

Welcome to Yale Cancer Center Answers with your hosts doctors Francine Foss, Anees Chagpar and Steven Gore. Dr. Foss is a Professor of Hematology in the Section of Medical Oncology at Yale Cancer Center, Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital and Dr. Gore is Director of Hematological Malignancies at Smilow. Yale Cancer Center Answers features weekly conversations about the research, diagnosis and treatment of cancer and if you would like to join the conversation, you can submit questions and comments to [canceranswers@yale.edu](mailto:canceranswers@yale.edu) or you can leave a voicemail message at 888-234-4YCC. This week you will hear a conversation about Pediatric Cancer Survivorship with Dr. Nina Kadan-Lottick. Dr. Kadan-Lottick is Associate Professor of Pediatrics and Hematology/Oncology and Medical Director of the HEROS Clinic at Yale School of Medicine. Here is Dr. Steven Gore.

Gore                      Tell us a little bit about yourself and what kind of cancers you treat?

Kadan-Lottick        I wear a couple of different hats at Yale Cancer Center. I have two passions, my first is cancer survivorship in children and adults and this started because I was realizing, as many of us have realized, that the survivor rates increase in individuals under the age of 21, it is now over 80% overall and we have this growing population of survivors and we need to give them the next step and take care of them.

Gore                      Are you saying that over 80% of children with cancer are cured now-a-days?

Kadan-Lottick        They are, and it's higher and higher each year, it's inching up, it is always highlighted as one of our modern medical miracles that happened in my lifetime and you cannot see me on the radio, but I am not too old.

Gore                      I will vouch for that.

Kadan-Lottick        It is amazing and it happened very rapidly over the recent decades, almost more rapidly than we realized how to take care of this growing population because now we have kids who were never expected to grow up, who we now want to succeed in school, grow up and feel good, have energy to live active lives every day, grow up and have their own children, be fertile enough to have their own children, and so my academic research interest is in understanding how to reduce late effects from cancer treatment in these

survivors and how to help these individuals live the fullest life as they grow up and that's why I started the HEROS Clinic at Yale.

Gore                      We obviously want to talk a lot of about survivorship and the HEROS Clinic, but just go back to this incredible cure rate, which is so exciting to hear about. I think many of us are familiar either because we read the news or many people have read the book that's name is escaping me, it is a biography of cancer, but we have all been exposed to it.

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Kadan-Lottick      The one from the Harvard author, I know what you mean.

Gore                      And he focuses on childhood acute lymphoblastic leukemia.

Kadan-Lottick      Yes.

Gore                      He focuses on childhood leukemia as sort of what started the whole success, but obviously that can't account, the high success rate in childhood leukemia, can't account for that whole 80%, right?

Kadan-Lottick      No, I am talking about all-comers, so in leukemia it is well over 90% and for the most common type of leukemia it is 97%.

Gore                      Wow!

Kadan-Lottick      It is really high and that goes to the other hat I wear and my other passion, and the reason it is so high is that we as pediatric oncologists work very closely together and for the last three decades we have had a research consortium, Yale is an important member of this consortium in which we work together, we meet twice a year and have exciting research trials with the newest and best ideas and we enroll our patients on them and we put aside our egos, it does not matter where you are from, and we all enroll our patients on them and in that way we have a participation rate of over 80% of children going on the research trial, so instead of just giving what we did 5 or 10 years ago, we

are always able to offer children the most up to date cutting-edge therapeutic options.

Gore                    I just remembered the name of the book, it is "The Emperor of All Maladies."

Kadan-Lottick        Yes, that sounds familiar, and I have read it.

Gore                    It is a wonderful book, so for anybody in the audience who is interested in learning the history of the modern anti-cancer movement and a lot about pediatrics, about the early days of the struggles to cure childhood leukemia, its reads like an adventure story.

Kadan-Lottick        It is really exciting and I am always freaked out because when I was born in the late 60s, I am always struck that if I had had childhood cancer, which now is almost 100% curable, I would not likely be here with you today, that is how fast it has been.

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Gore                    And I remember when I was in school, there would be a kid who would stop going to school and we would hear that he had leukemia and when you would ask your mom or dad what that was, it was a cancer and the likelihood was they were going to die. That was back in the 60s.

Kadan-Lottick        And now we talk to them about doing research studies about incorporating physical activity during treatment and working on school interventions already planning for when they are done with therapy, we start doing that during therapy because we want them to be ready to re-enter life.

Gore                    Wow, so what exactly is survivorship as a field, or even the term, it is not a term that I would use with my family or friends?

Kadan-Lottick        I think it is used in different ways. The National Cancer Institute would define it as anyone diagnosed with cancer or who has been affected by it, who is alive now, so it could be someone just diagnosed yesterday,



Gore                      Sixty years old, wow!

Kadan-Lottick      She is and she is amazing.

Gore                      She is a hero.

Kadan-Lottick      She is a hero and that is why we named it HEROS Clinic. We think of our patients very much as heroes and we think of their family members as heroes and we wanted that name because it reminds us every day how amazing our patients are.

Gore                      Is HEROS an acronym for something or is just a great name?

Kadan-Lottick      So we started with the HERO and then we went backwards and made it work because we wanted the word hero, so we made it stand for Health Education, Research Outcomes in Survivors, but the secret is that it started off with heroes, because that was what came to mind when we thought about our survivorship clinic.

Gore                      How long has this clinic been in existence?

Kadan-Lottick      I was recruited to Yale in 2003 to start this clinic, so it has been a little over 10 years and when we first started we were the first in Connecticut and we were one of the first few in the country. When I was doing my fellowship in pediatric oncology, I happened to have several kids who had fractures at the end of therapy and in the beginning of therapy and I started trying to figure out why and studied bone mineral density changes from steroids and methotrexate, and I did my research in that area during fellowship and then I sought out a postdoctoral fellowship and I did a postdoctoral fellowship in survivorship research in Minnesota, which has a large cohort of 12,000 survivors they are following.

Gore                      It is a big pediatric transplant program too right?

Kadan-Lottick It is a big transplant program, but also I am an investigator in the childhood cancer survivors study. My mentor is Dr. Les Robinson, it is kind of like the Framingham study. There are 12,000 childhood cancer survivors that are being followed every two years.

Gore Wow.

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Kadan-Lottick We see how they are doing, and these patients are now in their early 50s. So we have learned a lot from that group as well and a lot of publications that inform how we can take care of them best are from that group. We are contributing to that literature too with patients that come to our HEROS clinic. I really think of the HEROS clinic as a living laboratory, first and foremost, we take care of our patients and do what they need, but I want to feel that every year that they come to us, we will have something new to offer and we want to keep on learning. We do not want to just document what the problems are; we want to understand how to prevent them and how to make things better, so that is why we do intervention studies on improving neurocognitive outcomes and physical outcomes. We also try to teach the patients what to watch for so that they can identify issues before it becomes a problem, while we can still fix it.

Gore If I am a survivor of cancer, which presented before age 21, and I have come to the HEROS clinic, what could I expect there? Is it a classroom, is there a doctor's exam?

Kadan-Lottick So it is a little bit of everything, it is a multidisciplinary clinic. What would happen first is that we do a really good interview with the patient and figure out what worries the patient has if they are already adults. If they are younger, what worries their parents may have and then we ask our own questions screening for problems that we know people who are treated with their particular protocols could have. We have done a lot of work before they even come, we spend a few hours and actually summarize all of the treatments they received, calculate total doses of chemotherapy, radiations, types of surgeries, so we know what questions to ask and know what we need to be thinking about. We do a very thorough exam. We order and arrange all the tests and evaluations that would be recommended according to individualized exposure, so every patient will have a different experience depending on what treatments they had. For example, if a child or a young adult has had anthracycline or a chemo, they would get an Echo. If they had a certain drug, we would check to see if they

are going through puberty well with hormone tests and then we have a nurse educator who teaches them what to watch out for and a neuropsychologist to screen for cognitive problems.

Gore We are going to pick up on that after the break. Right now it is time to take a short break for a medical minute. Please stay tuned to learn more information about pediatric cancer survivorship with Dr. Nina Kadan-Lottick.

#### Medical

Minute The American Cancer Society estimates that in 2014 over 1500 people will be diagnosed with colorectal cancer in Connecticut and nearly 150,000, nationwide. When detected early colorectal cancer is easily treated and highly curable and as a result it is recommended that men and women over the age of 50 have regular colonoscopies to screen for the disease. Patients with colorectal cancer have more hope than ever before due to increased access to advanced therapies and specialized care. Clinical trials are currently underway at federally

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Gore Welcome back to Yale Cancer Center Answers. This is Dr. Steven Gore and I am joined tonight by my guest, Dr. Nina Kadan-Lottick. We are discussing pediatric cancer survivorship. Nina, before the break, you were telling us about the experience that a survivor of childhood cancer gets when they came in to your HEROS Survivorship Clinic and you mentioned that you spend a lot of time figuring out the various doses of drugs they have got and radiation and what kind of side effects to expect and then you ask them questions and you do some screening tests and one of the things we were talking about had to do with chemotherapy that seems to affect the heart, as one example. So you have the patients there, you know what kind of treatment they have had, and you ask the parents of the patient what their anxieties or concerns are, then what happens?

Kadan-Lottick Then we do screening tests according to what that particular patient had, because of course, cure is the initial goal, but very often the

therapies needed to cure a child can result in late effects and some examples include heart failure from radiation to the chest or a type of chemotherapy called anthracycline, one can get renal insufficiency.

Gore                      That is a kidney problem?

Kadan-Lottick      That is a kidney problem from cisplatin, you can also have hearing problems, you can have hormone problems so that you have trouble going through puberty or need help with a growth hormone to grow properly. You can get second cancers too unfortunately. Some of the chemo and radiation also causes an increased risk of subsequent cancers. It does not mean you are automatically going to get it, but some of our patients have a higher risk compared to other people their age and gender who did not have that cancer treatment and this sounds really scary I know.

Gore                      Yeah.

Kadan-Lottick      It is scary and our studies show that about two-third of survivors will have at least one problem that needs medical intervention.

Gore                      But not necessarily cancer?

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Kadan-Lottick      Not necessarily cancer. So the increased risk of cancer is in certain groups and it still means that most likely most people will not get cancer, just an increased risk compared to others, but because there is an increased risk we want to give them extra attention and hopefully prevent these problems. Even though a lot of patients, two-thirds, could get a late effect, most of these problems respond well to early detection such that you can prevent the problem from happening, for example, breast cancer is increased in girls who have had radiation to the chest, but we know to start mammograms early. So these girls start mammograms at age 25. Another example is there is a kind of cancer that can occur in the bladder and we know to screen these survivors with urinalysis looking for blood so we can catch things before they are an issue, and we have actually caught several breast cancers in our clinic in very young women before it was clinically apparent in any way or even to my exam. So that is important and I think of my clinic as a very positive clinic because most of the time we are able to improve people's health, give



them the knowledge they need to know, what to watch for and we call it a super check-up for keeping people healthy and we have a great team. It also includes Dr. Balsamo who is a neuropsychologist, who screens for cognitive and learning issues after chemotherapy and helps people, kids, students, and college kids and even adults, how to function at their best and she also supports people who are suffering with stress, or with anxiety because of their past diagnosis and we have Jamie a nurse educator who explains how to eat more healthy, to maximize fruits and vegetables which can halve the risk of cancer, five fruits and vegetables a day. But it is something simple that we really want our kids, especially, to do.

Gore                      You are saying fruits increase the risk of cancer or decrease the risk of cancer?

Kadan-Lottick      Decrease, so half. But it has to be five, three is not enough, and seven is better than five. One serving of fruit is half a cup and a serving of vegetables is one cup, but this is such good data and I am a researcher, it is so strong, it has been shown in the US. It has been shown in Canada. It has been reproduced. It is not like some of these days where you hear eat lots of lima beans and then next week, it is lots of grapes. This one has been reproduced, but you do need to eat a variety and it has to be frozen or fresh, or whole juice. It cannot be the processed juice. That has not shown a benefit. We talk about physical activity. We talk about how to do a self-exam, testicular, and breast self exams, because these are young people and they may feel shy about this or they may not get this in normal non-cancer checkups and so we talk about that and then Jamie spends a lot of time explaining to the patients our survivorship care plan. Basically what their treatments were and then the detailed list of what check-up tests they need and evaluations they need in the future. So that even if they move or go off to college, or whatever, they have that document that they can take to any doctor and tell them, this is what my check-up should look like and of course we also send a copy of this to all the survivors' doctors and anyone else they want to have it.

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Gore                      And do the patients, if they stay locally, continue to follow-up with you or it is kind of a one-time assessment and then they go back to the primary care physician?

Kadan-Lottick     We leave it up to the patients, most of them do stay with us yearly unless they move away but we have patients from parts of New York and Massachusetts, and Rhode Island as well and if they are coming from farther, sometimes they cannot come yearly and they take that information back, or even sometimes they just have a very close relationship with their primary care doctor as most people should actually, which I really encourage. That is one of the most important interventions we do, is make sure that we help people find primary care doctors who do not have one, but some of them do not want to come back to the cancer center, which is what you mentioned earlier, it can be traumatic to be in that same environment and so we give them the information they need, because the types of tests that are needed are not ones that need to be done in the cancer center. It is just that the doctor needs the knowledge to do them and know that this is what this particular person needs.

Gore                     And can you be in the HEROS Clinic if you have not been treated at Yale?

Kadan-Lottick     Yes, absolutely, we welcome any patients, the only thing is that we ask for patients that are diagnosed under the age of 21 because there are certain therapies that are given in that age group and certain issues that arise more as those people are growing up and that is where our expertise is and I am sure you are going to have Dr. Sanft on at another time, but she is the expert for survivors of adult cancer and so there is also an adult survivorship clinic for those patients.

Gore                     That is great. I know that at least some years ago, there was a lot of interest in pediatric leukemia and trying to dial back the intensity of the treatment for easier to cure cancers. Is that something that is continued and is that something that survivorship experts, like you, interface with people about, designing the studies to see if there are a lot of late effects on the heart or whatever, how does that work?

Kadan-Lottick     I mentioned that I have another passion and that is clinical trials and I am one of the members of the National Children's Oncology Group Leukemia Committee, ALL, this specific type that you talked about and our last trial was actually a dose reduction question. It is to see if we can give less steroids and less vincristine so that we can have less problems later with bone health and less problems with neuropathy, and that is very exciting. There are other diseases that we have been really successful with doing that. We had a recent trial in Hodgkin lymphoma, in which we studied giving sparing radiation and using therapies that are less likely to cause infertility later and we found that we could preserve those high cure rates and still give the survivors a better

future. The ALL study is still ongoing, the one that is looking at the less steroids and vincristine, but it is very exciting for me that we are at a point where we can look at that.

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Gore Do you find that it is hard to enroll patients in trials like that because it seems so scary to be getting less therapy than what works?

Kadan-Lottick I think that it is more a matter of explaining it to patients and talking about it. These ideas do not come totally out of the vacuum, they are not just experiments, there is preliminary data or pilot data, safety data with smaller groups of patients that showed that it works, so the larger studies are to prove it with absolute statistical significance. So that is one thing, and then the second thing is that I think that it is really a team effort taking care of patients and a very important part of the team is the patient and the family and I think it is very important to talk frankly about the risks and benefits because unfortunately I think we know this in life in general, nothing comes totally for free. There are always some risks and even in someone who is not on a protocol, if we have a young person, like an older teenager, where fertility is very important and it is an important life value and family value and that person is making a decision, I think that it is important to talk about options and talk about other protocols that are available that could help that person, have a risk benefit ratio that is more comfortable for that individual. I think it can be hard and it can be scary but I think it is about explaining things and being frank and certainly with late effects I think that if families understand that we expect the child to live, thankfully, and we also want them to live well I think they will also be able to understand but then they will have to make their own decision according to what they are comfortable with.

Gore At what age do kids get to have a say in this? Obviously you have the parents, you have the kids, but it is about the kids, at what age can they understand enough. I am sure it is different from family to family, I imagine?

Kadan-Lottick It is different and the Ethics Board requires parental consent for everyone under 18, but we would talk with every child separate from the written consent about the general idea, responding to where they are in their developmental stage. We would bring them into the discussion. A younger child we may just say, you are sick and you have to stay in the hospital and

we think we have a new medicine for you that will work, your parents are okay with it. We want to tell you what is happening. For an older teenager, we would explain the randomization or the different options and I would encourage them to talk with their parents and decide together.

Dr. Nina Kadan-Lottick is Associate Professor of Pediatrics in Hematology Oncology and Medical Director of the HEROS Clinic at the Yale School of Medicine. We invite you to share your questions and comments. You can send them to [canceranswers@yale.edu](mailto:canceranswers@yale.edu) or you can leave a voicemail message at 888-234-4YCC and as an additional resource archived programs are available in both audio and written form at [yalecancercenter.org](http://yalecancercenter.org). I am Bruce Barber hoping you will join us again next Sunday evening at 6:00 for another addition of Yale Cancer Center Answers right here on WNP, Connecticut's Public Media Source for news and ideas.