

From the NIH

No increased survival with bucindolol in patients with advanced chronic heart failure

Results of a study, in contrast with results of other studies of β -adrenergic-receptor antagonists, indicate that the β -blocker bucindolol hydrochloride did not significantly increase survival for patients with moderate to severe heart failure, according to a team of scientists funded by the National Heart, Lung, and Blood Institute, National Institutes of Health. Further, results indicate differences in race-specific responses to the drug, with African American patients with heart failure having a nonsignificant benefit, while non-African American patients who received the drug lived longer. There was a trend toward longer survival for bucindolol-treated participants who had less advanced heart failure.

Findings from the study that are consistent with findings of other β -blocker studies include fewer deaths from cardiovascular disease, fewer hospitalizations for heart failure, and fewer deaths and heart transplants for patients who received bucindolol, compared with placebo.

The study involved 2708 participants (average age, 60 years), 22% of whom were women and 30% of whom were from minority groups. Of these, 92% had moderately severe heart failure (New York Heart Association [NYHA] functional class III) and 8% had severe heart failure (NYHA class IV). Patients were assigned at random to receive either bucindolol or a placebo in addition to standard therapy for heart failure. A 2-year follow-up of participants indicated that 33% of the patients who received placebo and 30% of the patients who received bucindolol died.

The report of this study appears in the May 31, 2001, issue of the *New England Journal of Medicine*.

Long-acting β -agonists not as effective as inhaled corticosteroids for patients with asthma

Long-acting β -agonists (LABs) are not as effective for treating patients with asthma as inhaled corticosteroids (ICS), and the use of LABs as a supplement to ICS enables substantial reductions in steroid doses, according to a team of investigators of the Asthma Clinical Research Network of the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health. Two studies were initiated to address whether LABs should replace or supplement ICS in the treatment of adults with mild to moderate persistent asthma. Guidelines issued by the NHLBI for management of asthma recommend daily use of anti-inflammatory medications such as ICS and the addition of a LAB if low to moderate doses of ICS fail to reduce asthma symptoms.

Both studies included a 6-week phase in which all patients were treated with moderate doses of ICS. Of this group, 164 patients whose asthma was well controlled with ICS were entered into the Salmeterol or Corticosteroid (SOCS) study, while 175 patients whose asthma was not well controlled with ICS were entered into the Salmeterol $\pm$ Corticosteroid (SLIC) study.

Results of the SOCS study indicate that patients who received LAB alone had increased airway inflammation, four times more treatment failures, and three times more exacerbations than patients who continued treatment with the ICS alone or switched to a placebo. Results of the SLIC study indicate that patients who received the addition of a LAB to treatment with ICS were able to effect a 50% reduction in ICS dose without significant loss of asthma control. Finally, although LABs alone were highly effective in improving asthma symptoms and rescue medicine use, they were not effective in preventing asthma attacks or treatment failures.

The full report of study findings appears in the May 23/30, 2001 issue of *JAMA*.

Diet for hypertension also lowers cholesterol levels

The Dietary Approaches to Stop Hypertension (DASH) diet significantly lowers total cholesterol and low-density-lipoprotein cholesterol levels (LDL-C), according to researchers funded by the National Heart, Lung, and Blood Institute, National Institutes of Health.

A total of 459 participants were randomly assigned to groups using a diet enriched with fruits and vegetables, the DASH eating plan, or a control diet. Unlike the diet enriched with fruits and vegetables, the DASH diet—also rich in fruits and vegetables—is low in saturated fat, total fat, and cholesterol.

Participants on the DASH diet reduced total cholesterol levels by 7.3% and levels of LDL-C by 9%, compared with those on the control diet, which was designed to reflect American eating habits. In addition, participants on the DASH diet had an average decrease of 7.5% in the level of high-density-lipoprotein cholesterol (HDL-C)—a lipid considered protective of heart disease. Researchers suggest further study of this undesirable response to the DASH diet.

The size of the trial allowed researchers to observe how race and gender affect response to the DASH diet. Researchers note that although changes in HDL-C and triglyceride levels between men and women were similar, total and LDL-C levels fell significantly more in men than in women.

The study is reported in the July 2001 issue of the *American Journal of Clinical Nutrition*.

New tool facilitates early prediction of stroke outcome

A new tool that uses three factors for predicting degree of recovery for stroke patients

during the first several hours of hospitalization was developed by scientists at the National Institute of Neurological Disorders and Stroke, National Institutes of Health (NIH). The three factors are measurement of brain injury using magnetic resonance imaging (MRI), the patient's score on the NIH Stroke Scale, and the time from onset of symptoms to the MRI brain scan.

The study, published in the June 30, 2001 issue of *Lancet*, involved analysis of data for 129 stroke patients at two study locations and development of the tool for prediction of recovery.

The new tool proved to have high sensitivity and specificity in both study groups, with a small percentage of patients with low scores who recovered (6% and 8%, respectively) and a high percentage of patients with high scores who recovered (93% and 78%, respectively).

Scientists used a new type of brain imaging technology, magnetic resonance diffusion-weighted imaging, to measure the volume of the lesions that appear in the first hours after an ischemic stroke.

Study results indicate a correlation between this measurement and severity of stroke and outcome, with patients with a lesion volume of less than 14.1 mL five times more likely to recover, compared with patients with larger-volume lesions.

The second factor, the NIH Stroke Scale, was measured within 1 hour of the MRI scan. The mean score of patients in this study indicated mild to moderately severe impairment.

The third factor was time from onset of symptoms to time of brain scan. Scientists note that patients who had scans later were more likely to recover than patients who had scans earlier, possibly indicating instability in the earliest hours of stroke.

Of the three factors included in the new tool, researchers conclude that the combination of clinical and imaging data allows more reliable early prediction of stroke than any other single factor.

Heart muscle cells regenerate after heart attack

Large-scale replication of heart muscle cells was found in two regions of the hearts of patients who had heart attacks, according to scientists funded by the National Heart, Lung, and Blood Institute, National Insti-

tutes of Health. This finding challenges the long-held view that heart muscle cells do not regenerate after heart attack and clarifies the heart's mechanism of repair.

The study, reported in the June 7 issue of the *New England Journal of Medicine*, involved measuring a protein that is a strong indicator of cell division in the hearts of 13 patients within days of having a heart attack and in 10 patients who did not have cardiovascular disease. Samples of myocytes were taken from the site near the heart attack and from a more distant site. The number of myocytes multiplying in diseased hearts was 70 times higher at the heart attack site and 24 times higher in the remote site compared with that in healthy hearts.

Investigators note the need for research to determine if dividing myocytes are a subpopulation of known cells that retain their capacity to divide, or if myocytes originate from stem cells in the heart.

Launch of AIDS history Web site

To commemorate the 20-year anniversary of their first publication about the acquired immunodeficiency syndrome (AIDS), the National Institutes of Health announced the launch of a Web site titled "In Their Own Words: NIH Researchers Recall the Early Years of AIDS," which is available at <http://aidshistory.nih.gov>.

The site features interviews with physicians, scientists, nurses, and administrators involved in AIDS research at the NIH. The AIDS history project was begun in 1988 and documents how the NIH responded during the early years of the disease.

New test for Lyme disease

A new diagnostic test for Lyme disease that is sensitive to antibodies from both early and late stages has been developed in a collaborative effort with funding from the National Institute of Allergy and Infectious Diseases, National Institutes of Health.

The diagnostic test, developed by Immunetics, Inc, of Cambridge, Mass, uses a synthetic product based on components from the bacterium that causes Lyme disease and is effective at detecting Lyme disease in early stages and especially in later stages when antibodies fall to low levels. Further, the test produces no false-positive readings

for people who received the Lyme disease vaccine and fewer false-positive readings generally, compared with current methods of testing.

From the CDC

Intensive antibiotic treatment does not improve symptoms of chronic Lyme disease

Results of two trials funded by the National Institute of Allergy and Infectious Diseases indicate that a 90-day course of intravenous and oral antibiotics was no better at improving levels of significant pain and disabling symptoms in patients with chronic Lyme disease than placebo.

In the two identical studies, 129 participants with chronic symptoms of Lyme disease who had received one course of antibiotics were randomly assigned to receive further antibiotic treatment—either intravenous ceftriaxone sodium (2 g/d) for 30 days followed by oral doxycycline (200 mg/d) for 60 days—or placebo. Symptom improvement was based on patients' responses to a questionnaire given 90 days after completion of antibiotic treatment or placebo.

On the recommendation of a Data and Safety Monitoring Board, both trials were halted because there was no current or projected significant difference in the percentage of patients who received antibiotic treatment or placebo who thought that their symptoms had improved.

One trial involved 78 patients with chronic Lyme disease who tested positive for antibodies to the Lyme bacterium, while the other trial had 51 patients with chronic symptoms of Lyme disease but no antibodies. It is significant that none of 700 blood and cerebrospinal fluid samples from participants showed evidence of persistent infection with the Lyme disease agent, *Borrelia burgdorferi*.

Information from the studies indicates that the impact of Lyme disease on physical health is equal to the disability of patients with congestive heart failure or osteoarthritis.

Further information is available at www.niaid.nih.gov and in the July 12 issue of the *New England Journal of Medicine*. ♦