

Yale CANCER
CENTER

answers

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Hosts

Anees Chagpar MD

Associate Professor of
Surgical Oncology

Francine Foss MD

Professor of Medical
Oncology

**Survivor Perspective: Brain
Metastasis**

Guest Experts:

Harriet Kluger, MD

*Associate Professor of Medicine (Medical
Oncology), Yale School of Medicine*

Richard Metz

Melanoma cancer survivor

Yale Cancer Center Answers

is a weekly broadcast on

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Welcome to Yale Cancer Center Answers with doctors Francine Foss and Anees Chagpar. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1-888-234-4YCC. This week, guest host Peter Lamothe welcomes Dr. Harriet Kluger and Dick Metz for a survivor perspective on melanoma. Here is Peter Lamothe.

Lamothe Let's start off by having Dick tell us a little about himself and about his cancer diagnosis.

Metz Thank you Peter, I am 62 years old, and I live in Wilton, Connecticut and have lived there for the last 25 years. I have a beautiful wife and two boys and a couple of grandchildren with the third one on the way. Regarding my diagnosis, it was about 10 years ago, and I was going to my dermatologist and he saw a mole on my back. He did a biopsy and told me that it was stage II cancer, melanoma, and he said that I would have to go to Yale to have it surgically removed. I did go to Yale about two or three weeks after that and they went ahead, and because it was stage II it was little deeper than a stage I cancer, but they decided that they would have to do a sentinel node biopsy and check the lymph nodes to make sure that no cancer had spread into the lymph system. At that time, everything came out clear, they took wide margins from the surgery and I felt that I had dodged a bullet. About three years later, in 2006, I had a second primary melanoma also on my back and it was only a stage I cancer so it was a little better and I had pretty much the same procedure, but they did not have to do the sentinel node biopsy, but they went in with wide margins and they got the cancer on my skin. Once I had that first cancer, they asked me to come back each year to get checked and make sure that nothing had metastasized to other organs in my body and I had been doing that, but in 2007 I had missed my normal scheduled checkup by about six months or so and in the summer of 2007 I just was not feeling right. I was waking up in the middle of night two or three times, soaking wet, getting night sweats and frankly now I am much more sympathetic to women going through menopause because I guess this is the male version of menopause, but seriously, I knew something was not quite right. I went to my primary care physician and he ran some tests and saw that my liver enzymes levels were unusual so he asked me to go in for an ultrasound. When they did the scan they saw what he said was a mass on my liver which turned out to be an 11 cm tumor, and once it was biopsied that was when I found that the melanoma that was on my back had in fact metastasized and became what is called stage IV cancer and had gone to my liver.

Lamothe Dr. Kluger, could you explain to us briefly about the four stages of cancer and also cancer metastases?

Kluger Yes, so we think of cancer as originating in a single cell in one part of our body, and in fact our body makes cancer cells every day and for the most part gets rid of them. We have robust immune systems that get rid of rogue cells that should not really be there, but when a tumor evolves

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either the immune system is not taking note of it, or the new mutations, the new genetic changes within that cancer cell, are so powerful and so overwhelming that they are clever enough to evade the immune surveillance and grow to a certain size. When the cancer is still in the skin, you look at the depth to which it is underneath the superficial levels of the skin and stage I melanoma is a very thin melanoma, stage II for the most part is slightly thicker, if it goes to the lymph nodes that would be stage III melanoma, and stage IV melanoma refers to a situation where the melanoma cells have escaped into the bloodstream and gone into other organs or other skin sites that are quite a distance away from the original site.

Lamothe Dick, this was quite a lot to swallow. Tell us about your initial reaction?

Metz I would say initially it was a shock and surprise. I had gone through the treatment, I had been checked for three or four years after my initial melanoma was found on my back and so I felt I had dodged a bullet and I felt that I was cancer free. And I guess one good thing about melanoma is that you can usually see it on your skin, it is not like other cancers where it is in your body so here I feel like telling everybody that thank goodness that I have a dermatologist and that they have these treatments, but then once I realized that I really have melanoma I sort of went into what I call a fight mode and what I mean by that is a good friend of mine who also had cancer told me to become an expert in my disease and so I immediately went on the internet to find out any information I could, I checked with all my friends if anyone else had melanoma to find out from them what was going on, and I certainly consulted with Dr. Kluger because I wanted to get all the information I could to really understand what the treatments options are, and what the possible cures could be to beat this disease.

Lamothe Could you say a little bit about how you shared this news with your family and your friends?

Metz Initially I thought about how I wanted to share this and I felt that it was better to use full disclosure than to keep it to myself. So I was very open with everybody and as it turned out I think it was the best because they understood what I was going through and they were more supportive of me, so from that perspective I think it was a very good choice to make.

Lamothe So at this point, in late 2007 and early 2008, you are diagnosed with stage IV melanoma. Dr. Kluger, can you speak a little bit about the course of treatment that was chosen for Dick?

Kluger Yes, 2007 was the time of the initial diagnosis of stage IV disease and a lot has changed since then. The tools that we had to fight the melanoma at that time were very limited. We could give chemotherapy which tends not to work for a prolonged period of time, or we could give one of two immune therapies, the one immune therapy that was established at that time was a treatment called high-dose interleukin 2. We still use it and when it works, it works beautifully, but it works in a fairly small percentage of patients and we did give that to Dick initially, we did not see much

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of a response and Dick can talk a little bit more about the experience with the high dose interleukin 2, and then after that we sent him down to the National Cancer Institute for an experimental therapy which was the second option.

Lamotte Dick, about the high-dose interleukin 2, what was that like when you began that treatment?

Metz I went in somewhat positive, but really not knowing what it was like, and basically the way I describe it is as five days in the hospital because it is a fairly harsh treatment, then you're home for a week, then you go back for another five days and then you come back and in a few weeks after that you get a scan and see if there are any results. The way it works is when you get to the hospital they put a PICC line in because that is how the drug is administered into your body. The first few days for me really weren't all that bad, sitting around _____ taking my time reading books and all that. As the weeks went on, food started tasting very steely to me and I happened to be there in November during Thanksgiving and people were bringing turkey and mashed potatoes and all the great things you have at Thanksgiving and it tasted awful, I remember that. The other thing I should say is that you gain weight and they encouraged me to drink a lot of water plus you are on an IV line at the same time, so the first week I was there, in five days I gained 31 pounds, so my friends affectionately called me the Pillsbury Doughboy and actually gave me some sweat pants with the Pillsbury Doughboy on it, but they give you Lasix during that week off in between and it is great for people that want to lose a lot of weight quickly, I lost the 31 pounds in the matter of five days. Then I went back again, the second week, and Harriet you can clarify, but I think it is more cumulative, so you feel it more the second week than the first week and there are eight doses and as I got to maybe the 5th and 6th of the eight doses the rash, the itching, and all that got to be pretty intense. I describe it to people as, imagine you are in the words, you take off all your clothes, and you roll around in a patch of poison ivy for 15 to 20 minutes and imagine how you might feel about three or four days later. That is the best way to describe how I felt. It's a rashy, itchy feeling, but you come out of that, you take the Lasix, you lose your weight and a week after that I actually felt pretty much back to normal.

Kluger At that point, we wait a few weeks and rescan and see if things are changing and in the case of Dick's tumor, it was fairly stable. It did not have any major changes, but we also did not see obvious shrinkage. We then sent him down to the National Cancer Institute for an investigational therapy, but I do want to add that things have changed a lot and if we were going through the same sequence of events now, we are doing some of this adoptive cell therapy here at Yale. There are other FDA approved drugs which today he would be eligible for that were not available at that time. They have been approved in the last two years, but to go back in history, maybe Dick can tell us a little bit about what happened when he went down to the National Cancer Institute.

Metz In January of 2008, with Harriet's help, she got me an interview to go down there and I was hopeful that I would be able to get into this what they called TIL cell, tumor infiltrating

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lymphocyte therapy. The problem was when I did my blood test, my liver enzyme levels were sky high because my tumor was in the liver and I was not a candidate, but they decided that if they could do a surgery and they did not necessarily say, we will take it all out, they wanted to get out as much as they could, because the liver is one organ that can actually grow back, and that if they get most of it out, my liver, in theory at least, would recover and my liver enzyme levels would go down to more normal ranges and then I might be able to get into the TIL cell. As it turned out, I did go in for the surgery. They did get virtually all of the cancer that they could see out and so that was very successful. It was harsh, they told me when I was going in that if I did not have the surgery, I would probably only have two or three months to live, and there wasn't really much of a choice at that point, so that was my best and only option.

Kluger And what did they tell you the risk of the surgery was?

Metz Well that was the other thing. They said the risk was that I had a 15% to 20% chance of not making it through the surgery, because my tumor was so large and it was in a very vital organ, but the doctor I had down there was terrific and he did a terrific job. I was in ICU for a few days and about 8 or 10 days later I was back home and I was recovering.

Lamothe Terrific, when we come back from our break we are going to talk about Dick's next leg of the journey, but to set us up for that, Harriet, would you speak a little bit about what goes through your mind when you learn that a cancer has metastasized and how you respond to that to prepare a patient?

Kluger The first thought we have is, oh dear! I actually very clearly remember the day in the summer of 2007 that Dick called me and told me that he had sweats and that the physician that was working him up thought he might have an infection, something called a coccidial infection that one gets from exposure to sheep, and we knew obviously because of what we see every day that this cannot be the case and we brought him right in and if I remember correctly, we had a conversation that if we do not do anything, if we do not give you any treatment, the life expectancy is in the order of months. We actually do not have that conversation anymore, because the treatments have improved so much that we cannot really predict how long a patient is going to live after the diagnosis of stage IV disease, because it all depends on how they respond to the treatment and I think Dick's case is a testimony to that, because we thought the IL-2 had not done anything, but in fact once the major tumor was removed, there were other things in the body that did not grow very much or at all after that and Dick will give us some more details afterwards.

Lamothe We are going to take a short break for a medical minute. Please stay tuned to learn more about Dick's story of survivorship.

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*Medical
Minute*

This year over 200,000 Americans will be diagnosed with lung cancer and in Connecticut alone there will be over 2,000 new cases. More than 85% of lung cancer diagnoses are related to smoking and quitting, even after decades of use, can significantly reduce your risk of developing lung cancer. Each day patients with lung cancer are surviving, thanks to increased access to advanced therapies and specialized care, new treatment options and surgical technique are giving lung cancer survivors more hope than they ever had before. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatments for lung cancer. An option for lung cancer patients in need of surgery is a video-assisted thoracoscopic surgery also known as VATS procedure, which is a minimally invasive technique. This has been a medical minute. More information is available at yalecancercenter.org. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.

Lamothe Welcome back to Yale Cancer Center Answers. This is Peter Lamothe and I am joined by my two guests Dick Metz and Dr. Harriet Kluger, and we are discussing Dick's story and his cancer experience. Dick, tell us a little about your life outside of all of this, the cancer therapy and treatment, trips to Yale and trips to your primary care physician, trips to Washington, you had very intensive treatments, but you also had other things going on in your life.

Metz That is true, I would say my life in my mind went pretty much back to normal after my liver surgery in early 2008 I did have to go down to NIH occasionally to get scans to see how things were going and for the most part things were going fairly well. I was working normally, I was travelling, probably doing a little more traveling than normal, but I was really enjoying my life, but in February of 2011 when I was down at NIH and they did one of their normal scans, they saw that the cancer had metastasized to my brain and they also told me that I was now no longer a candidate for the TIL cell because they exclude people that have brain metastasis and they basically said, you need to go back to Yale to try to get some treatment. At that point, I was devastated, here I was thinking I had the TIL cell, and that was going to be my savior and now I am precluded from getting in. I immediately called Dr. Kluger and she calmed me down, which was good because it is a 4 hour or 5 hour drive back up here and she said, don't worry, we have lots of treatment options here at Yale, and as it turned out I came back up and she introduced me to Dr. Chiang, who is a neurosurgeon here at Yale and I went for the gamma knife procedure, which is noninvasive, with the exception of they have to fix a frame to your head, but frankly it is not that big a deal and it is a wonderful technology that they have today.

Lamothe Dr. Kluger, could you say a little bit about the purpose of the gamma knife surgery?

Kluger Gamma knife surgery is not really surgery, it is a bit of a misnomer. It is high doses of radiation. In the old days we used to give people whole brain radiation, which is lower fractions of radiation to the entire brain and over the years the technology improved and we have better imaging

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techniques and we can pick up these things when they are really small, as was the case for Dick, and we can deliver these very high fractions of radiation, which is about four fold the dose to a very small area of the brain. It is done by Dr. Veronica Chiang at Yale along with radiation therapists, specifically Ranjit Bindra and James Yu as well as Joseph Contessa. They do this procedure together, it is a one day procedure, outpatient, and essentially it requires a lot of high-tech technology, they use a very high resolution MRI scanner and a machine that can treat a good number of these in a single setting and they have become very proficient at doing this and we find that when you cherry pick these little lesions as they come along as opposed to treating the whole brain with lower fractions, we are better at controlling the disease and have way less side effects as well with the treatment, in fact we do not see many at all.

Lamothe That is fantastic. Dick, can you tell us a little bit more about what happened after this procedure?

Metz After the procedure in 2011 my life pretty much went back to normal again and about four to five months ago during one of my normal scans, it did come back to my brain and there was another small lesion, which was gamma knifed in April and I had another one only last week, gamma knifed, that was very small and as Harriet said, if we keep on top of this, it is really not that big a deal. So right now this is my course of treatment, I get scanned and should one pop up, I think I have a pretty good method of treatment that will take care of me.

Lamothe That is great news. Dr. Kluger, is it rare for melanoma patients to have brain metastases?

Kluger Not as rare as we'd like it to be. Unfortunately melanoma is the disease with the highest propensity for going to the brain. That has something to do with the biology of melanoma cells, in the embryonic life they originate from neuronal tissues, or from nerve tissue, and so that is probably why they are more conformable living in the brain and that is why they are able to survive there and grow. We see it in approximately 40% of melanoma patients.

Lamothe And what type of research are you conducting at Yale to investigate this?

Kluger We have started a fairly large program here to try to attack this problem. One of the big issues is the bias against treating the brain metastases specifically. As Dick is describing, he has had literally dots in the brain and we have a lot of patients who have dots in the brain, but disease in other places, and we cannot get them on clinical trials, as was the case with Dick back in 2011, because of this view of this problem as being the worst thing in the world because historically many, many, years ago, the median survival after diagnosis of brain metastases was in the order of two to four months and the reason was because we did not have the high resolution imaging to catch these things early, and so we were not really looking because there was not much we could

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do, and we did not have this gamma knife option. I also want to put a plug in here that that is not the only treatment modality we have available. Dr. Chiang is an expert in microsurgery and in relatively non-invasive surgical techniques that she uses to treat these lesions when they are very small.

Lamothe Dick, this is something, obviously, that has had a tremendous impact on your life, but thankfully you are doing extraordinarily well and you getting great care and you have a remarkable attitude and a really positive approach to all this. I know that you, like many cancer survivors in their families have chosen to give back, to take action, and have chosen to do something to help others. Can you say a little bit about what you are doing in the cancer community and in particular at Yale and at Smilow to do that?

Metz I never considered myself much of a religious person, but I think when you facing potential death you become a little bit more spiritual and as I thought about it I said, God kept me alive for a reason and there are a number of things that I have been doing over the past few years to try to give back, for example, at Yale-New Haven, I serve as the co-chair of the patient family advisory counsel, where we work with other volunteers along with different administrators to try to improve the whole patient family experience here at the hospital and I am happy to say that I have seen some of the results over the last three or four years. I think it is a much more welcoming environment for people coming in. I am pleased to see that we are making some progress on that. I am also on the board of Fairfield University School of Nursing, and my wife is a nurse, I went to Fairfield University, so I am giving back there and trying to improve the programs and actually looking for ways where we can bridge the nursing profession, which I think is so critical going forward, with some of the work that we are doing here in cancer care. I have also worked with another melanoma survivor, Bob Heffernan and I have doing some training for the freshman students of Trumbull High School over the past year on the importance of skin care and I guess on a more personal level, I have literally given my body. They have my blood, they have healthy tissue and some of my cancer tissue taken from the National Institutes of Health to do some research work on it. Yale is a research hospital and I would encourage everybody, if there is an opportunity where you can provide tissue and stuff like that, this to me is the secret, not the secret, but it will be the way that a lot of these terrible diseases are going to be cured.

Lamothe Dick, I know that in the last year so you have also done a remarkable amount of fundraising for brain cancer research, which has an extraordinary impact on the work that is being done and I would like Harriet to talk a little bit about that research and how that is moving your field forward.

Kluger We are trying very hard to approach the problem broadly. There are some patients who have small metastasis that do not come up very often, and then there are other people who really have a lot of them and the course of the disease is driven by what is going on in the brain. So, we have to have different approaches for different people. We also have to have clinical trials so that a brain metastasis patient can have early access to drugs, they are not waiting for years and years for

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something to be FDA approved before they can actually be given it, so we have our first brain metastasis protocol open right now to clinical trial. We are working on the second one. We are also working with the imaging people to improve our ability to differentiate between tumor and immune cells that sometimes surround these cancers and a lot of the research also has to happen in the lab. So, we are working with the immunobiology group, and Dr. Lieping Chen has a project that he started to work on about the immunity of the brain, because very little is actually known about it. We are trying to improve the radiation approaches as well and trying to find new genes within the cancer cells that are associated with the ability of these cells to live in the brain.

Lamothe It sounds to me like you have a whole team approach to this research, that it is not just you and another person conducting it but that you're harnessing all of this intellectual power and intellectual curiosity. Can you say how you put together this research and who brings our expertise to it, their backgrounds at the school and at the hospital?

Kluger We have to have a big multidisciplinary team and we have clinical researchers, what we call the translational researchers, and those are the people that are bridging the gap between the bench and the bedside and then the more basic science researchers. For basic science we have an immunobiologist, a radiobiologist and a geneticist, we have a molecular biologist involved, and on the clinical side, we have neurosurgeons, neuro-radiologists, radiation oncologists, and medical oncologists because we can also treat these tumors with systemic therapy, which means therapy that you give through an IV or by pill. I hope I have not forgotten anybody, we have statisticians, bioinformatics people who help us analyze the data, we have a group of people who help us make animal models, because in order to study whether a drug is effective in brain metastases you have to have a mass that you can study, and surprisingly, until recently, very little had been done, there were a couple of models out there but they were not very good, so we are now starting to develop new models so that we can study drugs in various treatment approaches in animals first before we take it into humans.

Lamothe It sounds to me like the combination of the research that you are conducting and Dick's passion to help fundraise and fuel it, means that we are going to be making considerable progress, hopefully in a relatively short period of time. Congratulations. Dick, we are going to be wrapping up and I would like you to speak a little bit to our audience about advice that you have for people who are going through this. What do you say to those patients and those families that you advise at the hospital as they embark on their journey?

Metz The first thing I would say is become an expert on your disease, stay informed. I do not know if Harriet will agree, but I think some of the best patients are the ones that are interactive because it shows that they care and they really want to get well. I think any doctor's reaction to somebody coming in who is really informed and inquisitive and talking is generally a positive thing and generally you get the best answers. One of the questions I always had was, I want to make sure that whatever you do, I have another option out there and I do not want to be precluded. The other

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thing is that having cancer is a journey. You are going to have your ups, you are going to have your downs, you are going to have some clean scans and you are going to be happy, you can have some bad scans, and you are going to be sad. That has been my experience, and it is probably most peoples' experience. I would say, try to stay somewhat even keeled. You will have your good days, but potentially you could have the bad ones, so do not let the bad days bring you down. Finally, surround yourself with support of friends and family. In my case, being open about opened up the support and I should say surround yourself with great doctors like I have here at Yale and lastly, I would say, have some trust in God, have some hope, there is a tremendous amount of work being done in the research field now that gives me hope that someday I will be totally healed.

Dick Metz is cancer survivor. If you have questions or would like to add your comments, visit yalecancercenter.org where you can also get the podcast and find written transcripts of past programs. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.