

# New Agents, Methods May Change Heart Imaging

BY MITCHEL L. ZOLER  
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NEW YORK — New agents and imaging methods will change the way that hearts are scanned in coming years, researchers said at the annual meeting of the American Society of Nuclear Cardiology.

## Myocardial Hyperemia Drugs

Adenosine and dipyridamole are the current mainstays of pharmacologic stress during nuclear imaging, but both agents cause many adverse events, including atrioventricular block in up to 8% of patients and bronchospasm in a small but significant fraction. Bothersome adverse effects such as flushing, chest pain, and dyspnea occur in 50%-80% of patients, said Robert C. Hendel, M.D., Rush University Medical Center in Chicago.

These features sparked an interest in developing more specific agonists for the A<sub>2A</sub> receptor that is responsible for coronary vasodilation. These agents have a reduced affinity for the A<sub>1</sub>, A<sub>2B</sub>, and A<sub>3</sub> receptors that are the source of the adverse effects caused by adenosine and dipyridamole. Two new drugs are now in phase III trials: binodenoson, developed by King Pharmaceuticals Inc., and regadenoson, developed by CV Therapeutics Inc. A third agent, BMS068645, developed by Bristol-Myers Squibb Co., is in phase II clinical studies.

Results from a phase II study with binodenoson that involved 203 patients showed that the new drug had "very good concordance with adenosine" for myocardial perfusion but with a "clear decrease in the overall adverse event profile," Dr. Hendel said. In this study, adenosine triggered a 92% rate of adverse effects, compared with a 33%-80% rate among patients treated with binodenoson, depending on the dosage. At a dosage of 1.5 mcg/kg, the

dosage being used in phase III studies, binodenoson produced no atrioventricular block and a "minimal" incidence of tachycardia in this small study, he said.

Regadenoson was tested in a crossover study with 36 patients, where it showed about an 85% concordance with the effect of adenosine on myocardial ischemia. A dosage of 400 mcg produced a 61% rate of adverse effects, compared with an 83% rate when adenosine was used.

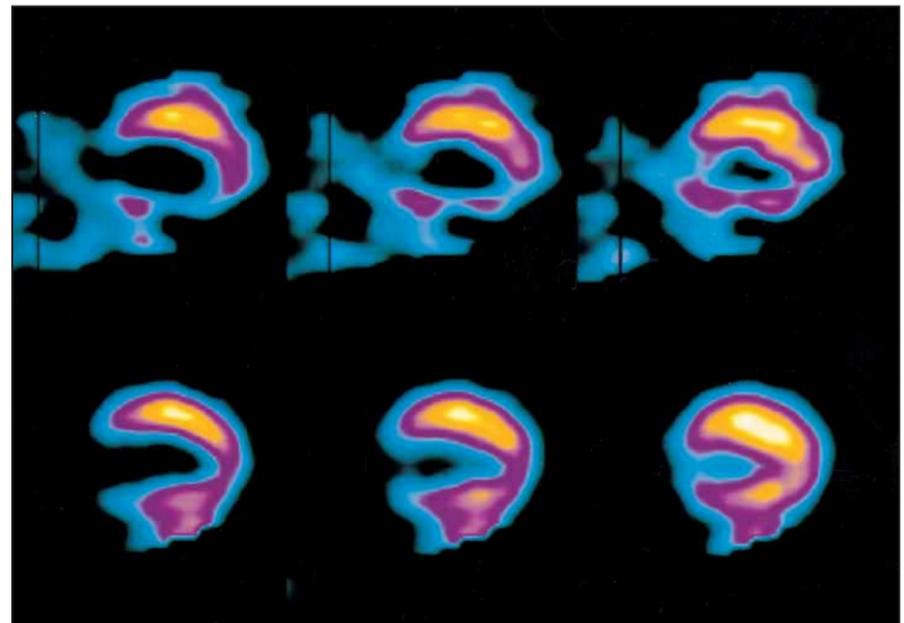
It's too early to say anything about the relative safety and efficacy of these new drugs, compared with each other, Dr. Hendel added.

## Ischemic Memory

A radionuclide that's just entering clinical testing in the United States has the potential to open a new avenue of cardiac imaging by tagging regions of the myocardium that were ischemic hours earlier. Known as BMIPP, this radioiodine tracer is a fatty acid analogue that takes advantage of the disturbed fatty acid metabolism that persists in tissues for a relatively prolonged period following ischemia, said James E. Udelson, M.D., director of the nuclear cardiology laboratory at Tufts-New England Medical Center in Boston. BMIPP has been used for several years in Japan.

The results from initial clinical studies in the United States have confirmed that BMIPP can selectively tag myocardium that has had ischemic stress more than 24 hours previously. "This agent may extend the time window for imaging ischemia beyond what we can do with a perfusion image," he said.

One especially attractive prospect is to use BMIPP simultaneously with a standard radionuclide marker of myocardial perfusion such as thallium-201 or technetium-99m sestamibi. This would allow physicians to get information on both metabolic



The bottom images show vertical long-axis views of a patient's heart labeled with <sup>99m</sup>Tc-sestamibi, at rest, showing that coronary perfusion and viability were preserved in this region. The top images are from the same view of the heart, taken simultaneously with <sup>123I</sup>-MIBG. The low uptake of <sup>123I</sup>-MIBG on the inferior wall, in a region with good perfusion and viability, indicates sympathetic denervation.

COURTESY DR. MARK TRAVIN

ischemia and resting perfusion "in one spin of the camera," Dr. Udelson said.

## Neuronal Imaging

Imaging the heart using a nuclear-tagged norepinephrine analogue, metaiodobenzylguanidine (MIBG), allows researchers to assess myocardial innervation and the abnormal denervation that's associated with pathology (see above). Pilot studies show that MIBG imaging can give new insights into both primary and secondary cardiomyopathies, said Mark I. Travin, M.D., a cardiologist at Montefiore Medical Center in New York. Cardiac imaging with MIBG can identify dysautonomias and may allow early detection and definitive diagnosis of Parkinson's disease. MIBG abnor-

malities also occur in patients with idiopathic ventricular tachycardia and fibrillation. MIBG imaging may be a way to identify patients who are at high risk for sudden cardiac death and are the best candidates for receiving an implantable cardioverter defibrillator. MIBG imaging can also follow the progress of cardiac transplants.

The most important potential use for MIBG may be to assess coronary artery disease and heart failure. Neuronal imaging may detect the early stages of coronary disease before it becomes clinically apparent, Dr. Travin said. Patients with congestive heart failure usually have MIBG-uptake abnormalities. This imaging may help guide therapy and provide a new way to assess efficacy. ■

## Prevalence of Valvular Heart Disease in the Elderly May Top 10%

BY MITCHEL L. ZOLER  
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NEW ORLEANS — Almost 12% of Americans aged 75 years or older have valvular heart disease, according to echocardiographic findings from an unselected population of 1,745 people.

The prevalence of valvular heart disease was also high (7.8%) in an unselected group of 3,879 Americans aged 65-74 years, Vuyisile T. Nkomo, M.D., reported in a poster at the annual scientific sessions of the American Heart Association.

This high prevalence of valvular heart disease in the elderly, many of whom were probably asymptomatic, suggests that physicians need to assess elderly patients carefully for valvular disease by their history and physical examination, said Dr. Nkomo, a cardiologist at the Mayo Clinic in Rochester, Minn. An echocardiogram, the definitive way to identify valvular heart disease, should be obtained for people who are suspected to have clinically significant valvular disease.

"Routine screening by echocardiography of all asymptomatic elderly people may be prohibitively expensive," he told this newspaper. "This may be where handheld echocardiography devices may be useful, if they come to be used as an ex-

pression of the physical examination.

"Waiting for symptoms to appear before making a diagnosis of valvular heart disease—or suspecting valvular disease but waiting for symptoms before getting an echocardiogram—may be waiting too long," Dr. Nkomo added. That's because of the excess risk for people who become symptomatic, compared with those who are still asymptomatic when their valvular disease is first diagnosed.

If an asymptomatic person is found to have, for example, moderately severe mitral regurgitation, then an

annual echocardiogram should be done to monitor whether the severity is progressing and intervention is needed, he said.

To examine the prevalence of valvular heart disease in the general population, Dr. Nkomo and his associates sorted through echocardiographic data collected on 11,911 people in three large, population-based studies that were sponsored by the National Heart, Lung, and Blood Institute. Data came from the Coronary Artery Risk Development in Young Adults (CARDIA) study, the Atherosclerosis Risk in Communities (ARIC) study, and the Cardiovascular Health Study (CHS). The echocardiograms were done between 1989 and 1996 in men and women who were at least 18 years old.

A total of 555 people had valvular heart disease that was of at least moderate severity, representing an overall, age- and gender-adjusted rate of 2.3%. But there was a striking link between age and the prevalence of valve disease: The rate was lowest in people under 45 years old, with a prevalence of 0.7%, and in those aged 45-54 years old, with a prevalence of 0.4%. The rate rose sharply among the next three age strata. The prevalence of valvular disease among people aged 55-64 years was 1.9%. The prevalence of all valvular diseases seen was roughly the same between men and women. ■

