myocardial infarction patients in cardiogenic shock refractory to standard therapy, including aggressive acute revascularization. The patients were elderly (mean age, 71 ± 10 years) with a mean left ventricular ejection fraction (LVEF) of 23 ± 5%. Intravenous L-NMMA (1 mg/kg bolus plus 1 mg/kg/h infusion for 5 hours) resulted in a rapid and substantial increase in mean arterial pressure, accompanied by a marked increase in urinary output. Interestingly, there was a small but short-lived increase in pulmonary capillary wedge pressure and a small but short-lived decrease in cardiac output. The overall clinical results were quite striking, with 7 of 11 patients surviving the inhospital phase and reported to be alive 1 to 3 months after discharge, with a mean LVEF of 31 ± 4%. The 4 nonsurvivors died of multiorgan failure, sepsis, sepsis and hemorrhage, or cholesterol embolism syndrome within the first week following administration of L-NMMA. The authors suggest that excessive activation of neurohormonal mediators, including nitric oxide, may contribute to and perpetuate the hemodynamic vicious cycle in cardiogenic shock and that manipulation of the nitric oxide pathway may emerge as a novel treatment for severe hemodynamic depression accompanying cardiogenic shock.

Although the overall results appear to be very impressive in a very high-risk cohort, the study is limited somewhat by the small number of subjects. This provocative study demonstrates a favorable survival effect of a novel agent with selective vasoconstrictor effects devoid of any chronotropic or cardiac stimulant actions. Further evaluation of L-NMMA and possibly of other modulators of the nitric oxide pathway, in conjunction with acute reperfusion and other supportive interventions in cardiogenic shock, appear warranted.

Coming in

REVIEWS IN CARDIOVASCULAR MEDICINE™

Update on the Management of Unstable Angina

Infection

Linking *Chlamydia* and Heart Disease

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Information is increasingly available on the relationship between inflammation and atherosclerosis, particularly the development of vulnerable plaque, which is a key factor in acute ischemic syndromes, including acute infarction and unstable angina. Pathology studies have yielded substantial data on how this plaque develops. A central component is a lipid-rich core that may occupy 50% of the plaque volume. Vulnerable plaque, however, is not always easy to detect. It may not be assessed as severe even by coronary angiography. Intense efforts are under way to improve the detection process, using temperature sensors, electron beam CT, and MRI, among others.

Inflammation plays a central role. In pathology studies, plaque-causing acute ischemic syndromes are characterized by local inflammation that includes mast cells, T lymphocytes, and monocyte macrophages. These cells are, in part, responsible for production of cytokines and proteases, particularly specific-matrix metalloendopeptidases. These agents result in weakening of the fibrous cap over the lipid-rich core, with destruction of the matrix and disorganization of collagen. Such weakening is the hallmark of vulnerable plaque; when subjected to a triggering stress, such plaque can rupture, with thrombus formation, leading to unstable angina, acute infarction, or sudden death.

Given the central role of inflammation in the genesis of vulnerable plaque, there has been substantial interest in an infectious etiology. Early studies showed that atherosclerosis developed in an animal model of lymphomatosis. Since then, other models and human tissue studies have suggested a possible infectious etiology. Several agents have been evaluated; prominent among them are *Chlamydia pneumoniae, Chlamydia psittaci,* and *Chlamydia trachomatis*. The exact mechanism by which *Chlamydia* may cause cardiovascular disease remains unclear but may involve production of an endotoxin and heat shock protein as well as an autoimmune process.

Chlamydia Infections and Heart Disease Linked Through Antigenic Mimicry

Bachmaier K, Neu N, de la Maza LM, et al.
Science. 1999;283:1238-1239.

Bachmaier and colleagues evaluated the relationship between *Chlamydia* and heart disease in a murine model. They specifically looked at the relationship between a heart muscle–specific α myosin heavy-chain peptide that has sequence homology with the cysteine-rich outer membrane proteins of *C pneumoniae, C trachomatis,* and *C psittaci*. A series of experiments tested the possibility of antigenic mimicry between the *Chlamydia* peptides and the α myosin heavy-chain peptide. Of importance is the fact that the immunogenic amino acids of the α myosin heavy chain are conserved between murine and human species and that those of the latter, when injected into mice, induce inflammatory heart disease.

The central findings of this study were that injection of both the α myosin heavy-chain peptide and the homologous *Chlamydia* peptides into this murine model resulted in perivascular mononuclear inflammation, fibrosis, and cardiac vessel occlusion. Fibrinous occlusion of at least 1 cardiac vessel was seen in 60% of mice immunized with *Chlamydia* peptides and 67% of those immunized with the α myosin heavy-chain peptide. There was marked triggering of T- and B-cell reactivity. In addition, *Chlamydia* DNA functioned as an adjuvant in triggering the peptide-induced inflammatory heart disease. The conclusion was that, in this model, the heart disease mediated by *Chlamydia,* which is characterized by inflammation and vessel occlusion, is induced by antigenic mimicry with a heart-specific α myosin heavy-chain peptide.

What is the relevance of this to the human arena of vulnerable plaque and inflammation? There are epidemiologic data that *Chlamydia* is one of the potential infectious agents involved in atherosclerosis and complex coronary lesions, including vulnerable plaque. The results of this current study provide both in vivo and in vitro evidence of molecular mimicry between bacterial antigens and heart-specific proteins that can result in heart disease characterized by inflammation, fibrosis, and vessel occlusion. ■

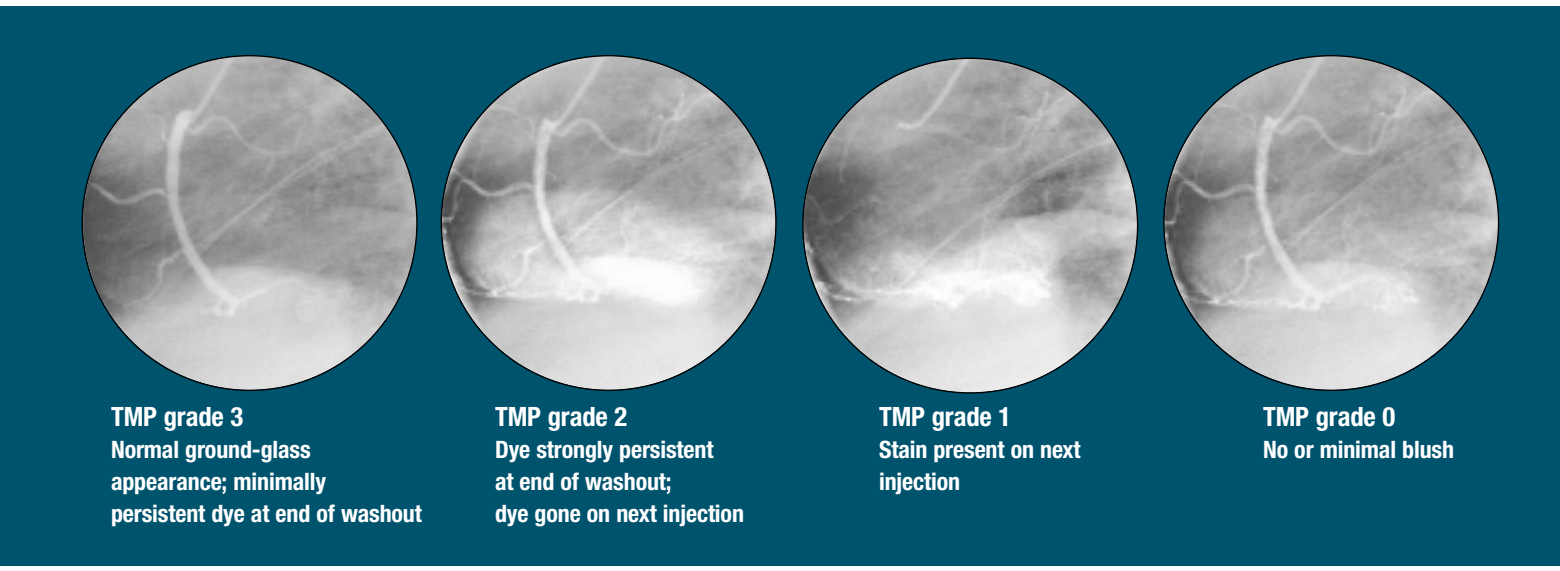

Figure 1. TIMI myocardial perfusion (TMP) grades. Diffuse myocardial blush characterizes TMP grade 3, giving a ground-glass appearance; at the end of the washout period, there is minimal or no dye. In TMP grade 2, dye enters the myocardium but accumulates and exits more slowly; dye in the myocardium strongly persists at the end of the washout phase. In TMP grade 1, dye stays in the myocardium; there is either a focal stain on the next injection or a diffuse glow of the myocardium. In TMP grade 0, dye does not enter the myocardium, and minimal or no blush is seen during the injection and washout phases. (TIMI, Thrombolysis in Myocardial Infarction.)

Figure 2. CS values and percentiles for 172 patients who underwent EBCT imaging following myocardial infarction. (CS, calcium score; EBCT, electron-beam CT.)