

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**

Dr. Shabbir Alibhai our April 16 speaker is an Associate Professor in the Department of Medicine, the Institute of Health Policy, Management, and Evaluation, and the Institute of Medical Sciences at the University of Toronto. He is a staff physician in the Division of General Internal Medicine and Geriatrics at the University Health Network and Mount Sinai Hospital, a senior scientist at the Toronto General Research Institute and the Toronto Rehabilitation Institute, and a Research Scientist of the Canadian Cancer Society. His research interests are in geriatric oncology, particularly in the impact of disease and treatment on quality of life among patients with prostate cancer or cancer-related fatigue and he conducts randomized trials of exercise to improve outcomes in older adults with Cancer. Come and hear what he has to say.

Meeting Date: April 16th, 2015

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

Time: 6:30 pm to 9:00 pm

Speaker Dr. Shabbir Alibhai

Subject: Impact of disease and your quality of life

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a member of the



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.

March Notes . . . Speaker Dr. Susanne Chan, Pathologist at Southlake

Subject: How your cancer is diagnosed and graded.

Dr., Chan gave an excellent Powerpoint presentation at our March meeting on how Pathologists go about diagnosing and grading our Prostate Cancer. Here is what she had to say.



I'm going to be talking about diagnosing and reporting on prostate cancer. But really the objectives of my talk are to have you understand these three questions by the time you leave this meeting. I want you to know who diagnosed your prostate cancer. That can be a mystery at times. How is your prostate cancer diagnosed. No one probably explained to you how we diagnose your prostate cancer. There are lots of elements in your prostate cancer report, either your biopsy report or your radical prostatectomy report that no one has explained to you. I hope by the end of this session you will know why these elements are on your prostate cancer report and what they mean.

The first question I want to answer is who diagnosed your prostate cancer? From the time of your initial visit to the treatment, you will see a lot of different doctors. Usually you will start with your family doctor, who may order in a PSA and/or digital rectal exam. They may do one on you and they will get a history from you. If they see anything that's kind of abnormal, they will send you for a biopsy. The biopsy is usually done by your urologist or sometimes a radiologist, less commonly but it is sometimes done by them. And then

your report will go to your urologist or your family doctor and they will say you have cancer. At that point, they will either decide you need treatment or you don't need treatment. Some people actually don't need treatment, they can have their cancer just watched and some people will require treatment. So you can be treated by your urologist, who will do a radical prostatectomy or you can be treated by a radiation oncologist who will do radiotherapy or a medical oncologist with hormones and chemotherapy but there is a step in between and no one really talks about that step but that is a diagnosis step and that is done by the pathologist.

So who is the pathologist? Well a pathologist is known as a doctor's doctor. They don't speak directly to patients, they actually report to the treating doctor. What they do is they help the treating doctor decide how you're going to be treated and they do that by giving a report on how bad the cancer is, how much it has spread etc. but unfortunately, you don't get to see that step.

Who exactly are pathologists? Well if you watch TV, see CSI, you see doctors in these morgues, these dark, dark rooms and they are cutting open dead bodies and doing autopsies and they're solving crimes and doing all of these interesting, crime solving procedures but really, most pathologists don't do this. Those are forensic pathologists. It is a form of pathology but often these pathologists are specialized. They will do extra training and they will specialize in murders and deaths that are suspicious. So I would say a very small proportion of pathologists are actually forensic pathologists. Most pathologists don't work in dark, dark rooms, we are not cutting open anybody. We actually sit at the desk and we have these our microscopes, which help us make the diagnosis of prostate cancer.

What are pathologists? Pathologists are doctors just like every other doctor. We do four years of medical school, we do five years of residency training. And in some cases like myself, I will do an extra year of training in another specialty. I did genitourinary pathology which is prostate, bladder, kidney. Pathologists are basically physicians who specialize in diagnosis of diseases such as cancer. Until the pathologist says you have cancer, you don't have cancer. Other doctors can say I think you have cancer, we suspect it but until the

pathologist says you have cancer, you don't actually have cancer.

So how exactly do pathologists diagnose prostate cancer? How can they be sure you have prostate cancer? Well there are really two steps, there is a technical step and there is a diagnostic step. The technical step is what we do for your radical prostatectomies and prostate biopsies. We have to process it in the lab. Most of you will have had at least a biopsy done. Basically the urologist or the radiologist will put a transducer into the rectum and they will put a needle into the prostate and they will take usually 12 samples from the prostate. The prostate can be divided into six regions; one is the right base – this is the top part of the prostate, the left base, the right mid, the left mid, the right apex and the left apex. The reason you want to spread out the samples is obvious, you don't want to sample just one area, you want to sample as many different areas of the prostate as possible. So that's why we take 12 samples.

These samples are then put into jars which contain a liquid called formalin because we need to preserve the tissue. If you don't put the tissue into formalin, it will decompose and we won't be able to read it. It's similar to anything like meats and vegetables, if you leave it out, it will decompose. So you need to preserve it somehow and we use formalin, which is the same material that we use to preserve corpse. In a funeral home, they will inject formalin into the corpse's body and that preserves the body so that it can be in that state for several days before the funeral.

That specimen gets sent to pathology lab, where we'll put a label on it. We put a barcode on it and we enter all your information into the computer. We want to be able to track your biopsy from the beginning to end. We don't want it to get lost, we don't want it to get mixed up with anybody else. We want to make sure that we are entering in the information properly and this biopsy belongs to you.

Your biopsy then gets sent to the grossing room, where we have a pathology assistant, who takes your prostate cores and puts them into what we call cassettes to protect the prostate biopsy. The reason you want to protect the prostate biopsy is we're going to put them into a processing machine. We load the cassettes into this machine and there's all these chemicals in there. Basically what the chemicals do is dry out the tissue, preserve it some more and prepare it to be read by the pathologist. This will run overnight, in the morning someone will take that tissue out and will put it into these metal molds. The technologists put the processed

tissue into the bottom of this mold and add hot liquid wax on it. When this cools it down, it becomes a wax block. So your tissue is actually in a piece of wax block and that sounds strange.

Why would you put tissue in a wax block? The reason is we need to cut this tissue into very, very, very, very thin sections. This section is about 3 to 4 microns thick. The reason we need to cut your tissue into such a small thin section is because we won't be able to read it if it is too thick. It has to be 3 to 4 microns thick. So one micron is basically one 1000th of a millimeter, so you can imagine how thin that is. We need to put the tissue in the wax so that it can cut to that thin level. The biopsy is clear. There is no color to it, it's just a clear piece of tissue. We can't read clear tissue, we need to actually add some color to it. So the biopsy goes into an automated system and the slides get put into different colored containers and your biopsy will come out kind of a pink color. That pink color allows us to read the biopsy because we can't read if it's clear. It has to have some color on it. So now you have a slide and your information will be on the slide and it will be given to the pathologist for the next step which is the diagnostic step.

The pathologist will put that slide under the microscope. *With the help of slides, Dr. Chan showed us the difference between a normal prostate and one with cancer. The prostate is made up of many glands that secrete fluid, which becomes part of your ejaculation. There are two layers to the glands: an inner layer, which makes the fluid and an outer layer, which protects it, so that nothing can come in or go out from the gland.*

In prostate cancer, you lose that protective layer. Then, if the inner layer decides it wants to grow, it can grow anywhere it wants. It can grow out of control and that's cancer. The minute you lose that outer layer, that's when you have prostate cancer. It is very difficult to see which cells are normal and which have lost the outer layer, so pathologist have little tricks they use. They use something called the immunohistochemistry. You may have seen these terms on your report, this is what they are referring to. We have a special stain that can highlight the protective layer, the basal layer. It will highlight it brown. If you have a normal prostate, you will have a nice brown protective layer around your glands. If however, you have prostate cancer, there's no more brown layer, it has disappeared. The glands that have cancer have no outer layer. So that's how we know if you have prostate cancer or not. We don't always just rely on what we see under the microscope, if we see

one layer or two layers. We actually order this test to make sure that the outer layer is missing. And the other thing – at least we do at Southlake – is we review all the prostate cancers. So anytime there's a diagnosis of prostate cancer, we have two pathologists look at your biopsy to make sure that it truly is prostate cancer, because we don't want to make a mistake. We don't want to tell someone they have prostate cancer when they don't. So all of our cancers get reviewed twice and we do that for breast cancer, lung cancer, skin cancer – all the cancers in the body. At Southlake two pathologists review everything.

I'm just going to move on to my third objective. What does my prostate report mean? You're going to get a biopsy report and possibly you're going to get a radical prostatectomy report. Some of this applies to the biopsy report and some applies to the radical prostatectomy report but I am going to talk about some of the more common terms you are going to see on your prostate cancer report. Everyone should have a Gleason score, so I'm going to talk about that and talk about **positive, negative margins that you will see in a radical prostatectomy. We will talk about extraprostatic extension, you will see it on the radical prostatectomy. Seminal vesicle invasion, again radical prostatectomy. Perineural invasion, you will see that in a biopsy report as well as a radical prostatectomy report.**

The Gleason scoring system was devised by pathologist Donald Gleason in 1966. Basically he determined that if you have a low Gleason score, you have low risk cancer. If you have a high risk Gleason score, you have a higher risk of cancer. The lower the score, the lower the risk and the higher the score, the higher the risk. The number that you see on your report consists of three numbers: one, the first number is going to be your Gleason score, the other two numbers are your Gleason grades. And it can get confusing, the Gleason score, and Gleason grades, don't get them confused because they are two different things.

I'm going to explain what Gleason grade is first and hopefully after that, I will explain what Gleason score is and how they work together. Initially Gleason identified five grades based on what the biopsies looked like under the microscope. Since grades 1, 2 and 3 look kind of the same, we just jump right to Gleason three nowadays, so everybody probably has a minimum of three somewhere on their report. Gleason grade 3, basically consists kind of oval or round glands. Again, these are glands that secrete that fluid and they have no pro-

tective layer around them. One thing that I was taught when I was training was that you can take a pencil and draw a line around the gland and you can actually outline each gland separately. They are not fused together, they are very respectful of one another, they keep separate from one another. If I saw this picture under the microscope, I would grade this pattern has Gleason grade 3. I call it Gleason grade 4 if I can no longer find where the gland ends, where the gland begins, if everything is kind of fused together. When it gets this complex, it's no longer Gleason 3 anymore, it's now Gleason 4. And when it even no longer resembles glands, then it's Gleason 5. *(Dr. Chan showed slides demonstrating the different grades)*

What does that have to do with Gleason score? Well Gleason score is calculated based on Gleason grade. So Gleason score is based on the most common Gleason grade in your biopsy plus the worst Gleason grade or the highest Gleason grade. So you have 6+3, the 6 is your Gleason score, the 3 is your most common grade and the other 3 is the worst Gleason grade.

I'll show you an example here. This is a Gleason score 6+3. Again, it has these nice glands where I can outline them, they are all separate. The most common one here is a 3 and the highest grade here is also 3. I don't see any 4, I don't see any 5, I only see 3. So this is a Gleason 6+3. Another is a Gleason 3+4. Why? Because again these glands that are separate from one another. I can draw a line around them. The most common one I see is 3 but there is also an area with a 4. I can't figure out where it ends, where it begins. It's all one big group of cells. So the highest grade or the worst grade would be a 4. So that becomes 3+4. If I saw some 5 here, that would be 3+5. A worst case scenario is a Gleason score 10. Again, the most common would be a 5. I'm not seeing those white spaces in those glands. And the highest grade is also a 5, you can't get anything higher than 5. So that's why we have Gleason score 10, 5+5.

Now it's a little different in radical prostatectomy. I just explained how to grade and calculate the score in biopsies but I didn't talk about radical prostatectomies. Radical prostatectomies are a little bit different; you are going to take the most common Gleason grade and you are going to add to it the second most common Gleason grade and that will be your score. If you had a radical prostatectomy, somewhere in your report it will say margins and it will either say positive or negative.

A negative margin is when the tumor is far away from where the surgeon cuts. It looks like the surgeon

probably cut out the entire tumor. They didn't leave anything behind. That's a negative margin, it's a good thing. In a positive margin the tumor is right on the edge of where they cut. So that means there probably is tumor here left behind in the body. They cut through the tumor and left some tumor in the body. If you have a positive margin, you're probably going to get extra treatment probably in the form of radiotherapy. So they will call it adjuvant radiotherapy. Extraprostatic extensions are another thing you might see in your radical prostatectomy reports. The prostate is called the capsule, it's not really a capsule but that's what people call it, The prostate capsule or the prostate boundary. This is where your prostate begins and ends. The area outside is called extraprostatic tissue. In most cases there is no extraprostatic extension because the prostate tumor stays inside the boundary of the prostate. If there's tumor that exits the prostate boundary and enters into this tissue, the extraprostatic tissue, then you have extraprostatic extension present. So if you see that on your report, this is what it means. It means there's tumor that is exiting your prostate into the tissue outside. And why is that important? Well they found that tumors that stay inside the prostate have a better prognosis. They act better whereas the tumors that exit the prostate, they are more

aggressive. So often, these patients will also have some adjuvant therapy such as radiotherapy because it is a bit of a more aggressive type of tumor.

Moving on to seminal vesicle invasion. This is something you're more likely going to see in a radical prostatectomy report. Seminal vesicles are two organs that sit right behind and near the top, the base of the prostate. What they do is they secrete fluid. This fluid along with the prostate fluid plus the sperm coming from the vas deferens, exit through the urethra and they make the ejaculate. So again, the seminal vesicle has nutrition in it to help support the sperm. If you don't have fluid from the seminal vesicle and from the prostate, the sperm will die so that's why you need these organs to produce fluid. If there's tumor involving the seminal vesicle, why is that important? Well that means the tumor has left the prostate, entered the extraprostatic tissue and not only that, has gone beyond the extraprostatic tissue into another organ. It's not only not contained in the prostate, it has actually spread quite far. It's called a seminal vesicle invasion. It's more aggressive and again, you will probably end up having a bit more treatment because it is a more aggressive tumor.

Perineural invasion – this is a term I included in



this talk only because it is so common. I think most of you will probably have perineural invasion in your reports somewhere. It is very, very common to the point that I don't think it is that important because if everybody has it then it doesn't really provide more information to the doctor. In the past, perineural invasion was very important and I think nowadays people are recognizing that it is less important compared to some of the other factors. Perineural invasion just means that the prostate cancer wraps around the nerve. So when we see this, we will report on your report perineural invasion.

This is a pretty short talk but we will have lots of time for questions. So I hope that now you will understand who diagnosed your prostate cancer. We are pathologists, we are physicians just like everybody else who diagnose except we specialize in diagnosis of diseases like cancer. How do we diagnose prostate cancer? Well there's two parts: there is a technical component – so the lab will have to process the biopsy or the radical prostatectomy specimen and then the pathologist will have to make a diagnosis. And in the prostate, the diagnosis is made by looking for that missing basal layer. If you're missing that protective layer then you have prostate cancer. And what does your prostate cancer report mean? Well Gleason score basically tells you how risky your prostate cancer is and that is calculated by taking your most common Gleason grade plus your highest Gleason grade or your worst Gleason grade and that is for prostate biopsies. Talked about positive and negative margins, that's basically saying how well did the surgeon cut out your prostate. Did they leave any tumor behind or did they take it all out? Extraprostatic extension means how aggressive was your prostate cancer. Did it leave the boundary of the prostate or did it stay inside the prostate? Seminal vesicle invasion again, how far did the prostate cancer go? In this case, did it actually enter into the seminal vesicles? And perineural invasion again is such a common thing, it just means did the pathologist see prostate cancer around a nerve.

So any questions? Yes.

Participant: How long does it take to diagnose?

Dr. Chan: Because we're diagnosing many other types of cancers, we have a big stack of slides on our desk, usually it's done within two weeks. But if it was an urgent case and someone said I need to get the diagnosis right away, I could probably do it in, depending on if I'm waiting on an immunohistochemistry a couple of days.

Participant: When they do a radical prostatectomy,

sometimes the surgeons take out the lymph nodes, do you look at that quickly before they proceed with the surgery?

Dr. Chan: The question is when you do a radical prostatectomy, sometimes the surgeons take out the lymph nodes, do you look at that quickly before they proceed with the surgery? The answer is yes in some cases and some cases no. It depends on who your surgeon is and what their preference is. So during the course of surgery, if they are taking out the lymph nodes and they feel like there might be a positive lymph node, there might be cancer there. They will call the pathologist, the pathologist will look at the tissue. We'll look at it using something called a frozen section. We will instantly freeze the tissue, look at it under the microscope and tell the doctor if there is cancer or not. If there's cancer, they might cancel the surgery at that point. If there isn't, they will continue on. It does happen once in a while when the surgeon just goes in and find a lymph node that they finds very suspicious. So they will send it to the pathologist and that takes about half an hour to get done. It adds about half an hour to your surgery.

Participant: I have questions and they are related to diagnosis. When the biopsy has been taken, does it concern you that you may not be seeing what's going on, on the other side of the prostate?

Dr. Chan: It's always a concern with prostate biopsies because the prostate gland is big and I am taking little cores of tissue. The surgeon is not able to keep biopsying it because if they did that would take them forever and they are just basically performing a radical prostatectomy. That's why they take only 12. They do try to spread it out though. So they will take it from both sides, they will take it from the right side and they will take it from the left side. The area that they might miss is the front because the needle can only go so far. They might miss some of the front where the urethra is, they might miss some of that. There are going to be certain areas that are not reached. The area around the urethra is called the transition zone. That area tends not to have high grade tumors. So they're willing to sacrifice not sampling that area. Having said that, what they will do is if they find that everything is negative, they don't see anything, they will follow your PSA. If they are still suspicious that something is wrong, they will go back and get another biopsy for you. Because really these 12 samples, you could miss cancer. There could still be cancer left behind. So unfortunately, this is not as thorough as we would like it to be but we do try to get every zone that we can access.