

a low-molecular-weight heparin, fare in comparison?

In this industry-supported study, investigators compared treatment with enoxaparin (throughout hospitalization) versus UFH (for >48 hours) in more than 20,000 patients with STEMI who were slated for thrombolysis. At 30 days, death or nonfatal recurrent MI had occurred significantly less often in the enoxaparin group than in the UFH group (9.9% vs. 12.0%). However, major bleeding was significantly more common in the enoxaparin group (2.1% vs. 1.4%). The combined safety-and-efficacy endpoint of death, nonfatal recurrent MI, and nonfatal intracranial hemorrhage occurred significantly less often in the enoxaparin group than in the UFH group (10.1% vs. 12.2%).

COMMENT:

Compared with UFH, enoxaparin throughout hospitalization was associated with better clinical outcomes. As an editorialist notes, because of the potential difference in duration of therapy, this study was not a true head-to-head comparison between the two agents. However, the results do provide good evidence that enoxaparin, given during incident hospitalization, is associated with fewer ischemic events, albeit at the cost of increased risk for bleeding.

— **Kirsten E. Fleischmann, MD, MPH**

Antman EM et al. Enoxaparin versus unfractionated heparin with fibrinolysis for ST-elevation myocardial infarction. N Engl J Med 2006 Apr 6; 354:1477-88.

Gibbons RJ and Fuster V. Therapy for acute coronary syndromes — New opportunities. N Engl J Med 2006 Apr 6; 354:1524-7.

Failure of One Type of Stem-Cell Therapy for Acute MI

Experiments in animals and humans have suggested that some types of stem cells can replace dead myocardial cells after acute myocardial infarction. Various types of adult stem cells — primarily hematopoietic stem cells — have been used, because they are so much easier to obtain than embryonic stem cells. In some procedures, they are injected into injured myocardium or infused through the coronary arteries.

In several small uncontrolled trials, researchers have reported encouraging results from a much simpler approach — infusions of granulocyte colony-stimulating factor (G-CSF). Such infu-

sions mobilize large numbers of hematopoietic stem cells, which then home to injured myocardial tissue. A German group has now conducted a randomized, controlled trial of this therapy in 114 patients with ST-segment-elevation acute MI who had undergone successful reperfusion within 12 hours. The researchers found no improvement in ventricular function or reduction of infarct size in the G-CSF group compared with the placebo group.

COMMENT:

Because many types of stem cells, and many ways to chemically treat and deliver stem cells, exist, the failure of this particular approach does not signal a death knell for all approaches to stem-cell therapy in acute MI. It does encourage skepticism toward encouraging results that are reported from small or uncontrolled studies.

— **Anthony L. Komaroff, MD**

Zobnibofor D et al. Stem cell mobilization by granulocyte colony-stimulating factor in patients with acute myocardial infarction: A randomized controlled trial. JAMA 2006 Mar 1; 295:1003-10.

Work Stress Linked with the Metabolic Syndrome

High stress has been associated with increased risk for coronary heart disease, but the mechanism for that association has remained elusive. This prospective cohort study from the U.K. provides one explanation.

Investigators evaluated 14-year follow-up data for 10,308 employed men and women (age range, 35-55) who were recruited from 1985 to 1988. During this time, self-reported work-related stress was measured on four occasions using standardized questionnaires. Presence of the metabolic syndrome, defined as presence of three or more risk factors (obesity, elevated triglyceride levels, reduced HDL cholesterol levels, hypertension, and elevated blood glucose levels), was assessed in 1999. A dose-response association was found between exposure to work stressors and metabolic syndrome. Men with chronic work stress (three or more stressors) were nearly twice as likely to develop the syndrome than were men with no exposure to work stress. Women with chronic work stress were five times more likely to develop the syndrome than were women with no work stress. Adjustment for age, employ-

ment grade, self-reported health behaviors, and obesity at baseline did not alter the association.

COMMENT:

This prospective study provides one possible mechanism by which exposure to chronic stress might increase risk for cardiovascular disease, based on the hypothesis that exposure to chronic stress can raise neuroendocrine activity that is associated with the metabolic syndrome. — **Keith I. Marton, MD**

Chandola T et al. Chronic stress at work and the metabolic syndrome: Prospective study. BMJ 2006 Mar 4; 332:521-4.

The full text of the original article is freely available at bmj.com

New Insights into Amyloid- β and Memory

Although the theory was controversial when we first reported it in *Journal Watch* (JW Nov 15 1990, p. 73, and *Science* 1990; 250:279), it is widely accepted now that the accumulation of amyloid- β (A β) protein is a cause of Alzheimer disease (AD). Yet, the correlation between A β concentration and memory deficits is inconsistent. For example, mice that have been genetically engineered to overproduce A β develop memory problems by about 6 months of age; these memory deficits plateau until about 15 months of age and then worsen. However, total accumulation of A β fibrils or plaques in mouse brains does not correlate very well with the extent of memory deficits.

Knowing that different size fragments of A β aggregate into clumps of different sizes, a multi-institutional U.S. team looked to see if fragments of any specific size might correlate closely with development of memory deficits. They found that a fragment called A β *56 did just that. Moreover, when that fragment (but not fragments of other sizes or saline control solutions) was injected into rat brains, the animals developed memory deficits.

COMMENT:

These findings support the hypothesis that A β plays a causal role in AD. More importantly, they identify a specific fragment of A β that is particularly vital in producing memory loss. Someday, this knowledge could lead to better early diagnosis of AD and to new prevention and treatment strategies.

— **Anthony L. Komaroff, MD**