

# CANADIAN PROSTATE CANCER SUPPORT GROUP

Newmarket, Ontario

Volume 13, Issue 1, September 15th, 2008

**A support group that provides understanding,  
hope and information to prostate cancer patients and their families**



Well you can put away your camping, fishing and swimming gear and get ready for a year full of great meetings with great speakers. We will be starting off on the September 18th meeting with one of our favourites in Padraig Warde from PMH. He's now spending time at Southlake setting up our new Regional Cancer Centre. Padraig has spoken to our group several times in the past and we've always enjoyed and learned from his talks. The subject of his talk will be, quite obviously " a look at the Cancer Centre at Southlake and all the bells and whistles they will be including in it. We will also be inviting a member each meeting to share their cancer story. We hope this will help new members in particular as they start down the treatment path.

**Meeting Date: September 18th, 2008**

**Place: Newmarket Seniors Meeting Place  
474 Davis Drive, Newmarket**

**Time: 7:00 to 9:00 pm**

**Speaker: Dr. Padraig Warde, Southlake Health Centre and  
Princess Margaret Hospital**

**Subject: The New Centre at Southlake**

Canadian Prostate Cancer Support Group,  
Newmarket, Ontario. 905-830-0447

a member of the



Canadian Prostate Cancer Network

Assisted by the Canadian Cancer Society  
Holland River Unit  
Cancer Information Service  
1 - 888 - 939 - 3333

## Your Executive

Ron Stevenson, <i>Chairman,</i>	905-836-1701
Dennis Allibon <i>Publicity,</i>	905-722-6392
Phil Harrison, <i>Secretary,</i>	905-895-1407
Derek Lawrence, <i>Treasurer, Exec. Consultant</i>	905-853-2665
Doug Bowers, <i>Speakers,</i>	905-841-2759
Bill Tuplin, <i>Speakers,</i>	705-458-4881
Jane & Frank Kennedy, <i>Newsletter,</i>	905-895-2263
Pat Stevenson, <i>Greeter,</i>	905-478-4012
Ulli Baumhard, <i>Member at large,</i>	905-478-8843
Dan Ho, <i>Member at large,</i>	416-953-8889

*The Newmarket Prostate Cancer Support Group does not recommend products, treatment modalities, medications, or physicians. All information is, however, freely shared.*

# June speaker notes **Dr. Jerome Green, Southlake Health Centre**

## **Subject: Testosterone and Hormone Therapy**

*Dr. Jerome Green, our speaker for the June 19th meeting is a Urologist practising out of Southlake Regional Health Centre. He spoke to us about "Testosterone and Hormone Therapy" bringing us up to date on the latest thinking on androgen deprivation therapy, the correct name for what we normally call Hormone Therapy. Here is what he had to say*



We're going to talk about testosterone and radical and hormone therapy tonight. Hormone therapy is not really the proper name for it, but if you look in your books or on the internet, everyone uses the name hormone therapy. The correct term, which you may or may not know, is androgen deprivation

therapy. Hormone therapy or androgen deprivation therapy doesn't necessarily apply to most patients who have prostate cancer. I am also going to talk about testosterone therapy which is sort of taboo in the prostate cancer world. By the end of this talk, I hope you can make up your mind as to whether testosterone is a good thing or a bad thing. I want to talk about testosterone, what it is and also talk about hormone therapy, what it is, why we use it, when and how we use it and then I'll talk about testosterone deficiency and potential replacement.

Testosterone is a steroid that's produced by the testicles and it's regulated by our brain and certain glands. Not all of our male hormones are testosterone, about 90% of them are, the rest are created by these little glands on top of our kidneys, called adrenal glands. They also produce some hormones that are considered sex hormones. Both women and men have them but not all of our hormones in our body are necessarily testosterone. You've got your hypothalamus. This is a gland which releases a messenger to tell the pituitary, another gland, to release a glutinizing hormone. The messenger is LHRH, a glutinizing hormone releasing hormone. It tells the pituitary gland to release LH, which circulates through the body, through the blood stream and works on the testicles and on certain other cells and these cells release testosterone. That's a simplified view of how testosterone is regulated. In fact, testosterone goes back and turns these off when there's high enough levels in the body. Testosterone is a very important hormone in our body. It's very important for our sexual function: sex drive, erections and also sperm production. Testosterone is also very important for our muscle mass and proper fat distribution. Without testosterone you tend to get what we call beer guts. It's very important for our bone health, as well as our overall mental well being.

How does it affect prostate cancer? Huggins, a Canadian-American surgeon scientist, won a Nobel prize in the mid-sixties for discovering that if you deprive the body of testosterone by removing the testicles, then the prostate cancer went into remission. He also gave a patient who had aggressive prostate cancer testosterone and, not surprising, that person's prostate cancer progressed very rapidly.

Androgen deprivation therapy, which is basically what it sounds like, removes the hormones and yet it's not a hormone therapy. If you think of it, hormone therapy means that you're giving hormones. ADT is one most effective therapies against any solid tumour out there. It's probably more effective than any of the chemotherapy drugs, so for solid tumours, it's a great treatment. Think of testosterone with prostate cancer, testosterone is a fuel. When prostate cancer starts it typically gets more aggressive when testosterone is present. The caveat to this is once you become more hormone refractory, meaning there are cells there that may not respond, they don't need that fuel to start moving around or start growing, in that state, obviously, the androgen deprivation therapy (ADT) potentially will not work and the testosterone deprivation will not be needed any more. All forms of ADT basically work by either lowering the levels of testosterone in your system or they tend to block binding of testosterone within the cell. So testosterone doesn't have any effects when it's moving throughout your body, it's only once it goes into your cell and binds with the receptor. By blocking the receptor, you get the same effect. Let's talk about types of therapy. The first type is called castration. There's medical and surgical castration. Surgical has been around much longer, basically by removing the testicles you're getting rid of the testosterone. We're currently doing more medical therapy by using LHRH Agonists and some of you may be on Aligard or Lupron or Zoladex. There's another type of pill which is called anti-androgens. These are Casodex or Biflutimide and other different anti-androgens. There is something called complete androgen blockade, sometimes it's called total androgen blockade or maximum androgen blockade and it's basically a combination of using one of those pills and a form of castration. There's something called LHRH Antagonists, The advantage of these is that they shut off the LHRH right away, so there's none of the initial rise in testosterone. Those are being studied now. They're not really available yet. There have been issues about their stability and how well they're working, so they're working on those and they are in Phase 3 trials now. The anti-androgens are typically not used on their own.

They're used initially to block the receptor and the advantage of this is that potentially it can preserve sexual function because your testosterone levels actually go up. Because there is no feed back through this whole mechanism, testosterone will actually go up initially and stay up. The problem is your sub-tissues don't respond as well because you're blocking that receptor. The disadvantage of this is, because your testosterone levels go up, you're estrogen levels climb and as the estrogen levels climb, this can potentially produce breast enlargement and breast pain, which is a common side effect. Most men are not very happy when they start growing breasts. We use these anti-androgen pills prior to giving the injection and the reason for this is, especially when they have evidence of you having disease in the spine, because you get that initial flare, that rise in testosterone initiall. If you don't have this on board, then you are feeding those prostate cancer cells. By blocking them with those pills, that initial rise really is no problem. So typically, before we give these, if there's any concern of potential metastatic disease, we give you the pills for two weeks, give you the injections, you continue with the pills for two weeks and then you stop the pills. Then you are just treated every 3 to 6 months with the injection. It's rarely used as mono-therapy. In some cases we use it just on it's own but again, the side effects, the breast tenderness are certainly significant. Usually these pills are used when you are already on the injections and your PSA starts to climb. Usually that's indicative that you are becoming hormone refractory, where your prostate cancer cells are not responding to testosterone deprivation. So they are starting to multiply and divide, not based on testosterone but based on other means. One of the things that it does actually start to divide in response to is the androgen itself. Those receptors mutate, they change. They become disregulated and when they become disregulated by giving them this anti-androgen, some prostate cancer cells start growing more quickly. So when we start to see that rise in PSA when you're on a complete blockade, by taking away this pill you slow down the rise. Up to 30% of patients who start having hormone refractory disease when they're on both the pill and the injection, by taking away the pill, about 50% of them will see a drop in their PSA, which may last up to five months. Most people are on the injection but, if there's any evidence that the cancer is outside the prostate, and there's a potential that they can have devastating effects from the flare, then they put them on the pill for a short term. There's no real survival advantage for the complete androgen blockade but, if you put people on the pill and the injection, there's no difference in survival. You're not allowing people to do better but you may be doing worse because of the side effects such as breast tenderness. There have been studies that looked at taking these pills alone. They do work temporarily but not as effective as the injections. You do have potentially improved sexual function but there have been some downsides. Initially, when we put people on Casodex alone, we prescribed 150 mg. a day. This was found to be detrimental and had cardiac effects. So people were dying

from heart disease quicker than they should have. In select patients, you can put them on the pill. Things tend to evolve in medicine. We look at what we're doing now, I'm hopeful that, still in my time, when I'm practicing Urology in 20 years from now, we won't be taking out prostates any more.

Let's talk about the complications. Basically everyone will suffer some side effects and I'm talking here mostly about the injections. Remember I told you about the role of testosterone, how it effects your over-all well being, your bone mass, your muscle mass, your sexual functioning.

Bone complications are common. Most men who are diagnosed with prostate are already in their sixties and their bone mass is already compromised. With four years of treatment most men drop into a much lower level. So we need to look at prevention. I always tell people to stop smoking and exercise always helps the bone density. All men should be on vitamin D and Calcium and there's some question as to whether or not men should be on bone stabilizing drugs, which strengthen your bones and help build them or maintain them, so you hopefully won't have any fractures or developing pain related to potential cancer, as well.

#### **Hot flashes:**

Most men on this medication have hot flashes. We don't know the mechanism of hot flashes but it's very common, up to 80%. We rarely see a patient who is on this medication who doesn't have hot flashes. One thing we tell them is that it is not life threatening. Sometimes they think they are having a heart attack because of the sweats, which can be quite profuse. It does tend to get better over time both in intensity and how often you get it. There are treatments but they also have side effects. There are anti-depressants or anti-androgens and sometimes progesterone can help if the hot flashes are severe.

#### **Sexual Dysfunction:**

You need to have testosterone to have normal erections. Studies have shown that up to 15% of the patients can maintain an erection during this treatment. Again, one of the problems goes back to age of the patients. Most men are already having a degree of this problem. So erectile function may be poor to begin with. Then, once you put them on hormones, it's probably going to be considerably worse. But, the sex drive is gone. Testosterone is very important to both men and women. In fact, sexual dysfunction is much more common in women than men because of estrogen loss and a lot of trials that are being done on women are usually testosterone supplementation. It's hard to improve the libido without giving some testosterone but certainly we can treat the erectile dysfunction. Unfortunately, all these drugs such as Viagra, etc. won't work if you don't have testosterone present. But there are injection therapy, vacuum devices.

So there's no question that as we get older, we don't think as well. There is evidence of cognitive decline with testosterone deprivation. There's a higher incidence of depression and there are treatments for that. Anti-depressants sometimes work and there's cognitive therapy but there certainly is an issue.

## **Anaemia:**

That's when your blood levels or your hemoglobin levels drop. Testosterone is very important for the hormone that is released through our kidneys that works to balance our red blood cells. Because you don't have it there's less of that hormone. Within a month of starting this therapy, your levels start to drop and usually it's only about 10% but some people can be worse. It usually levels off in two years. The problem are that men with extensive metastatic disease, or disease throughout their bones, their bone marrow is not responding anyway, so it might be more severe.

Because the estrogens level are higher, breast pain or breast enlargement are usually associated with the anti-androgens but there are people who get it with just the injections. There are treatments for this: Surgery to debulk the breast tissue there. Radiation has worked if there's no enlargement, just breast pain, Also Tamoxifen, which is commonly used in women for breast cancer, to cut down their estrogen receptors. Because estrogen levels are up, by giving prostate patients some of this it will help with the breast pain and enlargement.

## **Muscle Loss:**

This is a big problem for anyone who has prostate cancer. It's very important for all of you to be on an exercise program. Studies have shown that, not only men who are on these medications, but also men who have prostate cancer and are not on this therapy do much better in terms of PSA and progression and survival for those who are on exercise programs. We know that your weight increases and that's because of muscle loss and your fat increases when you're on hormone therapy and studies range from 5 lbs to 30 lbs. So guys do gain weight on this, so exercise is very important. We know that men who are obese have a higher risk of dying from their prostate cancer. Their PSAs tend to be lower because there's more fat and more estrogen effect, so even men who we see in screening, who are more obese, their PSAs are actually lower than they probably should be if they were not obese. Studies have shown that if men exercise for more than three hours a week, there's a 70% reduction in prostate cancer death.

There are other diseases which can be attributed to androgen deprivation therapy. Studies have shown that you're at high risk of developing diabetes, coronary disease, developing a heart attack. This was compared to men who were not on androgen deprivation therapy, do not have prostate cancer and then compared them to men who had castration or injections. For some reason, men with castrations were only high risk for developing diabetes and not for developing heart problems and we don't know why that is. This is just one study. The question is, why do we use all this? Why do we use hormone therapy? So the men who have low risk disease, localized disease, even in its aggressive form, like Gleason 8 or 9 or 10 and you've gotten rid of it, you don't put them on hormone therapy. That's because of their quality of life, for example the side effects, there's no survival advantage. If you

do a radical prostatectomy and they have a lymph node disease at that time, then there is a survival advantage in putting them on hormone therapy. That comes at a cost for the quality of life. The one study showed that, if you put someone on this therapy when they had lymph node positive disease, you extend their life by a few years. But, if you don't do it and wait until they need it, you can keep them off this therapy for a few years. So you're playing with the quality versus the quantity of life. In locally advanced disease, men who have bone metastases but have no symptoms, putting men on this therapy won't delay their progression, it will cut back on their metastatic disease. It will improve their chance of surviving prostate cancer, not necessarily long term but certainly short term but it does not improve their over-all survival. That's likely because of the detriment of what we're doing in terms of the heart function, diabetes and so forth. So, on one hand we're treating the cancer — I don't want to be a pessimist here — but, quality of life is very important and I don't expect everyone to run out of here and those who are on hormones say "To Hell with this! I'm not taking any." It does improve your survival, it improves your likelihood of not dying from prostate cancer but you may just die from something else. That's basically what I'm saying.

We don't use hormone treatment for radical prostatectomies. There was a study on radical prostatectomies, some of you may have been involved, this was late 90s or early 2000s. What they were looking at was putting people on hormones for three months or eight months or not at all, before they had their radical prostatectomy. Sounds great. Put them on a drug that shrinks the tumour. Maybe you get better margins or better control but it didn't translate into any difference in survival. So we don't recommend that any more. But, with radiation, if you have very high risk disease, a study has shown an almost 50% survival advantage if you have radiation with hormone or androgen deprivation therapy, compared to patients who just have radiation alone. It improved their chances of not having progression; it did improve their overall survival and improved their cancer specific survival. This is a short term therapy. It's only three years of hormone therapy, we're not talking life long therapy.

So how do you make the decisions? You need to talk to your doctor, he has all the tools but remember, 97% of the men who have prostate cancer die from something else. Only 3% of those diagnosed with prostate cancer, die from prostate cancer. There are no other cancers that have those odds, except maybe some skin cancers. So, if you look at patients who have had advanced disease. you take the prostate out, there's no evidence of lymph node disease but the PSA comes back early on. If you did nothing for them, the time for them to progress for the cancer to come into their bones takes an average of eight years. The time to death, this is without treatment, was five years after that. So you're talking 13 years. None of us have crystal balls, we don't know what's going to happen down the road 13 years from now. Heart attacks, other cancers, things like that. This was 1999, there's been

updated data from 2005 showing they have pushed this to almost 16 years. Although you all grapple with the PSA and the PSA is starting to come back, it doesn't equate to the median time. What you need to consider is your quality of life (quality of life and quantity of life are not the same thing). Anyone who goes on hormone therapy does not feel great. I'm not saying they're feeling awful, don't get me wrong, we have to be optimistic, but they don't feel great. If you can hold that off for a couple of years, potentially, with the down side meaning you'll live one less year but your going to live another 10, 12, 15 years anyways, you have to weigh the pros and cons of doing this. Discuss it with your physician.

This is for people who are going to be on hormone therapy long term. So how do people respond to this? Most people respond to it right away. How good a response will dictate how well you will do on the ADT. If your PSA drops very quickly and it drops to a very low level, I'd say you're going to do very well for a long time. If it doesn't drop as low, if it doesn't drop as quickly, then that's usually a sign that you have cells that are already there that tend not to respond, they don't need testosterone to fuel their existence and progression. So long term patients who are using ADT for advanced disease, the cancer will ultimately progress. That's because at the time of diagnosis, you have a few of these cells there that don't respond to testosterone and those, over time, will start building. So eventually your PSA starts to rise because you're not responding to the ADT. However, if you stop the ADT, there are still cells there that are responding to it. Those with hormone refractory disease still need to be on those medications or the injections.

### **Let's talk about intermittent therapy:**

Basically, it sounds like what it is. This started in the late 90s. The theory behind this was, can we delay that hormone refractory cancer? Can we wait and can we improve peoples quality of life by basically starting them on ADT, wait till their PSAs drop and then stop. Wait till their PSA rises and start again. The theory initially, we thought, well maybe we can prevent this hormone refractory stage. That doesn't happen. Then the big question was, is it going to affect my survival? There are lots of big studies on this, that looked at quality of life, survival, progression. Quality of life, there was no question. Once you come off the hormones, you start feeling better. So your quality of life is better on the intermittent therapy. Overall long term, there's no change in survival, there's no change in progression. Remember those side effects, diabetes, heart disease, etc., those potentially have a detrimental effect if you're on those drugs long term. So there's some question whether you might have a cardiac benefit as well.

### **Testosterone Deficiency:**

This applies to everyone. We're not talking to those on ADT, this is for the general population. You may have heard the term andropause. You've heard the female menopause, well this is the male menopause. This is a gradual, age re-

lated decline in your testosterone levels in your blood in older men, compared to younger men. Those signs and symptoms of testosterone deficiency are the same side effects of ADT. There are a whole bunch of Urologists who don't believe this exists, they're just in denial. They say, "Well, women it just shuts off, it's normal. Men, they decline, it's normal. So why treat them?" I argue that when you treat them, they feel better and that's a good reason to treat them. This is a gradual decline, once you reach your 30s, your levels start dropping 10% every year. It starts early, we weren't designed to live this long! The same thing happens as when you get ADT. When you get the lower testosterone levels, you loose muscle mass, you get more fatigued, you have more fat, you have some changes cognition wise, there may be mood changes, and some sexual dysfunction, to name a few. They've shown that lower levels of testosterone may be related to higher mortality.

You can replace people's testosterone, you can improve their bone density, you can improve their muscle mass, improve their sexual side effects with very few side effects. But, the reason people argue that this doesn't exist or "what's the point?" There's no proof that loss of testosterone will cause bone fractures. It probably doesn't prevent diabetes and heart attacks, mortality haven't changed. But there is a benefit, there's no question. It probably improves cardiac function but that's debatable. Your bad cholesterol tends to go down with testosterone and good cholesterol tends to not be affected. So you can give people testosterone with injections or pills or gells or you can wear a patch. We tend not to give this to anyone who has an active prostate or breast cancer. With prostate cancer, if you have the disease, we don't want to feed it. There are some potential side effects with it. People having benign disease, it may worsen that. People who have a bit of sleep apnea, it may worsen it. So, why not give testosterone replacement to everyone? There are two concerns. One is that people will bulk up with too much muscle but this doesn't happen. Two is that it may cause prostate cancer but that is not so. I think overall that testosterone is very important for our well being. Androgen Deprivation Therapy is certainly effective for treating prostate cancer. It does have a huge impact on the quality of life. There are many side effects due to the treatment but we have ways of coping with them. You should consider intermittent therapy because you're not going to change your quantity of life but you are going to improve your quality of life.

### *Doctors Jottings*

Discharge status: Alive but without permission

The patient refused an autopsy

She is numb from her toes down

When she fainted her eyes rolled around the room

Exam of Genitalia reveals that he is circus sized

The patient had a rash over his truck

# Hormone Therapy Shows Little Benefit Against Prostate Cancer

*Survival rates no different than “watchful waiting,” study shows*

*An increasingly common therapy used for localized prostate cancer may not bestow any survival benefits on the patient beyond those seen with a simple “wait-and-see” approach* By Amanda Gardner Tuesday, July 8 (HealthDay News).

Men taking androgen deprivation therapy, which shuts off male hormones that can promote tumor growth, even had a slightly *lower* prostate cancer-specific survival rate. “This might give pause, and probably should give pause to people thinking about using this approach,” said Dr. Robert Ennis, director of radiation oncology at St. Luke’s Roosevelt and Continuum Cancer Centers in New York City. “There’s always a gray area of patients. This might shift the balance.” But, Ennis added, “this is not an absolute, definitive, end-of-story type study.” The research, which is in the July 9 issue of the *Journal of the American Medical Association*, only looked at whether patients lived or died. There may be other outcomes of this therapy that would make it worthwhile, Ennis said. And androgen deprivation therapy has been shown to have a benefit in other scenarios, for example, when added to radiation therapy.

“This teaches us something about how we practice medicine, and it does give us reason for pause,” said Dr. Otis Brawley, chief medical officer of the American Cancer Society. “A lot of doctors give androgen deprivation therapy without any evidence that it’s a good thing for early-stage prostate cancer. One of the reasons we’re in such a quagmire on prostate cancer is so many doctors have practiced medicine not supporting the clinical trials but just treating it the way they think they ought to be treating it.”

“This is not the first research to show this. There are clinical trials out there that already suggest this is not beneficial, but people have done it anyway,” Brawley added. There is also evidence that androgen deprivation therapy can increase the risk of diabetes, stroke and death, among other things. “While it can be useful in a small number, it [can be] quite harmful and should not be used arbitrarily.”

“Prostate cancer is not as typical as some of other cancers. It grows at a slower pace, and it tends to occur in men that are elderly, so there a lot of other things going on like heart disease or lung disease or kidney disease or diabetes,”

explained study senior author Dr. Siu-Long Yao, a clinical assistant professor of medicine at the Cancer Institute of New Jersey in New Brunswick. “If you treat someone for prostate cancer, they could [still] drop dead from a heart attack. The key in this disease where it grows slower is prediction. Who’s going to drop dead of a heart attack and who’s going to have problems with prostate cancer. It leads to complexity. It’s a guessing game more so than in other cancers.”

Nowadays, however, more and more men, especially older men, are opting for primary androgen deprivation therapy (PADT) instead of the tried-and-true standards.

“A lot of men think surgery and radiation seem aggressive while observation seems like you’re doing nothing,” Yao said. “Men and their physicians have started looking for an alternative, which has become hormonal therapy. Use of [PADT] in this setting has grown tremendously in the last decade or two. It is the second most popular treatment [after surgery] but, in spite of that, nobody has really studied whether it works or not.”

Yao and his colleagues looked at 19,271 Medicare patients aged 66 and over, none of whom had received “definitive local therapy” such as surgery. Forty-one percent of the participants had received PADT for an average of 18 months; the rest had simply waited and watched. There was no increase in 10-year overall survival rates among men taking PADT compared with men undergoing conservative management. In fact, 19.9 percent of those taking PADT died of their prostate cancer within 10 years, compared with only 17.4 of those on the waiting approach.

A second study, this one presented at the European Society for Medical Oncology Lugano conference, found that the number of prostate tumor cells circulating in a patient’s bloodstream can predict how effective the treatment is. On average, the fewer the circulating tumor cells, said researchers from the Royal Marsden NHS Foundation Trust in the United Kingdom, the longer the survival.

## Speakers for our Fall 2008 meetings.

### Mark these dates on your calendar

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|----------------------------|--|
| September 18 <sup>th</sup> | Dr. Pdraig Warde. The new centre at Southlake          |
| October 16 <sup>th</sup>   | Dr. Shabbir Alibhai.TGH. Speaking on Osteoporosis      |
| November 20 <sup>th</sup>  | Dr. Loblaw. Timing of Hormones after treatment failure |
| December 18 <sup>th</sup>  | Christmas Party  |