Dominic D'Agostino - Interview (FL FEB 2017)

Dr. Eenfeldt: Today I'm going to talk to one of the world's top experts on ketogenic diets and ketone supplementation, professor Dominic D'Agostino. I'm here in his lab.

I'm Andreas Eenfeldt from DietDoctor.com and I'm here with Dominic D'Agostino. Thank you for having me.

Dr. D'Agostino: Thanks for coming, I appreciate it.

Dr. Eenfeldt: It's quite a setup you have here.

Dr. D'Agostino: Thank you yeah it's taken years to develop these technologies that actually gave us insight into the neuroprotective effects and anticancer effects of ketones.

Dr. Eenfeldt: You have been doing research on ketones and ketogenic diets for how long?

Dr. D'Agostino: It's been 10 years that I've gotten into this but... I am a pharmacologist and a physiologist so I was shifting my attention more towards drug research, to energy metabolites, because they had drug like effects that I was interested in exploring more.

Dr. Eenfeldt: So what's been the most interesting thing about this, your research into ketones and ketogenic diets... What made you so interested in this?

Dr. D'Agostino: Initially I was interested because I was funded by the Department of Defense, a branch of that is the Office of Navy Research and I'm in the Under See Medicine Program and I was funded through my grants to understand the cellular and molecular mechanism of oxygen toxicity seizures. And in the process of doing that I explored all the anticonvulsant, antiseizure strategies.

Dr. Eenfeldt: So that's basically divers getting seizures underwater... Could be fatal to them.

Dr. D'Agostino: Yeah, so a limitation of diving with a closed-circuit re-breather that the special operations community does is oxygen toxicity seizure. So it limits their mission capability and their safety. So we developed various technologies that allowed us to understand fundamentally what was going on at the level of the cell, the level the membrane and even the mitochondria.

And in the process of studying the fundamental roots of oxygen toxicity we made some observations with ketone metabolites that would suggest that that would be an effective strategy in testing various, you know, energy metabolites.

And to my surprise I kind of reinvested some time into looking at the dietary literature that I was kind of familiar with because my undergraduate work was on nutrition and it led me to

understanding the ketogenic diet as a century-old, you know, metabolic-based therapy for drug-resistant epilepsy. So I thought there was potential to exploring the mechanism of the ketogenic diet and harnessing that for oxygen toxicity seizures.

And either harnessing a specific formulation of the diet or to circumvent the diet altogether and develop synthetic ketone technologies that would allow us to exploit the benefits of altering or preserving brain energy metabolism in that face of an oxidative challenge which is occurring in these extreme environments of the undersea. In addition to that, kind of serendipitously I had a couple people contact me and one was Mike Denser from the UK and he had drug-resistant epilepsy and was going to have a part of his brain removed because of hippocampus.

And I mentioned the option of using the ketogenic diet, I was just exploring its use for epilepsy at that time while all of this was happening and when he tried the diet... And I was very familiar with how nothing worked for Mike, even high doses of multi-antiepileptic drugs... And when the diet worked remarkably well for him then you know I became increasingly confident that it could be used in this approach.

Because the diet tends to work for epilepsy, for seizure disorders independent of the etiology. So it works across many different types of seizures. And it probably works because it's bringing the brain back into homeostasis, into energy homeostasis and it does it remarkably well for a number of seizure types.

Dr. Eenfeldt: Could you just lay out in very simple terms what is ketosis and what are the potential benefits of it?

Dr. D'Agostino: I like to approach ketosis from the concept of fasting, because most of what we learn and what we teach to the medical students... They only know ketosis in the context of diabetic ketoacidosis which is very specific to type 1 diabetes. So I'm going to step back from that and talk about ketosis as a means for us to preserve brain energy fuel flow in the face of starvation or eliminate carbohydrate availability or limited food availability.

So in the face of starvation we liberate our fatty acids from adipose tissue and these are broken down in the liver to water-soluble fat molecules that can then go on and cross the blood brain barrier and continue to preserve brain energy metabolism after glycogen depletion in the face of limited glucose availability. And about a century ago it was observed that a carbohydrate restricted high-fat diet and moderate protein diet could mimic the metabolic state of fasting.

And this diet was termed the ketogenic diet, because there is an elevation of blood and urine metabolites that were ketone bodies. But anyway these ketone bodies have a broad range of functions on physiological processes and on specific tissues. Now we know that it's not just an energy source but it has anti-inflammatory effects, it has epigenetic effects and these are the things that we're also interested in exploring to help us understand how the ketogenic diet is conferring these therapeutic effects on so many different disorders.

Dr. Eenfeldt: So you eat ketogenic diet yourself?

Dr. D'Agostino: Yeah, I do.

Dr. Eenfeldt: All the time or most of the time, or...?

Dr. D'Agostino: I would say about 95% of time yeah...

Dr. Eenfeldt: Why?

Dr. D'Agostino: The meals would be ketogenic only because I feel better, because it's practical and I can eat in the morning and not get hungry in the afternoon and that has a practical advantage. And I actually like the food, I think of it as fairly indulgent, not very restrictive because your palette adapts over time and you gradually wean yourself off of sweet foods and you gain a liking to fatty, salty foods.

I like to increase the diversity of the carbohydrate-based foods that I have or fairly non glycemic carbohydrates like asparagus and Swiss chard and spinach, and salads, cauliflowers, kind of a staple cauliflower mashed potatoes.

Dr. Eenfeldt: Do you think it's important to eat a lot of vegetables for health reasons or could you like eat no vegetables at all?

Dr. D'Agostino: You know I feel totally fine eating vegetables and I'm a not as convinced as it's important as some people think that it is, but actually I like vegetables and it's part the pleasure of eating, is exploring, you know, making different types of salads. So if I'm about to eat dinner a lot of times I will just instinctively start eating the vegetables before I dig into the steak or the meat on my plate.

Dr. Eenfeldt: Yeah, I like it too.

Dr. D'Agostino: And I realize that kind of consciously sometimes I catch myself doing it. So I do miss vegetables if I don't have them. And they have this satiating filling effect because of the volume that you are eating.

Dr. Eenfeldt: What are the mistakes that people do if people want to get into ketosis, they want to do a ketogenic diet but they are not able to do it, they are not able to get into ketosis. What are the kinds of mistakes that are common and people make?

Dr. D'Agostino: So I would ask, you know, why are they doing a ketogenic diet. And that may influence my response. But I think for the large majority of people that want to lose weight and I don't think nutritional ketosis is definitely not absolutely necessary to lose weight. So I don't think they should be chasing ketones and trying to look at that, although ketones present in the urine or blood is an indication that your fat oxidation rate is very high.

Dr. Eenfeldt: So it's like a good sign.

Dr. D'Agostino: It's a good sign and I think it makes weight loss easier because if your ketones are elevated it's more or less keeping your brain happy, because you have a steady fuel flow to the brain. And I have had numerous people who told me that they just couldn't get into the groove of the ketogenic diet or feel well until they're able to get their ketones elevated and they had a certain clarity when in that metabolic state.

And their fat loss was proportional to the levels of ketones that they're able to maintain and that makes perfect sense from a metabolic physiology point of view. Most people initially I think you need to... so maybe do some intermittent fasting and that copes your body into a state of ketosis. And one way to go about it would be to do ketogenic intermittent fasting. So fasting throughout the day and then the meal that you are eating within your 4 to 6 hour window would be ketogenic in the macronutrient profile.

If someone's following a ketogenic diet and they just don't feel good and they are like, "What am I doing wrong?", I was like, "Maybe you shouldn't be doing the ketogenic diet." You know you need to explore what works right for you. But sometimes I'll get these people that they just do not feel good on the diet but they are dead set on doing it... And I would say, "Don't do it if you don't feel good. Even if your blood markers are improving, but if you don't feel good, that's an indication your body is not adapting."

Dr. Eenfeldt: This is something that sometimes is debated... Is it a bad thing or an okay thing to drift in and out of ketosis?

Dr. D'Agostino: I think it's probably better.

Dr. Eenfeldt: People potentially feel bad doing it, like they get less energy for the brain while they're sort of in between?

Dr. D'Agostino: It depends on what your goal is you now... An epilepsy patient I wouldn't recommend going in and out of ketosis, but if you are using it for general health reasons I think it's good to maintain your metabolic flexibility and to go in... And when you're not on a ketogenic diet it doesn't make sense to eat high carb but it would make sense to have some degree of carbohydrate restriction relative to what, you know, the general standard American diet is.

But I don't think there's any particular benefits to being in nutritional ketosis all the time. And maybe those relative changes are a good thing, because if we maintain that condition all the time then if we are put in front of us a situation where nutritional ketosis would be a benefit to us, whether we're going like on a hike, or a mission, or something, or had to deal with limited food availability for some reason or another, transitioning into ketosis may be a good thing for that period of time.

And I think our body works in cycles so I think it's good to vary our diets up. That may seem odd coming for me because I stick to the ketogenic diet almost all the time, but...

Dr. Eenfeldt: So do you do any like this breath test like Ketonix or doing strips?

Dr. D'Agostino: Yeah, I use Ketonix.

Dr. Eenfeldt: What do you see are the sort of pros and cons of different methods?

I don't mind pricking my finger to get blood. I still say that blood is the gold standard to look at that. And whenever I measure ketones I also measure blood glucose and I look at that ratio, the glucose-ketone index, which is a good measure, it gives you a single number you know. One being a one-to-one ratio of glucose to ketones in millimolar.

Dr. D'Agostino: And Prof. Thomas Seyfried has a paper on nutrition metabolism and we're trying to work towards getting meters. I'll actually give out a reading of the glucose ketone index to be used therapeutically. But I feel urine ketone strips are probably what you'd want to use if you're just starting out to confirm that you've even achieved the state of ketosis and you know you're not wasting blood ketone strips if you're not already in ketosis.

So if you're at moderate levels on a urine strip you're going to be measuring some elevation on a blood ketone strip. And a lot of parents had told me that their breath acetone levels or the breath ketone meter correlates very well with seizure control. And that would be in agreement with some of the publications that show that breath acetone correlates with seizure control.

So you're not going to have an elevation in acetone if your other ketone bodies are not elevated, beta hydroxybutyrate and acetoacetate. So it's a good noninvasive way and it's a useful device for adults and for kids too that don't want to get stuck in the finger.

Dr. Eenfeldt: One final subject that I'd like to discuss is ketone supplementation. What are your views on that? Who would it be beneficial for and who would probably be wasting his or her money?

Dr. D'Agostino: I think the benefits of ketone supplementation are numerous from the studies that we've done and other people have done and are expanding in various emerging applications. So the reason that I was specifically looking into ketone supplementation was for oxygen toxicity seizures. Something very specific and in a very small population of people. And my initial enthusiasm was to use the ketogenic diet. And there's not a whole lot of enthusiasm at the governmental level of switching the diet of a war fighter or an astronaut.

So they want to get the ketogenic diet in a pill or in a solution, or a powder, or whatever form an exogenous ketones would be in. So I was forced... I was steered in the direction of looking into developing and testing a broad range of ketogenic supplements that could be a ketone ester, a ketone mineral salt, even medium chain triglyceride oil and powders.

So I view from a therapeutic perspective, ketone supplementation can further augment the therapeutic efficacy of the ketogenic diet by enhancing the ketogenic ratio to further elevate ketones and probably ketones and even ketogenic fats like MCT oil or non-glycemic fats that have very little insulin response, so they further enhance this fasting like state that we call nutritional ketosis.

So they have applications for people who are already responding to the ketogenic diet. And for specific applications as it pertains to a war fighter in extreme environments, an astronaut on a shuttle, because the energy density is higher, or the average person who just is an athlete, who is a CEO in a company, who just wants to perform better, feel better, maybe look better, I think ketone supplementation, viewing ketones as a source of calories makes sense for me.

But we are still at the costs of understanding the science even and the application of exogenous ketones, like what would be optimal. We do know that when you added to a standard diet that's not carbohydrate restricted that you get remarkable neuroprotective, antiseizure effects. You get anticancer effects, you get antianxiety effects, you get lower blood glucose, you get metabolic effects.

So these effects are realized and documented even in the absence of the ketogenic diet. So we needed to do these studies to determine you know the effect of the agent by itself. And now you know as we screen at 20 different compounds and formulations of ketones we identify the ones that have the highest therapeutic efficacy, safety and palatability and then we can apply particular formulations to specific diseases, like Angelman syndrome, or glucose transporter deficiency or performance optimization, cognitive performance, physical performance, antianxiety.

And it's going to take screening the individual agent, independent of the ketogenic diet but supplemented to a standard diet to determine if it's the ketone supplementation actually having the effect. And the data that we're getting is pretty robust and very encouraging that these agents are having an effect independent of dietary restriction. So we're able to completely circumvent the need for dietary restriction and be able to realize the effects of nutritional ketosis with these ketogenic agents.

So therein lies the benefits, but I think the optimal use of these agents will be realized when they're combined with not necessarily a ketogenic diet, but with a low-carb nutrition which I think is optimal for metabolic physiology in most situations. And so I'm eager to get this work out of the way or we're testing it with the standard diet and then start formulating what I think may be the optimal diet and adding ketones to that and looking at performance optimization, antiseizure effect, stalling the progression of Alzheimer's disease in various animal models and also looking at the anticancer effects.

Dr. Eenfeldt: What are you most excited about looking into the future... ketogenic diets and ketone supplements? What's the most exciting thing for you right now?

Dr. D'Agostino: I think I'll have to kind of default back onto this idea of using exogenous ketones for emerging application. And I would have to say that some of the things that I'm most excited about is partnering with governments organizations like Department of Defense, and Office of Navy Research, and even NASA to incorporate the use of exogenous ketones in various military missions and also potential space missions.

So I am kind of in negotiations with them now and talking with them about strategies on how to do that and how to design an experiment that we can test this as an eating strategy or as a nutritional supplement as part of the program. So lots of interesting things coming up.

Dr. Eenfeldt: It's been super interesting to talk to you, thank you so much for letting us come to your lab.

Dr. D'Agostino: Thanks for having me and thanks for providing a platform for research scientists like myself to get the information out there, because we could be hiding in our labs and doing our thing and trying to publish in Science and Nature, but if we don't step out there and get the translatable, actionable kind of data from our lab to the public, that's kind of the most important thing. So there are things that we're doing in our lab today and that we've done that society can benefit from.

I really believe that and I know I have and people that I know have benefited tremendously from this idea. And it's not me doing the research, it's really the people working under me that are really in the trenches. you know, the students, the postdocs, the medical fellows that are you know implementing these approaches. They are really kind of at the forefront of this movement.