

Why Heart Attacks Occur in Many People With Normal Cholesterol Levels

James P. Meschino, DC, MS

There is no doubt high cholesterol levels increase risk for heart attack and other cardiovascular diseases. Your patients should strive to achieve a fasting blood cholesterol level below 3.9 mmol/L if possible, which is the safest level in regards to cardiovascular disease risk. However, there is more to the story than cholesterol alone when addressing the risk for cardiovascular disease, which remains the number-one cause of death in our society. Other factors, such as high blood pressure, diabetes, smoking, high blood levels of homocysteine, being overweight and high levels of stress, all are known to contribute to the development of heart attacks and other vascular problems. In addition, a state known as "endothelial dysfunction" recently has emerged as a significant cardiovascular disease risk factor, and its discovery has helped to explain the mechanisms through which smoking, diabetes and stress increase risk for heart attack, stroke, deep vein thrombosis and other vascular diseases.

Endothelial Dysfunction and Sudden Death

The endothelial cells (the endothelium) are the cells that line the inner surface of all blood vessels including arteries and veins (as well as the innermost lining of the heart and lymphatics). In addition to their structural function, endothelial cells participate in a number of activities that affect blood coagulation, blood stickiness and the degree of dilation/constriction of specific blood vessels from moment to moment, which largely determines how much blood will flow through them. Under normal circumstances, endothelial cells behave in a way that does not cause excessive blood stickiness and helps regulate the dilation of blood vessels according to the surrounding tissue's requirement for oxygen and other nutrients. If a tissue requires more blood, endothelial cells secrete nitric oxide (NO), which causes the muscular coat of the blood vessel wall to relax. This enables the local blood vessel to dilate, allowing more blood to circulate to the tissues it serves. A good example of this is the male penile erection, which occurs when endothelial cells secrete nitric oxide, allowing the blood vessels to open up. Drugs such as Viagra help overcome erectile dysfunction by increasing levels of nitric oxide in these blood vessels.

When endothelial cells function abnormally, it is known as "endothelial dysfunction." The endothelial cells secrete local chemicals that increase the stickiness of the blood and produce excessive blood-clotting activity. In many cases, the final event in a heart attack or an ischemic stroke is the clumping of blood platelets, which form a plug in the artery wall, often resulting from endothelial dysfunction. In turn, these plugs can completely block blood flow to a section of heart muscle or brain tissue. This is why doctors try to break down clots using powerful anticoagulant drugs when a heart attack occurs, and why they use anticoagulant drugs such as heparin and warfarin (Coumadin) to treat deep vein thrombosis. In addition, endothelial dysfunction involves an inability for endothelial cells to secrete appropriate amounts of nitric oxide. This results in constriction of the involved blood vessel, which severely restricts blood flow to the tissues it supplies. As such, endothelial dysfunction is a significant factor in the development of heart disease, ischemic stroke and deep vein thrombosis. It also is involved in angina attacks and erectile dysfunction.

What Causes Endothelial Dysfunction?

In recent years, we have learned a great deal about endothelial dysfunction in regard to what causes it and how to prevent it. Not surprisingly, much of the answer lies in our dietary and exercise behaviors. What we know is that high cholesterol levels increase the development of endothelial dysfunction. As such, people with already narrowed arteries from cholesterol buildup tend to have a greater propensity for endothelial dysfunction. It's a double whammy for these individuals. Let me state this again, as I have on numerous occasions: You should encourage your patients to eat a low animal-fat diet (with the exception of fish), consume foods that help to lower cholesterol (beans, peas, certain fruits and vegetables, ground flaxseed, psyllium husk fiber, salba grain, etc.), stay at their ideal weight and exercise regularly in order to help keep their cholesterol down.

But even if cholesterol levels are normal, endothelial dysfunction can occur from the ingestion of foods containing trans fats (margarine, shortenings, deep-fried foods, etc.) and/or high amounts of animal fat. The intake of highly refined sugars also has been shown to cause endothelial dysfunction. These factors should not be considered lightly, as evidenced by the fact that a study showed endothelial dysfunction was present in approximately half of women with chest pain, in the absence of overt blockages in their large coronary arteries.

Keep in mind that type 1 and type 2 diabetes also encourage endothelial dysfunction, which might further explain why diabetics have a much higher risk of cardiovascular complications. By remaining at an ideal weight and being physically fit, individuals dramatically reduce their chances of developing type 2 diabetes. If they already have been diagnosed with diabetes, the same principles apply to improving the management of their diabetic state. Cigarette smoking also has been implicated as a cause of endothelial dysfunction, which further explains the heightened risk for vascular disease that occurs in smokers. Uncontrolled high blood pressure also contributes to endothelial dysfunction.

Preventing and Combating Endothelial Dysfunction

From a dietary standpoint, we have learned that certain vitamins, minerals and other natural agents can help to reduce the development of, or reverse, endothelial dysfunction. For instance, the B vitamin folic acid has been shown to improve endothelial dysfunction. Other studies indicate that omega-3 fats improve endothelial function, as well as certain antioxidants such as vitamins E and C. Supplementation with these nutrients, as well as the amino acid L-arginine, has shown beneficial effects in reversing endothelial dysfunction.

Folic acid has been shown to increase the synthesis and release of nitric oxide from endothelial cells, thereby relaxing blood vessels and improving blood flow through the large, medium and small arteries of the body. Vitamins E and C decrease free radicals in the artery wall, promoting the release of endothelial agents that relax blood vessels and improve blood flow. Omega-3 fats encourage the production of endothelial agents known as prostacyclins, which also relax the blood vessel wall, improve blood flow and reduce blood stickiness. Vitamin E supplementation also reduces blood stickiness.

Supporting endothelial function is one of the reasons I recommend adults supplement a healthy diet with a high-potency multivitamin and mineral supplement that contains 1,000 mg of vitamin C, 400 IU of vitamin E, a B-50 complex (including 400 mcg of folic acid), as well as an essential fatty acid supplement containing 400 mg each of fish, flaxseed, and borage seed oils. Individuals over the age of 45 also should include a supplement containing 30-60 mg of coenzyme Q₁₀ and 37.5-75 mg of the herb hawthorn (standardized to 3 percent to 5 percent flavonoid content), as an

additional means to guard against endothelial dysfunction and cardiovascular disease. After age 60, the daily dosage of coenzyme Q₁₀ and hawthorn should be doubled.

Cardiovascular disease accounts for approximately 40 percent of all deaths in North America. Although genetic factors play a role, studies confirm that in more than 90 percent of cases, premature heart attacks, stroke, deep vein thrombosis and other vascular diseases result from faulty dietary and lifestyle patterns. In light of the importance of endothelial dysfunction as a cause of premature death from vascular disease, having a low cholesterol level and being thin are no longer acceptable reasons to regularly consume foods high in fats and refined sugars.

Resources

1. Brown A, Hu FB. Dietary modulation of endothelial function: implications for cardiovascular disease. *Am J Clin Nutr*, 2001;73;4:673-86.
2. De Bree A, Van Mierlo LA, Draijer R. Folic acid improves vascular reactivity in humans: a meta-analysis of randomized controlled trials. *Am J Clin Nutr*, 2007;86(3):610-7.
3. Stroes ESG, van Faassen E, Yo M, et al. Folic acid reverts dysfunction of endothelial nitric oxide synthase. *Circ Res*, 2000;86:1129-34.
4. Granato H. "Circulatory Function and Vascular Integrity." www.naturalproductsinsider.com.
5. Koukkou E, Ghosh P, Lowy C, Poston L. Offspring of normal and diabetic rats fed saturated fat in pregnancy demonstrate vascular dysfunction. *Circulation*, 1998;98:2899-904.
6. Gerber RT, Holemans K, O'Brien-Coker I, et al. Cholesterol-independent endothelial dysfunction in virgin and pregnant rats fed a diet high in saturated fat. *J Phys*, 1999;517(2):607-16.
7. Roberts CK, Barnard RJ, Sindhu RK, et al. A high-fat, refined-carbohydrate diet induces endothelial dysfunction and oxidant/antioxidant imbalance and depresses NOS protein expression. *J Appl Physiol*, 2004;98:203-10.
8. Zhang HY, Reddy S, Kotchen TA. A high sucrose, high linoleic acid diet potentiates hypertension in the Dahl salt sensitive rat. *Am J Hypertens*, 1999;12:183-7.
9. Lopez-Garcia E, Schulze MB, Meigs JB, et al. Consumption of trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. *J Nutr*. 2005;135(3):562-6.
10. Reis SE, Holubkov R, Smith AJC, et al. Coronary microvascular dysfunction is highly prevalent in women with chest pain in the absence of coronary artery disease: Results from the NHLBI WISE Study. *Am Heart J*, 2001;141(5):735-41.
11. Esper RJ, Nordaby RA, Vilarino JO, et al. Endothelial dysfunction: a comprehensive appraisal. *Cardiovasc Diabetol*, 2006;5:4.
12. Heitzer T, Yla-Herttuala S, Luomoa J. Cigarette smoking potentiates endothelial dysfunction of forearm resistance vessels in patients with hypercholesteolemia. *Circulation*, 1996;93:1346-53.

JULY 2008