

Yale CANCER  
CENTER  
*answers*

WNPR Connecticut Public Radio



*Hosts*

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**Colorectal Cancer Awareness  
Month 2013**

**Guest Experts:**

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**Yale Cancer Center Answers**

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*Welcome to Yale Cancer Center Answers with doctors Francine Foss and Anees Chagpar. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. If you would like to join the conversation, you can contact the doctors directly. The address is [canceranswers@yale.edu](mailto:canceranswers@yale.edu) and the phone number is 1-888-234-4YCC. This week, Dr. Chagpar welcomes Dr. Howard Hochster and Dr. Harry Aslanian for a conversation about colon cancer. Dr. Hochster is Professor of Medical Oncology, and Associate Director of Clinical Sciences at Yale Cancer Center and Clinical Program leader of the Gastrointestinal Cancers Program at Smilow Cancer Hospital. Dr. Aslanian is Associate Professor of Medicine in Digestive Disease and Associate Director of Endoscopy at Yale School of Medicine. Here is Dr. Anees Chagpar.*

Chagpar Let us start off by having you tell us a little bit about what each of you do? Harry, why don't you start by telling us a little bit about what your day to day looks like?

Aslanian I am a gastroenterologist at Yale and I specialize in different types of endoscopy. So, we see different types gastrointestinal problems and we try to solve and learn more about them. Using different types of endoscopy we can look in the colon with cameras in the upper intestinal tract and also with the combination of x-ray we can look into the bile ducts and pancreas ducts and get detailed pictures of the pancreas and the gallbladder from the stomach with ultrasound and endoscopy.

Chagpar Great and Howard, why don't you tell us a little bit more about what you do on a day to day basis?

Aslanian Thank you Anees, it's a pleasure to be here. I am a medical oncologist and my area of focus is gastrointestinal cancer including colon cancer and basically we are physicians, internists who focus on care of patients with cancer. We help manage the care of patients who have GI cancers. We give chemotherapy sometimes, and we work with our colleagues to come up with treatment plans for people who need treatment with cancer.

Chagpar As you know this is Colorectal Cancer Awareness Month and I think one of the things that we are hearing a lot about is the importance of picking up these cancers earlier with screening. Harry, can you tell us a little bit more about what the guidelines are for colorectal screening and what modalities are available to people? Who should get screened? How should they get screened and how often should they get screened?

Hochster Could I just interrupt for one second, you said that we should pick up cancers early but the whole idea of screening here is that we get polyps before they become cancer.

Chagpar Even better.

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- Hochster We know that there is a whole biologic process where DNA undergoes various steps in mutation to become cancer, but along the way they become growths that are polyps, adenomas, and if we remove those adenomas, and that's what Harry spends a lot of his time doing, going around picking off these polyps, they will not become cancer if we remove them at that point, so the screening is to totally prevent cancer.
- Chagpar Great.
- Aslanian That is an important point and screening is recommended for all individuals beginning at age 50, so even if you have no family history it is recommended to pursue screening at age 50 and it is important to know your family history for a variety of reasons and if you should have a family member who has developed colonic adenomas, which is a type of precancerous polyp or colon cancer, then you also want to know at what age they were when it developed and it is advised to begin screening 10 years before that, in particular if it is a first-degree relative, the closer the relative and the earlier the age that the cancer developed, the more pertinent it might be to an individual's own risk and the options for colon cancer screening are numerous, but colonoscopy is currently the preferred method. Alternative methods include screening the stool for small amounts of blood, as some cancers and occasionally polyps, will episodically bleed, and that is done by taking a stool sample and looking for evidence of microscopic amounts of blood, a shorter type of scope that looks at only the lower half of the colon called sigmoidoscopy can be pursued, but that has become less favorable because we know it is important to be able to see both the upper and lower part of the colon if possible. There has been interest in using what is called virtual colonoscopy, or using CT scan or MRI scan, however, a few specialized centers have had good results, but it has not widely applicable as a preferred method, and the problems with that study is that you still need to do the preparation, and there is radiation exposure with a CT scan and then if you find a polyp you need to have a colonoscopy to remove the polyp, so there are still some things that need to be worked out. Some other tests that are being worked on but still are not available is looking at the DNA of cancer of polyps that would be excreted into the stool, so a stool DNA test and perhaps a capsule or pill camera like we use for the small intestine, but that has not had good results in the colon so far.
- Chagpar If I am understanding you correctly, it sounds as if the whole purpose is to find these polyps and to pick off the polyps as Howard said, before they become cancer, and then even if you had a stool test and either found blood, or if you swallowed a camera and the camera saw a polyp, then you would still need to have a colonoscopy because as I understand that is the only way to really pick off these polyps. Is that right?
- Aslanian Exactly, that is a very important point. So the way that we are actually preventing colon cancer is by removal of the precancerous polyps so that they never have a chance to progress towards a cancer. Most polyps take roughly ten years to go from a precancerous polyp to develop into a

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cancer. So, it is a very unique setting where we can find precancerous lesions that can be removed and are visually identifiable and are slowly progressing so we can remove them before they ever become trouble.

- Hochster I think that what we were looking for in a screening tests is something that tells us who is not at risk, not a positive test, but a test that predicts who does not need a colonoscopy, and some of the DNA tests are getting to the point where they are pretty good about picking up the polyps, but again it needs to be a lot more sensitive before we tell people that they do not have anything and then those people do not need to get a test. So that would really be a much better prescreening kind of test if we get there, and Harry spends a lot of his time, as does his colleagues, doing colonoscopy on people with normal colons, and if we could cut that number in half and focus more on the people that need it, that would be more efficient.
- Chagpar When you talk about family history, some people may think that if they have a family history then they would be more at risk, whereas if nobody in your family has had colon cancer, do these people still need to be screened, or should they be screened with one of the stool tests instead of a colonoscopy, how does that work?
- Aslanian That is still being worked out, but even in individuals with no family history colonoscopy is currently the preferred method overall. Although that is a rapidly changing area and there are a number of complementary tests that could be useful if the performance can be improved somewhat in those other tests.
- Hochster There are about 50,000 to 60,000 cases of colon cancer deaths in the US every year and these could largely be prevented if we got people to undergo more rapid screening and 85% of these people have no family history, 85% of colon cancer is sporadic and there is no family history. So in people who do have a family history they need closer surveillance and start it earlier, but it is not going to be that relevant to most of the population.
- Chagpar You mentioned that people should get screened starting at the age of 50, or 10 years before the youngest family relative that was diagnosed. How frequently should that screening take place and does it matter what type of screening you have in terms of the interval, at which you should be screened?
- Aslanian Yes, once you have a screening test, if we identify adenomas then we know you are more likely to develop adenomas in the future, so in determining the frequency of the next test it would be a combination of family history, whether or not the individual had an adenoma detected and which test was performed. So if we look at colonoscopy, if say an individual who is 50 who has no family history and had no polyps, then the next screening test will be recommended in ten years and if they had a polyp, then it would typically be some combination of 3 to 5 years.

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- Chagpar In a lot of other cancers there has been a great deal of debate and changes recently in terms of screening guidelines with mammography for breast cancer, and with PSA for prostate cancer. How have guidelines changed or have they for colorectal cancer screening?
- Hochster There was a lot of debate originally about the benefit of screening colonoscopy, similar to the debates on things like screening mammography, but it became a lot more practical when people came up with these flexible colonoscopes where you could do widespread screening and then the studies came along pretty much and showed that you could actually reduce the incidence of cancers. Not only do you take out the polyps, but you actually reduce the incidence of cancer in the people who got colonoscopy, so that has been for the last 10 to 15, the standard recommendation. We have not really had a lot of improvement beyond that. I think that in the effort to be more cost effective people are looking at, could you do the stool blood tests, these hemoccult tests, together with a less invasive procedure, the sigmoidoscopy which just looks at the last part of the colon and does not go all the way around to the whole colon, and that might be a little bit more cost effective, but it is not that much better, so we have not really had a major technological advance in the last few years. I think the next thing will be probably the stool DNA test, but it still means that people have to take a stool sample and most people do not find that particularly acceptable, and that is part of the problem. It comes down to the whole thing of the clean-out, and if you are doing stool samples such as handling the stool sample, these are things that most people find unpleasant at best and there is a lot of reluctance to do it, but we are dealing with a kind of cancer that can be largely prevented with the right screening.
- Chagpar While we may think that the prep is not very pleasant, certainly getting colon cancer is not very pleasant either. Let us suppose, Harry, that somebody gets a colonoscopy and low and behold you find a polyp, what happens then?
- Aslanian Nearly all polyps we can remove right through the scope at the time of colonoscopy and that is where we are actually reducing that individual's risk, and by removing that polyp completely we take away the chance that it could ever progress towards cancer over the next five to ten years. So that is the most common scenario that we can remove the polyp right at the time of the colonoscopy, and as you heard from Howard, that is one of the persistent benefits of colonoscopy that we actually do a potentially therapeutic maneuver right at that time if we find a polyp and just to build on that further, we had some very exciting data that was recently published in the New England Journal that told us that colonoscopy reduces cancer mortality risks by 53% and that took about 16 years of follow-up to see that benefit and over that time period the technologies have improved dramatically, so I think we are doing better and better with that.
- Chagpar Fantastic, well on that note, we are going to take a break for a medical minute. Please stay tuned to learn more information about colorectal cancer and some of the new developments when we come back after the break.

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*Medical  
Minute*

*Breast cancer is the most common cancer in women. In Connecticut alone approximately 3000 women will be diagnosed with breast cancer this year. But there is new hope, earlier detection, noninvasive treatments, and novel therapies provide more options for patients to fight breast cancer. Women should schedule a baseline mammogram beginning at age 40 or earlier if they have risk factors associated with the disease. With screening, early detection, and a healthy lifestyle breast cancer can be defeated. Clinical trials are currently underway at federally designated comprehensive cancer center such as Yale Cancer Center to make innovative new treatments available to the patient. A potential breakthrough in treating chemotherapy resistant breast cancer is now being studied at Yale combining BSI-101, a PARP inhibitor with the chemotherapy drug irinotecan. This has been a medical minute brought to you as a public service by the Yale Cancer Center. More information is available at [yalecancercenter.org](http://yalecancercenter.org). You are listening to the WNPR Connecticut's Public Radio Station.*

Chagpar Welcome back to Yale Cancer Center Answers. This is Dr. Anees Chagpar and I am joined today by my guests Dr. Hochster and Dr. Aslanian and we are discussing colorectal cancer. Harry, I want to pick up where we left off before the medical minute, talking about the findings that were reported in the New England Journal that discusses the impact that colorectal screening is having. Tell us a little bit more about that paper and the effects that you have seen in terms of public awareness and whether that really has come to fruition or not.

Aslanian In disease entities that have a long time period, of say for a polyp to progress towards a cancer which may take many years to see the benefit, and it is very encouraging that we actually were able to document that we are preventing colon cancer deaths with the performance of colonoscopy and the removal of polyps, and they found that it takes about 10 years before you start to see a significant benefit from the polyp removal at the time of colonoscopy, but they documented a 53% reduction in colon cancer mortality in those people who had colonoscopy and had their polyps removed versus a group of the general population that did not pursue colon cancer screening. And I think on the converse you could say well 53%, why not closer to 100%, and I think that has been a mission amongst those performing colonoscopy and those looking to improve colon cancer screening, as to how we can reach closer to 100%. With colonoscopy we've pursued a number of quality measures, to say how can we be certain we are seeing the whole colon, how can we improve the preps and in particular we know that by looking very carefully at the colon and spending more time looking and training ourselves to see flat polyps, which are more like a carpet rather than a mushroom shape, and training ourselves to completely remove those polyps, we are seeing better and better efficacy and completely clearing the colon as much as possible of these precancerous lesions, and as Howard mentioned, the technologies are a moving target and the equipment for colonoscopy has improved and we are looking forward to these other technologies to continue to improve to make screening for patients easier and easier.

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- Chagpar Have you found with this that more patients are actually coming for colonoscopy, or is it as you say, Howard, still unpleasant?
- Hochster I think that it is still very unpleasant and most people do not want to deal with it but with the publicity where we have famous people getting colonoscopies on TV, it has become a lot more acceptable for people to think about it. Still, I have to say even amongst physicians we are not really as compliant as we should be with getting screened at age 50. So, it is still a big issue and how we can make this more user friendly and more accessible to the great majority of people. 150,000 to 160,000 people are diagnosed a year with colon cancer, but the incidence has gone down a little bit and that is due to more colonoscopies and better screening. We can probably cut that in half though.
- Chagpar That would be great. Harry, I want to get back to this sequence of events. So best case scenario, you do this colonoscopy, you find a polyp, you take the polyp out right then and there and it turns out that it is a benign polyp. But what happens if it is not a benign polyp?
- Aslanian The pathologist exams the polyp under the microscope and tells us the type and there are some polyps where it is a very superficial cancer and they determine if it was completely removed at the time of colonoscopy. If it is a more advanced polyp that requires additional treatment, then they would be referred to an oncologist and experts like Dr. Hochster and often in combination with a surgeon to determine what types of additional treatment might be necessary for that patient.
- Chagpar Howard, I want to turn to you and start the conversation about the treatment of colorectal cancer and what that entails. If the pathologist looks at the polyp that Harry just took out and says, Harry you did a great job you took out this polyp, but unfortunately it was not completely removed and it is a malignant polyp that we weren't able to catch before it transformed. What happens then and what are the courses of treatment that patients can expect? What are the side effects and what is the morbidity and mortality of colorectal cancer?
- Hochster The first thing I want to say is there are lots of treatments and many of them are curative, so one good thing about screening is that even if we find things that are a little beyond the benign polyp range, you are going to be better off because the treatment is usually less and more likely to cure you if we catch it earlier. So sometimes it is just a polyp that has got a tiny little bit of cancer that might be stage I, and if it is completely removed by the person who does the colonoscopy then you do not need anything else. More likely, if it has become cancer, it is more than just a polyp and it cannot all be removed by colonoscopy, and so they do a biopsy and it is kind of like a bulge that is halfway around the colon. So, they do a biopsy of that and if it is malignant but still in an early stage we would recommend surgery. You would see a surgeon, and they would remove a piece of your colon that includes that area. One thing that I want to reassure people about who are afraid of colon surgery because they think its means getting a colostomy and having a bag, but that is very rare actually. Most of the time they are going to take out the piece of the colon, sew it back together, and today with these laparoscopy techniques using long operating microscopes through

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kind of a periscope device they are very small incisions, so a week later you are back to normal and people would not even notice. So then assuming it's at that stage surgery may be all you need, but if it has gone a little bit beyond just the layer of the colon and it has gone to some of the lymph glands around the colon and these are the glands that we all over our body, people are most familiar with them in their neck when they get a sore throat, but you have those around your colon too. If cancer travels to the lymph nodes around the colon, which is kind of like the first stop on the way out, and we find it there, then we may have to give some additional treatment, which is most likely going to be a few courses of chemotherapy. Sometimes, if it is more advanced and a person does not go for screening and they start to have some symptoms like bleeding and it is even more advanced and the cancer had already spread beyond the lymph nodes into other parts of the body, then we might even skip the surgery and just treat it with chemotherapy alone.

Chagpar How well do patients do, in general? Let us suppose they actually heard the Harry/Howard message of get your colonoscopy and they went, but they still had a little cancer and they needed surgery or maybe surgery and a little bit of chemotherapy for a fairly early stage colon cancer, what can they expect in terms of five-year survival?

Aslanian Again, we can give better numbers depending on the stage, but the key thing for people know is that if it hasn't spread and is just in the colon and even in the lymph nodes, most people are cured, it is probably 75% to 85% at worst, for stage I, it is 95%, and for stage II, it is between 80 and 90%, so most of the time people will still be cured with the treatment we can give them, and surgery is the first modality that we use to treat this and the chemotherapy can improve your chances of being cured, but surgery alone will cure most people even with stage III colon cancer, more that 50% will be cured with surgery alone.

Chagpar It is always great news to hear that we can actually cure cancer and have really meaningful long term survival. Harry, I want to talk again with you a little bit about these polyps, so the idea is to catch them before they ever become cancer, but there is this progression between polyps that are precancerous to how they become cancer, right? Can you tell our audience a little bit about how that works? Does a polyp just wake up one morning and say, today is the day I am going to turn malignant?

Aslanian This was an important model in our understanding of cancer, this sort of polyp or adenoma progression towards cancer and researchers were able to look at polyps at different stages and then determine the different type of genetic mutations they had accumulated at each stage and begin to sort of put together a roadmap of what types of DNA injuries or genetic abnormalities are accumulated that cause some polyps to progress, some to spread as a malignant cancer, and some to just stay dormant. That has been an important step in our understanding of how cancers develop.

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- Chagpar      Howard, your other role is running clinical trials and so much of what we hear today in clinical trials and clinical research is about genetics and genomics, so how is that being exploited in the world of gastrointestinal cancers to help us to understand the biology of this disease and how we can push that cure rate even further?
- Hochster      This is a very important area of research and helps us understand a lot more about the biology and sometimes about the right kind of therapies. For GI cancers, the story is not as clear or as simple as in some cancers. In some cancers you have one mutation in a particular signaling molecule, something we call a driver mutation, and if you get a drug that turns off that driver mutation, then you are treated usually pretty well, maybe cured even, and that does not seem to be the case in colon cancer. Colon cancers seem to be a little bit more complicated in that there is some underlying mutation such as the mutation in the KRAS gene that is in 40%, and that is one of the earliest mutations and even most polyps and adenomas have KRAS mutations. So, from there other mutations are kind of accumulated along the way and it is a lot more complicated than just one target that we can turn off, but being able to identify these specific gene mutations in an individual helps us personalize the therapy for them and that is one of the therapeutic messages that we are trying to get out to the people at Smilow Cancer Hospital, is that we can treat you better by understanding the gene makeup of your cancer and that does not require any additional testing. Basically once the cancer is taken out or even biopsied by Dr. Aslanian and his colleagues, we can extract the DNA from the snip of the colon cancer and then we can use it to look at the DNA gene mutations and help understand your cancer better and give better treatment.
- Chagpar      We have about 45 seconds left in the program, and I want to get one final thought from you Harry and Howard, if you were going to tell our audience to remember nothing else from today's program, what would that be?
- Aslanian      I would encourage everyone to pursue colon cancer screening, discuss it with your primary doctor and I think people will be pleasantly surprised at how easy and perhaps even interesting the processes is.
- Chagpar      Howard?
- Hochster      I second that motion and would like to again emphasize that colonoscopy is a safe, simple procedure even though it is a little unpleasant for many people to have the prep but we can actually prevent cancer by removing the polyps. So, when they do the test and remove a polyp, it prevents you from getting cancer and can really help you avoid a lot of complications and problems down the road.

*Dr. Howard Hochster is a Professor of Medical Oncology and Associate Director for Clinical Science at Yale Cancer Center. Dr. Harry Aslanian is Associate Professor of Medicine in Digestive Diseases and Associate Director of Endoscopy at the Yale School of Medicine. If you have questions or would like to add your comments, visit [yalecancercenter.org](http://yalecancercenter.org), where you can also get the podcast and find written transcripts of past programs. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network*