

Yale CANCER CENTER *answers*

WNPR Connecticut Public Radio



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Testicular Cancer: Diagnosis and Treatment

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Welcome to Yale Cancer Center answers with Dr. Ed Chu and Dr. Ken Miller. I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center, and Dr. Miller is a Medical Oncologist specializing in pain and palliative care, and he also serves as the Director of the Connecticut Challenge Survivorship Clinic. If you would like to join the discussion, you can contact the doctors directly at canceranswers@yale.edu or 1-888-234-4YCC. This evening, Dr. Ed Chu welcomes Dr. Kevin Kelly. Dr. Kelly is the Co-Director of the Yale Cancer Center Prostate and Urologic Cancer Program and Associate Professor of Medical Oncology at the Yale Cancer Center.

Kelly Testicular cancer is a group of cancers that evolve or arise from the testicle itself. There are several types of testicular cancers. There are typically germ cell tumors. In germ cell tumors there are two main types called seminoma and nonseminomatous germ cell tumors. But, there are other types of testicular cancers that can arise in different areas of the testicles that either are more like a sarcoma or they can even be lymphomas or other types of tumors that arise, but the most common type that we see is the germ cell tumors, which are either seminomatous or nonseminomatous germ cell tumors.

Chu How common is this disease?

Kelly This is actually a very rare disease if you look at all malignancies. There are around 8,000 cases diagnosed in the United States per year. However, if you look at young male adults, it is the most common cancer that is diagnosed. It is more common than lymphomas and leukemia's combined. In patients from the age of around 15 to mid-20s, it is the most common tumor diagnosed.

Chu What are the usual presenting symptoms that a male needs to be aware of?

Kelly The major concern is increasing mass in the testicle itself. It could be painful or it may be asymptomatic. Some people do get breast tenderness, which is the first sign. Other patients present with back pain, which is a sign that the cancer may have spread. It is very important for young males, just like we teach with breast cancer, to do breast exams. Testicular exams are a very important component that should be taught to young males as they are growing up. A lot of this is being taught in the pediatric offices now, about the appropriate screening for testicular cancer.

Chu Interesting. What age should boys start self-testicular exams?

Kelly Once they start puberty is when they should actually start. Any abnormality in the testicle should be brought to the attention of their physician. Again, that is the best way to help detect testicular cancer early.

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Chu What are the main risk factors for developing testicular cancer?

Kelly There is a familial trait to germ cell tumors, a family history. Other risk factors are if you had an undescended testicle at birth and it was brought down, or you still have an undescended testicle. Syndromes such as Klinefelter syndrome have a higher incidence of testicular cancer.

Chu But for the majority of folks?

Kelly It's sporadic.

Chu Take us through the process Kevin, there is a mass in the testis, and you then go to your general internist or family doctor to have it evaluated?

Kelly Typically it is found by an internist or general practitioner who notices this abnormality, then it is seen by the urologist who can evaluate it because not all masses within the testicles are cancer. There are what we call benign masses and you really need an expert who sees this all the time to evaluate it, typically a urologist. If there is a suspicious mass, the first step is an ultrasound of the testicles. If there is something suspicious on the ultrasound, what we typically do is remove the testicle. We remove it through an incision in the groin and then the pathologist does examine the specimen at that point.

Chu There is no indication for a biopsy first before removing the entire testis?

Kelly No. The problem is that if there is a tumor in the testis, and you biopsy, you can track tumor through and infect the scrotal skin. If that happens then it is a more serious spread of the cancer. The most common way that we diagnose if there is a suspicious mass within the testicle is with what we call inguinal orchiectomy.

Chu What happens after the surgery is performed?

Kelly Typically before or after surgery we draw blood because germ cell tumors typically have tumor markers within the blood that are very diagnostic for certain types of tumors. There are three types that we look at. They are called alphafetoprotein, beta HCG and LDH. These three markers are very important to how we diagnose and manage germ cell tumors.

Chu Are those three markers elevated in all types of testicular cancer?

Kelly No they are not. Depending on what type, if you have seminoma versus nonseminomatous tumor, they would be differently elevated. But in the majority, one of those three is elevated in more advanced stages of germ cell tumor.

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- Chu Would one do any type of imaging study like CAT scan to see if the cancer is spread throughout the body?
- Kelly That is correct. The most common places where germ cell tumors spread to are the back, the abdomen, or what we call the retroperitoneum. A CT scan can visualize that very carefully. However, germ cell is very specialized because we know where exactly it goes into the body. Even a small lymph node may harbor cancer and physicians have to be very suspicious because germ cell can spread very quickly and very easily. An important point is that we know delay in diagnosis of the germ cell tumors actually has a dramatic impact on the overall outcome of the germ cell tumors. When a patient does have a testicular mass, it needs to be worked up efficiently and expeditiously because delay in diagnosis decreases the ability to cure that patient.
- Chu Presumably if there is a delay in the diagnosis the cancer has a chance to spread.
- Kelly Particularly the nonseminomatous germ cell tumors are rapidly growing tumors, and they can actually spread. Once we have diagnosed that, we work these patients up very quickly to ensure that they get the appropriate treatment to maximize the cure.
- Chu At the Yale Cancer Center, you oversee the genitourinary urologic cancers as a multi-disciplinary team. Can you tell our listeners out there who is involved in that team and why that team is so important?
- Kelly It is critical that there is a team of us that take care of these patients. It really exemplifies how a team approach can not only diagnose and treat but actually cure patients. It takes all three of us on the team to do it. It is composed of a medical oncologist, a urologic surgeon, and the radiation oncologist. Each have a role in the treatment of germ cell tumor and we will talk a little bit further about that, but the real role of each is to cure a patient with germ cell tumor. It will take a combination of all our specialties in order to have an optimum outcome for these patients.
- Chu Once you evaluate a patient with this multi-disciplinary approach and a diagnosis is made, the patient undergoes surgical resection and then you try to figure out what stage the disease is. Can you go through the different stages of testicular cancer?
- Kelly Typically we are talking of germ cell tumors not testicular cancers because germ cells are the most common tumors, and they are divided into two types. One is seminoma and one is nonseminomatous germ cell tumor. Once they have a surgical resection, typically we do a CAT scan of the chest, abdomen and pelvis to look at the extent of disease. We will repeat the tumor markers, which are the

beta HCG, alphafetoprotein and LDH after surgery, because if it is elevated beforehand and it comes down, it gives us more information. We watch those serially because we know that there is a certain half-life of these markers, and they should come down appropriately after resection of tumor or treatment. At that point, depending if you have a seminoma, or very localized disease, radiation therapy after the orchiectomy may be appropriate. For a patient who has a nonseminomatous germ cell tumor, depending on the pathology results, either chemotherapy or surgical resection of any residual or small lymph nodes in the back of the abdomen may be an appropriate first step.

Chu We would like to remind you to email your questions to canceranswers@yale.edu or call 1-888-234-4YCC. At this time, we are going to take a short break for medical minute. Please stay tuned to learn more information about testicular cancer with our special guest, Dr. Kevin Kelly.

Medical Minute

Over 170,000 Americans will be diagnosed with lung cancer this year, and more than 85% of these diagnoses are related to smoking. The important thing to understand is that quitting even after decades of use can significantly reduce your risk of developing lung cancer. Each days patients with lung cancer are surviving, thanks to increased access to advanced therapies and specialized care, and new treatment options are giving lung cancer survivors new hope. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatments for lung cancer. Patients enrolled in these trials are given access to medicines not yet approved by the Food and Drug Administration. This has been a medical minute, and you will find more information at www.yalecancercenter.org. You are listening to the WNPR health forum from Connecticut Public Radio.

Chu Welcome back to Yale Cancer Center Answers. This is Dr. Ed Chu, and I am here in the studio this evening with my special guest, Dr. Kevin Kelly talking about the latest treatment options and developments for testicular cancer. Kevin, before the break we were talking about the different stages of testicular cancer. For those just joining us after the break, can you review what the different stages of testicular cancer are, just in general?

Kelly In a broad sense you can actually divide the patients into stage I, II, and III. Stage I is more or less localized to the testicle. Stage II is if you have an involvement of the lymph nodes in the abdomen, and stage III is more advanced disease. What is interesting is that we can actually diagnose patients based on the risk categories, and we look at patients not only for the extent of disease based on stage, but their risk assessment. We can do that by looking at where the cancer is, what type of cancer it is, what the tumor markers are and whether HCG, alphafetoprotein, or LDH are elevated. We can divide them into what we call good risk, intermediate

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risk, and poor risk, and that helps our treatment. We know in seminomatous tumors that virtually all those tumors are only good risk and intermediate risk tumors. However, in the nonseminomatous germ cell tumors, you can have good risk, intermediate risk and poor risk tumors, and that really helps us designate what type of therapy these patients need.

Chu Do those different risk categories also give an idea as to how they would respond to treatment?

Kelly Absolutely, that is why they were designed. Germ cell tumor is the one tumor that we can actually cure, and that is an important point. Over 90% of patients, we can cure with the appropriate therapies; that includes surgery, radiotherapy, and chemotherapy. Depending on your risk category, we will modify the chemotherapy for the patients.

Chu Probably the most dramatic example of such effective treatment options for testicular cancer is the case of Lance Armstrong.

Kelly Absolutely. He is the poster child for germ cell tumors, but there are a lot of others out there with similar cases that also have been cured from the tumor. When Lance Armstrong was diagnosed he had very extensive disease, he even had disease to the brain, and through extensive therapy for over a year, and with resection of residual disease, he is cured from his cancer. One of the points I do want to make is that what we do cures a majority of germ cell tumors, but there is always a chance that tumor can come back. You get the treatment but it is a lifelong follow-up of these patients because these are young patients and they can have secondary complications to the therapy down the line.

Chu We can get back to that. When I was down in Bethesda, Maryland at the National Cancer Institute, we saw a number of young military males presenting with testicular cancer. I can remember the first question they would always ask was if they would become sterile once we started chemotherapy. What are your thoughts on that subject?

Kelly We are always concerned about the fertility of these young men, because most of them are not married, or newly married, and still are looking forward to having a family. Typically before we do either an orchiectomy or any therapy, we ask them to go to a sperm bank first. The majority of these patients, even with the diagnosis, have what we call low sperm counts, but after chemotherapy, their sperm count, or the ability to be fertile afterwards, markedly decreases. It is not zero, but it is markedly low. We encourage all of our patients to use a sperm bank before they start treatment, and that is a very easy process.

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Chu Can you give an approximation as to how many males might become infertile because of the chemotherapy?

Kelly What we always tell patients is that it is 100% will. We cannot count on it even if they do have sperm, we cannot tell them if they are going to be active, or if the number of sperm is going to be adequate to have their spouse become pregnant. That is why upfront we always encourage the sperm bank.

Chu What has always impressed me about testicular cancer is how sensitive it is to chemotherapy and radiation therapy. It is very different than other diseases that you also take care of such as prostate cancer and bladder cancer.

Kelly Yes.

Chu Is there any reason why this kind of cancer is so sensitive to chemotherapy and radiation therapy?

Kelly I thought you were going to tell me the answer Ed. That is a question that has been asked a lot, and unfortunately, I do not think we have a good explanation for it. Historically, germ cell tumors were always incurable tumors. If you look back in history, in the 1970s, this was a very fatal disease. It was not until the mid 1970s, when multi-agent chemotherapy came in, and there was a major effect when cisplatin-based chemotherapy was invented. It dramatically changed how we treat germ cell tumors. The impressive thing is what was done with germ cell tumors. You had a lot of smart people in the field that did very logical studies to optimize the treatment for germ cell tumors. It really showed that working together with our surgical colleagues, the urologist, the medical oncologist and the radiation oncologist, to develop the most optimal program for these patients, pays off. These trials are difficult to do because they are rare tumors; however, our colleagues in Europe and the United States worked together to do these large trials that showed us what the optimal treatments for germ cell tumors are.

Chu A significant advance came once cisplatinum was developed.

Kelly Exactly. That was a huge breakthrough at that time and it had a significant impact on germ cell tumors.

Chu What are some of the short-term, immediate consequences and side effects of the chemotherapy that you give patients with testicular cancer?

Kelly We give very aggressive chemotherapy to these patients and the typical drugs that we give are either what we call topoisomerase II inhibitors, cisplatinum or a third drug called bleomycin. Depending on what your risk category is at presentation, you may get two of those drugs or three of those drugs. The major side effects that we see

with chemotherapy are that they can lower your blood counts. Blood counts are 3 components, your white cells, red cells and platelets, and chemotherapy can affect all three. Young men typically tolerate very high doses of chemotherapy very well and bounce back, but there are medications that can help them with white counts and red counts to get through the therapy. Other side effects that they may have are nausea and vomiting. We give very high doses of cisplatin and that is one of the major difficulties. However, with the newer medications we have we can prevent nausea and over 90% of the patients seen are very aggressive with that. As we see these patients come through they actually have a very good quality of life and most of them continue to work while they receive chemotherapy. They do have other side effects such as hair loss; however, it all comes back within 4 to 6 weeks after the chemotherapy stops. Other things that can happen are that it can actually give you numbness and tingling in the hands and feet, but overtime it is reversible.

Chu As far as we know, are there any long-term consequences of chemotherapy treatment?

Kelly Yes, and as we are following these patients out 10 years, 15 years and 20 years, there are incidents where we particularly look at the incidence of leukemia, because a lot of these drugs can cause leukemia, but this occurs in around 2% of patients. That is one of the reasons why we have long-term follow-up of these patients. Another long-term side effect is cardiovascular risk. The cardiovascular risk increases as time goes out. We know that if you look at age control population, you see that the incidence of cardiovascular disease is higher at a younger age in these patients; so we need to watch them very carefully. Two other things that do happen is that you can get lung toxicities and this is particularly from one drug we give called bleomycin. We just have to monitor that. The other is a disease called Raynaud disease, which is very common with both cisplatin and bleomycin. This happens at a younger age than the natural history of Raynaud disease.

Chu What about if a patient is say, out 5 to 10 years from their treatment and they were cured, do you still have to worry about the risk of recurrence?

Kelly Absolutely. We still watch these patients out to around 5 years. We still see them on a yearly basis. We want to check their blood counts because that is one of the earliest signs we see in people with leukemia. We may want to still do a chest x-ray to make sure there is no recurrence. We will check their tumor markers and they should continue follow-up for at least 10 years, and subsequently even longer for any side effects from the chemotherapy.

Chu Who would typically then follow after say five years? Would it be the medical oncologist, the urologist or both working together?

- Kelly We typically work together, whether it is more convenient for the urologist or medical oncologist. Typically, in those patients who received chemotherapy or had more advanced disease, I have a tendency to follow them because I am looking for more of the side effects of chemotherapy. We are more tuned to that versus somebody who has a very local disease which is typically followed by the urologist.
- Chu Now suppose, God forbid, the testicular cancer comes back; the patient has been diagnosed with recurrent disease. Are there treatment options available at that point?
- Kelly Yes, there are, and the important thing is that this is still curable at that point too. There are what we call salvage chemotherapies which include a high-dose of chemotherapy. At times we even do what we call transplants or stem cell transplants in these patients. Even those who have the worst recurrence of disease, there is still a portion of those patients that we can cure.
- Chu If someone were out 8 to 10 years and presenting with new disease, would you go right away to the high-dose therapy or could you go back to the original therapy that they had received and had such good results with?
- Kelly The question we would have here is, is this truly a recurrent disease, or has this developed maybe in the opposite testicle? You would have to differentiate that. One of things that we also get concerned about with germ cell tumors is a rare phenomenon called malignant transformation of a disease. Germ cell tumors are very early cells of what we call primordial cells. Primordial cells are certain cells that grow and can be what we call teratoma, and those teratomas over time can transform into other types of tumors, a sarcoma for instance, or they can even become an adenocarcinoma. If we see a new mass, we always like to re-biopsy to reestablish a diagnosis to optimize the treatment for the patient.
- Chu In the setting of the teratoma that you just mentioned, would one want to have surgical resection of that teratoma so they wouldn't have to then worry about subsequent malignant transformation?
- Kelly Yes. Typically, after a patient gets chemotherapy upfront, we reevaluate the patient and if there is any evidence of a mass, whether in the lung, the back of the abdomen, or wherever, we take that out because there are three possibilities that could be in that residual mass; it could be a dead tumor, it could be a still residual tumor or what we call teratoma. Teratoma is not sensitive to chemotherapy and that is why we need to resect it. If we do not resect it, then it has a chance to do what we just discussed about malignant transformation.

Chu Over the final couple minutes of the show, Kevin, can you just tell our listeners what research is being done at the Yale Cancer Center focusing on testicular cancer?

Kelly One of the biggest quandaries that we're having in testicular cancer is that the incidences are actually increasing over each decade, and the epidemiology department here is looking at reasons why. There is some concern that there may be an environmental factor that is increasing the incidence of germ cell tumors. This is a study being conducted by Dr. Zeng, here in our epidemiology department, and also by other colleagues around the world.

Chu Kevin thanks so much for joining me this evening on the show. It has been a terrific session and I look forward to having you on a future show to discuss the further advances of testicular cancer.

Kelly It is a pleasure.

Chu Until next week, this is Dr. Ed Chu from the Yale Cancer Center wishing you a safe and healthy week.

If you have questions, comments, or would like to subscribe to our Podcast, go to www.yalecancercenter.or where you will also found transcripts of past broadcasts in written form. Next week, we will look at sexuality and cancer with Dr. Dr. Sharon Bober and Ellen Matloff.