

Testosterone Replacement Therapy (TRT) having been diagnosed with and treated for prostate cancer?

Compiled by Charles (Chuck) Maack – Prostate Cancer Advocate/Mentor

BEFORE BEGINNING TRT, PLEASE READ THE FOLLOWING IMPORTANT COMMENTS FROM THE CAREGIVER OF A PATIENT ON THIS SUBJECT:

TESTOSTERONE REPLACEMENT THERAPY? BEWARE!

It is important that men considering testosterone replacement therapy (TRT) be well aware that TRT, as well as Anabolic/Androgenic steroids, can have disastrous effects on some men that can lead to anger and rage unrecognized by the patient but most certainly recognized by family members. I bring this awareness having been informed by a caregiver of the terrible affect TRT had on her spouse that he did not even recognize nor accept when being told of his unusual change in behavior. Men should seriously discuss this possibility with their urologist or oncologist. Caregivers should be aware of this possibility so that should they recognize unusual changes in behavior, the caregiver should bring this change to the attention of the urologist or oncologist administering the TRT with recommendation that referral to a psychiatrist may be in order to work with the urologist or oncologist to determine if the increase in testosterone/androgen is interacting with other, until then, unknown health/mental issues of the patient. Many people are unaware of possible, up to the present, bi-polar or other mental issues because these conditions had remained dormant in the past, but the administration of TRT can trigger unexpected effects. Though very unlikely to affect most men, it is important to be aware that an increase in testosterone/androgen can have disastrous effects on others. Very close monitoring by physician, patient, and caregiver is important, and men are cautioned to “only” be administered such therapy by a urologist or oncologist very knowledgeable in its use.

Now, a few considerations regarding the “Yeas and Nays” of TRT:

Though renowned Medical Oncologist specializing in the treatment of advanced prostate cancer Bob Leibowitz is known to prescribe TRT, he does make this specific awareness to those being treated: "All of the men that I have treated with

TRT are aware that the only indication for using T in a man with prostate cancer is for quality of life issues."

In other words, no matter the success of temporarily disrupting PC cell development, it comes down to two things, he only supports and prescribes TRT at high dose to gain high levels of T to hopefully cause this disruption, but he does not prescribe it as a treatment expected to eradicate prostate cancer.

<http://www.compassionateoncology.org/pdfs/TRTHANDOUT.0206.pdf>

Most patients seeking to improve quality of life despite their cancer or having been treated for prostate cancer, are treated with low dose T replacement, and even Dr. Leibowitz is against such TRT since his research has indicated it is these low levels of TRT dosage and failure to rapidly escalate T to between 1800 and 3000ng/dl that results in prostate cancer cell development and proliferation, if there are any cancer cells still dormant somewhere.

Dr. Leibowitz ends the paper in the above URL with: "I cannot overemphasize that this paper should not be brought to your doctor along with a request for a testosterone prescription. Testosterone is contraindicated in men with prostate cancer. It has caused the death of some patients (fortunately, no one in my practice); permanent paralysis, increased bone pain, and new metastases. I do not recommend use of T for anyone with prostate cancer." (This last sentence is somewhat contradictory to his earlier statement in this same paper).

In summary, every patient is not a candidate to even attempt TRT, let alone high dose TRT. Even a physician with expertise in this area as is Dr. Leibowitz, is very selective of which patient may benefit from the temporary administration of TRT.

I would support TRT administration under the oversight of expert Medical Oncologists like Dr. Leibowitz, Stephen Strum, Charles Myers, and other notables of whom we are well aware have specific expertise in the treatment of prostate cancer. I have confidence in their expertise and knowledge to know how to monitor appropriate administration. I would not support TRT administration by any other physician.

The foregoing having been a preface, here is a PubMed paper regarding testosterone replacement therapy:

IMPORTANT to note in the below study was this specific sentence:

“Only patients with undetectable PSA values and negative surgical margins on pathologic specimen were offered TRT and included in the study.” And the "Conclusion" should have included that sentence, as well!

J Sex Med. 2009 Apr;6(4):1165-70. Epub 2009 Jan 22.

Testosterone replacement therapy following radical prostatectomy.

Khera M, Grober ED, Najari B, Colen JS, Mohamed O, Lamb DJ, Lipshultz LI.
Department of Urology, Baylor College of Medicine, Houston, TX, USA.
kheramohit@hotmail.com

INTRODUCTION: Controversy exists regarding testosterone replacement Therapy (TRT) in men following radical prostatectomy (RP). Many clinicians are hesitant to offer patients TRT after an RP, out of concern that the increased androgen levels may promote tumor progression or recurrence from residual tumor. Recently, several small studies have demonstrated the use of TRT in men following an RP and have shown an improvement in serum testosterone levels with no increase in prostate-specific antigen (PSA) values.

AIMS: The aim of this article is to assess changes in PSA and testosterone values in hypogonadal patients on TRT after RP and also to evaluate the impact of pathologic Gleason grade on ultimate PSA values.

METHODS: All hypogonadal men who were treated with TRT by members of our department following RP were retrospectively reviewed. PSA values before RP, after RP, and after TRT were evaluated. Serum testosterone levels before and after TRT were also examined. Only patients with undetectable PSA values and negative surgical margins on pathologic specimen were offered TRT and included in the study.

MAIN OUTCOME MEASURES: Main outcome measures were changes in PSA and testosterone values after initiation of TRT.

RESULTS: Fifty-seven men, ages 53-83 years (mean 64), were identified

as having initiated TRT following RP. Men received TRT for an average of 36 months following RP (range 1-136 months). Patients were followed an average of 13 months after initiation of TRT (range 1-99 months). The mean testosterone values rose from 255 ng/dL before TRT to 459 ng/dL after TRT ($P < 0.001$).

There was no increase in PSA values after initiation of TRT and thus no patient had a biochemical PSA recurrence.

CONCLUSION: TRT is effective in improving testosterone levels, without increasing PSA values, in hypogonadal men who have undergone RP.

PMID: 19207277 [PubMed - in process]

pubmed.gov

A paper regarding Testosterone Replacement Therapy written by Dr. Abraham Morgentaler was published in the December 28 edition of Life Extension Foundation (LEF) magazine and available at the below URL. My comments follow that URL:

http://www.lef.org/magazine/mag2008/dec2008_Destroying-the-Myth-about-Testosterone-Replacement-Prostate-Cancer_01.htm

Here is my take on Dr. Morgentaler's paper:

Regarding Abraham Morgentaler and testosterone replacement therapy (TRT): What is important to recognize in his paper is that he prescribes testosterone replacement therapy more to men who are not yet known to have prostate cancer but are experiencing hypogonadism/low testosterone levels, and TRT can improve the overall well-being of such men. He is much more cautious in recommending any such treatment to men who were already diagnosed with prostate cancer, and more particularly more advanced prostate cancer wherein their testosterone was inhibited by androgen deprivation medications to starve the PC cells. What I find more prevailing is that if a man treated for prostate cancer subsequently has a continuing consistent near undetectable PSA (under 0.05ng/ml) if having had the prostate removed, or a steady PSA at or near 0.2ng/ml if having received radiation treatment, thus indicating the cancer may have been eradicated or at least now

indolent, and maintaining these levels for at least a year as a reasonable length of time, then I would consider TRT may be reasonable if that man's testosterone has remained at a low level. If a man's PSA level fluctuates as an indication that cancer may still be present, I would see that as requiring caution with TRT, and I would only see such administration by a physician particularly skilled in both advanced prostate cancer treatment as well as TRT.

Excerpts I took note from Dr. Morgentaler's paper:

“That night in the basement of Countway Library, I pulled all the original studies I could find of LHRH agonists, as well as reports of bad outcomes due to the flare. As I read, two things became apparent. First, many of the bad outcomes attributed to testosterone flare occurred a month or more after initiation of treatment. This meant that these complications occurred not when testosterone levels were high, but when testosterone levels had already dropped for some time to castrate levels.”

(MY NOTE: Which appears to mean that Dr. Morgentaler believes that continuing on with testosterone replacement therapy should not be causal to a “flare” effect. My question is at what dosage and how often is the testosterone being administered, since I gather from Medical Oncologist Bob Leibowitz' paper on this subject, that he administers high dose TRT to raise the level of testosterone dramatically and to within a range of 1800ng/ml to 3000ng/ml or more)

“.....out of the substantial literature on LHRH agonists and prostate cancer, I could find only two articles that actually measured and reported PSA levels during the time of the testosterone flare. And here was the kicker: both articles showed absolutely no change in mean PSA values during the time of the testosterone flare! Curiously, neither article so much as mentioned this result.” **(MY NOTE: Which appears to indicate that as long as TRT continues a testosterone rise, there should be no “flare” effect.)**

“PSA is an excellent indicator of prostate cancer growth. The fact that PSA did not rise in these men during the testosterone flare strongly suggested that the cancers did not grow during this time. Perhaps the complications attributed to testosterone

flare were nothing more than the cancer progression that would have happened without any treatment at all.”

“It had been quite a day and night in the Countway Library. I left with my head spinning and a feeling that I had stumbled onto something very important. It was like the children’s story The Emperor’s New Clothes—we see what we want to see. And for two-thirds of a century, it had been assumed that raising testosterone increased prostate cancer growth. But maybe the emperor was naked.”

“Even in men with metastatic disease, there was no evidence I could find that raising testosterone made prostate cancer grow more than it would have anyway. Shockingly, the very publications cited so regularly to demonstrate a dangerous relationship between testosterone and prostate cancer contained evidence that this was not true.”

“The Paradox Resolved

Still, I was worried, because there was a bothersome unresolved paradox to explain. For decades, the storyline was that lowering testosterone levels caused prostate cancer to shrink away and raising testosterone levels caused it grow. The second part of this story was now seriously in doubt, yet the first part was obviously correct. In my own practice, I had seen the beneficial effects of lowering testosterone levels many times over in men with advanced prostate cancer. This part of Dr. Huggins’s work was indisputable. But if lowering testosterone levels caused these cancers to shrink, how was it possible that raising testosterone levels did not cause the cancers to grow? This was a paradox that needed to be solved if physicians were to accept the possibility that testosterone therapy may not increase the risk of prostate cancer.

The answer turns out to be not all that complicated. All the reports of testosterone causing rapid growth of prostate cancer occurred in men who already had extremely low testosterone levels, due to castration or estrogen treatment. Once we get beyond the near-castrate range, it is hard to find any evidence that changes in T concentrations matter at all to prostate cancer. This is essentially what Drs. Fowler and Whitmore described in their 1981 article when

they suggested that “near maximal” growth of prostate cancer is provided by naturally occurring T concentrations.

The experimental proof of this concept was provided by a landmark article published in 2006 using much more sophisticated means. In this study by Leonard Marks and colleagues, men with low testosterone received injections of testosterone or a placebo every two weeks for a total of six months. At the beginning and end of the study, measurements of testosterone and DHT (the more active form of testosterone within prostate tissue) were obtained from the blood and also from the prostate itself. The results showed that although blood concentrations of testosterone and DHT rose substantially in the T injection group, as expected, the concentration of testosterone and DHT within the prostate itself did not change at all and was similar to the group that received placebo injections. In addition, biochemical markers of prostate cell growth also did not change with T injections.

This study showed in elegant fashion that raising testosterone levels in the blood did not raise testosterone levels within the prostate. **(MY NOTE: That last sentence is interesting, since I expect it would also be applicable to men who no longer had a prostate – but would it be applicable to cancer cells that may still exist in the prostatic bed?)** It is as if once the prostate has been exposed to enough testosterone, any additional testosterone is treated as excess and does not accumulate in the prostate. In technical terms, we say the prostate has been saturated with regard to testosterone. And it is this saturation that resolves the paradox of testosterone and prostate cancer.

Saturation explains the paradox in this way. At very low levels of T, near the castrate range, prostate growth is very sensitive to changes in T concentration. Thus, severely lowering testosterone will definitely cause prostate cancer to shrink; adding testosterone back will cause the cancer to regrow. However, once we get above the point where the prostate is saturated with testosterone, adding more testosterone will have little, if any, further impact on prostate cancer growth. Experimental studies suggest the concentration at which this saturation occurs is quite low. **(MY NOTE: And my question then would be, is one’s current, steady testosterone considered already “saturating” whatever is supposed to**

be saturated (if one doesn't have a prostate gland), and thus adding TRT should have no effect on cancer cell development?)

In other words, the old analogy I learned in training was false. Testosterone is not like food for a hungry tumor. Instead, a much better analogy is, "Testosterone is like water for a thirsty tumor." Once the thirst has been satisfied, prostate tumors have no use for additional testosterone. **(MY NOTE: But what constitutes "satisfying that thirst?" If the "thirst" has not yet been satisfied to the prostate cancer cells, would that mean stimulating prostate cancer cell growth during that "saturation?")** And the vast majority of men with low testosterone appear to have prostates that are not particularly thirsty."

HOWEVER, Dr. Morgantaler goes on to say: "In men who do have metastatic prostate cancer and who have been given treatment that drops their blood levels of testosterone to near zero, starting treatment with testosterone (or stopping treatment that has lowered their testosterone to near zero) might increase the risk that residual cancer will again start to grow." **(MY NOTE: Thus, he would be hesitant to administer TRT to men who had received successful ADT.)**

"My perspective is that it is worth knowing the diagnosis, whether or not one chooses to be treated immediately. And because low testosterone seems to represent a small but definite increased risk, I feel that biopsy in men over fifty with low testosterone is worthwhile." **(MY NOTE: Of interest here is, before administering TRT, his practice of first performing a biopsy on men to make certain the biopsy indicates they DO NOT have prostate cancer. This indicates to me that if prostate cancer IS found, he would likely then hold back on administering TRT and rather have the patient decide on a traditional form of treatment for that cancer presence.)**

So, with my continuing questions, thus continuing concerns, I wonder how many others continue to have the same concerns. Very obviously any man considering TRT should be under the counsel and guidance of a physician with expertise in treating both advanced prostate cancer AND low testosterone.

In my opinion, the following advice given by Medical Oncologist Stephen Strum to a patient considering TRT whose PSA had remained at appropriate level for over 5 years post-treatment would be the prudent advice for any man considering TRT:

“TRT (testosterone replacement therapy). Issues to discuss with them (My Note: (Physicians) include:

1. Dosing of Androgel or any testosterone formulation, and what level of serum testosterone total and free testosterone should be achieved (BEPs).
2. Use of an aromatase inhibitor to prevent metabolic conversion of testosterone to estradiol which is further complicated by stimulation of prolactin increase which you do not want to have happen. Most often, using the aromatase inhibitor called Arimidex at 0.5mg to 1mg twice a week or three times a week is sufficient to keep serum estradiol levels (E2) well below upper limit of normal.
3. Checking DHT and considering use of 5ARI (5-alpha reductase inhibitor) like dutasteride (Avodart) since high levels of testosterone will result in metabolism to DHT which is 5x as potent stimulating PC (if any is present). Alternatively, measure the BEP of serum DHT & if it remains low then there may be no need to use an inhibitor of DHT.
4. Monitoring PSA monthly to make sure that no PC that may be present and lying dormant is awakened. If monthly levels remain unchanged from your baseline values then this is a good "stress test" to tell you that PC is almost certainly eradicated. If PSA starts to rise in a serial fashion than stop the TRT (testosterone replacement therapy), unless your physicians have some other form of strategy they discuss with you.

Most docs would tell you that you are cured with your PSA being what it has been for over 5 years. It is my belief that many men walk around with PC that is maintained in check or control by homeostatic (balance) mechanisms, that most likely involve the immune system as well as the status of other environmental or milieu factors (of all kinds). For this reason, looking at BEPs (Biological End Points), both good and bad are very important in my opinion.

If I were to return to academia and teach medical students and young physicians, I would try to imbue in them the following concepts that I have mentioned over many hundreds of posts on the Internet to patients and physicians:

1. Balance & Communication are the keys to health-love-peace at any level, from the cell on up to the universe.
2. Status & Strategy are logical, reasonable, relevant and crucial steps in interacting with all biological systems when quality & quantity of survival are at stake.
3. End-points (in medicine biological end-points or BEPs) must be used as measuring sticks to know that we are accomplishing that which we seek to achieve.
4. Our humanity lies in our human unity.

- Stephen B. Strum”

Disclaimer: Please recognize that I am not a Medical Doctor. I have been an avid student researching and studying prostate cancer as a survivor and continuing patient since 1992. The comments or recommendations I make are not intended to be the procedure for you to now follow; rather, they are to be reviewed along with the comments or recommendations of others for your own further research, study, and discussion with the physician providing your prostate cancer care to come to your own, personal conclusion.