**Depression–Heart Disease Link Probed**

Mike Mitka

**NEW ORLEANS**—People with cardiovascular disease are more likely to be clinically depressed and some seemingly healthy people with depression are at greater risk of developing heart problems. While scientists have yet to show that treating depression reduces cardiovascular mortality rates, evidence continues to mount that treating people with depression does improve their dysphoria and quality of life and may increase longevity (Glassman et al. JAMA. 2002;288:701-709; Musselman et al. Arch Gen Psychiatry. 1998;55:580-592).

Investigators are uncovering the ways depression is related to a variety of cardiovascular complications, opening new avenues for future treatment success. As research presented in November at the Scientific Sessions of the American Heart Association revealed, scientists are documenting the link among depression, infection, and immunity after coronary artery bypass grafting (CABG) and how treating major depression in such patients can prevent a decline in immunity and an increase in infection. They are also uncovering specific aspects of cardiovascular disease affected by depression and other psychological conditions. In addition, with the growing acknowledgment of the mental health–cardiovascular disease link, researchers are documenting defined patient populations at greater risk for depression and those whose psychological conditions are being missed by treating physicians.

**DEPRESSION AND IMMUNITY**

Lynn V. Doering, RN, DNSc, associate professor and chair of the acute care section at the University of California, Los Angeles, School of Nursing, said a pilot study of 52 women recovering from CABG found that major depression was associated with reduced natural killer cell levels and increased infectious illness.

**ATRIAL FIBRILLATION**

Also presented was a study on a link between depression, hostility, and overall psychological distress and an increased risk of developing atrial fibrillation. Charles M. Blatt, MD, an assistant professor of medicine at Harvard Medical School in Boston and director of research at Lown Cardiovascular Research Foundation in Brookline, Mass, and colleagues assessed depression, anxiety, hostility, and somatization in 354 men and 95 women (age range, 40 to 88 years) and followed them for 5 to 7 years.

The researchers found that patients scoring in a higher quartile for any of the measured psychological conditions were at greater risk of developing atrial fibrillation than those grouped in lower quartiles. Those in a higher quartile for anxiety and total psychological distress were more than twice as likely as those in a lower quartile to develop the condition. And patients scoring in a higher quartile for depression were 70%; hostility 60%; and somatization 50% more likely than those in a lower quartile to develop atrial fibrillation.

“The findings show that there’s something about patients with psychological stress developing atrial fibrillation—implicating either a common mechanism or shared mechanism on how the brain influences the heart,” said Blatt in an interview. “Physicians should be aware that depressed, anxious, or hostile patients who complain of palpitations may have a higher risk of having atrial fibrillation as the source of their palpitations.”

**FACTORS OF AGE, SEX, AND RACE**

Other studies presented at the meeting probed effects of sex, race, and age in the development of depression among patients with cardiovascular complications.

Prevalence of depression in patients who experienced a myocardial infarction was found to be more common in women than in men, especially in younger women, according to a study by Susmita Mallik, MD, an assistant professor at Emory University School of Medicine in Atlanta and colleagues. The study of 2219 patients, 712 of whom...
were women, found that 41% of women younger than 60 years had depression compared with 21% of women aged 60 years and older. In men, 21% of those younger than 60 years and 16% aged 60 years and older were depressed.

“We found that a significant proportion of patients are depressed after myocardial infarction,” said Mallik at a press briefing. “Thus, physicians should screen these patients for depression and they should be aware that younger women are a high-risk group [for depression] and especially should be screened.”

Another study found that physicians are less likely to recognize or treat depression in black patients hospitalized with acute coronary syndrome. Investigators led by Alpesh A. Amin, MD, a research fellow at St Luke’s Hospital Center for Innovation and Research, University of Missouri–Kansas City, interviewed 1181 hospitalized acute coronary syndrome patients, 194 of whom were black, and found 14.9% of whites and 29.9% of blacks had moderate to severe depressive symptoms. Of patients with moderate to severe depressive symptoms, only 10.3% of blacks were recognized by physicians as having these symptoms, compared with 31.2% of whites, despite the fact that rate of depression among black patients was twice that of white patients. Black patients also were less likely to be treated for their depression: 28.5% of white patients with moderate to severe depressive symptoms received antidepressant medications compared with only 3.6% of black patients with similar symptoms.

**Down Syndrome Protein Deters Cancer**

Scientists Reveal Molecular Mechanism

Tracy Hampton, PhD

Although the detrimental effects of Down syndrome such as mental retardation and congenital heart defects are well known to clinicians, less familiar are apparent benefits seen in many patients with the condition, such as decreased incidences of diabetic retinopathies, atherosomas, and some cancers (particularly solid tumors)—conditions linked to angiogenesis. Now, a new study offers a promising theory to explain this phenomenon and perhaps point the way to new antiangiogenic therapies (Minami et al. *J Biol Chem*. 2004;279:50537-50554).

It turns out that overexpression of a protein encoded by a gene found on chromosome 21 blocks the formation of new blood vessels and reduces tumor growth. (Three copies of chromosome 21 are present in cells of patients with Down syndrome rather than the normal chromosomal complement of two copies.) While the investigators did not set out to study this gene (called Down syndrome critical region 1, or DSCR-1) when they designed their experiments, the discovery piqued their interest.

Part of the reason we were quite excited by this finding is because it does add some mechanistic insight into why patients with Down syndrome have a reduced incidence of solid tumors. The biological plausibility is there, but it has yet to be proven,” said principal investigator William Aird, MD, chief of the Division of Molecular and Vascular Medicine at Beth Israel Deaconess Medical Center, in Boston.

Aird and colleagues in Boston and Tokyo stumbled upon their findings while they were looking for changes in gene expression following exposure of endothelial cells to vascular endothelial growth factor (VEGF) and thrombin. They were using DNA microarrays to look for different and common effects of the two molecules. “We had no idea we were going to pick up DSCR-1, but it popped out” as the gene that was most active after exposure to either VEGF or thrombin, said Aird.

Aird has been studying endothelial cells over the years because the cells are often dysfunctional in conditions with vascular components, including cancer, atherosclerosis, and inflammation. Because of his recent findings, Aird now plans to look at endothelial cells from individuals with Down syndrome. “There are endothelial cells from Down syndrome patients that we have that we’re propagating. We’re going to look to see whether DSCR-1 is overexpressed and to how it affects the cells.”

Mice injected with melanoma cells and induced to express the DSCR-1 gene develop smaller tumors with reduced blood vessel density compared with control mice. The finding may help explain the reduced risk of some cancers in people with Down syndrome, who have an extra copy of DSCR-1 (Image from *J Biol Chem*. 2004;279:50537-50554).