

Welcome to Yale Cancer Center Answers with Dr. Ed Chu and Dr. Ken Miller. I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and he is an internationally recognized expert on colorectal cancer. Dr. Miller is the Director of the Connecticut Challenge Survivorship Program and he is also the author of "Choices in Breast Cancer Treatment." If you would like to join the discussion, you can contact the doctors directly at canceranswers@yale.edu or 1-888-234-4YCC. This evening, as we reach the end of lung cancer awareness month, Ed and Ken welcome the Directors of the Yale Cancer Center Thoracic Oncology Program, Dr. Frank Detterbeck and Dr. Lynn Tanoue. Dr. Detterbeck is a Professor of thoracic surgery at Yale and Dr. Tanoue is a Professor of pulmonary medicine.

- Tanoue Unfortunately, lung cancer is a very common cancer. It is the most common cause of death from cancer, and if you add up the number of cancer deaths from lung cancer, it exceeds the combination of breast, prostate, colorectal, and pancreatic cancer deaths. More women will die of lung cancer than ovarian cancer and breast cancer, and more nonsmoking women will die of lung cancer than ovarian cancer, so it is a very common cancer. Unfortunately, it claims a lot of lives.
- Miller Let me ask you a little bit more about that. On one hand, it is not as common as breast cancer, but on the other hand, there are more women dying of it. How do you explain that?
- Tanoue We do not have a good way of early detection, and I think that is one of the important things that lung cancer research needs to focus, on a way to screen. We do not have that right now, and there is relatively poor awareness of the fact that lung cancer is so common, and breast and ovarian cancer have gotten a lot more attention over the last several decades; although that is changing.
- Chu When we think of lung cancer, what are the typical risk factors that one should be aware of?
- Detterbeck Certainly the thing that comes to everyone's mind is smoking, and there is no question that smoking is the major risk factor, but many people stop thinking after smoking, and there clearly are other risk factors. We certainly see lung cancer in non-smokers; in fact over half of the people that we diagnose with lung cancer now are people that quit smoking years and years ago. I am not talking about quitting two weeks ago, but 20-30 years ago. In fact, if you look at lung cancer in non-smokers, it is equal to people with lymphoma. It is not a minor group of people. What are other factors? Well, family history is clearly one. If you have a first-degree relative with lung cancer corrected for any second-hand smoke exposure or whatever, you clearly do. There clearly is some genetic factor. There are occupational exposures; asbestos is one of the major ones. If you have evidence of obstructive airways disease, emphysema, that is an independent risk factor, independent from whatever effect smoking may have had.

- Chu One thing that I think is commonly misunderstood, that I hear a lot from patients, is that they have quit smoking 15-20 years ago. Does the risk of developing lung cancer go completely to 0, or is there still a residual risk for developing lung cancer?
- Detterbeck There clearly is solid residual risk; it does not go to 0. Even the early studies, I think, were misinterpreted in suggesting that the risk goes down to 0. Certainly the risk diminishes relative to continued smoking, but it never goes down to that of a non-smoker. Whatever risk you have built up during your years of smoking you sort of maintain through your life. You do not build it up any higher, but you do not really lose whatever you have built up.
- Tanoue I just want to add something to what Dr. Detterbeck said, and that is that the risk diminishes when you stop smoking, and that is true no matter how old you are. So, people who stop smoking when they are 50 and 60 and 70, have a decrease in their lung cancer risk as well as, importantly, a decrease in their cardiovascular and cerebrovascular risks. The chance of having a heart attack or stroke goes down quickly, and the chance of having lung cancer goes down steadily over time. While it never reaches the level of a never smoker, it gets pretty low.
- Chu And what about this issue of second-hand smoke, we have heard a lot about that issue recently and I am just curious what each of you thinks about second-hand smoke and the risk for developing lung cancer?
- Detterbeck It clearly is a risk factor. There is no question about it, but I think it has been overblown. For example, the risk with a first-degree relative who had lung cancer is about 400% higher than that of a non-smoker without a first-degree relative. The risk with second-hand smoke is about 40% higher. We are talking 10 times higher with a family history, and yet we talk about second-hand smoke 10 times more than we talk about family history.
- Miller Let us say someone is at higher risk, and we will talk about a few populations; one are people that smoke, the second are people that were smokers, the third are people with a family history or some combinations of those, what constitutes good screening, is their any screening?
- Tanoue There is no recommendation to screen the population at large. For people who recognize that they have risk because they have a lot of factors such as they smoked, they have emphysema, they have a family history, and they may have had occupational exposure, that is different than the population; that is an individual decision. If an individual person feels they have excessive risk because of those factors, that is something they should speak about with their physicians and then a very conscious decision needs to be made about whether or not to

pursue an imaging study like a chest x-ray or maybe even a CT scan, but those are conversations that should happen between an individual and their own physician.

- Chu There has also been a lot recently in the news about the beneficial effects of CAT scans, as you just mentioned, and I am just curious, where do you weigh in on the role of CAT scan for early detection screening of lung cancer?
- Detterbeck Certainly CT has been studied a lot. There have been a lot of efforts towards having a screening test for lung cancer, but we are not there. One of the things we have realized with CT scan is that we are picking up a different spectrum of disease. We pick up things that are very slow growing, very indolent tumors that we did not really pick up as well, and I think we are still struggling to understand what we do about those tumors. We do not necessarily want to approach those with the same approach as the more aggressive lung cancer. Screening changes the spectrum of disease, you have to understand that as well, and without understanding it better, I do not think we can define where that fits at this point.
- Chu In your Thoracic Oncology Program, what do you recommend in terms of say an individual, like Ken said, that has a high risk for developing lung cancer?
- Tanoue I think those individuals, again, have to speak with their physicians who know their history and can appreciate all the nuances of their risks and an individual decision needs to be made as to whether to pursue any sort of imaging study to look in a more directed fashion. As a population though, there is no evidence right now that there should be screening done on a general level the way mammogram is done for breast cancer, PSA for prostate, and so forth.
- Detterbeck One of the issues with screening is that you really need to look at the risk, and I think that underscores what Lynn was saying. Patients should discuss it with their physician and put some thought towards it. Screening a broad population, people over 50 that smoked for some period in their life, we are not there to recommend anything on that, but if you can increase the pool of people that are at higher risk, now that is a different group of people to look at, that is a different situation, so I think that is a very important piece of it.
- Miller We get a number of E-mails from people saying, "What is the very best way to find out if I have breast cancer or prostate cancer?" Let me pose a clinical question. A patient sits in front of you and says, "Doctor, listen I want to be as vigilant as possible, I have been a smoker, I wish I had not been." What is the gold standard in terms of what you would tell that patient if he or she was sitting in front of you?
- Tanoue Again, there is not a gold standard, that is the problem. We certainly appreciate that mammography and PSA, even colonoscopy, will pick up lots of findings that

are abnormal, but not cancer, and we can deal with those, those are reasonably easy places for us to do a biopsy. The problem with CT scanning, which was supposed to help us with this, is that it is too sensitive. What I mean by that is that when you do a CT scan, particularly in a population of people who smoked even 10 packs a day for years, it is very, very likely you will find something. In fact, these studies, of which there have now been a number of, find abnormalities in one scan, just the first scan, in between 12% to over 50% of the people being screened. Of those many abnormalities, maybe 1% to 2% of them are cancerous, so you have to deal with the other 98% to 99% of them which are not cancers, but to know that confidently often requires many imaging studies over time. This requires waiting and being able to live with that, and invasive things like biopsies or even surgeries, and that is what Dr. Detterbeck was talking about with risk. These are procedures that can carry risks and complications, so at the present time the benefit of doing things like CT scanning is outweighed by the risk of those procedures and our increasing knowledge that some of these cancers that we pick up this way are probably never going to hurt people, the way that little prostate cancers that we pick up by high PSA often would not hurt somebody, but we do invasive procedures to figure that out. Weighing all those things right now it is probably more harmful to do the screening with CT studies on a population basis than not to do them.

Chu For prostate cancer, obviously we have PSA, and now there are some blood tests emerging to detect ovarian cancer at earlier stages. I am just curious, where are we in terms of trying to develop simple blood tests that might be able to identify high-risk populations who would have lung cancer?

Detterbeck There has been work done in that regard. There is actually a paper that was just published a few weeks ago from Yale by Joanne Weidhaas and Frank Slack. They looked at microRNAs, which are relatively new. It is something that had not been recognized for a long time, and the thing about microRNAs is that they can influence an abnormality and the microRNA can influence a lot of different genes so it potentially has a lot more effect. Previously they were not very well understood. What this study showed is that the incidence of a genetic mutation in a particular microRNA was much higher in people who develop lung cancer than in a baseline population. In other words, this potentially is a way of trying to figure out who is at higher risk. As we have talked about before, if we can figure out who is at higher risk, we are a whole lot further along in saying, perhaps this is an appropriate population to do CT screening on.

Miller Let me change the topic a little bit. You see a lot of new patients, unfortunately, with lung cancer, what symptoms do they report?

Tanoue Individuals should seek medical attention for things like persistent cough, if you

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are coughing up blood, if you have chest pain that does not resolve itself, fevers that do not go away, or symptoms that persist and are unusual. Definitely always seek medical attention.

Detterbeck I want to underscore that. We probably can detect lung cancers earlier if people pay more attention to subtle symptoms. It is another area of research that we want to pursue. Many people quit smoking for reasons that I think they are not entirely clear about, and then within a year they are diagnosed with a lung cancer. If we study this a little bit more, we realize that there are reasons why they quit smoking, and if we can pick up on that and be more aware of that, I think that we stand a chance to get an edge on those people that have a lung cancer already there.

Chu We are going to take a break. We will be back after a medical minute to hear more about lung cancer with Dr. Lynn Tanoue and Dr. Frank Detterbeck from Yale Cancer Center.

Medical Minute

Here in Connecticut, the American Cancer Society estimates that almost a thousand people will be diagnosed with colorectal cancer every month. The good news is that when you detect it early, colorectal cancer is easily treated and highly curable. That means that if you are over the age of 50 you should have regular colonoscopies to screen for this disease. In the case of patients that develop colorectal cancer there are more options than ever before thanks to increased access to advanced therapies and specialized care. Clinical trials are currently underway at Federally Designated Comprehensive Cancer Centers like the one at Yale to test innovative new treatments for colorectal cancer. Patients enrolled in these trials are given access to medicines not yet approved by the Food and Drug Administration. This has been a medical minute and you will find more information at www.yalecancercenter.org. You are listening to the WNPR Health Forum from Connecticut Public Radio.

Miller Welcome back to Yale Cancer Center Answers. This is Dr. Ken Miller and I am joined by my co-host Dr. Ed Chu and our guests, Dr. Frank Detterbeck and Dr. Lynn Tanoue from Yale Cancer Center. We are talking about lung cancer. So we were talking about these subtle symptoms that people may have that can perhaps give us some clues. When a patient has those types of symptoms, how would you evaluate it, and how do you make the diagnosis for that matter?

Detterbeck First of all, I would encourage people, if they have some subtle symptoms, that it is probably a good idea to talk with their physician about it and not blow it off for a long period of time.

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- Chu Who should they see, their family doctor, an internist, or should they go and see a pulmonary specialist such as Dr. Tanoue?
- Tanoue I think their family doctor, or their internist is always the best bet because that person usually knows the patient. Then if that physician feels that a referral should be made to a specialist, they can choose which appropriate specialist to make that referral to. I would strongly encourage everybody to keep their family doctor in the loop. You want somebody who will steer your little boat, even if there are many oars rowing.
- Chu Just following up with that, what kind of tests would be done once an individual goes to see their general family doctor?
- Detterbeck Certainly one of the straight forward tests is a chest x-ray, and while there is pretty good data from a number of studies done in the past that a screening chest x-ray just on a broad population is not really worthwhile, I think that is a very different situation from someone who comes in with some subtle symptoms and it is not so clear. That is a very different situation, and one should not say chest x-ray has proven not to be useful in that situation. I think we have gone a little bit wrong in that regard. We often see people who had some symptoms, they were seen, and yet it took six months before they ever got a chest x-ray.
- Miller After a patient is diagnosed, does everybody have surgery of some kind?
- Detterbeck No, I think you need a biopsy of some sort, but it used to be said that if you can't have surgery there is really nothing that can be done, and that is certainly not true. Surgery as a treatment for a lung cancer certainly is a major treatment, but we have excellent radiation and excellent chemotherapy drugs. In fact, I have backed off, and I think many in the surgical community have backed off in a number of situations, from doing a surgery because we get such good results with other treatments. Surgery is not necessarily the only treatment that works. The other thing though that we have learned is that a combination of treatments is in many situations more effective than just one treatment alone.
- Chu Can you tell us a little bit about what happens if a patient is diagnosed with lung cancer as is seen by your Thoracic Oncology Program at Yale? What goes into deciding what kind of treatment should be initiated for an individual patient?
- Tanoue The group consists of thoracic surgeons like Dr. Detterbeck, pulmonologists like myself, medical oncologists, radiation oncologists, social workers, pathologists, diagnostic imagers, nuclear medicine, and so forth. Our job at that initial evaluation of a new patient is to decide if they have a lung cancer, if a biopsy needs to be done, and what the stage is. Lung cancer, like all solid organ cancers,

is classified as different stages. For lung cancer it is I through IV. The initial assessment of what the best treatment is will be based on the stage, so the very important focus of the group of our tumor board is to decide what the likely stage is, because that guides the initial assessment about treatment.

Detterbeck Let me add to that in a general way, I think that many diseases have become more complex and there is a greater knowledge base. There is not any one person that knows everything about a disease. Everybody has sort of a different chunk of it and a different view. The key thing is to get that collective brain power and judgment working, so our policy is that all major decisions about patients, whether it is how they should be evaluated or how they should be treated, are made by the whole team. It does not mean the patient needs to see a whole bunch of different people, but it gets discussed so that the collective wisdom and judgment of that whole team can be brought to bear on making that decision.

Miller Frank, let me ask you about minimally invasive surgery for lung cancer, what does that mean?

Detterbeck Things have changed dramatically. It used to be an operation for lung cancer. It was a big incision, and often required removal of a rib, and it was very painful and a big ordeal. Now the majority of resections that we do for a lung cancer, or for anything really, are done with a video camera with about a quarter inch incision for the video camera and some other incisions that are about a half to three quarters of an inch long. It is much less invasive, and it is much less painful. Typically people are in the hospital about 2-1/2 to 3 days, and usually within a week or 2 people are getting around quite well. It is a very different experience because we have modified the incision and how invasive the operation is.

Chu As we were talking about earlier, many patients at risk for developing lung cancer have underlying lung disease. Is there a need requirement to try to assess their underlying lung function status before they can be taken for surgery?

Tanoue Absolutely, any patient who is going to be having thoracic surgery, whether it is in the old style with a big incision which is less common, or with a videoscopic approach, should have their lung function assessed. Particularly with the minimally invasive approach, the recovery is easier but that patient will have gone through a big surgery nonetheless, so it is important to assess their pulmonary function to see if there is something that can be done preoperatively to maximize that function, or to anticipate postoperatively if there might be any needs.

Detterbeck We also have to be careful about what we consider to be too high risk. There are a lot of nuances about that and certainly some of the data that we have applies to the old style operation, and it is pretty clear that with minimally invasive

techniques and newer things, mortality is lower. There is also a reason to select some people that have really poor lung function because in fact their lung function is going to be better, but you have to be careful about choosing those patients; it is not a simple answer.

- Chu When surgery is done, is there any role for follow-up therapy such as radiation therapy or chemotherapy?
- Detterbeck In many situations, as I had mentioned earlier, we do a lot more combination treatments. Not in all situations, in some situations we do so well with surgery alone that there is really no reason to add anything. But, in many situations, we know that we do fairly well with surgery, but we clearly do somewhat better by adding some additional treatment. Most often it is additional chemotherapy, and to a lesser extent, radiation.
- Miller There is a lot of exciting work going on throughout the country, and at Yale also, what are some of the trials you are working on and some of the projects that you are excited about?
- Tanoue We have clinical trials open for nearly every stage of lung cancer, and it is very important that patients have access to new drugs and new therapies because they take advantage of all the scientific discoveries that have been made over the past few years. For lung cancer, there have been some incredibly exciting advances that have changed the way that we approach patients. Five years ago we probably would not have given chemotherapy in addition to surgery for some patients with early stage lung cancer, but it is clear now that we can get improved survival and decreased death over time when we use these multiple approaches to patients even with early stage disease. We are really interested in the kind of research that Dr. Detterbeck discussed earlier, how can we define patients who are at higher risk? Can we predict whether patients who have had cancers are going to go on to relapse? We have been collaborating with colleagues at Yale, friends in the pathology division, to try to identify biochemical markers that we can see in biopsy specimens, and perhaps even in blood, to identify populations that might benefit from other therapy, novel therapies, and so forth.
- Detterbeck Just to add a little something about clinical trials, clinical trials sometimes represent a very new drug, for example one that we do not have a lot of experience with, but that is not the only situation. There are many clinical trials that use drugs that have been used quite a bit, but they are used in a slightly different combination. What it really represents is a very carefully thought out organized way of providing treatment, that some of the best minds in the country have gotten together and discussed, and think that this is a better way to do things. It is very well thought out, it is very well organized. That is a reason why, in general, people do better if they are treated on a clinical trial than if they get the

same treatment interventions but done off trial, it is just not as organized and it tends not to give us as good results.

Chu Frank, we are hearing a lot about the role of targeted therapies, either alone or in combination with chemotherapy, to treat patients with lung cancer. Following up on what you just said, could you tell us a little bit about what is going on in terms of trying to combine those new targeted molecules with traditional chemotherapy?

Detterbeck Clearly it has been an exciting time in lung cancer and targeted therapies. One of the reasons for that excitement is when we understand a particular tumor and why this tumor is growing, and when we can flip that switch off, we have dramatic results. Unfortunately, we do not understand quite as well how to pick those patients, and we only know that a switch exists for a relatively small number at this point, but we have come a long way to understanding that better and there is a lot of research going on in this area.

Miller Projecting into the future, if you had a crystal ball, which none of us have, but what do you think the big breakthroughs will be in terms of treating lung cancer?

Tanoue I think there will be many. We need to understand better how to define populations at risk, and we need to focus on understanding the biology of these tumors so that we can develop targeted therapy and broader treatment approaches for patients who do develop cancers.

Detterbeck I want to add how important it is to be treated and seen in an organized way and be appropriately staged. There is a recent study that suggests that by just doing a better job of evaluating patients we will increase the survival for patients with lung cancer about five times as much as for things that we call breakthrough new treatments.

Chu I think that is a terrific message to end the show on. You have been listening to Yale Cancer Center Answers and we would like to thank our guest experts, Dr. Frank Detterbeck and Dr. Lynn Tanoue for joining us this evening. We look forward, Lynn and Frank, to having you back on a future show to hear more about what is going on with the Thoracic Oncology Program. Until next time, I am Dr. Ed Chu from the Yale Cancer Center wishing you a safe and healthy week.

If you have questions for the doctors or would like to share your comments, go to www.yalecancercenter.org where you can also subscribe to our podcast and find written transcripts of past programs. Next week, Dr. John Colberg and Dr. Richard Peschel join Ed and Ken to talk about prostate cancer. I am Bruce Barber, and you are listening to the WNPR Health Forum from Connecticut Public Radio.