherent and invasive *E. coli* that are commonly found in Crohn's disease patients.

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- *Dec. 11th - 13th, 2015 • Las Vegas, NV*

A4M
- *May 18th - 21st, 2016 • Hollywood, FL*

AARM
- *14th Annual Conference*
- *Sep. 16th - 18th, 2016*
- *Hilton Head Island, SC*

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Merry Christmas

Best Wishes for Peace and Joy This Holiday Season and a New Year of Health, Happiness and Prosperity.

- From all of us at Diagnos-Techs

Dates will be announced.
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***Medical references can be found at diagnostechs.com/Pages/NewsLetter.aspx**

Evaluating Andropause and Low Testosterone in Men

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