

**CANCER
SURVIVORS**
SYMPOSIA SERIES
Issues & Solutions for Life After Cancer

**Living With "Survival":
Long-Term Effects of Cancer and Its Treatment**

March 19, 2007

Question & Answer Session

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We're going to turn the lights up. We're going to put a microphone down front for people who want to ask questions. I've been seeing people scribbling notes. We are recording this. It will be part of the CD-ROM, or computer access, or tape, or whatever, if you want to hear what we've talked about again and revisit it in your mind.

I want to thank your speakers for giving us a lot of things to think about and remind myself and remind you that one of the things Dr. McCarty said as we were putting this together, is that the intent of this session is to be very positive. We're looking at a small number of side effects, but in people who are living a long time after cancer care. That is the journey that we're most grateful for. Let me open for questions. If you can come to the microphone, that's great. If not, please talk loudly and we'll try to repeat them to whomever you wish.

Q: Dr. McCarty, you gave some statistics related to chemo versus bone marrow transplant. My question relates to when the patient has had the chemo treatment and then, due to recurrence, has stem cell or bone marrow transplant. How do those numbers or percentages change at that point?

JM: I'm not sure that anyone has those kinds of numbers. I guess by definition, though, everybody that comes to stem cell transplant has had upfront chemotherapy. So I think that the numbers you are describing for bone marrow transplant that were given there encompasses that group. Certainly, people who then go on and have a recurrence even after that and have to have a second transplant, yes, there are additive effects, both because of additional chemotherapy that needs to be given, plus the affect of the stem cell transplant effects on top of that as well. Those numbers I don't think we have because, again, now we're getting into numbers of

patients that meet the criteria for what's called an orphan disease where we can't really put together large enough numbers to make statistical sense and give you a number that means something.

MH: Yes, ma'am. Do you have a question?

JM: Reflex sympathetic dystrophy?

MH: It's probably more related to...I'll speak as a breast cancer physician...but we have seen some people have difficulty after lymph node dissection with...she's asking about problems with pain and discomfort in use of an arm after lymph node dissection...that's part of treatment for several different diseases. There are several different problems that sometimes people will have with nerve damage or nerve issues that happen after surgical and the key is seeing physical therapy, and there are a few pain specialists who work particularly with reflex dystrophy, which is a pain disorder following nerve damage. It can be very difficult. It can be very frustrating at times.

Q: [Inaudible.]

MH: Neurosurgeons know...that's their specialty, nerves. I think you're in good hands there because that's his specialty.

Q: [Inaudible.]

MH: I think working with...seeking care...and that's key, realizing that if something's not right, seeking a specialist in that area whether it be a nerve problem, you're seeing Dr. Desai, who is a hand specialist, is working with that, he's a surgeon who is a hand specialist, good plans there. You're welcome. Yes ma'am.

Q: I have a two-part question. Where can I find more information about asymptomatic chronic bone disease metastasized from the breast? And what about the side effects of long-term use of Zometa, more than three years?

MH: I'll take the second question first. Zometa is one of the bisphosphonates, many people have heard about it, it's an IV medication given to prevent bone loss. There has been a lot of increased question about how long it can be given safely. The biggest concern is that in some areas of the body, particularly the jaw, it may actually impact healing. There are no good studies right now that say you should stop it at one year, two years, three years, or five years. One of the problems of having long-term survivors is that we used to think people are going to be dead with their metastatic disease in two years, now they're not, they're living many more years. So we're still having to do additional research to see if we need to schedule it differently. There's no good answer to it yet. Certainly in

women with osteoporosis who are on the pill version of bisphosphonates, they continue on those for five, ten or fifteen years and do very well. The I.V. ones we have a lot to learn about. Asymptomatic bone disease with recurrent cancer, the statistics are all over the place in terms of how long they can live. Hormone-sensitive disease does the best. The key is continuing assessment and working with your oncologist.

Q: Is the Survivorship Clinic for adults now open?

MH: The Survivorship Clinic for adult cancer patients is open. It opened the end of January. They are taking names and numbers. We're focusing first on breast cancer patients and then we'll be adding other patient groups afterwards. They are going to be doing something similar to what Dr. Dunn talked about with the passport, a similar mechanism to put down what you've been treated with, to then be able to carry with you from physician to physician. Dr. Alton Hart, who is in the back corner here, is the director of that clinic. He will be leading our May session about how these survivor clinics will be working.

Q: The anthracycline drugs, I don't remember seeing how high is the risk for cardiac?

ND: I can speak for the pediatric population. The main identifiable risk factors include the age of the child at treatment, with the younger children being more sensitive than older children. The children under a year of age at the time they receive it are at the highest risk. In addition, the cumulative dose, you take all the anthracyclines, you add them together, and you do a calculation based on the patient's meter squared, and the higher the dose that the patient received the greater the risk of cardiac problems. The third risk factor is whether the patient also received radiation to the area around the heart because that potentiates the risk. You can have cardiac toxicity just with radiation, even if you don't receive anthracycline. It's hard to come up with figures. When we first started using anthracyclines they were hailed as wonder drugs because a number of patients who were terminal and not responding to anything else responded to these drugs. They were used very heavily when they first came out in the late 1960s and early 1970s, and then slowly the reports of the patient suddenly developing heart failure started to be reported. It took a while till physicians realized the cause and effect and went back and analyzed it and looked and saw that it was the patients who had the highest dosage levels that were getting into trouble during therapy or very shortly thereafter. So we developed a maximum dose beyond which we tried not to go, but we are now looking more carefully at the patients who in more modern times received less than that "maximum dose" and, if you look hard enough and try hard enough and do the right studies, even at "safe dose levels" with provocative tests we are finding that more and more patients have problems with these drugs. They may not be clinically

apparent until, for instance, a kid grows up, gets into high school or gets in college and starts participating in some college level sport and has a gung-ho coach and is doing extremes of exercise and prep work for the sport activity. We don't know if these are the patients that are going to drop dead on the basketball court or the football field. For females, we have a problem too, something that's a risk factor for females are the latter stages of pregnancy when the heart is pumping for two rather than one. So a patient may go along fine, they may be followed by us, they may be followed by cardiology, and their tests appear normal, but then they get pregnant and they get into trouble. So it's really, really hard to define who is safe and who isn't with these drugs.

Q: Thank you.

JM: One of the other things that we do in anyone who has received these kinds of drugs, very often we'll have an echocardiogram or some other test of heart function, because the other risk factor that we certainly follow, both with the kids and also with the adults, is whether there is a pre-existing abnormality in heart function. In those patients we may find alternatives or tailor the dose.

Q: As far as radiation at the heart, I'm a breast cancer survivor, mine was on the left. So with the radiation close to, does the radiation hit close to the heart?

MA: It can. It depends on the technique that was used. But it would be more likely to get at least a portion of the heart on the left side than it would, say, if it were on the right side. Since so many people are getting more than one type of therapy these days, and treatments are getting more and more multidisciplinary, it's much more common to see folks who are getting combinations of surgery and chemotherapy and radiation. I think we're more and more cognizant of the risks of the combinations of treatments, as well and how they may impact on the various organs.

Q: When it comes to x-rays, I've heard that having a lot of x-rays is not good for you because of the radiation. Is that the same type of radiation? Should you be cautious about having so many x-rays? Like if it's a chest x-ray, lung x-ray?

MA: It's probably a good idea to try and minimize your radiation exposure, but the relative dose that you would get from a chest x-ray would be infinitesimally small compared to what you probably had from one single day of your radiation therapy treatments.

Q: So from me getting radiation I should be very careful about getting any more, as far as x-rays?

MA: I wouldn't avoid them if it was thought they were necessary, because they're not going to significantly increase the dose proportional to what you had, and they're not going to significantly change the risk of any of the complications that you might be at risk for developing because of the treatment that you've already had. I think it's a different issue for the average person in the general population who hasn't been exposed to these types of treatments than it is for the cancer survivor who may need to have these done more frequently to try and pick up an early recurrence or to evaluate some other issue.

Q: Thank you.

Q: Can chemotherapy affect the function of the heart and cause atrial fibrillation?

JM: Not necessarily directly by causing an abnormal rhythm, but very often we see atrial fibrillation in patients whose heart function might be a little bit lower or where perhaps maybe even not directly ____ the heart where perhaps having a central line may have caused some asymptomatic blood clots, the blood pressure in the right side of the heart through the lung might increase, that can lead to atrial fibrillation. That one is harder to put together by saying, yes, there's a direct correlation. Usually by looking at what the heart function is with the echocardiogram or _____ scan, we can usually see if it's related and why.

Q: On March 25, 2000, I went in the house and I gargled and I spit up a lot of blood. I had an appointment the following Monday to have a colonoscopy, so that coming Monday I went in and the doctor said he treated both ends. I have stage IV squamous carcinoma _____ cancer. The doctor put up this thing that's that long and that big around. I've had 52 treatments of radiation at Duke University _____. This was the 25th of March 2000. I spent a week in the hospital having chemotherapy 24 hours a day. With that I was having two treatments of radiation as well, one in the morning and one in the evening. As a result of 52 treatments of radiation, a week in the hospital before this started, and a _____ later on, I haven't eaten anything since May of 2000. I'm getting a little hungry now. I've written an article for SPOHNC, if you're familiar with that. Are you or are you not? It's the Society for People with Oral and Head and Neck Cancer. [Inaudible.] Anyway, I was recommended to go up to Mt. Sinai Hospital as a result of me writing this article for this _____ and a fellow called me from New York and said he had the very same thing that I did and he went to Mt. Sinai and they took a clot out of his intestines and made a new epiglottis, because mine is closed. If I _____ then I've had it. I'm asking if there is anything at this point that either one of you know that I can do about taking care of this opening here so I can eat again?

MA: Nothing that I'm aware of, sir, other than if they're able to perform some type of reconstructive surgery like that to bypass the area of the stricture. That would probably be it. I'm not aware of any medical treatments that are available to try and deal with something like that, unfortunately.

Q: Basically nothing at this point, right? Is that what you're saying?

MA: Not yet. No, sir.

Q: You spoke of healing tissues from radiation. That's a lot of his problem.

MA: You can try it. It depends on the severity of the scar tissue that's developing in the area. Sometimes with the throat and pharynx there are muscles that have to function in a certain way to be able to make sure the food goes down without it going into your lungs and that may not recover. But you can try the medications – pentoxifylline and Vitamin E – it may help. It takes a very long time for those medicines to work. You may need to be on them for many years. But you could try it and see.

Q: It's been seven years. I just wondered how...?

MA: What the likelihood is that it would work? My guess is that it would be low because of the muscular function that you haven't had for this period of time.

Q: What about that treatment you had that somebody mentioned?

MA: Hyperbaric oxygen?

Q: Yes.

MA: Similarly, I wouldn't be optimistic. That also is more for painful areas of scar tissue and the muscles, but it tends not to relieve the scar tissue to the point that the muscles will begin to function again. I think situations like that, or particularly like you have, are particularly difficult because it's hard to restore the normal function of the organ.

Q: The main thing when he started off was that the epiglottis wouldn't close. Whatever he swallowed _____. There's no repairing that epiglottis?

MA: It sounds like you've had quite a bit of radiation and it just won't function like that anymore. But if they've developed, in New York, I'm just not familiar with it, but it's possible that they may have developed a reconstructive surgical procedure that may allow you to be able to close that off so that you can swallow. It might be something that you might want to call and ask.

JM: You have an excellent resource with Dr. Denardo. He may be a person to ask about what may be out there. He should have a fair idea, too.

Q: He was recommending the surgery where you go in and crack the jaw and everything and do all that. We discussed both ways. He thought this other way was easier because he could at least talk and he could do things that they said he might not be able to do.

MH: Right. Newer things coming out every day, which is a good thing.

Q: I was wondering if there has been a specific study done to address the memory loss that you can have due to the high dose chemo followed by the bone marrow transplants, and if that has been done has it answered to what degree memory loss can be attributed to that treatment? Or is it just what my husband says is my advancing age?

[Laughter.]

JM: Never let age be the reason. I think we're getting to a point where there are more studies to look at that. There have been emerging trials of different agents. They are not ready for prime time. There are questions of, for example, I think, Dr. Anscher can address this, even though there is some controversy now about some of the erythropoietins and those drugs in the news right now, that they may in some way be somewhat protective against some of the injury that happens cognitively. Just keeping the hemoglobin up may do it. But then again there can be too much of a good thing. I think it is an outgrowth, now that we have people who are able to ask for and demand a better quality of life because there are more of us to ask for it, that these studies are now being done. Nothing that we have right now, but a lot of the outgrowth of perhaps some of the, the drugs we're using for Alzheimer's for example, are being looked at in some of these same ways. It's not just high-dose therapy. When we have our consultations many people come to me and say either tape this or write this down because I'm having a hard time remembering things from the treatments I've just had. So I think it's an ongoing thing and a very important one. Don't have an answer yet, but I think we will.

Q: [Inaudible.]

JM: I think some of the studies do talk about, some of the studies actually, you can kind of tell the onset. If it's related to the treatment there is a reversible component. It does get better over time. Does it get to normal? Probably not necessarily, right now. But we also know that nerve injury takes very often months to years before we actually see the maximal effect of what may occur.

MH: One of the things we've done as part of our clinical trials, particularly with breast cancer and with some of our other cancers, is that we're now

acknowledging the fact that people do have chemo-brain and we are starting to do what they call cognitive testing. So not only are we trying to treat the cancer, but we are also trying to test the men and women who are on trial along the way to see if we can start to gain a better insight into it. We acknowledge that it is a real entity. Now the key is to figure out the lock-and-key method. There are some psychologists who are doing cognitive testing to try to help delineate if people have dementia versus an effect of the chemo. But still sometimes that gets to be a little bit murky. We have at least two psychologists in our community who are doing testing for that, just trying to help people get a grip on things. It's an expanding area.

Q: Dr. Anscher, on your slide that was entitled "What Works Now" you were referencing most of those things, if I understood it correctly, that were being used as treatments versus prophylaxes, I know you said the statins were in study now, and you just commented to this couple over here about the pentoxifylline and Vitamin E having to be used for long term. Are these recommended now on a prophylactic basis to ward off some of the long term?

MA: No, they haven't been utilized on a prophylactic basis. The things that have been used have been mainly to prevent dry mouth that people get as a result of radiation and drugs like _____. But the other agents, as a rule, especially hyperbaric oxygen, which is a big deal to get, the others have not really been used prophylactically.

Q: Is there anything in the pipeline for ERPR negative women for breast cancer? For the receptors that are negative, ERPR negative.

MH: In terms of a long term therapy or treatment?

Q: Yes.

MH: Other than doing the initial chemotherapy and treatment there is no new Tamoxifen-like drug available yet for that group of women. We're continuing to look at other ways to define the cancer, but nothing new yet.

Q: And one last comment, would anyone comment, or Dr. Anscher, about the effectiveness or usefulness of co-enzyme Q10 for cardiac, to help cardiac problems or prevention post-radiation?

MA: I can't give you an intelligent comment about that. I haven't seen any studies that have definitely reported anything on that one way or the other. There are a lot of nutritional agents that are being studied to see if they may have some preventive effects against radiation. One of the problems is that a lot of them tend to fall into the antioxidant categories and products of oxidation are important ways that radiation actually kills cancer cells. It becomes a little bit tricky as to how to recommend to folks to take some of

things. I generally recommend that a patient not be on them during radiation unless these things have been specifically tested and found not to interact adversely with radiation. Then afterwards most people will read something, they'll take it and see what happens. But we haven't really done the studies that we need to do to test these various agents that may actually have some beneficial effects.

Q: I have a radiation treatment question. It seems there are a lot of people now that are going for more targeted radiation treatments, like the prostatic BrachySeeds for prostate cancer, and the MammoSite treatments for breast cancer. The complication rates have just got to be less for those. But how about the success rate? I have a friend who just had the MammoSite treatment and in like five days it was over, her whole radiation treatment. Now she is having haunting questions about whether she should have gone for the full chest radiation. Is she going to have as good a chance with what she had as what she could have had?

MA: Probably yes. There is actually an ongoing research study right now, it's a big national cooperative research trial to try to answer just that question. But for properly selected patients we think that it's probably just as good as the conventional full breast radiation. The brachytherapy is equally as successful. Again, it's selection, selection, selection. For people with proper disease characteristics, it's just as effective as external beam radiation and surgery. The comparison of the complication profiles from brachytherapy versus external beam radiation is a whole lecture in and of itself. They are different. In a nutshell, the short term effects from brachytherapy tend to be more intense than the short term effects from the external beam radiation because you're getting this continuous radiation over weeks and months, but in the long run they're pretty similar in terms of risks of bladder problems. Beam radiation tends to cause a little higher incidence of rectal bleeding, and the seed implants tend to have a little lower incidence of erectile dysfunction.

Q: So my friend with the MammoSite, she probably was selected in such a manner that she'll have as good a result from this short treatment as she would have from the seven week, every day treatment?

MA: Most likely. In fact, she may even have elected to participate in the clinical trial because it's open in a number of sites in Richmond.

Q: Thank you.

MH: Time for one last question.

Q: All of these are related to the radiation, one is a technical term. I've had a gray versus a rad. Can you explain the difference?

MA: Physicists are like everybody else. They like to have job security so they change the terminology periodically. But basically one gray is equal to one hundred rad.

Q: Okay. Second is dealing with whole brain radiation. What are the long-term effects?

MA: The major ones that we see from whole brain radiation, the most obvious one, is hair loss. Unlike with chemotherapy, after radiation to the brain the hair often doesn't grow back very well. It can cause cognitive problems, oftentimes difficulty with short-term memory, and difficulty learning new things. People don't often forget things they already know but it may be more difficult to learn new things. And then it can depend also on the particular area of the brain that is effected so that you may get focal areas of the brain that are relatively damaged more than others. For example, in an area that may control the motor coordination in your hand, you may notice some problems there.

Q: You had mentioned one time about scarring of the blood vessels ... that could lead to dementia?

MA: It can lead to dementia, right. But in the brain you often don't see scar tissue like you do in other areas, but you can see the result of obliteration, of closing down of the very tiny blood vessels. That can cause micro-strokes which can lead to dementia.

Q: The last one, I've read that melanoma is radiation resistant. Your opinion?

MA: Unfortunately, that's true. Melanoma is pretty resistant to everything. The key to that, like everything else, is catching it really early.

JM: However, there are other treatments. There is immunotherapy for melanoma, using [intra-leukin-2?], some various trials that way. Some of those are being carried ...

Q: ... cross the blood brain barrier does it?

JM: It does not as well, no. It does not. The other thing that I wanted to address with whole brain radiation is that there are some treatment protocols that sometimes use both radiation and chemotherapy for treatment, for example, of lymphomas or leukemias that may be in the cerebral spinal fluid. Many of the concerns we have is when both treatment methods are used at the same time we actually see more effects for some patients as well.

MH: Thank you very much.

[END]