

Yale CANCER
CENTER

answers

WNPR Connecticut Public Radio



Hosts

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**Pancreatic Cancer Awareness
Month 2013**

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Yale Cancer Center Answers

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Welcome to Yale Cancer Center Answers with doctors Francine Foss and Anees Chagpar. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. 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, in observance of Pancreatic Cancer Awareness Month Dr. Chagpar is joined by Dr. James Farrell. Dr. Farrell is Director of The Yale Center for Pancreatic Diseases. Here is Anees Chagpar.

Chagpar Let's start off by talking about what pancreatic cancer is and what you do?

Farrell Pancreatic cancer is a cancer of the pancreatic organ. It is an organ that is pretty deep in the inner belly, sitting behind the stomach, and pancreatic cancer is increasingly becoming a more common cancer, there are about 44,000 cases of pancreatic cancer in this country every year. So my role in pancreatic cancer is I work as part of a large multidisciplinary group at Yale, whereby I am involved in both the diagnosis and the management as well as the palliation of treatment for patients with pancreatic cancer. By training I am an interventional gastroenterologist and endoscopist with a specific interest in pancreatic disease. I see a lot of patients who present with pancreatic disease. I see a lot of patients who are concerned about whether they have pancreatic disease, or whether they are at risk for getting pancreatic cancer, and I am involved in the initial evaluation of those patients with a variety of endoscopic tests. For the patients who ultimately do get a diagnosis of pancreatic cancer, we are involved with the management in terms of deciding which patients should undergo surgical management, which patients should have chemotherapy or radiation therapy as part of a larger multidisciplinary group that are all involved in the overall management of these patients from the beginning of the diagnostic workup.

Chagpar A lot of people do not know a whole lot about pancreatic cancer, but pancreatic cancer was what Patrick Swayze had right? And Steve Jobs?

Farrell Correct, there are a lot of notable people who have died as a result of pancreatic cancer. Patrick Swayze is one the more recent individuals. Steve Jobs, we believe, had a variant of pancreatic cancer of the endocrine neoplasm, or tumor of the pancreas, but still within the same broad family and can often be just as bad. But it is quite a common cancer. When you look at the overall list for pancreatic cancer it ranks about ninth overall in the country, but when you look at death from cancer it jumps up to the number 4 spot, and in fact, by 2025, it is estimated that it could be the number one, or leading cause of death from cancer, and there are a variety of reasons for that. It takes a lot of people by surprise. One is that it is really a disease of the elder generation, so the average age of onset is around 65 or so. So the population age is issue number 1. Number 2, is that a lot of the other cancers that we are very familiar with such as colon cancer, prostate, lung and breast cancers, there have been significant inroads in terms of early diagnosis and management, but not so much with respect to pancreatic cancer and so they are doing better and

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pancreatic cancer isn't and still the treatment regimens are available for pancreatic cancer and there have been some notable improvements. It is still a very difficult cancer to diagnose early and to treat effectively. So this is becoming a bigger issue and here in the State of Connecticut, for example, we have some of the highest rates of pancreatic cancer and some of the highest rising rates of pancreatic cancer in the country it is becoming an increasing issue. We see it predominantly in men, and a little more so in African-Americans. Smoking is a very significant risk factor for pancreatic cancer and everybody thinks about lung cancer, but the second most common smoking related cancer out there is pancreatic cancer after lung cancer, so it is a big issue.

Chagpar So our listeners may be really surprised to hear how prevalent it is today in Connecticut. Why is it that in Connecticut the rates are so high?

Farrell I do not think we have a really good handle on it. It certainly was alarming when I heard this, I had just moved to Connecticut from California and when I was doing my homework about moving to Connecticut I was looking at the data and it was surprising. I think some of it is actually because Connecticut has a very good track record frankly, of recording what goes on with its people and its patients, that is a part of it, but it is somewhat concerning that there is a definite increase in the incidence of pancreatic cancer. Again, it is not an alarming rate compared to the rest of the country, but it is certainly up there, and is at higher rates of smoking and I don't have an answer for that. Is it the age distribution of the population? There are many many factors but the specifics are actually quite hard to tease out.

Chagpar Let's talk about the risk factors for developing pancreatic cancer. Certainly you told us about smoking, but are there other things that put people at risk for developing the disease?

Ferrell There are and there has been much more research into this area of pancreatic cancer in the last 10 years than in the previous 100 years for a variety of reasons, and in fact, pancreatic cancer genetics is probably the most studied of all the cancer genetics out there because people have piled into this area to work things out. We definitely are beginning to understand that there is a familial component to pancreatic cancers. So we think about 10% of all pancreatic cancers have some sort of familial component and often the patients are unaware that this is going on and you begin to ask them and all of a sudden, an uncle or an aunt had a similar type of disease and the genetics of pancreatic cancer is being worked out so there are some clear cut genes that we can test for, like the BRCA1 and BRCA 2 genes, the P16 genes, but still the vast majority of familial pancreatic cancer has not really been worked out and in that field a lot of studies have arisen whereby we are actively engaging patients from families that have familial pancreatic cancer and trying to screen them at an early stage to see if they have lesions that might represent early pancreatic cancers. So the area of familial pancreatic cancer is certainly a concerning one. There are other areas such as in respect to diabetes. It is concerning for patients who develop a new onset of diabetes after the age of 50 or so, that they perhaps are at increased risk. Again it is a small absolute risk because diabetes is very common in the population but it is certainly a red flag when we hear about new

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onset diabetes after the age of 50. We also get concerned about patients with established diabetes where for some reason their sugar starts acting erratically after a long time of stability. So the world of diabetes is coming under our radar first to figure out, should we be looking at this group more closely as a risk factor for pancreatic cancer? Another big area that is also a concern, and we are being very proactive now at Yale in particular by doing this, is with the increasing use of CAT scans and MRIs in the community for a variety of reasons. We are picking up a lot of incidental cysts of small fluid collections in the pancreas and we know that some of these cysts are premalignant or precancerous. Now, there are a lot of these cysts out there and somewhere between 3% to 5% of the population between the age of 60 and 70 will have these cysts, but obviously not all of them are developing into serious pancreatic disease. So through a combination of our understanding of these diseases, we have a pancreatic cyst clinic and the use of more invasive endoscopic procedures to biopsy and sample these cysts, we are getting to be pretty good at identifying what patients we need to be very aggressive with by removing these as early lesions through surgery, or patients we can follow. So those are kind of the big three items in terms of risk factors. There is also the issue of chronic damage to the pancreas over time. The other big pancreatic disease, for example, is pancreatitis and everybody knows that alcohol is ultimately very deleterious to your pancreas. So if you develop damage to your pancreas from alcohol the disease is called chronic pancreatitis. It puts you at an increased risk of developing pancreatic cancer probably 8 fold compared to the rest of the population but there are other things that can cause chronic pancreatitis, and in fact there are hereditary forms of pancreatitis. This is different than familial pancreatic cancer and so this is being very well worked out. We know the genes that are involved. We know the families we can test for the genes, and those particular individuals are probably anywhere between a 40 to 60 fold increase of developing pancreatic cancer, so they need close attention. One of the very gratifying things about this field is that tremendous progress has been made in understanding and it is really up to us to put our knowledge to work to try and help some of these patients.

Chagpar Let's suppose, our listeners are listening to us on Yale Cancer Center Answers on Sunday evening and thinking, "I have a lot of those risk factors." What are the signs and symptoms that people should look for to prompt them to seek medical attention, or is a risk factor enough to go to your doctor and say, my sugars have been acting erratic and I just got diagnosed with diabetes after the age of 50, or, I am a smoker and have a history of chronic pancreatitis. What should people be looking for in terms of signs and symptoms?

Farrell I think it is governed by two issues, one of the unfortunate issues is the fact that a lot of pancreatic cancer in early stage is asymptomatic and so as a result of that I think we have begun to focus, and would tell people who fall into these high risk groups. So if there is a real family history of pancreatic cancer, if they have a pancreatic cyst, if there is something about their diabetes, again which is a very common disease, that they are concerned about, it is something that they should certainly bring up with their physician and then the physician can coordinate the proper

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management plan based on that. For people who do not really fall into those groups, the symptoms of pancreatic cancer, when it does become symptomatic, are unfortunately very non-specific. So we are talking about abdominal pain. We are talking about weight loss, which should certainly alarm anybody who has a new onset of abdominal pain or weight loss, it does not mean that it necessarily has to be pancreatic cancer, there are many other things that it could be, but those symptoms alone should be enough for someone to say, I need to get this sorted out. One of the problems with pancreatic cancer is the location of the pancreas itself, it is so deep that when you have the pancreas itself we have an area of the pancreas called the head of the pancreas and that is where the liver drains through. So when something goes wrong there, the liver gets backed up and the patient may turn yellow. So that can be an early warning sign for us. If you have something that is going on in the body or tail of the pancreas, unfortunately things can develop there for quite a while and the patient can be completely unaware of it. So it is a problem of very non-specific symptoms, and late presentations. We have also recognized some subgroups of patients such as diabetics or patients who develop pancreatitis or an inflamed pancreas, which in a certain age group says, we need to make sure that you do not have an early pancreatic cancer or something that could develop into cancer. But I think it is good medical advice for any patient with any sort of new symptoms to at least seek medical advice. We talked about some of the alarming rates of pancreatic cancer, but the absolute rates are still relatively low compared to heart disease and the lung disease. So I think patients need to keep those issues in mind as well.

Chagpar One of the things that you mentioned that I want to come back to is that there now are screening tests, because if we have people who are at high risk, potentially we can screen for cancers and pick them up early. Tell us a bit more about how you screen for pancreatic cancer, a lot of people know that they should get a mammogram to screen for breast cancer or a colonoscopy for colon cancer, but what do you do for pancreatic cancer and who should be getting screened?

Farrell It is still a very controversial subject and it again has come into an active area of work, but there have been some clear issues coming to mind. There is no simple blood test for example, whereby you can go out and get a blood test and say I do or I do not have pancreatic cancer. There is a tumor marker called CA19-9 but it lacks really what we called a sensitivity or specificity. So it is not the perfect test for it and so we do not recommend to be used routinely. There is a lot of work going on we are being involved ourselves in developing of the saliva based biomarkers. One of the big problems with a lot of these tests is that they are also found in patients who do not have pancreatic cancer and what our concern is, is that a certain number of patients will be falsely worried and anxious as we go through the screening process. So what we are working on is focusing on patients who are at higher risk and for those groups of patients we do a blood test, and we sometimes look at pancreatic juice that we collect from the pancreas. We use a variety of imaging tests, MRI scans of the pancreas, CT scans of the pancreas as well as endoscopic ultrasound to really begin to identify what is considered an early cancer or even possibly, the Holy

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Grail here, to find a pre-cancer or something before it develops into cancer and I think with those groups it is becoming reasonable to think about screening with an invasive procedure such as an endoscopic ultrasound, which is a very high resolution modality imaging for looking at the pancreas to see if we can pick a pancreatic cancer early.

Chagpar We are going to pick up on that conversation right after we take a break for a medical minute. Please stay tuned to learn more information about pancreatic cancer with our guest Dr. James Farrell.

*Medical
Minute*

The American Cancer Society estimates that over a thousand patients will be diagnosed with melanoma in Connecticut each year. 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 and new treatment options and surgical techniques are giving melanoma survivors more hope than they have ever had before. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatments for melanoma. The specialized programs of research excellence in skin cancer grant at Yale also known as the SPORE Grant will help establish national guidelines and 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.

Chagpar This is Dr. Anees Chagpar and I am joined today by my guest Dr. James Farrell and we are discussing pancreatic cancer, particularly given the fact that this is Pancreatic Cancer Awareness Month lest any of you did not know that, I certainly did not. James, right before the break you were telling us something that I found very intriguing, which was the fact that although it still seems to be in its infancy there are a variety of imaging modalities that we can use to kind of screen for pancreatic cancer, tell us more about what those tests are and how involved they are? What it is like for a patient?

Farrell We are beginning to use more tests such as MRI scans as well as CAT scans, but preferentially MRI scans because of the lack of radiation, and we get very good imaging of the pancreas with that. We are beginning to pick up very small lesions such as small cysts, which we think might be associated with the development of pancreatic cancer, so in the right population this becomes a very interesting finding for us. That is a non-invasive study, it does not require the patient to be sedated and takes about a half hour or so, it gives a lot of information about the pancreas in incredible detail. On account of a slightly higher level then we have to make decisions about whether we do more invasive, but safe procedures, and really a very common one is called endoscopic ultrasound and this is available at a variety of institutions around the country and it is becoming more common. It is like an upper endoscopy, so if have ever had an endoscopy to look

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for an ulcer or to check on heartburn, it is very similar to that, but it has an ultrasound probe that allows us to look very closely at the pancreas. So, we can see all aspects of the pancreas in incredible detail, but almost as importantly, it allows us to biopsy things within the pancreas very safely and so in former times if you wanted a biopsy of the pancreas it was a big production either involving CT scan with surgery, and now we can do a minimally invasive procedure such as the endoscopic ultrasound. We can stick a very small needle, very safely, painlessly into the pancreas, we can biopsy, we can collect fluid from these cysts and try and understand what is going on in a patient's pancreas. It is one of the great advances over the last 15 or 20 years or so and it has really pushed the area of pancreatic imaging, so that we are beginning to understand what we are dealing with again in certain populations.

Chagpar Can you tell me more about those populations, are those the people who would be genetically tested to be at higher risk? Who would those be and how frequently should they be getting these studies?

Farrell I think for the patient's who are incidentally being found to have a pancreatic cyst again through this kind of modern epidemic of imaging being done, and the patients found to have incidental abnormalities in their pancreas, they should certainly undergo an intensive evaluation initially with MRI scans, with endoscopic ultrasound, but then we end up stratifying and then we decide, you need to have this area removed of your pancreas or you need to be left alone for a couple of years and we will check in again in one or two years. We will be getting a better understanding of what patients we can leave alone and what patients we need to be aggressive about. For patients who do have a family history, a lot of those are being studied at places as Yale and other institutions around the country as part of protocols whereby they are enrolled, actively managed, they see a genetic counselor and their risk is assessed and then decisions about how often they need an MRI, for example, how often they need an endoscopic ultrasound, is decided upon and invariably they need some form of ongoing surveillance be it yearly with an MRI or every other year with an MRI and an endoscopic ultrasound.

Chagpar That sounds like that really is pushing the forefront of finding pancreatic cancer early?

Farrell It is important for us. There are two wars on pancreatic cancer, one is obviously a treatment and still there are a lot of patients presenting at very late stages with pancreatic cancer, it is one of the big issues of pancreatic cancer, but I think the other front is really in the world of early detection and how do we detect these lesions at an early stage that they could undergo surgery, so only about 15% of patients who present with pancreatic cancer are eligible to undergo surgical resection and they do better long-term, but only 15% of all patients are presenting that way, so if we can increase

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that number and try to pick up those patients earlier, that will be great. Again, as I said earlier, the Holy Grail would be to find patients before they develop into cancers, and so that is why there is such a hot area of interest in this world of pancreatic cysts and frankly looking at the patients who are considered to be at high risk.

Chagpar Let's talk about the management of pancreatic cancer. You mentioned that about 15% can be treated with surgery and that they do better then if they are not eligible to be treated with surgery, what is the surgery like?

Farrell The surgery for pancreatic cancer is a big proposition, and it involves removing all, or a portion, more often a portion, of the pancreas, and a lot of it depends on the location of the pancreatic cancer so if it is in we call the head of the pancreas, patients undergo a Whipple procedure which is named after the original inventor of the procedure, and it is a fairly involved procedure that really should only be done at an expert center by very experienced surgeons and that has been one of the great developments over the last 10 or 15 years is the realization that if you need pancreatic surgery, you really need to be in the hands of a very experienced surgeon at a high volume center. It is a big surgery, but now in good hands and in safe hands, the mortality is approaching zero percent. This is associated with more of the initiative recovery period, but I think for this group of patients because it does improve the odds, it is highly sought after and we do our best to try and identify patients who are eligible for pancreatic surgery, but unfortunately, it is still a relatively small number of the entire population.

Chagpar What happens to the other 85% of people?

Farrell So the other 85% people are not initially eligible for surgery, because they either have involvement of major blood vessels in the area or the disease has spread to the liver or lung for example, at the time of presentation. A small percentage of them over time and with treatment may become eligible for surgery, but the vast majority of them are still dependent on combinations of chemotherapy predominately, as well as radiation therapy and therein lies one of the big problems of pancreatic cancer, that we have really not had great drugs to try and tackle this disease. It is changing and there are a lot of new exciting developments in the area, but really for that 85% of the population, they are dependent on some form of chemotherapy with or without radiation treatment to try and help them.

Chagpar For a lot of cancers the big buzz words these days is targeted therapies and personalized medicine, where are we on that front in pancreatic cancer?

Farrell Personalized medicine in pancreatic cancer has been my personal hobby-horse for the last 15 years. In fact, I was involved in identifying a marker that was associated with a group of patients that did particularly well when they were given the common drug used in pancreatic cancer, which is gemcitabine, and so we are still studying that area, the particular marker is called hENT1 and it

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is a marker that allows the drug to get into the cell, for example. So, if your tumor has that marker and you get gemcitabine, you do well, so we are beginning to look more closely at this as a possible treatment option at least to identify that subgroup of patients that if they had that marker they would benefit from that treatment, and allow other patients who do not have that marker to go in a different direction with another treatment, and so I think, within the area of pancreatic cancer, like other cancers quite frankly, I think there was a big push and a big understanding now that not all these pancreatic cancers are the same, and they probably should not be treated and there are many subgroups, so we are beginning to understand it, we are beginning to see these subgroups, we are beginning to identify the drugs that these subgroups would benefit from. With respect to the issue of targeted therapy and better treatments for it, as I said, there has been much more work done on the genetics of pancreatic cancer than frankly any other cancer in the last 10 or 15 years. We know a lot about pancreatic cancer now by the mutations involved and people are developing ongoing treatments that are based on that but it is still in the early stages and it might require multiple drugs and multiple combinations of drugs. What has happened in the last two to three years or so are new drug trials and new combinations of treatment that have really advanced the management of patients with locally advanced and metastatic pancreatic cancer. For a long time, we depended on the drug called gemcitabine and in recent years we have added a drug called nab-paclitaxel and then recently FOLFIRINOX and these are really making a dent in patient's survival, but unfortunately with metastatic and locally advanced disease, there has been some progress, but I think the area of targeted therapy is still an evolution for pancreatic cancer as well as personalized medicine, but there are a lot of people who are pushing that agenda.

Chagpar The last thing that you mentioned in passing was radiation therapy, so we know that if you present really early you may be able to get surgery and do very well and then there is chemotherapy, but who needs radiation and what is that like?

Farrell The role of radiation therapy has actually been quite controversial in pancreatic cancer and for a period of time it went out of favor for the management of patients who had what we call locally advanced disease, so they have disease that is confined to their pancreas, but they are not able to have surgery because it is involving the major blood vessels and so radiation therapy had been used and is still used for that group of patients with a view that in addition to chemotherapy we are trying to shrink down the tumor. Also for patients who have undergone surgery, for example, and have had their tumor removed, there has been a role for radiation therapy in the management of those patients after surgery, but again it is still a controversial subject and I think as drug regimens get better most physicians and most treating physician would really like to push the concept of chemotherapy over radiation therapy, but again it is still kind of a controversial area.

Chagpar I want to get back to one of the statistics that you gave us early on in the show, which is that overtime, in the next decade or so, the mortality associated with pancreatic cancer may in fact be at

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the top of the charts in terms of all cancers and the mortality associated with that. Why is that? Is it that we are just finding it late, is it that all of this research is just going too slowly, what is it going to take to get that mortality back down where it belongs closer to zero?

Farrell I could tell you that there are a lot of people in the country and in the world who are passionate about getting this mortality rate down and the organizations that I am involved with are also very active here in Connecticut. PanCAN has set the goal for doubling the survivor related pancreatic cancer by 2025 and they are passionate about getting this done through research, by getting patients, and patients families and people interested in pancreatic disease involved, but the two big challenges are the issue of early detection and the issue of treatment and also the fact that yes there have been other gains made in other diseases and other cancers, and so those two things are being tackled and because there have been some advances in our understating as well frankly as the treatment of pancreatic cancer, I think, there is optimism that either a new treatment regimen or a treatment regimen for a subgroup of patients who have pancreatic cancer will benefit and will help move that needle a little bit and get to those goals by 2025, but it is a challenge and likewise with early detection, I think through combinations of new blood markers, our understanding of who is at risk, we are making slow dents in this overall statistics.

Chagpar And it seems to me that there is all kinds are really exciting research going on in the field of pancreatic cancer on all of those fronts, on early detection, on looking at the genetics of pancreatic cancer and on treatment, but all of this also requires the commitment of patients to participate in clinical trials. Can you talk a little bit about that?

Farrell It is a big issue for patients with pancreatic cancer and some recent studies have suggested that really the enrollment of patients with pancreatic cancer in trials is very low in this country and so PanCAN, for example, and other organizations are really pushing the agenda of increasing enrollment. We cannot begin to understand anything about disease without patient's involvement about understanding how the drugs work, why they work and moving forward in this field and I think the message is getting out and I think the message is that patients need to be counseled about the importance of being involved in pancreatic cancer trials and that is should not be seen necessarily as a negative or truly experimental thing, but that there is a probability now with some of these new regimens and they may actually receive a benefit and I think that word is getting out, but we have got a long way to go and it is a two-way street, we want to learn, we want to help as physicians and researchers and patients want to learn and patients want to be helped by this as do their families.

Dr. James Farrell is Director of the Yale center for pancreatic diseases. If you have questions or comments, we invite you to visit yalecancercenter.org or you can also get the podcast and find written transcripts of previously broadcast episodes. You are listening to the WNPR Connecticut Public Media Source for News and Ideas.