Heart News

Endothelial Dysfunction- Heart Disease in its Earliest Stages

Identifying the earliest stage of coronary atherosclerosis for vigorous treatment to prevent death, heart attack, bypass surgery or other invasive procedures is a major goal of the Weatherhead PET Center For Preventing and Reversing Atherosclerosis under the direction of K. Lance Gould MD. Toward that end, we are studying the function of the lining of the coronary arteries where atherosclerosis starts.

The thin, smooth lining of the coronary arteries is called the endothelium (pronounced end-o-the-lee-um). The normal healthy endothelium produces hormone like substances that cause the coronary blood vessels to enlarge (vasodilate) or constrict (vasoconstrict) in response to the heart’s need for more blood during exercise or stress. These hormone like substances, called vascular mediators, maintain a delicate balance between vasodilation and vasoconstriction. Nitric oxide is an important vascular mediator that dilates the coronary arteries and counterbalances another vascular mediator that is a powerful constrictor of the arteries called endothelin. This balance of the vascular mediators is disturbed in early coronary atherosclerosis and is termed endothelial dysfunction.

Smoking, high blood pressure, high blood sugar, high cholesterol levels, high fat food, excess weight and/or other risk factors injure the endothelium and impair its normal function. The loss of normal endothelial function may cause adverse vasoconstriction and/or blood clots in the artery (thrombosis) that reduce blood flow to the heart muscle. These adverse effects of injured or dysfunctional endothelium are illustrated in Figure 1 adapted from the book Heal Your Heart by Dr. Gould.

The vascular mediators produced by the endothelium also affect the aggregation or clumping of blood platelets, the small particles that instigate blood clots in arteries. Normally by inhibiting platelets, the healthy endothelium prevents blood clots from forming in the artery thereby maintaining blood flow through it. Damage to the normal endothelium impairs this protection against blood clots in the artery thereby making thrombosis more likely.

Endothelial dysfunction characterizes the earliest stage of coronary artery disease before narrowing of the artery develops and even before fully developed cholesterol plaques form. In the absence of reversal treatment, coronary artery disease progresses from endothelial dysfunction to early plaque formation and finally to progressively severe narrowing or to sudden breakdown
Living with "Blood Thinning Medications"

Most cardiac patients are instructed to take anticoagulant or anti-platelet medications such as Coumadin (warfarin), aspirin, or Plavix (clopidogrel) as part of their treatment regimen. These medications are designed to prevent abnormal blood clotting associated with coronary artery disease, irregular heart rhythms, or artificial heart valves. The risk of taking any "blood thinning" medications is the possibility of bleeding. Patients need to be able to recognize the common and expected side effects of the anticoagulant and anti platelet drugs as well as the uncommon and more serious side effects that need to be reported immediately.

Side Effects to expect while taking Aspirin, Plavix or Coumadin:

1. Skin will bruise very easily if injured.
2. Cuts, scratches, or injuries will bleed much longer than usual and may require long periods of pressure to stop bleeding.
3. Occasional small streaks of blood with "blowing nose" or small amount of bleeding after brushing teeth vigorously.
4. Occasional small nosebleed if nasal passages dry.

Side Effects to report immediately while taking Aspirin, Plavix, or Coumadin:

1. Spontaneous bruising with no apparent injury.
3. Coughing up blood.
4. Vomiting up blood.
5. Change in color of stool. Blood in stool may turn it dark in color and usually causes diarrhea.

Any medication that has the potential to help the body also has the potential to harm so all patients should monitor themselves for any changes and continue regular physician follow-up visits. Patients also need to make sure all physicians and dentists involved in their care are aware that they are taking these medications. Patients taking Coumadin should have their blood checked for the INR or protime monthly to adjust the dose. Green vegetables counteract the effects of Coumadin so that a higher dose is needed. Since green vegetables are essential for a healthy diet, it is important to eat approximately the same amount daily so that the dose of Coumadin required is stable. Some new drugs are being developed to replace Coumadin that do not require these monthly blood checks but they are not on the market yet.

Figure 2

Preventive treatment by lowering cholesterol, blood pressure, blood sugar and weight, stopping smoking, eating low fat food and controlling all risk factors heals the damaged endothelium. This healing restores function of the endothelium and the normal balance of vascular mediators with associated improvement in coronary blood flow. Such treatment also removes the cholesterol and reduces inflammation in the walls of the coronary artery. The plaque then stabilizes with markedly reduced risk of plaque rupture and corresponding reduction of heart attacks and deaths.

Until recently, endothelial dysfunction was identifiable only by an invasive arteriogram. However, most patients with endothelial dysfunction alone before narrowing of the coronary arteries don’t have symptoms of heart disease and have no reason to have an invasive arteriogram.

Over years of following patients with the risk factors for heart disease and studying their PET scans, Dr. Gould and his team have observed a patchy, uneven (heterogeneous) pattern on the PET scan at resting conditions that identifies dysfunction of the coronary endothelium as an early indicator of developing coronary continued on page 3
atherosclerosis. It is due to, and a picture of, the imbalance in the vascular mediators causing patchy constriction of the coronary blood vessels with a corresponding patchy, or heterogeneous, blood flow pattern. Figure 3, upper left panel, shows an example of a PET scan with this abnormal patchy pattern at resting conditions (single view). Commonly, this patchy pattern will improve during the stress images since the drug used for stress, dipyridamole, dilates the coronary blood vessels and overrides the constrictive effects of the dysfunctional endothelium. The PET image of this patient during stress improves with disappearance of this patchy pattern indicating that there is no flow limiting narrowing of the coronary arteries as in Figure 3, lower left panel. Three years of intense risk factor treatment improved this heterogeneous pattern, making it more uniform (homogeneous) at resting conditions, Figure 3 upper right panel, and after stress, lower right.

The significance of this patchy blood flow pattern in the heart at resting conditions was puzzling for many years since traditionally the stress images show blood flow abnormalities due to narrowing of the coronary arteries that do not affect blood flow to the heart muscle at resting conditions. The importance of this patchy pattern became apparent only after patients developed coronary artery disease years later at follow-up PET imaging before effective treatment was available as it is now. We also developed improved imaging technology and software to quantify this pattern that have been essential for understanding it better.

Dr. Gould had visually recognized this pattern on the PET images for many years but it was not widely accepted due to difficulty in proving the concept scientifically. However, over the past several years we developed a computerized mathematical model for quantifying the patchy pattern of blood flow in the heart muscle as being significantly different from normal and a strong predictor of early coronary artery disease. The scientific paper substantiating this observation was published in the Journal of Nuclear Medicine this month (J Nucl Med 2005; 46:1427-1437). This pattern of endothelial dysfunction on the resting PET scan is more sensitive predictor of early coronary artery disease than standard risk factors alone. Intervening at this early stage with vigorous combined lifestyle and pharmacologic treatment optimally prevents future heart attacks, deaths and surgical procedures.

However, we have not identified the specific vascular mediator causing this heterogeneous blood flow pattern, a step that is essential for complete scientific proof of this concept. Accordingly we are carrying out an additional study on the vascular mediator that we think is causing the abnormal pattern of blood flow in the heart as outlined in the next column.

Figure 3

PATIENTS NEEDED FOR STUDY OF ENDOTHELIAL DYSFUNCTION

Over the next year, a study will be carried out at the Weatherhead PET Center to help us understand more about the causes of endothelial dysfunction of the coronary arteries in early coronary atherosclerosis. We suspect that endothelin, a powerful vasoconstrictor is being produced excessively causing the patchy pattern of blood flow on resting PET images of the heart.

Our study will test a new drug called Darusentan, which blocks the effects of endothelin. Since excessive endothelin production has been identified as one cause of resistant high blood pressure, this drug has been studied in the past as a potential treatment for high blood pressure. However, the purpose of our study is to determine the effects of Darusentan on the PET images of patients with endothelial dysfunction. If this medication improves the blood flow in the heart muscle and eliminates the patchy pattern on the PET scans, we will have proven that endothelin is the most important vascular mediator causing the abnormal patchy pattern in the earliest stage of coronary artery disease.

The criteria for inclusion into the study are very specific and restricted to only those patients with a specific amount of the patchy pattern on their resting PET scan as measured by our computerized mathematical model. Patients who qualify for the study will undergo four PET scans over a 9-week period at no charge. Since there are specific inclusion criteria for admission into the study, we will call patients that qualify to provide details for those interested.
Living Healthy

The Importance of a Good Breakfast

It has been said many times that breakfast is the most important meal of the day. Now it appears that breakfast may also play an important role in reducing the risk of type 2 diabetes and cardiovascular disease. In a study presented at the American Heart Association’s Annual Conference on Cardiovascular Disease Epidemiology and Prevention, researchers found that risks of obesity and insulin resistance syndrome were 35 percent to 50 percent lower among people who ate breakfast every day compared to those who frequently skipped it.

Eating breakfast can have a profound effect on mood, energy level and even on eating habits for the rest of the day. Having protein with breakfast helps keep your energy level up and suppresses your appetite. Some people believe that skipping breakfast may help them lose weight but actually skipping meals often leads to overeating. Becoming over-hungry often leads to lack of control and eating more calories during the day than after an appropriate breakfast. When breakfast is skipped, you are likely to become tired when the brain and body run low on fuel. By mid-morning, a lot of people grab a cup of coffee, or a sugary snack to wake up again. This might work for a few minutes, but by lunchtime you are hungry, crabby, and perhaps your mood makes you a little more prone to making unhealthy choices at lunch. Eating a good breakfast sets the tone for the rest of the day and has also been proven to improve concentration, problem solving ability, mental performance, memory, and mood.

The most common obstacles to eating a good breakfast are not having enough time or not being a “morning person”. If you just can’t stomach food in the morning, try to have a little something with protein, such as a small container of yogurt, and bring along a mid-morning snack. Below are other suggestions for good portable breakfast items. Start your day off right by eating a nutritious breakfast with lots of protein that will decrease your craving for fattening snacks during the day, and provide the energy to accomplish the mental and physical tasks of the day.

Quick Protein Breakfast suggestions:
- Scrambled egg whites, low fat turkey bacon
- Low fat cottage cheese with fruit
- Protein shake

Cereals (Dry or with Skim Milk)
- Nutlettes soy protein Cereal (Dixie Diner)
- SMAPs maple flavored cereal (Dixie Diner)
- Protein Plus Brand Cereal (available at Rice) (a small amount of SPLENDA adds a lot of flavor)

Others
- Microwave a Tortilla rolled up with Canadian bacon and LF cheese
- LF yogurt and fruit
- LF mozzarella cheesesticks with grapes
- A glass of skim milk (with or without chocolate flavoring)
- No fat cheddar cheese melted or low fat/low carb bread (cheese toast).
- Soy or vege sausage patties
- Breakfast tortilla with scrambled egg whites and LF cheese

PET News is published twice annually for the patients and friends of the Weatherhead PET Imaging Center for the Prevention and Reversal of Heart Disease. We welcome your story ideas, comments, and suggestions.

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