Welcome to Yale Cancer Center Answers with Drs. Ed Chu and Ken Miller. I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and Dr. Miller is a medical oncologist specializing in pain and palliative care. He is also the director of the Connecticut Challenge Survivorship Clinic. If you would like to join the discussion, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1-888-234-4YCC. This evening Dr. Miller welcomes Dr. Nina Kadan-Lottick, the Director of the HEROS Clinic for Pediatric Cancer Survivors at Yale Cancer Center.

Miller — Let's start off by talking about the definition of a cancer survivor.

Kadan-Lottick — Recently we have realized that it has to be a broad definition, and currently, we as well as the Institute of Medicine, define it as anyone who has had a cancer diagnosis. We even broaden that definition to include family members and friends who have also been touched by the cancer diagnosis. The reason for this broad definition is that it is intended to incorporate all the ways that cancer touches the lives of people.

Miller — In many ways it is more than just a disease of one person; it is a disease that affects the whole family.

Kadan-Lottick — Definitely, and that is particularly true for children with cancer, but it is also true for adults. This definition is important because then we can really focus on how to improve quality of life. So, it is not just being alive, but making the most of being alive.

Miller — For a long time people said that if you are alive five years after a cancer diagnosis, then you are a cancer survivor. What happens to that definition?

Kadan-Lottick — I think that definition has a utility in defining whether a treatment works. We need to see if there is a good response at certain time periods after treatment, but what we are realizing is that we cannot just define successes of treatment by whether you are alive or not. Whether you are cured at five years is important, but what is also important is what your quality of life is after five years, what your health status is, are you doing everything to maximize your health and well-being to make the most out of being alive?

Miller — How many pediatric cancer survivors are there in the United States, and how has that changed over time?

Kadan-Lottick — It is difficult to give an exact number. The important thing to realize is that many people after they have been treated for their cancer diagnosis are lost to follow up because they do not recognize, and doctors have not recognized in the past, that they have unique health needs. So they are not in a general database that is easy to count. We do know that currently 80% of all children diagnosed with cancer under the age of 21 will be long-term survivors; they will survive at least five years after the diagnosis. That is a figure that steadily increases each year.

Miller Which is wonderful.

Kadan-Lottick Which is wonderful, and is really a medical accomplishment of our last generation. This would not have been true of the children I went to school with when I was a child. We have made major strides quickly in childhood cancer treatment, but what that does mean is that each year we have more and more cancer survivors entering our population and growing up. That is because they are cured and the numbers keep adding. The last time it was estimated was from rough figures of polling different institutions in 1997. It was thought then to be 10 million, but now here we are in 2008 and I am sure it is at least 20% to 30% more given the survival rate.

Miller So a lot of the children that were treated 15-20 years ago are adults now and they're out living their lives. What are some of the things that are different about them, from a medical and a non-medical standpoint, than their next-door neighbor or anyone else out there?

Kadan-Lottick It is very important to cure the cancer first, but often this comes at a cost because many therapies are toxic. They are needed in the short term to sustain life, but in the long term they can cause enduring problems in different organs such as the lung and the heart, and it can increase a person's risk of having heart disease, early heart attacks, having kidney problems, having ovaries and testes that do not function, problems with going through puberty and having children later in life. Another area that can be effected is the thyroid because radiation in the head and neck area causes the endocrine glands not to function well, especially the thyroid, but it can affect other endocrine areas.

Miller Do the majority of survivors have these problems, or do you think that your estimation is of the minority?

Kadan-Lottick The newest estimate we have for that is a study called the Childhood Cancer Survivor Study, of which I am one of the investigators. This is a multisite study around the country following 12,000 childhood cancer survivors in adolescence and now into adulthood. The oldest people in the cohort are in their 50s. From following them every two years we have learned that two-thirds of survivors have at least one medical problem, one-third will have none, and one-third will have at least one severe problem. On the optimistic side you can say that two-thirds of survivors will have no problems, or only a mild problem, but one-third will have a severe problem that requires regular medication, regular monitoring or even surgery or more extreme types of care. In general people are doing well, but what this does inform us of is that this population continues to have special health needs, and to maximize well being we need to make these survivors aware of the their unique health needs so that they can get specialized screening and specialized anticipatory guidance to help them. The good news is that many of these conditions are treatable and amenable to early screening.

Miller What kind of problem might they present with that you can help them with and you can have an impact on, what are some examples?

7:28 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Mar-09-08.mp3

Kadan-Lottick One example would be a young man who just got married a couple of years ago and is unable to father children. Actually what is interesting is that often these individuals do not even realize that this difficulty can be related to their past cancer diagnosis. Our technology has improved so much in reproductive endocrinology that even if the young man's sperm count is very low, using assistive technologies such as artificial insemination and in vitro fertilization, it is possible to father a child even with less sperm. It is important to do so in a timely way because the sperm count can vary in the periods after treatment and one would not want to wait too long. That is one example with reproduction. Another very important example where it is good to catch something early is that children who have had radiation to the head for leukemia or brain tumors have growth hormone deficiency. Often that is a clinically silent condition because it does not cause him to feel bad in any way. What will happen is that they will grow a bit with puberty, but not at the rate that they should so their final height will be much reduced. If we are aware that they had these treatment exposures, we can monitor their growth hormone production with more specialized testing. If someone is at risk of lower growth hormone production, we can replace that growth hormone in time so that their final height is not effected. But once your growth plates are too close during puberty, it is too late. Sometimes it is a matter of six months or a year that you have to catch this before it is too late.

Miller Do you get a sense that oncologists, pediatric oncologists and clinicians, are more aware of these long-term issues in survivorship than they used to be?

Kadan-Lottick Pediatric oncologists have led the way and I think that is because we have seen more quickly the strides in survival. We have had the privilege of enjoying watching our children grow up and that has led to the observation that as adults and adolescents these individuals are having certain problems. In that way my colleagues are becoming more aware, but I do think it is still a challenge and that is why I am so delighted to be on this radio show and to do my work at Yale, because it is something that is still not generally known in the oncology field. Many oncologists are still focused only on the time to cure because this has been the struggle for so many decades, and they do not have the same experience or awareness of current research in the time after the cure has happened. Another challenge is that many of these conditions are silent, so survivors do not identify themselves as having unique health needs. It is not as if they are going to feel sick like they did with their cancer, and that is important.

Miller We would like to remind you to email your questions at canceranswers@yale.edu. We are going to take a short break for a medical minute. Please stay tuned to learn more about pediatric cancer survivorship with Dr. Nina Kadan-Lottick from the Yale Cancer Center.

Medical Minute

There are over 10 Million cancer survivors in the US and the numbers keep growing. Completing treatment for cancer is a very exciting milestone, but cancer and its treatment can be a life changing experience. Following treatment, returning to normal activities and relationships may be difficult and cancer

survivors face many other long-term side effects of cancer including heart problems, osteoporosis, fertility issues, and an increased risk of second cancers. Recourses for cancer survivors are available at federally designated Comprehensive Cancer Centers such as the one at Yale to keep cancer survivors well and focused on healthy living. This has been a medical minute, and you will find more information at www.yalecancercenter.org. You are listening to the WNPR health forum from Connecticut public radio.

Miller Welcome back to Yale Cancer Center Answers. This is Dr. Ken Miller. I am here with Dr. Nina Kadan-Lottick who is Director of the HEROS Clinic at the Yale Cancer Center. Nina, I am going to ask the million-dollar question, how did you get the name HEROS Clinic, I think it is a great name.

Kadan-Lottick I have to tell you, we did it backwards. We loved the name HEROS because that is how we think of our patients and the family members, so we made it work. Thinking backwards, HEROS stands for Health, Education, Research Outcomes, and Survivors. It is a name that really resonates with our patients and that makes our clinic a positive experience which is really what we intend for it to be.

Miller It is an amazing name and it is great that you are able to make it fit so well. What happens when a patient comes to the HEROS Clinic, what is that experience like?

Kadan-Lottick It really starts a few weeks before they even come. We request all the medical records from the cancer therapy from the other treating institutions and the nursing staff and I review this in great detail and create a treatment summary that calculates all the specific chemotherapies and radiation they got and from that we have a pre-clinic conference that is attended by a psychologist, endocrinologist and an internist, as well as our pediatric oncology staff, in which we present each patient and discuss what specific issues that patient is at risk for. Then we plan the clinic visit, what studies we will do, what areas we will focus on in our discussions with the patient, and then a couple of weeks later we will have the clinic visit which lasts about an hour. During that visit the patient will spend time getting education from the nurse, talking and being examined by the physician, and also being interviewed by the psychologist for problems with depression and anxiety. They are also screened for problems in learning function because we have recognized that many of the therapies can result in problems in working memory, being able to focus and being able to organize one's thoughts. These can be subtle effects but can actually really affect the person's quality of life.

Miller It sounds like a lot of the work is done before you even see the patient.

Kadan-Lottick It has to be because each survivor is different. Their care depends on what specific therapies they got and what specific toxicities they experienced during therapy. The good news is that there are many patients who actually are not at increased risk for many of these problems, and they need to hear that. For those people we focus on general wellness strategies, nutrition, and exercise. Other individuals may be at a particular risk for issues and we try to highlight for each

individual what they need to do in their lives in terms of specialized healthcare and healthy habits that will make a difference for them.

Miller Let me ask you a bit more about the wellness part of it. Someone has been treated for cancer and there is a lot of anxiety and worry about it. You mentioned the word wellness, so in terms of wellness what are some things you would like to stress for your survivors of childhood cancer?

Kadan-Lottick I try to stress the idea that knowledge is power and that knowing they may be at an increased risk for certain problems does not mean that they are going to get the problem, but that they should be prepared to prevent the problem and to screen for the problem. In that way they have control over their destiny. I also stress that all the things that are recommended for all of us go up double and quadruple for them. We focus on eating more than five fruits and vegetables a day and trying to exercise at least 3 hours a week because there is good data that these interventions reduce the risk of cancer and also reduce the risk of cardiac disease and other health problems. In fact, we now have some data back from a study done in cooperation with Dr. Santacroce, one of the nurse practitioner faculty in our clinic, looking at how well our clinic is changing health habits in patients. We have found that there has been an incredible increase in healthy behaviors because of our clinic experience comparing what they report at the clinic visit to what they report at a phone follow-up weeks and months later.

Miller I am going to make a guess here, are they exercising more?

Kadan-Lottick They are exercising more; they are smoking less; they are getting the recommended screenings such as mammograms and in some cases early colonoscopy. For some of our patients we recommend very early mammograms, as early as 25 depending on the exposure, but we are seeing that these patients are doing it. We are also seeing that they are using sunscreen more and avoiding midday sun exposure which we are delighted about. What this really tells us is that these individuals can improve their health by having specialized care that focuses on these issues.

Miller You are a relatively small group of very dedicated researchers on childhood survivorship issues. Tell us a little bit about some of the latest research you are working on.

Kadan-Lottick My main areas of research are in how survivors do in terms of neurocognitive function later in life, and how they do in terms of depression and anxiety. We know from other studies that childhood cancer survivors are twice as likely to live with their parents as adults, less likely to graduate from high school and more likely to be underemployed relative to their potential. I am very interested in learning what the contributing factors for this are. My hypothesis has been that it is the subtle learning problems I discussed earlier, because all of those are important areas of thinking in order to be able to function and live independently. I was not sure if there was a greater role played by anxiety or depression, which we also know occurs in cancer survivors at higher rates than other survivors.

Some of my more recent research is suggesting that the more important factor seems to be the ability to have good short-term memory and to organize one's thoughts. These are preliminary studies, but I hope to test this in wider and larger samples because I would then like to focus on interventions that could improve neurocognitive functioning.

Miller If a child had to have chemotherapy or radiation therapy and does have short-term memory deficit, or a sort of executive functioning, are there other strategies to deal with that?

Kadan-Lottick An effective strategy is accommodation; helping the child, young adult or adult to have other tools to do this task. That includes learning how to organize one's day, choosing a career path that involves doing goal-oriented work instead of lots of multitasking so that one can be successful and use one's potential, using PDAs and choosing work where you have very organized structured days because then you can really succeed. The other part that can be helpful for some individuals is to take stimulants. A lower dose stimulant, such that are used traditionally for ADHD, seemed to also help with these areas of function. I have found that many of my survivors, after having had years of taking some new medicines, are hesitant to take medicines. While it is an effective strategy, we are finding in many studies that it may not be practical for many people because of the receptivity. We are also exploring whether some of the computer tools that are being investigated in older patients with early Alzheimer's, which ironically enough we have seen some of the same processing difficulties in early Alzheimer's, problems with working memory, organization of thoughts and ability to concentrate, can be used in our younger patients to improve areas of function.

Miller For young children are you optimistic that in fact you can help them overcome some of these issues?

Kadan-Lottick That is our hope. We know that the brain actively develops into a person's thirties, in terms of just developing into the mature brain. After that, we are learning that even with older patients, there is plasticity in terms of being able to heal from trauma and stroke, so one would hope, or hypothesize, that in younger people that would be even more so. That would be an exciting strategy because it could be something that could engage the family in a very positive way in helping their children.

Miller I am going to ask you about a different topic which has to do with survivors of childhood cancer moving on. Most of them go on and live long happy lives, but what about the risk of other cancers, is it higher, lower or is it the same?

Kadan-Lottick It is higher. From the Childhood Cancer Survivor Study, the 12,000-member cohort that I discussed with you earlier, we have learned that survivors in general are about 6 times more likely than other people of their age and gender to get cancer. That is a much increased risk. It is particularly high for certain groups, such as those who have gotten radiation, particularly those with Hodgkin's and sarcomas. But this does invite an area to feel empowered because if an individual

is aware that they can monitor their skin and tissue in the radiation field, and if they notice any lumps or bumps, they would be more likely to go to a doctor early on when something can be handled very easily rather than wait till it's progressed. The other issue we are learning about is that because of the second cancers, survivors are about 10 times more likely to have an early death than their peers, most of which is attributed to second cancers, but also cardiac disease and pulmonary disease. That is why, again, we think screening is very important. Earlier intervention for cardiac disease, maximizing lipids and exercise are very helpful strategies to decrease that.

Miller Thirty years ago some of these issues did not exist because childhood cancer survivors did not make it to be adults. So, on the one hand it is a blessing, but it is also a challenge.

Kadan-Lottick Absolutely, but I look at it in a hopeful way. It is a real privilege to be able to take care of cancer survivors because no one would want that diagnosis, or want their child to experience such a trauma, but in reality I often see, in many of our patients, that while they would not have chosen this experience, it has made these individuals realize that it gives their life purpose and that they are interested in accomplishing even more and using their experience to help others to go farther in life. Many of them also feel like they are not going to sweat the small stuff. They know what matters in life, and they are remarkable individuals making the most of their survivorship. That is really why I am so interested in this field. Anything we can do to improve their quality of life is going to help us bank on all the hard work we did in curing these individuals in the first place. It behooves us as clinicians to remain invested in these patients throughout their lives and to make sure that they make the most of them.

Miller Are you saying, in a sense, that for some people there are positive side effects of having cancer?

Kadan-Lottick There are, and some investigators have called this posttraumatic growth. It goes with the idea that, what does not kill you makes you stronger. I find that many individuals have found more spirituality in life, more meaning in life and have really engaged their social support groups and brought communities and families together. While we would not have chosen this for any child, looking back we can see how it has made these individuals truly remarkable.

Miller How old is the oldest patient in your survivorship program?

Kadan-Lottick I love saying this. I have a patient in her 50s who is a grandma in my clinic who comes down from Hartford. It really shows us the whole spectrum of survivorship and what we are aiming for.

Miller Hopefully we will have a chance to talk again on the air, and each year I will probably ask you about her. She is a hero, and so are you for that matter. Nina, I want to thank you for joining us on Yale Cancer Center Answers.

27:16 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Mar-09-08.mp3

Kadan-Lottick Thank you so much for the opportunity to share my work with you.

Miller Until next week, this is Dr. Ken Miller from the Yale Cancer Center wishing you a safe and a healthy week.

If you have questions, comments, or would like to subscribe to our Podcast, go to www.yalecancercenter.org, where you will also find transcripts of past broadcasts in written form. Next week, you will meet oncology nurses Judy Grasso and Marianne Davies.