

Dr. Kevin Kelly, Diagnosing and Treating Testicular Cancer January 31, 2010 Welcome to Yale Cancer Center Answers with Drs. Ed Chu and Francine Foss, I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1888-234-4YCC. This evening, Francine welcomes Dr. Kevin Kelly. Dr. Kelly is the Co-director of the Yale Cancer Center Prostate and Urologic Cancers Program and an Associate Professor of Medical Oncology at Yale School of Medicine.

Foss Could you tell us what the different types of testicular cancer are that are diagnosed? Kelly There can be several types of testicular cancer. There can be germ cell tumors, which we will talk about in a minute, but there can also be other tumors such as metastatic disease that actually goes to the testicle, you can have a lymphoma in the testicle, or from other structures within the testicles a tumor can arise. Typically, when we talk about testicular cancers, the most common type is what we call a germ cell tumor, and a germ cell tumor can be broken down into two categories. One is what we call a seminoma, and the other one is called non-seminoma germ cell tumor.

Foss Can you tell us a little bit about how frequently we see these types of testicular cancers and what age group they occur in? Kelly If you look at the germ cell tumors, they are typically the most common tumor that we see, that is usually between age 15 and 35. There are around 8000 cases per year of germ cell tumors. The other tumors that are not germ cell tumors can be found in the older population and they are actually fairly rare tumors.

Foss Say a young gentleman comes in with a testicular mass, and this happened in my clinic the other day in fact, can you tell us how commonly that would actually turn out to be a tumor as opposed to something else? Kelly Again, as you know, when patients have a testicular mass, they always should be checked out because germ cell tumors are curable tumors. But again, finding masses within testicles is fairly common and they need to be worked up appropriately. Workup would include a good physical exam by the physician and an ultrasound in a timely manner.

Foss How often do you actually see young men coming in with these masses that they don't know really what it is? Kelly As a primary physician, they typically will see around 10 of those a year, but there are a lot.

2:57 into mp3 file <http://www.yalecancercenter.org/podcast/jan3110-cancer-answers-kelly.mp3> of things in the groin and the scrotum that can actually feel like masses. There can be hernias down there, sometimes you can get a bruise or hematoma in the testicle, but what we get concerned about with a testicular mass is if there is pain, if there is growth in there and it doesn't go away. Those are the things that any young person should really be concerned about.

Foss For the average young person who may discover a mass there, first stop would be say the primary care doctor? Kelly That is correct, the primary care doctor should take a look at it and evaluate it.

Foss And the next step, if the primary care doctor is worried, would be to get an ultrasound? Kelly Yes, an ultrasound of the testes to evaluate whether it's a solid, or what we call a fluid filled mass.

Foss And

then what's the next step, say if it is something that's suspicious, what would happen next? Kelly Then he should be evaluated by a urologist who actually specializes in testicular cancer to evaluate it further. If there is something suspicious, if there is a solid mass in the testes, then further workup, which includes what we call an orchiectomy, or removal of the testicle, needs to be performed. This needs to be done in a special way by bringing it up through the groin instead of going through what we call the scrotal sac. Foss Is there ever a role to just stick a needle in one of these masses, or does it always end up being a surgical procedure? Kelly If it is a solid mass, there is no role for doing a needle aspirate right through the scrotum. There should be more of a surgical procedure at that point. They do biopsy the testicles by doing a small surgery to bring it up through the inguinal region and biopsy it that way. Foss Can you talk about some epidemiologic factors associated with testicular cancer, is there any connection with sexually transmitted diseases? Kelly No there is not. There is no association from estrogens, testicular trauma, HIV, or vasectomy. There is no correlation. The major correlation is to something called Klinefelter syndrome, and also undescended testicles can predisposes patients to testicular cancer. 5:28 into mp3 file <http://www.yalecancercenter.org/podcast/jan3110-cancer-answers-kelly.mp3> Foss In the setting of an undescended testicle, how much does a man have to worry about that and is there any screening that needs to be done? Kelly Anybody who has an undescended testicle needs to be evaluated and followed very closely. Typically, when they are found to have a descended testicle, it is brought down early in their life. But sometimes this is not done and these patients need to be watched very carefully. Foss Should all men be doing self exams? Kelly Absolutely, we teach women that breast exams are important, and testicular exams are also important. If there is any abnormality, they should go to their primary doctor. Foss At what age should a man start doing the testicular self exam? Kelly What we know is that the most common germ cells come between the age 18 and 35, so when you start puberty, or a little afterwards, you should start doing testicular exams. Foss Kevin, from a public health point of view, how often are primary care physicians and pediatricians keyed into this issue, and do they in fact instruct young man on how to do this? Kelly Unfortunately not. I think this is something that we have to do better with and educate our colleagues in primary care that we should be teaching young adults how to do testicular exams and the importance of doing health maintenance. Foss Let's talk a little bit about a patient now that has a diagnosis, so they have undergone a surgical procedure for a mass and they have a diagnosis of testicular cancer. First of all, you talked about a couple of different types. Could you go through a little bit with us what those types are and what the next steps would be? Kelly Yes, there are two main types of germ cell tumors, one is called the seminoma and one is called the non-seminomatous germ cell tumor. Again, these are different types of tumors and they actually have a different growth rate and also respond differently to different therapies. So, it is very important when you actually have a diagnosis of germ cell tumor to understand if you have a seminoma or non-seminomatous germ cell tumor. In addition, what is very important in germ cell tumors is looking

at what we call tumor markers. These are very characteristic for germ cell tumors and there are three main ones we look at. One is what we call the beta HCG, the other one is alpha-fetoprotein, and the last is LDH. Further workup, when you are diagnosed with a germ cell tumor, would be a CAT scan done of the chest,8:17 into mp3 file <http://www.yalecancercenter.org/podcast/jan3110-cancer-answers-kelly.mp3> abdomen and pelvis, and with the blood markers and CT scans, you can show the extent of the cancer.Foss Would these blood tests be done prior to the original biopsy, or are they only done after the diagnosis?Kelly Typically we try to get them before the orchiectomy, removal of the testicle, and then subsequently, after we have removed the testicle, we will repeat those blood tests.Foss So those blood tests are very good markers of whether or not there is metastases left behind, can you talk a little bit about how those markers change?Kelly We know that if the markers are very high, they are what we call prognostic, or predict how severe the cancer is, and actually, it helps us divide the patient's into what we call good risk, intermediate risk, or poor risk tumors. And based on the risk classification of this, a patient's treatment can be determined.Foss Are these markers available to the average practicing oncologist in their office, or do you have to come to a center to get these markers drawn?Kelly No, these are common blood tests, it can be drawn almost anywhere.Foss With respect to other blood tests, do you commonly see changes in say kidney function, liver function, or blood counts when patients present with testicular cancer?Kelly Typically not, perhaps in somebody who has very advanced stage of one of these cancers, you may see some abnormalities, but typically patient's can present with very large masses. They have some pain or discomfort but typically their other organ functions are intact.Foss Kevin, you talked about a CAT scan as being the diagnostic test that you do, we use PET scans a lot for other kinds of cancers. Can you talk about whether PET scanning has a role here?Kelly PET scanning has a significant role in staging. We do use it after treatment in what we call the seminomas to help us to differentiate if there is any residual tumor remaining, but that's still very controversial.10:37 into mp3 file <http://www.yalecancercenter.org/podcast/jan3110-cancer-answers-kelly.mp3> Foss With respect to metastases, do they pretty much go to all different organs or are there patterns of metastases that you look for?Kelly There are patterns that we look for. For seminoma, both germ cell tumors, they have a tendency to go to the lymph nodes in the back of the abdomen and they also spread to the lung, but in rare cases, it can go to bone, liver, or the brain.Foss When a patient presents with metastases, which I take is a common finding for these patients, what is your approach at that point? Do you need to go in and biopsy those metastases? Do you assume that you know that they are testicular cancer, and how does that change your treatment?Kelly In rare cases we wouldn't go in and re-biopsy if we find the diagnosis on the removal of the testicle, plus the blood markers are also good indication of the activity of distant disease. At this juncture, we would evaluate what stage they are and typically that is broken down into three stages; stage 1, 2, and 3, depending if he has localized disease of the testicle. Stage 2 would be disease in the back

of the abdomen, and 3 is anything that has spread beyond the lymph nodes in the back of the abdomen. We combine that with the blood markers and we can actually classify those patient's into the three risk categories; good risk, intermediate risk, or poor risk. Subsequently, it also depends on their cell type. We know that seminomas, almost all of those, are good risk. It is typically the non-seminomatous germ cell tumors that have the intermediate or poor risk features, and based on that we can actually determine whether radiotherapy, surgery, or chemotherapy followed by surgery is most appropriate for the patient.

Foss At what point do you get the radiation therapist involved in the management of these patients?

Kelly Typically the seminomas are the ones that are radiosensitive and those are the patients that will receive radiation therapy typically as adjuvant therapy in the back of the abdomen. If you have very small tumors or lymph nodes in the back of the abdomen, then radiation therapy may also be appropriate for that patient, but typically radiotherapy is not used in the management of non-seminomatous germ cell tumors.

Foss Thank you Kevin, we are going to take a break now. We are talking with Dr. Kevin Kelly on the management of testicular cancer.13:37 into mp3 file <http://www.yalecancercenter.org/podcast/jan3110-cancer-answers-kelly.mp3>

Foss Welcome back to Yale Cancer Center Answers. This is Dr. Francine Foss and I am here with Dr. Kevin Kelly, Co-director of the Yale Cancer Center Prostate and Urologic Cancers Program. Tonight we are talking about testicular cancer. Kevin, you told us a lot about the two different types of testicular cancer and how you diagnose patients and about the different prognostic groups, and I am wondering, how many of these patients actually present in the good prognostic group as opposed to the more advanced disease?

Kelly The majority actually are good prognosis, but the important thing about germ cell tumors is that an early diagnosis and treatment is directly related to the cure rate. So the earlier we find these patients, the quicker we work them up and diagnose them, the better off they are. We have to remember this is a germ cell tumor, this is the one tumor that we can actually cure. Over 90% of patients we can actually cure with the appropriate diagnosis and treatment of these patients.

Foss That's terrific news Kevin. I remember a long time ago now, when I was actually at the National Cancer Institute, and we were doing a lot of aggressive therapy for these types of patients and at that time we learned that the drug cisplatin really had a tremendous role in this disease. In fact, we still use that drug today, but can you step us through the treatment for patients with advanced testicular cancer and what happens after they complete their therapy?

Kelly Typically patients who don't have surgery or radiation therapy upfront, do get chemotherapy, and there are two main chemotherapies that we use. One is, as you described, based on cisplatin, which is a very potent chemotherapy. The other drug is called etoposide. Then again, there are some patients that it is appropriate to use another drug called bleomycin. Depending on what risk category they are we will either use two drugs or three drugs. As these patients get to around 12 weeks of chemotherapy, that is when we usually reevaluate to16:42 into mp3 file <http://www.yalecancercenter.org/podcast/jan3110-cancer-answers->

kelly.mp3see if there is any residual cancer remaining. If there is, then there is a very strong role for surgery to resect any residual amount of tumor tissue left behind.Foss Would the surgery typically be done in different parts of the body? Are there specific areas, say like the lungs, which you target for the surgical excision?Kelly Very typically what we will do is an abdominal surgery where we remove all the lymph nodes in the back of the abdomen and if there is any residual cancer in the lungs, we will go and resect those out of the lungs also.Foss And after that surgical excision do you give more therapy?Kelly In rare occasions we would give additional therapy, but in most cases if we have given appropriate chemotherapy upfront, and we can do an adequate surgical procedure, then patients will not need any further therapy.Foss The way we give this chemotherapy now, can you talk a little bit about the toxicities and the complications, because I know a drug like cisplatin can have a lot of neurologic toxicity?Kelly Yes, it can. We have come a long way over the last 20 years in terms of how we actually give chemotherapy. When I started treating these patients I actually had to treat them all as inpatients for days and weeks, but now all these treatments are done as outpatient. We have better medications to protect from any nausea or vomiting. We know that if we give adequate hydration and are very active upfront, patients can do very well with the chemotherapy, and most of my patients who are going through the therapy right now are still working at least part-time or full-time with it, or going to school.Foss Kevin, we hate to use the word cure because we are never sure with our patients, but after a patient goes through the chemotherapy and surgical excision, and everything is taken out, what do you tell them?Kelly We know that the probability of these patients, from many long-term studies we have found over the years, is that patients that have no tumor after the resection, the blood markers remain negative, and if they pass three to five years, the majority of those patients will not recur. But it is important to remember that we can't always predict who is going to be cured and not cured, while the majority are, we still have to monitor patients very closely afterwards not only for recurrence of the disease, but these are young patients and they can have complications from the chemotherapy and we have to monitor them for many years afterwards.19:40 into mp3 file <http://www.yalecancercenter.org/podcast/jan3110-cancer-answers-kelly.mp3>Foss I would like to talk a little bit more about that in a minute, but I just want to touch on the role of stem cell transplant. There still are some patients with testicular cancer that go on to get high dose therapy and a stem cell transplant. Can you talk about that a little?Kelly Yes, upfront chemotherapy or salvage chemotherapy can cure the majority of the patients, but there are small fractions of patients where the frontline chemotherapy does not work. Subsequently, we give very high doses of chemotherapy with peripheral stem cell rescue, these are cells that help to support the high dose chemotherapy and with that there are patients that can still be cured with high dose chemotherapy.Foss The stem cell transplant that we are talking about involves getting peripheral blood stem cells as opposed to bone marrow cells?Kelly That is correct Francine.Foss And it is pretty similar to what we do

for the hematologic malignancies. Kelly We took a chapter from your book. Foss Thank you. So, I guess the question is, how often do you actually do that? What percentages of patients actually go to a stem cell transplant? Kelly A small fraction overall, I would estimate around 10% to 20%. Foss You didn't mention any new drugs, and I know there are a lot of targeted therapies and antibodies out there now for other kinds of cancers. Are there any drugs like that that are applicable to the treatment of testicular cancer? Kelly As you know, this is one of the cancers that we have done well in trying to treat and cure. So, there hasn't been a huge initiative to look at new drugs because the drugs we have work so well; however, there are some new drugs, some of the targeted therapies, in patients who are really refractory, that we are trying, but since it's a rare tumor is very hard to do these clinical trials. Foss Also I understand it can be somewhat heterogenous in terms of the different cell types within some of these testicular cancers. Kelly That is correct. When it becomes more advanced and refractory to other therapies these are very difficult tumors to treat. 21:50 into mp3 file <http://www.yalecancercenter.org/podcast/jan3110-cancer-answers-kelly.mp3> Foss Another point is that in the case of brain metastasis, that is a situation where you often times do well by excising those. Kelly You can excise them, or even use radiation therapy even if it is non-seminoma, but typically even chemotherapy in this situation will cross the blood-brain barrier and also treat the brain metastases. Foss A patient who presents with brain metastases doesn't necessarily have a dismal prognosis? Kelly We have had some very famous people who have gone on and done very well with brain metastases. Foss You touched on the issue of complications of therapy and I would like to just get back to that right now, could you elaborate a little bit about that? Kelly There are a lot of complications in young men that can occur with the treatment of germ cell tumors. The first to start off is you remove one of the testicles, so they can have difficulty with fertility. Even just having germ cell tumor decreases the motility of the sperm and sperm count. Subsequently, we may have other therapies which actually influence the sperm count such as radiation therapy or chemotherapy. Before any patient ever goes through any therapy with germ cell tumors, we always recommend sperm banking. This allows them to have a family in the future. Other things that can happen is when these patients go through surgery a lot of times the nerves that help have appropriate erections and erectile functions are disrupted and they may get what we call retrograde ejaculation. Thus, that may also decrease the ability to have children in the future. So that's one of the areas. Subsequently, patients who actually have chemotherapy are at increase risk for leukemia. They can have problems with cardiac disease, lung problems, or peripheral vascular disease. These all are monitored for a prolonged period of time after therapy. Foss And how do you go about monitoring those? Kelly This is where we typically refer them back to the primary physician and we talk to the primary physician and tell them to look out for certain symptoms and signs. This includes doing the regular health maintenance workup, make sure of no cardiac disease, doing chest x-rays, looking and making sure they do a CBC on a yearly basis just

to monitor any long-term toxicity from the chemotherapy.Foss You talked about the sperm banking, I just wanted to clarify that for folks who don't know much about that. The sperm is banked and is kept forever?24:41 into mp3 file <http://www.yalecancercenter.org/podcast/jan3110-cancer-answers-kelly.mp3>Kelly Well it is cryo-preserved and is kept forever as long as you pay the bill, I guess.Foss Another question I had is touching on the psychosocial issues associated with say losing a testicle for a young man. Can you talk a little bit about that, I am sure that there are folks that work with you such as social workers that help with these patients.Kelly Yes, that is an issue, and a lot of times we do prosthesis within the scrotal sac so it appears to be normal. There are some circumstances where you know just the change in an appearance while they are getting chemotherapy does affect this young population, especially if they are in school, and we just have to support them thought this time and really encourage him that things will get better. We do have support groups here run by social workers, but we also have a very strong network of other germ cell tumor patients that work with our patients to assure them that they can have normal life after the treatment.Foss Kevin, what happens if a patient recurs?Kelly It's devastating but there is still a chance that we can cure these patients, but we still need some better drugs for those patients who recur at this juncture.Foss Are there national trials looking at new therapies for these patients?Kelly There are some, but again, it's a very rare tumor and it's very difficult to do these trials.Foss What do you see that's new on the forefront in the management or diagnosis of testicular cancer?Kelly I think that one of things is to better understand why young individuals develop germ cell tumors. What's interesting is there is an increasing trend of diagnosis, or there are increased trends of the number of germ cell tumor cases that are rising throughout the world. We actually have epidemiologic studies ongoing to understand why this is occurring. Most likely it is probably related to some of the environmental factors which are influencing the development of germ cell tumors. I think a better understanding about some environmental factors is important and why there is an increase in trend for the development of germ cell tumors is critical at this juncture.Foss And one thing we didn't touch on Kevin, is whether or not there is a racial predilection for germ cell tumors?27:14 into mp3 file <http://www.yalecancercenter.org/podcast/jan3110-cancer-answers-kelly.mp3>Kelly It is typically found in whites over African-Americans, but African-Americans still can develop germ cell tumors.Foss Well thank you Kevin, this was really a terrific discussion on a disease that fortunately is one of the ones that we can cure nowadays, and that's the good news here. You have been listening to Yale Cancer Center Answers and I would like to thank my guest Dr. Kevin Kelly for joining me tonight. From Yale Cancer Center this is Dr. Francine Foss wishing you a safe and healthy week.If you have any questions or would like to share your comments, you can go to [yalecancercenter.org](http://yalecancercenter.org), where you can also subscribe to our podcast and find written transcripts of past programs. I am Bruce Barber and you are listening to the WNPR Health Forum from Connecticut Public Radio.