

UNMC Chancellor Jeffrey P. Gold, MD: Hello and welcome, and, as promised, our returning guest today in November to give us an opportunity to focus on pancreatic cancer awareness is Dr. Sunil Hingorani, the director of the Pancreatic Cancer Center of Excellence. And Sunil, welcome back, it's great to be with you again today. I want to come back to where we left off and we had talked about the fortress. We've talked about the things that you've learned about pancreas cancer and literally turning things around to understand why tumor cells that were in a dish and growing seem to be susceptible. And then all of a sudden you put the same meds into a patient, and it doesn't work. So how does that translate into research? Is the research really focused on penetration of the tumor now, and how would you describe that and understand that? Just like our audience, I'm pretty naive in terms of the physics and the chemistry that will go into that.

Sunil Hingorani, MD, PhD: Well, I think you're being modest there. I know you have a good understanding of the physiology in general, but the lessons that we have learned are important for a number of reasons. They change the way we completely conceptualize this cancer, think about how it's constructed, and they give us an entirely new set of targets, therefore, to go after. Things that we didn't realize we needed to be going after. As one example, in a pancreas cancer, you probably want to try to increase the blood supply, increase the delivery of oxygen and nutrients, the same pathways, because that's the way we can get the chemotherapeutic drugs in. And that's paradoxical, you wouldn't normally want to try to do that.

Dr. Gold: You'd want to stop it.

Dr. Hingorani: You'd want to stop it. And more generally, I think this is the most important thing. And if I could convey this message to patients, I think this would be the most critical. We are in a completely different era now than we were even 10, 12, 15 years ago. And so the reputation that this cancer has deservedly earned over many decades is perhaps no longer fully appropriate. So, we are now increasingly seeing more and more cases of very long-term survival and even some cures for a cancer that notoriously, that was impossible to achieve. Moreover, the explanations we have now for why our previous strategies failed are so simple, so straightforward and so powerful that by simply flipping the switch on our approach, we are beginning to make inroads again in a way that we hadn't seen before. And so, the most important tool, most important weapon that a patient arrives with, is what I want to try to always promote and sustain and increase, and that's hope.

Dr. Gold: Absolutely.

Dr. Hingorani: So, what I would say to any patient is, first of all, don't believe what you read on the internet. A lot of it's doom and gloom, and it doesn't have the context. But most importantly, you are not alone. There are things that can be done, especially at specialty centers that bring a dedicated and concerted interdisciplinary team to treat the problem.

Dr. Gold: Well, I'm glad you mentioned that, because I think hope is critical to healing in almost any disease that we diagnose and treat. And having that very special fight by the patients and of course their loved ones, their family, their church, all of those people, it really is a team effort to get them engaged and to get them through that. And certainly when people lose hope, they lose a lot more in their overall prognosis. But you mentioned the team, the interdisciplinary approach, and I'd like to focus on that for a few minutes because when we've talked about the so-called Nebraska Way, which I've heard you discuss many times now, it is based upon that team approach, and let's share that with our audience today.

Dr. Hingorani: Well, I'm glad you mentioned that, and you brought that up because I think that's one of the most important aspects to the unique environment here. And frankly, a large part of, as you alluded to earlier, what got me to uproot myself in a place where I was perfectly happy and perfectly comfortable, but there was an opportunity to do things.

Dr. Gold: We have better weather.

Dr. Hingorani: I'm afraid I'm going to have to disagree with you on that point, but an opportunity to do things in a new way, but also on a much larger scale. And this interdisciplinary team is a great example. We do something here that is essentially unique in the country. Most often, when patients are faced with this diagnosis, they're left to their own devices to try to find the different types of doctors and disciplines that they might need to help take care of their disease. So they have to first potentially find a surgeon, then they try to find a medical oncologist, then maybe they're going to try to find a radiation oncologist. And each of these appointments usually take place individually, sometimes separated by days and even weeks. And so, you lose precious time during that period, but you also burden the patient and their families with the challenge of trying to navigate the health care system at a time when they're already overwhelmed with this diagnosis that they've just been given. And here's what became possible here, because of the spirit of collaboration and collegiality. Each of the doctors here in surgery, in oncology, in radiation therapy, in nutrition, in genetics, in pain management and more, were willing to completely change their clinic schedules so that they could all congregate together, 40-plus people, on a given afternoon, be present in the room simultaneously while patients are actually waiting in their clinic rooms. And together as a team, we review each patient's data, and we come up -- in a very robust and always respectful -- a dialogue with the best care plan that we can conceive of with all the players in the room simultaneously. And I can tell you, the comprehensive care plan that emerges when you have all of your colleagues in the room together at one time is very different than when each one of those specialists tries to come up with a plan in isolation. And that effort and that ability to create this kind of approach to a patient is truly unique in the country, and I believe transforms the quality of care that they get.

Dr. Gold: That's why we call it the Nebraska Way. Right?

Dr. Hingorani: Couldn't agree with you more. It literally is a new way, a better way, the Nebraska way.

Dr. Gold: Well, I love that concept, because it means that the 40 or so individuals sitting around the table can respectively disagree with each other. They can quote the most recent literature, or one of them might be aware of a clinical trial -- and we'll talk about that in just a second -- that a patient might be eligible for that would be uniquely suitable for that situation. And so this seems to me to make a lot of logical sense. It's kind of stunning that it took you and coming here to build this, and that the rest of the country is now going to be envious of the way this works. So, let's talk a little bit about clinical trials. I know that's something that's important, and there are quite a few patients that come here from across the state and actually across the country, and even around the world, to be enrolled in some of our clinical trials. Why is that so important, particularly in pancreas cancer?

Dr. Hingorani: Well, there's a couple of important reasons. Number one, I think of doing a clinical trial, trying a new approach to a disease in a scientific way, in a rigorous way, as a collaboration between

ourselves and the patient and their families. In other words, I recall being a family member, being the son of a patient with this disease. And I know that we as a family would've looked for any opportunity where we could find meaning and value to the experience that we're going through. Either by trying a new approach that might hopefully benefit that particular patient, in that case, my father, but even if not, in a way that might benefit future patients. And our patients come to us with that same spirit, and it's an extraordinarily generous approach, and they understand the situation that they're in. And so it's incumbent upon us, I think, to create not only the most novel and cutting-edge clinical trials, but also to find the appropriate trial for each patient to think of each patient as an individual entity and not a statistic. There's a reason that I never quote statistics when I'm in the clinic. I use them all the time in my laboratory research as you know, because it becomes essential. And in the laboratory, I might be studying a million cells or a billion cells, and so we're obligated to count them and to try to use statistics to understand the result. When I'm in the room with a patient, I'm dealing with one person. And for them, whatever we come up with is either going to be 100% or 0%. So I start out by taking all the statistics and throwing them out the window, and then you examine the person in front of you. You look at them as a human being. You look at their tumor by every different measure you can, the mutations that are in it, the way the cells are behaving, the other components, other cells that might be in their tumor, what the likelihood is that it might spread or not sooner rather than later. All of that goes into the thought process of the best approach, but also the best trial.

Dr. Gold: So, we've talked earlier about early diagnosis as being the best prognostic feature to allow for treatment, be it surgical treatment or others. What would our audience want to know about screening and what is the role of screening? We've talked a lot about screening in the area of breast cancer and colon cancer, and it's a lot of work going on now, of course, in lung cancer screening. But is there effective screening for pancreas cancer? And if so, what would the audience want to know about that?

Dr. Hingorani: Well, we're still coming up with the best ways to try to screen for and detect this disease. And a lot of the issues go back to, again, the anatomy -- where the pancreas is located. So unlike a colonoscopy, which is relatively straightforward to do, if not always entirely comfortable, it's easy to access the colon, to sample it, to look at it and examine it. It's relatively easy to examine radiographically the breast. And mammography, again, may not always be comfortable, but it's highly sensitive for trying to find a breast cancer.

We don't really have an easy way to access the pancreas except by an endoscope. And anytime you manipulate the pancreas, you run the risk of irritating it, because it has all the enzymes of digestion, and those can create an inflammatory response. And you get an entity called pancreatitis, which is very uncomfortable. So, that will never be a routine part of it.

Now, so how do you approach this challenge? One of the really fantastic programs that's been longstanding here and is wonderful both for the patients but also for the national and international effort to develop early detection markers, is this high-risk clinic. So there's a large cohort of families and patients that have a family history of pancreas cancer, as you and I have. And so, if you have a one first degree relative or two first degree relatives or three, the risk of pancreas cancer actually increases exponentially. And so what we want to do for those people and those families is create a surveillance program. We meet with them every six months. We do a physical exam, we take a detailed history, and if there's anything that seems slightly off, we will do a CAT scan or an endoscopic study at a much earlier time point than we might otherwise. And we also draw blood samples on them. Now, here's the beauty of that study. A small subset of those patients inevitably will develop pancreas cancer. And on those patients first, we will likely have caught it earlier because we've been following them so closely. But we'll also have their blood samples from one year before the diagnosis, and two years, and five years. Now

we can go back to those blood samples and ask “What's different there?” That's where we're going to find the marker, because we've enriched for, we've selected for the patients that are most likely to have those markers.

Dr. Gold: So, a higher likelihood that those screening blood samples will ultimately turn out to tell the story of even subtle changes. Well, I want to thank you. I want to thank you for giving up your very comfortable life out on the west coast and for joining us here in the community. And frankly, even more importantly, having had the experience that you and I did with our dads for giving us hope for what has been a pretty hopeless disease. And I think if there's a single message for our audience today is that there is hope and that the emperor of all maladies, watch out, Dr. Hingorani is on it. Thank you.

Dr. Hingorani: Well, thank you. I want to thank you for the pleasure and the privilege to be here and the opportunity to take this fight to the disease in a way that I might not have been able to do otherwise.

Dr. Gold: Thank you.