On the Pathogenesis of Unstable Angina

Over the past 20 years, there has been great speculation as to the pathogenesis of unstable angina. Early investigators suggested that subtle increases in myocardial oxygen demand preceded episodes of rest pain. In the 1970s, coronary spasm was implicated as its cause. The emphasis, therefore, changed to a decrease in myocardial oxygen supply rather than an increase in oxygen demand as the mechanism of ischemia. More recently, thrombus formation has also been incriminated in the pathogenesis of unstable angina. While transient decreases in myocardial oxygen supply probably explain most episodes of rest pain in unstable angina, it is perplexing as to why an artery should suddenly develop spasm or a thrombus. Furthermore, existing angiographic studies have shown that the distribution and percentage of stenosis of coronary lesions in patients with unstable angina are not different from patients with stable angina. What, then, is the basic mechanism responsible for this acute syndrome?

Pathologic and angiographic studies have shown that eccentric and irregular plaques are common in the ischemia-producing artery in unstable angina and myocardial infarction. Careful pathologic sectioning of these lesions indicates that they exhibit plaque disruption with thrombus formation. Disruption of an atherosclerotic plaque occurs when a tear develops in the fibrous cap overlying the plaque. This exposes the flowing blood to the undersurface of the plaque which is a potent thrombogenic surface. Platelet deposition and the formation of a white thrombus leads to thrombin generation and a red thrombus. The etiology of plaque disruption is poorly understood, but it may be a chance event caused by the normal twisting and bending of coronary arteries during systole. Furthermore, disruption of the plaque with thrombus formation appears to be the common link in all the acute coronary syndromes of unstable angina, myocardial infarction and even sudden death.

Angiographically, we have demonstrated in between 64 and 71 percent of patients with unstable angina, as well as patients with Q wave infarction and non-Q wave infarction, that an eccentric narrowing with overhanging edges and/or irregular borders (type 2 eccentric lesion) is present in the ischemia-producing artery. These lesions usually arose de novo from arteries that previously appeared normal or only had mild luminal irregularities. We have postulated that the type 2 eccentric lesion represents plaque disruption with thrombus formation. Angioscopic data in patients with unstable angina have supported this hypothesis.

In this issue, Haft et al (see page 609) have corroborated our previous findings of a particular coronary lesion in unstable angina. This lesion, which they call a T-lesion, was present in over 70 percent of patients with unstable angina. The incidence of this same lesion in stable angina was much higher in their study than in our previous work, (47 vs 16 percent, respectively). While patient selection between these two studies was relatively similar, the observed differences may be related to other factors. We feel strongly that to correlate morphology with the presentation of angina pectoris, one must attempt to identify the coronary morphology of the ischemia-producing artery. This is the lesion in a particular artery felt to be responsible for the patient's syndrome. Electrocardiographic and ventriculographic data may be necessary to identify the ischemia-producing artery in patients with multivessel disease. In addition, these complicated lesions are also seen in the majority of patients with a history of myocardial infarction and a patent infarct-related artery. The absence of these clinical data in the article by Haft et al makes comparison to our prior study difficult. Nevertheless, their study adds further support to the existence of a specific coronary lesion in unstable angina that presumably represents plaque disruption with intraluminal thrombus.

The Link Between Anatomy and Myocardial Ischemia in Unstable Angina

The eccentric and irregular plaque is the most common lesion in ischemia-producing arteries in unstable angina. This lesion, which likely represents a disrupted plaque with superimposed thrombus, is the anatomic substrate in most of these patients with acute angina. How these lesions produce the ischemic syndrome of unstable angina is still not completely understood. Whether decreases in coronary supply are related either to active vasomotion (coronary spasm) caused by the release of platelet-derived substances such as thromboxane, platelet-derived growth factor, etc, from aggregated platelets at the site of plaque
disruption or evanescent platelet plugs or thrombus formation at the site of the disrupted lesion, small changes in the diameter of a severe stenosis can cause profound drops in pressure across the stenosis. This potentially can lead to transient bouts of rest ischemia. Further evidence implicating thrombus as a potential mechanism in unstable angina has been shown by three clinical randomized trials in which either aspirin or heparin were effective in reducing short-term complications of unstable angina.15-17

Cardiology today is in the midst of a technical revolution of lasers, angioplasty, positron-emission tomography, magnetic resonance imaging, etc. Careful evaluation of the "ancient" techniques of coronary angiography can yet provide new and important information.

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Airflow Obstruction in Sarcoidosis

In pulmonary sarcoidosis, much emphasis has been placed on the functional restrictive ventilatory defect evident in this condition. Little emphasis has been placed on airway dysfunction.

In reviewing the pathology of sarcoidosis,1 it is not surprising that functional airway obstruction may be prevalent. Non-caseating granulomata occur in a perivascular, peribronchial distribution and may also be present in the bronchial mucosa. Bronchi in sarcoidosis may be affected by four different mechanisms: 1) airways may be narrowed by extrinsic compression by enlarged lymph nodes; 2) endobronchial sarcoidosis may occur in bronchi of any size, which may result in narrowing, occlusion, bronchial wall destruction and bronchiectasis; 3) fibrotic scarring of endobronchial lesions with resultant narrowing of bronchi may occur, as well as bronchial distortion by peribronchial, hilar or perihilar fibrosis; 4) extension of the granulomatous process into the bronchial wall from an extrabronchial location may ensue. It is of interest that severe bronchial stenoses of a number of segmental bronchi associated with severe airflow obstruction have been described in a patient with sarcoidosis, in whom resolution of the stenoses and improvement of physiologic function following the use of steroid therapy was reported.2 This study contrasts with that of Olsson et al3 who described six patients with single or multiple segmental bronchostenoses who presented with dyspnea and/or wheezing and in whom a poor response to steroid therapy was noted.

A number of studies have evaluated airway function in patients with sarcoidosis.4-10 In a study by Levinson et al,4 abnormal airway function was detected in 18 patients with sarcoidosis, all of whom had restrictive lung disease. In all patients, abnormal airway function was documented by at least one test and usually by multiple tests which included airway conductance,