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SPEAKERS Dr. Jeremy Jones, Narrator, Dr. Gazelka

Narrator 00:01 Coming up on Mayo Clinic Q&A:

Dr. Jeremy Jones 00:03

Which patients are going to be at highest risk of having colon cancer and trying to find them early? Because we know for a fact that finding early is probably the biggest prognostic indicator that we have.

Narrator 00:16

March is National colorectal cancer awareness month, a time to promote awareness and stress the importance of colorectal cancer screening and prevention.

Dr. Jeremy Jones 00:25

We are getting better at trying to sort of make this more palatable, more easier for patients to get screening. Because ultimately, that's the goal. We want to make it as easy as possible, as least invasive as possible, but to still keep it as effective as possible.

Dr. Gazelka 00:39

Welcome, everyone to Mayo Clinic Q&A. I'm Dr Halena Gazelka. It's March and that means that it's colorectal cancer awareness month. Colon cancer is a type of cancer that originates in the last portion of the large intestine where the colon is. Rectal cancer originates in the last several inches of the large intestine or the rectum. Together, they comprise a group of cancers called colorectal cancers. The National Cancer Institute estimates that 150,000 Americans were diagnosed with colorectal cancer in 2020, and over 53,000 individuals died. We have some good news today, though, and that is that when colorectal cancer is diagnosed early, that is before it has spread outside of the colon or the rectum, that the five year survival rate is over 90%. Here with us to discuss today is our expert, Dr. Jeremy Jones, who is a medical oncologist at Mayo Clinic in Florida. Thanks for being here today, Jeremy.

Dr. Jeremy Jones 01:42

Thank you so much for having me. I really appreciate it. I think that this is, you know, really a very pressing issue, and it really deserves all of the attention that we are giving it.

Dr. Gazelka 01:54

Well, it is wonderful to have you here to explain. You know, this is for our listeners. And I myself learn so much when we go over these things. So I'm excited to have you here. The first question I want to ask you, is can you tell us a little bit about what is colorectal cancer, and is anal cancer part of colorectal cancer?

Dr. Jeremy Jones 02:14

Yeah, so the short answer is that colorectal cancer is separate than anal cancer, it's actually two separate types of, when we traditionally speak of, it's two separate types of cancer cells. So it's the difference between what we call an adenocarcinoma or a gland forming cancer, which we predominantly see in the colon and the rectum. And a squamous cell carcinoma or sort of a lining type of cellular cells that we see in anal cancer. So in general, we separate those into two very distinct subpopulations, they're treated actually quite differently. And so, we'll focus mostly on colon and rectal cancer today. And so, more broadly, colon cancer, or rectal cancer is a cancer that arises within the glands of the colon. And what I like to tell patients is that essentially, these cells are normal cells, and then at some point along their development, they forget how to die. So a normal process for cells throughout our entire body is that they are they able to grow and to replicate when needed, and then also die when needed. And one of the unique things about cancer cells, and this is really throughout the body, is that these cells sort of forget how to die.

Dr. Gazelka 03:36

That is a really interesting, I thought that distinction that you made between the types of cancer was very fascinating as well, that it makes such a difference, what the cellular origin is of the cancer when you're considering how to treat it.

Dr. Jeremy Jones 03:48

It truly does. So you know, we think of these things as sort of anatomical landmarks, but the difference within the actual cell types makes a huge difference, because each different cell type is actually more susceptible to one therapy versus the other.

Dr. Gazelka 04:08

What causes colorectal cancer, Jeremy?

Dr. Jeremy Jones 04:11

So it's a great question. And it's a question that we don't have an answer for. There is a number of different things that can increase the risk of developing colon or rectal cancer. But we don't really have a great answer as to why one person gets it versus another person who doesn't. We know that there's a number of different risk factors, which we can talk about, that raise sort of the proportional risk, or you know, this population of people will have a 20% increased risk. But we don't really have a set if you

have this X, Y or Z, you will develop colon cancer with 100% certainty. And so unfortunately, that is sort of the case, really for all cancers, is that for the vast majority of the time, we don't know exactly what causes a specific cancer. What I tell my patients is the more that we study, the more that we learn about cancer in general, the more the question actually becomes how in the world do we not all have cancer? How does every cell, I mean there's just billions and billions of things that have to go exactly right, multiple times a day for us not to develop cancer. And so it truly is sort of a miracle that we don't see even more of these cancers. Now, obviously, we want to have zero cancers. But the more we learn, the more we realize that there's just so much interplay that's going on throughout. It's actually quite surprising that things work as well as they do.

Dr. Gazelka 05:34

I love that perspective, Jeremy, that it's miraculous how our cells recover every day. Would you tell us a little bit since you mentioned it earlier, what are the risks of developing colorectal cancer?

Dr. Jeremy Jones 05:46

So by far, the biggest risk that we know of is age. So advanced age is sort of going to be the highest risk population. Now, I say that with the caveat that has been sort of the traditional risk factor. And we'll get a little bit more into sort of the unfortunate trend that we've seen lately, in younger patients actually had been having significant increased risk, 50% increased risk of developing colon and rectal cancer over the last 30 years or so. So I think we should definitely get into that later. But if you look, from a population point of view, still age is one of the biggest risk factors. Having a family history, there are certain genetic predispositions can increase the risk, although again, that counts for a very small proportion of patients who actually have colon cancer. There's a number of other sort of small risk factors, not small risk factors, but relative proportion. So obesity, diets that are high in fat, low in fiber, smoking, alcohol use. But by and large, we don't really have sort of a good kind of, if you do this, you'll do that. We know that there's a bunch of things that will sort of increase your risk as a population. But, by and large, those risks ot the the absolute risk increase for an individual patient is relatively low.

Dr. Gazelka 07:12

I'm a little intrigued and horrified by the 50%, increased risk over the last decades. And I look forward to getting back to that. I'm wondering if you could tell us now Jeremy, what are the signs and symptoms of colorectal cancer? How would an individual know that they should be concerned?

Dr. Jeremy Jones 07:27

Yeah. So again, it's one of those things where you can really have any sign or symptom, but the things that I sort of would tell, you know, if my wife came to me and said, Hey, I'm having this symptom, I will be quite concerned. So anytime you have rectal bleeding, that really is a red flag, and it truly needs to be taken seriously. And in fact, one of the sort of disconcerting facts is that in these patients who are early onset, or young age, with rectal cancer or colon cancer, you know, they're 25, or 30, and they have rectal bleeding, which, you know, in a 70 year old is a very big risk factor. These risk factors, or these signs and symptoms have sort of been ignored, and in some part by the medical community, but by the patients as well. You know, I'm too young to have cancer. As it turns out, that's not the case. And so I think that, you know, certainly if you're having rectal bleeding, I would not really take you know, that this is just hemorrhoids, because that's sort of the classic is that when you have rectal

bleeding, it's hemorrhoidal bleeding until proven otherwise. And I think that, that's okay. But the proven otherwise part is very important. So I would not just sort of write it off. And unfortunately, you know, I see, unfortunately, a clinic full of patients who are young and otherwise healthy, who were told for sometimes six months, a year, that you know, this is hemorrhoidal bleeding, only to find out that there was actually a fairly sizable cancer that they had. And so, rectal bleeding, I think, is unique, and it's something that I would take seriously every time. Other signs, you know, changes in the caliber or frequency of your stooling, if you have, you know, persistent diarrhea or constipation, you know, you were previous previously very regular and then now these things are happening. If you have, again, persistent or severe abdominal pain that can be a sign or symptom. Unintentional significant weight loss 10 to 20% of your body weight, you know, those sorts of signs are, unfortunately generally sort of later on. And so, you know, the hope is that we're catching cancers before we get to the point where somebody is losing 10 or 20% of their of their body weight, because that generally portends that this is a sort of more advanced cancer.

Dr. Gazelka 09:36

Jeremy, I'm so glad that you mentioned the point about hemorrhoids because I think so often people maybe fail to present because they're worried that they're bothering their doctor or it's just something small and I don't really want to have to go in for this. So supposing that this individual does seek care, how do you diagnose colorectal cancers?

Dr. Jeremy Jones 09:57

So the foundation or the gold standard diagnosis of colon or rectal cancer is colonoscopy. And, there's a number of other ways that we sort of get to that diagnosis. But really this sort of, to confirm the diagnosis, the cornerstone is colonoscopy. There are non-invasive tests that can be done, one of which is Cologuard, which we actually had a hand at with Mayo Clinic helping develop. And it has really sort of revolutionized. It's a stool based test, you send it in, and for patients with average risk, it does a very good job. The testing characteristics are excellent. And so, for those patients who say, you know I'm not willing to do a colonoscopy, but I would do a stool test, that's a perfect test for them. I think that still colonoscopy remains the gold standard, if all things else are equal, I would recommend a colonoscopy, particularly in those patients who are at higher risk. But there's a significant proportion of the population that frankly, just are not interested in doing colonoscopy. And so, it's incumbent upon us as providers to try and find a way to help them get to a diagnosis early. The other thing I would say about colonoscopy is that it's unique and in the screening test, and that of all the screening tests that we have in medicine, I think it's the only one that I know of that is not only screening, but also preventative. And the reason why it is, is when they go in, when a GI doctor goes in and does a colonoscopy, they can remove precancerous lesions before they actually have a chance to become cancerous. And so, you know, it obviously plays quite a role in screening, but it is, it's quite important for prevention of colorectal cancer as well.

Dr. Gazelka 11:33

Jeremy, I hear so many people talk about, you know, adults talking about, oh, I have to have a colonoscopy, and they dread it and the bowel prep. Could you tell us a little bit about how is a colonoscopy performed? And what should an individual who's going to have one anticipate as they prepare? Yeah, so you know, I think that part of the problem, obviously, is that the colon needs to be

prepared for. Wen they use a colonoscopy, they're essentially sticking a camera in through the rectum and running it through the colon and looking to see is there any polyps or anything that looks suspicious. And so you can imagine that if there's a lot of stool within the colon, that camera is not very effective, you can't really see. And so, you know, the unfortunate part about colonoscopies, that people are not excited about is that there is a colonoscopic prep. There's a number of different ways that it can be done, it used to be that you get sort of a big jug of a gallon of fluid, and you drink that before. And I think that that's sort of what everybody thinks of. But there are other ways now that are a little bit less invasive. But at the end of the day, I think that for the patients out there who are sort of, you know, not inclined to consider colonoscopy, I would say that having a little bit of extra bowel movements for one or two days is probably quite a bit better than and, you know, and being able to catch a cancer early, is guite a bit better than, you know, skipping that, and then down the road being diagnosed with a more advanced cancer. So, you know, I really think that it's a risk benefit type situation, but we are getting better at trying to sort of make this more palatable, more you know, easier for patients to get screening, because ultimately, that's the goal. We want to make it as easy as possible, as least invasive as possible, but to still keep it as effective as possible. So Jeremy, we talked a little bit about potential signs and symptoms, but many individuals will not have signs or symptoms and you're doing the screening in people who have no evidence that they have colorectal cancer. And so can you explain what the screening guidelines are? I know, you mentioned both Cologuard and colonoscopy.

Dr. Jeremy Jones 13:44

Yeah, so so the screening guidelines have traditionally been since you know, I can remember learning, have always been in patients who are of standard risk. So don't have a hereditary syndrome, don't have a strong family history, has been to start screening either by flexible sigmoidoscopy or colonoscopy or now recently Cologuard at the age of 50. But like I said, we've seen actually a dramatic increase in patients younger than the age of 50. And so, the American Cancer Society has recently changed their guidelines and started screening at ages of 45. And I think that's actually a great move. Anytime we're doing screening recommendations, you know, there's a risk that you don't want to harm patients who don't have cancer trying to find those patients who do. But it's finding the balancing act in terms of which patients are going to be at highest risk of having cancer of colon cancer and trying to find them early. Because we know for a fact that finding early is probably the biggest prognostic indicator that we have.

Dr. Gazelka 14:48

And Jeremy, I imagine that by the time patients get to you they typically carry a diagnosis because you're an oncologist and you're planning to treat patients with cancer. But I would imagine that if individuals are concerned about or wondering what their screening pattern should be, that they should follow up with their primary care provider who can discuss not only preventatives in screening for colorectal cancer, but also for many other issues.

Dr. Jeremy Jones 15:16

Absolutely, the unfortunate reality is in the world of primary care, it's a job that, you know, as a subspecialist, I think, I don't know how somebody can do such a great job at primary care, because there's just so many things, you know, it's like a firehose of just all of these different issues that are going on, not to mention all of the screening recommendations that are quite important. So I think, from

a patient's point of view, I think that, you know, hopefully, your doctor has had time to sort of bring up screening. But if they haven't, I think, you know, being an advocate for yourself and saying, hey you know Doc, I read online that you know, that they've changed the screening guidelines to 45, and I just turned 45. Or, Doc, I know, you didn't ask me about this, but I have, you know, two siblings that have had colon cancer in their 40s. You know, that may be just sort of the reminder that tips off your doctor to say oh, you know what, I need to get them on with colonoscopies. And, you know, in some circumstances that can make all the difference.

Dr. Gazelka 16:15

Jeremy, we were talking earlier about a trend toward younger individuals being diagnosed. And I'm wondering if we could get back to that a little bit and talk about if there are preventative measures that people can undertake to lower their risk.

Dr. Jeremy Jones 16:31

So yeah, so like I said, we've seen, actually a greater than 50% increase in the rates of colorectal cancer in patients under the age of 50, which we would call early onset colon cancer. And in fact, in clinical practice, you know, it's not patients that are 45, or 48, you know, just sort of it's 25 year olds, 35 year olds. And so, there's clearly a trend, and this is a global trend, it's not just in westernized nations, we're seeing it all throughout the world. And so, there's a significant increasr, and you know, although we lump colon and rectal cancer together, if you look at the trends, actually rectal cancer is rising, actually quite a bit more even than colon cancer by itself. And so, in my mind, one of those sort of research interests that I have is sort of trying to see if we can look at is that a different disease. You know, we lump them together, because they do have very much similarities. But it is quite possible that there are different mechanisms and different levels of pathogenesis that are driving rectal cancer versus colon cancer. And in fact, this is a little bit off subject, but if you look at colorectal cancer, in general, we've learned over the past decade or so that a left sided colon cancer is actually significantly different than a right sided colon cancer. And you would think that, you know, it's one tube, it should be the whole disease, but in fact, it's not. And so the more that we can understand sort of the intricacies, the differences between a rectal cancer, a colon cancer, or a colorectal cancer and somebody who is young versus old. There's likely a difference in pathogenesis. And in my mind, that's sort of how we unlock the secrets and try to figure out why is it that we're seeing these differences? Because up to this point, we have a lot of hypothesis. But the truth is, is that we don't really know as a scientific community, we don't really know exactly why patients are or why we're seeing these trends. An answer to your question of, is there anything we can do? There's not a ton, unfortunately. I think that at the end of the day, screening is really probably the most important. There is some data to suggested patients who have you know, a healthy lifestyle will do better, or are less likely. And I think that that's actually a good rule. Just a good rule of thumb. But I can tell you in my clinic, you know, if you look at the data, it would suggested patients who are early onset colorectal cancer, are significantly more likely to be obese and have sort of bad habits as it were. I can tell you in clinic, that's just not what I see, you know, the patients that I see are the picture of health, you know, have really lived kind of a perfect life. no bad habits, no bad diet. And unfortunately, they still develop these cancers. And so I think that while it's a good idea, as a general rule to sort of live a healthy life, you know, try to decrease processed red meats, eat high fiber diets. I think that's probably, we do a disservice to patients who have done all of

those things, and unfortunately, still develop this bad outcome by focusing solely on that. I think that from a scientific community, we need to continue to try and figure out what exactly is at the heart of this.

Dr. Gazelka 19:40

Jeremy, this is my chance to ask you about what might be an old wives tale. But I remember learning when I was younger, or hearing when I was younger, way before I went to medical school, that eating things like white bread, and red meat and things like that, that, I think the term was that sat in your colon for longer were a stimulus for the development, potentially of colorectal cancers. Is there any truth to that?

Dr. Jeremy Jones 20:05

So like everything else, there's a little bit of truth to it. Certainly if you look at, you know, red meats or processed meats, there is an increased risk of colon cancer. With sort of high starch type foods, there is an increased risk as a population. However, I think if you look, you know, from an individual patient level, we see a large proportion of patients who have none of those risk factors. And so if we said, okay, well it's just diet, diet is sort of what's causing the change. It really doesn't fit with what we see in clinic. And so I think that, again, there's probably a small proportion, increased harm by having, you know, let's say eating, if you ate just strictly red meat, then that probably is a proportionate harm. But I don't think it tells us the full story. So yes, there is some evidence to suggest that is true. And I think that, you know, as a general rule, you know, don't just eat only red meat. That's it. That's just probably a good idea, just in general. But, I don't think it tells us the full story about what's going on.

Dr. Gazelka 21:15

It sounds like what we know that we can tell people overall is that a life of moderation is better. Try to be as healthy as you can, keep your weight appropriate, and do all those things that at least would prepare you to probably undergo a treatment better.

Dr. Jeremy Jones 21:30

I 100% agree. And in fact, you know, I tell patients that when I see them, it's obviously disheartening. When you see a patient who has done everything they can to take care of themselves their entire life, they say, you know, why did I develop this cancer? And obviously, I don't have an answer for that. But I think it means actually quite a bit to have a patient who is starting off healthy and strong. And so even though we may not be able to prevent these cancers, coming to me at a state where you are, you know, an otherwise robust person who is taking care of yourself, your liver is in good health, your body is in good health, it gives me sort of my full armamentarium to be able to treat you, you know, hopefully as least aggressive as possible, but to be able to treat you as full as we need.

Dr. Gazelka 22:15

Speaking of coming to see you, Jeremy, if an individual is diagnosed with colorectal cancer, and they come to see you in the office, what should they anticipate the conversation will be like, about treatment options?

Dr. Jeremy Jones 22:27

Yeah, so you know, my philosophy is that I try to understand the patient from the get go. I try to sort of understand what they've been through, what tests they've had, what they've heard previously, and try to sort of put that into perspective and to have a conversation with them. I think a lot of times, physicians and myself included, we sort of get into the mumbo jumbo, and we we don't sort of back up and kind of explain better. You know, what do we mean by colorectal cancer? What do we mean by, you know, surgery or radiation? Or why are we talking about, you know, a common question that comes up is, somebody has a surgery, and the surgeon removes all of the cancer that they can see. And then they come to see me, and we talk to them about chemotherapy. And they say, well why, why are we talking about chemotherapy, the surgeon told me, we removed everything we could see, and sort of letting patients know that what we're trying to do is actually reduce the risk. We're not telling you that chemotherapy is here to, you know, essentially kill the cancer that we know is there. But we know from a statistical percentage, there's a chance that the cancer will come back. And we know that if we can do chemotherapy, we might reduce that risk. So I think, you know, when I meet with a patient, I'm trying to really sort of help them understand the process and how we got to where we are. You know, we didn't always do adjuvant chemotherapy. And in fact, a study that was published by Dr. Moertel from from from Mayo Clinic, was the study that essentially changed the standard of care. And that was because we showed almost a 50% improvement in survival in patients who had adjuvant chemotherapy after surgery. And so trying to explain sort of how we got to where we are, I think it helps patients understand and you know, buy in to sort of what we're telling them.

Dr. Gazelka 24:07

And one way that I've heard that described, and correct me if I'm wrong, of course, is that while the surgeon can go in and see a tumor, or the gastroenterologist can see something with a colonoscope or we can see things with a CT scan, we can't see all of the cells that might have been distributed, that have cancer growing in them. And so the chemotherapies kind of to chase down and try to kill what's left.

Dr. Jeremy Jones 24:34

That's absolutely correct.

Dr. Gazelka 24:37

Great, thank you. Jeremy, how can an individual, or our listeners if they're wondering, how do you find out if you're getting the right care for your cancer or the best possible care that can be provided to you?

Dr. Jeremy Jones 24:50

Yeah, it's a difficult conversation. I think that you know, what I would recommend is the same thing I would recommend to my family is, you know, ask questions. Be involved in your care. I think that sometimes patients are concerned that they, you know, they may offend the doctor. That should never be a concern that you should have as a patient. You know, our goal, everything that we do is for you. It is to try and help you. It is to try and make this situation that none of us would want to be going through, to try and make it better, try to help you navigate. And so, I would recommend that you ask questions, to try and understand what's going on to understand, you know, what are your options? And, you know, I think it happens rarely, but if you have a physician who is not happy with you asking questions, to me, that would be somewhat of a red flag just as a patient because, you know, again, we're here to serve

the patient. We're here to sort of help them navigate through an extremely difficult situation. And so, our goal should always be to help educate them. You know, obviously, I'm biased, but I think that, you know, a second opinion is always helpful. And in fact, even when I see patients, you know, they tell me, Well, you know, I want to get a second opinion. Sometimes they tell me timidly, like, I'm going to be upset. And I say, Listen, I think that's a wonderful idea. You know, particularly in cancer, where there's very rarely black and white situations, it's generally very gray. So I think that having an extra mind, somebody else to think about things, to explain things to patients, I think, is quite important. And it's quite helpful for patients, even if you hear the exact same thing. And in fact, sometimes when you hear the exact same thing, it actually makes it easier for you to understand and to sort of buy in. So I think that for most of my patients and family, I think that, you know, I would say, in general get a second opinion, because it almost never will hurt. And, I think that most of the time it helps, even if you're getting exactly the same answer, I think it helps just to sort of have that recognition.

Dr. Gazelka 26:56

Jeremy, I love that you said that about a second opinion. Because isn't that the concept of Mayo Clinic that more heads are better than one. I work in the pain clinic, of course, and I often tell my patients that I will discuss their case with my colleagues, and see if they have other treatment options that I might not have thought to recommend. And I encourage them to get second opinions outside of Mayo Clinic if they desire and tell them that I'd be happy to speak with that provider as well. So I think we want our patients to feel comfortable that they're getting all of the information that they need.

Dr. Jeremy Jones 27:27

Absolutely, absolutely.

Dr. Gazelka 27:30

Tell me a little about clinical trials, Jeremy. Does Mayo Clinic have any ongoing clinical trials for individuals with colorectal cancer?

Dr. Jeremy Jones 27:39

We have a tremendous amount of clinical trials. And, you know, they're sort of always building. At the end of the day, particularly in cancer care, this is sort of, the field is moving forward. You know, I tell my trainees, I'm not that old, or at least I tell myself, I'm not that old When I went through medical school, what we knew about oncology care, is, you know, maybe 50% true now. And that's over, you know 10 or 12 years. So, you know, really everything that we are doing is constantly changing, based on trials that we're doing. And so we're learning more and more and more, and one of the things that fascinated me about oncology, when I was going through training is that it's sort of a black box, you know, it's somewhat of a overwhelming type feeling. But to me, it's very exciting that, you know, you can be the absolute expert at oncology in 2020, and by 2030, if you stop learning, you will be well out of touch. And so I think that it's a fascinating field. And, you know, obviously, it can be difficult, but we have a number of clinical trials that are open and accruing. And we're continuing to build on more. At the end of the day, we want to offer the best care that we possibly can to patients, and commonly that's on clinical trials.

Dr. Gazelka 29:03

I love what you said about the 50% of what you learned is no longer true. I had a professor say that in medical school, who said that it during the course of your career 50% of what we teach you today in medical school will be disproven. And it's fascinating to me how many things have already at this point in my career. So, I love hearing that from you as well.

Dr. Jeremy Jones 29:25 It is.

Dr. Gazelka 29:26

Jeremy, can you tell me a little bit about what kind of research is ongoing? You mentioned earlier about how treatment has changed in the last decade or so, because of research. So what things are researchers looking at now?

Dr. Jeremy Jones 29:41

So we're looking at a bunch of different ways to treat cancer. But I think from a fundamental standpoint, in my mind, we talk commonly about personalized therapy or, you know, targeted therapy. And from a fundamental standpoint, what that means to me is that there are certain patients with cancer who will have a good outcome, no matter what we do. And there are some patients who will have a bad outcome no matter what we do. What we need to try and figure out as a field, is how can we predict who of those people are a priority before we start getting into things. Because what we want to do is we want to tailor therapy. So if you're going to have a good outcome no matter what, we want to try and reduce the side effects as much as possible. So we don't want to treat those people as one patient, because we're going to give too much toxicity to one person with minimal benefit. And then we're going to give not enough benefit to the other person. And so what we're trying to do from a number of different standpoints, is figure out in prospect, which patients are going to sort of have the best outcome. And then in those patients, we want to try and de-escalate care, we want to try and deescalate the therapy that we're giving, because, you know, our therapies, unfortunately, do have toxicities associated with them. Generally, it's not as bad as what you read online. But our therapies do you have toxicities associated with them. And so the best chemotherapy is the one that I don't have to give. And so on the flip side of that is there are patients who no matter what we do based on standard therapies, they're going to have a bad outcome. And so those patients are in dire need of having better personalized therapy. And so, a lot of the research that I'm involved in, personally, is looking at this. So we're looking at what we call radiomic signatures. Essentially, if we look at an MRI after a little bit of treatment, can we predict those patients early on who are going to have either a better or worse outcome so that we can tailor treatment based on that. Just recently, we had a grant funded in my lab, where we're essentially going to take biopsies of the patient's tumors, both at the time of diagnosis, and then after they've had a little treatment. And we're going to grow those samples actually into what we call tumoroids. Which are essentially little spheres of tumor. The idea here is that there's a bunch of things that we're trying to do, but what we're trying to figure out is, what is it about one tumor or one patient's cancer that makes it so much more aggressive than the next patient? And we have a little bit of hints on some of these things. We look at single mutations, and we say, yeah, that single mutation causes it and there certainly are some. But the picture is much more difficult than that. Unfortunately, it's not going to be just one mutation, it's one mutation, and then how does that respond to X, Y, or Z

therapy. And then what mutation develops after that..or what we call secondary resistance. And so in my mind, the future of personalized medicine is actually going to be looking deeper. We, as a general rule, we hit a homerun with the first personalized medicine therapy. That was Gleevec. So it was a therapy that, you know, I was still in training at the time. But you know, when this drug came out, it sort of hit a home run, CML went from a universally fatal disease to a disease that rarely patients would die from. And so we thought, well, you know, every other step is just going to be an easy stepping stone from that. And and what I would say is that I don't think that we've had another home run since. We've had great personalized therapy drugs and targeted therapy. But I don't know that we've had a targeted drug that has changed the paradigm as much as Gleevec did in 2003. However, my overall thought is that the way that we're going to get to that is not just the first drug, because that's sort of what we're focusing on now. It's the first drug and then what do we do to target after that? And so these organoids, or what we call tumoroids, that will allow us to do that outside of the patient. You know, the problem is, we don't want to experiment, you know, just on a patient. Because, you know, let's say that the effect of the treatment is not effective, or the treatment has increased toxicity. We'd love to do that in a petri dish, and then come back to the patient and say, hey, you know what, we tested this. Although we haven't tested it in a human yet, we know that this drug will work to kill your cancer cells. And then, you know, along the process, obviously, this is a very long process that we have going on. But to me, it's the fundamental cornerstone of how we're going to proceed in the future and how we're going to make a difference for these sort of difficult to treat cases, these cases where right now we don't have a good option.

Dr. Gazelka 34:19

I think it's just exciting to hear that you and other researchers are enthusiastic and excited about the work ahead. I think that's just wonderful. Jeremy at Mayo, we have a keen desire to reach diverse populations, ethnicities, backgrounds of individuals, with both our research and our treatment. And I'm wondering, are there healthcare disparities related to colorectal cancer, it's treatment or it's research, that people should be aware of?

Dr. Jeremy Jones 34:53

Yeah, there certainly is. You know, if you look as a general rule in terms of research, African Americans are generally less represented than any other population group for all clinical trials. This is true in colorectal cancer and in terms of the risk of colorectal cancer, actually higher in patients of African American descent. Patients of American Indian descent have a similar downfall in terms of increased risk of having the cancer and also less represented in clinical trials. And so that's sort of like the worst case scenario. You know, we really want to target clinical trials. As I said, the best clinical trials are trials that are targeted towards the highest risk population, or the highest risk patient, and is, you know, evaluating those patients. And so I think that, right now we are, as a general medical community, this is unfortunately, not just at Mayo Clinic as it is across the globe, or across across the country. We have not done a good enough job of of getting to these communities and getting them involved in clinical research. And so, we have started trying to partner more with them in terms of screening programs, looking at genetic mutations. Because again, all of the data that we have, the vast majority of the data that we have, we look at, you know, colon cancer, and we say, well, this mutation occurs in 30% of patients. Well, the truth is, is that mutation occurs in 30% of Caucasian patients, we don't really have great data in terms of African American or, you know, Hispanics. And so part of trying

to move the field forward is understanding also, that these things may be completely different in different races. And we just haven't known because we haven't included them in trials, not because, you know, I don't think that we're trying to exclude them, obviously. But we clearly haven't done enough to try and move that forward and try to get those patients excited about clinical trial research. And so we have a very keen interest in that. And I think that it is, you know, moving forward. There's a lot that can be learned about colorectal cancer in general, just by including bigger populations of people or more diverse populations of people. Because, you know, the key to understanding the disease may actually be from us understanding the differences and how it presents in certain patients and subpopulations.

Dr. Gazelka 37:24

Yhat's very exciting work. If we have listeners or viewers who are interested in whether they or someone they know or love, may be a candidate for a clinical trial at Mayo Clinic or for care for their cancer at Mayo Clinic, how would they go about finding information Jeremy?

Dr. Jeremy Jones 37:43

Mayoclinic.org is a wonderful website, it has tons of information, both for how to contact us to get an appointment, asking your primary physician, whether that'd be an oncologist or whatever, reaching out to us directly are all great options.

Dr. Gazelka 38:04

Our thanks today to Dr. Jeremy Jones for being here with us to discuss not only treatment of colorectal cancer, but also research and appropriate screening. We're so glad to have had you here today.

Dr. Jeremy Jones 38:16

Thank you so much for having me, and I appreciate it. And I appreciate your emphasis on focusing on this disease that is unfortunately increasing in intensity.

Dr. Gazelka 38:26

Very important topic, particularly in March, which is colorectal cancer awareness month. I hope that you learned something today. I know that I did. We wish everyone a wonderful day.

Narrator 38:37

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