

## **ALL ABOUT LUNG CANCER**

**By: John Sprandio, M.D. 9/13/06**

I have been practicing in Delaware County for the past 18 years. Our practice exclusively deals with hematology and oncology issues that are blood disorders and cancer. My group and I have been affiliated with Fox Chase Network for the past 14 years. We have had a long relationship and a good relationship with them. We have been able to bring a lot of the latest treatment protocols and treatment strategies from Fox Chase to our community and the Fox Chase Network is a very broad network involved in 5 or 6 different counties in Pennsylvania and most recently the affiliation was extended to Crozer, Taylor and Springfield. So the effort, the oncology or the cancer program effort across the system has been very hardly supported by the administration and they have really helped us bring our program along and we in turn have brought a lot of new and innovative ways of approaching these diseases to the communities.

What I would like to do is talk about lung cancer in general initially. I want to talk about the way we are changing the treatment of the disease and treating it a little bit differently than we have in the last 50 years.

As many of you may or may not know, lung cancer is the leading cause of cancer deaths in the industrialized world, not just this country, but the industrialized world. One-third of all cancer deaths in this country are directly related to lung cancer. It is a huge number. Just to give you some other information, in 1920, only 1% of all cancer deaths were due to lung cancer. Just 1%; now it's 33%. In 1920, there were approximately three hundred million cigarettes smoked or sold in this country. Now there are six trillion cigarettes sold in this country. The rise in lung cancer is directly proportional to cigarette smoking.

Question: What is the relationship between lung cancer and cigarette smoking?

Answer: We are going to talk a little bit about that, but the first person to come up with the idea that there might be a relationship between cigarette smoking and lung cancer was a Dr. Asner in 1912. It wasn't until 1950 or 1960 that people started to really believe the connection was true and there were studies that were done in the 50's and 60's and the surgeon general warning came out in 1964. This was a very, very, very rare disease in 1920. One percent of all cancer deaths in this country were due to lung cancer. It has increased 33 fold. The bad part about this disease is the survival rate is unchanged since 1960. Now I say it is unchanged, it has gone from about 10% from about 14% in 1995 through 1999. There are changes that I am going to talk to you about that occurred in the 90's that are going to improve those numbers. Those numbers are being improved right now. People who are being treated now have a better prognosis than these historic numbers, but up until the late 90's survival rates were unchanged. Despite the advances in surgery, despite the advances in chemotherapy, despite the advances in radiation, didn't change the survival data at all. In terms of the survival data, only about, as I said, about 15% of people up until the 90's really survived, overall across the board.

Now there are two main types of lung cancer, one is called small cell lung cancer and of the 175,000 new cases each year, small cell lung cancer only accounts for about 35,000 and that is broken down into limited and extensive stage. Limited means it is confined to the chest, extensive means it is beyond the chest. So that is a relatively small number, about 20% of folks have small cell lung cancer. This number used to be larger. This number used to be close to 35%, but for some reason something in the environment or something in the biology of this disease has changed and now 80% of lung cancer patients have something

called non-small lung cancer and there is a couple different sub types of non-small lung cancer. There are 140,000 cases of non-small cell and 35,000 cases of small cell lung cancer diagnosed every single year in this country. It is a huge number. Now how does it compare to other common cancers. How does it compare to colorectal, breast and prostate cancer in terms of the frequency and in terms of the number of deaths. This slide really tells us a lot. Basically, if you include all breast cancers, even non-invasive breast cancers, the breast cancer is the most common, it is about 240,000 when you add the noninvasive cancers; it is about 240,000-250,000 breast cases per year in this country. There are 230,000 prostate cancer cases. There are 145,000 colorectal cases. There are 172-175,000 lung cases. Now over the years, if you look at the survival rates from the mid 1970's to the end of the 90's, we see the prostate cancer, the five year survival rates improved dramatically from 67% to 98%. There are lots of reasons behind that. Breast cancer survival improved from 75% overall to 88%. Colorectal cancer improved from 50% to 63%, and we wish these numbers were better, but they are pretty good; they are getting better all the time. Lung cancer was 13% in the 70's, it is 15% in the late 90's. If you add all the deaths from colorectal, breast and prostate cancer together, they don't match the number of deaths from lung cancer. It is a sobering set of numbers to look at. It is a major killer in this country.

Now let us talk a little bit about, or a lot if you want, about the risk factors. If you don't smoke, you have about a 1% chance of developing lung cancer in your lifetime. And why do you develop it? Well some of this might be predisposed genetically to developing lung cancer. Some of us might react differently to different environmental agents and 1% of nonsmokers will develop lung cancer. For someone who smokes, for example, say more than 10 pack years, that is a pack a day for 10 years, there risk increases. It does not increase to 30%, but it increases as you smoke more. If you smoke less than a pack a day, for 10 years, your risk might be 5 or 6%. If you smoke 2 packs a day for 30 years, your risk might be as high as 30%. So some people who are really heavy smokers, have almost a 1 in 3 chance of developing lung cancer. It really depends on how much you smoke and how long you smoke and it really also depends on how young you are when you start smoking. When they looked at second hand smoke, and I will talk about that again in a minute, people who are exposed to high levels of second hand smoke when they are children, have a greater risk than if they are exposed to second hand smoke when they are adults. But suffice it to say that your risk is 1% as a nonsmoker is somewhere between 1% and 30%, depending on how much you smoke over an extended period of time. 90% of the males and 80% of the females who have lung cancer smoke. So 20% of females and 10% of males who have lung cancer did not smoke and there are some other causes that we do not clearly understand. The majority of folks who have this disease smoked. And this the most preventable form of cancer in the world today.

Question: Does a person's risk of developing lung cancer decrease if he or she stops smoking?

Answer: What happens when you stop smoking, and this has been studied for the last 30 or 40 years, when a heavy smoker stops smoking, if you took 100 heavy smokers and they all stopped, at the same time, their risk of cancer would actually go up during the first year to 18 months; we don't know why that is; maybe it is the cells trying to repopulate and regenerate, maybe they have been revved up for all these years and they still have some disorder in their growth characteristics, but the risk increases a little bit when people stop smoking and then it goes down. Now it doesn't ever go back down to normal. If you have someone who smoked 30 years ago and they smoked a pack a day for 10 or 20 years and they've stopped and they didn't smoke for 30 years, their risk might be 5%, it might be 5 times the normal risk. It is not going to be 20 or 30 times, it might be 40 times the normal

risk, so it is going to be increased, but it is not going to be as bad as if you were still smoking. Also, I have to tell you for people who are smokers and can't quit, cutting down smoking, going from 20 cigarettes a day to 10 or to 8 cigarettes, decreases your risk over time. It is not as good as stopping, but it is clearly related to the amount of exposure and once you smoke a fair amount, you really don't go back to normal. The longer it is, the closer you get to normal, but you never get back to normal.

Now, second hand smoke, there have been a lot of issues about second hand smoke, a little debate about how significant it is, but we know that it probably does contribute to some cases in this country. The exact number of cases that are caused by second hand smoke are really unknown, but it is thought after a lot of research that maybe about 17% or maybe about 1 in 5 cases in nonsmokers is related to second hand smoke. That means about 17% of people who don't smoke; it is not related to second hand smoke. So there is a risk with second hand smoke; it is hard to quantitate. Generally the exposure that children get as infants and young children can be more detrimental than the exposure you get as an adult to second hand smoke.

Question: If you were exposed to smoke as a young child, and you are not exposed anymore for 30-40 years, do your lungs have an opportunity to cleanse themselves in a way that the rate will go down?

Answer: Yes, the rate really is down. If you never pick up the habit, no one really knows this, but you can imagine that the risk is going to be almost down to normal, but if you are a youngster and you are exposed to a lot of second hand smoke and you smoke, it just piles on any exposure that you had and then you really pile it on when you start smoking on your own. But second hand smoke is an issue.

Now radon is an issue, but no one really knows how many cases a year are caused by radon. Radon is an odorless, colorless gas that is produced when uranium degenerates. We happen to live on radon built. It begins somewhere in Kentucky or Tennessee and it comes up, it crosses the Appalachian trail, it comes up through Maryland, it comes up through Pennsylvania and up to New York and the highest recorded level of radon was recorded on Route 73 in Montgomery County. Ever recorded anywhere in the world was in the basement of a theological seminary on Route 73, it was in a house. But clearly, radon does increase the risk and that is why a lot of homes that are sold today have radon testing. The quality of the radon testing varies, but the fact is it can be fixed and your risks can be decreased. People who smoke and have a house that has a high radon level really have a higher risk at developing lung cancer.

Asbestos exposure, it was more of an issue 10-20 years ago when asbestos was not regulated. Now that asbestos is more regulated it is less of an issue, but again, people who have double the exposure who smoke and worked around asbestos had an extremely high risk of developing lung cancer. Patients or people who were exposed to asbestos also have a risk of developing a different type of cancer called Mesothelioma, which we see a fair amount of in Delaware County because of the previous work history and industry history here and basically, I have even seen patients who have developed mesothelioma in malignancy in their 30's and 40's because their dad works all around the stuff and brought the asbestos fibers home in his clothes. There is no other way to explain a couple of the cases that I have seen, except that their dad worked all around the stuff and there have been reports where wives can get mesothelioma with having no onsite industrial exposure. So asbestos was a real problem. You might think if you had a house or property that had asbestos in it and you thought that somebody was making a big deal about it, it is a big deal. It is a problem. It is less of a problem now though. There are also some other chemicals

and other metals that we have been exposed to in different industries that increase our risk of lung cancer, but everything pales even the radon in the second hand smoke. Everything pales in comparison to smoking. It is the issue.

I wanted to talk to you about some early symptoms or symptoms of lung cancer. There is nothing missing from this slide because there are no early symptoms of lung cancer. If anyone tells you that there are early symptoms of this disease, they don't understand the disease. There are no early symptoms. Unfortunately, there are symptoms of the disease though and this is not early disease. A cough that is changed in character or severity is an issue, it should be investigated. Seeing blood in your sputum; if you have a chronic cough in the morning and you have blood in your sputum, you have to get it checked out. If you have more shortness of breath than usual. If you have new localized wheezing; if you have asthma and you have diffuse wheezing, that is one thing, but localized wheezing can come when a tumor is blocking an air passageway. Some people present with lung cancer by having pneumonia that blocks an air passageway and there is an infection that occurs behind the blockage. Now these are relatively early symptoms, but they are late actually. These are all late symptoms. These are real late symptoms here. Weight loss, fatigue, bone pain, neurological symptoms, all of these are symptoms of advanced disease. So there are no early symptoms of this disease.

This looks a little busy, but I just want to go over some of the staging issues. There are all these different stages of lung cancer. These stages are potentially patients who are operable and these patients down here, these stages here are patients who can't be operated on, they cannot be cured of their disease. It spread beyond the chest. The majority of people in this country and I will show you some numbers from Delaware County are in this category, the vast majority. That is the problem. There are no early symptoms, so people who have Stage I and Stage 1A and Stage II disease, early stage disease here, they have absolutely no symptoms. The only people who are found to have early stage disease like this are people who might be getting a chest x-ray for some other reason, because there are no symptoms usually, unless you are really lucky; a strategic area that causes some symptoms like a cough. Again, just to show you the number of people who survive this disease. If someone is found to have Stage IA lesion, they have a 60% chance of being cured. They are fortunate; they have a 60% chance of being cured. They have a 40% chance of dying from this earliest stage of disease. If they have Stage II disease, it drops down pretty quickly from the 60's. The difference between 1A and 1B is the tumor is 3 cm. that is about an inch and a quarter vs. bigger than an inch and a quarter. It gets a little bit bigger, bigger than an inch and a quarter, guess what, big drop, a 24 point drop. If you have positive lymph nodes or if you have a really big tumor, even though it is Stage II disease, guess what, the odds are 65-75% that you are not going to survive. And patients who have more advanced disease, the numbers are progressively less in terms of 5 year survival rates.

Now let's take a look at some tumor registry data. The tumor registries are actually very important sources of information and we were able to pull the registry data from Crozer, Taylor, Springfield, Delaware County, Riddle and Mercy Fitzgerald and there were about almost 400 cases registered in these hospitals in 2003. The number of cases that were county wide has been pretty consistently about 500 cases a year in Delaware County. Those numbers have been pretty consistent for the past 5-6 years. They go up a little bit and down a little bit each year, but it is a ballpark number, it's about 500 new cases a year in this county, and about 400 of them were cared for by physician's were programs in these hospitals. Now here is the staging breakdown, this is accurate data from those almost 400 patients in 2003. About 13% had Stage IA or 1B disease. They were a fortunate group. About 6% had Stage II disease; 33% had Stage 3A and B disease, which usually is felt to

be inoperable; and 48%, almost half, clearly had inoperable disease from the day of diagnosis. So the majority of these patients here did not survive or will not survive their disease. Some of them may still be with us because we are treating them and we have better treatments now; a lot of them still may be with us, but that is 82% of all patients who were diagnosed in Delaware County in 2003 had inoperable disease essentially. 82%...and the reason is there are no early symptoms.

How are we doing as a county? Well, look at the 67 counties in Pennsylvania. Philadelphia has the highest death rate of lung cancer. Allegheny County, out by Pittsburgh, has the next highest; well we are right behind them and Bucks, Chester and Montgomery County have a little bit better death rates, but the point is, is that we look as a health symptom at some of the problems in our communities and we have to try to figure out ways to address them better and we have a problem in Delaware County, there is no question about it. Now some of this has to do with patient's presenting very late, not having access to healthcare, especially in Philadelphia and there are some economically depressed areas around in Allegheny County, but it is major care issue, its an access to care issue and its an issue regarding the nature history of this disease, the biology of this disease. So about 35 years ago, the medical oncology, the cancer community embraced the concept that cancer was a systemic disease; meaning that in patient's who ere diagnosed with breast cancer, all different stages of breast cancer, they had some risk of getting some cancer back. That was embraced 35 years ago. This was embraced regarding lung cancer. This is non-small cell lung cancer, this was embraced 5 years ago, acknowledged that it is a systemic disease from the outset. Well, it clearly is a systemic disease meaning that the majority of folks have disease elsewhere. If they have a nodule her and a lymph node here, guess what, they have had cancer cell in their bone marrow. The have cancer cells elsewhere. Now a lot of them aren't going to be equipped to grow and become a problem eventually, but some of them are and that is why this disease is so fatal. 40% of the patients with Stage I disease, the best one, die from lung cancer; that is a fact. 60% are cured, though. Tumor cells are found in the blood and bone marrow of all clinical stages, even the Stage I and size of primary lesions. Now it doesn't mean all patients, but 20% or 30% or 40% of patients in Stage I are going to have the disease found in their bone marrow. 100% of Stage IV are going to have it in their bone marrow or in their blood. Now the reason this is so deadly is about 1 cm. lesion, which is about that big may shed its thought between 3 and 6 million cells into the circulation every 24 hours. Now again, 99.99% of those cells aren't equipped to grow and present a problem in the areas where they land, but a small fraction of them are equipped and will grow. That is why this disease is fatal. It's systemic, it is spread beyond the site of origination from the outset and it metastasizes, this means the cancer cells are spreading, might occur in some cases when the tumor is 1-2 mm. in size. If it is destined to have the ability to spread, it spreads at an early time. Again, you would never have any symptoms from a 1 cm. lesion led along from a 1-2 mm. lesion. The majority of cases as you can imagine are diagnosed late in the natural history of the disease and they really do demonstrate the potential to remain localized or spread from the time of diagnosis. Now that sounds pretty dismal and it has been pretty dismal, but there is a change in the therapeutic and the diagnostic landscape that we are going to see in our lifetime. I'm going to talk about some things that are pretty early on in the development but we are moving in these directions. And not to give false hope, but to give you hope that things have already changed to a degree and are going to change a little bit more, for example, we now know from studies that if we take patients with Stage 1B disease, that tumor is greater than 3 cm. in size, greater than an inch and a quarter in size and just do surgery along, as many as 57% will survive 5 years. If you add Chemotherapy, we get a little bit of an increase, maybe a 3, 4, 5, 6% increase at this early stage. Now this group has not been studied that much. But there is now data, there is similar data now that there was for breast cancer in the 80's when everyone who had breast cancer and had an invasive lesion was getting

chemotherapy. There is data from Japan that suggests this number can go from the mid 60's to maybe the mid 70's with the chemotherapy agent. That chemotherapy agent is not available in this country. The studies have to be confirmed. We move along a little slowly, but there is data and it was published about a year and a half ago in the New England Journal that chemotherapy for Stage 1A disease is potentially going to be helpful in increasing the number of patients who are cured. A 5 year survivor essentially means cured in this disease. So there is some early data for Stage 1 disease, from Japan. There is some data that is real modest for Stage 1B disease in this country. The studies were done in this country, Europe and Canada. Now for Stage II disease, there is definite improvement with chemotherapy and this historically is given after the surgery. So if someone comes in, they have a nodule, they are fortunate enough to have it localized, they are in that small group, that 18 or 19% group in this county who has Stage I or Stage II disease, they have surgery, they survive the surgery, they get chemotherapy afterwards, we get about a 12-13% bump in Stage IIA disease. So if we give 4 cycles of chemotherapy, which is well tolerated, we can move this number considerably. Now you may look at it and say, gee it's not great, but we have been given chemotherapy to patients with breast cancer for the past 30 years for a 4% improvement in overall survival. This is not a small advance. This became obvious. This improvement with chemotherapy for lung cancer was suggested in the mid 90's in 1995 when they did an overall study of a whole bunch of studies they put together in something called a meta-analysis and it was suggested in 1995. It wasn't really confirmed until 2004. It took 9 years to confirm that initial impression. Also with Stage IIB disease, the same bump, about 12-13% improvement. Now this improvement which has become the standard of care only in the past two years is going to change those dismal survival statistics. From this point on it is going to be better. Now for Stage IIIA disease, we get a pretty good bump, again the majority of patients, only 41% are cured with the addition of chemotherapy, but that is a lot better than 25% and in IIIB disease, there is no data yet, but there may be some patients who are helped with IIIB disease. Again, it is just more advanced locally disease in the chest. There are some patients who are going to be cured. That 5% number is going to get better. I don't know if it is going to go 8 or 15%, but it is going to get better and we won't have that data for another 10 years. So for those patients who are potentially operable, which is the IIIA's, the IIIB's aren't really operable. A lot of times we go in thinking we have IIIA disease and we find IIIB disease. But for these people who have IIIB, IIIA, II and even some Stage I's, we can improve their chances of survival in a significant way 10, 12, 13% is significant in this business in a significant way by giving them 4 cycles of chemotherapy which they tolerate well and I will talk to you about chemotherapy later if you want just to give you an update on what has happened in the last 10 years, because everyone cringes when you hear the word chemotherapy.

Now what do we do for those folks that have advanced disease from the outset, Stage IV. Well, we have been giving chemotherapy, meaningful chemotherapy for the past 15 years. Until 1990, the chemotherapy regave. It worked for 4-6 months and made people feel a little bit better from their symptoms, but they got worn out by it. The side effects were too great. People did not do well and you had to be relatively young and healthy to take chemotherapy 15 years ago. The drugs have gotten better. They were better tolerated. We give them in a way that don't make people sick. There is some fatigue that people have with chemotherapy. It's not like taking Tylenol, there are some side effects, but the degree of side effects that we now have are controllable and they are much less than we used to have. First there was chemotherapy, starting in the mid 90's we were involved in some studies with Fox Chase and we used a regimen in the early 90's which is very well tolerated. Then about two years ago, chemotherapy combined with a drug called Avastin which prevents the development of new blood vessels was shown to be at a significant advantage to chemotherapy alone. These developments are all relatively new. So chemotherapy plus Avastin increases the response rates by about 10% which is substantial. It also improves

survival in patients. There is a measurable improvement in survival that have advanced disease with Avastin and chemotherapy. There is also a pill called Tarceva. This made a big splash in the papers starting about 5 years ago when its first close cousin Erysa was available, Tarceva is a better drug, but Tarceva is given now by itself. We have patients who we take care of who usually are women who are nonsmokers, who have lung cancer, or certain subtype of lung cancer, who respond to this pill. I have patients who have been stable to improving the past two years taking this one pill a day. They get a little rash, we adjust the dose, and the rash is controlled. But they are living with their cancer for 10 years without a drop of chemotherapy. Unfortunately, it is a small number of patients that qualify for this, but it is a start. Also, there was just a report in June when you combine this pill, which is not a standard chemotherapy drug, with this Avastin, which is again an anti-blood vessel forming drug, it prevents blood vessel formation. When you give that in combination to patients who have failed chemotherapy a certain number respond but overall 80% of patients benefit. They have stable disease and they do well for a period of time. They are not cured, but they live with it a lot better and they don't take chemotherapy. So I have some patients who I started on Tarceva two years ago and they are still doing ok and when they stop doing ok, guess what I'm going to do? I'm going to give them Avastin. And will probably get a bump in their response again with out having them have a drop of chemotherapy. So in a select group of patients, you can really utilize some of these newer tools. We have also been using some local forms of therapy. There is something called radiofrequency ablation which it essentially microwaves a tumor. I have had patient's who have had recurrent disease confined to the liver and what we do sometimes is give them two or three months of chemotherapy and if the tumor is small enough, if it's under three centimeters, an inch and a quarter, or three and a half centimeters, and that is always changing because they are making new probes, but if it is under a certain size, we can show the disease is responding to chemotherapy and we can zap it with radiofrequency ablation and guess what, they get a chemotherapy holiday, and we monitor them. Some patients go on for years because their disease was arrested at that point. Also, there is something called stereo tactic radiation. All the radiation therapy departments have now been trained on something called a cyber-knife. It doesn't belong to any health system, it's a free standing facility, but basically the radiation oncologist from Crozer and Delaware County, Bryn Mawr, have all been trained to use this. Now this is a specific tool that really concentrates radiation to a very well defined area. So if we have patients who have lung cancer and they can't be operated on because they are older or have some other medical problems, their tumor can be treated with a cyber-knife. We might give them some Tarceva afterwards. We might try something like that. So these advances from here on south, chemotherapy really became doable or more widely applicable to our patient population in the early to mid 90's, but all of these advances here, from here on down, really came in the last 3-4 years. So between the chemotherapy for patients who have surgically treatable disease which is only about 25% of patients; 75% aren't going to have surgically treatable disease, but for those folks who have surgically treatable disease, we are going to improve their survival with chemotherapy. We improve the quality way of life of patients with advanced disease with these forms of treatment. It is well documented in some big national studies that we participated in. We improved the quality of life and we either prevent or delay the complications of their cancer.

So the landscape is changing. Now when you have different tools, different drugs and different techniques, and different strategies that you can now use, you start as an oncologist, as a cancer doctor, you start to build a more meaningful program around this disease and basically that is what's happening in a lot of different centers. And basically we can now stage our patients better, not just with CAT scans and MRI's, but with PET scans. I will show you another slide where we are giving chemotherapy initially to patients or we can get prognostic information from comparing the first PET scan to the next PET scan even

before their surgery. We know which direction the disease is going. So there is better staging techniques. There is better evaluation with something called endoscopic ultrasound. We can take biopsies of lymph nodes in the center part of the chest less invasively. Every case within our practice is discussed with nine other medical oncologists each week to see if we have a protocol or a study that is applicable to our patient's with lung cancer. There is a group of physician's that get together and the pathologists never get any credit. They are the most important people almost in this whole business because we rely on their expertise to make a correct diagnosis. So there is a group of us that get together every week to discuss lung cases. There is going to be screening programs that are going to develop. If you want to, I will go through a few things that are currently happening and I will show you some direction we are going with that too. And there are treatment programs for patients who have had potentially operable disease that were developing within our campuses. Now one of the treatment programs that we are developing is that if we have someone that has lung cancer and whether it is Stage IB disease or II disease or IIIA disease, those potentially operable cases. We are now giving patients chemotherapy before they get their surgery. Now what is the reason for that? Well the reason for that is you immediately start treating the disease systemically. Chemotherapy is better tolerated when it is given preoperatively. Sometimes our patients are older, they have medical problems, and they don't get back to us for chemotherapy sometimes for 2 or 3 months after their surgery. So it is better tolerated and you treat patients systemically. You can access the tumor response. Why is that important? Well it is important because we don't just have 2 drugs anymore to choose from in terms of chemotherapy. We have about 8 drugs to choose from. We have 8 drugs, 8 different drugs; 15 years ago we had 2. So if someone doesn't have a good response to the preoperative treatment, they still go to surgery and we know how to refine our treatment postoperatively to give them a little bit better chance. And also, as I mentioned, we get a PET scan before treatment begins, we give 9 weeks of therapy, we get a PET scan before surgery and that gives us prognostic information. We know that if the PET scan reverts, the better the PET scan gets, the better the prognosis for the patient, the better the outlook. And we can tailor our treatments accordingly afterwards. We don't know how to do that yet, but we are going to put studies in place that will help us figure that out. Just to let you know what a PET scan is, CAT scans and MRI's give us anatomic information. They tell us how big an area is, if it's this big or this big we can tell easily with a CAT scan or MRI, anatomic information, a measurable disease. A PET scan gives us physiologic or metabolic information and it just so happens that cancer cells are very active metabolically. They consume a lot of sugar, a lot of glucose. So what a PET scan is basically you are injected with a small amount, labeled glucose and you wait ½ hour and you go into a machine which is actually a combination of a CAT scan and a PET scan so we can get precise overlay, we can tell if a nodule on the lung is something to be concerned about by using a PET scan. We can tell whether it has a high chance of being cancer or a very low chance of being cancer. We have patients who come to us with disease in different sites. I just saw someone last week who had three pulmonary nodules, three nodules in their lungs and it looked like a primary tumor in their liver. Well, these pulmonary nodules did not light up on PET and we found out later they were from pulmonary emboli, blood clots. So the PET scan is very, very helpful. It has drastically changed the way that we manage our patients. We have had access to it through the health system for the past five years. And we have had a CT PET machine for the past year, almost year and a half. So we have been supplied with great technology.

We can stop here or we can talk about...this is just kind of interesting...Everyone agrees that people should be screened for breast, cervical, colon cancer and prostate cancer, but you know it is really debatable. The value of screening for cancer is really highly debated in the medical community. There is something called randomized population trials and there have been a total of 18. These are big studies where half the patients get screened and half the

patients don't get screened. Then they try to measure that the survivorship disease free survival in the group that is screened and not screened. And only three of the 18 with breast, colon and lung were positive results. Not every breast study was positive, not every prostate study was positive. Two out of 10 with breast cancer were positive. We have a whole industry of screening with mammography based on 2 out of 10 studies that were positive were criticized in Europe for the way that we screen for breast cancer. We think it is really a value. I showed you the improvement in the numbers of survivorship for breast cancer. We believe it works, but these studies are exceedingly hard to do. They are hard to interpret. There have only been 1 out of 4 colorectal studies in this country that have proven to be a benefit and there was 0 out of 4 lung cancer screening studies. And two of these studies were completely misinterpreted. They occurred in the late 70's and reported in 1980.

Question: Did these lung cancer studies prove a direct link between having chest x-rays and rate of early detection of the disease?

Answer: No but these were all based on chest x-rays and the studies were poorly constructed. They have been criticized, they have been dissected, they have been hung out to dry and the interpretation was wrong. One of the biggest, 100 years from now, it's going to be looked back and it will be fought, I think. This is my opinion that one of the biggest health mistakes that were made in the late 1900's was the doctrine that was spread screening for lung cancer is not a benefit. The screening is a really hot issue. The agencies that regulate and make recommendations have changed a lot since 1996 to 2004. This kind of sums it up. Every medical student that was taught from 1980 until 2004 that lung cancer screening was a no-no. Every insurance company denied any attempt at lung cancer screening. You can never write as a doctor, screening for lung cancer, they would not pay for the study whether it is a chest x-ray or a CAT scan. I'll just read this real quick, now the American Cancer Society says based on information that, this is a long story, I'm giving you the short version; but physicians along with high risk asymptomatic persons, that is people who smoke who don't have symptoms should determine if a chest x-ray is indicated. Decision to screen should be made on an individual basis weighing the potential benefits and harms. This is similar to the recommendations for screening for prostate cancer, PSA. So now it is opening the door for screening potentially for lung cancer. I said that the studies years ago said the chest x-rays were useless, well the NCI knows that those studies were fraud, so they started a study, it's completed. They put 150,000 subjects who had a bunch of screening tests done and half of them received chest x-rays on a regular basis and half of them didn't. These results are going to out in 2009, so they went back 35 years to look at chest x-rays. So the jury is still out. There has been new data using low dose CT scans. We know that using low dose CT you can detect more lung cancers than a chest x-ray. They are smaller. Survival is better. Most cancers are diagnosed early and when you put someone in a screening program, they stop smoking at a higher rate. And it also picks up some other cancers and diseases. So there is CAT scan strategies. There are screening studies that are going emerge. There is already data in the cooker on a national level and we are going to use that data to act locally as well.

I didn't talk about small cell lung cancer. We are making advances in small cell lung cancer, but unfortunately the vast majority of folks who have a disease, that even has a tendency to spread quicker than non-small cell lung cancers. So the vast majority of folks are not in a curative situation at the time of diagnosis and we generally don't operate on those patients. Now we do operate on some selected patients with small cell lung cancer. I've had patients operated on who I saw who had peripheral lesions and you have a higher cure rate if you give them chemotherapy and operate on them, but the majority of folks with small cell lung cancer have advanced disease at the outset. There are newer studies that

we are participating in utilizing chemotherapy plus Avastin for those patients and we are hopeful that we can do a little bit better. These improvements are incremental improvements. It seems like its slow, but it actually is happening. Our job has gotten a lot easier and a lot less happy. We are not completely happy yet by any stretch of imagination, but we've been more effective in the last 5-7 years in this disease than we have in the last 15.

Question: Why doesn't everyone just have a PET scan done? Is it because of the expense?

Answer: its a couple things. First of all, PET scans aren't full proof. And just like CAT scans aren't. And generally it probably makes much more sense from a cost stand point. The actual cost from a low dose CT scan, including the radiologist fee is about \$150.00. That's it; for a lose dose CT. The cost for a PET is about \$1,500.00, the actual cost. Now that's not the charges; the charges in different health systems is \$6,000.00 and the insurance company you have to pay is God knows what. But the actual cost for the glucose, the machine time and everything else is about \$1500. So the algorithm that I showed you looked kind of crazy. We know that if someone has a low dose CT, we know that in this part of the county about 25% of people will have an abnormality. We also know that if you give them a course of antibiotics and you wait a month, half of them are going to go away. The CT scans have gotten more precise. We now know, when you have a cold and you get a CAT scan, they may see something. It might be 4 or 5 mm., there might be 2 or 3 of them, there might be 6 of them and you take a course of antibiotics, guess what? Whether you take the antibiotics or not, those abnormalities are going to go away. So we know that we can cut down the number of patients with an abnormal low dose CT down to about 12% after a course of antibiotics. Then the question becomes, well what do you do with these folks? Do you worry them unnecessarily, how do you work them up? Well it turns out that there is data now, mostly from Europe, there is an Italian study and a Spanish study that utilized PET scanning in conjunction with low dose CT. You can direct the work up much more effectively if you put PET in the algorithm. Using the information from the Italian and the Spanish data, we think we know how to put that in the steps, the algorithm that we have laid out. So you don't want to worry somebody unnecessarily, you don't want people to get unnecessary biopsies. Biopsies aren't benign. People can have a pneumothorax, a lung can collapse with a biopsy. They can have a complication if we try to biopsy a lymph node that looks suspicious, that might not really be suspicious. So using the combination of a low dose CT and the PET is, I think, going to be a major break through and we have pulmonary discussions with the administration in the health system and I think we are going to see that available within the next year. I'm very supportive in the administration,

Question: What types of lung cancer treatment does health insurance cover?

Answer: I would tell you not to worry about it, I'll tell you what the charges are and the insurance companies pay for that type of treatment. This is not something that you have to be wealthy to have this treatment. That is the stereotatic radiation of the cyberknife and that's what they were talking about. The charge that the radiation departments submit to the insurance company is about \$25,000. It's not cheap, but I have to tell you for the right patient, guess what, it's worth it. And that same treatment is available at Temple, its available locally in Delaware County up on West Chester Pike and the radiation oncologist from the different health systems have been trained to use that machine. I think the different health systems will eventually, once they understand it better will get one, but it costs a lot of money. It cost about four million dollars for the machine.

Question: Is there any value to having a chest x-ray to screen for lung cancer?

Answer: The American Cancer Society says that you should have a conversation with your primary care doctor and after you both understand the risks...quite frankly, I think that I think a chest x-ray does have value. People have built careers evaluating those four studies that were done in the late 70's and critiquing them and understanding them better. People have built whole academic careers around them. A chest x-ray does have some value and if I smoked, I would get at least an annual chest x-ray, I would really get an annual CAT scan because CAT scans do have data. There is data all around the world that CAT scans are better picking up smaller tumors than chest x-ray. So a CAT scan or a chest x-ray...and everyone of my patients I follow that had lung cancer, they all get PET scans every year. The people with the highest risk of lung cancer are patients who have had a history of lung cancer. They have a 3% chance per year that is cumulative for over a 10 year period to a 30% chance of getting another lung cancer. And guess what's happened, we have patients who were diagnosed in 1994, we started using chemotherapy for early staged disease 9 years before the rest of the world caught up because there are exposure to these programs at Fox Chase; a lot of them have lived and they have developed their second lung cancers and we've cured them of their second lung cancer. They have lived to develop laryngeal cancers; we've cured them of those and by following them with some imaging studies on an annual basis, we've picked them up earlier. So I think that it's going to become standard practice. It's not going to become standard practice over night, but it's going to become standard practice over a 10-12 year period. Maybe 15 years. That's how long it takes to work these things out. But the question is what do I do now? You have at least 400 of the 500 people that we have data on in this county, 82% of them had advanced disease. What do you do? How do you address this major health problem in this county? That is the challenge. We don't know the exact answer, but we know we can take some steps in that direction.

Question: Which drugs are most effective in treating lung cancer?

Answer: There are about 50 different drugs that we use. But drugs that have proven good activity in lung cancer, there is about 8 of them and from 1980 through 1991 we had 2 and they were toxic as could be. We could help people for a couple of months, but then after the third or fourth month of treatment, they got sicker from the chemotherapy. But now we have a much better drug.

Question: Do people have genetic predisposition to getting lung cancer?

Answer: Well we don't really know that. We do know that in some cases, there may be some predisposition. That is a whole other area that is going to become clearer in your lifetime. Over the next 20 years we are going to get a lot smarter and we are going to find out that every one of us in this room might have a genetic predisposition to half a dozen different cancers, and only 25% of us are going to get cancer. How strong is that predisposition that has to be quantitated? How strong is it if you have other environmental factors? If you work in a factory that has exposure to god knows what and you have a moderate predisposition to lung cancer. Guess what, your risk might be higher. We are going to get smarter about that, but we do know that we have treated patients and their families where they have had siblings that had lung cancer. We have had young people in their 40's come to us with lung cancer whose father or mother might have had lung cancer when they were 50. When you see a young case, almost all the time, they had a parent, not all the time, but it seems like a lot, they had a parent who had it a relatively young age.

Question: If a person had smoked very little and then had quit 30 years ago, would they still have a risk of contracting lung cancer?

Answer: Well one of the, for this screening program...the answer is we don't know. We don't know the right thing to do. By smoking that little and stopping 30 years ago, he really substantially reduced his risk in a major way. But the American Cancer Society specifically said something about chest x-rays, but there is a United States prevention task force that leaves the door open to CAT scans too and it is really a discussion, the patient has to take the initiative because all of the docs now were raised and trained in a period of time where if they have thought about screening for lung cancer, they got their wrists slapped. The test was denied. The test was not paid for. So these attitudes are not easy to change and every physician in this country should have changed their attitude when the NCI set up one of those studies and it wasn't low dose CT vs. nothing, it was low dose CT vs. chest x-ray and they know that in the way that the study is constructed, chest x-rays probably have some value.

Question: Do cancer patients at DCMH benefit from your partnership with Fox Chase?

Answer: Yes, Dr. \_\_\_\_\_ is here primarily. What happened was when the Fox Chase affiliation went system wide, all of the hospitals now have these protocol developing, but basically we had a lot of patients from this primary zip code area and the patients in this community are commendably loyal to this hospital and they are very loyal to this hospital and we offer these patients who are from this zip code areas the option of coming here, closer to home, or staying at Drexel Hill, so now we are here five days a week. But this is a rapidly changing field and thank God it is changing for the better in these last half a dozen years.

Question: What are the primary early symptoms of lung cancer?

Answer: Well, certainly you could have a cough or if you feel short of breath and if you are a smoker, you can ask for a chest x-ray or a CAT scan because you want to be screened and ideally, the American Cancer Society thinks there should be dialog about the potential benefits and risks of screening and what to do with the information. For nonsmokers, they have about a 1% chance of developing lung cancer in their whole lifetime. Generally for a nonsmoker, with no family history, this study that we are going to start is going to leave the door open for people who have a family history of lung cancer who are nonsmokers. So they may have a genetic predisposition, so we are going to open the door for screening for them. But if you are a nonsmoker, if you don't have any symptoms, you probably don't really need a chest x-ray or a CAT scan.

Question: Are you planning on conducting lung cancer studies?

Answer: What we are doing now is we are kind of doing the ground work to do this as a formal study. We have gotten the health system to agree to donate the low dose CT. We have gotten the radiologist to agree to read them for free in the initial studies and now we are trying to raise some money for data management. It is a big deal to have a screening program. You can't just screen people and not counsel them adequately. It takes time. It's best to couple a screening program with a smoking sensation program. It's very effective in the studies that have been done before, combining them, you get much more compliance in terms of the discontinuation of smoking. But initially what we might do is open up the studying on a pilot basis for hospital and health system employees. Get some of the kinks out of it and open it up to the public.

Question: How long does a person with lung cancer need to be in remission to be considered cured?

Answer: Generally if people are destined to have it come back, lung cancer comes back pretty quick if it is going to come back, so if you are a year or two years, even a year and a half since the diagnosis and you haven't had a recurrence, that's pretty good. The majority of people, probably 85-90% of people who are destined to get it back after a successful surgery, most of them are going to get it back in the first 18 months, 18-24 months. Now there are another 10-15% that get it back later, 3 and 4 years later, but the majority get it back very quickly because it is a systemic disease at the outset. It is either there and it is going to grow within a year and a half or two years or it is not there and you are cured. So to answer your question, his chances of survival to be cured improve with each passing month.