

BY RICHARD WASSERSUG Ph.D.

PSYCHOLOGICAL SIDE EFFECTS OF HORMONE THERAPY

About half of all men treated for prostate cancer will be prescribed hormone therapy—more accurately known as Androgen Deprivation Therapy (ADT)—at some time along their cancer journey. ADT is often started prior to radiotherapy to improve the efficiency of that treatment. When used that way, it is called neo-adjuvant therapy. ADT is also used as a second line therapy when patients experience a continuing rise in PSA or have other evidence of residual disease after either a radical prostatectomy or some form of radiotherapy undertaken with the intent to cure the disease. In those situations ADT is considered adjuvant therapy. Lastly, ADT is used as a systemic therapy to treat the disease when it has spread beyond the prostate gland.

AD deprives the body of the main androgen, testosterone, the key hormone that normally promotes prostate cell growth. Although ADT is not considered curative, for many patients it can hold prostate cancer in check for years, sometimes for decades. In the early stage of metastatic disease, ADT can also cause some painful metastases to regress, improving patients' quality of life.

ADT obviously benefits many patients. The downside is that ADT is now known to cause an array of side effects and some of those are substantial. Long-term use of ADT increases the risk of osteoporosis, bone fracture, anemia, weight gained as fat with a concomitant loss

of muscle mass (that combination is called sarcopenic obesity), and possibly cardiovascular disease, kidney disease and diabetes. Much has been written about strategies for reducing the more serious metabolic and musculoskeletal side effects of ADT. Less attention has been given to the psychological impact of ADT, which I am focusing on here.

Let's start with the normal roles of testosterone in the body. Testosterone (along with its more potent derivative, dihydrotestosterone) gives men the multitude of features that define males as men and distinguishes them from most females. This includes their more muscular bodies, their facial hair, and their propensity to go bald in middle

age. Most notably, testosterone gives men their sex drive, which is diminished in most men on ADT.





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But psychologically testosterone does more than that. Testosterone has been described as a “social hormone” [1] for it not only regulates men’s desire for sex, but also their propensity to compete with other individuals; i.e., in popular lingo it gives men their “machismo.” Many studies report men feeling less energetic, less motivated, and to some degree less macho while on ADT. In sum, ADT impacts on how men feel about themselves and interact with others. This is revealed in many ways, and is discussed further below.

Depression

Although low testosterone is not necessarily a primal cause of depression, testosterone levels decline naturally with age, and low testosterone has been associated with depression in some middle-age and older men, who are not cancer patients. In cancer patients, depression may be linked to some extent with anxiety associated with disease progression. Putting men on ADT doesn’t make that situation any better. DiBlasio et al. [2] reported “a three-fold increase...between rates of pre-ADT psychiatric illness and development of de novo illness” after starting on ADT. More recently Lee et al. [3] confirmed in a controlled study that ADT is most notably associated with an increased risk of depression. Those authors make a plea for clinicians to both screen patients on ADT for depression and intervene when they find it.

Cognition

There have been several studies suggesting that ADT also impacts cognitive functions. Cognitive functions are those mental processes involved in how we perceive, think, reason, and remember. Patients anecdotally report memory problems on ADT, but some of that may be due to normal aging. Back in 2008, Nelson et al. [4] however reported that between 47% and 69% of men on ADT experience some impairment in at least one cognitive domain. They concluded that ADT “is linked to subtle, but significant cognitive declines in men with prostate cancer” and felt that clinicians should “inform and monitor patients for this possible side effect of treatment.”

Recently McGinty et al. [5] revisited this topic with a meta-analysis of studies completed to date on ADT and cognition. They flagged visuomotor tasks as the domain where patients on ADT were most likely to experience cognitive decline. In real life, this can manifest itself in problems with finding papers on a messy desk, car keys left somewhere about the house, and even locating the car itself in a large parking lot. McGinty et al. reinforce Nelson et al.’s conclusion, asserting that “knowledge of the cognitive effects of ADT may help patients and [healthcare] providers better understand the impact of ADT on quality of life.”

Men & Emotions

Changes in emotionality have been repeatedly reported for androgen-

deprived prostate cancer patients (as well as male-to-female transsexuals, who similarly go on androgen-depriving treatments), but these have not been precisely characterized and may be manifested in different ways by different men. In general terms, they range from men becoming more sentimental to more irritable [6].

The most conspicuous change that has been reported is an increase in tearfulness. In our society women may cry, but in the cultural stereotype for the western world “real men” don’t cry. Increased tearfulness can thus be embarrassing to men on ADT.

How men see this increased emotional ability, and whether they accept it or not, may have a great impact on how well they adapt to ADT in general. It is not inconsequential that for half of our species, crying is seen as empathetic and not necessarily a negative personality trait. I have met a fair number of patients on ADT, who announced that they now share tissues with their partner when they go to a dramatic movie...and feel closer to their partner as a consequence. However such open acceptance of the changes brought on by ADT is not always easy. Some men, who are not comfortable with the changes they are experiencing, feel ashamed or out of control at being seen by others as acting, or reacting, differently than they did before ADT. In contrast to the patients who acknowledge and accept emo-



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tional change, they strive to hide it and perhaps hope that it will go away...or at least go unnoticed. They then get distressed and even angry if it is recognized and commented on by someone else.

Impact on The Partners

The “someone else” is often the patient's partner, who sees ADT-induced changes in their partner's personality before he sees them in himself. This can lead to conflict between patients and partners if they have different coping strategies. Often women find it beneficial to talk out problems, whereas men often resort to denial as a defensive mechanism, particularly when facing problems they cannot easily solve. That can lead to frustration and then depression in the patient's partner, who may feel rebuffed and rejected, when the patient wants to neither acknowledge nor discuss how different he feels on ADT. [Various research groups have described versions of this conflict when heterosexual couples are challenged by ADT; the impact of ADT on same sex couples has yet to be investigated.]

In sum, ADT can negatively impact on a man's interactions with the person he is normally closest to, and this can have repercussions on that person's health. In general, the psychological distress associated with cancer is greater on females than on males whether they are the patient or the partner [7]! This has recently been documented for a variety of cancers, including prostate cancer,

where the female partners show persistently higher levels of anxiety than the male patients [8]. In fact, over 20 years ago Kornblith et al. [9] reported greater psychological distress in the partners than the patients on ADT.

To put this in slightly glib terms, ADT can cause a “communicable iatrogenic psychiatric disorder”. In other words he is medically emasculated, not acting quite like he used to, and she is now depressed. As a part of informed consent, when starting patients on ADT, one might suppose that patients and partners would be informed of this possibility as part of routine clinical practice. But that doesn't always happen. In defense of the healthcare establishment, the depth and breath of this problem has become much worse over the last 20 years as more men are living much longer on ADT. And out of fairness to uro-oncologists, the care they provide should be focused on the patient. After all, keeping him from dying of prostate cancer is a major step in the right direction for reducing distress in his partner. However there is reason for healthcare providers to be particularly concerned about the psychological burden on the partners of prostate cancer patients since the distress in the partners correlates with the distress in patients. In fact Kim et al. [10] showed that there is “evidence of partner effects, at least for women. That is, women's distress predict[s] men's physical health, over and above the men's distress, ...age, and

cancer stage.” Seen in that light, all of us—patients, partners, and healthcare providers—should be concerned about the health and welfare of not just patients on ADT, but also their partners.

Helping Patients & Partners Deal with The Adverse Effects of ADT

Going one step further, I would argue that we should be concerned not just about the individuals, but about preserving their partnership as a co-supportive dyad. Too often cancer treatments can be so debilitating that they cause co-supportive partnerships to devolve into a patient/caregiver dynamic. Our job should be to help prevent that. Strong partnerships are first and foremost built on intimacy, which means sharing something with someone that one doesn't share with others. When we are young, sex is a bonding act, an intimate act that builds partnership. But when we age—and in particular for patients on ADT whose sexual desire is depressed—maintaining intimacy and protecting partnership can be challenging.

When it comes to dealing with ADT side effects, whether they are the physiological ones affecting the cardiovascular and musculoskeletal systems, or the psychological ones affecting the patient's mood and emotionality, there is one intervention that can help across the board. That is physical exercise. Not only can exercise protect the heart, bones, and muscles, but it can improve mood and

memory, reduce depression and fatigue, and recently it has even been shown to improve sexual function for patients on ADT [11].

To bring this back to the psychological impact of ADT on patients and its indirect impact on partners, exercising together can help maintain intimacy and thus help keep prostate cancer couples together. In that regard, I am particularly impressed with the “Exercising Together” program for prostate cancer patients developed at the Oregon Health & Science

University (OHSU) in Portland, Oregon [12]. This is a partnered, strength-training program for prostate cancer couples, which essentially trains patient and partner to work as a training team, partly by being the fitness trainer for each other and partly by doing exercises in tandem. The final results of that study are soon to be submitted for publication, but preliminary analyses show that partnered exercise is helpful not just in strengthening patients’ and partners’ bodies and minds, but also strengthening their spousal bond. The Vancouver Prostate

Cancer Supportive Care program where I work is now piloting a modified version of the program.

Not all prostate cancer patients have life partners, but having one and keeping one’s partnership strong and healthy is one of the most effective treatments for prostate cancer. As Aizer et al. [13] noted, the survival benefit for prostate cancer patients in having a supportive spouse (call it marriage if you will) beats any benefit of chemotherapy. □

References can be found online at PCRI.org

Bone Health & Prostate Cancer

Understanding Your Risk of Osteoporosis

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Your skeletal system is a system of organs - a living, growing, integral part of your overall health, just like any other organ system within your body. Each bone is considered an organ in and of itself. Keeping your bones healthy can have multiple benefits, the greatest of which is preventing fracture. This article is intended to give you a better understanding of your risk of osteoporosis, and develop the right questions to research for yourself, and ask your physician(s).



Osteoporosis is not just a ‘condition’ – it is a ‘disease’. This may surprise you, but the National Osteoporosis Foundation states that men older than 50 are more likely to break a bone due to osteoporosis, than they are to get prostate cancer.

The International Society for Clinical Densitometry (ICSD) states that “Osteoporosis is under-recognized and under-treated. Testing for bone loss, or osteoporosis (DEXA Scan, QCT) in men is not done routinely. There is a prevalent misconception that osteoporosis is a disease of women.” About 20% of people with osteoporosis are reported to be men.

When Should You Ask for A Bone Density Test?

Start by asking your primary care physician, or your medical oncologist. Sometimes initiating the conversation with a nurse can be helpful. Understanding some background information about osteoporosis will help you carry on a more informed conversation.