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000:00.000 --> 00:13.200 Support for Yale Cancer Answers comes from AstraZeneca, working side by side with leading scientists to better understand how complex data can be converted into innovative treatments. More information at astrazeneca-us.com.

00:13.200 --> 00:48.600 Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about colon cancer with Dr. Charles Fuchs. Dr. Fuchs is Director of Yale Cancer Center and Physician-in-Chief at Smilow Cancer Hospital , and Dr. Gore is a Professor of Internal Medicine and Hematology at Yale and Director of Hematologic Malignancies at Smilow.

 $00:48.600 \rightarrow 01:15.500 < vGore>When you were on our show a couple of years ago, when you first arrived, it was an interesting time for you, but we are not going to talk about that now that you are all settled in and we'll talk about where your career has led, which is really in colon cancer.$

01:15.500 --> 01:54.900 <vFuchs>Absolutely. I think it is an interesting time in understanding colon cancer and it is a major burden of cancer right. This year, the American Cancer Society expects about 150,000 cases of colon cancer in the US, regrettably about 50,000 Americans die each year of this malignancy. It is a major contributor to the burden of cancer. So, on a public health basis, it is really important and really from the onset of my career, I have been committed to understanding the biology of the disease and figuring out how we can better treat it, how we can prevent it, and ultimately developing new drugs for patients.

 $01:54.900 \rightarrow 02:37.800 < vGore > It is my impression now with my lay-person hat on that colon cancer is not really in the news like it was for a while and I was just sitting here thinking, is that because we have done so much better with colon cancer that it is not such a big problem or is it just that we have not had the celebrities? Is colon cancer not in the buzz or are we just at a different place with that disease?$

 $02:37.800 \rightarrow 03:17.200 < vFuchs > No.$ I suspect that the other cancers are getting appropriately a lot more attention, and they should. Colon cancer is a major problem. Perhaps, one reason we are not hearing as much about it is that the revolution in cancer therapy over the past 3 years or so has been development of immunotherapies, which has been incredibly exciting and transformative. And colon cancer has lagged behind in that area. That is to say that, the immune-based approaches for cancer which work in a variety of malignancies do not seem to work for the majority of patients with colon cancer and that is one aspect of our work that we are looking to rectify.

 $03:17.200 \rightarrow 03:39.600 < vGore > And we see a lot of buzz about those immune therapies on TV with ads with balloons and people with lung cancer with balloons$

loons and there is always balloons for some reasons it seems to me. But, you know, I just realized even as a cancer doctor how much of my impression of the world of cancer gets filtered through through media.

03:39.600 --> 04:02.200 <vFuchs>You and I have been doing this for a while and the hype is real. You are right. We are not there yet with the immunotherapy, but you and I have been doing this for a long time with the idea that somehow we should leverage the immune therapy to treat cancer and the fact that at least we have these inroads that show success, it is extraordinary and it is really just the beginning I think of revolution in cancer therapy.

04:02.200 --> 04:21.500 <vGore>Right. And colon cancer, you know from where I sit, and again I would be happy to have been proven wrong by now, but really the key is early discovery and early definitive and curative therapy, which is usually surgical right?

04:21.500 --> 05:17.000 <vFuchs>It is. So, early detection is a critical component of what we do. And it makes sense, why? Because the vast majority of colon cancers arise from benign polyps. And so, if you find that polyp and remove it typically with a colonoscopy, you then eradicate that person's risk from that polyp becoming cancer. So, as a result, early detection and screening fundamentally improve mortality from colon cancer and the results show that. In fact, and I credit Katie Couric for a lot of this, in 2000, about 20% of the US population was getting colonoscopies in circumstances where they should. That is, for instance, people over the age of 50. So, 20% of people who should have gotten a colonoscopy got one. That is, 80% did not. Now, it is roughly about 60%.

05:17.000 - 05:18.100 < vGore > Wow! 60% to get them?

 $05:18.100 \rightarrow 06:09.400 < vFuchs > Are getting them. Yeah. That is not 100%, but tripling that frequency since 2000 is amazing and I think the work of Katie Couric, getting on television, telling her story and the story of her husband, a variety of other organizations really across the US and the globe have brought attention to that. So, it is making a difference. There is now a variety of techniques to detect colon cancer, tests on the stool which have some measured success though not as good as colonoscopy, but the American Cancer Society, and the National Cancer Institute among others, what they are recommending to people is get some kind of screening test. Ideally, colonoscopy but if colonoscopy is not an option, that some of the newer stool-based tests are also an option though they are not as sensitive.$

 $06:09.400 \rightarrow 06:16.100 < vGore>So$, that 60% really refers specifically to classical colonoscopy and does not include these alternative tests?

 $06:16.100 \rightarrow 06:17.000 < vFuchs > That is exactly right.$

 $06:17.000 \rightarrow 06:29.800 < vGore > Gotcha$. And at least for a while we were hearing with these so-called virtual colonoscopies or CAT-scan based colonoscopy is that in the metric, what's up with that?

 $06:29.800 \rightarrow 06:56.500 < vFuchs >$ For the past 20 years, this technology which is using the CAT scanner to visualize the inside of the colon and find polyps and cancers as a means of early detection, that does not require a scope, has been something being developed, but here is the problem, you still need to do the prep because you have to clean the colon to find these.

 $06:56.500 \rightarrow 06:55.800 < vGore > Which is what everybody dreads.$

 $06:55.800 \rightarrow 07:22.500 < vFuchs > Right.$ And if you find something, you have to get a colonoscopy. And lastly, the tests are not as sensitive. I know that there have been some studies saying that they find cancers as well as colonoscopy, okay, but small polyps, they do not find as well. So, I think it is an interesting technology but if it were my patient, my friend, my relative, I would recommend a colonoscopy.

 $07:22.500 \rightarrow 07:27.600 < vGore > And I guess one difference would be you probably do not need to be anesthetized for the virtual colonoscopy?$

 $07:27.600 \rightarrow 07:36.700 < vFuchs > That is true. So, there may be circumstances if the patient is at high risk where you cannot give them conscious sedation, you know putting them to sleep.$

07:36.700 --> 07:36.900 <vGore>Light?

 $07:36.900 \rightarrow 07:48.000 < vFuchs > Light sedation as you put it, then it is an option. But ideally, I think a colonoscopy, which is a very safe procedure done as an outpatient really should be the standard.$

 $07:48.000 \rightarrow 07:59.000 < vGore>I$ can say that I have had my 2 on schedule, which tells you how old I am and they have been a piece of cake.

07:59.000 --> 08:03.300 <vFuchs>We need to advocate this as practitioners.

 $08:03.300 \rightarrow 08:14.500 < vGore>Yeah$, now it is about nothing but the prep, you know the prep is a little bit of a nuisance, but not so terrible really. And you know, it is nice to come out with a truly clean bill of colonic health.

 $08:14.500 \rightarrow 08:27.400 < vFuchs > Yeah$, and I think one thing your listeners should be aware of, and I am sure you are aware as well, Steve, is that the American Cancer Society has moved the bar from starting at age 50 to age 45.

08:27.400 --> 08:26.300 <vGore>Yeah. So, tell me about that, I have heard that.

 $08:26.300 \rightarrow 09:24.700 < vFuchs > Right.$ So, whereas we are making inroads in reducing the rates of colon cancer in the United States largely through early detection, the rates of colon cancer in younger people, that is people under the age of 45 is rising faster than almost any other cancer in the US. It is still uncommon among young people, but it is clearly increasing. And it is sort of a great deal of consternation to us as to why is this? Why is this younger population of Americans more likely than ever to get colon cancer and I do not think we know the answer. One aspect of that story is the rising rates of adolescent obesity. Because obesity is a well-established risk factor for colon cancer. So, it is clear that is part of it, but it does not explain all of it and we need to sort this out, but in the meantime, the American Cancer Society has acted by saying we are going to move the recommendation 5 years earlier at age 45.

 $09{:}24.700 \dashrightarrow 09{:}32.300 <\!\!\mathrm{vGore}\!\!> \mathrm{And}$ that is regardless of body mass index or obesity measurements?

09:32.300 --> 09:59.100 <vFuchs>That's exactly right. And you referred to an interesting thing these sort of precision prevention approaches as they are based on either the demographics of patients or sometimes even genetic features. Those things I think need to play into all of our prevention efforts. So, if you have a family history, then you should start at age 30, perhaps even younger if the family member is one of the high-risk syndromes.

 $09:59.100 \rightarrow 10:09.500 < vGore > So$, can we be a little more specific about that, so anyone with a first-degree relative who has had colon cancer, meaning parents or siblings, should they start screening at age 30?

 $10:09.500 \rightarrow 10:20.400 < vFuchs > Yes$, that's exactly right. So, a first-degree relative, a parent or sibling, you should start somewhere in the range of 30-35.

 $10{:}20{.}400 \dashrightarrow 10{:}20{.}000 <\!\!\mathrm{vGore}\!\!>\!\!\mathrm{And}$ it is still every 10 years if you are clean or?

10:20.000 --> 10:49.400 <vFuchs>That's exactly right. Now, I think it depends on the nature of the family history. So, if you have a family history, I would encourage not only starting earlier but talking to your physician, your gastroenterologist, whoever it is that is advising you about the frequency because I think it does depend on sort of the nature, the characteristics of what happens in your family. And also, for the patients like that, it is sometimes worth getting genetic testing, which is increasingly a part of what we do in risk assessment.

 $10:49.400 \rightarrow 11:10.700 < vGore > And who are the people where the family history should really be ringing a red flag? Is it several cases of colon cancer, or is it colon cancer with other people in the family having different cancer, who should be thinking, I wonder if there is something up with my family?$

11:10.700 --> 12:50.800 <vFuchs>I think anyone who has multiple cancers of which one is colon cancer in their family should talk to their physician about whether they should be screened genetically. I think we are still learning who should be screened. It used to be when I started this, if you have 3 members of your family with colon cancer right. That is not the case any more. We realized that there are people who are harboring a genetic proclivity to cancer, colon cancer, with less robust family histories. So, if you have colon cancer in your family and there are other individuals in the family with cancer, then I think it is worth noting. I will just share one anecdote, a personal anecdote, which is my wife was diagnosed with colon cancer at age 42 and at that time, the only person we knew that had cancer was her father, who regrettably died of a cancer of the

esophagus. Since that time, her sister and her sister's daughter have had cancer, but not colon. And what is also interesting and my wife is comfortable with me sharing this was that at the diagnosis, when they did the genetic panel, they did not find anything. But we have gotten better in understanding these genes. So, she actually repeated the panel last year and they did not find one but two genes that put her family members at risk for both colon, breast and other cancers. So, it is always hard to find those things out, but what we are pleased about is, that our family can actually use that information for the benefit of all in terms of how we screen.

 $12:50.800 \rightarrow 13:00.800 < vGore>Because it likely impacts not only your children but your extended family.$

13:00.800 --> 13:08.700 <vFuchs>Yeah. My sisters-in-law, my wife's sisters are getting checked and the family is getting checked and you know we want to sort through this.

13:08.700 --> 13:13.000 <vGore>Knowledge is power.

 $13{:}13{.}000 \dashrightarrow 13{:}13{.}200 <\!\!\mathrm{vFuchs}\!\!>\!\!\mathrm{Absolutely}.$

 $13{:}13{.}200$ --> $13{:}15{.}100$ <vG ore>Well, that was a fast first half, but we need to take a break for a medical minute.

13:15.100 --> 13:27.600 Medical Minute Support for Yale Cancer Answers comes from AstraZeneca, dedicated to advancing options and providing hope for people living with cancer. More information at astrazeneca-us.com.

13:27.600 --> 14:13.500 This is a medical minute about melanoma. While melanoma accounts for only about 4% of skin cancer cases, it causes the most skin cancer deaths. When detected early, however, melanoma is easily treated and highly curable. Clinical trials are currently underway to test innovative new treatments for melanoma. The goal of the Specialized Programs of Research Excellence in Skin Cancer or SPORE grant is to better understand the biology of skin cancer with a focus on discovering targets that will lead to improved diagnosis and treatment. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio.

14:13.500 --> 14:38.300 <vGore> Welcome back to Yale Cancer Answers. This is Dr. Steven Gore. I am joined tonight by my guest Dr. Charles Fuchs and we have been discussing colon cancer. Charlie, before I forget, you had mentioned the stool testing for early detection and you know we hear a lot about this on the radio and I know some of my family members, a physician, who recommends it to her patients. Can you tell us about this test or these tests?

14:38.300 --> 16:01.600 <vFuchs> Absolutely. Historically, physicians have done these tests where what you are really looking for is microscopic pieces of blood or blood cells in the stool. And that test is relatively insensitive. That is, sometimes there is a cancer, but there is no blood in the stool. So, you do pick up patients with colon cancers but you miss a lot. It has been enhanced

now so that we know that when there is cancer, that cancer sheds its DNA into the stool and that cancer-mutated DNA can be found in the stool through genetic testing. So, the current generation of stool tests which you can send the stool to the companies that do these tests, they test for blood and for those genetic mutations in the stool. It definitely increases the sensitivity of those tests, but it is not 100% and it does not pick up polyps as well and realize, if it is positive, you are going to get a colonoscopy, and if it is negative, that is somewhat reassuring but not a guarantee that there is not a polyp in your colon. So, if the person is unwilling to do a colonoscopy, then it is an option and it therefore does increase our rates of screening, that is a good, but I would still rather get a colonoscopy.

16:01.600 --> 16:39.600 <vGore> Gotcha. Yeah, I think that makes sense. Interesting. So, what I would like to go to next I think is your favorite subject of obesity. I know it is your favorite subject, but it is the one that sticks out to me because the last time we were talking about it, I think we made a commitment to like being 10 pounds thinner the next time we did this interview and the good news is that I am not any greater, although there may have had been a little blip up in the meantime. So, it is hard for some of us less lean people to hear but why don't you give us the straight dope on that.

16:39.600 --> 17:21.400 <vFuchs>I have been committed to understanding the biology of colon cancer and developing new treatments, but one thing that I took an interest in a while ago was not only early detection but primary prevention. What do we mean by that? Well, yes you can find it early but what if people, what if we can find ways that people never get it at all. And the reason I took an interest in that is, it is clearly that diet and lifestyle drive the risk of colon cancer. How do I know that? Well, if you look at the western parts of the world, like the US and Western Europe, our rates of colon cancer are 40 times higher than the underdeveloped parts of the world.

 $17{:}21.400 \dashrightarrow 17{:}22.900 <\!\!\mathrm{vGore}\!\!>\!\!\mathrm{Its}$ incredible.

17:22.900 --> 18:52.000 <vFuchs>Now, some people say well that is just because they cannot diagnose colon cancer. No, they diagnose it. Some say that it is because they do not have the genetic proclivity, they do not get it because they do not have those genes, it is not that. And in fact, if you look at migration studies, that is, people who move from those parts of the world to the west, the US or Western Europe, those families have the same rate of colon cancer as we do within a generation. So, it is something we are doing that is effecting risk. And what we have learned is, is that our western behaviors drive the risk of colon cancer dramatically. So, what does that mean? People who are obese have a significantly higher rate of colon cancer, people who are sedentary have a higher rate, in fact people who exercise can reduce their of colon cancer. Some studies show that just a western diet in general, significantly increases the risk of colon cancer. And then frankly, smoking and alcohol which we know are problems for a variety of cancers also increase the risk of colon cancer. So, a lot of modifiable behaviors here, right, and what we have shown is that people who do modify their behavior, significantly lower their risk.

 $18:52.000 \rightarrow 19:10.300 < vGore >$ It makes a difference. Well, there are lots of reasons why healthy lifestyle and healthy weight are things that we should strive for and certainly cancer is one of them and of course cardiovascular problems, all sorts of reasons to live the healthy lifestyle.

19:10.300 --> 19:37.100 <vFuchs>Absolutely, and if I may just expand on this one bit, which is, you know, you make an important point, which is we all think we are indestructible and it is really hard to do all those things, you know for healthy people to do those things. And what is really interesting is the people who pay the most attention to that literature are people diagnosed with cancer right.

19:37.100 -- > 19:39.800 < vGore > Sure, what can I do now? Its too late, its not too late but.

19:39.800 --> 20:32.900 <vFuchs>Exactly. It is not too late, and in fact, studies show that 75% of cancer patients believe that there is some diet or supplement that will improve their chances of cure, 75%. The problem is that we just have not done those kinds of studies, and as you know, at our center, we are doing those studies and we have now moved this research into patients, and we have done studies of colon cancer patients, we have asked them about their diet and lifestyle, and I will tell you what we find is - it matters, that we find patients, colon cancer patients, who exercise regularly have a higher cure rate. Patients who avoid high western diets, avoid high-carbohydrate diets have a better cure rates. Patients who avoid lots of sugar sweetened beverages have a higher cure rates. So, these things matter even for patients.

 $20{:}32{.}900$ --> $20{:}37{.}600$ <vGore>Fascinating. And you have recently done a study that involves vitamins as I understand it.

20:37.600 --> 22:25.500 <vFuchs>We have. Yes, thanks for asking. So, as you probably know, the multivitamin industry is a 24-billion dollar industry in the US, and for the most part, multivitamins have an uncertain benefit. I mean, people take them whether they help or not, but one vitamin that we have been interested in is vitamin D. That vitamin that we need for the health of our bones right. It builds strong bones. So, why did we get interested in that. We actually found in the laboratory that if you take away vitamin D from animals with colon cancer, the cancers grow faster and if you then administer vitamin D, you can actually reduce the rate of growth of colon cancer. So, we have done studies in patients where we find that patients with higher blood levels of vitamin D seem to do better. So, we decided to put our money where our mouth is, that is, to do a clinical trial. And we did a clinical trial with about 140 patients with colon cancer where they all got standard first-line chemotherapy, but they were then randomly assigned to get either a high-dose version of vitamin D with their treatment or just a very low dose of vitamin D. And what we found is, the patients who were randomly assigned to receive the high-dose vitamin D, those patients getting the high dose had a significantly greater benefit from the treatment. So, the time to progression of a cancer, the length of time to which the treatment worked was much longer if you continued on vitamin D.

22:25.500 --> 22:28.200 <vGore>That's amazing. I mean, that sounds very meaningful indeed.

 $22:28.200 \rightarrow 22:53.600 < vFuchs > Yeah.$ It was about 40% better. The treatment was 40% better if you took a high-dose vitamin D. Now, let me be clear. That is a relatively small study. We are working with the National Cancer Institute to do a larger confirmatory study. So, I think anybody who is contemplating doing these things should talk to their doctor, but it is encouraging and one that we want to follow through.

22:53.600 --> 22:59.800 <vGore>And I guess you've got to be careful that if people are taking a lot of vitamin D and calcium not under medical supervision, they can get into trouble right because their calcium might go too high.

 $22{:}59.800 \dashrightarrow> 23{:}03.900 <\!\!\mathrm{vFuchs}\!\!>\!\!\mathrm{That}$ is a great point. So, too much of vitamin D is a bad thing.

23:03.900 --> 23:04.400 <vGore> So, do not do this at home without consulting.

 $23:04.400 \rightarrow 23:13.100 < vFuchs > Talk to your doctor and if your doctor suggests trying it, talk about what the dose should be first, so that you make sure you are not taking too much.$

 $23:13.100 \rightarrow 23:21.400 < vGore$ Right. And we know that vitamin D certainly levels are impacted by your sun exposure. Should people be going to tanning salons?

23:21.400 --> 23:46.500 <vFuchs>Great question. So, the answer is no because we do not want people to get melanoma or skin cancer. So, there are ways to supplement your vitamin D levels through oral supplements, but again the jury I do not think is in right. We have one very exciting small trial. Before we start recommending this routinely, let us do a larger clinical trial and in the meantime talk to your doctor.

 $23:46.500 \rightarrow 23:50.600 < vGore > And we cannot get my insurance company to pay for trip to Guadeloupe or somewhere like that.$

23:50.600 --> 23:55.000 <vFuchs> Well, vitamin D tablets are cheap.

 $23{:}55.000 \dashrightarrow 24{:}00.000 <\!\!\mathrm{vGore}\!\!>$ And more cost effective, but may be less fun. And have to remember to take them.

 $24:00.000 \rightarrow 24:03.100 < vFuchs > Yes$, once a day, we can do it.

 $24:03.100 \rightarrow 24:14.600 < vGore > Vitamin C is the one we hear I think traditionally a lot about from patients right. I think people are still talking about vitamin C, how about that?$

24:14.600 --> 24:25.000 <vFuchs>Yeah. And actually maybe that was unintentional but worthy of discussion. So, vitamin C has been under discussion for cancer for years.

 $24:25.000 \rightarrow 24:26.600 < vGore > Since I was in college I think.$

24:26.600 --> 24:37.000 <vFuchs> Or before. There was a Nobel prize winner, chemist, Linus Pauling, who was an advocate of vitamin C as a treatment for cancer.

24:37.000--> 24:37.100 <vGore> Megadose?

24:37.100 --> 25:19.300 <vFuchs>Megadose. It did not pan out, but there has actually been some recent literature looking at alternative forms of vitamin C administered in a particular way that may have an effect for cancers with certain molecular genetic alterations. So, we have grant from Stand Up To Cancer where we are working with other centers to try to look further in that vitamin C story, but there I think we are really at the early stages. To be clear, previous studies of vitamin C have not shown a benefit and whether we can find a benefit by vitamin C with alternative preparations of the vitamin and picking the right patients remains to be seen.

25:19.300 --> 25:30.100 <vGore>But there is certainly nothing wrong with eating citrus fruit as part of a healthy diet? And what about plant-based diets versus non-plant-based diets?

 $25:30.100 \rightarrow 26:39.200 < vFuchs>$ Yeah. So, we actually looked at dietary patterns in colon cancer patients, and you can actually take a food frequency questionnaire, diet questionnaire and you can take the aggregative data and you can then create 2 patterns - one is what is a western pattern of diet characterized by all the things we enjoy eating, but are not healthy versus a prudent diet, which I think is what you are referring to sort of fruits, vegetables, legumes, not refined grains and things like that. And what is interesting is, that higher consumption of a prudent diet did not improve the outcome for colon cancer patients. It was not worse, but it was not better. It is the same. But, a higher intake of a western diet, conferred a significantly worse outcome. So, western diet was bad. What do I take from that? Well, I think you want to avoid an excessive western diet -- red meats, lot of fats, carbs. You want to not do that, but do you need to eat hay or vegan, no.

26:39.200 --> 26:41.300 <vGore> No macrobiosis for you?

 $26:41.300 \rightarrow 26:51.500 < vFuchs > You can do it and there is no harm to it, but we could not find evidence that sort of those more extreme diets, which may have other benefits, necessarily benefit colon cancer.$

 $26:51.500 \rightarrow 27:15.400 < vGore$ You know, off topic a little bit as a non-meat eater, I have been very interested in these new laboratory-based meat substitutes that taste like meat, one is called the impossible burger, as a company called

Beyond Meat that makes both hamburger-type things and sausage and they are delicious. And I wonder if that is a good thing or a bad thing.

 $27:15.400 \rightarrow 27:21.900 < vFuchs > I actually think it is a good thing. I recently had one of those and you are right, you cannot tell the difference.$

27:21.900 --> 27:23.700 <vGore> It is delicious.

 $27:23.700 \rightarrow 27:40.700 < vFuchs > It is. I also want to be clear in our studies, it is not to say that having red meat once a week or twice a week is a bad thing, but if you are having it 5 days a week or every day, that is when we start to see increases in the risk of colon cancer.$

 $27:40.700 \rightarrow 28:04.300 < vGore > Got it. We are running out of time Charlie. So, the take home that I am hearing from you is, talk to your doctor about when colon cancer screening is appropriate for you, have some idea of your family history, think about how you are living your life and that may be a good monitor for us all for lots of reasons.$

 $28:04.300 \rightarrow 28:25.600 < vFuchs > Absolutely and I appreciate the points you made. We want to get more Americans screened for this disease, it is preventable. We want to put Charlie Fuchs out of business in terms of his work in colon cancer. And I think with early detection, better science, better treatment, we are going to get there.$

28:25.600 --> 29:00.000 Dr. Charles Fuchs is Director of Yale Cancer Center and Physician-in-Chief at Smilow Cancer Hospital. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. We hope you will join us next week to learn more about the fight against cancer here on Connecticut Public Radio.