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0:00:11.6 -> 0:00:47 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 colorectal cancer with Dr. Xavier Llor. Dr. Llor is a Professor of Medicine and Medical Director of the Cancer Screening and Prevention Program at Smilow Cancer Hospital. Dr. Gore is a Professor of Internal Medicine and Hematology at Yale School of Medicine and Director of Hematologic Malignancies at Yale Cancer Center.

0:00:47 -> 0:01:10.3 I think colon cancer is something that has touched a lot of people and it has been brought into the public awareness by Katie Couric and others. There has been a big boost to getting everybody screened, how successful has that been?

0:01:10.3 -> 0:01:53.3 Definitely colon cancer screening has been a big success in the US and I think that has decisively contributed to the decrease in colorectal cancer incidence. I think it is a collective win from that standpoint. We are a little bit stuck at this point in the upper 60s in terms of percentage of people who are getting screened, who should be screened and are getting screened. So, we still have a third of the people who really need to be screened and we are not being that successful in reaching out to that population. We really need to work harder in getting more people screened, particularly because we do know that it does work, it does prevent colon cancer and saves lives.

0:01:53.3 -> 0:01:53.2 Who should be screened?

0:01:53.2 -> 0:02:39.5 In general, for average-risk individuals, meaning no family history or any other things related to that, the common screening age is starting at age 50. Some organizations have recommended screening starting at 45 for African-Americans because of the higher risk and lower rate of diagnosis, and recently the American Cancer Society has extended their recommendation to all groups starting at 45 just because of the significant increase in the younger individuals that we have seen over the last 10-15 years. So, between 45 and 50, again maybe trending more towards 45 because of the reasons I just said.

0:02:39.5 -> 0:02:41 Well, that's a big change from what I was used to. I was used to 50.

0:02:41 -> 0:02:45.3 Absolutely.

0:02:45.3 -> 0:02:52.1 And if I am not mistaken, maybe this has changed too - if you get a clean colonoscopy at your screening, then it goes to every 10 years, is that right?

0:02:52.1 -> 0:03:11.6 Correct. Yeah, if it is done through colonoscopy, every

10 years still seems a reasonable option and that is still the recommendation. If you do get screening through other options, like a stool-based test, that is a different framework and basically it is every year that you keep getting screened.

0:03:11.6 -> 0:03:29 Wow. There have been a lot of advertisements that I hear. I do not know if it is on TV or I am tuned in on radio or something, where they are advertising this Cologuard screen. Tell us about these stool-based screens, I do not know if that is the only one that is available or if there are others.

0:03:29 -> 0:04:41.8 Actually stool-based tests were the initial tests that we used for colorectal cancer screening, and basically the initial ones and the ones that are still on the market that are called FIT tests, those are the ones that are based on finding occult blood, just traces of blood in the stool. That has been extensively used. This is one of the more common ways of screening populations around the world, not so much in the US, but around the world, definitely the most used one. Cologuard is also a stool-based test that includes not only the detection of occult blood but also some particular changes in the DNA that go with malignant changes of cells, being shredded off from the colon. So, what Cologuard does is again, it is a molecular test to the already existing test for detection of occult blood in the stool, increasing the sensitivity a little bit and providing then a little bit of a higher detection rate than the FIT test, which is the traditional stool-based test.

0:04:41.8 -> 0:04:45.4 Are either of these tests as sensitive or useful as a colonoscopy?

0:04:45.4 -> 0:05:53.3 The gold standard is still colonoscopy for colorectal cancer screening and again we should also remind our audience that when we do stool-based testing, the positive ones need a colonoscopy to complete that screening. So, we could kind of call them prescreening tests. Colonoscopy is still the gold standard, but we do know from a lot of very well-done studies that from a population standpoint, using either one of these tests does prevent both colon cancer and colon cancer-related mortality. We often say that the best screening test is the one that gets done. And that is why we are emphasizing more choices; some people may not be that interested in colonoscopy, yet they could go with a stool test because it is something that you can do home, you do not need to prep, there are a lot of different reasons for that. Again, the best one is the one that gets done and I think that is the emphasis.

0:05:53.3 -> 0:06:04.5 And just to be clear from what you said before, if you have any of these stool-based tests and it is a negative screen, then you repeat it every year?

0:06:04.5 -> 0:06:19.2 For FIT test, it is every year. For the Cologuard, right now it is approved every 3 years. So, that is where we stand right now in terms of the stool-based tests. But for the stool-based test to be effective, it has to be every year.

0:06:19.2 -> 0:06:20.2 Even the Cologuard?

0:06:20.2 -> 0:06:38.7 No. The Cologuard, basically the FDA approved every 3 years even though the data is not extremely strong, part of the data is extrapolated from the FIT test because FIT is within the Cologuard test. But, if you are doing FIT, it is every year and if you are doing Cologuard, every 3 years.

0:06:38.7 -> 0:06:55.2 Gotcha. And it seems to me, you said it is a prescreen, but it sounds like you are accepting a negative result is meaning you do not need a colonoscopy right now?

0:06:55.2 -> 0:07:19.5 Correct. That is exactly the nature of the test. If you have a negative test and obviously we are not talking about anyone having any symptoms or anything like that, that would be a totally different story. We are talking about people who feel perfectly fine, who have no family history and no symptoms, feel well, then a negative is a negative and you just repeat it in a year and no need for colonoscopy if it is negative.

0:07:19.5 -> 0:07:41.6 Gotcha. Well, let us just take the population of otherwise healthy 50-year-olds who do not have a family history or anything worrisome, do not have symptoms, no bleeding in the stool or anything like that, and let us say 100 of them were to get colonoscopy, what percent would you expect to have cancer and what percent would have polyps or some other premalignant lesion?

0:07:41.6 -> 0:07:45.7 You are talking about 50 year olds?

0:07:45.7 -> 0:07:52.3 Well, or 45, whatever age you are going to start screening. Let us say 50, because that is a fashioned one.

0:07:52.3 -> 0:08:42.5 If it is 50, we know in the US population, about 30% of them would have a polyp, and probably around 1.5% or so that we will be finding a cancer at different stages. And the polyp detection rate is really high and so obviously not everyone who does have polyps would develop into a cancer because colon cancer is much less common than polyp detection, but we continue removing all the polyps just because we still do not have a good handle on which ones would end up being a cancer and which ones which just stay or even regress, which there is some evidence and maybe we are actually regressing some of them. But certainly the number of polyps we find is much bigger than the number of cancers, yet we know there is a very strong relationship between polyp development and cancer.

0:08:42.5 -> 0:08:50 Gotcha. And if you have polyps, will they show on the Cologuard test or is this something you only see in colonoscopy?

0:08:50 -> 0:09:24.8 The detection of polyps is much better with colonoscopy than the stool-based studies even though the Cologuard test seems to detect better dense polyps than the FIT test on its own. But the discussion here and the argument again is going back to which polyps are significant and which ones are not. And that may have a lot to do with the fact that these stool-based studies are still pretty good from a population standpoint in terms of preventing particularly colon cancer death.

0:09:24.8 -> 0:09:32.9 Gotcha. Why are people afraid to get colonoscopy if your insurance will pay for it?

0:09:32.9 -> 0:10:30.9 Well, I think there are still a lot of reasons. One of them is, you have to pause in your life for at least a day and a half and prep yourself, prep - taking that whole solution and all that seems to be a big barrier for a lot of patients, and then there are other issues too, which is the fact that it is an invasive test, it does have a very small percentage of risk, but it does have risk of complications too that we should know upfront about. So, if we think about a screening test, usually we like to see tests that are totally risk free. Well, this is close to that, but it is not 100%. People do get that choice offered and they should be told about the potential risks, they are there and that is something that some people consider in their choice in terms of getting a colonoscopy.

0:10:30.9 -> 0:10:40 When you said that 60% of the targeted population who should be getting screened, is getting screened, does that include the stool test as well as colonoscopy?

0:10:40 -> 0:11:15.5 Correct. That includes everyone. The way the data is being looked at is basically people who are up-to-date with screening, people who should be undergoing screening for colorectal cancer and their up-to-date with the screening. So, if they are having screening through stool-based test, they have it every year. If it is colonoscopy and it was negative - the initial one, then in 10 years. Everyone who is within the timeframe that is recommended for every screening choice, that is being up-to-date with screening.

0:11:15.5 -> 0:11:26 So, 60% is obviously not 100%, but it means a lot of people are getting what you would consider adequate screening?

0:11:26 -> 0:12:12.6 Absolutely. And I think that has a lot to do with the steady decreases in colorectal cancer incidence that we have seen since the 1980s. So, I think it is a big success of collective success here because we have been taking screening seriously and again you mentioned Katie Couric at the beginning of the program, and people like her have had a big impact. It has been documented that there are big spikes in terms of people going for screening after the televised colonoscopy that she underwent, Oprah Winfrey also that was a big one too, so the power of the media in this sense is definitely out there.

0:12:12.6 -> 0:12:19.7 How has the incidence or death rate from colorectal cancer changed since the 1980s?

0:12:19.7 -> 0:13:31.3 The incidence has gone down in a very steady way with a caveat here that we are all very concerned about, which is the steady increase in younger individuals developing colorectal cancer. Since the mid 1990s, we have seen about a 1.5% yearly increase in colorectal cancer in individuals younger than 50, which is really very worrisome. So, while the numbers have gone nicely down overall, the younger individuals have gone up and that has been really concerning and that is the trend that we need to tackle, and in response to that, that is why for instance, the ACS went down with their recommendations

for colorectal cancer screening to 45 instead of 50. That is the main reason. They did some modeling calculations, sophisticated modeling calculations that basically looked like it was cost effective to start at 45 instead of at age 50 just because of these changes in the incidence and that trend which has been again very steady since the 1990s.

0:13:31.3 -> 0:13:39.5 Well, that is very encouraging news and I am going to want to talk about those younger people in a bit, but right now, we need to take a short break for a medical minute.

0:13:39.5 -> 0:13:54.6 Medical Minute Support for Yale Cancer Answers comes from AstraZeneca, dedicated to providing innovative treatment options for people living with cancer. Learn more at astrazeneca-us.com.

0:13:54.6 -> 0:14:44.6 This is a medical minute about breast cancer. The most common cancer in women. In Connecticut alone, approximately 3000 women will be diagnosed with breast cancer this year, but thanks to earlier detection, noninvasive treatments and novel therapies, there are more options for patients to fight breast cancer than ever before. Women should schedule a baseline mammogram beginning at age 40 or earlier if they have risk factors associated with breast cancer. Digital breast tomosynthesis or 3D mammography is transforming breast screening by significantly reducing unnecessary procedures while picking up more cancers and eliminating some of the fear and anxiety many women experience. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio.

0:14:44.6 -> 0:15:13.4 Welcome back to Yale Cancer Answers. This is Dr. Steven Gore. I am joined tonight by my guest Dr. Xavier Llor. We have been discussing colon cancer in honor of colorectal cancer awareness month. Xavier, before the break, we were talking about the general decrease in the incidence of colon and colorectal cancer since the 80s, what has been the sort of absolute percentage difference, has it gone down 5%, 2%, 10%?

0:15:13.4 -> 0:15:18.8 So, we have seen close to 15% decrease.

0:15:18.8 -> 0:15:21.3 That is a lot. And does that affect the death rate as well due to colon cancer?

0:15:21.3 -> 0:15:37.6 Yes, that is a lot. It has affected the death rate, but obviously that has also to do with the improvement in treatment. So, both detecting earlier cancers and improving the treatment, which clearly has been seen has really contributed to that too.

0:15:37.6 -> 0:15:48.9 Right, and even though there has been great progress in treating advanced cancers, is it not still true that getting rid of the early ones is the best way to not have people die?

0:15:48.9 -> 0:15:50.6 Absolutely.

0:15:50.6 -> 0:16:01 So getting your screening early and getting those premalignant polyps taken out is a big thing right? Why do you think it is that younger

people are getting colon cancers? Is it related to the obesity epidemic?

0:16:01 -> 0:17:30.8 Absolutely. Obviously it is going to be environmental, it is going to be related to either what we breathe, what we eat, what we drink because we would not think about genetics when you are seeing such a fast change in a very short period of time. So, looking at what is different, there are some studies that they look at factors like this one - obesity, and the relationship has been found to be moderate. So, certainly, it has something to do with it, but it is not a big chunk of the explanation of why the change. There are a lot of other issues like the big increases being seen in the US, in Appalachia, in the western states like Washington and Oregon and also a little bit less but also in the northeast, that is where the bigger increases have been seen. So, there are a lot of theories about what is behind these changes - is it the water that we are drinking. Obviously, there is a good relationship between other risk factors like smoking and all that, we know that, but what is behind that change in the younger individuals, we really do not have a good handle. Obesity can play a role, but from all we know so far, it would not justify that big jump that we are seeing.

0:17:30.8 -> 0:17:46.6 I see. And one more thing on the screening before we move onto some other topic that I would like to cover - a few years ago, there was a lot of hubbub about the so-called virtual colonoscopy that used CAT scan or something like that, is that still a thing, where does that fit?

0:17:46.6 -> 0:18:45.5 It is still a thing, but most of the guidelines have stopped recommending it as an option. One of the important aspects about that is that even though technically it has gotten much better with detection of very small polyps, one of the important issues is unintended consequences of doing CAT scans in individuals is that in over 30% of cases, there are incidental findings, things that are found that are not related to the colon that need some follow-up and so there is a lot of concern about using that particular approach for colon cancer screening and ending up with a lot of expensive follow-up that has nothing to do with that and again they can really be very costly. So, there has been a lot of cooling down in terms of using that option though it is still an option.

0:18:45.5 -> 0:18:52 For example, you might see a lymph node that looks a little too big and that may lead to a biopsy for nothing, that kind of thing?

0:18:52 -> 0:18:56 Exactly. And this number is a pretty significant one.

0:18:56 -> 0:19:02.9 And if I am not mistaken, you still need to do some kind of prep for the virtual colonoscopy, don't you?

0:19:02.9 -> 0:19:24.7 Correct. You still have to prep even though the software has gotten much better and they do have a software that can kind of factor in the stool and all that, so it has continued to improve, but you still have to take your prep. So, if you are looking for an alternative that would spare you from that prep, it may not be the best.

0:19:24.7 -> 0:20:39.6 That is not the one. I can definitely testify that I myself signed up for my first colonoscopy right before my 50th birthday, I went when I was 50 plus 1 month and I did the same with my 60th birthday and I saw them as presents of health to myself and they were both great experiences really and the prep was really not so terrible at all and with the propafol anesthesia, it is like you just missed an hour of your life, you just do not even realize it and no after effects whatsoever and then when you get the negative result, which fortunately I was able to get negative results both times, you just feel really great and good to go for 10 years. So, just for our listening audience, the prep is really nothing to worry about and the procedure itself for me at least was certainly no big deal. Now, are there difficulties in access to appropriate screening for people with different kinds of insurance or with no insurance, how does that fit?

0:20:39.6 -> 0:21:30.5 It is still a big issue, particularly there are some important areas in the US that their availability for colonoscopy, not only just using it as a primary source for screening, but also in areas where the main program is stool based and then they need for the positive test to access a colonoscopy. That is still a big issue. And probably in our area, this is much less of an issue though we still have some capability issues here, but there are some areas, I am just thinking a program in South Carolina for instance, they had the hardest time trying to get their positive stool test, get a colonoscopy just because there were no endoscopies in the area available, and obviously in the states that have not expanded Medicaid, that is still a big problem.

0:21:30.5 -> 0:21:46.1 Yeah, and I imagine if you are in a big state that is rural, say Wyoming or some place like that, if you are already reluctant to get a prep done and then you have to travel 300 miles to get your colonoscopy, that is really quite a big distance I would suppose?

0:21:46.1 -> 0:22:09.2 Absolutely, yes. Sometimes, it is hard for us, we are in an urban area, it is very hard to imagine these types of barriers, but a lot of individuals in the US do have these type of barriers, they live in much less populated rural areas and often we have the same issue with urban areas where there is plenty of possibilities but the insurance becomes an issue.

0:22:09.2 -> 0:22:15.7 Yeah. And what about the affordable care act? Did that change laws about reimbursement for colon cancer screening?

0:22:15.7 -> 0:23:17 Right. That was obviously a big improvement from what we had before. There has been a loophole with the affordable care act, which is that the minute we are doing a biopsy, for instance removing a polyp or something like that, the procedure gets changed from screening to a diagnostic test and then you could apply co-pays. So, that has been an issue for the longest time. It has taken forever, a lot of medical institutions and the American Cancer Society are trying to lobby to change that aspect of the law to make sure that no one would get an unexpected bill just because there was a polyp found and all of a sudden that is no longer a screening colonoscopy. This seems to be on the way to being resolved, but it has been extremely painful and a lot of resources being

dedicated to really covering the loophole because that was a very unfortunate aspect that was not well covered under the ACA.

0:23:17 -> 0:23:28.9 But to be clear for our listening audience, the ACA does mandate that people of the appropriate age and risk group will not have to have a co-pay for the screening in general right?

0:23:28.9 -> 0:23:47.7 Exactly. It was something that was not as clearly written and that is why some insurance took advantage of that, but the ACA is very clear about that your approved screening test should be covered.

0:23:47.7 -> 0:24:20.7 But it behooves people to at least find or know that it is possible if they were to get a biopsy, there might be some cost associated with that, of course better to find a way to pay for that I think than to have an untreated cancer or a precancerous lesion right? So, that hopefully will not be a barrier for too many people. So, I know that one of your scientific interests is in familial or inherited cancer syndromes that lead to colon cancer right? Who should be worried about that?

0:24:20.7 -> 0:25:21.8 Absolutely. Certainly if in a family there are several family members not only with colorectal cancer but also other types of cancers that are commonly associated with that, like endometrial cancer or uterine cancer or other GI tract cancers, that should raise a red flag for sure. Other cases would be young onset; in general, as we said young-onset colon cancer has been growing and behind that it is not going to be genetics, but we take a group of individuals who are younger than 50, the incidence or the number of individuals who will have a genetic defect is much bigger than if you take a group of individuals who develop colon cancer after age 50. On average, you have about 15-18% of those younger individuals who will have a genetic defect, yet if you look at the older individuals, it would be more like 5%. So, there is a big difference, that is why younger age diagnosis for a cancer is usually a red flag too.

0:25:21.8 -> 0:25:31.6 So, let us say somebody is 45 or 40 and has colon cancer, will that colon cancer be screened for genetic abnormalities that might be familial?

0:25:31.6 -> 0:26:05.6 So, in general, that young age diagnosis would be an indication for screening. One of the things that is being recommended and currently done in many institutions is testing all colon cancers and endometrial cancers for a particular test that is like a prescreening test for lynch syndrome, which is the most common colon cancer syndrome, that is already done systematically but we are also moving towards a genetic testing to most individuals who are young at onset.

0:26:05.6 -> 0:26:16.4 And if the cancer indicates one of those syndromes, then do the children necessarily need to be tested?

0:26:16.4 -> 0:26:44.7 So in general, there are only a couple of cases where you would test children because that is when they can start having complications

as kids, but in lynch syndrome, the most common one, we do not usually test until age 20-25 because until that age, we usually do not do anything in terms of starting screening because the risk of cancer is still very, very low in that age.

0:26:44.7 -> 0:26:56 And when you test the individual that is 20 or 25, you are testing the genetics of their tissue or are they getting a colonoscopy?

0:26:56 -> 0:27:23.1 So, what we are doing is, we are doing germline testing which is looking at their DNA and looking if any of those genes that have been associated with a cancer syndrome are in their own DNA, that is what we are looking at. If that is the case, then usually at age 25 or so, we start the screening program according to the recommendations for every particular gene because they do change also by gene.

0:27:23.1 -> 0:27:29.2 And that DNA screening could be done by swabbing the inside of the mouth for example?

0:27:29.2 -> 0:27:30.3 Correct, yeah.

0:27:30.3 -> 0:27:30.1 So, it is not a painful or anything.

0:27:30.1 -> 0:27:33 Does not even need to be a blood test. It could be just the saliva.

0:27:33 -> 0:27:39.8 But if the parents' cancer does not have any of these genes, then what?

0:27:39.8 -> 0:28:17 So, if the parents' cancer does not have any of these genes, only the very uncommon one that we call familial adenomatous polyposis is really the only possibility in general because there is a significant percentage of cases of those that they can appear for the first time and so someone all of a sudden develops that mutation, yet their parents did not have the mutation. When it comes to lynch syndrome and the other common ones, those new mutations are extremely uncommon, so usually you have to have it inherited either from mom or from dad.

0:28:17 -> 0:28:29.6 Okay, so let me just get this straight. If your parent has young-age onset colon cancer and the colon cancer does not screen positive for any of these familial syndromes, do the children need any kind of screening before the usual age?

0:28:29.6 -> 0:28:58.5 When that happens, we do know that they still have higher chances of developing colon cancer even though we have not found any of those genetic defects. So, we think that there is still information that we are missing or maybe some shared environmental factors. Whatever it is, the recommendation is - if they develop early, we would start screening them with colonoscopy 10 years before the age of diagnosis of the parent.

0:28:58.5 -> 0:29:02.4 Gotcha. So, it is important for them to know because we do not really know all the genes probably yet right.

0:29:02.4 -> 0:29:18 Correct. And also important to know if we are parents or any first-degree relatives have had what we call advanced adenomas, because we do know that the risk of cancer is also higher and then we do recommend earlier colonoscopies and colonoscopy every 5 years.

0:29:18 -> 0:29:19.9 Advanced adenomas being the big polyps.

0:29:19.9 -> 0:29:31.4 Exactly. Big polyps are the ones that usually goes together with the size, but ones that have what we call advanced histology when the pathologist look at them.

0:29:31.4 -> 0:29:33.2 Precancerous?

0:29:33.2 -> 0:29:32.5 Exactly.

0:29:32.5 -> 0:29:59.6 Dr. Xavier Llor is a Professor of Medicine and Medical Director of the Cancer Screening and Prevention Program 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 Yale-CancerCenter.org. We hope you will join us next week to learn more about the fight against cancer here on Connecticut Public Radio.