

Love Your Endothelium

By Jessica Garcia

Put your hand over your chest and feel the rhythmic beatings of your heart. Listen to what it has to say as it pumps your blood throughout your body. Is your heart happy, healthy, at peace? Or is it unsettled, stressed, and overworked? Take good care of your heart because if you don't, there is a chance that one day atherosclerosis may creep up on you.

Atherosclerosis frequently leads to heart attack and stroke, and is one of the most prevalent causes of death both in the United States and throughout the world. Evidence shows that people with high cholesterol, high blood pressure, diabetes, or tobacco exposure are more likely to develop atherosclerosis. However, there are mysteries with regards to who will develop atherosclerosis. For instance, if two individuals have high cholesterol, one may develop atherosclerosis while the other may not. To better understand the nature of heart disease and the ways we can minimize its effects, we must ask why some people develop atherosclerosis, and among those people with atherosclerosis, what factors contribute to the onset of heart attack or stroke.

Recent research by Dr. John Cooke, Professor of Medicine and Director of the National Institutes of Health funded Program in Vascular Biology and Medicine at Stanford, has shown that the answers to these questions appear to lie within the endothelium.

The Endothelium and Atherosclerosis

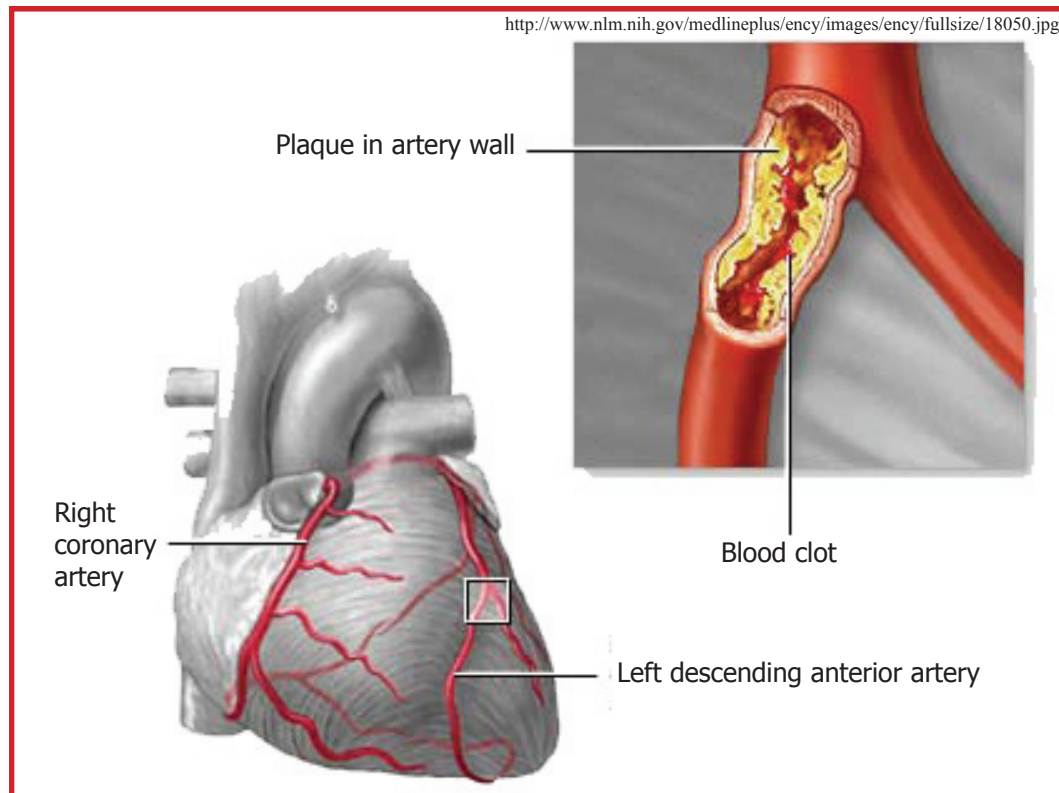
The endothelium is the innermost lining of the blood vessels, just one cell layer thick. This thin film of tissue plays an integral role in the health of the vessel, instrumental in contraction, blood flow, clotting, and inflammation. A healthy endothelium provides a protective coating. When it is damaged, white blood cells stick to the endothelial cells and penetrate the vessel wall, causing the wall to thicken.

Atherosclerosis—a buildup of cholesterol and lipids creating a plaque in the vessel wall—also thickens the wall and restricts blood flow. A plaque is especially dangerous when it ruptures because it can completely obstruct blood flow and cause a heart attack or stroke.

Atherosclerosis tends to occur in bends and branches of vessels. These are areas of disturbed flow and recirculating eddies that can cause biological changes to occur in the endothelium. Such biological changes can weaken or remodel the endothelium, leaving it susceptible to the infiltration of fatty material.

Endothelial Research: Say Yes To NO

There are many labs around the world that focus on different aspects of atherosclerosis and the endotheli-



< In atherosclerosis, fatty material builds up inside a blood vessel wall, which can lead to total blockage of blood flow. The disease most commonly affects the coronary arteries of the heart.

um. Here at Stanford, Dr. John Cooke's lab focuses on the study of the endothelium's role in atherosclerosis and angiogenesis, or blood vessel formation.

Dr. Cooke's lab has discovered that nitric oxide (NO) performs functions that protect the endothelium. NO is expressed by NO synthase in endothelial cells. It diffuses freely across cell membranes into smooth muscle cells, causing them to relax and assisting blood flow through the vessels. NO inhibits blood cell adhesion, aggregation, cell proliferation, and inflammation. It also exhibits antioxidant effects by scavenging free radicals that damage blood vessels. Indirectly, NO helps to widen blood vessels, which in turn lowers blood pressure.

Although research has shown that NO has several antiatherogenic functions which protect the endothelium, researchers have yet to prove whether NO actually inhibits atherosclerosis. Nonetheless, Dr. Cooke believes that an individual with a healthy endothelium will maintain healthy blood vessels and resist the development of cardiovascular disease. His philosophy is "You are only as old as your endothelium."

What You Can Do To Improve Endothelial Function

Explaining the importance of endothelial health, Dr. Cooke has published a book entitled "The Cardiovascular Cure: How to Strengthen Your Self-Defense Against Heart Attack and Stroke." The book describes in detail what can be done to improve endothelial health, especially with regard to choosing beneficial foods.

For instance, you may know that those people who

consume more fish, and specifically cold-water fish such as salmon, tuna, and mackerel, are less likely to have heart disease. The reason is that fish oil contains protective factors known as omega-3 fatty acids.

Omega-3 is a polyunsaturated fat that the body uses to construct cell membranes, including those of the endothelium. If the body does not receive a sufficient supply of polyunsaturated omega-3s, it will construct the membranes from saturated fat instead. As a result, the membranes are less elastic, making it more difficult for the heart and blood vessels to expand and contract. This puts stress on the circulatory system and can contribute to the development of cardiovascular disease.

Finding a reliable way of measuring endothelial health could give us early warning of developing atherosclerosis.

In short, increased consumption of foods containing polyunsaturated fats such as omega-3 will make your endothelium less rigid, making it easier for your heart and circulatory system to pump and flow. This helps to keep your heart healthy and decreases the chance of death from cardiovascular disease.

Chocolate Is Good For You?

If you have a sweet tooth and enjoy dark chocolate,

you may be happy to hear that dark chocolate also contains potent anti-oxidants. Dark chocolate contains “flavanols” that can improve both blood flow and the health of your endothelium, in part by increasing the concentration of circulating NO. Chocolate bar manufacturer Mars has developed a new dark chocolate bar, Cocoa Via, that is packed with flavanols. The bars are relatively low in calories—80 per serving—and also contain plant sterols that help lower blood cholesterol.

Genetic research may help to explain why different people with similar diets can have different susceptibilities to developing atherosclerosis.

Future Directions For Endothelial Research

Dr. Cooke’s lab has done a great deal of work advancing the understanding of the endothelium’s dynamic role in heart health as well as constructing ideas for future research. One area of endothelial research that can improve our chances of detecting and inhibiting atherosclerosis is to find early warning markers. In other words, finding a reliable way of measuring endothelial health could give us early warning of developing atherosclerosis, and could predict the risk for heart attack and stroke.

Dr. Cooke believes that this early warning beacon includes measuring the level of asymmetrical dimethylarginine (ADMA). ADMA is a molecule that inhibits NO synthesis and therefore interferes with its protective effects. Dr. Cooke’s lab has shown that ADMA inhibits angiogenesis, plays a significant role in causing vascular disease, and is elevated in disorders associated with endothelial dysfunction. Perhaps early detection of elevated ADMA levels followed by targeted inhibition of ADMA may provide the protection necessary to keep the endothelium healthy and ward off atherosclerosis.

Genetic research may help to explain why different people with similar diets can have different susceptibilities to developing atherosclerosis. The levels of expression of NO or ADMA under normal conditions may vary among individuals, giving some more endothelial protection than others.

In the future, drugs targeted to improving endothelial health may be able to protect blood vessels from disease and prevent heart attack and stroke. Only time will tell how critical the endothelium is for maintaining health. For now, research seems to suggest that if you love your endothelium, it will in turn love you. **S**

Omega-3 fatty acids are found in cold-water fish like salmon and in flaxseed and canola oils.



<http://www.nlm.nih.gov/medlineplus/ency/imagepages/19302.htm>

^ Certain habit changes, such as consuming more foods rich in omega-3 fatty acids, will help maintain heart health and reduce one’s chances of developing cardiovascular disease.

Jessica Garcia is a junior at Stanford majoring in Biology. She has a strong interest in cardiovascular research, and in her spare time enjoys running and swimming.