Prostate Cancer Canada Network - NEWMARKET

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

Our speaker for the March meeting is Dr. Susanne Chan, MD, FRCPC. She is a staff pathologist at Southlake Regional Health Centre. In her presentation, she'll take you through the steps involved in making a diagnosis of prostate cancer. This includes the initial processing of the prostate tissue in the laboratory, the diagnosis of prostate cancer and how it's reported. Much of the presentation will be spent explaining report elements such as Gleason grading, extraprostatic extension, positive margin etc.. Please take this opportunity to learn more about how your prostate cancer was diagnosed.

Meeting Date: March 19th, 2014

Place: **Newmarket Seniors Meeting Place,**
474 Davis Drive, Newmarket (Side Entrance)

Time: **6:30 pm to 9:00 pm**

Speaker **Dr. Susanne Chan, Pathologist at Southlake**

Subject: **How your cancer is diagnosed and graded.**

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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.

February Notes . . . Speaker Dr. Yasmin Rahim Hematologist & Oncologist

Her Comments on PSA, Watchful Waiting and Active Surveillance

One of the first comments Yasmin made was asking us to interact with her. If there was something we didn't understand, to stop her and ask a question. She started off tackling the questions, What is PSA? What is the significance of it? What is its roll in screening? Dr. Rahim relied very heavily on her Powerpoint presentation and referred often to graphics on the screen.

The prostate gland, just like any other gland in any other part of the body, has two sections. One is the gland, and the other is the duct. The cells in the gland secrete this glycol protein which is called prostate specific antigen (PSA), This is secreted mainly inside the gland but part of it may escape into the blood, which is what we measure in a blood test for PSA.

Prostate cancer is the biggest cause of cancer in men. 22,300, compared to 12,000 in a year that would have lung cancer and about 11,000 of colorectal cancer. Even though the number of cases diagnosed in a year is so much higher for prostate cancer, the death rate is only 4,000. Of 24,000 (men and women) diagnosed with lung cancer, 19,000 die. It's really a deadly disease, whereas prostate cancer can go on for years and years. People actually die of other causes rather than of prostate cancer itself.

Having a very useful test like PSA, the automatic thought was, "This is a good test, we can screen people and can detect the cancer early and that's exactly what happened in the 1990s. When this test was developed, the whole idea was that people who already had prostate cancer could take this test and then we could monitor them after the treatment, to follow up if the prostate cancer was coming back or, even if it's back. It was a good way to screen it and monitor how they were responding to treatment or not. The rationale for any kind of screening for any kind of cancer or any disease is first of all that cancer has to have a high incidence over a good chunk of the population. On average, Canadian men have a lifetime risk of prostate cancer of about 14.3%. Interestingly enough, the incidence of prostate cancer being that high, the risk of that person dying from prostate cancer is much lower, 3.6%. The most important thing is, if you do a test, apart from the fact that it has to be safe, cost effective, standardized, easy to be done, etc., the important thing is that the test should save lives. That test should also cause less risk of harm to the population that it serves. The harms, when we talk about screening for prostate carcinoma, are the harms related to the biopsy, related to the over diagnosis and related to the fact that there is unnecessary therapy, with lots of side effects.

Looking back at past studies, we can see that in the 1990s there was a dramatic rise in prostate carcinoma diagnoses as a result of the new PSA testing. The mortality, or

death from prostate cancer, had not taken a dive down while the incidence of cancer had gone higher. There is probably just a 2 or 3% decrease in the mortality while the incidence has gone much higher. Also, interestingly enough, when the PSA testing became popular in the 1990s, most of the cases diagnosed were early stage prostate cancer, very localized, early stage. So at that time, when PSA testing became the standard for prostate cancer diagnosis for men above 55, there wasn't really much evidence. There were no randomized, controlled trials in which they would actually divide the population: half having it and half not having the PSA testing and then knowing that it made a difference.

It was only a couple of years ago, when a few trials matured, some big European trials and the U.S. and some other smaller trials that led people actually to analyze all the data. The first that came out saying they would not recommend PSA screening was the U.S. Then came our Canadian Task Force in November of last year, which came out with the publication of its task force on prevention. They looked at all the evidence and they said based on the evidence of all these trials, that they would strongly recommend not to test people for PSA for prostate cancer screening in men who are less than 55 and in men who are more than 70 years of age. Then they left, as a vague recommendation, that aged 55 to 69 they do not recommend screening for prostate can-

cer. Almost all the other urological associations from many countries endorsed that PSA testing should not be routinely used as a screening for prostate cancer.

However, there are some caveats. Some of the urological associations would recommend that patients should be screened but that screening should take place after having a very clear discussion about the benefits and the harms of this screening. Secondly that it has to be done in populations where you would see that their life expectancy is at least 10 or 15 years or more than that, rather than doing it in people who may have a life expectancy of less than 10 years, just because of other conditions that they have or just because of their age .

In answer to a question, Dr. Rahim said that the Canadian Task Force did not actually comment on the digital rectal exam (DRE), they just focused on the PSA testing. However, if you look at the recommendations of some of the urological associations, they all do recommend the DRE. How often? It's all up in the air because their hasn't really been any evidence collected on that. That leaves family doctors scratching their heads. To do or not to do?

I thought I'd break it down to some of the truths and not so truths about the screening. The screening does increase the diagnosis but also over diagnoses cases of prostate cancer in over 40% of patients, where it probably would not have made any difference in their lives, had they not known that they had prostate carcinoma. It also probably prompts us as health care professionals to over treat these patients resulting in the harms that are associated with these treatments. The people that sit on the other side of the fence argue that the screening should still be done because it causes stage migration, when detecting it later when they have more symptoms. If you do screening you detect the cancer at a much earlier stage rather than a later stage. Even though all these trials, their details mature at 13 or 14 years, people argue that prostate cancer is a chronic disease and maybe the data needs to mature a little more. Maybe there should be 20 year data. The European study did show that it saved 12 patients from dying out of 10,000 people. The U.S. study showed no difference in terms of lives saved.

The question is what to do? And I think the majority of us advocate that family doctors and urologists should sit down and have a discussion with men above 55 years of age about having a PSA testing done, about the harms related to the testing and the benefits of it. You can go on Google at www.canadiantaskforce and it will give the details of the harm and benefits to people. I think it is still something that should be looked at in people who have a high risk of prostate cancer: people who have genetic tendencies or people who have had family members who have had prostate carcinoma and people who are African American where the tendency is far greater.

In response to a question, Dr. Rahim emphasized that active surveillance is something that men should consider when they have been diagnosed with moderate prostate cancer. Health professionals need to be educated as to when a person should be put into active surveillance.

Regarding PSA, I'm not an advocate for the Task Force but I believe that it's a test that is available, that it should be offered to people who want it, with good explanation as to what it actually means. I'm just putting down what is there and what is coming out in the literature. I think balance is what's needed. Over diagnosis and over treatment which may cause harm is what we really want to avoid.

Going into the prostate cancer itself, once it's been diagnosed, I like to put it into three categories: one is the early stage, one is called locally advanced and the other one is called metastatic. The majority of the cancers diagnosed are in the early stage or locally advanced category. About 10 to 15%, or even less than that, are diagnosed first time in the metastatic category. In the metastatic diagnosis they are castrate sensitive, which means they are very sensitive to the hormone manipulation that is being done. There are patients who are diagnosed and who would do well for ever and ever and die of another cause; and there are patients who are diagnosed and their life is very limited. Th0e.re are lots of factors that define how they are going to progress and what their prognosis is going to be. About half of the patients who have prostate carcinoma, it's like a chronic disease and they can go on for years and years without any problem. Then there are about 35% where it's unpredictable and these are people that you really have to carefully follow and then there are about 15% that are really aggressive, they just go. These are people who have what we call undifferentiated cancer, have Gleason scores of 9 and then there are patients who have associated some other kinds of cancers with it. There's a lot of variety of prostate carcinoma and that's why they must be treated differently. Each person is his own statistic.

Dr. Rahim talked at length about the differences between Active Surveillance and Watchful Waiting. With Active Surveillance you are going to offer definitive treatment, because you're going to follow them regularly and if you see any change, you offer them treatment. Either because the life expectancy is low or the person has a variety of other medical conditions, which makes them ineligible for any radical treatment, that is the category where it's called Watchful Waiting. If these patients start showing symptoms or problems then the treatment is given. but the intent is very different. The intent in the Active Surveillance population is to give the treatment when it is needed, so it may be needed right away or it may be needed in five years or ten years down the road. Whereas in Watchful Waiting, it's not with curative intent.

This is different from Post Treatment Surveillance. There are no defined guidelines and you may see variations in practice but men who have had treatment, either radiation or surgery, they routinely continue to be followed by the urologist. They get the history physical, DRE and they get PSA done on a routine basis. It is not recommended they undergo CT scans or anything else on a regular basis.

It's mainly PSA, checking how you're doing, any symptoms, which may prompt a CAT scan or something... or not. What happens if, after you've received the treatment, the PSA starts going up? You've been followed regularly, the PSA starts going up, you have no symptoms, there is nothing else that anyone can find on exam. We look at the doubling time of your PSA, which is the amount of time that it takes to double. If it doubles in less than three months that indicates some problems, that's pretty bad, particularly if you have had treatment for Prostate Cancer. If it's a doubling time of less than a year or less than three years if you are in the Active Surveillance group that's not good. Similarly, if the initial Gleason grade was 8, you know that they have much more aggressive cancer cells, compared to somebody who had a Gleason grade of three or four, or five. If the PSA goes to zero after whatever the primary treatment is or even after androgen deprivation, they do a lot better compared to people who have had the treatment and it never goes to zero. These are some of the factors that are being considered. Dr. Rahim showed a graph of men whose PSA doubling point was less than 6 months. At three years their chance of developing metastases was close to 70%, compared to someone whose PSA doubling is eighteen months or greater, that's 30%. There's a vast difference in the rate of progression based on the PSA doubling time.

So, what if the PSA comes back up? You've had treatment, you've been followed in whichever group you were and now the PSA starts coming back up. This is when androgen deprivation therapy is started. That is time to get the testosterone level down to zero because the prostate cancer cells feed on testosterone. Basically what is needed is to deprive the cancer cells of androgen. Usually it works very well and the PSA comes down. It can remain down for a period of time but then it starts to go up again. Then it goes up and down with different treatments until we have no treatments left. What we do if the prostate cancer spreads in spite of androgen therapy, when we reach the point where the cancer has spread to the bones, we know that giving them medication to strengthen the bones is very helpful, so they don't run into problems with fractures or compression of the cord, etc.

Two important points I want to make: Some people can go on with androgen therapy, that can continue for the rest of their life, that doesn't stop; the other thing is that not everyone gets a high PSA, there is a small proportion, about 10 or 15% of patients may have PSA but it's not very high. This can be because the tumour is very aggressive and so it doesn't secrete PSA, it doesn't want to secrete PSA, and those patients may have disease spread but not have a high PSA. That's just two important caveats to keep in mind but the PSA is still a good guide for the majority of patients.

Things have changed quite a bit and we've learned a lot about prostate cancer. Since 2009, we have had a mixture different anti-androgens. One of the things we've learned is that, when deprived of testosterone, the cancer cells themselves will start producing their own. The other thing we've found that when the testosterone comes inside the cells, there's something called androgen receptors, where the testosterone sits and then it gives a signal to the DNA machinery and the nucleus to say, "Now you multiply." And what we learned is that quite a lot of times, these androgen receptors may have a very tiny amount of testosterone and they would just proliferate. They don't need too much. Sometimes they don't even need that, they just proliferate. The improvement of the understanding of prostate cancer has led us to finding many more treatment options. We have multiple options now, it has really exploded. The only resort we had before was chemotherapy, now we have many more before and after chemo.

Dr. Rahim finished her talk with a fairly lengthy question and answer period covering such subjects as a new immunotherapy being tried in the U.S. This takes white cells from the patient's blood, which are then exposed to other proteins, making them more robust and infusing them back into the patient. Unfortunately, we only have room for one more question.

Q. What percentage of patients relapse after primary treatment?

A. Depending upon the stage and the grade, the majority of patients are actually cured, so they don't relapse. Quite of lot times, given time, say 15 years, 20 years, they may relapse. To give you an absolute number depends on the grade, etc. but it's less than a quarter.