Manitoba Prostate Cancer SUPPORT GROUP

Newsletter

**Vol. 282** 1,300 copies printed/e-mailed **January 2015**

# Hormonal Therapy - Systemic Therapy

Systemic therapies are medicines that circulate via the bloodstream throughout the whole body. The term systemic therapy encompasses various types of treatments including hormone treatment, immune treatments, chemotherapy, medicines to block angiogenesis, and injected radiation such as Xofigo.

**Testosterone Inactivating Pharmaceuticals (TIP) for Prostate Cancer**

Blocking testosterone is proven to prolong life in randomized prospective trials. Testosterone Inactivating Pharmaceuticals (TIP), otherwise known as androgen deprivation or hormone blockade consist of FDA approved medicines used either alone or with radiation to treat various stages of prostate cancer. Despite widespread experience, there are many controversies about the optimal way to use TIP. Probably the biggest issue is side effects. TIP impacts quality of life. So there is an art to picking the right amount of TIP for each individual. The goal is to give enough TIP to get the job done, without going overboard. The optimal methodology for using TIP varies from situation to situation because prostate cancer comes in a spectrum of "stages" ranging from low-risk which can be safely monitored, to metastatic castrate-resistant disease.

**Testosterone**

Testosterone is manufactured

*(Continued on page 2)*

## Medical Advisors

Paul Daeninck M.D.
Pain Management

Darrel Drachenberg
M.D. Urologist

Graham Glezerson
M.D. Urologist

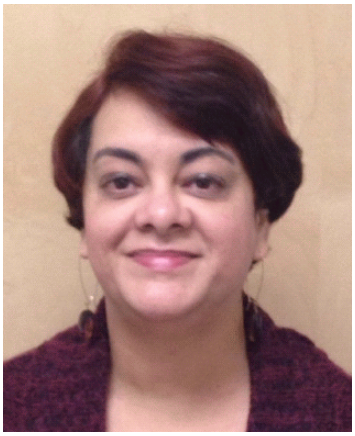
Ross MacMahon
M.D. Urologist

John Milner
M.D. Urologist

Jeff Sisler M.D.
Family Practitioner

*Thanks!*

**Next meeting**: January 15, 2015
Dr. Rashmi Koul, Radiation Oncologist
**Topic**: Prostate Cancer and Bone Health
**Location**: Main Floor Auditorium
Seven Oaks General Hospital
Leila and McPhillips
**Time**: 7 to 9 p.m.



SHARING IS CARING

*The Manitoba Prostate Cancer Support Group does not recommend treatment modalities, medications, or physicians.*

Thought of The Day

***A good time to keep your mouth shut is when you're in deep water!***

*(Continued from page 1)*

intracellularly from cholesterol and progesterone, mainly in the testicles. Dihydrotestosterone (DHT), a substantially more potent form of testosterone, is converted from testosterone by the enzyme 5-alpha reductase which is located in the prostate and the liver. Dehydroepiandosterone (DHEA) and androstenedione (ANDRO), weaker androgens, are synthesized in the adrenal glands, located above each kidney. The adrenal glands are where other common hormones such as cortisone and adrenaline are created. DHEA and ANDRO are synthesized from cholesterol and progesterone just like testosterone.

Prostate cancer cannot survive without testosterone. Prior to puberty the prostate gland is only a vestigial nubbin, but when the time comes it blossoms into a walnut sized gland to manufacture semen. After puberty, if testosterone is removed, the gland involutes and atrophies. Prostate cancer cells (which are derived from the prostate gland) also need testosterone to survive. Prostate cancer cells grow and proliferate when testosterone is present; they shrivel and die when testosterone is absent. When testosterone levels in the blood drop, the cancer cells "commit suicide" through a process called apoptosis.

**Testosterone Inactivating Pharmaceuticals**

There are different varieties of Testosterone Inactivating Pharmaceuticals (TIP). However, they fall into five categories. In the first category are the LHRH agonists such as Lupron, Zoladex, Eilgard, and Vantas. These medicines are administered by injection on a monthly, quarterly, semi-annual or yearly basis. They work by suppressing the pituitary gland (at the base of the brain) which in turn sends a suppressive hormonal signal to the testicles.

In the second category are the anti-androgens such as Casodex, Eulexin and Nilutamide. These pills work at the molecular level to block testosterone from reaching the androgen receptor (the switch in the cell that enhances cell growth when it's turned on).

In the third category are the 5-alpha-reductase inhibitors such as Proscar and Avodart. They work by blocking the conversion of testosterone into its more potent analogue, DHT.

Zytiga (abiraterone), the fourth type of hormone therapy, interrupts the pathway of biochemical synthesis of testosterone. Since it also blocks normal cortisone synthesis in the adrenal gland men on Zytiga should also receive prednisone. Ketoconazole also blocks testosterone synthesis. However, Ketoconazole is less potent than Zytiga. Ketoconazole can also cause a variety of troublesome side effects.

Xtandi is a totally new androgen receptor blocker. Like Casodex it blocks testosterone from activating the androgen receptor. However, unlike Casodex it also blocks the androgen receptor from getting into the cell nucleus and attaching to DNA.

**Combinations**

These medications can be used in combination to attain more complete testosterone suppression and thus increase the anti-cancer effect. However, urologists throughout the world more commonly employ single-drug therapy with LHRH agonists alone. This policy is rooted in studies done back in the 1990s that showed that anti-androgens added to LHRH agonists only enhanced survival by a couple months. Also many urologists at that time were concerned about the high cost of Casodex. Unfortunately, this policy of using LHRH agonists without Casodex persists, even though these days Casodex is generic and much more affordable.

Adding medicines from the third category, the 5-alpha reductase inhibitors like Proscar or Avodart, is often justified with the rationale that, "It can't hurt, and it might help." While using drugs from all three categories is popular in some circles, clinical studies are lacking. Studies do however confirm that Proscar and Avodart have some anti-cancer effects.

**TIP Added to Radiation Improves Survival**

The most convincing proof that TIP enhances survival comes from studies of men who are undergoing radiation. In the studies, men receiving little or no TIP are compared with men in whom TIP administered for a more prolonged period. The two groups are monitored over time to determine if one group has superior survival. Men receiving longer periods of TIP show consistently better survival. However, the optimal duration of TIP is still unknown. Treatment periods between 8 and 24 months are worthy of consideration. In our practice we often recommend 12-18 months depending on the individual characteristics of each patient.

Even without radiation, TIP as sole treatment effectively controls prostate cancer for many years. In a prospective trial in men with proven

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lymph node spread (stage D1), better long-term survival was seen when TIP was started immediately as compared to TIP initiated at the time of cancer progression. However, in another prospective trial with locally advanced prostate cancer (seminal vesicle invasion or stage T3b), better survival occurred when radiation was added to TIP, compared to men who were treated with TIP alone.

To summarize - when the disease is aggressive, TIP and radiation together appear best, but only up to a point. Once the disease becomes metastatic, TIP alone is considered standard. At the other end of the spectrum are the men with intermediate-risk disease. For the more "favorable type" of intermediate-risk disease, combination treatment is unnecessary. Men with this type of disease should be treated with a single treatment rather than a combination. Men with the more "unfavorable type" of intermediate-risk disease should consider combination treatment, but only with short-term TIP for four months.

**Casodex Monotherapy**

Traditionally, anti-androgen medications have been used in combination with LHRH agonists to block testosterone. When anti-androgens are used alone it is called anti-androgen monotherapy. This approach is attractive for some men because it causes in a milder degree of testosterone blockade with less side effects. There are three anti-androgen agents - Casodex, Flutamide, and Nilutamide. They work by keeping testosterone away from the androgen receptor, an enzymatic "switch" inside the prostate cancer cell. This switch stimulates cell growth when it's turned on. Anti-androgens keep the switch in the "off" position. Because anti-androgens do not eliminate testosterone altogether, they have fewer side effects than the LHRH agonists such as Lupron, Trelstar, Eligard and Zoladex.

Clinicians with experience using Casodex monotherapy estimate that Casodex monotherapy is about 70% as effective as the LHRH agonists but with only 30% of the toxicity. Anti-androgens have been studied in prospective randomized trials as stand-alone therapy and combined with radiation. Overall, compared to LHRH agonists, side effects are certainly less. And compared to placebo, they clearly retard prostate cancer growth. The only caveat with Casodex monotherapy is a higher risk of breast growth. This can be partially or completely prevented with prophylactic breast radiation or an estrogen blocking pill called Femara.

**Quality of Life**

Whenever the action of testosterone is inhibited, side effects ensue--hot flashes, osteoporosis, loss of muscle and loss of libido are typical. Many other side effects can also occur. Casodex monotherapy is less likely to induce muscle loss and less likely to reduce libido than the LHRH agonists. For example, only about 50% of younger men lose their libido whereas about 80% of men lose their libido with LHRH agonists.

There is one side effect that is more common with Casodex monotherapy than with LHRH agonists - breast enlargement. The medical term is gynecomastia. Gynecomastia occurs in 10% to 20% of men treated with LHRH agonists and in 50% to 60% of men on AAM. Gynecomastia can be prevented with radiation or an estrogen blocking pill called Femara. However, once breast tissue develops, it can only be removed with liposuction or surgery. To be effectively prevented, the radiation or the Femara must be started prior to starting treatment.

**Length of Life**

The attraction of Casodex monotherapy is fewer side effects. But to what degree do we sacrifice anti-cancer effectiveness and long-term survival? Studies performed to answer to this question have various flaws. For example, low-dose Casodex (50 mg daily) has been compared with LHRH agonists in men with advanced metastatic prostate cancer. Survival was shorter in men treated with low-dose Casodex compared to men who received Lupron or Zoladex.

Higher doses of Casodex (150 mg daily) have been compared with Zoladex, a LHRH agonist, in men with fairly advanced cancer that had not quite yet spread to the bones. After six years, men treated with Zoladex lived an average of six months longer than the men treated with Casodex 150 mg daily. However, the statisticians were concerned that there were an insufficient number of participants for the trial to be conclusive. Similar conclusions have been drawn from another study in men with advanced metastatic disease.

**Practical Considerations**

The side effects of Casodex monotherapy are less than with LHRH agonists. However, in regards to anti-cancer effectiveness, it is possible, even likely, that Casodex alone is somewhat less effective in controlling cancer than the LHRH agonists. LHRH agonists should be considered standard when cure is the goal. For example, when testosterone blockade is given in conjunction with surgery or radiation or when younger patients relapse soon after surgery or radiation with fast PSA doubling times. On the other hand, Casodex monotherapy is a good choice for older patients or men who are less tolerant of side effects and need milder treatment to maintain quality of life.

***Source:*** *Prostate Oncology Specialists*

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# Genomic Analysis of Prostate Cancer Indicates Best Course of Action After Surgery

PHILADELPHIA - July 29, 2014 - There is controversy over how best to treat patients after they've undergone surgery for prostate cancer, but a new study published in the *International Journal of Radiation Oncology, Biology, Physics* shows that a genomic tool can help doctors and patients make a more informed decision.

"We are moving away from treating everyone the same," said Robert Den, MD, Thomas Jefferson University, Philadelphia, Pennsylvania. "Genomic tools are letting us gauge which cancers are more aggressive and should be treated earlier with radiation, and which ones are unlikely to benefit from additional therapy."

Although surgery for prostate cancer is meant to be curative, in some men, the cancer can recur. Doctors have developed high-risk criteria based on clinical factors, but these criteria are imperfect predictors of recurrence. Only about 50% of high-risk patients ever go on to develop metastases, raising the question of whether those who receive additional therapy are being over-treated.

In an attempt to better understand how to treat their patient population, researchers assessed whether a genomic test designed to predict prostate cancer metastasis could also predict which patients would most benefit from radiation treatment after surgery.

The test, called Decipher, (see description below) generates a gene signature from a patient's cancer tissue sample. Based on this signature, the test stratifies patients into high, intermediate, or low risk for cancer recurrence and metastases.

The researchers tested the genomes from tumour samples of 139 patients who had received radiation therapy following prostate surgery at Jefferson. Using medical records, the researchers grouped the patients by the treatments they received after surgery, and matched their records to the results of the genomic analysis.

The genomic analysis correctly predicted outcomes. The patients with a high Decipher score were more likely to develop metastases than those with a low score. In addition, those with a high Decipher score who received radiation earlier had longer survival than those who did not receive radiation immediately after surgery. The results showed that patients treated with radiation after surgery maintained low prostate-specific antigen (PSA) levels for twice as long than those who were not treated with radiation.

"Our analysis suggests that genomic analysis scores could be used, in concert with other diagnostic measures such as PSA testing, to help determine which patients would benefit from additional radiation therapy and more aggressive measures, and which are less likely to benefit," said Dr. Den.

**About Decipher®**

The Decipher Prostate Cancer Classifier directly measures the biological risk of metastatic prostate cancer. By assessing the activity of multiple genomic markers associated with metastatic disease, Decipher provides information about the aggressiveness of a patient's tumor – information distinct from that provided by PSA and other clinical tools. Through an extensive program of clinical studies, Decipher continues to demonstrate its ability to more accurately distinguish metastatic disease and impact treatment decisions for men with prostate cancer.

**About GenomeDx**

GenomeDx Biosciences develops and commercializes genomic tests for prostate and other urologic cancers that impact treatment decision-making, improve patient outcomes and ultimately reduce healthcare costs. GenomeDx has developed the Decipher Prostate Cancer Classifier, the first and only commercially available genomic test that predicts the risk of developing metastatic prostate cancer independently of PSA and other conventional risk assessment tools. GenomeDx is based in San Diego, California and Vancouver, British Columbia.

***Source:*** *dgnews.docguide.com*

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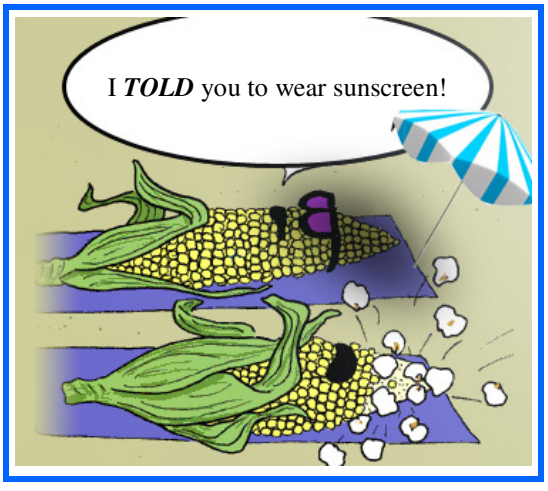

# Quality of Life After Standard Therapies for Localized Prostate Cancer

Assessment of patient quality of life (QoL) after standard forms of treatment for localized prostate cancer is difficult for many reasons — not least because there is no real agreement among members of the research community about the best ways to measure QoL or patient satisfaction after treatment.

What is very clear, however, is that relatively few patients are "satisfied" with their erectile/sexual function after standard forms of treatment — and this is a key driver behind the development of newer forms of treatment (such as the various forms of high-intensity focused ultrasound [HIFU] and focal forms of therapy).

A recent paper by Nicholaisen et al. (in the *Journal of Clinical Nursing*) looked, in considerable detail, at patient quality of life and satisfaction with information provided to a cohort of Norwegian patients at 3 to 4 years after three types of standard treatment: radical prostatectomy, radical external beam radiotherapy, and post-surgical radiotherapy.

The results of this study can be summarized as follows (and there are no real surprises associated with these results):

- The study cohort included 143 men, all treated at a single Norwegian hospital between January 2008 and December 2008 (and still alive in the autumn of 2011).
- QoL among these men at 3 to 4 years post-treatment is best described as "fair".
- QoL scores were generally very low with regard to sexual factors (regardless of treatment type).
- As a whole, the study population reported a lower overall QoL than similar men in the normal, healthy population.
- QoL factors affecting mental and physical summary domains appear to have an important impact on overall QoL regardless of treatment type.
- Patients receiving more information and detail about treatment and post-treatment effects before their treatment reported higher levels of satisfaction with the information provided and also reported high QoL scores.

The study confirms what many prostate cancer advocates have argued for many years … which is that many patients are under-informed about the potential consequences of prostate cancer treatment when they make the decision to have specific types of treatment. Regardless of what the treating physician may think that he (or she) has communicated to the patient, the fact is that all too often patients either haven't been given that information in a neutral manner, with full disclosure of the risks of treatment as compared to the benefits, ***or*** haven't really heard and absorbed that information.

The sexual function factor is a particularly important part of this equation because so many men define their quality of life (at least in part, and rightly or wrongly) by their personal perception of their own sexual potency and abilities. Failure on the part of the medical community to fully acknowledge this male trait, and therefore to avoid dealing honestly and accurately with the impact of prostate cancer treatment on erectile and sexual function can be devastating to many men and their families once the realities start to "sink in".

The "New" Prostate Cancer InfoLink is well aware that there are many physicians who do make considerable efforts to ensure that their patients understand the potential consequences of standard forms of treatment on erectile and sexual function. However, it is also all too clear that there are many physicians who make little to no efforts to do this. Worse still, there can be a tendency to brush the whole thing off and under-acknowledge the risks with statements like, "I expect most of my patients to be capable of intercourse within a few months post-surgery." The problem here is that whatever a physician may think he or she means by that, it certainly doesn't reflect reality.

Post-treatment quality of life for the vast majority of prostate cancer patients is going to be lower than it is for their otherwise healthy peers. How much

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lower may depend to a very large extent on: (a) the individual patient's ability to simply handle this type of adversity and (b) the expectations of the patient about quality of life post-treatment based on what he knows pre-treatment.

The "New" Prostate Cancer InfoLink would point out — yet again — that there is a moral and ethical obligation on the provider community to make the risks of prostate cancer treatment (of all types) very clear to patients. Failure to do this is one of the prime drivers of over-treatment. And while hoping for good, high-quality outcomes is certainly wise, acknowledging the reality that this only happens some of the time is probably even wiser.

***Source:*** *prostatecancerinfolink.net July 2014*

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## What Triggers Hot Flashes in Men?

*Channing J. Paller, M.D., Assistant Professor of Oncology at the Johns Hopkins University School of Medicine, talks about hot flashes, a common side effect of androgen deprivation therapy.*

One minute you're fine, but suddenly, and for the next few minutes, your head and neck heat up, your face turns red, and you're sweating -- perhaps profusely. You may even feel nauseated or anxious.

This complex of sensations, better known as hot flashes, or hot flushes, is familiar to most postmenopausal women, but the symptoms are a common side effect of androgen deprivation therapy (ADT) as well. In fact, up to 80 percent of men receiving ADT for prostate cancer report having hot flashes during treatment, and the symptoms may continue for months to years after ADT ends.

These hot flushing episodes include feelings of increased warmth in the upper body and face; the skin may also redden, and sweating is common. Hot flashes occur for no discernible reason, and may last for just seconds, but for many men they continue for several minutes. For some, the incidence of hot flashes decreases over time but, unfortunately, in other patients the flushing continues unabated for years.

**What triggers hot flashes?** For some, it's the second glass of red wine that brings on a hot flash. For others, it's a rise in blood pressure, that third cup of coffee, taking a hot shower, smoking, or vigorous exercise that can cause the bothersome flushes.

**Keep a journal.** To see if you have predictable triggers for your hot flashes, keep a notebook handy and record when the flash occurs and what you were doing at the time. Knowing the particular trigger(s) will allow you to better manage the flashes and take appropriate steps to possibly reduce their incidence and severity.

***Source:*** *Johns Hopkins Health Alerts*

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Pictured above are members of the Campfire Junkies who entertained us at our Pot Luck Christmas party on Nov. 20th. The Junkies had everyone clapping and singing along for over an hour. It was indeed a lively and fun evening.

Everyone enjoyed the goodies on the food tables – thanks to the many donors. Special thanks to **Liz and Pat Feschuk** for their organization and planning of this event. Liz makes the world's best meatballs!

Thanks to **Irene Schade** for sharing her photo of the band. The performing members of the Campfire Junkies were **Mark Galbon** (leader), Sheila Hawkes, Bev Self, Khandias Carewick, Sheila Tagesen, Leona Rawluk, Bruce Mazur, Jim Walld, John Janzen, Henry Kliewer, Daryl Weremy, Bruce Penner, Teresa Beauregard, Karen Thomas, and Paul Sinclair.

# PCa Treatment Ups Heart-Related Deaths

**Androgen deprivation therapy, which lowers hormones in the body, could lead to death in men who already have heart problems. 'For men with significant heart problems, we should try to avoid ADT when it is not necessary,' one researcher said.**

Some treatments for prostate cancer may do more harm than good.

Androgen deprivation therapy is linked a higher risk of death from heart-related causes in men with heart problems, according to a new Boston-based study.

Researchers from the Dana-Farber/ Brigham and Women's Cancer Center and Harvard Medical School analyzed 5,077 men with prostate cancer — 30% who received this type of treatment and 70% who didn't.

Androgen deprivation therapy, a common way to treat prostate cancer, lowers the amount of male hormones in the body so that they don't spur cancer cells. But it's been known to lead to heart problems, such as heart attacks and sudden cardiac death. The researchers wanted to investigate this link.

After a five-year follow-up, there was no risk found between ADT and heart problems in men without heart risk factors. But there was three times the risk of heart-related deaths in men who had previous risk factors.

Still, the actual number of deaths was small: 7% of men who got ADT vs. 2% who did not.

"I would still say that for men with significant heart problems, we should try to avoid ADT when it is not necessary — such as for men with low-risk disease or men receiving ADT only to shrink the prostate prior to radiation," said study author Paul Nguyen of the Dana-Farber/ Brigham and Women's Cancer Center. "However, for men with high-risk disease, in whom the prostate-cancer benefits of ADT likely outweigh any potential cardiac harms, ADT should be given even if they have heart problems, but the patient should be followed closely by a cardiologist to ensure that he is being carefully watched and optimized from a cardiac perspective."

Source: *nydailynews.com* October 2014

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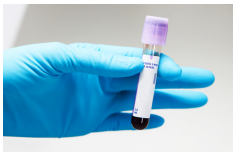
# The Manitoba Prostate Cancer Support Group Supports PSA Testing

The Manitoba Prostate Cancer Support Group (MPCSG) would like to respond to the recent guidelines released from the Canadian Task Force on Preventive Health Care (CTFPHC) recommending that the Prostate Specific Antigen (PSA) test should be eliminated as a screening tool for prostate cancer.



The MPCSG strongly disagree with these guidelines. When performed on a regular basis, the benefit of the PSA as a screening tool can go as far as directly saving lives.

Most men with prostate cancer have an increased level of PSA in the blood. It is sometimes the case that PSA levels can be high when actually there is no cancer present. Conversely, men can have low PSA levels yet have a significant amount of prostate cancer. Rising PSA levels have been clearly shown to indicate cancer growth. For this reason, we recommend that all men over the age of 40 be tested for prostate cancer to create a baseline PSA number.

We have consistently been telling men how important it is to get a "baseline number" in their medical file, so their family doctors have a comparative measure with subsequent PSA tests. This allows men to be properly monitored and any changes to be duly noted. Knowing and tracking their PSA level helps men take a proactive step in fighting this disease. Without the availability of the test, men would be unaware of any change in their PSA level.

We encourage all men and their loved ones to speak out against these recommendations and insist on their rights to make choices based on informed decision-making.

The **PSA test may not be perfect** but it is the best indicator in clinical practice today and an important red flag to show that something **may** be wrong.

*Editor's Note: The full CTFPHC report can be read on the internet.*

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Winnipeg R3M 3S7

Publications Agreement
# 40037332

The Manitoba Prostate Cancer Support Group has been providing services for 20 years:
**Newsletter – Website - Monthly Meetings - Hospital visits - Presentations**
Your **DONATIONS** make it all possible. **We Thank You.**

Donor's Name: _____
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*A tax deductible receipt will be issued. Charity number: 88907 1882 RR0001
*Credit card donations can be made by going to our website at* www.manpros.org *and clicking on the* donate *tab. Canada Helps will issue a tax receipt.*

# *Many Thanks*

**The Canadian Bridge Federation Charitable Foundation** has recently made a generous donation to our Support Group. The CBF disperses money raised each year by the Canadian Bridge Club players to various charities.

We appreciate that they have considered us as worthy recipients again this year. We would like to express our gratitude for their recognition of the work that we do in the community.

Many thanks to all the bridge players for their kindness.

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Email - manpros@mts.net ALL MEMBER INFORMATION IS KEPT CONFIDENTIAL
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**Receive this newsletter by email ~ Please notify us and we'll make the changes.** ***Thank-you***

## 2015 MEETINGS

**January 15** ..... Dr. Rashmi Koul
– Head of Radiation Oncology, CancerCare Manitoba
Topic: "Prostate Cancer & Bone Health".
**February 19** ..... Bill Martin – Gimli author
Topic: "Ripped Out: One Man's Journey Surviving Prostate Cancer".
**March 19** ..... TBA
**April 16** ..... Dr. Sabeer Rehsia, Urologist.
**May 21** ..... TBA
**June 18** ..... TBA
**July** ..... NO MEETING
**August 20** ..... TBA
**September** ..... Prostate Cancer Awareness Evening
– Caboto Centre – 1055 Wilkes Ave.
**October 15** ..... Kelli Berzuk
– Incontinence & pelvic Pain Clinic
**November 19** ... Christmas Pot Luck Party
**December** ..... NO MEETING

All meetings are held at
Seven Oaks General Hospital Auditorium
7-9 p.m.
Everyone welcome

## MPCSG BOARD

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