

# *THE SATURDAY EVENING POST*

## Health/Fitness

### Battling the Blues

#### Ongoing research shows that omega-3 fatty acids help treat depression.

By Patrick Perry

Several years ago, **Dr. Andrew Stoll**, director of the Psychopharmacology Research Laboratory at Harvard Medical School-**McLean Hospital**, conducted a landmark study on the role of omega-3 fatty acids in bipolar disorder and came up with some surprising results. The researcher discovered that when patients with bipolar disorder consumed omega-3 from fish oil, they experienced a marked reduction in episodes of mania and depression. Extensive research continues to demonstrate that omega-3 fatty acids form the foundation of a solid, healthy diet, while also reducing the risk of heart disease, stroke, hypertension, and arthritis, among other conditions.

Depletion of the essential omega-3 fatty acids in the typical American diet is linked to chronic disease and the huge increase in the rates of depression. Researchers now speculate that the increase in depression correlates well with the progressive depletion of omega-3s in our diet throughout the 20th century. The shift from rural community life to fast-paced urban sprawl also ushered in an era of fast foods, low fiber, and foods high in saturated fats, trans-fatty acids, and excessive intake of omega-6 fatty acids.

Omega-6 fatty acids are converted by the body into a number of strongly inflammatory hormones, collectively known as eicosanoids. Prostaglandins are the most well-known class of eicosanoids. If omega-6-derived eicosanoids are produced in excess over time, the risk of developing heart disease, other inflammatory medical conditions, and, apparently, depression and bipolar disorder skyrockets.

The omega-3 fatty acid eicosapentaenoic acid (EPA) is converted into eicosanoids as well, competing directly with omega-6 fatty acids for access to the enzymes that convert these fatty acids into eicosanoids. Whichever acid wins the competition for these eicosanoid-producing enzymes depends solely on the ratio of omega-6 versus omega-3 consumption in the diet. This is crucial, because the omega-3-derived eicosanoids are largely anti-inflammatory hormones and have the role of keeping the omega-6-derived eicosanoids in check. Now, omega-6 fatty acids aren't bad, unless there is an excess over time.

Therefore, essential fats such as the omega-3s EPA and docosahexaenoic acid (DHA) are necessary for optimal health.

Historically, scientists believe that our ancestors consumed close to a one-to-one dietary ratio of omega-3, found primarily in certain fish, to omega-6, commonly found in vegetable and seed oils. Today, researchers estimate that the ratio of omega-6 to omega-3 fatty acid consumption is somewhere between 20:1 and 50:1 in the United States, with an abundance of omega-6 over omega-3 fatty acids, which pushes us in a pro-inflammatory direction, more susceptible to heart disease, arthritis, and to illnesses related to inflammation, and perhaps depression and bipolar disorder.

To update readers about Dr. Stoll's ongoing research into the role of omega-3 fatty acids in depression, the Post spoke with the Harvard researcher and author.

Post: Do omega-3 fatty acids continue to demonstrate mood-stabilizing benefits?

Dr. Stoll: No one has replicated the findings of our original study as yet. The real story now is that there are now numerous positive studies on the benefits of omega-3 in unipolar depression, schizophrenia, borderline personality disorder, ADHD, and Huntington's disease. It seems that many disorders respond to omega-3s. Three of the four studies in depression used EPA, or EPA plus DHA, and they worked. The fourth study used pure DHA—important for developing babies, pregnant women, and nursing mothers—and it failed. People hold onto stores of DHA for a long time, so you don't need to replenish levels as often as with EPA, which is turned over constantly, by conversion into eicosanoid hormones.

Post: Does EPA have anti-inflammatory properties?

Dr. Stoll: Exactly. The anti-inflammatory action of omega-3s has been definitively shown to help prevent heart attacks, in part by reducing atherosclerosis (hardening of the arteries). Omega-3s also appear to help cut down on the need for medications to treat rheumatoid arthritis, ulcerative colitis, Crohn's disease, and a number of other medical conditions. Omega-3s may also work in osteoarthritis. Research on omega-3s is exploding—and not just in psychiatry.

Post: Are you continuing your research into the relationship between fats and mental health, particularly omega-3 fish oils in bipolar disorder?

Dr. Stoll: Yes. We published the results of our first bipolar study, and the results were very promising. We went out on a limb to do this study with no funding and with colleagues sometimes ridiculing us. But the study was logical and rational, and patients, as well as informed and open-minded physicians, liked the approach. We tried it randomly and it worked. The same pathways are activated during bipolar disorder and depression, so EPA may perform the anti-inflammatory action.

Post: Do your patients, who were part of the original study, continue to take omega-3 and experience relief from their symptoms?

Dr. Stoll: I still see some of these people. All continue to take omega-3 supplements. In my practice, I am in favor of it, so I advise people to take it—if not for the psychiatric benefits, then for the general health benefits.

Post: Is there a downside to supplementing with omega-3?

Dr. Stoll: There isn't. Some people may experience GI distress if they take a large amount of a low-quality supplement. But the highest good-quality fish oil is not rancid and has little or no taste and has no side effects. Another issue that people worry about is bleeding, because EPA inhibits platelet aggregation. But we scoured the scientific literature, and there has never been a documented case of bleeding due to omega-3 fatty acids.

We recently reviewed about 18,000 people who participated in clinical trials with omega-3s, largely in cardiology studies, and we couldn't find one instance of bleeding in any of the trials. There was no bleeding, even if used in IVs prescribed before and during cardiac surgery. I think this perception is a myth because omega-3s don't inhibit the platelets as strongly as aspirin—perhaps 60 to 70 percent as much as aspirin—and unlike aspirin, the effect is reversible.

Post: When a patient is on blood thinners, such as coumadin, should they exercise caution when supplementing with omega-3?

Dr. Stoll: In that situation, I usually recommend a lower dose, not exceeding one or two grams of EPA per day. At this dosage, there should be no effect on the action of coumadin. The unanswered question is, together are they providing too much anticoagulation? Nonetheless, there may be some minute risk of a negative interaction with anticoagulants, such as warfarin (coumadin), high-dose aspirin, or ibuprofen-like medications, based on animal data and anecdotal reports in humans.

However, large-scale controlled clinical trials with patients receiving omega-3 fatty acid supplements with either aspirin or warfarin observed no cases of bleeding even after one year of the combined treatments. It would be a shame if cardiac patients or their physicians avoided the use of omega-3 supplements out of fear. I am thoroughly convinced that the dramatic and lifesaving cardiac actions of omega-3s far outweigh the very small or nonexistent risk of bleeding.

Post: What dosage do you recommend for patients with bipolar and/or depression?

Dr. Stoll: Our omega-3-fatty-acids-in-bipolar study was the first controlled study in psychiatry. We really had no way of knowing what the minimum effective dosage was, so we decided to use a moderately high dosage that had been successfully used in omega-3 studies of rheumatoid arthritis and other medical disorders. This dosage was about 10 grams per day (6.5 grams of EPA and 3.5 grams of DHA daily). Most of the newer omega-3 studies in major depression used a very low dosage of pure EPA added to partially effective or noneffective antidepressants. For example, in one small study, Dr. Malcolm Peet and colleagues from England compared one gram a day of EPA to two grams a day of EPA, and up to four grams of EPA per day. One gram of EPA did the best by far. The most recent depression study, done by a group from Taiwan, was another unipolar study where they added omega-3 to an antidepressant regimen that was not working. They used the same exact formulation that we did—nearly 10 grams of EPA plus DHA in about a 3:2 ratio—with good results.

So, the question of optimal dosage remains unanswered. Practically, I start patients on one gram of EPA per day, and go up on the dosage gradually until an effect is seen on a person's mood. I usually do not have to exceed six grams of EPA per day. The amount of omega-3 in a supplement may be calculated from the side of the bottle.

It is important to know that the amount of active ingredients in supplements is listed on the label by serving size, not necessarily by how much of an ingredient or compound is in one capsule. Companies can make the serving size one, two, three, or a hundred capsules—as big or small as they want.

To determine omega-3 content, simply take the amount of EPA or EPA plus DHA per serving, as listed on the label, and divide it by the serving size to determine how much omega-3 is in each capsule. That's not understood well by many people. It is important that people read labels carefully. They get fooled.

The FDA requires that supplement manufacturers list the ingredients or nutrients by serving size. But the company can put in any serving size they want, so it may look like there is a lot of EPA, for example, in a product, but the serving size may be 10 capsules. Consumers should be sure to divide whatever value is in the column for the amount of EPA by the number of capsules in a serving, and read labels carefully.

Post: What dose of omega-3 do you recommend and find most effective?

Dr. Stoll: I will distinguish the doses. I usually start everyone on one gram of EPA per day. I prefer to have a little bit of DHA in the formula. They should be at least in a 3:2 or 2:1 EPA to DHA ratio. If one gram doesn't help after one to two weeks, I will raise the dosage to two grams a day of EPA. I definitely use lower doses than I used to, based on the depression data. Occasionally, someone will call or e-mail

me with an anecdote that they didn't respond until they were taking 10 grams a day—the original dose in our study. Hopefully, we will resolve that issue in the next few years.

Post: When consumers are looking at supplements, what is the ideal ratio of EPA to DHA that they should look for?

Dr. Stoll: This remains an unresolved issue, but I like a 7:1 ratio of EPA to DHA. That high ratio delivers plenty of EPA—the presumed active ingredient—and also provides an adequate amount of DHA. More DHA is required during pregnancy or while nursing to replenish stores. Most adults and children seem to have adequate or nearly adequate stores of DHA in their brains. Believe it or not, these DHA stores in the membranes of brain cells date back to a person's fetal life and is provided by their mothers. DHA turns over very slowly, so you don't need much to get by. In contrast, EPA is turned over very rapidly, as it is used for eicosanoid synthesis. For this reason, we think people are also much more depleted in EPA than DHA.

Post: Today, people are faced with a lot of conflicting information. Eat more fish, get more omega-3, but at the same time, they are warned about the mercury content of certain fish. What should the consumer do?

Dr. Stoll: It's a real problem. People thought farmed fish were safe, but it turns out that they have as much or more mercury and PCBs as wild fish. For salmon, the increased mercury and other chemicals occur because the salmon are carnivores and are fed pellets containing mercury-laden wild fish. Eating fish in low doses is okay—one or two meals a week is enough to begin to reduce your cardiac risk, yet it is probably not enough to raise your mercury levels much. For pregnant or nursing mothers and young children, it may be best to avoid fish altogether. Some omega-3-containing fish have little or no contamination. Little fish, like mackerel, sardines, and anchovies that do not live a long time and are nonpredatory, are cleaner and contain less or no toxic contaminants. Large predatory fish, like tuna, tend to be the most contaminated.

Fish oil never has mercury or PCBs because the mercury stays with the solids and does not go into the oil. But PCBs and pesticides, on the other hand, which are organic carcinogens from human pollution, will go into the oil. That is why I like the high concentration fish oil supplements—50 to 90 percent omega-3 in the formulation. Fish oil supplements are distilled, which lifts the oil away from the contaminants. There are multiple distillation steps in order to arrive at formulations of 90 percent omega-3 concentration, which produces very pure oil.

There is a useful Web site called [www.consumerlabs.com](http://www.consumerlabs.com), where you can actually find the best brands. It's a watchdog agency. Companies voluntarily submit their products to Consumer Lab for analysis. They seem to be pretty honest. They fail companies, even though the supplement makers pay to review products. I trust them 95 percent. They reviewed whole classes of supplements, including omega-3s. You can see that they measured for organic carcinogens, mercury, cadmium, lead, and other contaminants, which is comforting.

If a person can't easily afford some of the omega-3 capsules, they can reduce the required dosage of their supplement by eating a couple of fish meals per week. Make sure that it is an oily type of fish, such as salmon, mackerel, or sardines. Another, somewhat less expensive, option is to use flaxseed oil or ground flaxseed (flaxmeal). I occasionally buy flaxseeds and grind them up fresh and put them on foods. When I was in Greece for an omega-3 conference, they served yogurt with flax meal sprinkled on top with honey and walnuts. It was one of the most delicious things that I ever ate in my life, which I continue to make at home along with flaxseed pancakes with a couple of tablespoons of flaxmeal mixed into the batter.

Another thing about flax oil is that there are conflicting epidemiological studies from different investigators in different countries showing that elevations of alpha-linolenic acid (ALA)—the omega-3 fatty acid in flaxseed—is correlated with prostate cancer. Some people scoff at these studies. It makes no sense because EPA is an anticancer compound. But until someone clarifies the issue, I avoid recommending flax to older men, just in case. High doses of flaxseed also can cause thyroid toxicity, so you don't want to consume more than three or four tablespoons per day.