

Welcome to Yale Cancer Center Answers with doctors Francine Foss and Lynn Wilson. I am Bruce Barber. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Wilson is a Professor of Therapeutic Radiology and an expert in the use of radiation to treat lung cancers and cutaneous 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 1-888-234-4YCC. This evening, Francine and Lynn are joined by Dr. Michael Hurwitz. Dr. Hurwitz is an Assistant Professor of Medicine at Yale Cancer Center and is here this evening for a conversation about the treatment and research of genitourinary cancers. Here is Francine Foss. Foss Can you start off by just telling us a little bit about yourself? Hurwitz I have not been here that long, I actually got here about a year ago, and prior to that I was up in Boston at Massachusetts General Hospital, where I was seeing patients with genitourinary malignancies and doing research. Foss Can you tell us what genitourinary cancer is? Hurwitz Genitourinary cancer is also called urologic oncology, or urologic cancers, and these are cancers of the degenerative urinary system, so the kidneys down to the ureters, which bring the urine from the kidneys to the bladder, and then from the bladder to urethra and prostate in men, which surrounds the urethra, and then down through the penis and the testicles. So we deal with cancers of the kidney, the bladder, the prostate, and the testicles, primarily. Wilson That is a number of different diseases within one organ system group, so speak. Which is the most common? And also tell us about some of your clinical and research interests. Hurwitz Yes, it is a very broad range of cancers and certainly the most common is prostate cancer, as there are about 220,000 to 240,000 diagnoses a year and about 32,000 people die of that every year. Prostate cancer is in its own sort of category because we know that we under diagnose it massively. We know that a huge number of men have it, in fact, by age 80, the estimates are that about three quarters of men actually have some prostate cancer but we also noted that the vast majority of it is not significant, unlike a lot of other cancers. Most of us will die with prostate cancer, not of prostate cancer, so that one is about 250,000 cases to 240,000 cases a year. The other is kidney cancer which is about 58,000 cases a year as of last year and about 13,000 deaths a year. Bladder cancer is about 70,000 cases and also about 13,000 deaths, and then testicular cancer, while it is particularly important because it's a cancer of the young, it is relatively rare with 8,000 cases a year and about 300 people, 350, die of that. Wilson You mentioned not significant when you were talking about prostate cancer, so that would mean that someone might have it if they did a biopsy or removed the prostate and looked for it, but it is 3:27 into mp3 file http://medicine.yale.edu/cancer/podcasts/2011_0626_YCC_Answers_-_Dr_Hurwitz.mp3 not significant in the sense that the patient feels fine, it is not bothering them, it is not interfering with their life or survival in any significant way? Hurwitz It is a counterintuitive fact, so just to be very clear about it, they have done studies on people who have died for other causes and looked at the autopsies and actually looked at prostates, and again, when

you reach the age of 80, 75% of men have some prostate cancer in there. It appears that some kinds of prostate cancer are just aging, which is something that naturally happens, but they are not going to spread. The big problem is that we do not yet know how to differentiate between those that will spread and those that will not spread. There are clues that you can use to figure this out and we use those the best we can to decide who to treat and who not treat, and so when I see someone who has come to clinic because he has had a biopsy say of the prostate that showed some prostate cancer in there, often times I am in the odd position of telling people, what you need to do is nothing. You need to be watched very closely by us. We have to actively observe you but we do not want to treat you because the flip side of treating is side effects and there are significant side effects, which I am guessing if we talk about prostate cancer, we will talk about today. Foss Can you back track a little bit and tell our audience again what the PSA is and how you use the PSA and does an elevated PSA mean that you have prostate cancer? Hurwitz An excellent point, PSA is the prostate specific antigen and it is a protein that is produced by prostate tissue, so normal prostate tissue makes PSA, however, there are two things that cause the PSA level to go up. One thing that causes it to go up is the prostate getting enlarged, and a very common problem amongst men as we age is that the prostate gets enlarged and there is a term for this which is benign prostatic hypertrophy, and concentrate on the benign. This is not a condition that causes cancer, it just means the prostate gets enlarged and that can result in problems such as literally pressing on the urethra which makes it either hard to urinate or you suddenly have the urge to urinate, and that can cause an elevated PSA because you have more prostate tissue and more PSA has been made. The other thing that causes the PSA to go up though is cancer and the PSA itself, while it goes up with age naturally and while a lot of men are going to have some prostate cancer and some of this benign prostatic hypertrophy going on at the same time, if the PSA is elevated it can mean that there is prostate cancer there and depending on the elevation and the rate of elevation, it can mean that it is a prostate cancer that can be dangerous to you. If I sound like I am hemming and hawing it is because there are no black and white borders between what a bad PSA is, what a dangerous PSA is, and exactly how to manage it. In general, in America, if your PSA has gone above 4, we often consider that a warning sign and it might be worth getting a biopsy. Now there are caveats to everything, so as you age the PSA goes up, if you are 65-75 a PSA of 4 might not be significant, and in fact this is probably in the normal range. Everything I have said so far refers to Caucasians, if you are African American, then actually the risks are higher and we probably would biopsy at a lower number. It is a sort of moving target and there is a little bit more complexity to the PSA than just the number. 7:37 into mp3 file http://medicine.yale.edu/cancer/podcasts/2011_0626_YCC_Answers_-_Dr_Hurwitz.mp3 Foss Can you go through what the recommendations are for checking PSA in the United States. Hurwitz This is also an area of a lot of controversy. There are different societies of doctors who come up with different recommendations about whether you should be checking or

not. In general, the recommendations have turned into the idea that if you have a normal risk of prostate cancer, then at age 50 or above, your doctor should recommend that you have the PSA test and explain some of the things that I have said, specifically that it is not a perfect test, and it does not necessarily mean there is cancer there, but it can warn us that we should biopsy, however. And there are false positives and the biopsy is unpleasant so you may actually be going through things you don't need to go through, however, the test can show there is prostate cancer. In general, age 50 is when we test. For African Americans we feel if we are going to test it should start a little earlier, because the disease is more aggressive and if you have a family member that is a brother or father who has had prostate cancer, then your risk is a little bit higher and you should have it done at 45, or 10 years before the age at which he was diagnosed. Wilson Tell us a little bit about some of your research interests and what you are working on. Hurwitz My research interests are very different from this, I work on extremely basic science and my particular research interest primarily is on how cells move. Within the body cells move for a lot of reasons, a lot of normal cells move. Your immune system is made of cells that have to move throughout your body to attack infection, nerve cells move, and there are a lot of these migrations that occur. It turns out that cancer cells also move and when they move that can be a major problem, because as cancer cells spread, you can get invasion from the organ that they originate to other organs, or they can actually jump, what we call metastasis to a far away organ, and all of that requires the cells to have the ability to move on their own. The reason that I work on how cells move, is that it turns out that in many respects the way a cancer cell move is identical to the way a normal cell moves. The only difference is that is doing it at the wrong time and into the wrong place, and then once it gets to where it's going, it does things that it should not doing. However, since it is such a fundamental part of cancer biology, the thought behind the research is that if we understand how cells move we can block it when it is doing it at the wrong time and we can learn exactly when cancer cells might be moving to places they should not be, and to make it even more basic, I do most of this work in a small worm called *Caenorhabditis elegans*, which is a system people have been studying this in for the last 30 years. Foss Can you talk to us about how the studies that you are doing in the worm actually relate to humans? Hurwitz I hope I can do that because if I cannot then no one is going to fund my research. The way that relates is that we already know that many of the factors that cause cell movement in worms are exactly the same ones that happen in humans, and as I alluded to, the same thing that happens in normal cells in humans for cell movement, happens in cancer cells for cell movements. I work on a set of proteins. These proteins are actually central for cancer cell movement, and I work 11:30 into mp3 file http://medicine.yale.edu/cancer/podcasts/2011_0626_YCC_Answers_-_Dr_Hurwitz.mp3 particularly on how you can block this process. For example, one of the proteins that I work on is something call the Abl kinase. The Abl kinase apparently is involved in blocking cell

movement. It also happens to be one of the few proteins that we have a very effective, actually multiple effective, blocking drugs for. So, if you can figure out how that is involved in worms, if I can figure out exactly how that blocks movement, then I could translate that into humans and human cell movement and then translate that back, ideally, into human cell cancer movement. Wilson

Getting back to the clinical realm, you mentioned some of the differences in screening between Caucasians and African Americans, what are some of the risks for GU cancers and do genetics play a role in any of these diseases? Hurwitz

For prostate cancer, we think that genetics plays a role in that there have been studies in twins that have shown that about 40% of prostate cancer can be attributed to genetics. That is sort of an unclear statement. It sounds very clear and simple, but I think it just means that yes there are risk factor. If it is in your family, it is more likely that you will develop prostate cancer, but it is such a prevalent disease that in some ways it is not as important to worry about genetics in prostate cancer. You just have to worry about getting it. The risks for prostate cancer are if it metastasizes, if it spreads, then it can kill you, and the later it is caught, the more aggressive the therapy and the therapies in prostate cancer are pretty difficult and can have a lot of side effects. That would be for prostate cancer. For bladder cancer, it is a similar thing, in that again, if bladder cancer is not caught it can become metastatic, it can be very aggressive and it can kill you. The earlier you catch it the better, and you might be able to prevent some of the more difficult therapies, the difficult therapy being either chemotherapy or actually removal of the bladder. In kidney cancer, which at Yale Cancer Center is actually treated by specific kidney cancer doctors so I do not see those patients, but for kidney cancer, again, if you have an aggressive one it can eventually lead to death through metastasis and the earlier it is caught, the more likely you can just take care of it with pretty benign treatments. Foss

We are going to take a short break for a medical minute. Please stay tuned to learn more information about GU cancers with Dr. Michael Hurwitz. MedicalMinute

The American Cancer Society estimates that last year there were over 65,000 new cases of melanoma in this country. And over 1,000 patients are diagnosed annually in Connecticut alone. While melanoma accounts for only about 4% of skin cancer cases, it causes the most skin cancer deaths. Early detection is the key. When detected early, melanoma is easily treated and highly curable. New treatment options and surgical techniques are giving melanoma survivors more hope than they have ever had before. Clinical trials are currently underway at Yale Cancer Center, Connecticut's federally designated comprehensive cancer center, to test innovative new treatments for melanoma. The Specialized Programs of Research Excellence and Skin Cancer 14:58 into mp3 file http://medicine.yale.edu/cancer/podcasts/2011_0626_YCC_Answers_-_Dr_Hurwitz.mp3 Grant at Yale, also known as the SPORE grant, will help establish national guidelines on modifying behavior and on prevention as well as identification of new drug targets. This has been a medical minute brought to you as a public service by Yale Cancer Center. More information is available at YaleCancerCenter.org. You are listening to the WNPR Health Forum on

the Connecticut Public Broadcasting Network. Wilson Welcome back to Yale Cancer Center Answers. This is Dr. Lynn Wilson and I am joined by my co-host Dr. Francine Foss. Today we are joined by Michael Hurwitz and we are discussing GU cancers. Michael, you have explained some of the risks associated with some of the diseases, but how about risk factors? What are some other risk factors that would lead to bladder cancer for example, or testicular cancer? Hurwitz

The primary risk for bladder cancer is really smoking, and there are other industrial risks. The bladder is one of the places in the body where obviously urine collects and there are a number of chemicals that could be concentrated there. There are sort of organic compounds that can be in certain industries. Most of us are not exposed to that and that is probably a small part of the risk, smoking is the big one. For prostate cancer, there have been a large number of things people have looked at, and the data is not entirely clear. Smoking is always bad, do not smoke because for almost everything smoking is some sort of a risk factor, but other than that for prostate cancer, there is nothing truly obvious. In the case of testicular cancer the main risk factor is actually something called cryptorchidism, or undescended testes, and that is something that you find out early on in life and if that is fixed early that can alter the risk, but if it is not fixed then that commonly can lead to testicular cancer. The other risk for testicular cancer, is having a testicular cancer. If you have one in one testicle it is more likely you will have one in the other, and that is true for kidney cancer also. Kidney cancer is another one where for the most part there are not that many risk factors, smoking has been shown to be a moderate one but it is not a huge risk, but there are a few genetic syndromes that are high risk for us, there is something von Hippel-Lindau syndrome. These people have a very high rate of getting kidney cancer and as a side note, when researchers figured out what causes that syndrome, they found that the same thing that causes it in people who have this disease, it turns out that same problem can happen sporadically or sort of at random and the vast majority of normal kidney cancer, in people who do not have the genetic disorder, it is the same molecular mechanism that is causing it, so sometimes these rare things actually lead us to great advances and that actually led to a massive change in the way we treat kidney cancer, it has been a huge change in the last few years. Foss

Can you talk to us about the presentation of most patients; you mentioned that a lot of prostate patients do not have symptoms but what about the bladder cancer patients and the advanced prostate patients? Hurwitz

For both bladder cancer and kidney cancer, one of the common presentations is blood in the urine, and usually it's painless. So, you are peeing and the urine comes out pink or obviously bloody, 18:26 into mp3 file http://medicine.yale.edu/cancer/podcasts/2011_0626_YCC_Answers_-_Dr_Hurwitz.mp3 that is probably the most common presentation. There are presentations of pain, sometimes belly pain in the case of bladder cancer or pain sort of in the back or flank in the case of kidney cancer. It is not as common but that does happen occasionally. I would say in the case of prostate cancer, since the advent of PSA testing which began in 1991, so it is not that old, almost everybody gets diagnosed by a PSA elevation, but if you

do not get diagnosed that way then you can get diagnosed by having severe difficulty urinating and that can sometimes mean the prostate has enlarged and something is blocking the urethra. Wilson Tells us about some of the different treatment modalities that are used, starting with the kidney down through the testicles, for example. Hurwitz With the kidney, again because of changes that have happened, we diagnose differently from the way we used to. Most people these days who are diagnosed with kidney cancer had a belly ache and got a CAT scan for something entirely different and they find there is something unusual on the kidney. For those people usually it is a small lesion and they usually just take out that section of the kidney and that is called partial nephrectomy. There are many institutions that also will directly destroy that tumor nodule with basically a probe that goes in and uses cold or heat to kill it. So those are the things that happen. If it is a more advanced kidney cancer, they take the entire kidney out. Kidney cancers are not terribly responsive to chemotherapy or to radiation type therapies. So, if it is more advanced we usually use a pill of some sort. There are a number of pills that have all come out since about 2005 and now there are five or six different kinds and they are used in various orders to treat the tumor. There is also something called immunotherapy, which is treatment to boost your immune system and that also can be effective in kidney cancer. That is sort of the whole gamut from localized kidney cancer to kidney cancer that has spread. With bladder cancer, going sort of down the urinary tract, there are different levels of tumor, so sometimes you will have a cancer but it is just superficial that is sitting in the inside of the bladder but not really invading into the bladder itself, and with those tumors you remove it, a urologist or urological surgeon takes it out, and then depending, sometimes they can put a therapy directly into the bladder, they actually can infuse something into the bladder that will kill off the rest of the tumor cells. If it has become more advanced and is actually invading into the wall of the bladder then what I would say is the most standard regimen, although there is nothing totally standard unfortunately for bladder cancer as it is one of the trickier tumors, is to treat with chemotherapy followed by removal of the tumor or removal of the entire bladder. Bladder cancers have a way of showing up in multiple parts of the bladder. There are some organs where a tumor in one part of the organ does not predict tumors in other part of the organs. However, both prostate and bladder are like that and so with the bladder cancer, often, depending on how aggressive the bladder cancer is, that will tell you if new ones will pop up and sometimes you take the bladder out. If it escapes the bladder, then we give chemotherapy. In the case of prostate cancer which is by far the most complex, there are a few things that we look at. We look at the PSA value that was brought up earlier, we look at what the cancer tissue looks like under the microscope and there is something people may have heard of called the 22:17 into mp3 file http://medicine.yale.edu/cancer/podcasts/2011_0626_YCC_Answers_-_Dr_Hurwitz.mp3 Gleason score, which is a scoring system for how aggressive the tumor looks and based on the Gleason score, the PSA number and how big the tumor is and where it is in the prostate, we decide what therapies

are available. When they look the least aggressive, the options are what we will call active observation, which is very close watching, but no treatment or radiation therapy of the prostate or removal of the prostate. And as far as we know there is no difference in these treatments for effectiveness. It is actually being studied in England right now, but no one knows if there is any difference in the effectiveness of these treatments for early prostate cancers. What we do know is that if you get either radiation or surgery, you are very likely to have a number of important and serious side effects. The biggest one is impotence and difficulty with erections. Radiation can also cause some damage to the bowel nearby and the bladder nearby. And surgery can, in about 2% to 4% of people, can cause some urinary incontinence. These procedures are not taken lightly and that is why if we can avoid procedures for people, we do. If the tumor is more advanced in the prostate then it is usually either surgery or radiation, and the radiation in that case is in combination with an injection, something we call androgen deprivation therapy. All prostate cells and early prostate cancer cells are very sensitive to testosterone. They need it to survive and when you block off testosterone then they will not live, they will die, and so we often treat people with that while we give them radiation because it will attack the prostate and specifically shrink the prostate cancer cells down. So those are the early treatments. Once it has spread beyond that, then the treatment is generally these anti-testosterone treatments called androgen deprivation therapy or hormonal therapy. And that can work for many years and then there are further manipulations to keep testosterone down, and when that is over, eventually we talk about chemotherapy. Foss

What are the complications of those hormone based therapies? Hurwitz The complications of the hormonal-based therapies are also important. The big one is libido and erectile dysfunction and also less interest in sex. Other really important ones are that there can be fatigue and hot flashes, so sweating and flushing and turning red and this is can happen multiple times a day, there is risk of bone loss and this is significant bone loss including bone breakages in men, just like women get osteoporosis, men who are on therapy that removes testosterone are much more prone to this. The other thing is there can be body mass changes, that is less muscle, more fat, central obesity, and lastly we are finding out now that it can have major effects on the cardiovascular system, meaning you are more prone to heart attacks, more prone to stroke, and just overall cardiac health can be decreased by this. Foss

There are a number of men out there who are using testosterone now to improve sexual function. Can you just clarify for those men whether the use of testosterone will increase their risk of prostate cancer? Hurwitz I wish I could, I think it is risky behavior from that standpoint. It is not that it will increase the likelihood that they will have a prostate cancer, that probably happens independent of whether you 26:09 into mp3 file http://medicine.yale.edu/cancer/podcasts/2011_0626_YCC_Answers_-_Dr_Hurwitz.mp3 take testosterone, but will it increase the likelihood that it will spread, it certainly might. One of the reasons it is difficult to talk about this is due to the fact that the vast majority of us have prostate cancers, when

we get old enough, and what we do not know is are there prostate cancers that even if you try to sort of strengthen them with testosterone , if they'll never go anywhere anyway, or if you can take a prostate cancer that would otherwise be relatively quiet and make it more aggressive with testosterone, but my personal view is that it is a risky behavior, I would be wary of it. Wilson Getting a little bit more general for a second, tell us about some of the benefits in the multidisciplinary approach. Hurwitz I think there is a huge benefit. We know that if you go to a surgeon it is more likely you will receive surgery, if you go to a radiotherapist or radiation oncologist you are more likely to receive radiation therapy for your prostate cancer, not because it is wrong. In fact, it turns out that we do not know which one is better in most cases and the fact is as far as we can tell, they are very similar in effectiveness. The advantage of the multidisciplinary approach is that when you are talking about multiple therapies all that seem to be equally effective, it is best to find out what is going to be better for you. This is one of the few cancers where if you come in with this cancer, you will be told you really have a choice of your treatment and it is best if you have a choice of treatment to be told all the pros and cons by everybody and that really is significant for this disease because, for example, if you have a very early stage prostate cancer you may not have to have it treated at all and that is fine. You come to my office and I say you do not have to have it treated. However, if you are going to be up all night for the next ten years of your life sweating because you are terrified of this prostate cancer inside you, than it is just not the right thing for you and that is why it is important to hear from everybody and know what the side effects might be because this is really one of those things which is a real balancing act. Dr. Michael Hurwitz is Assistant Professor of Medicine at Yale Cancer Center. If you have questions or would like to share your comments, visit yalecancercenter.org, where you can also get the podcast and find written transcripts of past programs. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.