One of the fastest-growing areas in medicine today is the use of testosterone in men, particularly during the middle years. Most of my academic credentials within medicine come from my work with testosterone, as I was one of the first to recognize that healthy men can experience an age-related natural decline in hormones that affects their sexuality and vitality, and which can be treated successfully with testosterone therapy. Although testosterone has been used since the 1930s, it was a small backwater in medicine until the last 20 years or so. I feel as if I were there at its modern-era birth and have taken a degree of uncertain pride as I’ve watched the field expand. Although I’ve published many articles on the benefits of testosterone, my greatest contribution has been to show that the long-held belief that testosterone is risky for prostate cancer is false. As the fear of testosterone has declined, physicians have become more comfortable with it, leading to a crescendo of interest in its use.
Men Are Also Hormonal

Over the last 10 years, the fastest pharmaceutical sector is testosterone, growing at more than 10% per year. There are a huge number of men out there who have the symptoms of low levels of testosterone. As this problem gained attention from physicians about 10 to 15 years ago, there was a push to talk about andropause, a male version of menopause.

I started to use the term low T in the office and during lectures to describe the condition that has otherwise been called hypogonadism, or testosterone deficiency syndrome. My colleagues thought low T was too simplistic a term, but it worked for me and my patients, and I continue to use it. Nonetheless, I was surprised to hear one day that my verbal shorthand had been co-opted by the industry. Now, television and print ads ask, “Is it low T?”

Are Men Like Lizards?

We think of testosterone as the male sex hormone, and to a great extent, this is true. However, testosterone is involved in so many biological functions for men that it is difficult to come up with a biological system that is not affected by testosterone. What is remarkable is that researchers have been studying testosterone in animals for many decades, yet with humans it is as if we are just beginning to learn about something brand new.

When I graduated from my urological residency in 1988 and came on staff as a young attending physician, I was curious about testosterone because of research I had done as an undergraduate. During my training I had been taught that testosterone was important for sex drive but not much else, and that a man needed to have almost no testosterone left at all before his low T levels caused sexual issues. There was some grudging acknowledgment that perhaps testosterone treatment might help some men with erection issues, perhaps 5% at most, but this number was so small that no one was spending much time looking into treatments.

In my sophomore year at college, I started on a boring, tedious project, mapping out which parts of the lizard brain took up radioactive samples of hormones that had been previously injected into the bloodstream. The lizards I worked with were the American chameleon, Anolis carolinensis. When a normal male lizard is placed in a cage with a female, the two of them go through what is called a sexual behavior, much like a dance. The male will extend the bright reddish orange flap of skin under his jaw, called a dewlap. He then does what we call a “stuttering push-up,” bobbing his head up and down rapidly. In response, the female will do a stately, single push-up, indicating she is receptive. The male will approach and repeat the behavior, extending his dewlap and performing his stuttering push-up. After a few repetitions, the male will grasp the female by the nape of her neck and mount her.

However, when the males were castrated, that is, had their testicles removed, they did none of this. They behaved as if they couldn’t have cared less. If testosterone levels in the blood were restored in these animals, the males would again perform their usual sexual behavior. The sexual “dance” was a testosterone effect.

The exciting part of my research project was to see what would happen if I implanted hormones directly into the sexual centers in the brain.
I didn’t quite know what to expect after I’d done my first testosterone insertions.

The experiment was a home run. Castrated males behaved sexually just like normal males if testosterone was inserted in the correct part of their brains. What this experiment proved was that testosterone is a brain hormone, and its actions on the brain are enough to organize the entire set of behavioral responses.

Involved in male sexual behavior are attraction, behavioral display, and mating. I spent nearly three years in the lab and published my first three scientific papers from that experience and related experiments.

Once I had my own practice seeing patients who had come to see me for weak erections or diminished libido, I couldn’t help but wonder whether there might be a testosterone connection, given my research experience with lizards. So I started obtaining testosterone blood tests in my patients. I was immediately surprised by how many of these men had low testosterone levels.

Testosterone acts on the brains of humans, just as it does in male lizards, rats, and any number of species, to create sexual desire.

Testosterone controls the production of nitric oxide, the chemical signal in the penis that initiates erections. And it is also necessary for the maintenance of penile smooth muscle, responsible for the control of blood flow into and out of the corpora cavernosa.

The Big Fear

For the last 20 years, the greatest impediment to the use of testosterone therapy has been the fear that raising testosterone levels is dangerous for prostate cancer. It started with a publication in 1941 by Charles Huggins, MD, and his co-author, Clarence Hodges, MD, in which they demonstrated for the first time that cancers can be sensitive to hormonal manipulation. These two researchers from the University of Chicago castrated men with metastatic prostate cancer and showed that levels of a chemical called acid phosphatase were reduced, indicating improvement in the cancer. This was the first treatment for advanced prostate cancer that had shown any efficacy. Within a few years, castration had become a standard treatment around the world, and Huggins, as the lead investigator, became famous, ultimately being awarded the Nobel Prize in Physiology or Medicine in 1966.

Huggins and Hodges also reported that “in all cases,” the injection of testosterone to these same men with metastatic prostate cancer caused acid phosphatase levels to rise. They concluded that testosterone causes “activation” of prostate cancer and an “enhanced rate of growth.” From that point forward, medical students around the world have been taught that high testosterone levels cause prostate cancer; low testosterone levels protect the prostate from cancer; and providing testosterone to a man with prostate cancer is like “pouring gasoline on a fire” or “feeding a hungry tumor.”

Once I started seeing the benefits of testosterone therapy in men, my greatest concern was that the treatment I was offering might be like a pact with the devil: If these men were restored to youthful vitality and sexuality, it was at the expense of developing prostate cancer. What followed for me was a 20-year exploration into the relationship of T and prostate cancer, eventually resulting in the widespread, albeit not yet universal, rejection of those long-standing concerns.

In the early 1990s, I began performing prostate biopsies in men with low T even though they had normal levels of PSA, the blood test used to diagnose prostate cancer, since I wanted to make sure these men didn’t harbor a hidden cancer in their prostates, which might grow out of control if I treated them with testosterone. Although it was taught that men with low T are at extremely low risk for prostate cancer, I found an astonishingly high number of cancers in these men. In 1996, my colleagues and I published these results in the Journal of the American Medical Association, reporting that low T appeared to be as great a risk for prostate cancer as an elevated PSA. Low T was not protective at all.
Yet for a time I still clung to the belief that high levels of testosterone must be risky. In 2004, I published with my fellow, Ernani Rhoden, MD, from Brazil, an article for The New England Journal of Medicine on the risks of T therapy. After reviewing approximately 200 medical articles, we could not find a single one that showed a compelling, worrisome relationship between high levels of T and prostate cancer. This was beyond strange. It had been universally accepted for decades that high testosterone is dangerous for prostate cancer and low T is protective, yet there appeared to be no evidence to support either of these beliefs.

To discover the source for these universally held beliefs, I made my way to the basement of the Countway Library at Harvard Medical School, which contains centuries-old medical journals. The very oldest of these are kept locked or under glass, but in the archives in the basement are volumes from the 1800s, waiting to be read by medical “archaeologists.”

I found the volume holding the Huggins and Hodges article from the 1941 edition of Cancer Research, and as I pored over the text I had a “Eureka!” moment, like an electric buzz throughout my body. Although Huggins and Hodges had claimed that every one of their patients with metastatic prostate cancer who received testosterone developed an ominous increase in acid phosphatase concentrations, my close reading revealed they had administered testosterone to only three men. Of these, they only provided results for two. And one of these men had already been treated in another way, which made it impossible to determine the effect of testosterone alone. For the last seven decades, the belief that testosterone makes prostate cancer grow like wildfire was based on the results of a blood test from a single patient!

It turns out that prostate cancer does need some testosterone to grow optimally, but it can only use a little bit. Once the need for testosterone has been satisfied by the tumor, any additional testosterone is simply excess. A good analogy is a houseplant and water. The houseplant (think prostate cancer) definitely needs water (think testosterone), but once it’s been adequately watered, no matter how much additional water one gives it will not cause it to grow as tall as a sequoia tree. So it is with prostate cancer and testosterone.

Based on these findings, and despite warnings from colleagues several years ago, I started offering testosterone therapy to men with known prostate cancer. Today, men with prostate cancer fly from around the country to see me, each hoping that I will find him to be a reasonable candidate for T therapy to treat his ED. Many of them are.

In May 2011, I published with my colleagues Larry Lipshultz, MD, and Mohit Khera, MD, from Baylor Medical College, a report in the Journal of Urology on 13 men with untreated prostate cancer who received testosterone therapy for an average of two-and-a-half years. They had an average of two sets of follow-up prostate biopsies. None of the men showed any progression of their cancers, and in 54% of the biopsies, we couldn’t find any trace of the cancer that had been there earlier. It was a small study, so we must be careful not to overstate the conclusions; however, this was the very first time since Huggins in 1941 that anyone had bothered to look directly at what actually happens to an existing localized prostate cancer when a man receives testosterone treatment. The answer appears to be: “Not much.” I’ve since treated many more of these men, with similar, good results.

Testosterone affects not only men’s sexual desire and performance, but also their mood, thinking, muscle, fat, and sense of vitality and well-being. When testosterone levels drop far enough, men get suddenly sweaty and can even experience hot flashes, just like menopausal women. Testosterone production declines with age, but even young men can have low levels. I’ve treated teenagers and men in their early twenties for low T, but most men I see with low T are in their forties and above. It’s also extremely common, with some studies showing that as many as 40% of men over the age of 45 have low levels of testosterone.
Treatment is quite safe, so it’s very reasonable for a man with characteristic symptoms—low desire, weak erections, chronic tiredness—to ask his physician to have his blood checked for low T. Just be aware that many of the labs categorize a testosterone result as “low” only if it is very low, which means that if a man has symptoms and a T level that is at the low end of normal, it may still be worthwhile to consider a three-month trial of treatment. As my colleagues and I have published, men with symptoms and these below-normal testosterone levels respond just as well to treatment as men with unquestionably low testosterone.

Since testosterone levels decline with age, some have argued this means the decline should be considered a normal part of aging and therefore should not be treated. It’s an argument that we hear elsewhere: Why do we have to medicalize normal aging? My response is simple. Normal aging stinks. Aging is associated with bad eyesight, bad hearing, bad teeth, bad joints, bad blood vessels, bad hearts, and cancer. We treat all of these in order to improve our lives and, in some cases, our longevity. Just because a condition becomes common as we age doesn’t mean we should resign ourselves to it if treatment is helpful and safe.

I had exceptionally good eyesight until my early forties, at which point I found I had to hold books farther and farther away from my face in order to read them due to the “normal” age-related decline in near vision called presbyopia. Now I wear an artificial contraption of metal and plastic on the front of my face in order to read. Am I somehow disobeying the laws of nature by wearing glasses? I think not. Similarly, if a man with low T wants testosterone therapy in order to feel better and more sexual, I see no reason to deprive him of a trial of treatment just because many men his age are experiencing the same problem.

Here is a medication that can make men feel more energetic, improve erections and sexual desire, increase muscle strength and mass, decrease fat, strengthen bones, improve mood, and make men feel that their minds are sharper. Can anything really be that good? The answer is, simply, “Yes.” Of course, not everyone responds to T therapy, and of those who do, the response is not always so dramatic.

As I see it, low T is underrecognized, underdiagnosed, and undertreated. In my own practice I have seen far too many men with low T who had been discouraged from trying T therapy or told they didn’t even have the condition. Many of those men have responded to T therapy beautifully and feel that they are healthier, happier, in addition to being better sexually. Now that the fear of prostate cancer from T therapy is finally waning, there is no good reason to deprive men of a treatment that may help them regain their mojo.