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CENTER

*answers*

WNPR Connecticut Public Radio



*Hosts*

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**A New Take on Lung Cancer**

**Guest Expert:**

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**Yale Cancer Center Answers**

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Sunday Evenings at 6:00 PM

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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](mailto:canceranswers@yale.edu) and the phone number is 1-888-234-4YCC. This week Dr. Foss welcomes Dr. Rogerio Lilenbaum. Dr. Lilenbaum is Chief Medical Officer of Smilow Cancer Hospital at Yale-New Haven. Here is Francine Foss.*

Foss Let's start off by having you give us a brief summary of where you were before you came to Smilow Cancer Hospital and your role is here at Smilow?

Lilenbaum I spent most of my professional life in South Florida, at a hospital called Mount Sinai and then I moved to the Cleveland Clinic in Florida where I spent two years before I came up to Yale-New Haven Hospital, so I had a variety of roles in both those hospitals. I worked in patient care and clinical research and also administrative functions and then had an opportunity to come here to be Chief Medical Officer of Smilow.

Foss So here you are part of the clinical care team as well, and your expertise is in lung cancer. Can you talk a little bit about how got interested in lung cancer?

Lilenbaum This has been a passion of mine for a long time, and it started actually in the middle of my fellowship training. I had completed my clinical training in general hematology/oncology and had the opportunity to work very closely with an exceptional mentor who was a lung cancer expert, and at that time he was at the University of California in San Diego. So, after my clinical training in Saint Louis, I spent 2-1/2 years with Dr. Mark Greene learning about lung cancer, about clinical research in lung cancer, and I never left that field since then.

Foss Lung cancer is one of the more common cancers. Can you talk a little bit about the number of cases per year and some of the major causes are? I think we all know about smoking, but are there some new things to talk about?

Lilenbaum Of course, so lung cancer, and it is important to note this, is not the most common cancer in women, that happens to be breast cancer, and it is not the most common cancer in men, that is prostate cancer, but on the other hand lung cancer is by far the number one cause of cancer death in the United States. In fact, lung cancer accounts for more death from cancer than breast cancer, colon cancer, and prostate cancer combined.

Foss Sounds like we are not doing that well with lung cancer then?

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Lilenbaum We still have a long way to go. I think we are probably doing a little better than we were 15 to 20 years ago, but our overall survival from lung cancer has not changed as much as we would like it to.

Foss You have been involved in clinical research for a number of years. Could one then conclude that our treatments have not improved that much?

Lilenbaum I think that is one conclusion, and I do not think it would be wrong to conclude that. We have not been able to accomplish as much as we would like to. On the other hand, I think part of the problem is the fact that by the time this disease is diagnosed, it is advanced in the vast majority of patients.

Foss Let's go back then and talk a little bit about first of all the risk factors and how patients clinically present. We know about smoking. Can you talk a little bit about whether smoking is on the rise, or on the decline, and how many lung cancer cases are attributed to smoking?

Lilenbaum Approximately 85% of patients with a diagnosis of lung cancer will be either current smokers or former smokers, so there is still 15% of patients who never actively smoked, they may have been exposed to second hand smoking though, so that is an important issue. They may have been exposed to radon, that is a second risk factor and we're beginning to see that independent of these risk factors, we have individuals who just have a predisposition to lung cancer based on how that disease evolves from a molecular standpoint. So I think that has not changed. Smoking continues to be a significant issue for us in the United States. It has been cut down significantly from what it was two decades ago, but in the past few years we have seen that smoking rates among young adults has plateaued, and in women it actually has gone up a little bit. So we are not where we need to be, we are still at about 20% to 25% of the population in the United States who are active smokers.

Foss Do you think that there is enough education around smoking? Particularly for young people, do you think that the educational interventions have made a difference and should we be looking at women differently? Do they have an increased risk, say for smoking?

Lilenbaum I think educational efforts have been significant, but they have not been enforced to the extent that we would like. If you look at a state like California, for example, they have seen a measurable decrease in the incidence of lung cancer after two decades of very stringent laws in terms of smoking. We have not been able to replicate that in other sections of the country, so I think that is one issue. It is not so much what to do but how to enforce it in many ways. I think it is different for women and that there is something else about smoking that attracts women differently than men, and we just have to know how to tackle women differently in terms of efforts to decrease smoking. It is not the same as men from a social standpoint.

Foss Can you talk about symptoms and how patients present? You alluded to the fact that most people have very advanced disease, but we also hear about people going to get a chest x-ray and

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something small is found and they are operated on and that is it. How frequently do you see people advanced and how frequently are they picked up incidentally?

Lilenbaum That is great a question. About a quarter of all patients diagnosed with lung cancer will have early stage disease; therefore three quarters of patients will have advanced disease. Let me step back for a second and talk a little bit about the different types of lung cancer and then I can go into the stages. Lung cancer has two major types, one is the small cell lung cancer type, which accounts for a little less than 15% of all patients with lung cancer, and then everybody else almost by default has what is called non-small cell lung cancer and this is just based on the way the cancer cells look under the microscope. Small cell lung cancer has two stages. It is either limited to the chest or it is beyond the chest, in which case it is called extensive disease. Unfortunately, again, most patients with small cell will have extensive disease at presentation or at the time of the diagnosis. This is not so much because we do not have a good screening technique, and will discuss that later on, but it is also because this is a disease that tends to spread quickly. For non-small cell lung cancer, which is the majority of our patients, we have four stages, I and II are considered early stage disease and therefore are almost always managed by surgical treatments. Patients who have stage III and stage IV disease end up receiving a combination of chemotherapy and radiation therapies, so again we are talking about 75% of our patients with non-small cell lung cancer being diagnosed with either stage III or stage IV. So not many patients come to us as you said with an incidental finding, we still see that in approximately 10% to 15% of patients. They were supposed to have a hernia operation, or they were supposed to have some sort of plastic procedure, and then they get a chest x-ray and something is seen on the chest x-ray that leads eventually to the diagnosis of lung cancer. Other patients have early disease but have symptoms, which can happen depending on the location of the tumor. A cough that never goes away is something patients need to be aware of, pain, chest pain, is also important because if the tumor is located next to the chest wall or adjacent to a rib, it will hurt and then sometimes there is a general sense of fatigue and lack of energy, and I know that is not a specific symptom. A lot of people have that for a variety of reasons but it is something that should trigger an investigation.

Foss What about coughing up blood? A lot of people equate coughing of blood with cancer? How often do you see hemoptysis as a clinical presentation?

Lilenbaum Coughing up blood is absolutely a dire symptom, and so when that happens on a consistent basis, then the patient needs to seek medical attention right away. It is important, however, to differentiate that from patients who have, for example, chronic bronchitis and/or emphysema, so called COPD that we see advertised on TV, and then once in a while they will have a little blood mixed with their sputum. But when you are coughing up blood, that is a symptom that should immediately lead you to pursue or seek medical advice. That happens in about 15% to 20% of patients with lung cancer and again it does not always indicate advanced disease. It has much more to do with the location of the tumor than necessarily the stage of the tumor.

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- Foss So all of these things apply whether they are smoker or not a smoker? Even if you are not a smoker and you cough up blood, do you need to worry?
- Lilenbaum Yes, as we discussed a few minutes ago, approximately 15% of patients with lung cancer are never smokers. They have never smoked in their lives. So it is important to keep in mind that you are still at risk for developing lung cancers. It is not the same as in someone who has a heavy smoking history, but it is important to think about that in the differential diagnosis.
- Foss Rogerio, there are a couple of types of lung cancer that occur in nonsmokers that are not that frequent, could you talk a little bit about those?
- Lilenbaum Of course, small cell, for example, which we discussed a few minutes ago, almost never happens in never smokers, in fact, in my entire career I have probably seen two patients with small cell lung cancer who never smoked and even those two patients had some slight issues with their pathology. It was not classical small cell lung cancer. For the majority of patients who are never smokers and have lung cancer, they will have non-small cell and of the subtypes of non-small cell, they will have adenocarcinoma, it is very unusual for a never smoker to have squamous cell cancer or even large cell cancer. It happens once in a while, but it is not that common, and this is one of the reasons for the misconception that adenocarcinoma of the lung is not associated with smoking, that is not correct. It is just that when never smokers get lung cancer, they get adenocarcinoma.
- Foss Can you talk a little bit about other risk factors? You mentioned other kinds of cancer syndromes and we have heard about these cancer syndrome with breast and ovarian for instance. Are there cancer syndromes that have lung cancer as a component? Somebody comes in and says, there is a lot of cancer in my family, is that going to predispose them to lung cancer?
- Lilenbaum That is a great question, and not to the extent that we see in breast cancer or ovarian cancer or brain tumors for example, we do not have specific genetic syndromes that make you more susceptible to lung cancer. However, there is some degree of familial clustering. It is more likely for someone who has a first degree relative with lung cancer to develop lung cancer, but it is not because we associate that with a specific genetic syndrome, and again all of this pales in comparison to smoking as a risk factor. If you really think about it, this is a disease that could be largely eliminated if smoking were to be completely banned. It would still take several decades for that to happen, but this is a disease that our society can eliminate for future generations.
- Foss It is kind of the equivalent of polio and infectious diseases where you come up with a vaccine and you eliminate it from the population.

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Lilenbaum Absolutely.

Foss We are going to take a break now for a medical minute. This is Dr. Francine Foss with Dr. Lilenbaum and we are talking about lung cancer.

*Medical  
Minute*

*The American Cancer Society estimates that over 1000 patients are 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 and skin cancer grant at Yale, also known as the SPORE grant, will help establish national guidelines on modifying behavior and on prevention as well as identification of new drug targets. This has been a medical minute, brought to you as a public service by Yale Cancer Center. More information is available at [yalecancercenter.org](http://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. Rogerio Lilenbaum and we are discussing lung cancer. We talked a little bit before the break about some of the different types of lung cancers and how many of our patients present with advanced stage disease, could we talk a little bit now about ways to prevent that? We talked about smoking as a major risk factor, but how do we actually screen people, how we do screen smokers and how do we screen, or should we screen nonsmokers?

Lilenbaum I think this is the single most significant progress that has made in lung cancer in the past 50 years or so. As you know, and most people know, we do not have an effective screening technique for lung cancer as we have for breast cancer for example, or for colon cancer, in fact, the studies that were done several decades ago looking at chest x-ray do not show a decrease in the overall mortality from lung cancer. Not too long ago, approximately two years ago, we heard the initial result of a major study conducted by the National Cancer Institute looking at CAT scans, or a CT scan, in patients at risk for lung cancer, and the comparison was between a CT scan and a chest x-ray and over 50,000 people participated in that clinical trial, now who were considered to be at risk for lung cancer? Patients between the ages of 55 and 74 who had at least a 30 pack per year of smoking, and that usually means one pack a day for 30 , or two packs a day for 15 years, etc. and so those individuals were then randomly allocated to either a CAT scan or a chest x-ray, which were done at certain intervals depending on the findings, and at the end of that study it was shown that the CAT scan decreased mortality from lung cancer, which is a pretty high bar, by about 20%. To put that in perspective, this is approximately the same

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degree of reduction in mortality that we see from breast cancer when mammogram is optimally utilized. We do not know exactly what that is yet, but when mammograms are used in breast cancer, we also see about a 20% reduction in mortality from breast cancer, so it is the same in lung cancer. This is a huge step forward because up until now we have no effective technique to identify individuals before they develop symptoms and as we just discussed, people who develop symptoms from the lung cancer, by the time they are diagnosed they usually have advanced disease.

Foss So these patients had the CAT scans done on a regular basis in the study?

Lilenbaum The original CAT scan was done at one year, and if it was negative it was repeated annually for three years, so there were three CAT scans done for the duration of the study as opposed to chest x-rays. Now that raises questions in terms of how that can be applied to clinical practice, why stop at three years? Number one, what is the duration of the screening, should we do it every year, should we do it every two years, and we are just beginning to open up that entire field of investigation as to how this can be applied to clinical practice and to be quite honest, I do not think that we have seen the impact of this screening in our population at all, in fact, if anything, for a variety of reasons, CT screening has not really reached as many people as we would want.

Foss What is the standard of care with respect to screening?

Lilenbaum We do have a screening program and please understand that the CAT scans required for that study are not yet approved by most healthcare insurances. So this too has to be an out of pocket expense, which is a significant problem for people. Some insurances are beginning to look at this and they understand that if you catch this disease early, there would be a significant cost reduction in the future in terms of decreasing costs of treating patients with more advanced disease, but we do have screening programs. At our hospital we still charge these individuals for the CAT scan, but we are in the process of investigating how we can make this more accessible to individuals without incurring significant expense. If anybody is interested in undergoing a CAT scan at Smilow they can call us and we will point them in the right direction.

Foss When folks out there are examining their own risks, we mention smoking, and this study was a 30-pack-year history of smoking, but can you talk about who should come to the screening clinic, who is at risk?

Lilenbaum The selection for the trial was somewhat strict, and so I, for example believe if that is somebody is 50 years of age as opposed to 55 and they have a 30-pack-year history of smoking, I would consider that individual eligible for a CT screening, the problem is when you start deviating a little bit from the data, from what we know, then it opens it up for a lot of other people who want to have screening and probably would not benefit in the same way. For example, we get

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questions all the time from individuals whose parents had lung cancer because their parents smoked, and they never smoked, but should those individuals be screened? And the answer to that is, not at this time, based on the available evidence we do not recommend it. It is important to also note that CT screening has its risks because there are findings in the chest that are not cancers, right? And those findings may lead to invasive procedures and biopsies or even surgeries that in the end are unnecessary and these procedures tend to be more complicated than they would be in the breast, because it is less accessible.

Foss So for people who only have had passive smoking exposure, in the workplace or at home, there is no screening recommendation for them at this time?

Lilenbaum Not at this time.

Foss Can you clarify for us again what a pack-year is? We talk about a 30-pack-year history, what does that mean?

Lilenbaum So if you smoke one pack a day for 30 years, that is a 30-pack-year history, if you smoke two packs a day for 15 years, that is the same thing, or if you smoke three packs a day for 10 years, so it the multiplication of the number of packs by the number of years.

Foss And again that was an arbitrary designation in the study, it does not mean that if you smoked less than that you are not at risk?

Lilenbaum I agree 100%.

Foss Are there other things that could be done for screening that are not as expensive as a CAT scan, we mentioned chest x-ray, but what about a blood test?

Lilenbaum There is an immense amount of research being done to identify certain markers in the blood that would identify individuals at high risk, and some progress has been made, but we are not yet at a time where we have a blood test that can reliably identify individuals, not just with the disease, but even those at higher risk for developing the disease. So, right now this is not recommended in clinical practice, but I would not be surprised if we sit here again in 5 or certainly 10 years from now and that answer is different.

Foss So, at this point, there are no ongoing clinical trials looking at any particular markers in the blood or anything that could potentially be a factor?

Lilenbaum There are studies looking at blood markers, they are not of the same magnitude as the screening studies that we discussed with CT scans, but there are some very interesting preliminary studies showing that in the future we may identify markers in the blood.

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- Foss Great, can we talk a little bit now about people that actually have lung cancer. Once you are diagnosed, and I presume you are diagnosed based on a biopsy, can you talk a little bit about that process of diagnosis and then we can talk about treatment.
- Lilenbaum Let's think about a patient who is found to have a tumor in the lung which is how this disease usually presents, so, there are a couple of ways in which you can get a biopsy as you said, one would be by putting a needle through the chest and our colleagues in interventional radiology usually do that, or sometimes the lung specialists or the pulmonologist will do a biopsy from inside which is called the bronchoscopy, so it is similar to an endoscope looking at the stomach but it is looking at the lungs and those techniques depend on the location of the tumor. Sometimes the disease will be beyond the lung, will be in a lymph node or even outside the chest, and in those cases we tend to pursue a biopsy of those spots because then we can both diagnose the disease and stage the disease at the same time.
- Foss So once you have your diagnosis, and again that is a pathologic diagnosis under the microscope, what is your next step?
- Lilenbaum The next step is to stage the disease. As we discussed we have limited stage and extensive stage in small cell, or in the case of non-small cell we have four different stages. Stage I being the earliest, and stage IV being the most advanced. Usually we accomplish that by doing scans and the one that we use most often, not in everyone, but in the majority of our patients, is a PET scan and a PET scan will identify sometimes small tumors that can be located in the chest or outside the chest that may not be seen on a regular CT scan and we also tend, although it is a little debatable, to scan the brain of most of our patients because that is another common site for disease in lung cancer.
- Foss I understand that both chemotherapy and radiotherapy are used in lung cancer, can you talk a little bit about the role of both of those?
- Lilenbaum If we think about those patients we discussed at the beginning with stage I and II, who can have surgery, let's say lung function is good, the heart function is good, they can undergo general anesthesia, they go to surgery and a portion or segment of the lung is removed. In some cases, that is all that is needed, no further treatment, and there is a pretty good chance that the lung cancer will never return. Sometimes, however, there is a higher risk of what we call recurrence of that tumor and in those patients we give what we refer to as preventive chemotherapy, just like in breast cancer or in colon cancer, we try to decrease the likelihood of a recurrence in the future by giving chemotherapy for a limited number of cycles. So that is how most patients with stage I and stage II disease are treated. When you get to stage III disease, those are patients who have disease that is more advanced within the chest but the disease has not spread outside the chest. So with those patients you can't cut out all the disease by surgery, even if you give chemo afterwards. So in those patients we use typically two different treatments, chemotherapy with radiation, sometimes even three, chemotherapy with radiation followed by

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surgery. So, this is a big group of patients, almost 40% of our patients have stage III disease and each patient is managed individually, but the basic understanding of that group of patients is that they will need more than one type of treatment and sometimes the chemo and the radiation are given together, and sometimes one is given before the other, there are different techniques to do that.

Foss It sounds like we have made a lot of exciting advances in lung cancer. In the one minute left, I wonder if you could just give us one highlight for the future.

Lilenbaum I think that what has changed the landscape for this disease, even for patients with more advanced disease, is the discovery of specific mutations within their tumors that allow us to use what we call targeted agents. These are very specific drugs that are incredibly active and when used they can change the prognosis and the survival of these patients very significantly.

*Dr. Rogerio Lilenbaum is Chief Medical Officer of Smilow Cancer Hospital at Yale-New Haven. If you have questions or would like to add your comments, visit [yalecancercenter.org](http://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.*