Is Testosterone The New Therapy for Prostate Cancer?

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A board-certified internist and medical oncologist, Jeffrey Turner, MD, may have the most extensive experience administering testosterone to men with prostate cancer. Testosterone deprivation has been a mainstay in prostate cancer therapy for decades. In men whose cancer is under control, testosterone deficiency may need to be addressed with replacement. This article will also explore the far more controversial topic of using testosterone to treat prostate cancer, an area where Dr. Turner's experience is unmatched.

Low testosterone ("Low T") or hypogonadism is typically encountered by men when they arrive at middle or late stages of life. The symptoms are increased body fat, weight gain, low sex drive, fatigue, anemia, depression, poor memory, osteoporosis, and a higher risk of diabetes. The first step when considering whether testosterone replacement is appropriate is to determine if the cause is primary or secondary. "Primary hypogonadism" is when the testicles themselves fail to produce adequate amounts of testosterone. "Secondary hypogonadism" occurs when the pituitary gland stops producing sufficient amounts of LH (leutinizing hormone), the hormonal factor that stimulates the testicles to produce testosterone.

When a diagnosis of primary hypogonadism is made, direct replacement with testosterone is a reasonable course of action. In secondary hypogonadism, men can take medications, such as Clomid, which work by stimulating the pituitary gland to produce more LH, which in turn stimulates increased production of testosterone from the testicles.

Why do we care about the specific methodology of increasing testosterone? Because long-term testosterone replacement can further suppress any residual testosterone production from the testicles causing testicular atrophy. By stimulating natural production with Clomid, the functionality of the testicles is maintained in a natural state.

Even though testosterone is a natural hormone, supplementation or replacement is not completely free of potential side effects. Higher testosterone levels can enlarge the prostate, cause balding, acne, fluid retention, breast enlargement, testicular atro-

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If you've spent time perusing the internet or television, you must have noticed the ads of Dr. Jeffrey Life, the physician in his 70's who has a body that rivals those seen in FLEX magazine. Advertising sells, so the attraction to using testosterone has been growing. Constant media exposure to testosterone continues to stir up interest, whether you're visualizing a career in the NFL or Hugh Hefner looking for limitless libido to keep up with the Playboy Playmate of the month. Judging by all the excitement, "low T" has reached almost epidemic proportions and many men are seeking ways to increase their testosterone levels.

phy, emotional lability, decreased sperm count, and an excess of red blood cells. Due to this latter factor of increased red cell production, there is even a potential risk of heart attack and stroke if men who are treated with testosterone fail to be monitored.

For those who have prostate cancer or a history of prostate cancer, the use of testosterone is even more controversial. Historically, more than 99% of physicians would never consider supplementing a patient who has ever been diagnosed with prostate cancer in the past. This is because most doctors believe that testosterone will fuel prostate cancer growth. This association between testosterone and prostate cancer growth was documented back in 1941 by urologist Dr. Charles Huggins.

There is, however, no concrete evidence whatsoever that testosterone causes prostate cancer though it is clear that testosterone can stimulate existing prostate cancer cells to grow. The take home message, therefore, is that men who appear to have been cured of prostate cancer can indeed consider taking testosterone without concern that it will induce new tumors. There is currently a wealth of studies (including randomized controlled trials) in patients who have been treated with surgery or radiation who went on to use testosterone replacement without any evidence of higher relapse rates. This is, of course, a very different scenario from patients who have existing cancers, especially those who have aggressive, widespread, and castrate-resistant disease. Potentially such individuals could be harmed by taking testosterone.

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Despite historical evidence indicating that testosterone is universally bad for men with active cancers, some avant-garde researchers have been hypothesizing that testosterone administration to castrate-resistant patients may help in restoring hormone-sensitivity and thus aid in transforming bad cancers into a less aggressive phenotype. The emergence of something termed "Bipolar Androgen Therapy" has now surfaced. Bipolar therapy is the concept of rapid cycling between high blood levels of testosterone and low blood levels of testosterone using hormone blockade and testosterone supplementation in a cyclical fashion. Preliminary studies done on tissue cultures in the lab have demonstrated that in certain cases high doses of testosterone do cause suppression of prostate cancer cell growth, whereas normal doses of testosterone stimulate cell growth. This concept that high dose testosterone may suppress cancer growth has been tested in men with prostate cancer in very small, retrospective studies. In one study, for example, that evaluated giving large doses of testosterone on a cyclical

basis to 10 men with metastatic castrate-resistant prostate cancer resulted in lower PSA levels and radiologic evidence of tumor shrinkage.

These findings mirror my own experience using high-dose testosterone to treat men with prostate cancer. On a number of occasions, I have certainly used both standard doses of testosterone and high doses of testosterone to treat prostate cancer patients. What I have found is that it is much safer to use testosterone in patients who are in remission after treatment with previous surgery or radiation. Supplementing castrate-resistant men with high doses of testosterone is a much riskier proposition. Even so, I have indeed seen rare cases where men with castrate-resistant prostate cancer have been able to cycle between hormone blockade and testosterone replacement and keep their disease in check for over 10 years without developing radiologic progression of their disease. Unfortunately, for every one of these success stories, I have encountered far more cases where the disease not only failed to respond but the cancer appeared to progress more rapidly due to the high doses of testosterone.

So in my judgement, using high-dose testosterone in men who are hormone resistant is a RISKY proposition. What I believe is particularly inappropriate is administering testosterone to men with large tumors in the prostate or who have metastases in the spine. Such men risk catastrophic events such as urinary obstruction, spinal cord compression and paraplegia/quadriplegia due to progression of disease. Most of the men who I have treated with metastatic castrate-resistant disease first underwent aggressive cancer debulking with hormone blockade and chemotherapy. But even with this aggressive preparatory protocol, the results were discouraging in the vast majority. Men would typically develop a relatively rapid rise in PSA and manifest radiologic progression quickly, prompting a return to aggressive therapy with chemo and hormone blockade. It is true that a small minority of men with high-risk prostate cancer seemed to have their disease suppressed for a longer duration of time with high doses of testosterone. However, I found it to be impossible to determine in advance who might benefit and who would end up with rapid disease progression.

In conclusion, testosterone replacement is a viable option for prostate cancer patients who are suffering from the symptoms of low testosterone, as long as they are monitored closely. Monitoring should include regular PSA testing, digital rectal examination, and ideally prostate imaging such as color Doppler ultrasound or multiparametric MRI. Patients need to be fully informed regarding all the potential risks. In my experience, testosterone replacement is quite safe in low-risk patients who have undergone adequate local therapy and are considered to be in remission. Testosterone replacement in men with more advanced cases with metastatic castrate-resistance disease is far more risky. Further studies to evaluate testosterone in this role are ongoing. For the present, I recommend patients exhibit cautious skepticism before embarking on such a treatment outside of a clinical trial as the risks may certainly outweigh the benefits.