

## Giving Testosterone Levels a Boost

HEALTH IMPACT OF "LOW NORMAL" T AND HOW TO HELP PATIENTS.

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In an analysis of more than 7,000 blood tests, [one source](#) reported, "More than 80% of men tested had less than optimal testosterone blood levels."<sup>1</sup> ABC News, quoting the *Journal of Clinical Endocrinology & Metabolism*, stated, "1 in 4 Men Over 30 Has Low testosterone."<sup>2-3</sup> Conservatively, this translates to more than 16 million men suffering with less than optimal testosterone in the United States today.<sup>4</sup>

A man suffering with "low normal" testosterone typically experiences mild to moderate fatigue, lethargy, tiredness and/or sapped motivation that just won't go away. Men contribute largely to the success of the "energy drink market," as they continually seek some form of artificial energy boost like caffeine throughout the day to attempt to feel "normal." Other symptoms of low testosterone are weight gain - especially abdominal fat, sagging physical stamina, loss of muscle tone, mild depression or mood swings.

The good news is that naturally enhancing this [core hormone](#) quickly and positively revitalizes every aspect of what it is to be a man, benefiting protein synthesis, enhancing skeletal muscle mass and bone density, and revitalizing mood, motivation, physical stamina; as well as improving cognitive functions like memory, mental performance and speed of reaction. In more subjective terms - restoring testosterone makes a man feel like he did when he was younger, more energetic, and vibrant.

### More Science-Based "Low Normal" Testosterone Facts

- "Low normal" total testosterone concentrations are associated with reductions in motivation, initiative, self-confidence, concentration and memory, sleep quality, muscle bulk and strength, diminished physical or work performance, feeling sad or blue, depressed mood, mild anemia, and increased body fat and body mass index.<sup>5-6</sup>
- Low normal serum testosterone concentrations are associated with reduced male sexual desire, function, performance and potency.<sup>5-20</sup>
- Low normal serum testosterone concentrations increase the risk for premature death from any cause.<sup>21-29</sup>
- Low normal serum testosterone concentrations increase the risk for death from cardiovascular disease,<sup>21,23,25,28-29</sup> and increase the combined risk for suffering a first stroke or first transient ischemic attack.<sup>30</sup>
- Low normal serum testosterone concentrations increase the risk for both memory loss<sup>31</sup> and developing clinical depression.<sup>32</sup>
- Low normal serum testosterone concentrations increase the risk of developing an increased level of systemic inflammation.<sup>33-37</sup>

### Defining "Healthy" Testosterone

Multiple peer-reviewed papers state that "testosterone deficiencies" are more prevalent and "desirable testosterone" levels in men are actually much higher than what is currently being

considered as "normal" in doctors' practices across the country. Case in point: A cross-sectional study of Swedish men ages 69 to 80 years showed the risk for premature death from any cause<sup>26</sup> and the risk for suffering a major cardiovascular event<sup>27</sup> were inversely correlated with the total serum testosterone concentration (i.e., the higher the testosterone levels, the lower the risk of death).

Specifically with regards to cardiovascular events, men in the highest quartile of testosterone (at or higher than 550 ng/dL) had a lower risk of cardiovascular events compared with men with lower testosterone.<sup>27</sup>

More importantly, details from this study show that it did not matter if a man's total testosterone was very low (below 340 ng/dL ) or moderately low (up to 549 ng/dL ) - all men with T levels below 549 ng/dL had a similar increased risk for suffering a cardiovascular event. Only when total testosterone exceeded 550 ng/dL did cardiovascular risk drop.

This is truly alarming, as cardiovascular disease is the No. 1 killer of men in the United States and even more - this study was published in the *Journal of the American College of Cardiology*. These researchers documented a 30 percent reduction in cardiovascular events as well as a decrease in cerebrovascular disease incidence. Men with the highest total testosterone had a 24 percent reduced risk of transient ischemic attack or full-blown stroke.<sup>27</sup> Clearly, based on this study, the only target for "healthy testosterone" is to maintain total testosterone at or above 550 ng/dL.

As a health care practitioner, please note the following:

- According to LabCorp, the "healthy reference range" for total testosterone is 348-1,197 ng/dL. So, the lower part of this range completely ignores recent science that shows total testosterone levels need to be maintained above 550 ng/dL.
- Subjectively, this broad range is ridiculous. As any 45-year-old man who has suffered with low normal testosterone knows, there is a world of difference in how a man feels and performs (both mentally and physically) when testosterone is "low normal" versus higher up the healthy "normal" reference range.

Stress / Cortisol: The "Testosterone Switch"

Acting through the classic glucocorticoid receptor, cortisol directly inhibits testosterone production in testicles by Leydig cells.<sup>38-40</sup> The cortisol-receptor complex suppresses testosterone synthesis via inhibition of the expression of the steroidogenic acute regulatory protein - the very first step in testosterone synthesis.<sup>41</sup> Even worse, hypercortisolemia inhibits testosterone synthesis,<sup>38-44</sup> reduces the total testosterone concentration<sup>38-44</sup> and accelerates the apoptosis (cell death) of Leydig cells.<sup>44</sup> This is alarming because it means:

- Cortisol stops testosterone synthesis dead in its tracks at the very start of testosterone synthesis.
- Even worse, cortisol kills the cells in the testicles responsible for making testosterone in the future.

So, controlling hypercortisolemia is the key to generating healthy testosterone now *and* protecting testicular Leydig cells so they can continue to do their job and make testosterone in the future.

Cortisol Stimulates the Activity of the Aromatase Complex

Even worse (if there can be such a thing), cortisol stimulates the activity of the aromatase complex in human male fibroblasts and adipocytes in fat deposits throughout the body.<sup>45-48</sup> Through this separate mechanism (completely different from inhibition of testosterone synthesis and secretion via Leydig cells, as just described), hypercortisolemia increases the conversion of circulating testosterone into estradiol, increases the serum estradiol concentration, decreases the serum total testosterone concentration, and increases the ratio of the serum estradiol concentration to the serum total testosterone concentration in men.<sup>38-40,42,43,45-48</sup>

### Acute Stress Increases Cortisol, Decreases Testosterone

Acute stress, whether psychological (mentally stressed at work, finances, home, family, etc.) or the result of a physical challenge (surgery, injury or intense exercise), induces a significant increase in cortisol secretion in healthy men.<sup>49-50</sup> For example, healthy men participating in a simulated job interview followed by a mental arithmetic test (real-world experiences designed to generate acute psychological stress), experienced a rapid significant increase in serum cortisol concentrations.<sup>51</sup>

Stress-induced elevations in [serum cortisol concentration](#) are associated with rapid declines in testosterone production by Leydig cells in the testicles.<sup>40</sup> When male members of the ground crew of military aircraft were passengers on an acrobatic flight, they experienced acute anxiety that was accompanied by increased serum cortisol concentrations and decreased serum total testosterone concentrations.<sup>52</sup> Similarly, young men about to board an aircraft for their first skydiving attempt (a purely psychological stressor) experienced an acute increase in cortisol concentration and an acute decrease in total testosterone concentration.<sup>53</sup>

During exposure to spontaneously occurring workplace psychological stress, 51-year-old men exhibited significantly decreased serum total testosterone concentrations.<sup>54</sup> Healthy men receiving painful electrical shocks also experienced an acute increase in cortisol concentration and an acute decrease in total testosterone concentration.<sup>55</sup>

*Editor's note:* Look for part 2 of this article, in which Dr. Smith discusses treatment strategies for combating low normal testosterone, in an upcoming issue of *DC*.

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