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The ERA JUMP Study: Reevaluating the Omega-3 Index

OMEGA-3 FATTY ACIDS

Hosted By: Dr. Larry Kaskel.

Presented by the National Lipid Association.

Guest: Dr. William Harris, Director of Metabolism and Nutrition Research at Sanford Research at the University of South Dakota, and Research Professor of Medicine at the Sanford School of Medicine at the University of South Dakota, and the developer of the Omega-3 Index.

DR. LARRY KASKEL:

Well, there is a recent study that just came out about fish oil and its benefits in decreasing coronary calcium and potentially decreasing events called the ERA jump. Can you tell us a little bit about that trial.

DR. WILLIAM HARRIS:

Yeah, that is a study that, I must admit, I did not do, I did write an editorial about the paper, so I am at least a little familiar with it. It was a study that was done in three cohorts of men, Japanese in Japan, Japanese in Hawaii, and white men in Pennsylvania, and these guys are all the same age, are all post World War II, from a Japanese point of view, that is important, in age, and what was interesting about the study, they looked at the cardiovascular risk factors among all three of these groups, (01:30) and they found that to somewhat my surprise that the Japanese in Japan had pretty much the same lipid risk factors as the folks here in America, whether in Hawaii or in Pennsylvania, so there was not much difference about their lipid risk factors. Blood pressure tended to be a

little higher among the Japanese in Japan, smoking rates were higher, diabetes was slightly higher, but when they looked at coronary calciums and intima-medial thickness, they found less atherosclerosis in the Japanese in Japan, and so the question was why is that and so they went on to measure serum levels of omega-3 fatty acids and found that voila the difference between these groups was a glaring difference in omega-3 levels.

DR. LARRY KASKEL:

Now, this was not an outcome study, was it?

DR. WILLIAM HARRIS:

No, it was not. It was really a cross-section of a three-cohort study.

DR. LARRY KASKEL:

Did any of these people have preexisting disease as far as we knew?

DR. WILLIAM HARRIS:

It is a cohort that has been followed; they may have included people who already had an event.

DR. LARRY KASKEL:

There was a very high correlation association between omega-3 levels and calcification in IMT, so I would like for you to tell us why that is?

DR. WILLIAM HARRIS:

The reason why I think that is, is that a chronic long-term intake of omega-3 fatty acids, that is what I think with the Japanese level which is around approximately 1 g a day of (03:00) EPA and DHA, the two fish oil omega-3's. I think a long-term intake of that produces a chronically less inflamed environment and that I think probably adds up to long-term reduction in vascular disease.

DR. LARRY KASKEL:

But there is a lot of mechanisms that you are aware have been postulated how omega-3 fatty acids can reduce coronary risk. There is decrease in from arrhythmogenicity; there is decrease in thrombogenicity, there are decreases in triglycerides. Do you think that there is something going on with perhaps adhesion molecules, nitric oxide? What do you think is the mechanism that is really giving these fish oils the bang for their buck?

DR. WILLIAM HARRIS:

If you are talking about sudden cardiac death, I think we are talking about antiarrhythmogenic effects, which is the omega-3 fatty acids becoming incorporated into the lipid bilayer membrane of the heart, stabilizing the heart against ischemic stress that would in other situations throw it into a V-tach and a V-fib post MI and reduce the risk of those fatal arrhythmias that has been shown in animals, and there is evidence in humans that that is what they seem to do at fairly low intakes, that's the intake that the Japanese are typically taking around 1 gram a day. I think that in this particular study they are not looking at sudden death or arrhythmic mechanisms at all. (04:30) They are looking at atherosclerosis, deposition of plaque, and as a function of the anti-inflammatory effect, there is less adhesion molecule expression. I think there probably is more nitric oxide so slightly more nitric oxide release. We have looked at the vascular endothelial function with omega-3 and that has improved, and so in the supplementation study, this is a chronic life-long situation from that. I think that is an important point that it may be that it takes years and years of the right dose of omega-3, a nutritionally achievable dose by the way. One does not need prescriptions or one does not need supplements to do this if you are willing to eat some fish. That I think is what it probably takes as a long time of chronic exposure.

DR. LARRY KASKEL:

If you have just turned in, you are listening to Lipid Luminations on ReachMD XM157. I am your host, Dr. Larry Kaskel. My guest today is Dr. William Harris of the Sanford School of Medicine and developer of the Omega-3 Index, and we are talking about omega-3 fatty acids. Bill, how do you measure someone's blood omega-3 level. Is there a widely available test?

DR. WILLIAM HARRIS:

No, there is not a widely available test right now, and there is no widely standardized method of doing this which is slowing things down. In our laboratory the way we measure it, we measured in red blood cells. We take a purple top tube; actually green top, blue top, any tube that gives you plasma and liquid red cells. (06:00) We take the red cells out, we treat them with some reagents, we analyze them on a gas chromatograph, and we come up with what we call the Omega-3 Index which is the amount of EPA and DHA in the red cell membrane as a percent of the total fatty acids in the membrane.

DR. LARRY KASKEL:

Have you measured your own?

DR. WILLIAM HARRIS:

Yeah! My blood is the high control for our assay. I am going around 10% EPA/DHA, and what we have proposed, and we have got some experimental evidence to support this is that a omega-3 index of around 4% is pretty typical of Americans and that's the low end and that's we don't want to be. The Japanese are around 8-9% omega-3 index, and we think that there is good evidence that that is the target people would want to shoot for if they want to raise their omega-3 to some level and that would be the one to go for.

DR. LARRY KASKEL:

Bill, is there any reason why someone should not take this? It sounds like it's a win-win, that there is no real downside.

DR. WILLIAM HARRIS:

There really is no downside certainly to increasing your omega-3 intake from eating the oily fish that the salmon, the mackerel, the rainbow trout, herring, sardines, albacore, tuna, etc., those kinds of fish. When we say oily fish, some people think you are talking about deep fried fish and that's not the idea; stay away from those as they don't have much omega-3. (07:30) People have been concerned about bleeding, but really on careful examination of the literature and surgical intervention studies are not finding any increased risk of bleeding in people who are on omega-3. Even if they are also on anticoagulants at the same time, it does not make a difference.

DR. LARRY KASKEL:

How did you get interested in this topic?

DR. WILLIAM HARRIS:

I did a post-doctoral fellowship in the late 70s in a laboratory in Portland, Oregon, where we were trying to understand the effects of different oils on cholesterol levels. We knew vegetable oils were polyunsaturated and that they lowered cholesterol, but nobody really looked at fish oils which are also polyunsaturated in a different way with the omega-3's to the omega-6, and we wondered if the fish oils lowered cholesterol, and we found out that they were just like the vegetable oils in lowering cholesterol, but they were also very good in lowering triglycerides.

DR. LARRY KASKEL:

You and I both know that taking a high dose of fish oil will actually raise your LDL a little bit.

DR. WILLIAM HARRIS:

If you are hypertriglyceridemic.

DR. LARRY KASKEL:

Okay, so it kind of speaks a little against the lipid hypothesis of heart disease and more towards the inflammatory hypothesis, that this is really a chronic inflammatory disease gone haywire.

DR. WILLIAM HARRIS:

I am not sure it speaks against the lipid hypothesis in the same sense that taking aspirin lowers risk for heart attacks, but does not lower your LDL, doesn't mean that the lipid hypothesis isn't true. It just means that, yes, but there are other things too, (09:00) and this is one of those other things like aspirin it's doing something that's completely unrelated to lipoproteins, and as aspirin does, to reduce risk for events.

DR. LARRY KASKEL:

Are there any oils that you researched or have come across that also have beneficial effects?

DR. WILLIAM HARRIS:

Nothing like this, nothing like with the omega-3's where you have actually large randomized controlled trials showing cardiovascular benefit. These are the only oils I know of that has ever been done for.

DR. LARRY KASKEL:

And what about the Lyon Heart Study where we looked at olive oil.

DR. WILLIAM HARRIS:

Well, I didn't really look at olive in that one. In that study they provided a margarine to the group that had canola oil, that was provided some alpha-linolenic acid in small amount, but the Lyon Heart Study, I do not consider an omega-3 study or even an oil

study. That's a complete dietary pattern change from fruits and vegetables to the kind of meat they ate, to the amount of cheese they ate, I mean, everything changed. So that's a whole diet plan, and I don't think you can pick out one aspect of that and say well it was the alpha-linolenic acid or it was the vegetables that did, it is a whole package and so that study is useful only in so far as it shows a major change in diet to a Mediterranean style.

DR. LARRY KASKEL:

Bill, are there any primary prevention (10:30) trials or studies that show the benefits of fish oil. I know there have been a lot of secondary preventions which have all been very positive.

DR. WILLIAM HARRIS:

Yes. Recently, another study from Japan called the JELIS trial. There were 18,000 people randomized to EPA alone or not. For some reason, they don't believe until they see those in Japan. So it was an essentially open labeled trial. About three-fourths of the people in that trial were primary prevention. They had hypercholesterolemia, and they were all on a statin, but three-fourths of them had not had an event yet, so just the EPA added on top of a Japanese diet already which is a kind of a remarkable finding did reduce risk for events. It was not statistically significant. It was the same effect size as was seen with the people who were on secondary prevention because the secondary prevention people had much higher risk than the primary about an 18 or 19% reduction in events for both the primary and the secondary group, just that the primary group was not large enough to show to have a statistically significant event.

DR. LARRY KASKEL:

I guess the last question is for a physician listening to this show if he has any patient that has documented coronary artery disease or documented carotid disease, (12:00) would you say it is standard of care that that patient should be on some fish oil?

DR. WILLIAM HARRIS:

It is certainly not a fact or standard of care, it is the recommendation of the American Heart Association that patients should be on about a gram of long-chain omega-3, but it is far from standard of care. Certainly, it has not been the subject of Heart Association, Cardiology College Conference to establish it as a guideline. I would like to see that they come, but it has not come yet.

DR. LARRY KASKEL:

Well, Dr. William Harris of the Sanford School of Medicine, thank you very much for coming on Lipid Luminations.