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### **The Cardiometabolic Risk Syndrome**

#### **Part IV – Endothelium Dysfunction**

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**Your Life Your Health**

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To continue our discussion of the cardiometabolic risk syndrome, we have to learn some biology. Bear with this, it will make a great deal of sense when you finish and it will help you paint a mental picture of what you are doing to your body when you abuse it with overeating, eating the wrong foods, not exercising, gaining weight, smoking and/or not taking care of your health in many other ways.

There was a time when it was thought that blood vessels were passive conduits, like a piece of pipe, which allowed the blood to be transported from one place in the body to another. Now we know that blood vessels are very active organs which contribute greatly to our health, or when abused, to the development of illness.

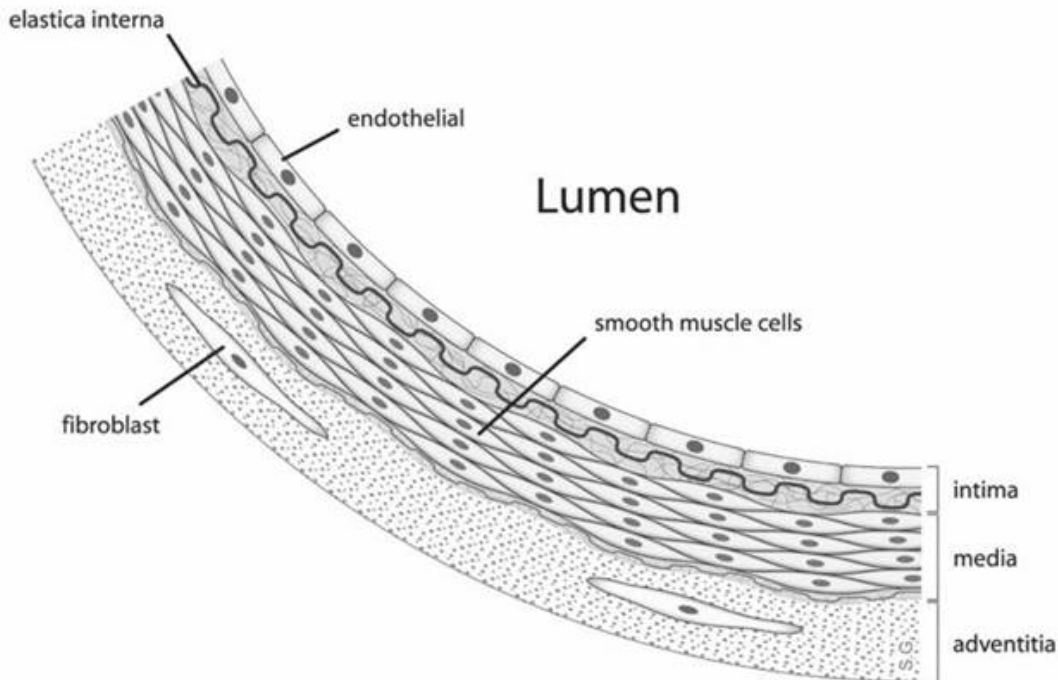
Here is the science. There are four basic types of tissue in the human. These compose all the organs, structures and other contents.

- Epithelium -- Tissues composed of layers of cells that cover organ surfaces such as the surface of the skin and inner lining of the digestive tract. These are the tissues that serve for protection, secretion, and absorption.
- Connective Tissue --As the name suggests, connective tissue holds everything together. Some people consider blood a connective tissue.
- Muscle Tissue - Muscle cells contain contractile filaments that move past each other and change the size of the cell. Muscle tissue also is separated into three distinct categories: visceral or smooth muscle, which is found in the inner linings of organs; skeletal muscle, which is found attached to bone in order for mobility to take place; and cardiac muscle which is found in the heart.
- Nervous Tissue - Cells forming the brain, spinal cord and peripheral nervous system.

The endothelium is the layer of thin specialized cells that line the interior surface of blood vessels, forming an interface between circulating blood in the lumen of the vessel and the rest of the vessel wall. Remember the concept of an “interface.” It differs from a barrier. An interface helps things cross from one place to another while a barrier simply separates things. An interface creates a dynamic exchange between the two “entities” which it connects. The blood vessel is a barrier but it is an active barrier; it has many functions in addition to getting blood from one place to another.

Endothelial cells line the entire circulatory system, from the heart to the smallest capillary. Both blood and lymphatic capillaries are composed of a single layer of endothelial cells. The following is a drawing of the artery. It shows that the endothelium is a one-cell thick layer on the inside of the artery. As we learn more about this

remarkable organ, we will see why a great deal of our efforts at preventive health should be targeted to keeping the endothelium healthy and actively performing its functions.



Endothelial cells have many functions; among the principle ones are:

- The constriction and dilation of the blood vessels which helps control your blood pressure
- The clotting of the blood (thombosis) and the prevention of the clotting of the blood (fibrinolysis). Health is dependent upon the proper balance of these two.
- Is were the process of atherosclerosis starts by which “hardening of the arteries” take place and by which we get heart disease, strokes and peripheral vascular disease.
- The formation of new blood vessels which is a good thing from exercise and a bad thing from tumor formation.
- The inflammation which contributes to atherosclerosis and edema (swelling) in the limbs.

Endothelial cells also control the passage of materials including white blood cells into and out of the bloodstream. When the function of the enthothelium in the arteries is compromised, disease develops. Those with the cardiometabolic risk syndrome are at great risk for diabetes, hypertension and heart disease. Endothelial dysfunction is a result of these processes and is also a contributing cause to them.

## **Endothelial Dysfunction**

Endothelial Dysfunction is one of the cardinal features of the cardiometabolic risk syndrome. Endothelial Dysfunction is both a cause and an effect of:

- Hypertension
- Atherosclerosis
- Heart Disease
- Diabetes Mellitus
- Kidney Disease

Endothelial dysfunction can result from disease processes, as occurs in shock due to infection, high blood pressure, elevated cholesterol, diabetes mellitus such as from smoking tobacco products and excessive alcohol use. A sedentary life style also will result in endothelial dysfunction as will obesity.

Endothelial dysfunction is thought to be a key event in the development of heart disease and predates clinically obvious vascular pathology by many years. Endothelial dysfunction has also been shown to be of prognostic significance in predicting vascular events including stroke and heart attacks.

## **Dilating Arteries**

A key feature of endothelial dysfunction is the inability of arteries to dilate fully in response to an appropriate stimulus. Dysfunctional endothelial cells are unable to produce nitric oxide to the same extent (or there is increased and rapid destruction of NO) as healthy endothelial cells and therefore vasodilatation is reduced. This creates a detectable difference in subjects with endothelial dysfunction verses a normal, healthy endothelium.

## **Diet and Endothelium Dysfunction: Trans Fats**

Endothelial function can be improved significantly by exercise and improved diet. A study published in 2005 has determined that a positive relationship exists between the consumption of trans fat (commonly found in hydrogenated products such as margarine) and the development of endothelial dysfunction. Other factors have been identified as improving endothelial function and include cessation of smoking, loss of weight and treatment of high blood pressure and high cholesterol among other things.

Endothelial dysfunction has been observed in a 2001 study of women where it was found that this disorder is present in approximately half of women with chest pain, in the absence of overt blockages in large coronary arteries. This endothelial dysfunction cannot be predicted by typical risk factors for atherosclerosis (e.g., obesity, cholesterol, smoking) and hormones.

## **From Endothelial Dysfunction to heart disease**

Atherosclerosis has been considered as a disease of "four concepts"; those four concepts are:

1. Atherosclerosis is a wide spread disease; therefore if you have decreased blood supply to your legs (peripheral vascular disease) due to hardening of the arteries, you probably have heart disease as well.
2. Atherosclerosis is a heterogeneous and multi-form disease, which means simply that while you may have severe vascular disease in your legs, you may have only mild disease in your heart.
3. The quality of the plaque (blockage in your arteries) is more important than the size. In advanced stages of arteriosclerosis, two types of lesions can be distinguished: Stable, or fibrous plaque and High Risk, unstable or vulnerable plaque.
4. Atherosclerosis is an inflammatory, immunological, polygenic and multi-factorial disease – this means simply that genetics, infection, immune reaction and inflammation are all involved in the hardening of the arteries.

In atherosclerotic disease, classical and new emerging risk factors play an important part. All of these are associated with the cardiometabolic risk syndrome and all are associated with endothelial dysfunction. They are:

- high cholesterol serum levels
- high blood pressure
- smoking
- obesity
- sedentary lifestyle
- hyperhomocysteinemia – elevated homocysteine in the blood.
- Lp(a) lipoprotein – a particular kind of cholesterol particle which is inherited and which is very atherogenic (very likely to cause heart disease).
- Cytomegalovirus – an infectious organism
- Chlamydia pneumoniae – a common infection which has been found to contribute to heart disease.
- Helicobacter pilorae – another infectious organism which is associated with a higher risk of heart disease.
- Bacteroides gingivalis – a gum infection which contributes to heart and heart valve disease.
- genetic factors
- C-reactive protein – a marker of inflammation in the body.
- serum-A amyloid protein – another inflammatory marker.
- Plasminogen Activator Inhibitor I – an important element in the body balancing blood clotting. Too much PAI-1 increases the chance of having a blood clot (thrombus)
- D-dimer – another element which can promote excessive blood clotting

- Fibrinogen – another element involved in blood clotting.
- von Willebrand -- another form of excessive clot formation.
- Microalbuminemia – this is protein in the urine which indicates endothelial dysfunction in the kidney. If it is present in the kidney, it is likely present in the arteries.

All the experience obtained in the last years, suggests that the endothelium's dysfunction is not only the initial stage of the atherosclerotic disease that generates plaque formation, but endothelial dysfunction also causes the high risk plaque leading to the development of a vascular event, i.e., heart attack, stroke, etc.

The good news is news is that endothelium dysfunction like all of the other features of the cardiometabolic risk syndrome will respond to the following steps:

1. Magnesium supplement in the diet. This helps the body balance the clotting/not clotting mechanisms in the body. Calcium promotes clotting; magnesium promotes not clotting. The balance between your calcium and magnesium can be expressed in a ratio which partially reflects your vascular health.
2. Statins – these medications which decrease your cholesterol, improves the function of your endothelium and also helps stabilize any plaques which you have in your arteries. Remember, getting rid of your plaques is valuable but changing them from the highly unstable to the stable plaques is critical.
3. Ace Inhibitors – this is a class of medication used for blood pressure control which helps improve the function of your endothelium particularly in the kidney. If you have diabetes or if you have protein in your urine, these medications can be very helpful in preventing the advancement of kidney disease.
4. N-Acetyl Cystiene (NAC) – the use of dietary supplements is controversial, but there is growing evidence that the antioxidant benefits of NAC have many positive benefits as we age.
5. Vitamin C and Folic Acid – both have shown benefit in improving nitric oxide production in the endothelium and may have significant benefit for those with endothelial dysfunction. Some research has contradicted this potential benefit.

Improvement in endothelial function has been demonstrated by improving the control of diabetes as evidenced by normalizing hemoglobin A1C. Controlling cholesterol and insulin levels also improve endothelial function. All three of these factors respond to diet, exercise, weight loss and smoking cessation.

Endothelium function is also improved by the improvement of plasminogen activator inhibitor-1, homocysteine, C - reactive protein and fibrinogen. Each of these will be discussed in future parts of this series on the cardiopulmonary risk syndrome. All of them can be clinically measured.

It is important for you to know if you have the cardiometabolic risk syndrome. Ask your doctor to evaluate you for this condition and to recommend a treatment program to avoid it, cure it or control it. Remember, it is your life and it is your health.