Understanding Eicosanoids

Hormones that are Key to Our Health

by Dr. Barry Sears

Strange, mysterious, and almost mystical, eicosanoids are the key to our health because they control the flow of information in our body. Why are eicosanoids so important? They were the first hormones developed by living organisms more than 550 million years ago. As such they can be considered “super-hormones” because they control the hormonal actions of other hormones. Furthermore, you don’t have an eicosanoid gland since every one of your 60 trillion cells can make eicosanoids.

Even though they are earliest hormones, eicosanoids only were identified in 1929 starting with the discovery of essential fatty acids. It was found that if fat in the diet was totally removed, rats would soon die. Adding back certain essential fats (then called Vitamin F) was found to enable fat-deprived rats to live. Eventually as technologies advanced, researchers realized that essential fats were composed of both Omega-6 and Omega-3 fatty acids that both needed to be obtained in the diet because the body could not synthesize them. The word eicosanoid is derived from the Greek word for 20 which is eicosa, since all of these hormones are synthesized from essential fatty acids that are 20 carbon atoms in length.

The first actual eicosanoids were discovered in 1935 by Ulf von Euler. These first eicosanoids were isolated from the prostate gland (an exceptionally rich source of eicosanoids), and were called prostaglandins (a small subset of the much larger family of eicosanoids). Since it was thought at that time that all hormones had to originate from a discrete gland, it made perfect sense to name this new hormone a prostaglandin. With time it became clear that every living cell in the body could make eicosanoids, and that there was no discrete organ or gland that was the center of eicosanoid synthesis.

To date biochemists have identified more than 100 eicosanoids and are finding more each year. The breakthrough in eicosanoids research occurred in 1971 when John Vane finally discovered how aspirin (the wonder drug of the 20th century) actually worked: It changed the levels of these critical hormones. Yet ask most physicians what an eicosanoid is, and you will usually get a blank stare.

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Bergelson for their discovery of how eicosanoids play a role in human disease.

This is where my journey with eicosanoids first started 20 years ago. It was apparent to me that if certain “bad” eicosanoids were associated with chronic disease conditions (like heart disease, cancer, arthritis, and so on), then the key to wellness would be to induce the body to make more “good” eicosanoids and fewer “bad” eicosanoids. Rather than using drugs to achieve that goal, I reasoned I could use food as if it were a drug. All I needed to do was figure out the right balance of protein, carbohydrate, and fat that would turn food into this beneficial drug. After more than 20 years, I think I’ve come pretty close to that “drug” as described in my book, OmegaRx Zone.

Of course, my colleagues in academic medicine didn’t quite share my initial enthusiasm. Almost overnight, I went from being a respected research scientist with numerous patents in the area of intravenous drug delivery systems for cancer drugs, to being called a snake-oil salesman because of my constant refrain that the appropriate diet could change the balance of eicosanoids throughout the body. Part of the problem was that very few of them even knew what an eicosanoid was.

I believe that the foundation of 21st century medicine will be the manipulation of eicosanoids. Yet ask most physicians and medical researchers what an eicosanoid is, and you will usually get a blank stare. As unknown as they are to the medical community, eicosanoids are the hormones that maintain the information fidelity of your “Biological Internet”, which means they become the key to health and longevity.
Certain drugs can affect eicosanoid formation. The most well known is aspirin which literally destroys a cyclooxygenase enzyme on a one-on-one basis. This is what is known as a suicide inhibitor. When you are suffering from a headache or arthritic pain, you are overproducing "bad" eicosanoids, but in particular "bad" prostaglandins. The aspirin temporally shuts down all prostaglandin formation (but not leukotriene formation), until the cell can make more of the cyclooxygenase enzyme to replace the ones destroyed by the aspirin. However, you can’t be using these suicidal soldiers forever, as aspirin also shuts down the synthesis of "good" prostaglandins, especially those that protect the stomach from dissolving itself. When that happens, you get internal bleeding. This is why there are more than 10,000 deaths per year associated with the over-use of aspirin.

Other drugs known as non-steroidal anti-inflammatory drugs (NSAID’s) also inhibit the cyclooxygenase enzyme but not the lipo-oxygenase enzyme that makes leukotrienes. The common names for these NSAIDs are Motrin, Advil, Aleve, and others. Continued use of these NSAIDs generates the same problems as does long-term aspirin use.

The most common types of anti-inflammatory drugs are those that can only affect those eicosanoids that are synthesized via the cyclooxygenase enzyme or COX. It was recently discovered there are two forms of this enzyme known as COX-1 and COX-2. COX-1 enzymes are a constant fixture of the vascular cells that line the bloodstream or in stomach cells that secrete bicarbonate to neutralize stomach acid. COX-2 appears to be an enzyme that is synthesized only in response to inflammation. Standard drugs like aspirin and NSAIDs don’t discriminate between these specific forms of the COX enzyme, which is why they have side-effects associated with their long-term use.

For example, it appears that the anti-cancer benefits of aspirin may stem from its inhibition of COX-2, whereas the side-effects (like an increased risk of internal bleeding) come from its simultaneous inhibition of COX-1. However, this same inhibition of the COX-1 enzyme appears to convey the cardiovascular benefits associated with aspirin. This may explain why long-term use of COX-2 inhibitors may not work to decrease heart attack rates: they don’t target the COX-1 enzyme. Weighing the risks against the benefits presents a dilemma associated with all drugs that affect eicosanoid synthesis.

Unlike inhibitors of the COX enzymes, there are very few inhibitors of the LOX enzymes. Since leukotrienes (particular LTB4) represent a primary mediator of pain, the only way to affect their production is to use corticosteroids with all of their associated side effects.

Drug companies are racing to develop new patentable drugs—ones that affect the downstream enzymes that control eicosanoid production from arachidonic acid. Overlooked in this frenzy by the drug companies seeking new and more expensive drugs, is that there is an existing “drug” that can achieve all of these benefits without any side effects: high-dose fish oil. Elevated levels of EPA from high-dose fish oil will reduce the production of “bad” eicosanoids.

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It’s important to mention that you cannot control eicosanoid levels without controlling insulin first. Insulin is an activator of the delta-5-desaturase enzyme. The role of excess insulin in negatively affecting eicosanoid balance also explains why excess insulin is highly associated with heart disease. It’s not that insulin is a cause, but that it drives the metabolism of essential fatty acids to make more arachidonic acid, and therefore more “bad” eicosanoids. The more “bad” eicosanoids you make, the more likely you will promote platelet aggregation and increased vasoconstriction, the underlying factors for a heart attack.

The only way to control insulin requires controlling the protein-to-carbohydrate ratio at every meal. But what should the optimal ratio of protein-to-carbohydrate be? Fortunately, such an estimate was established in research published in an 1985 issue of *The New England Journal of Medicine*. Using anthropological data and comparing a large number of existing hunter-gatherer tribes, these researchers estimated the average protein-to-carbohydrate ratio in neopalolithic diets to be approximately 3 grams of protein for every 4 grams of carbohydrate, or a protein-to-carbohydrate ratio of 0.75. Using this research as a starting point, I began developing a diet that would control the protein-to-carbohydrate ratio in a range between 0.5 and 1.0 at every meal, so that the balance of insulin and glucagon would be maintained from meal to meal. This is the foundation of the insulin control component of my dietary recommendations.

Thus, my dietary program controls both the ratio of long-chain Omega-3 fatty acids to Omega-6 fatty acids as well as the balance of protein-to-carbohydrate at every meal—while restricting total calories. This dietary strategy maintains the dynamic balance of eicosanoids by controlling the levels of the actual precursors and the hormones responsible for activating the critical enzymes in essential fatty acid metabolism. By keeping the balance of eicosanoid precursors in an appropriate zone (after all, you need some “bad” eicosanoids to survive), you also control the information flow of your Biological Internet. Control that flow and avoid hormonal miscommunication, and you have begun to reverse the aging process.

The development of chronic diseases (heart disease, diabetes, cancer, and arthritis) associated with aging does not occur overnight but is the result of constant hormonal insults to your body. But by the time they do appear, significant and potentially irreversible organ damage may have occurred. So if eicosanoids act as master hormones that control this complex hormonal communication system, is there some way we can continue to monitor and fine-tune this ultimate mechanism of aging before chronic disease conditions appear? Yes! I believe that your blood parameter can be changed rapidly within 30 days by following certain dietary guidelines such as balancing the ratio of proteins to carbohydrates at every meal, restricting your total calories, and daily consumption of pharmaceutical-grade Omega-3 supplements.

Learn more about Dr. Sear’s Zone Diet at www.zonediet.com

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