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New Bone Clinic at Smilow Cancer Hospital

Guest Expert:

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Yale Cancer Center Answers

is a weekly broadcast on

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Welcome to Yale Cancer Center Answers with doctors Francine Foss and Lynn Wilson. 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 week, Francine welcomes Dr. John Wysolmerski. Dr. Wysolmerski is the Director of the new Bone Clinic at Smilow Cancer Hospital. Here is Francine Foss.

Foss Let's start off by learning a little bit about you. Could you tell me a little bit about your background and how you got to the Smilow Cancer Hospital?

Wysolmerski Certainly, I am a practicing endocrinologist. I did my endocrine training here and have been at Yale since 1990 now and specialize in metabolic bone disease in patients with calcium disorders. Primarily we see patients with osteoporosis, but also other disorders of abnormal bone metabolism such as Paget's disease as well as abnormalities in patients with hyperparathyroidism, other abnormalities in the parathyroid glands and in hormones such as parathyroid hormone and vitamin D that lead to changes in bone and calcium metabolism. So, that is my clinical interest. My research focus is on normal breast development and physiology, especially interactions that occur between the breast and the skeleton during lactation in order to support milk production. We believe that many of these interactions that are important for the normal physiology of lactation in terms of liberating calcium for milk production are recapitulated in breast cancer and we can understand some of the alterations in bone and calcium complications that happen during breast cancer by better understanding the normal physiology. Basically, that combination of an interest in cancer biology and a clinical interest in metabolic bone disease was a natural marriage to form this bone health program at Smilow Cancer Hospital.

Foss Can you tell us briefly why you think a cancer center needs a bone health center?

Wysolmerski There are many complications of cancer that affect the skeleton. Of course, the most feared is bone metastases. At least initially we are not going to directly deal with that problem, but a peripheral or secondary effect of both cancer itself and especially treatment for cancer, is bone loss, and as therapy for cancer continually improves, it is important to understand and treat the long-term consequences of treatment on other organs such as the skeleton. Among both endocrinologists like myself and oncologists like yourself, we have realized increasingly that many aspects of cancer and its treatment impact the skeleton and can lead to premature osteoporosis and fractures. This is, as you know, particularly true of cancers where we manipulate hormones that are important for bone metabolism, but it is true for all cancers and we

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are seeing more and more patients in our bone clinic with these problems that coexisted with their treatment for cancer, and when Smilow Hospital opened, we thought it was a good time to try to tackle this problem and create a systematic program to help prevent this complication.

Foss John, is this a unique program, or do other cancer centers also now have bone health programs?

Wysolmerski Many of the leading cancer centers do have some programs that are directed at this issue. Many of those exist in terms of coming up with treatment guidelines, which is something that we are doing as well, but I think we are among the few cancer centers that will actually have a dedicated bone clinic within the oncology clinic itself, within the same cancer hospital that will be dedicated to seeing patients only with cancer who are suffering these complications.

Foss That sounds great. Is the clinic actually open now?

Wysolmerski It is not quite open, we are still in the planning phase. We are hoping for October 1, 2011 and still have a few little details to work out, but sometime this fall we are going to start scheduling patients and open our doors. I just came from the clinic this morning actually, and so I see patients with these complications, but I have to go to a different building, it is less convenient, and I am not in close enough contact with my oncology colleagues to develop the kind of multispecialty approach that we really want.

Foss Can we take a giant step back and talk a little bit about bone loss itself? How is bone loss detected and do you think that oncologists are not looking for bone loss often enough?

Wysolmerski First of all, one of the issues with osteoporosis is that it is silent until you have a fracture. So you have to be very vigilant and the standard way right now to know whether patients have osteoporosis is to do a test called a bone density test. There are several different techniques but the standard one is called dual-energy x-ray absorptiometry, which involves using a very small amount of radiation, about a tenth of what is in a typical chest x-ray, with the general idea that the more dense your bones are the more that radiation gets absorbed by the bone and the less it gets transmitted to a detector. This is the standard screening test that many women have when they go through menopause and some men also get if there are risks for osteoporosis. The key is knowing which patients to do that test in, so one of the things that we are involved upfront with this is to go through disease by disease. We have started with breast cancer. Next we are going to prostate cancer and work our way through solid tumors as well as hematologic malignancies and come up with disease-specific institutional guidelines as to when people should be thinking about screening patients for this complication, and then based on the results of those screening

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tests, what kind of therapy, either conservative therapy or drug therapy, should be instituted to prevent further bone loss in patients with osteoporosis or patients with cancer who may develop osteoporosis. To go back to your original question, I think that oncologists are very keyed in to this idea, I think that they are busy dealing with all the various problems of patients that they treat, especially if they are on active chemotherapy. I think a little guidance both upfront with these guidelines as well as having a bone specialist actually in Smilow to serve as consultants will help improve both the sensitivity to this problem and then make sure that the patients who need to be screened are screened, and then preventative measures are taken in those patients.

Foss We typically think about osteoporosis in women, but do not think about it as often in men. Can you talk a little bit about the incidence between men and women and what things we should be looking for? What men are at higher risk for developing osteoporosis?

Wysolmerski The reason that we think about osteoporosis primarily in women is that women go through menopause. Their primary sex hormone is estrogen, and that decreases after menopause and that puts them at risk for accelerated bone loss and developing osteoporosis. The same thing happens in men, but it tends to happen more gradually, and it tends to happen 10 or 15 years later. Typically women can present in their 70s and 80s with fractures, sometimes sooner than that. Men also develop osteoporosis but they do it in another decade or a decade and a half later. So, men with hip fractures, for instance, often are in their late 80s and 90s as opposed to 70s and 80s. That can happen in an accelerated fashion in men when they have an orchiectomy either for treatment, for instance, for prostate cancer, or as a result of chemotherapy, or because they had an accident or for some other reason. So, if they lose testosterone levels, just like women lose estrogen levels, then they develop accelerated bone loss and osteoporosis. It can also happen in patients that have a variety of other long-term illnesses and especially in organ transplantation we see men with osteoporosis as well.

Foss Can you talk about screening? When we think about screening in a normal population, how is that different and how should we be screening our cancer patients?

Wysolmerski That is a bit of a controversial topic in the general osteoporosis world, but it is generally recommended that women be screened by age 65, and based on those results, be stratified into patients who might consider pharmacologic treatment for osteoporosis or not. There are not any set screening guidelines for men in the general population for osteoporosis, it is left to the discretion of the primary care doctor, or if men have hypogonadism or other metabolic problems that might predispose them to osteoporosis. In the setting of cancer, it is different, of course. Cancer patients are often younger than that. Any woman who as a result of her therapy at whatever age loses ovarian function or ovarian function is interrupted for a prolonged period of

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time, or if she is exposed to high-dose glucocorticoids, which we know damage bone for prolonged period of time, then that person should be screened for osteoporosis. Similar in men, men who would be treated with drugs that interfere with either androgen production or action for the treatment of prostate cancer or men who are treated with cytotoxic chemotherapy that would interfere with testicular function should be screened earlier no matter what age they are at the time that they clearly pronounce themselves as being hypogonadal. That is easier in women because they lose menstrual function. In men, it is a little bit harder. You have to ask them specific questions directed at whether or not their testosterone levels are adequate.

Foss Primarily, those would be men with prostate cancer who are undergoing various hormonal manipulations or have had radiation?

Wysolmerski Yes, by and large that is the largest population of people.

Foss When you talk about radiation by itself, what is the risk with just radiation therapy inciting bone loss in a patient, and does it really matter what kind of cancer they have or what area is radiated, is that really a risk factor?

Wysolmerski There is a transient loss of bone mass that can happen as a direct result of radiation therapy. That is not typically the same kind of osteoporosis as we see. It is not the result of metabolic activity in the bone cells but instead a direct damaging effect of the radiation. That is often transient. It often goes down and then comes back, and many times when we see those patients, we follow them conservatively and often their bone mass returns after the radiation therapy is completed. There are some side effects of radiation that if there is radiation therapy to the abdomen that can interfere with the ability of the intestine to absorb calcium properly, those patients because of long-term calcium malabsorption, can then be at risk for accelerated bone loss and osteoporosis, but that is more of the long-term side effect of radiation than direct effect of the radiation itself.

Foss We are going to take a break now for a medical minute. Please stay tuned to learn more information about the Bone Clinic at Smilow Cancer Hospital with Dr. John Wysolmerski.

*Medical
Minute*

Breast cancer is the most common cancer in women. In Connecticut alone, approximately 3,000 women will be diagnosed with breast cancer this year, and nearly 200,000 nation-wide, but there is new hope for these women. Earlier detection, non-invasive treatments, and novel therapies provide more options for patients to fight breast cancer. In 2010, more women are learning to live with this disease than ever before. Women should schedule a baseline mammogram

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beginning at age 40, or earlier if they have risk factors associated with the disease. With screening, early detection, and a healthy lifestyle, breast cancer can be defeated. Clinical trials are currently under way at federally designated comprehensive cancer centers such as Yale Cancer Center, to make innovative new treatments available to patients. A potential breakthrough in treating chemotherapy-resistant breast cancer is now being studied at Yale combining BSI-101, a PARP inhibitor with a chemotherapy drug, irinotecan. This has been a medical minute, brought to you as a public service by the Yale Cancer Center. More information is available at yalecancercenter.org. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.

Foss Welcome back to Yale Cancer Center Answers. This is Dr. Francine Foss and I am joined today by my guest, Dr. Wysolmerski, who is here today talking to us about the new bone health clinic at the Smilow Cancer Hospital. We talked a lot about screening and the fact that cancer patients in general are at increased risk for developing bone loss. Can you talk specifically about bone metastases? Are bone metastases by themselves a risk factor?

Wysolmerski Bone metastases can be a risk factor for fractures. They are not in and of themselves a risk factor for bone loss in other parts of the skeleton. That is something that scientifically we have an interest in, especially in the setting of how breast cancer cells recapitulate some of the same processes that they are engaged in during normal breast cells during lactation. The way I think of it is that the breast during lactation, one of its jobs is to take calcium out of the skeleton to provide for milk production. So, breast cancers cells recapitulate some of that same physiology, and when they land in the skeleton, they actually use some of the same mechanisms that the normal breast uses to take calcium from the skeleton, but over a short geographic distance now, and they cause bone resorption and osteolysis. So if it is large enough or in a critical place, it can dissolve the bone enough to cause a pathologic fracture, and that is something that we in this clinic are not going to deal with directly because that really falls under the job description of the oncologist taking care of the patient to worry about bone metastases per se, but eventually, hopefully, as the science improves and as we have better therapy directed specifically at bone metastases, it would be nice if this bone health program were to include a multidisciplinary team that might explore more efficacious treatment for bone metastases.

Foss Can you talk a little bit about the treatment options for patients who have osteoporosis who have bone loss either because they are getting older or because they have cancer, what are the different options for those patients?

Wysolmerski In the last 10 or 15 years, we now have a series of many medications that are available for postmenopausal osteoporosis, not all of which are really suitable for patients with cancer. So, we

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have a little bit more of a restricted armamentarium of medications that we can use to treat patients with bone loss and cancer. First of all, what we do when we see patients is we think of osteoporosis somewhat like coronary disease in the sense that there are many metabolic factors that contribute, and we try to make sure that even though a patient has cancer that they do not have some other easily correctable metabolic issue that is going on. So, we do a full workup looking at all the hormones that can affect bone metabolism as well as study carefully the calcium metabolism of each patient in order to ensure that whatever supplements or not that they are taking that their body thinks they are sufficient in calcium, and sometimes we have to tailor specific calcium and vitamin D regimens for those patients. The second thing we do is make sure that all patients have enough vitamin D and calcium, and so we will have recommended doses of both calcium supplements and vitamin D for these patients, but as I said before, we sometimes tailor that and increase or decrease the doses depending on their individual calcium metabolism. Finally, medication for cancer-related bone loss really consists of two different classes of medications. The first are bisphosphonates, which are a mainstay of osteoporosis therapy. Those drugs, some of the brand names of which are Fosamax, Actonel, and Reclast, are used to slow down the cells that resorb bone and therefore preserve bone mass and interfere with the bone resorption that causes the accelerated bone loss. The other drug that is new to the market is a humanized monoclonal antibody against a molecule called RANK ligand, which is important in the development and action of the cells that are involved in bone loss, and that drug is called Denosumab and that is the other mainstay of therapy for patients who have bone loss and cancer. The other treatments such as estrogen replacement or parathyroid hormone have theoretical problems with them and we tend to stay away from those treatments in patients with cancer.

Foss If you are a cancer patient and you do not have bone loss at this point and you are getting chemotherapy, say, or hormonal therapy, do you recommend the prophylactic use of calcium and vitamin D?

Wysolmerski I think that that is a wise thing to do in all patients who are at risk for bone loss even if it does not get to the degree to which they might be labeled as having osteoporosis.

Foss Is there any such thing as taking too much of these vitamins?

Wysolmerski Yeah, you can take too much, especially of vitamin D, and there has been some recent controversy about this. This is back and forth in the endocrine literature, and it became very fashionable within the last several years to take very large doses of vitamin D based on extrapolation from some clinical data, and the Institute of Medicine recently came out with a

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report that kind of said, hold on, you can overdo this and it can be dangerous. It can cause kidney stones and high calcium levels and anything more than 1,000 to 2,000 units of vitamin D is probably unnecessary except in very few patients.

Foss What about if you drink milk and use dairy? Do you still have to take vitamin D and calcium?

Wysolmerski It depends on how much dairy product you take. To get enough calcium for a typical postmenopausal woman, you have to drink a liter and a half of milk a day and most women do not do that. I usually recommend some combination of dairy products and calcium supplements. As far as vitamin D goes, part of the issue was that there is a lot of vitamin D fortified in food. So, you probably do not need to take mega doses of vitamin D to get your vitamin D levels in a reasonable range.

Foss John, can we switch back again to talk about the bone health clinic at Smilow? Are you working there by yourself or are you part of a multidisciplinary team? Can you tell us a little bit about it?

Wysolmerski Well right now when the clinic opens, it is going to be myself and endocrine fellows that are rotating through that clinic that will see patients. We hope to involve the oncology trainees as well and eventually help this as the clinic program grows depending on what the patient demand is, that we make it a multidisciplinary clinic in the terms of actually seeing patients. Behind the scenes, of course, we are already involved with discussions with oncologists and developing the institutional guidelines that will be used to decide which patients get screened, and which patients get referred to this bone clinic, and we will dictate which patients get treated with what kind of therapies. One of the things that we would like to do in setting up this program, and we really like to think of it as more than a clinic but really a program, is kind of a three-pronged approach. One is to increase education through outreach as well as talking to my colleagues and hopefully regionally increasing awareness of this problem. Second is by working with the oncologists to develop institutional guidelines, we hope to standardize and improve the treatment of these patients so that everyone is on the same page in terms of what kind of evaluation is necessary, what kind of steps need to be done and what kind of patients need to be thought of as being offered therapy in addition to the calcium and vitamin D and exercise, which everyone should do. Then finally, by doing that we hope to ask patients to allow that all of their data goes into a single database, and so this will serve as, we hope, a springboard to two kinds of investigation; one is to follow up on our programs to see if they are efficacious, do they actually stop bone loss, are they helping patients or not? And as new drugs come out that are targeted at this population that we would be a site for clinical trials to investigate new agents and allow patients to have access to those new agents as part of trials that are ongoing in this region.

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Foss It is interesting that you talk about the guidelines, and I think that is a very important part of this whole thing. In cancer we have what we call the NCCN guidelines, which are national guidelines that dictate how we treat cancer patients, but I do not think that we really have good guidelines looking at supportive and ancillary care for those patients. Is there a national guideline addressing this issue of following bone loss?

Wysolmerski Because of my research interest, we started this with breast cancer and, of course, those are patients who are particularly at risk because of the use of medications that lower their estrogen levels to low levels such as aromatase inhibitors, and there are not any officially adopted guidelines and they are kind of all over the place. So, what we did in developing the guidelines for breast cancer is reviewed all that literature, got in a room with my breast cancer oncology colleagues and discussed all this, and then I also talked to people at other cancer centers at MD Anderson, at University of Michigan, Seattle, and talked about what they did, and they were kind enough to share with me their institutional guidelines. We put all that together and we decided what would work best for Smilow Cancer Hospital, and we came up with our own set of guidelines. One of the things we would like to do in starting this program since I had these conversations, and hopefully, once we are up and running, we can do this, is start a cooperative group somewhat similar to the cooperative groups for chemotherapy trials with people across the country including those cancer centers I just mentioned that have a similar interest in metabolic bone disease in the setting of cancer and come up with trials that will involve many institutions to test to see whether the therapies that have been suggested actually prevent fractures. In order to do that, you can measure changes in bone density, but what we really want to do is prevent people from having fractures. In order to do that, you need very large numbers of patients. So, we are hoping that we will start a cooperative bone health group; I am not sure exactly what we will call it yet but that we will be able to do studies that involve Smilow but also these other cancer centers across the nation.

Foss What about cancer survivors? Are they eligible to come to your clinic as well?

Wysolmerski Sure, I kind of see ourselves as overlapping with the survivorship program because bone loss, especially in patients with breast cancer, is an ongoing issue, especially patients on either tamoxifen or aromatase inhibitors for many years after they have been cancer-free sometimes. We see this as spilling over into an issue that is an ongoing issue for patients and they have been left with low testosterone levels or low estrogen levels as a result of their cancer therapy. So, this will be a lifelong issue for them that they will have to continue to pay attention to it.

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Foss And you would hope that you would intervene in this clinic sooner before they end up at the end of their treatment with issues?

Wysolmerski Right, the paradigm, for instance, in breast cancer, is that we know that these drugs that are used to lower estrogen levels cause accelerated bone loss. So, can we can stratify patients, intervene at the time that they have therapy, and prevent them from ever developing osteoporosis in the first place.

Dr. John Wysolmerski is the Director of new Bone Clinic at Smilow Cancer Hospital. If you have questions or would like to add 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.