

Dr. Edward Chu, Colorectal Cancer Awareness 2009 March 1, 2009 Welcome to Yale Cancer Center Answers with Dr. Ed Chu and Dr. Francine Foss, I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and an internationally recognized expert on colorectal cancer. Dr. Foss is a Professor of Medical Oncology and Dermatology and is an expert in the treatment of lymphomas. If you would like to join the discussion, you can contact the doctors directly at canceranswers@yale.edu or 1888-234-4YCC. This evening, in recognition of the fact that March is Colorectal Cancer Awareness Month, Dr. Foss sits down for a chat on this subject with her co-host Dr. Chu.

Foss Ed, I know that you have been interested in colon cancer for a long time and worked on this at the National Cancer Institute. Can you relate to us what first got you interested in colorectal cancer, and a little bit about your research work as well?

Chu I think it was probably a bit of genetics and environment. As you know, both of my parents were cancer researchers and initially started their careers at Yale Cancer Center and then moved up to Brown. They both were involved in basic research focusing on colorectal cancer, so I think having grown up in that environment influenced me. My research in college and at med school focused on colon cancer, and then when I went to do my fellowship at the National Cancer Institute I worked closely with Carmen Allegra and Bruce Chabner and I focused initially on the basic research of colon cancer and trying to understand how drugs work and do not work in colon cancer. I then extended my interest to developing new agents for the treatment of colorectal cancer.

Foss So I guess things were a little bit unusual in your household; you probably talked about colon cancer from the time you were very young. How common is the disease? Most people hear about it and a lot of us have questions about who is getting it and who is at risk.

Chu Even in 2009 colon cancer remains a major public health problem in the United States and worldwide. To give you some perspective, there will be about 150,000 new cases of colon cancer diagnosed in the U.S. this year. It is the number three cause of cancer in this country and it is the number two cause of cancer death. There will be about 46,000-47,000 deaths associated with this disease, and bringing it closer to home, here in the State of Connecticut, in 2009 it is estimated that there will be about 2,200 new cases of colon cancer diagnosed.

Foss What are major risk factors for colon cancer; who has to worry about this?

Chu By far and away the number one risk factor for developing colon cancer is age; age greater than 50. The general recommendation for anyone who is over 50 is that colon cancer screening must be initiated. One of the things I would like to emphasize, and the reason we are doing this show in March, is that March is Colorectal Cancer Awareness Month and I3:27 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Mar-01-09.mp3 think the key drive for us as healthcare professionals is to highlight the importance of colon cancer screening.

Foss Can you tell us a little bit about the screening process? Who should be screened and what is involved in getting screened?

Chu Again, age by far and away, is the number one risk factor, and anyone who is older than 50 should get colon cancer screening. The one thing that is important to recognize is that individuals with a family history of colon

cancer, especially for those whose family members have developed colon cancer before the age of 50, should start getting screened much earlier. Maybe one of the other reasons why I developed a strong interest in colorectal cancer is because one of my mom's younger brothers, in fact her baby brother, was first diagnosed with colon cancer at the age of 42. Fortunately for him, he went about 10 years with the diagnosis, but unfortunately succumbed to the disease. Yours truly, in fact, started getting screened for colon cancer when I was in my late 20s. I actually just had my fourth colonoscopy one week ago.

Foss People who have certain other diseases could be at risk as well, and I have heard that people with inflammatory bowel disease, or people that have had polyps, should be screened more often. Can you talk a little bit about that?

Chu That is an important point. Patients with inflammatory bowel disease, either ulcerative colitis or Crohn's colitis, and in particular individuals who have had the disease for over 10 years duration and who have had pretty extensive involvement of their colon, are certainly at increased risk. The other important risk factors, just to note, are individuals with a family history of colon cancer, but interesting enough, also a family history of other types of cancer such as breast cancer, ovarian cancer, stomach cancer, even brain cancer. There is a familial syndrome, called Lynch syndrome in which there is a higher incidence of colon cancer along with those other cancers.

Foss At what age should a patient like that start to be screened?

Chu In someone who has a very strong family history of colon cancer, those other cancers, or in a situation where there is a very strong history of polyps, generally screening may start as early as the 20s.

Foss Can you talk a little bit about screening? What tests are actually done?

Chu There are a number of tests that have been recommended by the American Cancer Society into mp3 file http://www.yalecancercenter.org/podcast/Answers_Mar-01-09.mp3 and the Centers for Disease Control. The simplest test is actually a physical exam in which the physician does a rectal exam. If they can obtain a stool specimen, they can test the stool to see if blood is present. You may not actually see the blood as a bright red color, but you can then do a stain to see if in fact there is microscopic blood in the stool. Unfortunately, the physical exam and the stool testing are pretty insensitive, so the gold standard for colon cancer screening and early detection is a test called colonoscopy. What a colonoscopy basically is, is a tube with a light at the end that is inserted in the rectum and goes all the way to the end of the large bowel so you can actually visualize the entire colon.

Foss People who have had colonoscopies give kind of horror stories about how difficult it is, I know you have said you have had colonoscopies, and I have had them myself, and I think it is important for us to talk a little bit to people about this procedure and how it does not necessarily have to be something to worry about.

Chu That is a great point that we need to highlight. I think that what people actually get very squeamish about is the preparation. You need to drink a fluid to try to cleanse the entire bowel so that the procedure can visualize the bowel. Now, as I said, my very first colonoscopy was quite some time ago and back then I think I had to drink three or four gallons of a fluid called GoLYTELY. It was really kind of a misnomer because it was

not so GoLYTELY. You have to drink this big bolus of fluid, you get bloated and then you actually discharge. Now it has gotten to the point, as I said one week ago I had my colonoscopy, where I took pills with fluid and I found it to be much simpler and just as effective in getting the appropriate prep for the procedure.

Foss Can you talk a little bit about the role of x-rays in making a diagnosis of colon cancer, and whether or not there are blood tests that are helpful?

Chu There has been a lot publicized recently about a test called virtual colonoscopy, and what that is, is basically a very sophisticated high tech CT scanning of the bowel. The advantage of virtual colonoscopy is that it takes about 10 or 15 minutes and basically once the procedure is done the individual can go back to work. It is important to note that you still need to take the same prep as you do with the real colonoscopy, and the other potential issue is that with very small polyps, small tumors, it is not as sensitive at picking them up as colonoscopy. If there is anything suspicious that is seen on the virtual colonoscopy, that individual still needs to then have the colonoscopy and have a biopsy performed.

Foss Should people worry that something might be missed if they have a virtual colonoscopy?

Chu If the virtual colonoscopy is entirely normal, then that is a discussion that needs to be had.

9:56 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Mar-01-09.mp3 with the individual's primary care physician and GI specialist. What we are also finding is that not all virtual colonoscopies are created equal. By that I mean that it needs to be done at centers that have done a certain number; they need to have a certain level of experience. We are also finding that radiologists need to be specially trained in order to interpret the CT scan images, and you need to have the very high powered, very sophisticated software, that can basically take the CT scans and turn them into images much as you would see with a colonoscopy. While there will be reports that everyone can do them, I think it is still not ready for primetime for all community centers.

Foss So most of us will probably still have a basic colonoscopy. If a diagnosis of cancer is made on a colonoscopy, can you take us step-by-step through what happens after that?

Chu It is important to note why a colonoscopy is so important. It can visualize polyps, and if polyps are seen they typically are removed. That is important because we now know with about 20 to 25 years worth of research that colon cancer arises from polyps, so if the colonoscopy can basically remove the polyps, in essence you remove one of the main causes for developing colon cancer. The other thing is that if in fact a colon cancer is present, the hope is that the colonoscopy is catching it at an earlier stage. We now know that when colon cancer is found and detected at the earlier stages, we can cure up to 90% of those patients.

Foss What percent of patients actually have early stage disease when they are diagnosed?

Chu I would say probably somewhere between 25% and 40% are actually diagnosed with early stage colon cancer.

Foss Let's step back a minute and talk a little bit about the symptoms. We talked about the screening process with colonoscopy, but what symptoms would a patient who has colon cancer experience?

Chu The classic symptoms are a change in bowel habits; there may be a change in the color, typically we ask if there is blood in the stool or if the stool has

changed to kind of a tarry black color. There can also be a change in the size, shape, and caliber of the stools. The classic shape is actually pencil thin stools. There can also be associated abdominal cramps, a little bit of bloating, change in appetite, reduced appetite with weight loss, and sometimes it is generalized fatigue. So those are the classic symptoms. But again, to stress the critical importance of screening, a good number of patients who receive a diagnosis of colon cancer have absolutely no symptoms and so that can be very misleading to an individual. They think that if they do not have symptoms, there is no need to get screening done, and that is absolutely wrong.13:22 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Mar-01-09.mp3Foss That points out the critical need for us to follow the recommendations in terms of screening. You mentioned that if you have a family history that you need to be screened more often, but for the average person age 50 and over, can you quickly reiterate how often a patient needs to get a screening colonoscopy?Chu For an average risk individual, someone who does not have a prior history of colon cancer, prior history of polyps, or a family history of colon cancer and other cancers, they should have a colonoscopy once they turn 50. If that is completely negative, probably the next time you need to get a repeat colonoscopy is 10 years later.Foss Thank you very much for this information. We will be back in a few minutes to talk a little bit more about the treatment for colon cancer. You are listening to Yale Cancer Center Answers and we are here discussing colorectal cancer with Dr. Ed Chu.Foss Welcome back to Yale Cancer Center Answers, this is Dr. Francine Foss and I am joined by my co-host Dr. Ed Chu discussing treatment options for colorectal cancer. Ed, we talked a little bit about the risk factors for colorectal cancer, but I am wondering, is there a difference in the incidence of this cancer in men versus women, or are there any differences between different races?Chu I am glad you asked that question Francine. What we found over the years is that the incidence in colon cancer is absolutely the same between males and females. If you look at how many men, and how many women get screened for colon cancer, women get screened about half as frequently as men. The reason for that is that there is this misperception that women are at a much lower risk for developing colon cancer than their male counterparts, but that absolutely is incorrect. Also, I think what typically happens is that their primary care16:02 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Mar-01-09.mp3 physicians and gynecological physicians obviously focus on breast cancer and cervical cancer, for which we also have good screening techniques, but the key is that women should get screening just like men. With respect to race there is also some very interesting new data coming out suggesting that African-Americans seem to develop colon cancer at an earlier age than their Caucasian counterparts. And when they do present they also tend to present with more aggressive disease. Therefore, the American College of Gastroenterology and the American Cancer Society have suggested that African-Americans start screening at least 5 years earlier than the magic number that we have been talking about which is 50. So, in general, African-Americans probably should start at 45, but perhaps maybe even as early as

age 40. Foss Can you address the question of diet and colon cancer and colon cancer prevention? We have all been told that if we eat high fiber and bulky type diets that would prevent colon cancer. Chu There is no question that diet is an important risk factor for developing colon cancer, and diets that are rich in fatty foods, red meats, and low in fiber content does increase the risk of colon cancer. Probably the best evidence for this is when you look at individuals who grow up in Africa and in Asia where typically they have a diet that is very rich in fiber, and fruits and vegetables; the incidence of colon cancer is much lower. In this country there have been a number of studies to try to address the question of whether or not a diet that is rich in fiber and fruits and vegetables can reduce the incidence of polyps and colon cancer. The studies, unfortunately, have been all negative, but I think the problem is that those studies only go on for about a year or two and the damage has already been done, especially if patients on these trials are say age 50 or older. The key is to try to do these dietary interventions as early as possible. Foss What about calcium and vitamin D? Chu There is some very interesting data that calcium, vitamin D supplementation, and also folic acid supplementation, may reduce the risk of developing colon cancer. Foss Do you have a recommendation for patients who might be at high risk, such as those who have a family history of colon cancer? Chu What I generally recommend is to focus on a diet that is rich in lean meats, white meats, high in fiber, fruits and vegetables, and try to avoid alcohol because alcohol seems to increase the potential risk for developing colon cancer. Also, abstain from smoking, and to live a good natural lifestyle, try to have daily exercise. The recommendations that are given by the ACS19:20 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Mar-01-09.mp3 for good healthy living, and to prevent other cancers, also hold true for trying to prevent colon cancer. Foss Can you talk a little bit with us about patients who have colon cancer? What has changed in the treatment of colon cancer over the last 10 or 15 years? Chu There have been a number of major advances. The first one is that we now know that this is a disease that requires a multidisciplinary team to approach each individual patient and then come up with treatment recommendations. As part of that multidisciplinary team it is critically important to have a medical oncologist, a surgical oncologist, and a radiation oncologist, each of whom specializes in the treatment of colorectal cancer. When I think back to when we were fellows at the National Cancer Institute, back in the 1980s, for colon cancer we had only one drug and that drug was 5-fluorouracil; basically we had that drug for about 40 years and nothing else. Within the last 8 to 10 years we have three new, what are called, anticancer drugs that can be used to treat colon cancer, and we have three new target agents that can also be used to treat colon cancer. So, the availability of new agents and new treatment regimens to treat both early stage colon cancer and metastatic colon cancer has really exploded. Foss Ed, I know that you are very intimately involved in the Developmental Therapeutics Program and in developing novel therapies for colon cancer. Can you tell us a little bit about what you have been doing? Chu I would be very happy to. We have a very interesting agent, in fact it is a Chinese herbal medicine called PHY906 that my

close colleague, Professor Tommy Cheng who has been on the show previously to talk about this, first identified a few years ago. Interestingly enough this herb has been used in the Orient for nearly 2000 years to treat everyday nausea, vomiting, abdominal cramps, and diarrhea. Our thinking was that since most of the cancer drugs that we use to treat colon cancer have as their main side effects nausea, vomiting, and diarrhea, wouldn't it be interesting to see if could combine this herb with our traditional chemotherapy. In fact, we actually did a study about three years ago testing this herb in combination with a drug called irinotecan, and really, not to our surprise, this herb significantly protected against nausea, vomiting, and diarrhea. Our colleague Dr. Wasif Saif, who is co-Director of our GI program at Yale Cancer Center, just started a phase I/II study looking at this herb in combination with this drug irinotecan in patients who have been previously treated with other chemotherapy.

Foss: How does a patient get access to this kind of a new treatment?

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Chu: I think the best thing is for patients to go to the Yale Cancer Center website which is www.yalecancercenter.org. There they can click on to our website and go to either the Developmental Therapeutics Program or the GI team. If someone wants to get in contact with me directly, they can call my office at 203-785-6879.

Foss: Ed, we talked a little bit about some of the treatments that patients are getting and I think you bring up a very important point, which is the importance of symptomatic control and looking at side effects of treatments and addressing what is important for a patient as they go through the treatment for a disease like colon cancer. Can you talk a little bit about what kind of treatment the average patient would get if they need chemotherapy, how long that would last, and what happens after they finish chemotherapy?

Chu: How often do they need to come back and get screened?

Chu: As I said, one of the great advances that we have seen in 2008-2009 is the amazing number of treatment options that are available to patients. Typically it would involve a combination of the traditional chemotherapy as well as incorporating one of these new target therapies. Typically what we would do is we would start a regimen, follow that patient for two to three months, see how they are doing and how they are tolerating it, and also look at how the tumor is responding. If in fact the tumor is showing a nice response, and the patient is not experiencing any adverse side effects, we would continue for another two to three months, and we would continue until there is either evidence of the tumor no longer responding, or at anytime the patient says they are just experiencing too many side effects. One of the really significant advances that we have seen is that many years ago, with that one drug, 5-fluorouracil, we were talking about a median overall survival of only about 10-12 months. Now, with very aggressive treatments and sequential treatments and very effective salvage treatments, we are now talking about survivals approaching 28 to 30 months; in some cases 3 years. We have really seen a pretty significant prolongation in survival of patients who have colon cancer that has spread throughout the body, and that is why it is particularly important to not only give these very effective, active therapies, but also try to maintain their quality

of life. What we want patients to do, and I know it is the same way in your area of expertise, is try to maintain as best as possible their normal activities of daily living and maintain their quality of life. Foss You make a very good point here, and I think it is important to stress this point to patients. I remember back, as you said, 5-10 years ago when patients with metastatic colon cancer had a very bad prognosis. Because of some of the recent advances that you mentioned, these patients can have a meaningful survival and can live a couple of years with their disease, maybe even longer in some cases. I think it is important for patients to start thinking about 26:08 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Mar-01-09.mp3 the positive aspects of some of these new developments in therapy, and with regard to that, I would like to switch gears and talk about biological therapy. We talk a lot about biological treatments in the context of lymphomas and breast cancer, but I am just wondering if there are biological therapies for colon cancer as well? Chu As it turns out there are three new biologic target therapies. These are antibodies that target key pathways that we now know are critical for the growth of colon cancer. There is one drug called Avastin which targets the VEGF signaling pathway, and we feel that this pathway is important for angiogenesis, which is critical for the growth and proliferation of tumors. There are other antibodies that target a growth factor receptor called the epidermal growth factor receptor, which we also know is critical for the growth and proliferation of colon tumors. Foss Are there clinical trials at Yale Cancer Center looking at some of these novel agents? Chu Yes, in fact we have studies looking at those antibodies in combination with newer antibodies and newer target therapies because one of the challenges with treating colon cancer, and other cancers, is that not only can we inhibit those pathways, we need to make sure we can inhibit other pathways that contribute to the growth of colon cancer tumors. Foss Thank you very much. This was a very informative program. You have been listening to Yale Cancer Center Answers. I would like to thank my co-host and this week's guest Dr. Ed Chu for joining me. Until next time, I am Dr. Francine Foss from Yale Cancer Center wishing you a safe and healthy week. If you have questions or would like to share your comments, go to 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.