Saint Luke's Regional Laboratories
Clinical Laboratory Letter
June 2013

Testing for Low T

More than $100 million was spent by drug companies on advertisements for androgen replacement therapy (ART) in 2012. The ads appear to be successful because the number of prescriptions for ART among men 40 years or older has more than tripled since 2001 (JAMA Intern Med online June 3, 2013). Interestingly, among all new androgen users, only 74.7% had their testosterone level measured in the prior 12 months. The proportion of men with low testosterone could not be determined in this study. Common diagnoses in the year prior to testosterone replacement therapy included hypogonadism (50.6%), fatigue (34.5%), erectile dysfunction (31.9%) and psychosexual dysfunction (11.8%).

Despite the claims touted in these ads, randomized clinical trials have shown that testosterone therapy results in only small improvements in lean body mass and body fat, libido, sexual satisfaction and has inconsistent or no effect on weight, depression, and lower extremity strength (J Clin Endocrinol Metab 2010;95(6):2536-59).

Testosterone circulates in the blood 98% bound to protein. In men, approximately 40% is bound with high affinity to sex hormone binding globulin (SHBG) and approximately 60% is bound weakly to albumin. The testosterone fraction that is bound to albumin dissociates freely in the capillary bed, becoming available for tissue uptake. Only 2 to 3% of testosterone exists in the free state. All non-SHBG bound testosterone is considered to be bioavailable.

After the age of 40 years, men's total testosterone levels begin to decline about 0.4% per year. Men with chronic illnesses have testosterone levels that are 10–15% below that of healthy age-matched men. SHBG increases with age, causing bioavailable testosterone to decrease to a greater extent than total testosterone. Gonadotropins usually do not increase above the normal range with aging.

Young men have a circadian rhythm of testosterone, with the zenith occurring in the morning between 0600 and 0800 hours and the nadir in the late afternoon between 1700 and 1800 hours. This circadian rhythm disappears in elderly men. The difference in testosterone levels between young and elderly men is most pronounced when measurements are made in the morning.

Common practice has been to order both total and free testosterone in the evaluation of testosterone deficiency. To meet the growing demand, most laboratories measure free testosterone with an automated androgen analog immunoassay. Unfortunately, an increasing number of studies have demonstrated that these free testosterone assays do not accurately measure free testosterone and are often falsely low. Analysis of total and free testosterone results from 240 males performed by Saint Luke's Regional Laboratories between May 1 and June 15 showed concordance in 64% of cases. In 65 samples (27%) total testosterone was normal and free testosterone was decreased. Our local data supports the published findings that automated free testosterone assays produce a large number of falsely low results.

The Endocrine Society recommends against the use of automated free testosterone assays(J Clin Endocrinol Metab 2010;95(6):2536-59). Recently, Saint Luke's Endocrinologists have requested that Saint Luke's Regional Laboratories discontinue free testosterone testing. Accordingly, the laboratory ceased free testosterone testing on June 25.

The Endocrine Society Clinical Practice Guideline does not recommend screening for androgen deficiency in the general population. The Guideline recommends making a diagnosis of androgen deficiency only in men with consistent symptoms and signs and unequivocally low serum testosterone levels. The initial test should be a total testosterone level measured on a sample collected during the morning. Low levels should be confirmed by repeat testing of total testosterone. Men who

have total testosterone levels near the lower limit of normal or who may have a sex hormone binding globulin abnormality can be further investigated using bioavailable testosterone levels. Total testosterone is performed at Saint Luke's Hospital laboratory. Reference range is 240-813 ng/mL. Bioavailable testosterone is sent to a reference laboratory.

Middle East Respiratory Syndrome Coronavirus

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is a novel coronavirus first reported to cause respiratory illness in Saudi Arabia in September 2012. Genetic sequencing shows this new virus is different from other known human coronaviruses, including the one that caused severe acute respiratory syndrome (SARS). As of June 7, 2013, 55 laboratory-confirmed cases of MERS-CoV infection have been reported to WHO—two from France, three from Italy, two from Jordan, two from Qatar, 40 from Saudi Arabia, two from Tunisia, one from the United Arab Emirates, and three from the United Kingdom (UK). Thirty-one of the 55 patients have died (mortality rate 56%). To date, all cases have a direct or indirect link to one of four countries: Saudi Arabia, Qatar, Jordan, and the United Arab Emirates. Human to human transmission and nosocomial transmission are confirmed. No cases have been reported in the United States as of June 7.

Incubation period for MERS CoV may be 1-14 days, and persons with chronic medical conditions or immunosuppression are particularly vulnerable to infection. The CDC advises that persons who develop severe acute lower respiratory illness within 14 days after traveling from the Arabian Peninsula or neighboring countries should be evaluated for MERS CoV according to the following guidelines:

- A person with an acute respiratory infection, which may include fever (≥ 38°C , 100.4°F) and cough; AND
- suspicion of pulmonary parenchymal disease (e.g., pneumonia or acute respiratory distress syndrome based on clinical or radiological evidence of consolidation); AND
- history of travel from the Arabian Peninsula or neighboring countries within 14 days; AND
- not already explained by any other infection or etiology, including all clinically indicated tests for community-acquired pneumonia according to local management guidelines.

In addition, the following persons may be considered for evaluation:

- Persons who develop severe acute lower respiratory illness of known etiology within 14 days after traveling from the Arabian Peninsula or neighboring countries but who do not respond to appropriate therapy; OR
- Persons who develop severe acute lower respiratory illness who are close contacts of a symptomatic traveler who developed fever and acute respiratory illness within 14 days of traveling from the Arabian Peninsula or neighboring countries.

Persons who meet these criteria should be reported to state and local health departments. There is no specific treatment for MERS-CoV infection; care is supportive.

Diagnosis of MERS-CoV can only be made through specific real-time PCR testing, currently available exclusively through CDC and state health departments. Commercially available respiratory virus PCR panels, including Saint Luke's Microbiology's respiratory PCR, do not detect MERS-CoV. Submission of respiratory specimens for testing requires consultation with the CDC and state health laboratory. Additional information is available at the CDC MERS website at: http://www.cdc.gov/coronavirus/mers/index.html .

Potassium Reference Range Change

The reference range for plasma potassium was changed from 3.5-5.1 to 3.5-5.3 mEq/L on May 29 at all Saint Luke's Health System Laboratories.