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## Innovative Nutritional Intervention: A Science-Based Approach to Supporting Metabolic Health

Announcer:

Welcome to ReachMD.

This medical industry feature, titled "*Innovative Nutritional Intervention: A Science-Based Approach to Supporting Metabolic Health*" is sponsored by L-Nutra, and is intended for healthcare professionals.

Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:

The obesity epidemic is now recognized as a global chronic disease with significant metabolic consequences. And even with all of medicine's modern advances, should we be turning to fasting, a long-time healing tradition to promote metabolic health? This is ReachMD, and I'm your host Dr. Jennifer Caudle. Joining me to discuss a new regimen is Dr. Joanna Mitri, who is an endocrinologist at Joslin Diabetes Center. She is also a clinical instructor at Harvard Medical School, and we also have Dr. Pouya Shafipour, a primary care physician and attending physician at St. John Hospital in Santa Monica, California. Dr. Mitri and Dr. Shafipour, thank you so much for being here today.

Dr. Mitri:

Thank you for having us.

Dr. Shafipour:

Happy to be here.

Dr. Caudle:

Absolutely. Well, I'm – I'm really excited to have you both. So to start us off, Dr. Mitri, could you define fasting and describe the different forms of fasting and how they could benefit our patients?

Dr. Mitri:

Yeah. As you know, fasting has been part of human evolution. Unlike our ancestors, people now eat three large regular meals per day with snacking in between. Our human ancestors were occupied with looking for food. So, as a species, we are here because of our bodies' ability to adapt during times when energy or food is scarce.

Many religions of the world use fasting as part of their spiritual ritual. When people go for routine bloodwork, they're often instructed to fast prior to coming in. So what does fasting mean? In simple terms, it means not eating for a period of time. There's overnight fast, and this is where the word breakfast comes from. Meaning to break one's overnight fast. Let's start with the term, intermittent fasting, which is very popular these days. It's an umbrella term for various fasting modalities, which involves complete or partial 24-hour restriction done one or more times per week. Intermittent means irregular intervals and it's not continuous – steady or continuous. Intermittent fasting has gained a lot of popularity recently and there has been an increased interest in learning more about it. I think of intermittent fasting as a way of eating that focuses more on when you eat rather than what you eat. In humans, the three most widely studied intermittent fasting regimens are one, the alternate day fasting; two, what we call the five to two intermittent fasting. This means that you would fast two days each week. Um, and that this – uh, during those days, you typically consume about 500 calories and you do them on nonconsecutive days. Uh, and, uh, and lastly, uh, you have, the daily time restricted feeding which is the most common type. Most people refer to this type of fasting when they use the term intermittent fasting. In a nutshell, people eat during a window of time throughout the day, anywhere between 8 – to 8 – 12 hours and then they would refrain from eating or fasting during the other time. Note,

that some of that time would include sleeping. There's also the prolonged or periodic fasting. Typically, this involves water fasting where people only drink water for anywhere from two to five days, but this form is quite dangerous and should only be done in a supervised setting. At the end of the day, this plan help people to become more aware and mindful about the frequency of their eating and how much their food intake is impulse driven and unrelated to hunger. As you stated, at the top of the interview, diseases of excess are the top causes of death globally. So, I see this shift in meal timing and then allowing the body time to rest from digestion as a good thing. The good news is that there are numerous studies being conducted around the world looking at various fasting modalities and its impact on the body and the health.

Dr. Caudle:

Dr. Mitri, thank you so much for that. It was excellent. Um, so now that we understand the various fasting methods, I would really like to dive into the newest approach to fasting, which is the fasting mimicking diet. So, Dr. Shafipour, we are going to – um – we are going to go to you now. How does this nutritional intervention compare to the ones described by Dr. Mitri?

Dr. Shafipour:

So the fasting mimicking diet or for short, FMD, was created by Dr. Valter Longo at the University of Southern California's Longevity Institute. Based on years of observing and studying, eating and physical activity patterns of people in centenarian regions for so-called blue zones, where many people live to be at least 100 years old or more. What they've noticed that, uh, these people all have in common is that they eat predominantly plant-based food and they do not consume excessive amounts of animal-based protein. And they're do – all – some type of fasting a few times a year. FMD was developed to allow consumers to reap the benefits of water fasting while being nourished with plant-based food and precise macro and micronutrient contents that does not really turn on the nutrient-sensing pathways of the body. So patients can avoid the burden and dangers of conventional water fasting. Now, let's discuss these nutrient-sensing pathways. Uh, there is usually three, uh – uh, nutrient-sensing pathways in the body. One of them is called the protein kinase A or PKA pathway, which is typically activated by glucose and there's also IGF-1 and mTOR, which are activated by protein and amino acids. So, earlier in his career, Dr. Longo was studying the impacts of prolonged fasting or water fasting on longevity, but he faced difficulty recruiting and keeping study participants, obviously. Uh, so he developed the FMD out of desire and need to make prolonged fasting more doable by allowing study participants consume foods with specific micronutrient breakdown that does not recognize the body because the food typically goes under the nutrient-sensing pathways radar in the body. So the FMD was developed, uh, the researchers at USC as a result of over \$30 million dollars in grant from, uh, - some of which was from NIH and NIA.

And as of now, it's the only patented nutritional program for longevity and health span. So, how does FMD work? It works by providing specific plant-based foods and macro and micronutrient contents and ratios that put the body in a physiologic and molecular and cellular fast. Typically, it's a five-day diet and it's, uh, the first day is about 1100 calories and then it follows by 800 calories, uh, or less the rest of the days people are typically eating foods like soups, uh, nut-based bars, olives, and some teas.

But the body senses these as fasting because of the low protein content, low carbohydrate content and also with the very low-calorie content of food.

Which, as discussed before, does not trigger any type of nutrient-sensing pathways. It's convenient for patients because they're eating food, but, uh, also it's convenient for the body that's resting and is in, uh, a fat – fasting state.

Dr. Caudle:

So, you know, tell us now that you described the – the process, how does the body actually react during these five days?

Dr. Shafipour:

So, on day one, the body gradually transitions into a fasting state and it starts going into fat-burning state typically end of day one, beginning of day two and also we see some intercellular, uh, process called autophagy, which is, uh, Auto means cell, phagy means eat, so basically the body starts dismantling, uh, old and worn out intercellular components and repurposes them for other uses and, uh, almost like, uh, body starts recycling and cleaning itself. And, on day three, the recycling continues, uh, and people sometimes reach fat-burning or ketotic state, although for different people, uh, this would be different.

And then, uh, we have autophagy continuing day four and five, uh, and day six, typically, people transition to a normal diet that they were on before. But what we see, uh, clinically in people, is that after going through this, uh, five days of fasting mimicking, they typically improve their eating habits and they don't necessarily go to an unhealthy diet, especially because they seem some weight loss.

They see some decrease in abdominal fate – with fat, uh, waist circumference, and they typically do not feel like they are losing any type of lean, uh, body mass. Other things that people, uh, usually report is improved focus, energy, better relationship with food, and a sense of pride and achievement. Also, what I have seen in patients, is that really – they – they really have this sense of pride that they could survive on so little food.

Dr. Caudle:  
Interesting.

Dr. Shafipour:

And, uh, in five days. Um, uh, we typically recommend people do the diet at least, uh, once a month for three months and then periodically, uh, depending on their goals and, uh, health condition. What we've seen in clinical, uh, trials, uh, and studies after three consecutive methods of the FMD five days a month for three months in a row is that about approximately six pounds of body, uh, weight loss. Also people have referred – uh – reported abdominal and visceral fat loss. We've seen that with, uh, measuring the body fat. Also, the waist circumference, and also the other markers, such as systolic blood pressure has gone down, the – uh – a lot of the inflammatory markers go down. And, uh – uh, people have been able to maintain a very healthy levels of the insulin-like growth factor 1 or IGF-1.

Also, as I mentioned before, they get a lot emotional benefits and better relationship with food and they're able to break the, uh, some of the food impulses an addiction and as a results, they have a sense of pride after finishing this. In terms of clinical studies, there is about 49 clinical studies that are planned and ongoing and – or near completion in the United States, Europe, uh, that are studying the effects of FMD and – some of – some of the number of conditions such as diabetes, cancer, and also other several other immune disorders.

Dr. Caudle:

So, Dr. Shafipour, I think we need to talk about what evidence there is to support the regimen you just discussed. So, can you review the science, uh, behind the fasting mimicking diet or FMD and what makes this method work?

Dr. Shafipour:

So, in a randomized controlled study of 100 subjects by Min Wei published in *Science Translational Medicine* in 2017, participants who completed the three monthly rounds of FMD had reductions in IGF-1 and systolic blood pressure and also they lost an average of five pounds and, uh, we also noticed reductions of abdominal adiposity, waist circumference, and preservation of lean body mass. Also they were – most participants were able to maintain these benefits for three months post-completion of the FMD.

Dr. Caudle:

Great and looking at this on the other side, Dr. Mitri, let's come back to you. Are there potential risks that are associated with these nutritional interventions that our listeners really should be communicating with their patients?

Dr. Mitri:

Yeah, absolutely. First the majority of clinical studies have focused mainly on overweight, young, and middle age adults, but despite the evidence for the health benefits of intermittent fasting, there are certainly some impediments to the widespread adoption of intermittent fasting as a long term way of eating. Some people may experience hunger or retabulating and a reduced ability to concentrate during periods of food restriction. These happen typically during the initial period within one month, but they do substy – subside after that. So, we need to learn more about the long term benefits of this way of eating, but we also hear of extreme forms of fasting, so it is important that we take the opportunity to remind ourselves and our patients about safer ways to try fasting. Some of those risk associated with these extreme versions of fasting or ab – abstaining from food may be gallstones, passing out, hypoglycemia, dehydration, and so on.

Dr. Caudle:

Excellent. Um, and lastly, Dr. Shafipour, are there any contraindications across patient populations that we really should be aware of? And also, what types of activities should be avoided during fasting or – or using – uh – while using the fasting-mimicking diet?

Dr. Shafipour:

So we usually do not recommend doing the fasting-mimicking diet for children under 18, women who are pregnant or nursing, individuals who are allergic to nuts and soy, which is a part of the diet. Also, underweight individuals, body mass index under 18 is our limit, um. The other people that we usually recommend against it, is people with serious health conditions and illnesses unless we have approval from their physician. Also, people that feel very weak or by certain diseases, anyone who is on prescription medications, we usually again need to review the medications with their physicians, especially people on diabetic medications, hypertensive medications, metformin, insulin, uh – um – uh, that we need to – we need to talk to their physician to make sure, uh, we have a regimen for, um, for the while they are on fasting. We also, uh, um, do not recommend fasting, uh, for individuals with particular metabolic diseases, such as those effecting gluconeogenesis. Uh, the other individuals would be people with congestive heart failure, especially New York Heart Association Grade 2 or more that have ejection fraction less than 40%, uh – uh, patient with history of syncope or fainting and also calorie restriction, other – that can be significantly affected by calorie restrictions. Also, there is certain dietary needs that people have that might be incompatible with the FMD meal plan. The other group would be people with liver or kidney disorders, uh, that can be affected by low glucose or protein content of the diet, uh, that are – uh – contraindicated for.

Dr. Caudle:

Okay.

Dr. Shafipour:

In terms of activities, uh, this is a form of fasting.

Dr. Caudle:

Right.

Dr. Shafipour:

So this is a form that puts the body in the state of fasting so any type of intense physical activity, one of the popular ones right now is high intensity interval training.

Dr. Shafipour:

There are lot of people -

Dr. Caudle:

Right.

Dr. Shafipour:

-that participates, so we don't recommend that because of again risk of syncope, but regular light cardio activities, such as walking, gardening, light yoga, are things that, um – uh, are allowed and recommended during the fasting.

Dr. Caudle:

Excellent. Excellent. Well, those are all really great things for us to keep in mind. Uh, unfortunately, however, we're all out of time here, so I – I would really like to thank my guests, Dr. Joanna Mitri and Dr. Shafipour, for helping us really better understand the fasting mimicking diet. It was really great having you both on the program. Thank you.

Dr. Mitri:

Thank you.

Dr. Shafipour:

Thank you.

Announcer Close

This program was sponsored by LNutra. If you missed any part of this discussion, visit [reach-m-d-dot-com-slash-Medical-Industry-Feature](https://reach-m-d-dot-com-slash-Medical-Industry-Feature). This is ReachMD. Be part of the knowledge.