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## **Cardiometabolic Risk Syndrome Part X**

### **Inflammation Altered by Diet**

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**Your Life Your Health**

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As we try to create mental pictures which will enable us to initiate and sustain healthy changes in our habits and as we continue to examine the inflammatory effect of the cardiometabolic risk syndrome, we need to understand "eicosanoids." The inflammation which contributes to heart disease, elevated blood pressure, arthritis and all other disease processes, are mediated by eicosanoids. Generally, as we age, the "bad" eicosanoids increase in our bodies, thus causing and/or contributing to disease. There are "good" and "bad" eicosanoids and you can influence which "kind" you produce. Diet is one of the principle way so of regulating your eicosanoid balance.

The word eicosanoids is derived from the Greek word for twenty, *eicosa*, since all these hormones are synthesized from essential fatty acids that are twenty carbon atoms in length. The first eicosanoids were discovered in 1936 and were isolated from the prostate gland and were therefore called "prostaglandins", which are a small subset of the much larger eicosanoid family. Every living cell in the body can make eicosanoids. Biochemists have identified more than a hundred eicosanoids and are finding more each year. In 1971, it was discovered that aspirin actually works by changing the level of eicosanoids.

### **Eicosanoids' mission**

As autocrine hormones, they are secreted by the cell to test the external environment and then report back to the cell what is just outside by interacting with its receptor on the cell surface. On the basis of this information, the cell can take the appropriate biological action (via the appropriate second messenger) to respond to any change in its environment. The following is a summary of the effects of "good" and "bad" eicosanoids.

### **Good Eicosanoids**

1. inhibit platelet aggregation -- this decreases your risk for heart attacks and for strokes.
2. promote vasodilatation -- this decreases your risk of developing hypertension and heart disease.
3. inhibit cellular proliferation -- this decreases the probability of your developing cancer and other conditions which depend upon cells dividing. There also appears to be some benefit in the fighting of viral infections including HIV.
4. stimulate immune response -- this helps you fight off infections, bacterial and viral.

5. anti-inflammatory -- this controls the inflammatory response mechanisms in your body which helps prevent and/or ameliorate diseases such as rheumatoid arthritis, Crohn's disease and ulcerative colitis.
6. decrease pain transmission -- this helps the body cope with illnesses which were not prevented and prevents debilitation from degenerative conditions such as osteoarthritis.

### **Bad Eicosanoids**

1. promote platelet aggregation -- this promotes heart attacks and strokes.
2. promote vasoconstriction -- this promotes hypertension and heart disease.
3. promote cellular proliferation -- this facilitates the development and spread of cancer.
4. depress immune response -- this inhibits the body's defenses against infections and inflammation.
5. pro-inflammatory -- this promotes inflammatory illnesses, such as arthritis and other autoimmune diseases.
6. increase pain transmission -- this debilitates the body and robs strength and vitality.

### **General Concepts about eicosanoids**

The eicosanoids that generate increased production of cyclic AMP are your key to maintaining wellness because Cyclic AMP is the second messenger used by a number of endocrine hormones to transmit their biological information to the appropriate target cell. Thus, an eicosanoid's effect on second messengers becomes the definition of a "good" or "bad" eicosanoid. A "good" eicosanoid will increase the levels of cyclic AMP in a cell, whereas a "bad" eicosanoid will decrease the level of cyclic AMP. Wellness really is a function of balance between "good" and "bad" eicosanoids.

The AA/EPA ration (AA -- arachidonic acid, EP -- eicosapentaenoic acid) in the blood will indicate where you stand in terms of such a balance between good and bad eicosanoids. It is the balance between arachidonic acid and eicosapentaenoic acid (EPA, an omega-3 fatty acid found in fish oil) which determines whether you will produce health-promoting "good" eicosanoids, or age and disease-promoting, "bad" eicosanoids.

### **Promoting "good" eicosanoids**

The principle influence on this is your diet. Controlling your insulin levels, whether or not you are a diabetic is key. That is why balancing your carbohydrate intake, which generally stimulates insulin production, with protein and fat, which generally moderate insulin production, is key to this entire process. Because the western diet is typically deficient in omega-3 fatty acids, we must supplement our diet with omega-3 fatty acids. (see *The Examiner* from September 4, 2003 or [www.jameslhollymd.com](http://www.jameslhollymd.com) Your Life Your Health for a list of ways to increase your dietary intake of omega-3 fatty acids.)

## **Eicosanoids are hormones**

A hormone is any chemical that can transmit information as essentially hormones are messengers. "Hormone" is derived from the Greek word meaning "impelling, exciting, or setting into motion." Within our bodies lies a biological internet that is vastly more complex than the electronic internet. Some sixty trillion cells need to maintain constant communication with one another. This communication system is controlled by hormones, which can be modified by diet.

### **There are three distinct classes of hormones:**

1. **Endocrine** --- these are like microwave towers that send your telephone conversation into the air when you speak.
2. **Paracrine** -- these hormones don't travel randomly in the bloodstream. They are cell-to-cell regulators that have very defined constraints on how far they can travel. They are more like the physical telephone wires that come directly into your house after the signal is received by the microwave tower. Neurotransmitters like serotonin and dopamine are paracrine hormones.
3. **Autocrine** -- These hormones are sent out from the cell to test the immediate environment and then come back to report to that cell what lies just outside its perimeter. These hormones are like the receiver on your telephone. The most important autocrine hormones are the eicosanoids, because they ultimately drive your biological Internet, just as electrons drive the Internet you access by your computer.

## **Second Messengers**

These are the ultimate key to hormonal action and act through the following sequence of events:

1. A hormone like insulin docks on a cell receptor
2. The receptor which spans the membrane of the cell undergoes a change that is transmitted to the interior of the cell.
3. Depending on the receptor and the hormone that has activated it, another molecule is synthesized within the cell that completes the message.
4. These new molecules are called second messengers of which there are two primary kind:
  - Cyclic AMP, which is considered the "green light" for cells. "Good" eicosanoids interact with receptors that produce this second messenger;
  - Inositol triphosphate/diacylglycerol (IP<sub>3</sub>/DAG) which is equivalent to the "red light" for the cell and usually has a physiological action opposite to that of cyclic AMP. Both insulin and "bad" eicosanoids use this pathway.

If the green light and red lights are balanced and working smoothly, the result is wellness. If you have excess of red lights, then your traffic signals are out of balance, the result is

the development of chronic disease. The great complexity of your biological internet comes down to maintaining the appropriate balance of green and red lights in each of the trillions of cells throughout the body.

### **Omega-3 Oils and Eicosanoids**

If you simply take high-dose fish oil, you would automatically alter the balance of the traffic signals wince you would be making more "good" and fewer "bad" eicosanoids. By changing the levels of these second messengers, you can ultimately control cellular function moment by moment. Once you learn to control your hormones, you have a "magical drug" -- your diet -- that can help:

- Prevent heart disease
- Reverse cancer
- Reduce pain and inflammation
- Treat neurological disease.

But if you can treat those diseases with this "drug," then the same "drug" can also:

- Slow or even possibly reverse the aging process
- Make you smarter
- Make you thinner
- Improve your physical performance
- Improve your relationships with others

How to control your hormones:

1. Balancing protein and carbohydrate at every meal -- this controls insulin levels
2. Calorie restriction without hunger or deprivation -- this is the only proven way to increase longevity
3. Supplementation with high-dose fish oil -- this alters eicosanoid

The reality is that your diet does three things:

1. Controls eicosanoid formation
2. Alters eicosanoid balance in the body
3. Determines how eicosanoids become central players in your health.

### **PGE1**

When your diet is properly balanced, the primary "good" eicosanoid produced is called "PGE1 (Prostaglandin E1) which has the following effects on the body. PGE1 is a(an):

1. Powerful vasodilator
2. Inhibitor of platelet aggregation
3. Reduces the secretion of insulin from the pancreas.

4. Increases the synthesis of a wide variety of hormones that normally decrease during the aging process such as those from the thyroid, adrenal and pituitary glands -- including human growth hormone.
5. Helps cut down the liver manufacture of cholesterol.
6. Controls the release of lymphokines, the natural substances that "prime" the immune system to take action.
7. Reduces the proliferation of immune-system cells, which can sometimes overreact and begin attacking other cells in the body.
8. Cuts down on the release of histamine, thus helping to put the brakes on a wide variety of allergic reactions.
9. Reduces pain.
10. Reduces the secretion of acid from the stomach.
11. Relaxes tissues in the bronchial tubes, helping to reduce the intensity of asthma attacks.
12. Controls the neuro-transmitters which acts as the nervous system's chemical messengers. By increasing the uptake and release of these messengers, PGE1 can reduce the need for sleep and it can help alleviate depression.

PGE1 does all this because it causes an increase in the production of cyclic AMP.

### **PGA1**

Another eicosanoid whose production is stimulated by increased Omega-3 oil in the diet is PGA1, which is:

1. The most powerful suppressor of viral replication, especially HIV transcription.
2. Inhibits the nuclear transcription factor (NFkappa B) necessary for synthesis of a wide variety of pro-inflammatory cytokines thus making it another anti-inflammatory eicosanoid.

How do you help your body block excess arachidonic acid formation and tilt the balance back toward a favorable balance between "good" and "bad" eicosanoids?

1. By making sure your body has an adequate amount of eicosapentaenoic acid (EPA, which is an omega-3 oil found in fish oil). EPA acts as a feedback inhibitor of the enzyme which produces "bad" eicosanoids. The higher the EPA in the diet, the more the enzyme is inhibited and the less "bad" eicosanoids are produced.
2. By decreasing the arachidonic acid in your diet. Foods high in arachidonic acid are egg yolks, red meat and organ meats.

There is no "medicine" or "magic pill" which will increase your good eicosanoids and decrease your bad ones. It is only via your diet that you can "modulate" your hormone balance to change your body's chemistry to improve your health.

## **Omega-3 Fatty Acids -- Summary**

1. EPA (omega-3 fatty acid) restricts the flow of any omega-6 fatty acids into "bad" eicosanoids.
2. Because the levels of omega-3 and omega-6 fatty acids needed in the diet are relatively low, you must "supplement" these with other fats. These fats should be monosaturated fat which can't be made into eicosanoids "good" or "bad."
3. Because monosaturated fats have no effect on eicosanoids or on insulin, they can provide the necessary fats to control the rate of entry of carbohydrates into the bloodstream without disturbing the hormonal balance you are trying to achieve.

This may seem complicated and in some ways it is. Reviewed several times, however, it will begin to make sense which may motivate you, maybe for the first time in your life, to change your life by changing the way you eat. Also, I would recommend you reading Dr. Barry Sears' book, *The OmegaRX Zone*, which is the source of much of this summary. More than ever, the responsibility for improving and the opportunity to improve your health are yours. Remember, it is your life and it is your health.