

## Advances in the Treatment of Testicular Cancer

Webcast

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### **Michael's Story**

#### **Andrew Schorr:**

Hello and welcome once again to Patient Power. This is what we do with M. D. Anderson every two weeks. I'm Andrew Schorr, and as we do it every time we connect you with leading medical experts from M. D. Anderson and always-inspiring patients. One of the cancers that you may have heard about and men may wonder about, but I don't think we know a lot about is testicular cancer, and it can affect younger men. You are about to meet a younger man who was diagnosed with it, came out of the blue. Could happen when you are older but typically younger men. And we're also going to meet a leading expert who treats and helps people hopefully have a good prognosis. We are going to learn all about the full range of testicular cancer.

Let's meet our first guest, and that is someone who has lived with it. That's Michael Pellon, who is normally from North Houston, north side of Houston, but he goes to graduate school up at the University of Vermont. And, Michael, you are 22 now, but going back about, what, three years ago or so you were diagnosed with testicular cancer, and it was fairly advanced, wasn't it?

#### **Michael:**

Yes, it was.

#### **Andrew Schorr:**

You were at Trinity University in San Antonio, tell us the story of being diagnosed.

#### **Michael:**

I was in school. I actually finished out my freshman year, and when I was kind of towards the end of the school year I was developing quite a cough, went home, saw my physician back home on numerous occasions over a short period, and just antibiotics weren't doing it, and good rest, that wasn't doing it. Didn't seem to be allergies. So from there a chest x-ray was done and determined I had some quite large tumors in both my lungs. From there I was moved to a local hospital where I had an orchiectomy done and then from there referred to Dr. Pagliaro and the team down at M. D. Anderson where they carried out the chemotherapy and subsequent treatment.

**Andrew Schorr:**

Well, you tell it pretty matter of factly. We are going to meet your doctor, Dr. Pagliaro, in just a minute who is an expert in research and treatment of testicular cancer, which is what you were diagnosed with. So there you are, you are a college student, Michael. You think you have a cough, and they tell you you have metastatic cancer in your chest. That must have just been devastating.

**Michael:**

Yes. I don't know if I want to say devastating, because again it didn't really set in, quote-unquote, I would say ever. It still hasn't kind of set in that it happened because again it just happened so fast. And it became just kind of, well, I was going to go to a summer job, but this kind of getting healthy became my new summer job. And that's how I looked at it through the whole time.

**Andrew Schorr:**

Well, we should mention that you have been getting healthy, and so you had surgery. And we are going to learn more about that with the long word, what is it, orchiectomy?

**Michael:**

Orchiectomy.

**Andrew Schorr:**

So you had surgery, testicular surgery, but you also had several rounds of chemo beginning that fall and then as we mentioned there were these masses in your chest, so on Christmas vacation in 2005, you had one lung surgery, and then spring vacation you had another one, right?

**Michael:**

Right. So two double thoracotomies.

**Andrew Schorr:**

How are you doing now in 2008?

**Michael:**

I am doing great. I'm up there at grad school staying busy, so healthy and active.

**Andrew Schorr:**

And what sort of activities do you do?

**Michael:**

Well, now I am in Vermont, I can actually enjoy hiking in actual mountains and fresh spring air and cycling, actually.

**Andrew Schorr:**

Wow. Well, good for you. Well, let's meet your doctor. So we mentioned that you were referred when it was noted that this had spread. I think smart people said let's get you to an expert in testicular cancer, and that's Lance Pagliaro, who is associate professor of medicine, and he's in the department of genitourinary medical oncology at M. D. Anderson. Thank you, Doctor, for joining us.

**Dr. Pagliaro:**

Hello, Andrew. Hello, Michael.

**Symptoms and Diagnosis**

**Andrew Schorr:**

Doctor, tell us about Michael's case first. So here's a fellow--Michael, had you had any symptoms at all?

**Michael:**

No. Like I said really the only kind of just in your face symptom, there was a cough, and there was no really direct way to point that towards testicular cancer.

**Andrew Schorr:**

Doctor, tell us about that. What can be the symptoms of testicular cancer where maybe it could be noted earlier? I would think that would be a good thing, but then how does it slip by that it spreads like this and there were no apparent symptoms that Michael noted?

**Dr. Pagliaro:**

Right. The chance of cure is best when it's detected earlier. The earlier the detection, the better the chance of cure. And testicular cancer can begin with many different types of symptoms, commonly a testicular mass, but not always. Michael was a 19-year-old college student, and that's very typical for testicular cancer. It's the most common cancer in men 15 to 25 years old. In Michael's case the primary tumor in the testicle was small, but the tumors that had spread to the lungs were large, and so the symptoms that ultimately brought it to attention were the breathing and coughing symptoms caused by the tumor spread.

**Andrew Schorr:**

So I have a kid who is a freshman in college. What should younger men be looking for? Is there something they should be doing that might give them an indication if they are, you know, one of the 7,000 US men diagnosed each year? It's not a common cancer, but it's certainly not one you would want.

**Dr. Pagliaro:**

Right. Well, it's estimated there will be over 8,000 cases in the United States alone in 2008. Men should be aware that although at that age people are generally

healthy and particularly don't commonly get cancer that is the peak age for testicular cancer. But the testicles are sensitive. They are in a location that they can be examined easily, and most men who have a mass on the testicle will be aware of it at some point, and that by far and away is the most common clue that they are going to detect.

And again Michael's case was different. He had a small tumor which actually was dissolving spontaneously even before we started treatment. But then in terms of other symptoms, if a person of any age or any gender is experiencing weight loss or cough or breathing difficulty that doesn't go away in a few days the way a cold should do, then they need to get that checked out.

## **Testing**

### **Andrew Schorr:**

All right. Let's carry this further. So Michael's cancer had spread. Tell us about the kinds of tumor cells there are. How are these different? We have talked about a lot of different cancers on Patient Power, so is there anything unique about the cancers that form in the testicles and then how they spread?

### **Dr. Pagliaro:**

The uniqueness of testicular cancer, there are several things. Most testicular cancers are what we call germ cell tumors. They are tumors of the reproductive tissue, and so like an embryo or like reproductive tissue they can differentiate. They can transform into different cell types. Unlike many solid tumors, testicular cancers can be cured with a combination of chemotherapy and surgery, and with modern treatment we can cure more than 90 percent of testicular cancers.

### **Andrew Schorr:**

Well, that's good news. Now, he mentioned this type of surgery. Tell us that again that Michael had. Tell us about the surgery and where that comes in.

### **Michael:**

It's an orchiectomy.

### **Dr. Pagliaro:**

Radical orchiectomy, that is just a fancy term for removal of the testicle. And in this case the incision is not made in the scrotum as a person might think. The incision is made in the groin and so that the testicle can be removed in one package without disturbing the tumor, without causing any further tumor spread.

### **Andrew Schorr:**

Now, there was a part I didn't understand. Michael, had you had any kind of ultrasounds or any kind of diagnostic exams to confirm it was cancer before the surgery?

**Michael:**

Right. I mean, they did the chest x-ray, and I was moved to a like I said a regional hospital where an ultrasound and CAT scans were done as well as tumor markers were taken. So blood was drawn to look for the presence of certain proteins in the blood.

**Andrew Schorr:**

All right. Doctor, tell us about that. So how do you confirm the diagnosis before you do the surgery?

**Dr. Pagliaro:**

Usually it's done with ultrasound, and ultrasound examination, it's a painless, noninvasive test that can be done right in the doctor's office. It's usually in a urologist's office. And the ultrasound tells us whether the testicular swelling is solid or cystic, that is, whether it's a fleshy tumor or something fluid that may be benign, and it also tells us whether it's within the substance of the testicle or perhaps something that's not within the testicle but also within the scrotum. If we see a solid mass that's within the testicle, that's presumed to be cancer. We do not do a biopsy, but that would be a case for surgical removal.

**Andrew Schorr:**

Okay. Now, are there different--I know like with prostatectomy for men, there are sort of different levels of it. There is radical, there is nerve sparing, and I know here too there can be times when you take lymph nodes out and other times when you don't. Tell us about that.

**Dr. Pagliaro:**

Well, the radical orchiectomy procedure does not vary tremendously in part because the lymph nodes that are affected are not really in that location. They are way up in the abdomen just under the kidneys, and so to reach those lymph nodes requires a different procedure. But the cancer cells from the testicle, they are conducted through the lymph system which travels all the way up to that location near the kidneys and then they settle in what are called retroperitoneal lymph nodes.

**Andrew Schorr:**

So typically are the lymph nodes, some lymph nodes removed or not always?

**Dr. Pagliaro:**

Well, again that would be as a separate procedure, and the answer is not always. And in some cases lymph nodes are removed prophylactically, you know, without

immediate evidence of cancer but to see if there is cancer there and to hopefully remove microscopic cancer. In other cases they are removed after chemotherapy, much the way Michael had operations on his lungs after chemotherapy.

### **Stages of Testicular Cancer**

**Andrew Schorr:**

Tell us about the stages, if you will. So help us understand different stages of testicular cancer and then what modalities come into play, whether it's surgery and radiation and chemo or some combination of all of the above or not all of the above.

**Dr. Pagliaro:**

Right. Well, I mentioned the pathway of spread through the lymph system to the lymph nodes. And like many other cancers testicular cancers can spread either through the lymph system or through the circulation, through the blood stream. And when cancer cells spread through the blood stream, then they can settle in other organs. And in testicular cancer most commonly that is the lungs, which was the case in Michael's cancer.

So then in the staging system we talk about stage I, which is a tumor confined to the testicle without spread. Stage II are those that have spread through the lymph system to the lymph nodes but not to any other organs. And stage III, which is the highest stage in the testicular cancer staging system, are those that have spread beyond the lymph nodes to other organs such as the lungs.

**Andrew Schorr:**

All right. And tell us about the treatment approaches and how they might be tied to the stages.

**Dr. Pagliaro:**

The treatment for testicular cancer varies depending on the cell type. We will probably talk later about seminoma and nonseminoma for example.

**Andrew Schorr:**

Right.

**Dr. Pagliaro:**

In the case of seminoma, radiation is a very important modality, but less so with nonseminoma. With nonseminoma, treatment consists of chemotherapy and surgery, and often, and Michael's case is typical in this way, to achieve cure requires both chemotherapy and surgery. It's not just one or the other.

**Andrew Schorr:**

All right. Well, I think what we will do is we are going to take a little break, and

when we come back we will learn about these different tumor types because as we have discussed on Patient Power so many times it's the biology of the cancer cells that makes a difference too and not just where the cancer is or how big a tumor is. Am I right about that, Doctor? Did I get it right?

**Dr. Pagliaro:**

That's correct. It's the extent of the disease and also the cell type.

**Andrew Schorr:**

We are going to take a quick break, and when we come back we are going to learn more about the biology of testicular cancer tumors and understand then how that makes personalized treatment important and also what the prognosis can be. You heard that Michael is cycling and living a full life now, and we hope that that goes on forever as he studies computer science and applied mathematics at the University of Vermont. We will be back with much more of Patient Power sponsored by M. D. Anderson Cancer Center right after this.

**Seminoma and Nonseminoma**

**Andrew Schorr:**

Welcome back to Patient Power. Andrew Schorr here as we visit with Michael Pellon who is from Houston originally, but he is studying, he's getting a Ph.D. in applied mathematics and computer science, and all of that after--he is 22 now, but after being age 19 and being diagnosed with testicular cancer that had actually spread to his lungs, and he went through treatment in part at M. D. Anderson. And his doctor who is an expert in testicular cancer, Dr. Lance Pagliaro, is with us today. So we are going to learn more about that.

Dr. Pagliaro, let's understand the different biological types of testicular cancer, is one more common than the other, and then why they might be approached differently.

**Dr. Pagliaro:**

Well, most testicular cancers are what we call germ cell tumors. There are a small percentage that are non germ cell tumors. And the germ cell tumors we divide broadly into what are called seminoma and nonseminoma. Seminoma makes up about half of germ cell tumors, and by that we mean pure seminoma, and everything else is nonseminoma, which are other pure cell types. And there are also mixed germ cell tumors which may include a percentage of seminoma, but are not a pure seminoma.

**Andrew Schorr:**

All right. So take us through that now and how--well, how do you figure out which you are dealing with?

**Dr. Pagliaro:**

Well, that's good question. There are several elements to establish that it's a pure seminoma, and it's partly a diagnosis of exclusion. If there is any sign or symptom of nonseminoma, then you know it's that, but if everything checks out to be pure seminoma with, you know, with no exceptions, then that would be the diagnosis.

The first thing is the way the tumor looks under the microscope, and that's determined by the pathologist after the testicle is removed. The next thing is the blood test called tumor markers. There are three that we look at at the time of diagnosis that are called HCG, AFP, and LDH. And we know that with seminoma there is a certain pattern of tumor markers which would be a normal AFP, a slightly elevated or normal HCG, and a normal or elevated LDH. And then any deviation from that pattern, for example an elevated AFP, would tell us that it can't be pure seminoma. It must be nonseminoma.

**Treatment: Surgery, Radiation and Chemotherapy**

**Andrew Schorr:**

So now we have talked about the stages. And now we are learning about the biology. So now take us through the drugs that come into play, and when you use drugs, and also I also wonder does radiation come into play at all too?

**Dr. Pagliaro:**

Right. That's a good question. We do use chemotherapy and radiation and surgery for the treatment and cure of germ cell tumors. Radiation is used almost exclusively for pure seminoma, but we do use chemotherapy in all types depending on the stage and the particular presentation. And chemotherapy really revolutionized the treatment of germ cell tumors and brought us into an era where the majority of young men with germ cell tumors are cured, and that occurred in the 1970s.

**Andrew Schorr:**

Well, that's neat, and of course people see Lance Armstrong who they know is a testicular cancer survivor. Now he is I think talking about trying to go for the Tour de France again. So you know, what an inspiration to people. So what is it about the drugs you have and these germ cell tumors that make them so sensitive to the drug therapies? Why does it work so well in this type of cancer when sometimes in others it doesn't work so well?

**Dr. Pagliaro:**

Boy, I wish I knew the answer to that question. I might be on my way to Stockholm right now. One of the key questions in cancer science and cancer medicine is why do some tumors respond well or are cured with chemotherapy and others are not. And you could also ask the question in testicular cancer, why are some patients with testicular cancer cured and others we are not able to cure who

die of the disease. A lot of work is going into understanding drug resistance and understanding why malignant tumors are so stubborn and difficult to cure. There are biological differences in germ cell tumors. We know for example P-53 mutations, that's a gene called P-53, which is commonly mutated in other cancers, is not commonly mutated in germ cell tumors, and that may make them more susceptible to the cancer-killing effects of chemotherapy.

**Andrew Schorr:**

Now, is there a way to tell? So when someone like Michael comes to you, maybe it has spread, maybe it hasn't, is there anything in the testing where you can tell them what their future might be or how likely the chemo is to work? Is there a way to tell, or you just have to start?

**Dr. Pagliaro:**

Well, there certainly is a way to tell. We have a system that divides patients into three groups, and we know that the good prognosis group we can cure with standard treatment some 80 to 90 percent of the time. And now we are talking about tumors that have spread. Okay? And in the intermediate prognosis group the cure rate is a little lower, 70 to 80 percent. And there is unfortunately a poor prognosis group whose cure rate is a little less than 50 percent. But we are able to identify those patients at the time of diagnosis, and we can adjust their treatment to be more or less aggressive and also their follow-up to be more or less frequent according to the likelihood of cure.

**Andrew Schorr:**

All right. Tell us about the drug therapy. Since that comes into play often, what are the typical courses of treatment? What are the drugs you use? How long does somebody have therapy? Just help us understand, the new patient who may be listening and where drug therapy is recommended, what they might be in for. And I know it's individualized, but just generally.

**Dr. Pagliaro:**

Right. Well, on the one hand there is a standard regimen for example that we use in nonseminomatous germ cell tumors which has been selected over the course of many clinical trials to optimize the beneficial effects, the cure rate, and minimize the side effects. But on the other hand this is a disease which does respond to a variety of drugs, so we are by no means limited to the standard. There are many, many options so that if we need to, say, customize the therapy to avoid a certain side effect or accommodate some other illness the patients may have, we have the wherewithal to do that.

**Andrew Schorr:**

Now, these are probably, typically younger people who are reasonably healthy often, so does that allow you to hit the cancer harder, if you will, or use more drugs more aggressively to try to have a better chance for cure? In other words, does age come into play and general better health?

**Dr. Pagliaro:**

Men can get germ cell tumor at any age, but the most common age is in the teen age or early 20s, and yes. We can give drugs and we can give doses and intensity of therapy in young, otherwise healthy people that would be difficult or impossible in older folks or particularly those who may have had years of cigarette smoking or may have other diseases that are already going on. Having said that, we can still cure the older patients or those that have other complicating problems. It just requires a little more creativity in selecting the drugs and looking at alternatives and how to modify the treatment to best suit that patient.

**Andrew Schorr:**

Michael, tell us a little bit about your course of therapy. So when you started chemo how often did you have it and how long did it go on for?

**Michael:**

Right. Like I said, I started in May of 2005, and the courses ran to that September. And correct me if I'm wrong, Dr. Pagliaro--five courses of chemo. Each course was I would stay at M. D. Anderson for roughly a week and receive chemo throughout that week, go home for about two weeks and pretty much do nothing because I was pretty fatigued. It's like running a marathon every week. And kind of get healthy again ready to come back and hit it again hard that following week at M. D. Anderson for another course.

**Andrew Schorr:**

Now, Doctor, is that still, we are three years later, is it still--would that be representative of what would happen today?

**Dr. Pagliaro:**

Sure. For a more advanced germ cell tumor, five courses using the drugs that Michael received would be typical. The standard chemotherapy for germ cell testicular cancers that have spread is three or four courses of chemotherapy. In Michael's case because the bulk of the disease required additional duration of treatment.

And also something else we can talk about in terms of the individual drugs, one of the medicines that we use to treat nonseminomatous germ cell tumors is called bleomycin, which is a very important drug, but can injure the lungs. For example you mentioned Lance Armstrong who chose not to receive bleomycin because that might have impaired his athletic performance, so his doctors were able to choose

other drugs to use. In Michael's case we avoided bleomycin initially. We later did use it, but when there started to be some inflammation we, you know, like the case of Lance Armstrong, we had to avoid bleomycin.

## **Fertility**

### **Andrew Schorr:**

One of the questions I have got to ask along the way, we are talking about younger men and, Michael, you I imagine are still single, right?

### **Michael:**

Correct.

### **Andrew Schorr:**

Okay. So fertility comes into play. Talk to us about the discussion that a younger man might have with their doctor about trying to preserve fertility recognizing that some powerful drugs may well be used.

### **Michael:**

Right. Initially after our first meeting with Dr. Pagliaro, one of the big topics was sperm banking. Again, knock on wood, in Houston, we're sitting at the heart of Texas Medical Center, so it was literally a drive down the street to Baylor College of Medicine to bank sperm before the chemo started. Now, it doesn't necessarily mean that I am infertile. There is just an increased chance of that, and we have got kind of a safeguard set up there.

### **Andrew Schorr:**

Right. Good for you. Okay, Doctor, so tell us about that discussion and whether that's an important one to have.

### **Dr. Pagliaro:**

Michael stated it very well. Men who undergo chemotherapy for testicular cancer often do father children, and infertility is by no means inevitable in those cases. And the loss of a testicle because of a tumor and the need for orchiectomy actually does not impact fertility at all, so a man can be as fertile with one testicle as with two.

But there can be other medical factors that affect fertility in any individual, with or without cancer, and one of the side effects of chemotherapy in terms of what it does to healthy tissues, it may damage the testicle in a way that makes it harder to father children at a later point in time. And sperm banking is the best way we have to give men the best possible range of options so that with assisted reproduction if they have difficulty conceiving, you know, they may still have that option in the future.

## **Follow-up and the Possibility of Recurrence**

### **Andrew Schorr:**

Now, we are talking about someone who hopes to have a very long life ahead of him and be cured, but we have talked also about powerful medicines. You mentioned the one with possible effects to the lungs. Does someone who is treated for testicular cancer have to be checked out in a certain way over many years just to guard against not just a recurrence but some late effects of the medicines that were used?

### **Dr. Pagliaro:**

Absolutely. And we follow our patients indefinitely, even after the risk of recurrence or relapse is essentially zero. We know that there can be, even decades later, there can be second cancers that may be in part related to prior treatment with radiation or chemotherapy, and we also know that both radiation and chemotherapy can predispose to cardiovascular disease.

### **Andrew Schorr:**

So, Michael, you are probably attentive for having regular checkups I would think.

### **Michael:**

Right. I mean I actually see Dr. Pagliaro about every three to four months, and we have just started to space it out now.

### **Andrew Schorr:**

Okay. Well, yeah. We have done some programs actually on younger adults with cancer, and I know it's something to be very attentive to throughout the rest of your life.

We are going to talk more after the break about are there some people who are more at risk for testicular cancer because I am sure, Michael, you wondered, well, where did this come from. And we will educate the public on that after we take a break. We are going to continue our discussion with Michael Pellon, who was treated three years ago for testicular cancer and is now doing really well, and also his doctor who is an expert in testicular cancer, Dr. Lance Pagliaro from M. D. Anderson. We will be right back with much more of Patient Power.

## **Combination Therapy**

### **Andrew Schorr:**

Welcome back to Patient Power. Andrew Schorr here with our discussion about testicular cancer. Now, it is not a common cancer. Maybe seven or eight thousand American men will be diagnosed in 2008 with it. About 80 to 90 percent of the cases are very successfully treated. Obviously there are different forms of it and everybody needs really personalized medicine to see what you are dealing with, but

as you have been hearing on our program Michael Pellon, who had cancer that had spread to his lungs and surgery, not just on his having a testicle removed, but also surgery on his lungs, he is in graduate school, and he is cycling, and he is doing well. So there is a lot to be very hopeful about. But let's learn more about it.

I want to go back to our medical expert, Dr. Lance Pagliaro. Doctor, help us understand, there are treatments you mentioned, a lot of drug choices so that can be personalized. Is it typically a combination of drugs that are used when chemotherapy is indicated?

**Dr. Pagliaro:**

Yes. For tumors that have spread and particularly for nonseminomatous germ cell tumors we always use a combination of chemotherapy drugs, which helps to overcome drug resistance which may occur. Any one cancer cell may be resistant to this or that drug, but by having a combination of drugs we are able to achieve a more efficient eradication of tumor cells. The standard regimen which is most commonly used for nonseminoma testicular cancers that have spread is the three-drug combination of bleomycin, etoposide and cisplatin.

**Andrew Schorr:**

All right. Now, you mentioned, though, that bleomycin can be left out sometimes. Is there another drug that's been substituted?

**Dr. Pagliaro:**

Well, there are many, many other drugs that have activity in the disease that would be used for example in second line treatment for cases where the disease comes back but still can be cured. There are high-dose chemotherapy regimens which are done in conjunction with autologous stem cell transplant, which is sometimes called bone marrow transplant. And in certain cases of nonseminoma that has spread which are in what we call the good prognosis category which are not too advanced, we have a choice of either giving the three-drug regimen for three courses or just two drugs, the etoposide and cisplatin, for four courses. And so we consider the relative risks in terms of whether the patient has preexisting lung disease or a habit of cigarette smoking, and we also discuss with the patient their lifestyle, their interests, their habits, and what is their preference. If the patient is a singer or a professional, you know, a champion cyclist like Lance Armstrong, it may be more important for them to avoid the drug that can harm the lungs.

**Andrew Schorr:**

Now, Michael, you went through a lot with your lungs, you know, had lung surgery, it had spread to your lungs. But you're cycling. How do you feel your lung health is these days?

**Michael:**

Well, it's definitely not anywhere near champion cycling league, you know, in that area, but it doesn't stop me from doing what I want to do in a normal, you know, not just normal everyday life, but even being active outside of that. Like I said I have been going hiking and cycling, not really slowed down tremendously. Throughout the process, it's worth mentioning that Dr. Pagliaro along with, even while I was on bleomycin and well before and after, they are doing what they call pulmonary function tests. And throughout the whole period they are monitoring my lung function to ensure that it's not decreasing at all. So M. D. Anderson pays very close attention to not just treating the cancer but treating the whole body and just keep making sure that while these very powerful drugs are flowing through your system you are not injuring some other portions of the body as well.

**Early Detection**

**Andrew Schorr:**

Right. No, I found that too being a patient there.

Doctor, I want to back up for a second. So men are listening, and maybe they were diagnosed with this so they sought out this program or a family member did. Now, there are some men who won't need these powerful drugs, right? We have talked about the cancer spreading, but when it has not, could surgery be enough?

**Dr. Pagliaro:**

Absolutely. Testicular cancer often causes pain or swelling in the testicle which a man will detect and hopefully will report to his physician. I just want to emphasize here especially to young men, you know, in high school or college that if they ever detect pain or swelling in a testicle to let somebody know right away, either a doctor or a parent or a teacher. I unfortunately have seen many cases of young men who were embarrassed or just were too busy to worry about it until their tumor becomes very advanced, so it is something you want to get checked out right away.

**Andrew Schorr:**

Right. Well, I have two young boys, one, you know, in college, and he is a busy bee, a freshman in college, as I am sure, Michael, you were. And so would he, with a cough that didn't go away, would he go to the doctor? Probably so. If he felt some pain in his scrotum unless it was really serious, if it was just annoying, would he go to the doctor? Maybe not. So I think we have a message about this.

Now, is there also a message to primary care healthcare providers, whether pediatricians or internists or nurses, because many of them may never even think about testicular cancer since it's not common, but is there any statement you want to make to them?

**Dr. Pagliaro:**

Well, many times these young men will first see their pediatrician. And I think fortunately pediatricians and family medicine physicians are attuned to the possibility of testicular cancer in young men, and in my experience usually those types of visits quickly result in referral to a urologist. I would want to emphasize again, and I think we mentioned this before, the urologist can do an ultrasound test, which is a painless test that can be done right in the office and very quickly gives some confirmation yes or no whether this could be a testicular cancer.

And you had asked about do all patients require chemotherapy or can some be managed with surgery? The earlier we detect it the less likely it is to require chemotherapy. And those that are confined to the testicle, once the testicle is removed, those patients can be managed either with watchful waiting, where they have checkups periodically and treatment is only given if and when they need it, or they can receive preventive treatment, which immediately lowers the risk. Still requires careful follow-up, but with a much lower chance that additional treatment would be required.

**Risk Factors**

**Andrew Schorr:**

Now, what leads to this cancer? Do we have a clue? Is there any correlation between anything that could put someone at a higher risk?

**Dr. Pagliaro:**

Right. We know that there are some groups of people who are more likely to get testicular cancer than others. We know of a few risk factors, but we don't know the exact cause of why one person gets it and another does not. So just to list a few of those, boys who had undescended testicles, or an undescended testicle in infancy have a higher risk of developing testicular cancer at some point later in life.

**Andrew Schorr:**

I mentioned I am one who shares my history. I talk about my leukemia all the time. So I was a little boy who did have an undescended testicle and actually had minor surgery for that when I was about five to push it down. Interestingly, nobody, and I mean nobody and I am 58 years old, has mentioned that risk to me. So am I at risk now in my late 50s? You know, we mentioned all about younger men, but if I had that possible correlation would that show up typically when you are younger or could it be at any time?

**Dr. Pagliaro:**

Well, the risk is lifelong, and men or boys can get testicular cancer at any age. The most common age is in the teens and early 20s, 15 to 25. There is a second peak of incidence later in life in men in their 50s and 60s which are almost entirely pure seminoma, so those are a particular subgroup. But it really can happen at any age.

And the men who have had a history of undescended testicles only make up two to three percent of the patients that we see. So, you know, it is a risk factor, and statistically the risk is higher for those patients, but it is still uncommon.

**Andrew Schorr:**

Okay. What about other factors? Like what about injuries? So you know, we tell our kids, I have kids who are active in athletics, and the boys wear cups, you know, but I can remember like many of us older, before they always told us to do it, play baseball, and if you get hit there somehow and you are in terrible pain, but is there any correlation with injury?

**Dr. Pagliaro:**

No, there is no established relationship between trauma and germ cell tumors. There are other cancers that can be associated with chronic inflammation or trauma, and having a history of trauma or, you know, a preexisting lump or swelling may mask the diagnosis or cause a delay in seeking help. But that is not an established risk factor that would be related to the cause of germ cell tumor.

**Andrew Schorr:**

All right. Now, what about, so take Michael. So if Michael has children, would his male children be at any higher risk?

**Dr. Pagliaro:**

Well, that's a good question. There is some evidence that first-degree male relatives of patients with testicular cancer have a higher risk of developing testicular cancer themselves, as there is a higher risk of the patient developing a second testicular cancer in the other testicle. So both of these observations point to some risk factor relating to genes that we inherit from our parents, something in our genetic background that may predispose to testicular cancer.

Another clue in that direction is the racial differences in incidence of testicular cancer. It's much more common in Caucasians than in Asians or African-Americans or people in sub Saharan Africa.

**Andrew Schorr:**

Do we have any idea why?

**Dr. Pagliaro:**

We don't. And it's striking. I do have patients who are African-American, but, you know, they are a distinctly small percentage of the total.

**Andrew Schorr:**

All right. Well, we are going to take another break, but before we do, I just want to recap a couple of things you said, Doctor. So obviously younger men in particular should be attentive to any kind of pain or swelling they have, and earlier detection

and treatment makes a big difference. And yet happily in most cases you can do a lot in fighting this cancer, and not all the time, but most of the time you have talked about, you have used the cure rate. You have used the cure word, I should say. So that's very encouraging.

When we come back, we are going to learn more about where you are in research so that everybody can be helped or a much higher percentage and then how you are doing that through clinical trials. And so there is a lot more to talk about as we continue Patient Power. We are talking about testicular cancer, and we will be right back.

### **Advanced Testicular Cancer**

#### **Andrew Schorr:**

Welcome back to our final segment in our discussion about testicular cancer on Patient Power brought to you by M. D. Anderson Cancer Center, and we are hearing from people in the know. Michael Pellon, who is 22 now, but just at 19 he was diagnosed with more advanced testicular cancer, but he is doing well. Went through a lot. He had three different surgeries, one testicle removed, and then it had spread to his lungs. So on Christmas vacation one year he had one lung surgery, and then he had another lung surgery on spring vacation following and a lot of chemo, but he is doing well. And then his doctor is with us who is a hematologist, oncologist, and a specialist in testicular cancer, Lance Pagliaro. He is an associate professor of medicine in the department of genitourinary medical oncology at M. D. Anderson.

Let's continue our discussion, gentlemen. So, Doctor, so sometimes the cancer is more advanced than in Michael's situation. What does that look like? Do you still do surgery, and do you take a look at whether in standard practice or now in research being even more aggressive in chemotherapy, Doctor?

#### **Dr. Pagliaro:**

Right. And probably the best known case of what we call poor prognosis germ cell tumor, the most advanced type, would be Lance Armstrong. He was one of those cases, and I think as most people know was successfully treated with chemotherapy and surgery. For those patients it's especially important to be seen by a physician and begin treatment as quickly as possible. Complications such as bleeding in the lungs, bleeding in the brain and other complications can result in death even before treatment is started. So time is of the essence, and we really treat those cases as a medical emergency.

#### **Andrew Schorr:**

Now, related to chemo, though, so somebody might see a primary care doctor, as Michael did, go to a urologist, maybe something might even be done at a

community hospital, are you saying that when there are these signs that it's more advanced it's like do not pass go, you really, if you can, want to see a testicular cancer specialist such as yourself?

**Dr. Pagliaro:**

That's absolutely correct. And we can identify who are at the greatest risk of death from testicular cancer or germ cell tumors by the stage, which is relating mainly to the organs that are involved and also by blood tests called tumor markers. If they are above a certain range we know that those have a worse prognosis. And also by the location of the primary tumor. We haven't talked about what we call the extragonadal germ cell tumors. There are germ cell tumors that do not arise in the testicles, and one in particular, which is called mediastinal germ cell tumor which occurs in the chest, those that are the nonseminomatous mediastinal germ cell tumors are also in this worst, most difficult to cure category.

**Andrew Schorr:**

All right. So let me see, it's not really testicular cancer. Testicular cancers are usually germ cell cancers, right?

**Dr. Pagliaro:**

That's correct.

**Andrew Schorr:**

Okay. So now we are saying, well, we are not talking about in the testicle. We are talking about it in the chest. So how, what is the sign of that? How would you know you had that?

**Dr. Pagliaro:**

Right. Most commonly cough or chest pain or shoulder pain or shortness of breath. Mediastinal germ cell tumors can be seminoma or nonseminoma. They have a similar diversity of cell types as what you see in the testicles. They still can be cured. In fact, the pure seminoma in the mediastinum has a good prognosis, as good as a testicular tumor. It may require surgery on the chest. Obviously the anatomical considerations are different. And those are distinctly uncommon. That's less than five percent, probably less than one percent of germ cell tumors are mediastinal germ cell tumors.

**Dose Dense Chemotherapy**

**Andrew Schorr:**

Okay. Now, I understand you are doing research in what's called dose dense chemotherapy, and I have actually done programs about it in breast cancer as well. And the idea is to give kind of more--higher doses and more frequently I know to try to beat the cancer, and then support the patient related to the side effects that otherwise you might have of those powerful medicines being given so frequently.

Where are you with that? And what's the theory behind why this might be effective for people with more advanced cancer?

**Dr. Pagliaro:**

Right. Well, a little background to that. There are a couple of ways to intensify chemotherapy. One is by giving a higher dose, and one commonly used technique is what's called stem cell transplant or bone marrow transplant, where the patient's own bone marrow is actually removed and frozen or stored at cold temperature. The patient is given a very high dose of chemotherapy, and then their bone marrow is returned.

At M. D. Anderson we are doing a slightly different approach, which is using a number of chemotherapy drugs, more than just three, and giving them at more frequent intervals, that's referred to as dose dense chemotherapy, to give the cancer cells less time to recover in between each treatment.

**Andrew Schorr:**

And this of course is in research right now. So what would the discussion be for someone with more advanced testicular cancer, a germ cell cancer, would be with someone like yourself is what's standard therapy, what are clinical trials, and let's have a discussion about whether these should be considered in my case.

**Dr. Pagliaro:**

Well, with what are referred to as poor prognosis germ cell tumors, unfortunately the cure rate with the standard four courses of bleomycin, etoposide and cisplatin chemotherapy, cure rate is less than 50 percent. More than half of those patients die of the disease. Now, we have other drugs that are also effective against testicular cancer or germ cell tumors. We can give those drugs. We know that they will have more side effects, but we don't know that they will cure more people.

So in the clinical trial we have some patients receiving the standard chemotherapy and some patients receiving a more aggressive treatment that has more drugs given more frequently with a greater risk of side effects. And we won't know until we finish the trial whether giving the more aggressive treatment results in a better cure rate that would offset the greater risk from the treatment itself.

**Advice for Others and Hope for the Future**

**Andrew Schorr:**

Well, I was part of a phase II clinical trial, and it worked out. And, now, I was not in the more advanced case, so mine was for previously untreated patients and patients that maybe had a pretty good prognosis, but the treatment that I received, the three-drug combination, is what most people get now. And I am happy that I could help and it worked for me too. So I would always encourage people to look at clinical trials.

Michael, I have some questions for you. So you have been listening, and of course you have been living with this now for three years, and I think as you mentioned you are still kind of processing what happened. But there are people who may be listening now, maybe young men who were just diagnosed, came out of nowhere, as it did for you, and their families. What would you say to them to help them get through it and hopefully have a result like you have so far where you are going to grad school and biking and going about your life?

**Michael:**

Certainly. I think the biggest single message, if you could encapsulate everything in one word of the past three, three and a half years, it's been perspective. You have to really just keep a perspective about you. I mean, initially honestly it kind of set in as a shock, but I knew quickly that I had to turn to, well, again this is going to be my job for this short interval in my life unfortunately where I would have to work very intimately with Dr. Pagliaro. And, you know, he can only do so much. I mean, he can prescribe medicine and all that, but equally important is my job and the patient's job on that side of staying as healthy as you can and keeping a positive attitude about it. It's amazing what having a good, positive attitude can do to affect your outcome. So keeping a good perspective, keeping, you know, family members involved, encouraging the support of other relatives and close family, and as well as just keep going about your normal life as best as you can.

As I mentioned, I received chemo in the summer and kind of had to take a break out from being a normal 19-year-old, but as soon as my chemo was done there was really no reason for me to be in Houston, and Dr. Pagliaro encouraged, you know, well, go back to school. You know, obviously there is some things you need to be cautious about. You know, you still have some lower white blood cell counts. You are still a little more susceptible to most diseases, but he knew going in that being in a more positive atmosphere, a normal atmosphere for a 19-year-old was going to do at that extra, you know, oomph to help get cured.

**Andrew Schorr:**

What's your outlook for the future, Michael?

**Michael:**

It's great right now. I guess it's another five years of graduate school, but it's great to be involved with programs like this and stay involved with other activities. I mean, I have seen both my parents volunteer their weekends and stuff. So it's great to just kind of stay involved, and I love talking with people about it, talking to my friends and encouraging them. And I encourage everybody out there listening to take that step even it is scary to get checked or to check yourself, self-examination. Or if you are unsure or you feel uncomfortable examining yourself, asking a physician or medical professional to assist you.

**Andrew Schorr:**

Good idea. And you are a real inspiration, and I wish you well. You know, we did get an e-mail question in, Doctor, that maybe is important to cover. Jeff from Phoenix wrote in, and he said, "I know this sounds bad, but I have had a small, pea-sized lump on the bottom of my left testicle for a few years and have never thought anything about it until now. It has stayed the same size until recently, and I don't have any pain. Should I be concerned? And what other symptoms should I look for?"

Now, I would be interested to know what you say about him, but I also wonder whether you want to just take a minute and talk about, you know, we are all focused on if there is anything with the testicle, oh, my god, it's cancer. Couldn't it be other things too?

**Dr. Pagliaro:**

Sure. And a urologist or even a family doctor just by examining the testicles may be able to determine that it is more likely to be epididymitis or some other benign condition. But, you know, we don't know enough about the case to say that at this point. Certainly Jeff or any man of any age really who has a swelling of the testicle needs to see his physician, get it checked out. It may be something that can be resolved with antibiotics. If there is any question, they will do the test called an ultrasound that we talked about. It's painless, it's simple, it's quick, and that will right away give an indication of if this is something that needs to be worked up further.

**Research and Clinical Trials**

**Andrew Schorr:**

Good advice. Yeah. I think I actually did that one time, and I really breathed a sigh of relief afterwards.

So, Doctor, putting it all in perspective as we draw to a close, this is a cancer, not common, but where most of the time the treatment modalities you have, whether it's surgery, sometimes radiation, chemotherapy, more often are going to have people go back to a normal life. They need to be followed, and sperm banking we talked about. A man can go ahead and have children. So I think it's a more upbeat story, but can we hope as you are involved in research that it can help even more people as time goes on?

**Dr. Pagliaro:**

Yes. You know, as I mentioned we are performing our clinical trial. It's a randomized trial where patients receive either standard treatment or a newer type of treatment, but there is no placebo involved in this trial. There is no secret about what the patients are getting. Everyone is getting treatment that is curative in many cases. And, you know, by doing these clinical trials and by patients

participating we hope to learn, and if we can identify a new treatment which is more effective which results in a greater cure rate, you know, a better batting average, so to speak, then that would become the standard of treatment in the future. And it's only through those kind of clinical trials.

In this case our goal is to have 240 patients worldwide on this clinical trial. As you can imagine with a rare disease, that takes a long time and a lot of effort to complete, but only by doing that with that large number of patients can we really learn and move the ball down the field.

**Andrew Schorr:**

Well, I encourage people to be part of clinical trials again.

And, Michael, I want to wish you all the best in your studies. I think it's interesting to note in your case that it looks like you are applying your mathematics and computer science to the medical field, aren't you?

**Michael:**

Yes. It's kind of ironic that I am working with an advisor who works closely with the college of medicine here.

**Andrew Schorr:**

Yeah. Well, good for you, and if you come back to Houston, maybe you will work with M. D. Anderson, bring your brain power and your experience as a patient as well. So all the best to you.

Dr. Lance Pagliaro, I want to wish you all the best in your work and your dedication to patients like Michael, and thank you for joining us today as well.

**Dr. Pagliaro:**

Thank you. I've enjoyed talking with you.

**Andrew Schorr:**

All right. Well, this is what we do on Patient Power. Every two weeks I am just thrilled that I get to host these programs with leading M. D. Anderson experts, very inspiring people like Michael Pellon today, and help bring people around the world information about very serious diagnoses.

Now, if you want to hear this again of course or share the transcript, you always can go there, recommend it to a friend. And remember that every two weeks we will have another program maybe on another cancer, but often we do programs on issues that touch everybody. Michael mentioned about the fatigue he was going through during treatment. Well, he is a pretty upbeat, kind of go straight ahead guy, but other people deal with depression or anxiety or their family members might. We have discussed that in our library of programs. And then also we have



talked about the issue of being a long-term survivor, the opportunity. And as you have heard there needs to be monitoring as well, whether for a second cancer or a recurrence. So lots to talk about, and I think our library of M. D. Anderson programs is unmatched.

So thank you so much for joining us on our Patient Power program brought to you by M. D. Anderson. I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.

Please remember the opinions expressed on Patient Power are not necessarily the views of M. D. Anderson Cancer Center, its medical staff or Patient Power. Our discussions are not a substitute for seeking medical advice or care from your own doctor. That's how you'll get care that's most appropriate for you.