The New Understanding of Heart Attacks

Before discussing how you can dramatically reduce your risk of a heart attack, it is important to understand the process of heart disease. Recent large-scale follow-up studies of patients, as well as new scanning technologies that provide an unprecedented clear view of what is actually going on in the coronary arteries, have completed changed our understanding of the disease.

The long-held model of heart disease as basically a plumbing problem has been shown to be fatally flawed, as recent studies of the two most popular forms of heart surgery have shown. A major study of 2,300 heart patients, both men and women, published in 2007 in the prestigious *New England Journal of Medicine*, studied the effectiveness of angioplasty, the most common form of heart surgery. This surgery involves smashing the deposits blocking the coronary arteries – the arteries that provide blood to the heart itself – up against the arterial walls and inserting a "stent" (a wire mesh tube to keep the artery open). All of the patients in this study were considered candidates for angioplasty according to the standard surgical criteria and were divided into two groups. One group received angioplasty surgery plus standard medical care, which included lifestyle recommendations and standard-of-care cardiac medications such as aspirin (to reduce blood clots), beta blockers (to reduce strain on the heart) and statin drugs (to lower "bad" cholesterol levels and inflammation). The control group received the same standard medical care but no surgery. Both groups of patients were followed for 4 ½ years, but, incredibly, *no* benefit was seen from the surgery in reducing heart attacks or deaths.

Looking at the numerous studies that have been done, the only circumstance in which angioplasty has been shown to aid survival is when it is administered immediately after a heart

attack. In all other cases, including this major study, it was shown to provide no more value than not performing the surgery.

Proponents of angioplasty and stenting countered that even though the patients who underwent these procedures had no reduction in heart attacks or deaths, the surgery was still worth doing since these patients would have less angina or chest pain. Yet, this new study also found that patients who underwent these procedures didn't have less chest pain either. Even though these procedures haven't been shown to provide value in reducing any of the things it is designed to treat – heart attacks, death rate or angina – they are still done over 1.2 million times a year. At an average cost of about $44,000, the American public is spending more than $50 billion a year unnecessarily.

The second most common type of heart surgery is coronary artery bypass grafting (CABG). This is an extremely invasive surgery in which occluded arteries are bypassed with grafted veins or mammary arteries. The surgery involves stopping the heart, maintaining the patient on a heart-lung machine during surgery, and then restarting the heart when the bypass surgery is completed. But, about one in fifty patients who has a CABG does not survive it. In addition, more than half of the patients experience a significant decline in mental function and mood, including cognitive decline, depression, and mood swings after bypass surgery - a phenomenon called "pump head," referring to the effect of the heart-lung pump on the brain.

Defenders of CABG originally claimed that this effect was temporary, but studies, such as one reported in the *New England Journal of Medicine,* have found that the mental and mood decline is permanent for about half of all bypass patients. Other profoundly negative side effects and complications include serious infections, collapse of the lungs, heart rhythm problems and others.

Studies of the effectiveness of bypass surgery show the same thing as for angioplasty - essentially no benefit in reducing subsequent heart attacks and deaths. CABG is somewhat more effective than angioplasty in reducing angina pain, but there are much less expensive and safer, noninvasive ways to accomplish the same thing, such as judicious use of cardiac medications and the non-invasive procedure known as enhanced external counterpulsation (EECP).

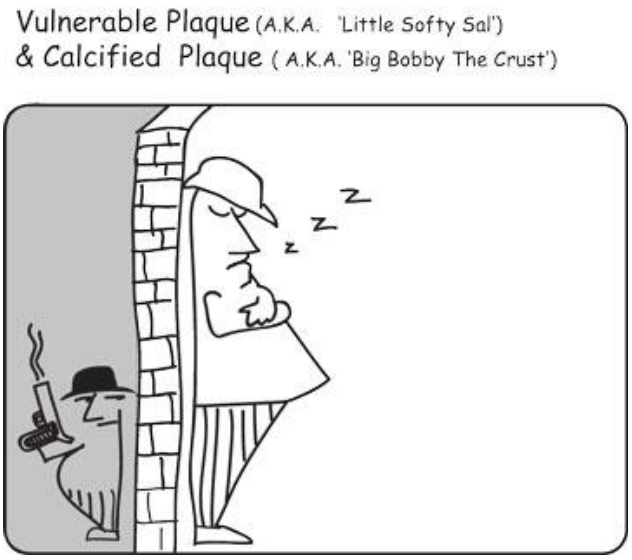
Approximately 470,000 bypasses are performed each year at an average cost about $85,000, which totals $40 billion a year. This means about $90 billion each year for these two surgeries is spent. The American Heart Association estimates that heart disease is responsible for an additional $150 billion of indirect costs such as lost productivity.

You might wonder why angioplasty and bypass surgery constitute a $90 billion industry in the U.S. when they cause so many side effects with little documented benefit. One factor might be leaving surgical decisions to the very people who benefit financially from the decisions, but we'll leave the economics of health care to others. For our purposes, the point we want to make is that these two surgeries are based on an old and scientifically discredited theory of heart disease – that it is a plumbing problem that can be fixed by unclogging or bypassing stopped up pipes.

Let's compare the old plumbing model with our new understanding, because all of our recommendations stem from a proper understanding of the real causes of heart attacks. The old model works like this: hard, calcified plaque builds up in your arteries, gradually occluding them. Then, when an artery became sufficiently blocked - 75 percent or more – there is a risk that a clot will get stuck in the narrowed opening. When that happens, the artery becomes completely blocked, no blood can get through to the heart muscle – and that's a heart attack.

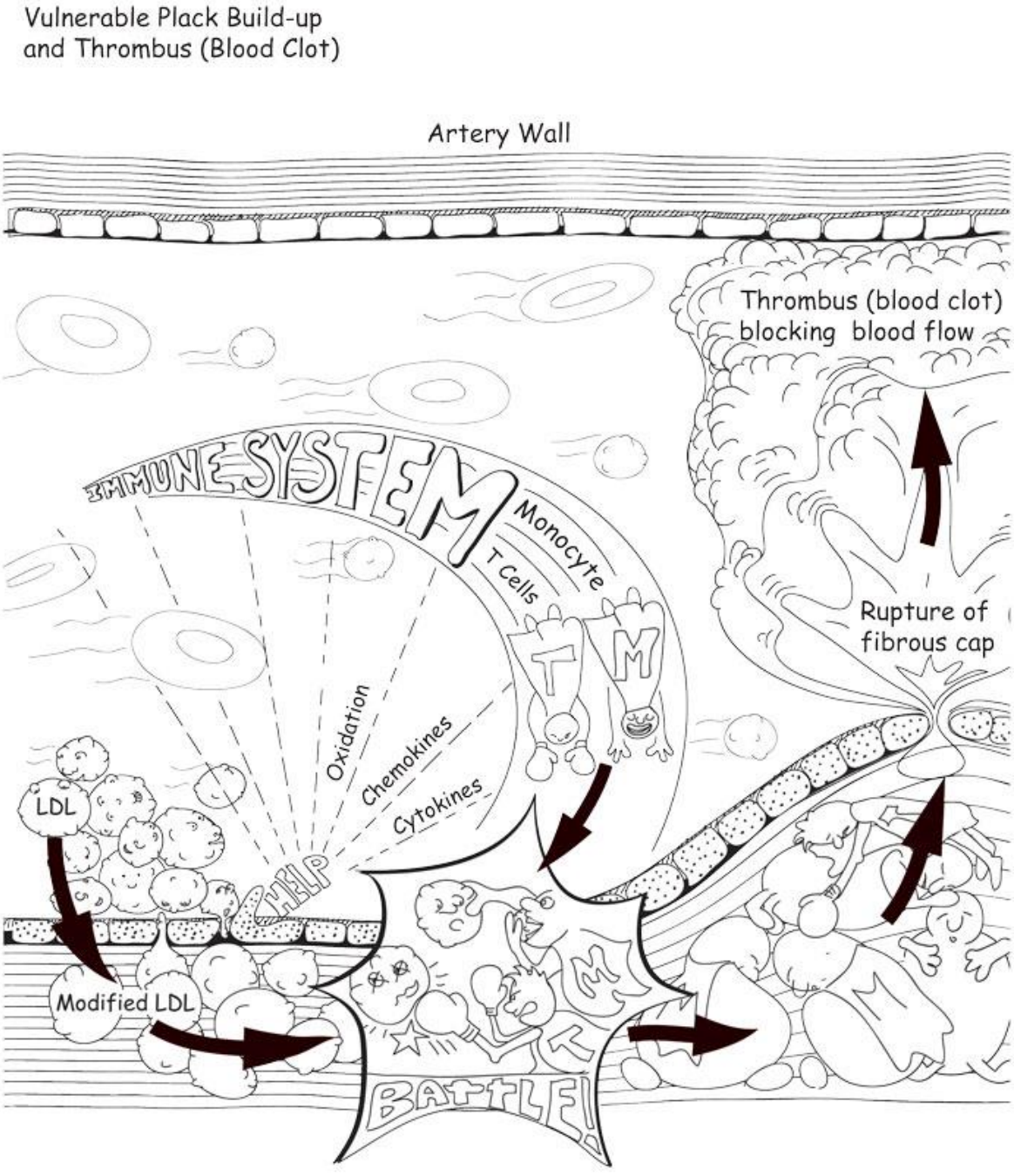
Every day, thousands of patients the world over are being shown pictures of their blocked coronary arteries by their cardiologists and cardiac surgeons. These pictures were taken when the patients underwent their angiograms (itself an invasive procedure in which a catheter is inserted in the groin and threaded up the aorta into the heart, where dye is then injected and pictures taken). As they look at these pictures of their blocked arteries, the patients are often told that they are "walking time bombs" and need to undergo angioplasty or bypass surgery immediately. These patients may very well be walking time bombs, but for an entirely different reason, and these surgeries will do nothing to change the risk.

We now know that the vast majority of heart attacks do not result from arteries blocked with hard calcified deposits or *calcified plaque* that patients are shown by their surgeons. In fact, this type of hard plaque is almost never the cause of heart attacks; rather, it appears to be the *result* of the body's attempt to wall off the real culprit, which is soft, non-calcified or *vulnerable* plaque. Vulnerable plaque is flexible and dynamic. It rarely produces symptoms, does not appreciably block arteries and is difficult to see on angiograms. Yet, vulnerable plaque is the real villain in the story.



This new understanding replaces the old model of heart disease as a plumbing problem and looks at it instead as a dynamic multi-step process in which *inflammation* (the over-activation of the immune system) works first to create vulnerable plaque and then to lead it

through an intricate and insidious cascade of events which ultimately ends in a heart attack. It is worthwhile to review the steps in the process that leads up to a heart attack because it guides our



thinking on how to thwart this process at every stage.

The story begins with LDL (low-density lipoprotein) cholesterol particles – the aptly named "bad" cholesterol. We should note that LDL is not all bad; indeed we could not survive

without it. LDL transports cholesterol from the liver to the body's tissues where it is needed to keep cell membranes healthy. It is also a precursor of our sex hormones. But when levels of LDL are higher than we need for these vital life processes, it accumulates inside the artery walls where it can undergo pathological changes. LDL can react with oxygen to become oxidized and with excess glucose in a process called glycation (binding with sugar molecules). Once modified in this way, the LDL particles take on a different appearance. They no longer look friendly to the immune system and are easily mistaken for foreign invaders. The immune system responds by sending in different types of white blood cells including monocytes and T lymphocytes in an attempt to destroy the pathological LDL molecules.

After the monocytes encounter the LDL deposits, they become *macrophages* and begin to gobble up these deposits. These macrophages (from the Latin *macro* for big and *phage* for eater) have such big appetites, they eventually become stuffed with the LDL particles and become "foam cells," so named because they look like bubbles of foam. This is the beginning of vulnerable plaque, which at this stage is called a "fatty streak." Autopsies of soldiers killed in battle have shown that this early form of vulnerable plaque is quite common in 20 year olds, and can even be found in children.

Note that the entire process above is one of inflammation, basically an over activation of the immune system. Inflammation, in fact, underlies every stage of this process. In the next step, inflammation causes the blood vessel's smooth muscle cells to grow over the foam cells and form a fibrous cap. This is now a mature vulnerable plaque, which typically does not restrict blood flow but just appears as a slight bulge in the outer diameter of the blood vessel. Vulnerable plaque has been notoriously difficult to visualize, but recently, we have begun to be

able to see images of vulnerable plaque in arteries on a beating heart using a new generation of non-invasive scanners, and this is emerging as a promising diagnostic tool.

The stage is now set for the coup-de-gras event of a heart attack, and is again fueled by inflammation. Prompted by substances produced by an overactive immune system, the fibrous cap can rupture spilling the contents of the foam cells and other dangerous chemicals that they have produced. Specific elements in the blood stream respond by forming a blood clot or thrombus to keep the contents of the foam cells from entering the bloodstream. If the thrombus that forms is large enough to completely block the coronary artery, that's called a coronary thrombosis or heart attack. The region of the heart normally supplied by this artery is now deprived of oxygen and other nutrients and will die if the blockage is not quickly reversed. It is important to note that in most cases until just moments before the heart attack, the artery was *not* blocked to any significant degree by the vulnerable plaque. The thrombus formed suddenly after the rupture of the fibrous cap with devastating consequences.

This new understanding motivates all of our recommendations for heart attack prevention. Since the process starts with excess LDL particles, keeping LDL at healthy low levels is our first recommendation. In addition to LDL, there is a form of cholesterol called HDL (high density lipoprotein cholesterol), the "good cholesterol," which clears LDL particles from the bloodstream and carries them back to the liver. So, keeping HDL levels high is another important approach.

Keeping in mind that that every stage leading to a heart attack is fueled by inflammation, we see once again another way in which our evolutionary Stone Age heritage is not on our side when we get to middle age. Infections were the most common form of death tens of thousands of years ago, so having a strong and highly reactive immune system was critical to the survival

of the human species. At this earlier time in our evolution, very few people lived long enough to die from heart attacks, so there was little need to worry about the downsides of an overly active immune system that might cause a heart attack later in life. Many aspects of our modern lifestyle such as the wrong diet and excessive stress also increase the activation of the immune system and increase inflammation. So, our next and perhaps the most important strategy in preventing heart attacks is keeping our immune system robust enough to combat infections, but avoiding its over activation and subsequent inflammation.