

HeartFacts

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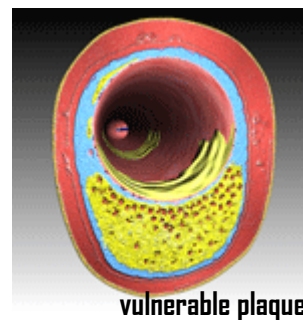
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Why Does Plaque Rupture?

Plaque rupture is the inciting event in the **acute coronary syndromes**. The subsequent extrusion of plaque contents into a coronary lumen initiates the clotting cascade and results in thrombus formation at the rupture/erosion site. If the vessel occludes, an ST elevation myocardial infarction results. If it simply obstructs, then either a non ST elevation infarct occurs or unstable angina is the clinical expression (depending on the degree of lumen obstruction). But why does plaque rupture in the first place?

an inflammatory process. It may also have a link to certain infections, for example chlamydia. It is thus possible to think of a vulnerable plaque as a pustule protruding into the arterial lumen. There it is exposed to a number of blood born effects, both through the channel itself and via the fine network of capillaries in the arterial media called the vasa vasorum. As if in battle, the pustule may be attacked frontally, from the flanks, and from the rear. That point at which the plaque is most vulnerable appears to be the shoulders.

Plaque which is destined to rupture is referred to conceptually as **vulnerable plaque**. As opposed to the tight, often calcified plaque of stable coronary disease, vulnerable plaque is younger, softer, lipid rich, and encroaches less on the lumen. Additionally, the population of these plaques may be 5-10 times more numerous in a given patient than chronic, severely stenotic plaque. A thin fibrous cap is all that separates the



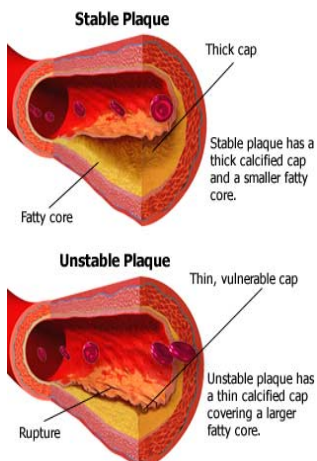
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thrombogenic pool of lipid from the vessel channel. A variety of forces combine to disrupt and tear the fibrous cap. Again, the point of attack is often the shoulders. Sheer forces from elevated blood pressure weaken this zone much in the way that high winds might lift the flap of a tent. Blood mixes with the lipid core and thrombosis is initiated.

Plaque which has ruptured is frequently found at postmortem examination to contain an infiltrate of inflammatory cells. These are principally macrophages but also T-lymphocytes and mast cells. Their presence suggests an inflammatory response to the tissue irritant effect of subendothelial LDL. Macrophages are rich in enzymes called metalloproteinases

that are highly proteolytic. While these enzymes are advantageous in the war against bacterial or viral intruders, in the setting of vulnerable plaque they attack and weaken the collagen and elastin that tether the fibrous cap to adjacent normal endothelium. Measurable thinning of the cap occurs and the likelihood of disruption is enhanced.

What can primary physicians do to mitigate this process? Interventions which reduce sheer forces on the coronary endothelium are highly attractive. Thus, beta-blockers and cessation of tobacco are known to be highly beneficial. Emotional trauma should be avoided. Regular cardiovascular exercise trains the



We must remember that plaque formation is now thought to be

Why Does Plaque Rupture? (continued)

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circulation so that the heart rate and blood pressure response to sudden exertion is blunted. All of these interventions reduce shear force at the shoulder of plaque.

A vegetarian diet has been shown to slow plaque buildup in approximately one-third of patients and to produce regression in a third. Low-fat, low cholesterol diets have a less certain basis.

Far and away the best data on plaque stabilization are found in the statin trials. Lovastatin, pravastatin, and simvastatin have all been shown to reduce clinical ischemic events early in the active arms of their respective trials. Data on pravastatin have shown a parallel reduction in highly sensitive CRP suggesting that statins in addition to their LDL modulating effects are anti-inflammatory. Thus coronary patients should receive statins even if serum LDL is not particularly elevated. Individuals at high risk of coronary events due to multiple cardiovascular risk factors should also be considered for statin therapy. Currently we believe the drug should be titrated to achieve an LDL < 100. Because statins slow LDL infiltration and are also apparently anti-inflammatory they represent a powerful double barreled shotgun in the war against plaque rupture and ischemic events.

Ramipril has been shown in the HOPE trial to reduce clinical ischemic events. ACE inhibitors are known to normalize the endothelial production of nitric oxide, a powerful endogenous vasodilator. This increases luminal diameter upstream and downstream from plaque and thus reduces shear forces.

Lastly, aspirin therapy inhibits platelet aggregation and may reduce the amount of thrombus which accumulates on disrupted plaque.

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Lawrence R. O'Connor, M.D.



Y. Joseph Wen, M.D.

Our next event is confirmed...

You're once again invited to our next "Seminar at Cinnabar".

Save the date:

Thursday, September 25, 2003 at 6:30 pm at Cinnabar Restaurant.

Invitations will be sent out in advance.

See you there.

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