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Inflammation, Depression and N—3 Fatty Acids: A Proof of Concept Study

Q: What role does inflammation play in Major Depression?

A: Well, I think that inflammation probably plays two roles. I think the most important role will be for individuals who have chronic inflammation. A certain number of individuals with Major Depressive Disorder, actually have a chronic inflammatory state. Just as you have with people who have rheumatoid arthritis or Cohn's disease. I think there, inflammation is driving the signs and symptoms we see associated with what we call depression. In those cases. Inflammation drives the sad mood; it drives the problems with lack of interest, problems with concentration. It drives the problems with appetite and sleep disturbance. That is a subset of people that are resistant to most of our standard treatments, because our standard treatments don't get at the inflammation. I think there is another group of individuals who are acutely ill and acutely stressed and in these acutely ill individuals, you will see a transient increase in markers of inflammation. Those tend to resolve when the depression resolves. That is a different subgroup of people. So, there are these two different subgroups of people that are involved.

Q: What major clinical disorders are associated with inflammation?

A: Inflammation is part of so many different disorders in the body. It's associated with metabolic syndrome, heart disease, cancer, and diabetes. What we are learning is this chronic inflammation has a variety of different effects. So, what we need to begin to understand is who are the individuals who are susceptible to chronic inflammation leading to a cancer phenotype, versus a depressed phenotype, versus heart disease; and whether or not there is actually an overlap between those phenotypes. We don't know that right now.

Q: Would you talk about the N-3 Fatty Acid therapy?

A: There has been a lot of interest in Omega-3 fatty acids throughout medicine. A lot of the original work started because of epidemiological studies that were done in cardiology. What they were able to discern was that individuals that had diets that were richer in Omega-3 than Omega-6 fatty acids, tended to have less heart disease, less problems with strokes. This led to some work by Joe Hibbein and John Davis, where they showed that looking in the epidemiological data that there seemed to be a decrease in depression associated with diets that were rich in Omega-3 fatty acids.

A: (continued) There have been a variety of studies of the use of Omega-3 supplements in a myriad of medical conditions. If we look at the literature in mood disorders, what we see is that it is really mixed. The reason that it is mixed is because depression itself is this heterogeneous syndrome with many different causes. What we believe is that for Omega-3s to work, you have to have a certain subtype of depression. In our hands, it looks like these are people who have continuous signs of chronic inflammation. We believe that those are the people who are most responsive to Omega-3s.

There has been an interesting study that came out that if you can increase levels of Omega-3 in the body, you can actually decrease the rate of interferon-induced depression for people who are getting Hepatitis C treatment. That again suggests that what you are doing is shifting the body into a more anti-inflammatory role. So, this is stuff that we are really interested in. The literature with supplements is a lot more complicated than the literature with diets itself. In fact, there is a wonderful series of studies in the *New England Journal of Medicine*, showing that if you can get people to eat a diet rich in Omega-3s, you can decrease the rate of heart disease in those individuals. I think there is a lot of opportunity there either with supplements or with changing our diets.

