00;00;00;19 - 00;00;32;08 WNPR Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital. Welcome to Yale Cancer Answers. The director of the Yale Cancer Center is Dr. Eric Winer. Yale Cancer Answers features conversations with oncologists and specialists who are on the forefront of the battle to fight cancer. Here's Dr. Winer.

00;00;33;05 - 00;01;03;20 Dr. Winer We're now in the month of August, and you may not know this about this very hot month, but it is Appendix Cancer Awareness Month. You actually may not even know very much about appendix cancer. Of course, mostly we hear about the appendix when people need appendectomies because they have an infection in the appendix. And while that can be life threatening, it's usually dealt with quite readily by our surgical colleagues. But the appendix can also be a place rarely where cancer forms. It's not a common problem.

00;01;03;20 - 00;01;37;21 Dr. Winer According to the National Cancer Institute, appendix cancer only affects 1 to 2 people per million annually in the U.S. So this is indeed a relatively small number of individuals, but it seems to be increasing and increasing, perhaps more so in younger adults. There was a recent study in the annals of internal Medicine that found that appendix cancer cases had tripled for Americans between the ages of 49 and 54.

00;01;38;11 - 00;02;08;08 Dr. Winer There are still many questions, but this, of course, raises some concern. Here to help us understand cancer of the appendix is Dr. Kiran Turaga, division chief of surgical oncology at Yale School of Medicine's Department of Surgery. He's also the assistant medical director of the Cancer Center Clinical Trials Office. Kiran, thanks so much for joining us this evening.

Dr. Turaga Thank you, Eric.

00;02;09;15 - 00;02;41;20 Dr. Winer You're relatively new at Yale. You've been here now, I think, pushing three years and you came here from the University of Chicago. Is that correct?

Dr. Turaga Yeah. Yeah, that's correct. I was at the University of Chicago for six years prior to joining Yale. And it's been a wonderful time here.

Dr. Winer And you've been interested in this area of cancer, of the appendix and in general in abdominal malignancies for really your whole career.

00;02;42;16 - 00;03;14;04 Dr. Turaga Yeah, I think, you know, I was affected by patients that I saw during my surgical training who dealt with cancers of the appendix that had spread to the lining of the abdomen called the peritoneum, and certainly came across some mentors that guided me in this field that allowed me to develop my skills and learn more about this disease and over the last 15 years have dedicated my career to the study and treatment of patients with appendix cancer and those that have metastases.

00;03;15;13 - 00;03;47;03 Dr. Turaga And I think sometimes people, when they

hear the word oncologist, they think about medical oncologists. Oftentimes there are surgeons, particularly in the past, who did a mix of cancer cases and lots of other different kinds of surgery. And increasingly, there's a whole group of people like you who are really every bit as much oncologists as medical oncologist. It's just the focus is a little different.

00;03;47;18 - 00;04;33;01 Dr. Turaga Yeah, you know, I think people forget that, you know, chemotherapy and a lot of cured of intense treatments for what we call solid tumors. So tumors like the breast, prostate, lung, GI, cancers, appendix cancers is actually surgical. So a lot of absolutely a lot of cancers are treated and even cured with surgery alone. And I think the there was a society named the James Ewing Society at Memorial Sloan Kettering that sort of fostered this thinking where we thought of ourselves not as surgeons as much as we thought of ourselves as cancer doctors who had a specific modality that we use to treat cancers.

00;04;33;01 - 00;04;57;26 Dr. Turaga And I think the advantage of thinking like that is you're thinking more holistically for the patient. And I think many surgical oncologists will probably agree with me and ascribe to this philosophy that, you know, come a day where we don't have to do a surgery on patients with cancer, we would we would actually be delighted. So I think, you know, just to remember that our focus is on treating and curing the cancer with the modalities we have available, which is surgery.

00;04;57;26 - 00;05;26;08 Dr. Turaga But working in a multidisciplinary fashion with medical oncologist, radiation oncologist, geneticists, pathologists, you know, I think is the key to this.

Dr. Winer Well, and I think as a medical oncologist, I would just chime in and say this — we hope there's a day when there's no more chemotherapy or other treatments that cause significant side effects. And I mean, ultimately the goal is that we just won't have cancer and will prevent it.

00;05;27;10 - 00;05;58;00 Dr. Winer But it is striking over the last decade or two how cancer care for patients with solid tumors. So this is everything. But patients who have leukemia and lymphoma who are really cared for by hematologist or medical oncologist. But for the rest of of our patients, it's really a multidisciplinary approach. And we have surgeons and medical oncologist and radiation oncologist and and nurses and social workers and many others involved.

00;05;58;25 - 00;06;25;19 Dr. Turaga And of course, you know, none of us could do without our friends in pathology and radiology as well who are sort of behind the scenes, but support itself all the time. I mean, I think the tougher the problem, the better the team you need. And I think, you know, we clearly all agree that cancer is one of the striking problems of humankind right now.

00;06;25;19 - 00;06;47;19 Dr. Turaga I mean, it's overtaking heart disease, as you know, the number one cause of mortality for humans. And so I think we

just need all the smart minds to get together and figure out how we're going to both cure it as well as reduce suffering from it, whether it's, you know, physical, emotional or financial or others. Absolutely.

00;06;48;00 - 00;07;17;28 Dr. Winer So let's get into talking about cancer. So can you just explain to our listeners what cancer of the appendix is? Maybe you could make a few comments about how common it is. I realize I addressed that just very briefly in the introduction. And anything else on your mind about cancer of the appendix?

Dr. Turaga Yeah, I think, you know, I'll start off by just talking a little bit about the appendix itself.

00;07;18;23 - 00;07;40;22 Dr. Turaga You know, the appendix is an organ that we've for a very long thought was vestigial. We thought it didn't have any function and it was just an evolutionary remnant in human beings. And I think recently there's been several studies that have identified the important role of the appendix in both maintaining normal bacteria as well as the important role it has in the immune system.

00;07;41;04 - 00;08;01;18 Dr. Turaga It sits right at the junction of the colon and the small intestine, so the large and the small intestine, but is distinct from both of them. So if you actually look at it, it actually under the microscope looks very distinct from both of them. And I think that's a very interesting aspect of the appendix. And when you think of appendix cancer, it's a very heterogenous disease.

00;08;01;18 - 00;08;30;24 Dr. Turaga So while we would love to think of appendix cancer as one problem or one entity, it's actually a combination of different entities which can range from being very simple, very benign, very treatable, very consistent with long survival to this very aggressive, very malignant type of cancer. And so I think it's a it's a simple word that that encompasses this sort of very complex set of diseases that occur in the appendix.

00;08;30;24 - 00;08;49;05 Dr. Turaga The fortunately, it's not a very common cancer. So I think as you alluded to, Eric, it's you know, we used to think it's about one in a million. And I think as we're going to talk about in the study, you know, we're thinking it's actually becoming one in 100,000. So it's still not as common as, say, the common cancers, you know, breast, skull and lung, prostate.

00;08;49;19 - 00;09;18;04 Dr. Winer But I think still alarming to think about, you know, this cancer increase that's occurring and what what proportion of patients are just diagnosed when they have an appendectomy for presumably rule out appendicitis. And there's just a little spot of cancer there. Is that a common presentation or do people tend to be symptomatic from the cancer itself?

00;09;18;04 - 00;09;41;10 Dr. Turaga So I think we can we can think about this in two ways. So if you think of all patients with appendix cancer, a third of

them will present with appendicitis. So not all appendix cancers will present symptomatically. So often patients will be asymptomatic and it's either found on a scan or they're having symptoms that are different than appendicitis, you know, fullness, bloating.

00;09;41;24 - 00;10;00;28 Dr. Winer And is the appendicitis related to the cancer when people develop this?

Dr. Turaga Yeah, absolutely. So I think the appendix is sort of this channel. It's a very thin sort of organ like the earthworm, and inside it needs sort of normal circulation of mucus and fluids and everything needs to come in and out from the colon in the small intestine.

00;10;01;10 - 00;10;27;05 Dr. Turaga And sometimes these tumors or polyps can actually block that very thin channel. And that's how appendicitis occurs. Very similar to, say, a stool ball called the fecal it or certain bacteria. So one-third of them will present with appendicitis. But if you take all patients who have appendicitis, who then say, have surgery and you look at that pathology, you know, less than 8% of patients will have any kind of sort of pathology.

00;10;27;05 - 00;11;01;24 Dr. Turaga And the number of patients that will have a tumor is less than a percent. So it's not a very common occurrence from having an appendectomy to have a tumor. So if somebody presents with appendicitis and they're going in for surgery, their family member, that shouldn't be worrying that they have cancer. That's correct. I think the key thing that they and their family members should do is to make sure that the appendix is appropriately studied by a pathologist and that they have certainly looked at the appendix to make sure there aren't any tumors in it.

00;11;01;24 - 00;11;27;07 Dr. Turaga I think that's pretty much what is standard of care, at least in the United States. But it's fascinating, Eric, and in countries such as, you know, developing countries or underdeveloped countries, many times these specimens are not even examined. The appendix is taken out and it's basically thrown in the trash bucket. And so I think our plea has always been at least to make sure that a competent pathologist looks at it, make sure there's nothing unusual and deep.

00;11;27;17 - 00;11;53;15 Dr. Winer And it's done that way in those countries, because so commonly it's just nothing.

Dr. Turaga That's exactly right. And plus, it's obviously a resource, right. So if you if you need someone to look at stuff, it's more money. And then for patients who don't initially have appendicitis, the cancer is found with other symptoms or routinely, as you mentioned, on scans.

00;11;54;04 - 00;12;37;02 Dr. Turaga Yeah. So the appendix is an unusual organ. You know, unlike, say, colon cancer, which tends to spread to the liver, the lungs and other organs, appendix cancer is predominant, tend to spread to the peritoneum. In fact, there are certain appendix cancers that will never spread to the lungs or the liver. And so it's a very unique problem where

patients will present often with sort of bloating, fullness, inability to eat, and then they get a CT scan and then you see fluid in fact, it's difficult to actually see the cancer itself or sometimes they're getting a scan for something else and you see some nodules or some lumps or you see some thickening or fluid and

00;12;37;02 - 00;12;59;19 Dr. Turaga Then, you know, you investigate it further to find out what it is.

Dr. Winer And how old are these patients generally?

Dr. Turaga So I think the average age of patients with appendix cancer is in the fourth and fifth decade of their life. So most patients. So the average age we see here at Yale is about 52. And I think most patients are diagnosed in that sort of age cohort.

00;13;00;21 - 00;13;26;25 Dr. Turaga So relatively young, younger than some cancers for sure. I think, you know, it's scary that we're starting to see, you know, 19 year olds and 30 year olds and 20 year olds in our clinic now being diagnosed with appendix cancer, which is why we're all alarmed with this rising incidence of appendix cancer.

Dr. Winer And just a couple of quick questions before we take our break. 00;13;27;22 - 00;13;53;18 Any predominate predominance in terms of men versus women?

Dr. Turaga We saw different studies have found slightly different findings. So it's a little difficult to say which one is more common. We think women tend to have a slightly higher predominance of certain subtypes of mRNA subtypes and men may be goblet cells, but I think the study, it's not very clear.

00;13;53;18 - 00;14;24;18 Dr. Turaga So I would say right now we think both sexes that are affected and any known risk factors there are and I think this is also a big area of research for us as well as nationally, the big things. So the three sort of big things to think about is, number one, we've found that about 10% of patients with appendix cancer have hereditary mutations, so they have germline mutations, which is a new finding which has been corroborated and validated in multiple different studies.

00;14;24;18 - 00;14;48;20 Dr. Turaga And so I think that's something that is interesting. The second we've found a connection of appendix cancers with autoimmune diseases. So diseases like lupus, rheumatoid arthritis, ulcerative colitis, a third of patients with appendix cancer will have an autoimmune disease compared to, say about 10% of other cancers like breast or colon. So it's a much higher incidence of that.

00;14;49;14 - 00;15;14;23 Dr. Turaga And I think there's a lot of interest in this theory that microbial ah, dysbiosis, which means that different types of bacteria in the appendix are associated with appendix cancers. One of the bacteria that's been implicated in colon cancer called Fusobacterium is often found at a very

high proportion and in the appendix as well. So I think it's something that, you know, all of us that study appendix cancer are very fascinated by.

00;15;16;19 - 00;15;47;25 Dr. Winer Well, we're going to take a break. We'll be back in just a minute with our guest, Dr. Karen Turaga, who is the chief of surgery oncology at Yale School of Medicine.

WNPR Funding for Yale Cancer answers comes from Smilow Cancer Hospital, which provides a multidisciplinary approach for treating appendix cancer, including advanced surgical techniques like hypothermic intraperitoneal chemotherapy. Learn more at Smilow Cancer Hospital dot org. 00;15;48;06 - 00;16;18;14 There are over 16.9 million cancer survivors in the US and over 240,000 here in Connecticut completing treatment for cancer is a very exciting milestone, but cancer and its treatment can be a life changing experience. The return to normal activities and relationships may be difficult and cancer survivors may face other long term side effects of cancer, including heart problems, osteoporosis, fertility issues, and an increased risk of second cancers. 00;16;18;29 - 00;16;47;25 Resources for cancer survivors are available at federally designated comprehensive cancer centers such as the Yale Cancer Center and its Smilow Cancer Hospital to keep cancer survivors well and focused on healthy living. The Smilow Cancer Hospital Survivorship Clinic focuses on providing guidance and direction to empower survivors to take steps to maximize their health, quality of life and longevity. More information is available at Yale Cancer Center dot org. 00;16;48;06 - 00;17;27;23 You're listening to Connecticut Public Radio.

Dr. Winer Hello again and welcome back to your Cancer answers. I'm Eric Winer. And tonight I've been speaking with Dr. Kieran Turaga, division chief of surgical oncology at Yale School of Medicine, and who is a surgeon at Smilow Cancer Hospital focusing on appendix cancers, but more broadly on intra-abdominal cancers in the first half of the show, we talked about how rare appendix cancer is, although maybe a little more common than at least some of us had thought in the past.

00;17;28;09 - 00;18;08;14 Dr. Winer And we talked about how it is that patients come to be diagnosed with appendix cancer. We ended talking about a bacteria that might be found more commonly in the appendix than one would expect otherwise. And more and more in the past few years, we've been hearing about the microbiome and cancer. And I'm wondering, Kiran, if you could just comment about that and your thoughts about it, both related to appendices cancer, but more broadly in terms of GI cancers?

00;18;09;21 - 00;18;35;28 Dr. Turaga Yeah, I think, you know, the important thing about the gastrointestinal tract is that we have a very large population of bacteria in it and normal health of the colon, the intestines, the stomach and any of the GI organs relies on having normal bacteria. And these are called commensal. So which means usually the bacteria are just hanging out in these intestines.

00;18;35;28 - 00;19;04;22 Dr. Turaga They help with digestion. They help

with, you know, promoting some of these normal physiological functions of these intestines and organs. And as our diets have changed, as we are exposed to different environmental factors, antibiotics that are prescribed very often and differently than, say, 100 years ago, we are also noticing that the composition of these bacteria inside the human intestines has changed quite dramatically.

00;19;05;15 - 00;19;29;16 Dr. Turaga And right now, very clearly it's been shown in almost all cancers that the type of bacteria that are in the intestines, in the colon are very distinct.

Dr. Winer When folks develop cancers of, say, the colon, the the small intestine, the appendix, as well as other organs. The thing that is still an area of investigation is how do they contribute to this?

00;19;29;16 - 00;19;49;21 Dr. Winer So are they causal or are they associated? Are these is the change in the bacteria causing these cancers or is the change in the bacteria a result of something that is causing the cancer but also causing the change of the bacteria?

Dr. Turaga So I think that's the area of highest investigation right now. Yeah, No, it's it's a fascinating area.

00;19;49;21 - 00;20;21;25 And of course, there's also talk about the microbiome affecting the response that that patients have to immunotherapy and potentially other treatments as well. Yeah, And I think, you know, what is particularly interesting for us as surgeons is that when we cut intestines or colon and we so it together, we've also found that the type of bacteria in the colon actually predicts for leakages from these connections.

00;20;21;25 - 00;20;55;29 Dr. Turaga Really. So it's a very interesting. So surgical complications, surgical complications, liver failure after liver resections. So all of these have also been implicated based on the type of bacteria in your intestine. And in fact, now there's a lot of studies where pre-surgery patients are being given an altered diet, a diet that's not quite like the high fat Western diet, but a more Mediterranean diet, diet where patients can repopulate their their microbiome a little bit in order to do recover better from surgery.

00;20;56;01 - 00;21;48;14 Dr. Turaga And now I'm really sort of veering off course. But people talk frequently about the overuse of antibiotics. And of course, one of the concerns about antibiotics is they just dramatically alter the normal bacteria in one's GI tract. And so, again, you know, this track is really, really important. So as a surgeon who has focused on cancer for years, I have no doubt that you have seen innumerable patients who had symptoms that went on for a long time before they were diagnosed and that's probably even more true in younger patients where nobody thinks anybody young has anything wrong with them.

00;21;49;13 - 00;22;18;16 Dr. winer And do you have thoughts about this and any comments to our listeners about how they should be advocates for themselves when when these problems arise?

Dr. Turaga Yeah, I think just like you, Eric, you know, this this phenomenon is so pervasive where majority of our patients have some degree of symptoms. You know, they know their bodies very well, and they'll go to the physicians and say, hey, you know, this is not right or this is not right.

00;22;18;16 - 00;22;38;25 Dr. Turaga And they're the challenges we have specifically for both the, you know, appendix cancer and intra-abdominal cancers in general is that it's not easily detectable on scans. There's no easy blood test that finds it. And so often these young patients will go to doctors, get scans or even not even get scans. You know, many times they're just like, oh, you're fine.

00;22;38;25 - 00;23;05;16 Dr. Turaga Just go take care of it, or it's irritable bowel. And then by the time they're diagnosed, they're it's either very advanced stage four or just very difficult. And the second problem with appendix cancers is that we don't actually have good knowledge around it in the community. So in fact, many times these patients that would actually be cured of their disease or live a very long time will be told by well-meaning doctors that you're going to live only three months or four months.

00;23;05;16 - 00;23;27;24 Dr. Turaga And so I think, you know, things like the appendix, cancer awareness Month that you alluded to earlier, bringing people together to kind of share knowledge and growth. But I think the most important thing is that patient health care team partnership. And as a patient, if you are one of those folks that is being told that don't worry about it, don't worry about it, but there is something that bothers you.

00;23;28;02 - 00;24;01;14 Dr. Turaga And I think advocating for you incessantly or yourself incessantly is the only thing that we as cancer doctors can can strongly say is important.

Dr. Winer Where I think that's very well said and I can't say it often enough, which is that for patients that if they feel like they're not being listened to by the people who are seeing them, that they really just need to move on and make sure that people listen to them.

00;24;02;24 - 00;24;57;24 Dr. Winer It's and it's and of course, it's a challenge for doctors because doctors are oftentimes seeing large numbers of patients. And many of those patients will have symptoms that turn out to be nothing serious. But at the same time, you have to listen carefully. And we all, of course, can do better there. I want to move on and spend a few minutes on your research as someone who has been very interested in cancer of the appendix and other abdominal malignancies that spread within the GI cavity, you've really been at the forefront of looking at new treatment approaches for these patients.

00;24;57;24 - 00;25;25;15 Dr. Winer And maybe you could talk for a minute about how cancer spreads within the abdominal cavity and then about some potential options.

Dr. Turaga Yeah, no, thanks for that question, Eric. I think when you think

of how cancers spread, there's three sort of broad mechanisms. We think about cancer spreading. One is through the bloodstream, which is often how it goes to the lungs and liver and brain and bone.

00;25;25;26 - 00;25;45;19 Dr. Turaga The other is through the lymphatic channels, which is often what you'd hear in things like breast cancer, melanoma, colon cancer. It kind of spreads through the lymph channels as well. And the third is what we call peritoneal dissemination, which is sort of like if you had a balloon filled of mucus, put it in a room and popped it when the mucus kind of spreads along all the surfaces, it's touching all the surfaces.

00;25;45;19 - 00;26;09;12 Dr. Turaga It's not actually growing through the wall or through the floor, but it's sort of there. And that's the peritoneal dissemination, which is an area of interest for me. And the fascinating thing is when cancer spread to the bloodstream, if you look at the DNA in the blood, you can actually catch this cancer in the blood. So in fact, things like liquid biopsies where you're using blood to detect these cancers becomes very attractive.

00;26;09;27 - 00;26;36;10 Dr. Ruraga But when it spreads to the lining, the crazy thing is that the cancer tends to stay in there and this peritoneum is a remarkable barrier of letting this cancer not leak, walled in, walled in. And so it's a great way of trying to target it with just regional treatments where we treat this cavity with surgery, with chemotherapy inside the belly novel, agents.

00;26;36;10 - 00;27;05;22 Dr. Turaga And that's sort of an area of interest for me both.

Dr. Winer How do you find these cancers early and then how do you actually treat them with novel stuff inside the peritoneal cavity and how effective is that when the cancer from the appendix spreads within the abdominal cavity?

Dr. Turaga I think it depends on the type of cancer. So in fact, there's some types of appendix cancer where we tell patients they're going to get cured or live, you know, 20 years, 30 years and live a fairly normal life.

00;27;05;22 - 00;27;30;28 Dr. Turaga And there are some cancers in which patients will die within 2 to 3 years despite our best efforts at trying to treat it. So I think really getting a good sense of pathology is very important. Understanding the real drivers of this cancer is it mutated in a certain type. You know, we call these mutations gene or Cress Samad for and Tp53 sort of the four hallmark mutations that you've got to look for in these appendix cancers.

00;27;31;14 - 00;27;49;21 Dr. Turaga And then, of course, the type of treatment can we actually do surgery and clean it out? What kind of intraperitoneal chemotherapy do we place or do we just not do chemotherapy? So these are options and they were kind of IV chemotherapy. So really it's a multidisciplinary approach to thinking about the best way of taking care of patients with this.

00;27;50;07 - 00;28;15;20 Dr. Winer And of course, when patients are facing these kinds of problems while living two or three or four years may sound like a

short period of time, we don't know what's going to be available in two or three or four years.

Dr. Turaga Yeah, I think, you know, this is a journey that I'm sure you will agree with as well. You know, the first part of my career, we barely saw any new drugs, any new treatment for cancer.

00;28;15;20 - 00;28;40;09 Dr. Turaga I mean, there were slightly better. There were. Okay. And just in the last five years, it is just remarkable to see the pace of progress. And I think this is also, you know, not to distract too much, but why it's important to invest in medical research, because this is really why we're now in a different place.

WNPR Dr. Kiran Turaga is division chief of surgical oncology at the Yale School of Medicine's Department of Surgery. 00;28;40;24 - 00;28;59;01 If you have questions, email questions to canceranswers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. We hope you'll join us next time to learn more about the fight against cancer. Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital.