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Integrative Oncologist Dawn Lemanne, MD Discusses Ketogenic Diets

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LS: Today I have the pleasure of interviewing Dr. Dawn Lemanne. Dr. Lemanne is an integrative oncologist who will be presenting at our upcoming **Restorative Medicine Conference in San Diego** . Dr. Lemanne, please tell us a little about your background and what drew you to integrative oncology.

DL: I'm a completely conventionally trained oncologist. I went to medical school at the University of California, San Francisco, and did a residency in internal medicine at a program associated with the University of Michigan School of Medicine. Following that I did my oncology fellowship at Stanford University. I actually became interested in oncology as a child. Cancer seemed really mysterious to me as a kid. I was always interested in health and how people stayed healthy, and I had some inkling that nutrition and exercise were important and played a role. That was how I came to the integrative part. But I also went for conventional oncology training so that I would have all the tools that one could possibly have in my hands when I was treating patients. Basically, I'm a conventionally trained oncologist, board certified and fellowship trained. Then I've also added the integrative methods to my practice that I think are very important, and which research is showing are very important to patient recovery.

LS: I know that diet and nutrition are a core part of your therapeutic approach. Could you speak a little to how you incorporate intermittent fasting, carbohydrate restriction, and the ketogenic diet into your practice?

DL: The first thing I want to say is that each patient gets a very different diet. I have some patients for whom I recommend something more along the lines of a raw vegan diet, and other patients for whom I will recommend something like the ketogenic diet, which is a high fat diet that can be done as a vegetarian diet, although it's very difficult to do it that way. I also use fasting with many patients, but not all of them. The diets are very personalized. Different cancers require different diets. A single patient may have a cancer that will be susceptible to one diet during one part of their course of treatment or recovery, but susceptible to a different diet, or even resistant to the first diet, at a different point in time. It's really important to figure out as much as possible where your patient's dietary needs lie at that moment, and to go from there.

Another thing I tell patients is that at strategic moments in their cancer care, it may be more important to consider not eating for various lengths of time. Of course what you're eating is very important, but at certain points it may be more important to fast than to be very particular about diet or even supplements. Evidence from animal studies suggests that fasting judiciously and strategically may be a couple of orders of magnitude more

powerful than following a particular diet, no matter how wonderful that diet may be! I incorporate fasting into a lot of patient protocols whether they're on treatment or not. With patients who are on treatment, I will often use fasting during a chemotherapy infusion period; 24 hours before and 24 hours after the infusion. There are studies that show a decrease in certain types of collateral damage with that approach to fasting during cancer treatment, especially with particular chemotherapy agents. In fact, I think the evidence suggests that everyone should fast for short periods at various points in their lives. Not eating is turning out to be as important as what we eat, and perhaps even a little bit more important.

LS: In general do your patients take to fasting readily?

DL: Yes, my experience has been that most patients take to fasting very well, and they often want to do more than I want them to do. Fasting becomes, for most people, much easier the more they do it. Once you've up-regulated the enzymes that allow you to tap into your fat reserves for fuel, it becomes easier. The first couple of days are the hardest, especially for someone new to fasting. For people who are on a vegetarian diet, or another type of diet very high in carbohydrates, it will be harder to get into ketosis, which is when the engines of fasting rev up and you start feeling a little bit better. But people who have been on a ketogenic diet or who are experienced fasters will be able to metabolize fat pretty easily, and will slip into the fasting mode quite quickly.

I read an interesting study of a marathon runner named Frank Shorter. Marathon runners do best when they can tap into their fat reserves while they're running because in a 26-mile race, you use up your glycogen reserves in the first few miles. If you can then tap into your fat reserves, you don't have to constantly stop and drink Gatorade and eat bars and other sources of carbohydrate during the race. Frank Shorter was a champion marathon runner. People did a lot of physiologic examinations on him just to figure out how he was so good. One of the things I found really interesting was that when they took him into the room with the treadmill on which they were going to have him run while they did all the testing, he started burning fat just by *looking* at the treadmill! You up-regulate your metabolism in terms of being able to burn fat by practicing burning fat. People get better at fasting and it becomes easier and easier for them.

LS: I imagine some physicians might be reticent about fasting a cancer patient because of cancer cachexia. How would you respond to that?

DL: You wouldn’t want to place a cancer patient with cachexia on no calories, but the ketogenic diet is a nice thing to use in those patients, because cancer cachexia is a problem of inflammation. It's not a problem of lack of calories, it's a problem of inflammation and the result of insulin resistance. Often patients with cancer cachexia are told to just get some calories in. The easiest way to get calories is to eat carbohydrates. They'll be drinking sweet drinks and milkshakes and things like that. But if you're insulin resistant from inflammation, you can't use the carbohydrate that you have, and you're just going to keep getting thinner and thinner. The ketogenic diet is really much more helpful in cancer cachexia than just stuffing calories from any source into those patients. In fact, that's detrimental. If you eat fat, it decreases the amount of oxygen needed to make ATP or energy compared to carbohydrate metabolism. So if you're eating fat, you're making more ATP with fewer molecules of oxygen, and you have less oxidative stress. That is very anti-inflammatory. The ketogenic diet is a nice anti-inflammatory diet. It decreases the inflammation that patients with cancer cachexia have, and it decreases their insulin resistance.

The ketogenic diet can be useful in patients with cancer cachexia along with other things such as anti-inflammatory medications. Sometimes you’ll want to add anabolic steroids and there are other drugs as well, but that's a big area of research, and a little bit complex to go into here.

LS: How do you assure that a patient has reached ketosis?

DL: I insist that my patients check their blood with a finger prick and a blood ketone meter. Unless they do that, I'm never sure that they're in ketosis, and they aren't sure either. I like to know what their blood ketone level is at any moment, and I like to see how it changes with their diet. A lot of times people will think they're following a ketogenic diet, and it may be ketogenic for their neighbor, but it might not be ketogenic for them. They may need to tighten up the diet and lower their carbohydrate intake more to get into ketosis.

You don't always have to have hugely deep levels of ketosis. If a patient is no longer receiving treatment, is feeling pretty well, and has no signs of cancer, it may not be appropriate to have a Glucose Ketone Index of 1 at every moment. You might be leaving some nutrients on the table that could be good for you. My sense is that you want to loosen up the diet somewhat when you can, and let the patient take advantage of a wider variety of foods. This is why I insist my patients use a blood ketone meter: So that I know they're in ketosis, and that their level of ketosis is appropriate for what we're trying to accomplish. If somebody is on treatment, let's say they're receiving radiation for a brain tumor, and you're trying to augment the protocol with the ketogenic diet, then you really want the Glucose Ketone Index to be near 1, if you can get it there, so we need to measure it to make sure we're accomplishing that.

LS: Where do you stand on the use of antioxidant supplementation during chemotherapy or radiation?

DL: This is one of those really interesting questions that no one has a good answer to. I don't really stand anywhere on it. I try to make sense of the information as it comes in. I did pay attention to the studies that showed that N-acetylcysteine may increase the number of lung metastases in laboratory animals injected with human cancer cells. Does that translate across the board to humans? I don't know.

Mice can make vitamin C, so they have a different way of metabolizing and dealing with antioxidants than human beings, since we can't make vitamin C ourselves. Would all antioxidants have the same effect? I don't think the answers are completely in.

There are interesting case reports of people taking high dose IV vitamin C after a diagnosis of cancer and having an excellent response even without treatment. But those are rare. There are also studies that suggest vitamin C during chemotherapy might cut down on some of the side effects. But those are hard studies to do and hard studies to interpret. High dose vitamin C seems to be very, very safe, which is interesting in itself, because certainly our conventional cancer treatments are not safe. Is it efficacious in treating cancer? In my experience, I have not seen dramatic responses to vitamin C either alone or in combination with conventional treatment. I have read about a couple of seemingly miraculous results. For somebody, somewhere, vitamin C seemed to do a lot, and it seems to be safe, so it's hard to argue against that. It doesn't seem to interfere with conventional treatment, as best we can tell. But again, we don't know for sure.

LS: Thank you for that thoughtful response. it just really points to the necessity to study those outlier patient cases, which is not happening as comprehensively as we wish.

DL: Yes. I think it's important to study the outliers very closely. There's a rich trove of information in those situations.

LS: One of the things you'll be talking about in San Diego is the new field of adaptive therapy. Can you give us a preview of what that is and how it integrates evolutionary principles such as natural selection into its approach?

DL: This is a really exciting area right now. One of the issues in oncology is that the way we treat cancer is to give big doses of treatment in periods as close together as we can without hurting or killing the patient. Treatments are often given in large doses every two, three, or four weeks apart, even in patients whose disease we consider incurable, and most cancers are usually considered incurable once they're metastatic. If a patient has a curable cancer, this approach is exactly what you need to do. You need to treat vigorously and for a long time until the cancer is gone. But in general, with some exceptions that I'll discuss in my presentation, if you give high doses of treatment close together to a patient whose condition is not considered imminently curable, you engineer treatment resistance. For the first couple of rounds of treatment, the scans look better, but in effect what is happening is you're killing off all the treatment-sensitive cancer cells. What you're not doing is having any effect on the treatment-resistant cancer cells, which were in the minority when the patient started out. At the beginning, most of the cancer cells are sensitive to treatment, but Darwinian forces actually play a role here. It's hard for treatment-resistant cells to out-compete the treatment-sensitive cells. Treatment-resistant cells have to have a drug pump or some other way of resisting treatment, and they have to maintain that at all times, whether or not there's any drug around -- whether the patient is undergoing treatment or not. There's an evolutionary or fitness cost to that. They can't reproduce as quickly and as successfully as the treatment-sensitive cells. The sensitive cells outnumber the resistant cells just because they can use all their resources to grow and reproduce.

Researchers I've worked with at the University of South Florida, Moffitt Cancer Center in Tampa, have discovered, using mathematical modeling, that treating very, very minimally and far apart with low doses and very intermittent treatments, not even metronomic, but very intermittent, should improve survival in those patients with incurable cancers. And early pilot trials appear to bear this out. Essentially, we are figuring out how to minimize and slow the development of drug resistance. There may be more skillful ways of administering chemotherapy, and we're trying to figure that out.

LS: That sounds like a very exciting new paradigm in a field that could do with it.

DL: Yes. Oncology desperately needs some new ideas. I'm very happy to have found some of these new ideas with diet and fasting, and an evolutionary approach to giving treatments that offers some hope to patients that really didn't have any.

LS: Thank you so much, Dr. Lemanne, for your compelling and comprehensive clinical observations.

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