

Scott Redding: Welcome to the 3Ps of Cancer Podcast, where we'll discuss prevention, preparedness and progress in cancer treatments and research, brought to you by the University of Michigan Rogel Cancer Center. I'm Scott Redding. We're here with University of Michigan professor of Pulmonary and Critical Care Medicine, Doug Arenberg, to talk about lung cancer screening and prevention. Dr. Arenberg leads the Rogel Cancer Center's Lung Cancer Screening Program, and is part of the multidisciplinary lung cancer team. He has been with Michigan Medicine since 1990. Welcome, Doug.

Doug Arenberg: Thanks for having me.

Scott Redding: I'd like to start off with, how is lung cancer screening performed? What is the way it's screened?

Doug Arenberg: Yeah, the way we screen for lung cancer is by looking for hopefully small nodules in the lungs with a test called a low dose CT scan. Most people are familiar with CT scans, or sometimes referred to as CAT scans. They use radiation. In this case, it is a computerized reconstruction of the anatomy of the lung. After scanning people in a scanner, it's open. It's not like an MRI where you're closed in. The scan itself probably takes 30 seconds. Hold your breath, get zipped through the scanner and with the modern technology that we have and the computer power behind current imaging, we get really stunningly detailed images of the lungs, and what we're looking for is evidence of tiny pulmonary nodules.

Now the downside of this is that, and this is something that'll probably come up again throughout our conversation, is that lung nodules are extraordinarily common and most of them are not cancer. So, the real work comes after you've found an abnormality, determining what to do about it. I will sometimes use the analogy lung freckles, because everybody can relate to a freckle. I'm a pale guy with a lot of freckles and my wife is a dermatologist. Most people can recognize that some freckles or moles and some holes can be skin cancer, but most aren't. So a lot of times when I meet with a patient who's been told they have a lung nodule, most of whom have gone to the internet and googled lung nodule and read all sorts of horrifying things, I use the term lung freckle because it's a little bit of a disarming term.

As I said, we can all relate to what a freckle is for the most part, and we know most of them are harmless. But enough of them are enough concern that we'll get advice, example from our dermatologist to say, "Keep an eye on that one and if it changes come and see me," and it's very similar to what we do when we find the lung nodule. Most of it is we say to the patient, "Let's keep an eye on that and make sure that it behaves in a benign way." We're looking for ones that have the potential to be cancer and most of that just involves additional imaging, perhaps in the form of surveillance. But the short answer to your question is, lung cancer screening is done with CAT scans and the key is doing it in the right population of patients.



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Scott Redding:

When you get to that point where you're going to monitor a lung nodule, when is it determined for a patient to actually get screened to have those nodules detected? You hear most people that get lung cancer, it's usually later at an advanced stage.

Doug Arenberg:

Sure. Getting back I guess to a better answer to your original question, what we're really looking for with screening is to find lung cancer when our best treatments are most effective. Most cancer up until 10 years ago, the vast majority of cancer was diagnosed when it was stage three or four when treatments are far less likely to result in a cure. If we find lung cancer in the past, we were most enthusiastic about it when we found it by accident. We had a CAT scan or an X-ray for some other reason, and then were found to have a small nodule that prompted further investigation. In those cases, we found that treatment usually in the form of surgery or something, some folks who can't or don't want to have surgery, radiation therapy is very effective for early stage lung cancer.

So what we're really trying to do with screening is take a population of people that we think are at high risk and look for cancers before they advance to stage three or four, catch them at stage one if we can when treatment is both a little simpler, and a little more likely to result in a long term cure. If we do find a nodule in the lungs when we're screening somebody ... As I said, most of them are benign. Our job is to sort out the ones that have the potential to be cancer from the ones that don't. And ultimately some of these nodules, most of them won't but some might require, for example, a biopsy if we're not sure. That's where we start getting into some of the downsides of screening, which is that if we're not careful, some of these nodules that we find in the lung that are benign, if we start doing a lot of biopsies in people that don't have lung cancer, we're liable to do more harm than good.

Now, we're pretty good at avoiding that. We've had many, many years, decades if you will of experience in pulmonary medicine, and in thoracic surgery, and in radiology. Experience in knowing when to do a biopsy and when not to. But what we're really looking for when we do screening is we're taking a population of folks that we think are at high risk of dying from lung cancer, and doing a test that reduces their chances of dying from that disease. That's the purpose of any cancer screening program. It's not sufficient to just talk about early diagnosis or catching it early, which is a catchphrase I think most people can relate to. But by itself, catching it early is not sufficient reason for introducing a public health screening program. The real purpose is to recognize that we think for example, dying of lung cancer, or breast cancer, or colon cancer, these are particularly bad ways to have to die.

Life is 100% fatal and we really want quality of life to be the major focus. So when we have a test that reduces your chances of dying from lung cancer, or breast cancer, or colon cancer for instance, that's the purpose of screening. By itself early detection is necessary, but not sufficient to achieve that goal. You want to be able to detect it at a time when treatment is likely to essentially yield



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a complete cure. So when we're screening for lung cancer, we're looking for people who are otherwise potentially going to die from lung cancer, and catching it before it's able to spread basically.

Scott Redding: You talked about the screening and the CT scans. Is there guidelines of when a patient should be considered for a CT scan screening?

Doug Arenberg: Absolutely. The guidelines that exist now are actually in the process of being reevaluated, but let's talk about the existing guidelines before we talk about the proposed changes. We currently in the US recommend lung cancer screening for people between certain ages, so above the age of 55, up through about the age of 80. In that age range, we want to screen people who meet a couple of very important criteria. One is, they're cigarette smokers who have either quit within the last 15 years, or who have continued to smoke throughout adulthood. We use these criteria because we think they identify the people who are most likely to benefit from screening. So, we want people who are current or recent smokers.

And, we want people who smoked what we call a pack-year, 30 pack-years or more. An example of what that means is if you smoked a pack of cigarettes per day for 30 years, that would be 30 pack-years. If you smoked two packs of cigarettes a day for 20 years, that would be 40 pack-years. You take the number of packs per day and multiply it by the number of years you've been smoking, and there is your pack-year criteria. The criteria for current recommendations for screening are between the ages of 55 and 80, and 30 pack-years or more of smoking history. And if you have quit, then you quit within the last 15 years. The rationale behind that, it's intended to identify people who are at very, very high risk for getting lung cancer.

Now even within that population, most people will not get lung cancer. It is a misconception that if you smoke, you're destined to get lung cancer. The problem with smoking is that it causes all kinds of other diseases like emphysema, heart disease, stroke, all of which can compete if you will, with lung cancer for mortality. Essentially when we screen for cancer, whether it's lung, or colon, or breast or cervical, we're rooting for our patient to die from something else. That's a weird way to put it, but until you stated this and understand it that way, it's hard to I think, institute a screening program and do it correctly.

Let me give you an example. One thing that we shouldn't be doing, for example, is focusing just on those screening criteria and then ignoring the fact that a lot of people who meet those criteria may have other very serious illnesses. For example, a patient with severe congestive heart failure and kidney failure from years of diabetes and cigarette smoking, and what other lifestyle choices that have been impacting their health. Such an individual is likely to die from something else, even if they have lung cancer. And if they do have lung cancer, our ability to treat and diagnose it is significantly reduced. So, we're not looking for people who just meet these criteria. The fine print if you will, by the United



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States Preventive Services Task Force, and it's an area I think a lot of people overlook, is that you really need to be otherwise pretty healthy to benefit from any cancer screening, but it's particularly true of lung cancer screening. So, we're looking for people who are otherwise healthy that meet these age and pack-year criteria.

Scott Redding: Being that you need to meet some of that criteria, the pack-years and so forth, is it more likely that smokers are going to be diagnosed earlier than maybe nonsmokers who end up with lung cancer just because they maybe have some of these other issues that they're dealing with as well?

Doug Arenberg: Yeah. This is a very different question, which ... We get very uncomfortable interactions with our friends who are in the advocacy field. Advocates for lung cancer, because many of them became advocates because they got lung cancer in spite of never having been tobacco users. The problem with tobacco users is not that they are to be blamed for their habit. Addiction is not a choice, and we as a profession and as a society need to stop doing the work of the tobacco industry, which is to say that tobacco is some kind of choice. It's not. Most adults who smoke started as teenagers. Teenagers do not generally make rational long term decisions about their behaviors. Whether it's speeding, texting and driving, jumping off cliffs, or smoking, they're making risky decisions. It's part of the way the teenage brain works, and I'm going to get off on a tangent here.

But when we talk about smokers and nonsmokers, unfortunately there's almost a wedge between them when it comes to being advocates for better public policy and better research funding of lung cancer. That's sad, because there aren't enough survivors to advocate for themselves like there are for instance, for breast cancer. The vast majority of women diagnosed with breast cancer are going to die from something else. They have a lifetime of advocacy in front of them and it shows in the way the public funds and the supports with tax dollars, scientific research. With that in mind, one of the major challenges with this problem, which is lung cancer among never smokers is the third or fourth leading cause of cancer related death in the Western world. So it's not a trivial issue, and it's a bigger issue in Asian countries where there is almost an epidemic of lung cancer amongst nonsmokers and that's particularly true of women.

Now, whether this is due to air pollution or other genetic factors is beyond, I think, the scope of this discussion but it's true. I think the issue with people who don't smoke is that we as physicians may tend to think of the possibility of lung cancer less readily than if somebody walked in having been a lifelong smoker with a new cough. So when we see somebody with symptoms of respiratory illness, we may be less likely to order a chest X-ray or a CAT scan on a nonsmoker, and that's just simple common sense. We have to use common sense when we approach any problem in medicine, but it's these incidentally discovered things that have to be taken seriously, whether you're a smoker or not. If we're doing our job correctly, take these symptoms seriously enough.



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If you start talking about symptoms, you're really getting away from screening. Screening is by definition, something that we do in people that have no symptoms of the disease you're looking for. In particular in lung cancer screening, we really want to discourage screening in people who have concerning symptoms. Part of the reason for that is, if you look up the symptoms of lung cancer, every textbook out there will give you a table and that table includes things like cough, a new cough, changing cough. Most people who walk in your office with those symptoms don't have cancer. But, if you start screaming people simply because the thought of it was triggered because the patient reported new symptoms to you, you're going to have a lot more false positives.

That is, you'll find abnormalities that look like they could be cancer but aren't, and that's where the trouble comes in with screening. And I have seen examples personally in my own practice of people that had biopsies because somebody did a screening CT, and only did it because the patient had reported symptoms to them. And the doctor, you can almost see the thought process. Thy connected the dots, "Smoker, symptoms, let's get a CAT scan." Unfortunately, that's not a good practice. We want to discourage cancer screening in the context of symptoms. Now if you do have symptoms, that's a different story. That's a diagnostic workup and it may be appropriate to do a scan, but how you approach the results from that scan would be very different than somebody who showed up asymptomatic.

I'm going down a rabbit hole you probably didn't want to go down, but I think it's really important to emphasize that screening is something that we do on healthy, asymptomatic individuals. That is the definition of disease screening in the context of lung cancer. CT screening for lung cancer should be reserved for healthy, high risk, asymptomatic individuals, those three characteristics. We couldn't possibly overemphasize the importance of that.

Scott Redding:

So if I do have symptoms, I have a cough, maybe I've noticed I've got a little ... Maybe some blood when I cough or something, and maybe I'm getting a little too much like what I see in shows where they have that or other symptoms, what would happen then? I would come in, I'd make an appointment either with my primary care doctor and they'd recommend me to a pulmonologist? How does that work once the symptoms start to show up, just to clarify that difference between screening and me coming with symptoms?

Doug Arenberg:

Let's take your example of you've got a cough and let's look at the world of cough. Acute cough that's been there for a couple weeks. 98, 99% of people have a viral infection and it's going to go away on its own. You don't need antibiotics, you probably don't need an X-ray. But if you come back to me 3, 4, 5, 6 weeks later and your cough is still there, I think at that point in time I might get an X-ray. If you're a smoker, I might get a CAT scan if the X-ray is normal. But most of the things that cause cough are not going to be cancer. We'll take a history. We'll ask you how long your cough has been there. What's it like? Is it



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dry? Is it wet? What makes it better? What makes it worse? Have you taken anything for it over the counter? Do you have a history of having asthma?

Putting all these pieces together, medicine is really playing the odds. I mean, a good doctor is always creating in your head if you will, a differential diagnosis. What are the things that can account for this? I like to look at it almost as a pie chart, and the biggest slice of that pie is viral bronchitis. Just an infection, a cold, post nasal drip, asthma. These are common things and by far, even in people who are heavy smokers. If you have a cough that's been present nagging cough for less than a few weeks, it's going to be something that'll go away on its own. So, taking a good history is the first place to start, but recognizing that imaging has a role to play once it starts to behave in a way that it shouldn't, if it's truly a viral infection for instance.

Scott Redding: Going back to the screening a little bit. I'm 49 and I quit smoking over 20 years ago. Would I be a candidate? As far as I know, I'm pretty healthy. Would I be a candidate for screening?

Doug Arenberg: In the current environment, the short answer is no. As I alluded to earlier, there are proposed new criteria that are being published pretty soon by the United States Preventive Services Task Force. So let's first take a step back and ask, what is the USPSTF? It is a group of volunteer experts in preventive medicine. Most of them are physicians, some of them are epidemiologists, all of them are experts, they are volunteers. It is a committee of people that rotate and basically develop preventive service recommendations for all the United States, whether it's preventing a stroke from high blood pressure, when to do cancer screening, when to screen for diabetes and everything in between. So, their current recommendations are what we talked about earlier. Over age 55, 30 pack-years or more of tobacco use. And if you've quit, you quit within the last 15 years.

Now, the recommendations may be changing to essentially cast a broader net to screen people as young as age 50 and with a slightly smaller pack-year history, maybe down to 20 pack-years. What that's going to do is dramatically increase the number of people that they believe we should be screening, but it's going to screen a much lower risk population. Because that population is generally at lower risk, you'll need to screen more people to find that one cancer that might potentially save a life. There is a term in preventive medicine called the number needed to screen. What that really is, is quite simple, how many people do you need to screen in order to believe you've save one life from cancer?

The original data from the National Lung Screening Trial, which is where we got most of our information suggested that on average, if you just took the average subject in that study, it was around 300. You need to screen 300 people to save a life from lung cancer. To put that into perspective, mammography, which I think a lot of people look at as one of the gold standard screening tests, at least in terms of overall acceptance, average risk women over age 50, the number



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needed to screen is over 1,000. In other words, I need to screen 1,000 women for 10 years. That's 10,000 mammograms, and from that one person's life will have been saved from breast cancer, which I think is ... When I have that conversation with people I see a lot of surprised looks, but this is what the data tells us. And that's actually a pretty good screening test, but my reason for dwelling on this is that it really puts into perspective how very effective lung cancer screening is from a public health perspective.

Now, these numbers aren't completely comparable. It's not like you're going to the store and buying a dozen apples for \$1 versus \$3. There's very different outcomes from cancer screening with lung cancer and cancer screening for breast cancer. The downside of lung cancer screening is that if you end up doing a biopsy of the lungs that otherwise would not have been done on somebody with a benign condition, that has a potential to lead to some bad outcomes, puncturing the lung, bleeding. These are much bigger complications than a minor complication from, say, a breast biopsy. You aren't necessarily comparing apples to oranges here but from a public health perspective, lung cancer screening is very effective.

Now that number, that 300 or so that we screen currently to save a life, that's going to go up if we accept these new screening criteria, which are to screen a younger population with perhaps a little bit less tobacco history. Your screening if you're 49 and quit 20 years ago, you have already done two things that have reduced your risk of cancer far better than I can. One is you quit smoking, so you should pat yourself on the back for that because nobody should underestimate how hard that is. The tobacco industry has spent a century creating a product that is nearly impossible to quit. If you ask any ex smoker, a lot of them will tell you it's the hardest thing they ever did, and there's a reason for that. The tobacco industry has created a product ... Imagine any other product that when used as directed, killed 50% of its users. That's the cigarette.

So, your quitting 20 years ago has reduced your risk of dying from lung cancer by about as much as can be done, and me screening you with a CAT scan probably can't reduce it much further. That's one way to look at whether or not you're eligible for cancer screening and the good news is, your risk is pretty low. Now, there are things that can change that risk. If you were to tell me that both your parents and three of your brothers had lung cancer at a young age, we might consider that very different. It's very hard to incorporate family history into decisions about whether or not to screen, but I think it is important to have that conversation. We do know that that moves the needle in terms of your risk, as do some other things. For example, a diagnosis of emphysema. If a doctor has ever told you that you have emphysema, that by itself increases your risk of lung cancer, even if you never smoke.

As a field, we're in a period of debate as to whether or not to include some of these models, if you will, that use characteristics like that to predict risk for dying from lung cancer and whether that should be used to decide who we would offer screening to and who we shouldn't. But for now, the simplest



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answer is sticking with these age and pack-year criteria, we're relatively early on in an era where lung cancer screening is even recommended. We're now 40 or 50 years almost into mammography screening and a good 20 to 30 years into colonoscopy screening.

We really haven't learned some of the lessons from these others, which is that even 20 or 30 years after learning that colonoscopy is such a very effective screening test for colon cancer, we're at maybe 60% of the population who's eligible for that test. Only about 60% are getting it done. So we need to learn some things about implementation science that get primary care doctors, and specialists like me and patients, and public health advocates and payers all on the same page about how to do the simple things well like promoting smoking cessation and other preventive services. Under that umbrella would be something like lung cancer screening for the right population of folks. We have a lot to learn about how to do this better. I think we're learning to crawl, and pretty soon hopefully we can learn to walk and then start to run.

Scott Redding: You know, a lot of mentions that you've brought up talking about screening has also brought up mentions about prevention. What are preventative measures for lung cancer? Hopefully not getting lung cancer, and I would even say maybe even other lung diseases since there's multiple lung diseases that I'm sure can benefit.

Doug Arenberg: Well, obviously the 800 pound gorilla in lung disease is tobacco, combustible tobacco. I've spent a lot of years giving talks about tobacco and e-cigarette, and debates that raged back and forth on this. But, there should be no mistake about our understanding that the enemy if you will, from a pulmonary perspective as a lung doctor, the enemy is combustible tobacco. Followed by a very distant second place, but very important second place, which is air quality. We live in a world where air quality is increasingly recognized as an important factor in determining longevity. Some of the most important health disparities, whether it's across national boundaries or continental boundaries or even within the state, some of the most important disparities in health can be accounted for in part by exposure to particulate air pollution.

So what I think of when I think of cigarettes is, it's self induced air pollution. Anything that you burn and inhale into your lungs has the potential to cause lung disease, the most common of which would be emphysema followed by lung cancers and others, but other lung diseases. The lungs are not meant to inhale combusted organic material, and that includes diesel fuel as it does tobacco and other things. So, the major driving force in lung health is the air we breathe. 10,000 liters of air every day goes through your lungs and your health is in part determined by where you live, which is unfortunate but that's true.

And then it's determined by the choices that you make early in your youth, and ways you can avoid the peer pressure and the media pressure from tobacco advertising, and now the social media pressure from tobacco advertising. If you can avoid those things and resist them and stay away from combustible



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tobacco, you've done yourself a huge favor. And if you become dependent on nicotine through combustible tobacco, then quitting is the single most important thing that you can do. And I'd hate to say it, but writing your legislators and asking them to support anything that improves clean air will also go a long way towards improving lung health.

Scott Redding: Combustible tobacco. I mean, does that include stuff like vaping, which is very popular with young kids? Marijuana now that it's becoming more legal in more and more states?

Doug Arenberg: Sure. So like I said, anything you burn and then put in your lungs. Now the difference is vaping, you're not combusting anything. You're heating a liquid that has something in it. If you want to start a debate amongst public health experts, I'll use that term lightly since I'm on the call with you. I'll put experts in air quotes. If you want to start a debate, start talking about electronic cigarettes. I guess what I would like to do is highlight, or perhaps introduce the idea of driving a wedge between two very, very relevant and important aspects of the electronic cigarette debate.

On one hand, we have this recent uptake of electronic cigarettes by teens and other youth who probably never would've in their life dreamt of using combustible tobacco. People who would've gone throughout their lives and not become dependent on nicotine are finding a new route to nicotine dependence, which is electronic cigarettes. That no matter how you look at it cannot be considered a good thing, because these are not ... Essentially what you're doing with vaping, and let's just assume you're only vaping nicotine. You're taking a liquid, usually glycerin and glycerol, and heating it up and taking it into your lungs. We don't fully understand the health effects of that yet.

But if anybody's betting that that's not bad for your lungs, I'll take that bet in a heartbeat because I'm pretty sure long term we'll learn of some health effects of vaping in youth lungs, particularly since most people who are youth e-cigarette users have not fully reached their adult lung function. So, one of the major concerns about long term health disease is that the lung is still developing in most people who are, say under age 25. Let's set that aside for a second and let's talk about the other side of that public health coin.

If I could take every single adult user of combustible tobacco today and switch them over to electronic cigarettes or some other electronic nicotine delivery system, the public health benefit of that would be almost too big to measure. So you have this potential to have an enormous public health impact for people who are current users of combustible tobacco, who can't quit no matter how hard they try. That enormous public health benefit is being challenged, if you will, by this uptake of nicotine dependence by as I said, folks who would never have dreamed of taking up cigarette smoking. So, I think the problem with this is looking at the behavior of the tobacco industry should tell us a lot.



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In over 100 years of existence, the tobacco industry has never ever placed a losing bet. And to see their behavior now and the literally hundreds of millions if not billions of dollars they're putting into marketing electronic cigarettes and electronic nicotine delivery devices to the youth, to people who aren't legally allowed to buy these things, it should tell us everything that we need to know about how the tobacco industry views these. Now, I think we've blown it from a public health perspective in allowing the narrative about electronic cigarettes to become a black and white narrative. We have to figure out a way to potentially make these available to adults on the assumption that they are going to reduce the harm from combustible tobacco and really avoid creating a generation or two or more of nicotine dependent youth, because we just don't know what the long term health effects of these are in the developing lungs. We shouldn't be putting anything other than air into the lungs of developing teens.

Scott Redding: I guess my question then would be younger kids, teens, they have developing lungs, but you're saying that it might be okay maybe from a way of getting adults off of cigarettes to actually use e-cigarettes instead?

Doug Arenberg: Well, we don't know that yet and we've never ... There have been a few trials that have looked at the role of electronic cigarettes as smoking cessation aids. The pharmaceutical use of electronic cigarettes, that has been studied in some way, shape or form, and the results were I would say, encouraging, though by no means definitive. Some of the problem is the way some of these studies were done really didn't allow you to draw the conclusion that the study was intended to arrive at. So, we think as ... I'll tell you my personal opinion. My personal opinion as a pulmonary doctor is that I will do everything I can to help my patients make an attempt to quit, and then give them everything they need to secure the success of that attempt.

Now in 2020, what that means to me is I'm going to start with the currently seven FDA approved medications for tobacco cessation in the United States. Five of them are some form of nicotine and the other two are pill forms. They all increase the odds of a successful quit attempt. So, my first job is to make sure that my patient's on board with, "Yes, I really do want to quit, and yes, I recognize that my chances of succeeding are better with one of these medications." The reality of the situation is, the practical reality of the situation is that even with all of these FDA approved medications, there are people who remain nicotine dependent who cannot stop using combustible tobacco.

And if they come to me and they say, "You know, Dr. Arenberg," and they say it sheepishly, I can almost tell what they're about to tell me. They say, "You know, I've been using electronic cigarettes," and I say, "That's okay." I would not encourage that as a first means of smoking cessation because I have other ways that I know are proven safe and effective, but if you tell me right now that the only way you can avoid combustible tobacco is by using that electronic cigarette that you bought at the drugstore, I will pat you on the back and say, "Listen, I really, really appreciate your persistence in this. I want to congratulate you. Eventually we want to get you off all nicotine but for now, if you can completely



avoid combustible tobacco with electronic cigarettes, you have my support." That's the way I approach it in a practical setting.

I will say that one of the things that I really try to avoid or try to have my patients avoid is the substitution of electronic cigarettes for combustible tobacco, that is smoking cigarettes here and there. In other words, dual use. That is something that we should be discouraging, because really at that point you're not getting any of the benefits, and you might be compounding your risks. So I tell people, job one, let's try to help to make a quit attempt. Let's try to agree that this is something we can do. Number two is, let's put FDA approved medications in your hands because we know they increase your chances of success. And we stick with it and recognize that this is a ... Tobacco cessation is an ongoing battle. It's not a one-time thing.

This is a struggle, and you probably can tell me better than I can tell you. It's a struggle that you fight again, and again, and again, even years after you've quit. I've had people tell me they still fight cravings. So I try to make it clear that this is a long haul battle, not a short haul battle and that I'm on their side, and I believe in them. But if I can help my patient quit and only help them quit through the support of their choice to use electronic cigarettes, I'm never going to veto that if you will as a doctor. The enemy as I keep saying to my trainees and my residents and my fellows, the enemy is combustible tobacco.

Scott Redding:

It sounds like although we're talking about the potential of one or the other, nicotine is still between those and that's what the addiction is too. So is nicotine the stronger culprit in potential of lung cancer, or is it just the fact of inhaling the combustible, the organic smoke if you will, coming into the lungs?

Doug Arenberg:

With a cigarette, you get a really rapid delivery of nicotine to the brain and it's that rapid delivery that reinforces dependence, the psychological and chemical dependence. That's the addiction. If you take nicotine out of cigarettes, you won't have addiction anymore. It's the other 4,000 chemicals that come with the cigarette smoke that likely lead to lung cancer. Now, nicotine by itself probably doesn't cause cancer. Nicotine causes high blood pressure and a fast heart rate and some other troubles, so long term we want to get everybody off nicotine, but the major health effects of a cigarette come not just from the nicotine. It's a package deal if you will.

So the nicotine changes the chemistry in your brain. When you're a smoker and you wake up in the morning and your brain hasn't had nicotine overnight, the first thing your brain says is, "Do whatever you got to do, but get us some nicotine." If you ask a smoker, that first cigarette of the day is always the most satisfying one because of the, if you will, the deficit of nicotine in a brain that is starved for it. When you create that dependence, it's a cycle that never really breaks. So the nicotine by itself is not a harmful chemical that causes lung cancer but if you can eliminate that from the cigarettes, then you don't have the addiction and nobody is going to smoke. Cigarettes are very, very unpleasant. Anything that you burn purposely to inhale in your lungs is purposely



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unpleasant. So a lot of the chemical manipulation of tobacco is to make that less unpleasant, to introduce flavors that mask the harshness of it and allow the nicotine addiction to just do its job, which is to make tobacco executives really, really wealthy.

Scott Redding: You mentioned about research with the vaping with the e-cigarettes. What other kind of research is currently happening that you're aware of, either nationally or at Michigan Medicine?

Doug Arenberg: I guess I'll touch on a couple. One is, go back to this nodule problem which is that even if you don't do lung cancer screening, we do CAT scans now for so many more reasons than we ever used to do. A lot of times the question I get from a patient, "Isn't there some blood test that you can do to find out if this is lung cancer?" This sad answer is right now there just isn't, but an enormous amount of research is being put into using the blood as a source of what we call biomarkers. That is, is there something there that we should be worried about? There are many ways that you can use a biomarker. You can use a biomarker that might increase the probability that a disease is present. So if the biomarker test is positive, then it incentivizes you to go look, "Where is that disease?"

The most useful biomarker for us in the pulmonary world would be what we call a rule out biomarker. That is, if your biomarker is negative, then you really can't have the disease we're looking for. A great example of this and one that I'd like to see a parallel for in lung cancer, a great example this are a test called a D-dimer. I won't go into a lot of detail, but if you go into the emergency room and you have a D-dimer test that's negative, the emergency room doctor will immediately cross off the list of things that might be wrong with you, pulmonary embolism. Very, very useful test that has what we call a high negative predictive value, very useful test.

What we as pulmonologists have been digging for, for many years is we want the D-dimer for lung cancer. We want the one that says when it's negative, we can really reassure the patient that this nodule shouldn't be something that keeps anybody awake at night, it's probably benign. We're much better at telling people what it isn't than it is, but we know it's not lung cancer. We're currently enrolling people in a couple of different studies that evaluate the value of these biomarkers. So when patients come to see me over the next year or two, one of the things we'll be talking about in addition to what we recommend clinically to evaluate them is, would we get them interested in being a volunteer for one of these studies that allows us to test the role of these biomarkers?

That's a really big area of interest. That's an area that we've known of for years, that regardless of the results of these screening trials, which as we waited for the screening trials to come back and tell us whether screening really worked or not, we always knew that these biomarkers were going to be a part of this process. That's a long winded answer, but I'm very excited about that as you can tell. If we can work on getting better at that, that would be one really good area.



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Then the other course, is other ways to help people address tobacco dependence. Anything that we can do to move that needle even a little bit. Just a few people quitting tobacco has a huge public health impact.

Scott Redding: Doug, I really appreciate all the great information. If there's one thing that you want to make sure that everyone walks away from this with, what would that be?

Doug Arenberg: First one is, understand that lung cancer screening is highly effective if we choose the right population. The right population is people who are at high risk, and otherwise healthy with no symptoms. High risk, otherwise healthy, no symptoms. I would love for people to understand that that is the population for whom lung cancer screening should be considered. And the other is if you smoke, there are a lot of resources out there to help you quit. Those resources include your doctor's office, state funded quit lines. 1-800-QUIT-NOW is available in every state in the United States and many of them will give you free tobacco cessation medications, and your friends and family who want you to quit. So, use the resources available to help you set goals and reach them by one day at a time, never quit quitting. Those are my two. Thanks for that.

Scott Redding: Great. I really appreciate the time. Thank you.

Doug Arenberg: Thank you.

Scott Redding: Thank you for listening, and tell us what you think of this podcast by rating and reviewing us. If you have suggestions for additional topics, you can send them to cancercenter@med.umich.edu, or message us on Twitter @UMRogelCancer. You can continue to explore the 3Ps of Cancer by visiting rogelcancercenter.org.



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