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A Fresh Approach to Tackling Obstacles of Obesity

Dr. McDonough:
When people try to lose weight, there are lots of challenges and there aren't many approaches. I remember once I interviewed a physician who said that he had about 2,000 books in his library, and each one had the best cure, the best way to lose weight. Obviously, there's not 1 answer and there are not 2,000 answers, but there are certain things we should have that are consistent as we approach this. I'm Dr. Brian McDonough, and welcome to Primary Care Today on ReachMD. I have a very special guest today, Dr. Lou Aronne. He is the Director of the Comprehensive Weight Control Center at Cornell Medicine New York Presbyterian, and he's been kind enough to join us. First of all, welcome to the program.

Dr. Aronne:
Thank you very much, Brian.

Dr. McDonough:
Let's talk a little bit about obesity and weight loss. We know it's a major health problem. The physicians in our audience are dealing with patients every day. What's your approach, and what do you think we need to know?

Dr. Aronne:
Well, one of the key things I think that physicians need to understand is that obesity is a disease. So, now you're going to ask, "What's the disease?" And what research is showing is that hypothalamic neurons, the nerves that carry signals from the stomach, the fat cell, the intestine to the rest of the brain telling the brain how much fat is stored, how much has been eaten, the evidence is they're damaged in the process of weight gain, so what we believe happens is that bad habits and the environment of too many calories, too much food, not enough exercise, causes a physical change in signaling pathways, and that's what makes it so hard for people to lose weight. They have these physical changes whereby the neurons become less sensitive to hormonal signals. And so, when you look at how you can approach this, in the past we've used reducing calorie intake and increasing energy expenditure, but that hasn't been completely successful. If it were, I would not have this job. I love telling people that. If all those diet books worked, we would not have the Comprehensive Weight Control Center at Weill Cornell. And so something more is going on, and that something is a shift in the set point. How do we manage it? Well, in addition to reducing calorie intake and in addition to increasing physical activity, we have more sophisticated strategies. Surgery has proven its health benefit, but we have on one side diet and physical activity and then do nothing until we do bariatric surgery, and I believe that we are coming to an era where using rationally designed medical therapies and some old therapies that are now being used in a more medically rational way are going to become increasingly common.

Dr. McDonough:
When you look at it and you look at your approach to dealing with this, what advice do you have for doctors? We're dealing with patients all the time. In many cases we ourselves are fighting issues with weight. What do you suggest?

Dr. Aronne:
Well, one of the things we find commonly is that medicine that we as physicians prescribe can cause weight gain. And I can't tell you how many cases we see. We've estimated that about 15% of serious problems with obesity are related to drugs that we prescribe. So, for example, today we were meeting with colleagues from Memorial Sloan Kettering, across the street from us, and they have and it's been recognized that in the treatment of breast cancer, weight gain is very common because of the use of aromatase inhibitors as well as some of the antinausea medicines, steroids, strong antihistamines like diphenhydramine. So, what happens in the treatment of breast cancer is women gain weight, but the evidence is that a 5 to 10% weight gain increases the risk of recurrence, and so we're seeing many physicians in very specific areas looking for strategies to manage weight. And so the first thing we always look for when

we manage someone are medicines that could be causing weight gain and which we could change to something else that would encourage weight loss, and that's a topic, perhaps, for another day. The second thing we do is look for problems like sleep apnea, which make it hard for patients to comply. Sleep apnea is a common comorbid condition. Patients have difficulty focusing when they develop it, and often they look depressed and wind up getting treated with antidepressants that can cause further weight gain. And then, of course, we look for the typical behavioral issues as far as eating, stress, lifestyle, and how we can change those. So, we take a very problem-solving approach where we look for the issues, some of which are very concrete and some not, and try to help the patient to solve those problems. Now, if that works that's great, we're thrilled, but if it doesn't we don't give up. We go to the next step, and we believe that the use of pharmacotherapy would be the next step in this process.

Dr. McDonough:
You know, it's funny how it's evolved. I remember how people used to say, "Well, just some people are overweight, and you gotta cut down the calories." We've really learned, well, sure, diet plays a very important, maybe the most important part, but there are so many other things we can do, and I think a lot of us as physicians are kind of late to the party because we keep saying, "Watch your diet, cut the calories," but that may not always be the answer, and I think you're alluding to that.

Dr. Aronne:
I am, but when it comes to those kinds of recommendations, "push away from the table" and things like that, there are very concrete recommendations that we make for patients. So, one of the things that has been recognized over the past few years is that no diet works for everybody, so we have a number of different approaches that we utilize. For most of our patients, but certainly not all, a lower carbohydrate or a low glycemic diet seems to be quite effective. It allows people to reduce their calorie intake by changing the macronutrient composition of their diet. Other people, on the other hand, like to count calories, so they can eat virtually anything, but they count the exact number of calories. Two new techniques are intermittent fasting. One technique is where someone cuts their calorie intake to 800 calories or even less 2 days per week. That's been shown to be as effective as dieting every single day. And then time-restricted fasting where you eat for a period of 8 hours a day or 12 hours a day and then don't eat for the other 16 to 12 hours, that, too, has been shown to be effective. So, we don't just give vague advice. We give very specific advice which we… We kind of negotiate with the patient to see what they can do in their lifestyle. You know, "Can you do it?" That's the kind of discussion we have with patients where we ask them what can they do. If they're on board, then we'll try something.

Dr. McDonough:
I'm Dr. Brian McDonough. You're listening to Primary Care Today on ReachMD. My guest is Dr. Louis Aronne. We're talking about weight loss, and I really like the fact that you're bringing the patient into the conversation, because you're right, I think a lot of us more or less say, "Okay, this is what you need to do. Read this. Follow this diet," whatever. You're making them a partner. And, I mean, I've been practicing so many years, I'm realizing the more I make patients a partner the better shot I have.

Dr. Aronne:
I agree completely, especially when it comes to these behavioral changes. It's easy for me to tell someone, "Don't eat any carbs and you're gonna lose weight." That will happen every time. But, can someone actually do that on a regular basis? Now, you'll find 1 person who can do it and they wind up in an article in the newspaper that they lost 100 pounds doing this, but I promise you that 99 other people do the exact same thing and it doesn't work, so it really has to be customized to the patient and their needs and what they can do within their life.

Dr. McDonough:
I teach young residents. As I say, I don't know if this is good or bad, but as I move through life, I tend to, when I talk to patients, say, "Well, I tried this and it didn't work," or, "I tried that and it didn't work." What about that approach? Do you find yourself sometimes saying, "Look, this is what most people do," and do you ever use yourself as the so-called foil to try to help them along?

Dr. Aronne:
Sometimes we do that. Generally, we'll give them examples of patients who've succeeded and we tried this and this worked in this patient or that patient, so teaching by example can work, but when it comes to something like weight, it's so individualized. I mean, when you look at a lot of the diet books that are written by celebrities, it's basically, "I lost weight, and everyone in the world should lose weight doing the exact same thing." It doesn't work that way, so we don't tell people, "I lost weight doing this. You should do it." But we will give them examples as we move forward. In certain situations, if someone has prediabetes or they have early type 2, it's pretty clear what we need to do in a situation like that. We try to reduce their carb intake, we give them metformin, those kinds of things, but in more sophisticated situations, we will use examples.

Dr. McDonough:
It's so funny, because having worked in television, I remember one time I went on this diet to show you can lose weight, but they also

paid for the trainer, they paid for the workouts, they paid for things that most people are not going to have access to, and they're certainly not going to get the top people helping them, and that was one of the points of the story, which I remember it frustrated people. I said, "Well, I was given this, this and this, but what do we do without it?" and that really became the most important part of the story. What does the average person do? And I think a lot of things you're talking about fall into that category of what is realistic and what can you individually do. You mentioned metformin and you mentioned prediabetes, and a lot of what at least I'm reading and learning about is initiating medical treatment a little earlier than we did in the past. What about that?

Dr. Aronne:
Well, I think that the future of obesity treatment, that medication will play an increasing role. Metformin has been around for 50 years. We know that it causes weight loss in people with prediabetes. It's not indicated for that, but we find it can be quite effective in that situation, in patients with prediabetes. So, when you combine metformin with a lower carbohydrate diet of some type, we find that we often get very good weight loss. We'll have patients referred to us who are on metformin. The doctor says, "Oh, here's a patient. I put him on metformin because I see you do it. They didn't lose weight." What they didn't do is put the patient on a diet. And again, metformin should be used with a lower carbohydrate diet—not no carbohydrate but a lower carb diet. But going beyond metformin, we have a number of medications. The one that's most widely used is phentermine, and one of the things we found about phentermine… Everyone knows phentermine. It's been around for 50, more than 50 years—

Dr. McDonough:
Right.

Dr. Aronne:
—but much lower doses than have been previously prescribed are effective, and we use the equivalent of a quarter of a phentermine tablet to start in most of our patients. We published a phase 2 trial a number of years ago showing that a quarter of a phentermine, half of a phentermine, you're starting to hit the plateau of weight loss. So, when it comes to the side effect profile that we associate with weight loss medicines, one of the reasons that we've been seeing it is lack of understanding of the mechanisms of weight regulations, so we have been overdosing people by trying to get more weight loss by using too much medicine, by just pushing the dose. What our research has shown and the research of other people has shown is that combining medicines is what can really today, with the medicines we have right now, break through the plateau phenomenon. So, we have a medicine that's a combination of 2, phentermine and topiramate, topiramate which is used most widely for migraine headaches and seizures. When you add those, we've shown that you can get additive weight loss between those 2 agents, and phentermine topiramate is approved for obesity treatment. And there are others. The combination of bupropion, which is used as an antidepressant, used for smoking cessation, along with naltrexone, which is used for alcoholism and narcotic treatment, those 2 together can produce greater weight loss. And finally, as an individual agent, there's liraglutide. It was originally approved for type 2 diabetes. In a higher dose it's turned out to be effective, probably the most effective single agent for weight loss. There's a new agent that's a more lipid-soluble version that's coming on the market for diabetes, produces even greater weight loss. And finally, there's lorcaserin. Lorcaserin is a serotonin agonist that produces significant weight loss, very few side effects, very well tolerated, just had an outcome study which came out today—the results of which we first heard about today—showing no increase in risk, and we hope that with further analysis we'll see a decrease in risk in people who lose weight. If you look at some of the agents that we're studying now, we're seeing significantly greater weight loss than even these. We're seeing 10, 15, even the potential for 20% weight loss in agents that are currently in development.

Dr. McDonough:
Dr. Louis Aronne, I want to thank you for joining us. I have to tell you, I had the opportunity with a colleague of mine to give a lecture at the American Academy of Family Physicians conference on obesity, spent months on it. We got a 1-hour lecture. You, in 15 minutes, summarized so effectively what I probably spent 40 hours on. I really appreciate what you did, and I think a lot of people listening appreciate what you did, because you have a good knowledge of it, and you can express it really rapidly and effectively. So, thanks so much for joining us on the program.

Dr. Aronne:
Thanks for having me, Brian.

Dr. McDonough:
This is Dr. Brian McDonough. If you missed any of this discussion, please visit ReachMD.com/primarycaretoday. You can download the podcast. You can learn about the series. Thank you for listening and Being a Part of the Knowledge.