

CANADIAN PROSTATE CANCER SUPPORT GROUP

Newmarket, Ontario

Volume 13, Issue 3, November 15th, 2008

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

Dr. Hans T. Chung of the Sunnybrook Odette Cancer Centre will be our speaker for the November 20 meeting. He is an Assistant Professor, Department of Radiation Oncology, University of Toronto. Dr. Chung joined Sunnybrook Health Sciences Centre in September 2008 specializing in prostate cancer and gastrointestinal cancer, especially external-beam radiotherapy and prostate brachytherapy. Before coming to Sunnybrook, he worked for 3 years as a Consultant in Singapore, where he set up a prostate brachytherapy program and a prostate IMRT program. Come and get an update on the latest developments on these treatments.

Meeting Date: November 20th, 2008

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

Time: 7:00 to 9:00 pm

Speaker: Dr. Hans T. Chung, Sunnybrook Health Sciences Centre

Subject: Brachytherapy and IMRT

Canadian Prostate Cancer Support Group,
Newmarket, Ontario. 905-830-0447
a member of the



Canadian Prostate Cancer Network

Assisted by the Canadian Cancer Society
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The Newmarket Prostate Cancer Support Group does not recommend products, treatment modalities, medications, or physicians. All information is, however, freely shared.

September Speaker notes **Dr. Shabbir Alibhai, Toronto General Hospital.**

Subject: Osteoporosis

Dr. Shabbir Alibhai our speaker for the November 20 meeting talked about the potential side effects hormone treatments have on Osteoporosis, He specializes in geriatric oncology, with a primary focus in prostate cancer. His major research projects include examining the impact of androgen deprivation therapy on health outcomes (including quality of life, physical function, cognitive function, and bone mineral density). Here is what he had to say



I am a geriatrician. My focus is on prostate cancer and more broadly, cancer in older adults. I'm particularly interested in how cancer and its treatment effects the older person and how we can minimize the impact of cancer and its treatment and all the negative things it might do to older people. I was asked to spend

some time talking about osteoporosis, particularly with regards to men with prostate cancer who are on hormone therapy.

I'll talk first about what osteoporosis is. The causes of osteoporosis, particularly in men. There are differences, obviously, between men and women in terms of how their bones age and what the impact of different things, such as hormones, might do to bones, depending on one's gender. I'll spend a few minutes reminding those of you who are not familiar with Androgen Deprivation Therapy, what exactly it is, how it works and why it has implications for the bones. We'll then talk a little bit about how to diagnose osteoporosis and then how to prevent it and then how to treat it.

So, what is osteoporosis? It's a bone disease. It's characterized by a couple of key features. There is loss of bone mass and there is deterioration of the bone architecture or the skeleton of the bone. The bones over time become weak and brittle, instead of being nice and strong and firm. If you think of a piece of wood starting to rot from inside, it's much easier to crack. Up to one in four women over the age of 50 will develop osteoporosis and up to one in eight men. So, it's common and, unfortunately, until one gets their first fracture, it is a completely silent disease. You will have no symptoms. If you have back pain or leg pain and so on, that's not osteoporosis, that's arthritis or other things but osteoporosis is silent until your first fracture, unless it's picked up by special screening tests. As your bone density drops, as you get more severe osteoporosis, the risk of fracture keeps going up. One thinks about bone both in terms of density of the bone, how much bone there is per cubic millimetre or centimetre, for example, and also the quality of the bone — can it withstand the weight that we put on it every day or the weight that might be transferred onto it if we have a fall? As the osteoporosis progresses, the bone becomes more porous, or holey. That's, of course, a problem, because the more porous the bone be-

comes the more likely that even a small injury or force applied to it by a fall, can lead to fracture. In severe enough osteoporosis, I have patients who fracture when they sneeze, it can get that bad, or when they roll over in bed, they occasionally end up fracturing. It can be severe and it can be very uncomfortable. Bone strength includes both the quality of the bone and the density. I'm going to spend most of the rest of the time when I talk about bones, about bone density because that's easier for us to measure. The big black box in osteoporosis is how to understand how to measure bone quality because we need to understand how to measure the turnover of the bone. (Bone is always remodeling, there's new bone coming, there's old bone going and it's a dynamic process. Bone isn't dead, it's full of life and things move around and reshape every day.) But architectural bone and the damage that it accumulates and how the calcium gets into the bone and leaches out of the bone and associated proteins, all of these things impact on bone quality independent of bone density. We're very good at measuring bone density. We have a lot more to learn about how to measure bone quality. Nevertheless, we do know some important things about bones and how to prevent and how to treat osteoporosis but the focus is on bone density, not bone quality.

The typical image of osteoporosis is of the dowagers hump but osteoporosis is not just a disease of older women. One in eight older men will have the disease and that increases for men on hormone therapy. As people get older, the risk of fracture goes up. For any given age women seem to have a higher risk of fracture than men, but as men get older, they start to catch up, particularly when you get into your 70s or 80s, the risk really starts to rise for hip and spine fractures. That's for all men, not just men with prostate cancer and hormone treatment. Now, besides hormones, there are other things that can cause osteoporosis in men. In particular, roughly half the cases of osteoporosis in men will be from aging or unknown causes. Steroids that people may take, like prednisone, or drugs like it, can cause a significant proportion of cases of osteoporosis. Low levels of male sex hormones, which can be caused by Androgen Deprivation Therapy (ADT), can lead to male osteoporosis. For half the patients, it's due to aging or unknown factors, and almost one in four is due to hypogonadism (lack of male hormones), primarily from hormone therapy and that's going up. There are other risk factors. I already mentioned that age is a risk factor; family history, particularly in women, increases the risk if there's a history in your family; a low calcium diet, lack of exercise; a low

body weight again, particularly in women, the magic number is about 45 kg or 99 lbs; smoking over many years; a high caffeine intake; and, of course, hormone deficiencies, particularly low testosterone from drugs like ADT and then some other medications and illnesses. So, there are a number of risk factors. They can, of course, combine. The more risk factors you have, the more you should really be checking your bones and paying attention.

How do these male sex hormones impact on bone, anyways? Well, men have higher levels of androgens, or male sex hormones, like testosterone and by the time they reach the age of 18, they already have a higher peak bone mass. This means that their bones are stronger by the time they reach that age, they tend to have more muscles as well, simply because of their testosterone being a major factor. The periosteal bone, meaning around the actual edge of the bone, tends to be stimulated by male sex hormones, tends to be built up faster and, if you don't have enough androgens, then you tend to get a reduction in the height or the width of the vertebrae, or the spine bones, and you tend to get a reduction in the femoral neck, which is part of your hip (if they have a hip fracture, these men tend to have lower male hormones) and, where the bones are constantly changing at the level of the actual cells that are remodelling the bone every day, you tend to have less bone formation when you don't have enough testosterone on board. So testosterone plays a role. Just as important, or maybe more important, it's still not really appreciated but estrogen, or the female sex hormone, in fact plays a bigger role in male osteoporosis and male bone formation than testosterone. People don't appreciate that, many physicians don't appreciate that but, in fact, it's a major determinant of your peak bone mass and you really need both. The double whammy of hormone therapy is that, not only does it lower your male sex hormones, it also tends to lower your estrogen levels a little bit. So it accelerates bone loss through affecting both pathways. The exact mechanisms of how estrogen helps the bones isn't that important but I want to point out that both androgens and estrogens help the bone.

ADT or hormonal therapy reduces levels of these androgens, brings them down to virtually unmeasurable levels. Why do we use it? Because androgens stimulate the prostate cells, help them to grow. They are nutrition for the prostate cells. If you can block the androgens, prostate cells shrink – both benign prostate cells but, more importantly, prostate cancer cells will stop their growth. So ADT is part of the routine management of many men who have prostate cancer. It's used in combination with radiation or surgery. We also know that if you start to get that annoying rise in PSA after radiation or surgery, some men are put on hormones to try to prevent the spread of the disease to the bones. If you already have spread of the disease to the bones, or (metastases), hormone therapy, if you've never been on it, helps to slow down spread of the disease further, also improves symptoms such as pain and energy in those men who have metastatic prostate cancer. Hormones don't work forever but they can often work for years

to slow down the growth of prostate cells. The major methods of doing this either involve orchiectomy, which is surgical removal of the testicles, which is rarely done in North America any more or the majority get it through injections of drugs that are called agonists, also called LHRH agonists. Injections may be once a month or up to every six months. The injections block the levels of the hormone in your body that stimulates testosterone and the levels go down, almost the exact same as if you had surgery to remove the testicles. They are used in the vast majority of men who get hormone therapy now in North America, sometimes in combination with a pill. In the United States today, if you are diagnosed with prostate cancer, you have about a 50% chance before you die of getting exposed to hormones. Probably half the men diagnosed with prostate cancer will be put on hormones so it's extraordinarily common and you all know how common prostate cancer is. So lots and lots of men are on hormone therapy – there are at least 500,00 men in the United States who are on hormone therapy right now. In Canada, we're not that much farther behind.

Men and women, by the time you reach your early to mid thirties you have reached your peak bone mass. In women, there is a rapid drop because of menopause when you lose estrogen and we know estrogen is needed for bones, so osteoporosis is much more common in women after menopause. In men, it's a little bit different because we don't have the same kind of andropause that is abrupt. We have a peak in bone mass and we get a slow but steady decline in bone density once we reach about the age of 40, all the way until we die. There is nothing that we can do to stop that in terms of the aging phenomena itself. There are things we can do to stop it in terms of preventative therapies, like calcium. Aging alone is responsible for the majority of bone density decline. But, if you're on hormone therapy, there is a significant acceleration of the drop in bone density.

Let's look at how we make the diagnosis of osteoporosis. Most people do not have symptoms at the time they are diagnosed unless they've already had a fracture. It's a silent disease until your first event and the problem is, the first event can be quite traumatic. If you have a hip fracture, 50% of men or women, within one year of a hip fracture will be dead or permanently disabled. So these fractures can be very serious. The usual guidelines to screen people who have no symptoms for osteoporosis are: if you're over the age of 65; if you have a history of one or more wrist, spine or hip fractures, particularly after the age of 50 because then it's likely to be a non-traumatic, low trauma fragility type fracture (which means that your bones are weak and you didn't fall skiing but you fell to the ground, less energy fractures so the bones are probably weaker); if there's a family history of osteoporosis or if have other risk factors— if you are a smoker (shame on you if you are), if you have a life long low calcium diet because you have irritable bowel or some problem with absorption; lots of different factors increase the risk.

The screening test to pick up osteoporosis, at least in

North America for most people, is a bone density. I encourage you to ask your doctor to sit down with the printout of the test and go over it with you. The printout gives you a number called a T score and a Z score. The bottom line is, the numbers you need to know are the T score. It's a number that says what's your bone density like relative to the average young adult. Not people your age, because if everybody your age has osteoporosis, it's no good being just as bad as everyone else. You want to compare to what you should have been, if you could have preserved yourself from when you were 30 up until whatever age you are now. As you get older, your bones will decline but the T score helps you to know how bad is the decline. The World Health Organization has given us some numbers to try to put things in context. If your T score is -1.0 or higher, so it could be 0, +1, +2 because it's relative to a young adult peak bone mass, then you're fine. You have normal bone density, your risk of fracture is low. If your T score is between -1 and -2.5 you have what we call osteopenia. Nowadays, in fact, many people are moving this number down to -2.0 and if you're lower than that they're saying that's higher risk. If you have had a fracture that is low trauma fragility type with that horrible T score, you are called severe osteoporosis, as if mild osteoporosis is a good thing to have anyways. If you're on androgen deprivation, what happens to your bones? Looking at men who do not have androgen deprivation therapy your bone density will go down on average about 1%, maximum 2%, a year. Men who are on androgen deprivation therapy will go down more in all the test areas. The longer you're on ADT, the lower your bone density – the more your bones decline in terms of their strength. The first one to two years is the worst, then things decline a little less but continue to decline and it affects every single bone in the body, including your teeth. Some bones are much more prone to acting up with fractures than others. So although almost every bone can be affected, those bones that are responsible for carrying a lot of your weight or being involved in a lot of activity, your arms or legs or spine, they tend to be affected more and to decline more.

Several studies have shown that men on all kinds of Androgen Deprivation Therapy are much more likely to have significant loss in bone density and many more fractures. In one very large study, we looked at 20,000 men in Ontario over 12 years. We found that men with prostate cancer who were on hormone therapy showed an increased risk of having a fracture over those who were not on hormones. 6 1/2 years later, 17% of men on ADT have had a fracture, compared to 12.7% of controls. It's not a huge difference but, what it means is that, for every 20 men or so who are on hormone therapy, one or more of them will fracture. This data from many studies show that the risk with ADT is real. It's not just a numbers game, it's not just pretty X-rays, it impacts on fracture risk. The other frightening thing is that, not only does osteoporosis affect every bone but a study looked at 19 different sites in the body and every single site had a greater risk of damage in hormone users. Even the skull, as hard as it

is to skull fracture, every single part of the body, the hands, the fingers, the forearm, the shoulder, the back, the hip, every single bone they looked at they had extra risk. It's a very wide spread phenomena. Now you have to consider a trade-off if you're taking hormones to lower your PSA. This is the part of medicine we hate. What you have to decide, you and your prostate doctor, is, how high is the risk of getting progressive disease from the prostate cancer versus how high is the risk of breaking a bone? More importantly, are there other risk factors for your bones that you should know about that might impact on the risk of the hormones and what is your bone density? Because that's obviously a major question. If you start off with osteoporosis versus starting off with normal bones, you are in a very different situation in terms of the risk of fracture. In order to answer that, you have to look at what is the stage of your cancer, what is your bone density and what other risk factors do you have for osteoporosis? Then you and your doctor could have a better discussion. It's not just choosing one or the other because we do have therapies which can preserve bone in men who are on hormone therapy. It's not that everyone's going to get osteoporosis and wither away and die. We have therapies that can slow down or even reverse the bone loss of ADT. It's just you need to be aware of them and we need to advocate and use them where appropriate. There is hope because they're looking at intermittent therapy instead of continuous in major trials and also there are new osteoporosis drugs that are being studied that are looking at agents to reduce the risk of fracture. For some it is an issue of survival. You will live longer on hormone therapy but we're just trying to help you live better.

If you are on hormone therapy, our guidelines tell us that you should be aware that one of the side effects is bone density loss and a greater risk of fragility fractures and osteoporosis among the 50 other side effects of ADT. For example, in a study we looked at the practices of urologists and oncologists in Princess Margaret and other cancer centres in Ontario who had put men on hormones, because all of the men in my study did not have metastases. We found that the rates of men being told within six months of starting hormone therapy that there is a risk of bone side effects, even as general as that, was less than 25%. People just weren't being told and this was just last year, it's not exactly old data. It's not just the community doctors, it's also in the big city centres, we still have a long way to go. It's still only a minority of doctors who are discussing this issue with their patients.

Let's take a look at prevention. In terms of prevention, the standard recommendations are that everybody should be doing some things in diet; some lifestyle changes; and then we can talk about drugs. In terms of diet, calcium is one of the first things and it's not something that you should be starting now, you should have started it when you were six. The earlier you start, the better for you. Unfortunately, most young women and young men, your children and grandchildren, are not getting enough calcium in their diets and the earlier you start, the better to achieve peak bone mass. Once you achieve

peak bone mass, it's downhill from there. Calcium, however, even in your 50s, 60s and 70s will help to slow down bone loss, so it's important to get enough in your diet. The rule of thumb is about 1,000 mg. minimum in your diet, preferably 1500 mg. of elemental calcium. That's the actual calcium, not the calcium combined with a salt for absorption, so it's the actual calcium stuff that you need. If you have a glass of milk, it's got about 300 mg. of calcium in it, which means you should be drinking 3 1/3 glasses of milk every day, which is difficult for many people to do. Or, 2/3 cup yogurt, or 50 g of cheese or even a scoop of icecream. Any of those will give you 300 mg. of elemental calcium, so you need to have more than one of these more than once a day. There are other options, you can go to kale and other things to get your calcium, these seem to be the best sources for most people. You can get it from canned salmon and sardines. If milk bothers your stomach, there are three easy options which will help the vast majority of people: soy milk, lactase containing tablets and lactose free milk. Most people who are intolerant of lactose, can still tolerate one glass of lactose containing milk without a problem. Even though they think they can't.

Vitamin D, the second option in terms of diet. Vitamin D is probably two to three times more important than calcium these days, in terms of trying to help your bones. Vitamin D has a reputation these days as being good for all kinds of things, it helps alzheimers, it helps cancer, it helps your bones, your heart, your muscles and the list goes on and on, it's incredible. Many of these are really based on good evidence. Before the age of 65, everybody should be getting at least 400 units of Vitamin D. Some people are now recommending higher. If you are over the age of 65, everybody should be getting 800 to 1,000 units of Vitamin D a day. Some experts are now recommending 2,000 units, which is very difficult to achieve in the diet, especially if you don't live in places like Florida. You can get Vitamin D in food, there's not that many easy sources in food but your body makes it when you're exposed to sunlight. The problem is, we don't get a lot of sunlight in winter. The other problem is, when you get older, your body is less efficient at making Vitamin D, even if you do get sunlight. So, if you get 30 minutes of sunlight at the age of 50, once a day, you will be able to make anywhere from 2,000 to 10,000 units of Vitamin D. Sunlight's great but be careful not to put on too much sunscreen because you block out the Vitamin D. However, if you don't put on enough sunscreen, you might get sun burn on your skin and get a skin cancer. It's a difficult trade off. However, windows block out about anywhere from 30 to 90% of the actual sunlight that helps you make Vitamin D. Many dairy products come fortified and some orange juice. In terms of lifestyle: **STOP SMOKING!** Those of you who have never smoked, good for you. For those of you who did smoke and stopped, that's still excellent. Within one to seven years most of your risks will drop to that of a non-smoker and, if you're still smoking, you still have hope. Regular exercise is also helpful in terms of walking two to three times a week, 25 to 30

minutes a day. More important, however, is light weight lifting if your bones will allow it. By light weights, anything from 5 to 20 lb weights are sufficient. Ten repetitions, two to three times a day is enough, a couple of days a week, to get your bones stimulated to be able to get stronger. Cutting down caffeine intake to about two, maximum three cups a day if you're getting caffeinated products, either coffee, tea or colas will also be useful in terms of helping your bones, because caffeine and some of the other chemicals in coffee and tea particularly, leach calcium out of your bones. So it's not good for you. Particularly tea, there are phytates and tannins in tea that help leach calcium out of your bones.

Then, of course, there are medications. For those of us who cannot get enough calcium in the diet, there are lots of calcium tablets out there in various forms. This is where things get a little tricky. Calcium comes attached to a salt, to be able to turn it into a tablet that you can swallow. In the body, it breaks down and the calcium floats around by itself in little ions. In the food or in the pills, it comes attached to a salt. Calcium carbonate is the most common one, that's what chalk is made out of and many of you who take tablets, know that they taste like chalk, because, literally you are eating chalk, so enjoy it. Roughly 40% of the calcium carbonate is elemental calcium. Remember you need 1,000 mg. of elemental calcium, not the calcium carbonate. So, if you had a 625 mg. tablet of calcium carbonate, which is the typical one on the market, you're getting 250 mg. of elemental calcium, just under one glass of milk. So you need to be taking three of those tablets a day at a minimum, if you cannot take milk or other dairy products. Take with meals for better absorption. There are easier forms of calcium to swallow, if you can't swallow the calcium carbonate, you could chew Tums. Calcium Citrate is easier to absorb. Taking calcium with Vitamin C may make it easier on the stomach to absorb. You can get liquid forms of calcium or fizzy tablets. Beyond the calcium, of course, you can also get Vitamin D, either in a multiple vitamin supplement or you can get separate Vitamin D tablets. Be aware that most multivitamin supplements contain only 400 units of vitamin D a day, so you would need to take two of those and there are a lot of other minerals and vitamins in there that you probably don't want to take too much of, so check with your pharmacist to see if it's O.K. to take two of them. Otherwise you may take one multivitamin and one Vitamin D at 400 or 600 units. It's better to take your Vitamin D with a meal for better absorption.

What about prescription drugs to prevent osteoporosis in men who are on ADT? The trials that have been done have not been finished. The large studies that are looking at prevention are still going on. The small studies have shown that you can slow down and you can improve bone density for sure in these men who are on these drugs but the studies are primarily focussed on men who already have osteopenia or osteoporosis. At the moment, the benefits are uncertain if you have normal bone density to start with. Most experts don't suggest that you start taking these drugs for prevention.

Curry Fights Prostate Cancer

Ladies, if you love your man, give him cauliflower curry with a side of kale for dinner. It may stave off prostate cancer, according to research released by Rutgers University.

Though they don't often make the favorite menus of most men, cauliflower and kale — along with cabbage, broccoli, brussels sprouts, kohlrabi, watercress and turnips — contain a chemical that is a significant cancer-preventive.

But add curry powder to the mix, the researchers say, and the vegetables and spice are effective in treating established prostate cancers.

It all boils down to a pair of crucial chemicals that “hold real potential for the treatment and prevention of prostate cancer,” the Rutgers study stated. The vegetables contain phenethyl isothiocyanate, or PEITC, while the curry contains curcumin, a yellow pigment found in the spice itself. Both are considered phytochemicals — nonnutritive substances in plants that have protective, antioxidant or anti-disease qualities.

The bottom line is that PEITC and curcumin, alone or in combination, demonstrate significant cancer-preventive qualities in lab mice, and the combination of PEITC and curcumin could be effective in treating established prostate cancers,” said Ah-Ng Tony Kong, the study's lead author and

a professor of pharmaceuticals at Rutgers.

While prostate cancer is common in the U.S., the disease is rare in India, where plant-based diets and curry are the norm. Curry itself has prompted other significant findings. The University of Texas found it inhibited the growth of both skin cancer and breast cancer cells, while the University of California at Los Angeles found it stopped the spread of harmful brain plaque in patients with Alzheimer's disease.

Mr. Kong had previously found convincing evidence, he said, that the two chemical compounds quelled prostate cancer cells grown in the laboratory. He has since tested his theory on mice injected with the cancer cells. Three times a week for a month, the test mice then received injections of PEITC and curcumin. Separately, the compounds “significantly retarded the growth of cancerous tumors, Using PEITC and curcumin in tandem produced even stronger effects.” The research team also evaluated therapeutic potential of the compounds in mice with advanced prostate cancer to find they “significantly reduced tumor growth.”

The study was published by Cancer Research, a journal of the Philadelphia-based American Association for Cancer Research.

When to wait and when to treat? program will search for biomarkers to help find an answer

Researchers at Fred Hutchinson Cancer Research Center have a lead role in a new public/private partnership creating the first systematic surveillance program of men with prostate cancer to look for biological clues to help determine when to wait and when to treat the disease. They are enrolling men in a cancer-surveillance study to look for biomarkers — proteins in the blood that could predict prostate-tumor aggressiveness.

The study is meant to help answer a key question that has vexed physicians and researchers: "When is it best to treat prostate cancer versus observation or “watchful waiting” For most men with prostate cancer, the disease never progresses to become a serious health problem, yet most receive some sort of treatment, such as radiation or surgery. Such treatments can have side effects, such as impotence and incontinence, which can be worse than the low-grade cancer. Currently it is challenging to accurately predict when inactive or slow-growing prostate tumors will become aggressive.

“There's an emerging consensus that we dramatically over treat prostate cancer in general,” said Nelson. “The overall prevalence of the disease in the population

far exceeds the number of men whose disease progresses to cause serious problems. Yet, there are clearly many prostate cancers that behave aggressively and patients benefit from treatment. It is a challenging problem.”

In the study, men diagnosed with early-stage prostate cancer are not treated right away but are closely followed in an active surveillance program involving regular collection of blood and urine samples as well as prostate biopsies. A new repository for blood and DNA samples is located at the Hutchinson Center.

The samples will be tested for candidate biomarkers — proteins in the blood — that can signal when indolent disease has progressed to more aggressive illness. Such biomarkers could help physicians better determine when to initiate treatment versus watchful waiting.

Each of the study institutions also has a “retrospective” tissue collection of samples taken from unrelated studies. These will also be examined to ascertain the accuracy of predictive biomarkers.

“Through collaboration we can make bigger strides in providing better, more individualized treatment for prostate-cancer patients.”