Controversial Warning for Heart Drug

Two new studies of nifedipine, a drug commonly prescribed for high blood pressure and heart disease, have generated fierce controversy over the safety of calcium-channel blockers, the class of compounds to which nifedipine belongs. In response, the National Heart, Lung, and Blood Institute (NHLBI) in Bethesda, Md., last week issued a warning that one version of nifedipine be used "with great caution (if at all)."

In the September CIRCULATION, researchers describe their reanalysis of pooled data from 16 previous studies in which physicians administered either a short-acting form of nifedipine, which must be taken three or four times daily, or a placebo to 8,350 people with heart disease. The scientists conclude that high doses—80 milligrams a day or more—of the short-acting drug increase a patient's risk of death.

This kind of review, known as metanalysis, offers investigators great statistical power in reaching conclusions but remains controversial. One major reason is that it often combines studies that have very different designs.

The metanalysis comes on the heels of a report in the Aug. 23/30 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION (JAMA) analyzing the medical records of people treated for high blood pressure. Investigators compared the treatment of those who had had heart attacks to those who had not. They concluded that patients taking short-acting nifedipine had a greater risk of heart attack than those taking diuretics or beta-blockers, two other common classes of hypertension drugs.

"What really troubles me is the consistency of the findings," says Curt D. Furberg of Wake Forest University's Bowman Gray School of Medicine in Winston-Salem, N.C., an author of both studies. These results, Furberg adds, make him question the safety of all calcium-channel blockers, particularly the newer, long-acting forms of nifedipine, which are taken once a day and are now more commonly prescribed than the older, short-acting versions.

"Since we have treatment alternatives, use those drugs," advises Furberg.

Patients often have trouble tolerating beta-blockers and diuretics, however. Among other side effects, the drugs can make them tired or impotent.

The JAMA and CIRCULATION studies have drawn both praise and harsh criticism, the latter coming in particular from Pfizer and Bayer, two companies that make nifedipine. Pfizer labeled the metanalysis a "flawed rehash of old data" and distributed comments from cardiologists denouncing the research.

In addition, three commentaries in CIRCULATION and one in JAMA offered sometimes conflicting opinions on the studies' quality and on the proper use of calcium-channel blockers.

The NHLBI, though endorsing Furberg's concerns about short-acting nifedipine, avoided extending its warning to all calcium-channel blockers, including the long-acting forms of nifedipine. A panel reviewing the relevant research concluded that it was "unclear" whether the concern over short-acting nifedipine could be generalized.

"We're leaning on the side that they're OK to use until proven dangerous," says panel member Michael J. Horan, director of NHLBI's division of heart and vascular diseases. Studies in progress may resolve the issue, but not for many years, he adds.

Raymond L. Woosley, a pharmacologist at Georgetown University Medical Center in Washington, D.C., notes that many calcium-channel blockers are pharmacologically distinct, making it difficult to extrapolate the dangers of one to another. For example, short-acting nifedipine raises heart rate, whereas the long-acting version lowers it. "The rate at which you give a drug is as important as the drug you give," Woosley explains.

"There are so many alternatives, including long-acting nifedipine. Talk to your physician," counsels Horan. —*J. Travis*

Quest for condensate turns up another find

Not long after one group set the theme, another composed a variation.

In July, researchers in Colorado reported having observed the elusive state of matter known as the Bose-Einstein condensate in the form of a cloud of rubidium-87 atoms chilled to near absolute zero (SN: 7/15/95, p.36). Now, Randall G. Hulet and colleagues at Rice University in Houston report in the Aug. 28 PHYSICAL REVIEW LETTERS that they've done the same with lithium-7, an element theorists previously thought would not undergo this condensation.

Other researchers, however, are reserving judgment until they see additional proof.

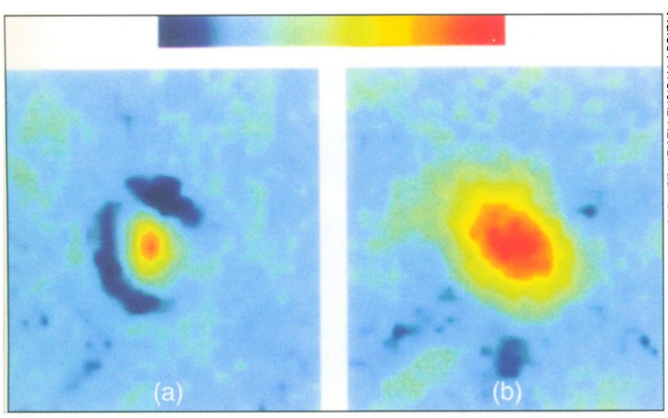
Their skepticism originates from the more indirect nature of the Rice group's evidence, says William Phillips of the National Institute of Standards and Technology in Gaithersburg, Md. After creating physical conditions that would encourage the lithium atoms to form a Bose-Einstein condensate, the researchers shone a laser beam at the cold atom cloud and saw an unusual halo appear. They attributed the halo to light diffracted by the dense condensate.

But since no one fully understands yet how the condensate interacts with light, the pattern could be caused by something else, Phillips suggests.

Hulet agrees. "Unfortunately, our measurement isn't as direct as the Colorado group's," he says. Those researchers measured the velocity of the rubidium atoms as the cloud expanded and saw a clear peak at zero.

The Rice researchers can't take velocity measurements because of their experimental setup. The magnetic trap they used to confine the atoms has permanent magnets instead of adjustable electromagnets. This turned out to be both an advantage and a disadvantage, Hulet explains. The trap held the atoms like a "magnetic bowl," but the field couldn't be turned off to let the atom cloud expand.

Though they find the existing evidence "significant and compelling," Hulet and his colleagues plan to do microwave spectroscopy on the atom cloud to get a more direct, highly resolved image of the condensate. They also want to get a more accurate count of the number of atoms in the condensate, since many more seem to be there than the theory predicts. —*C. Wu*



Hulet/PHYSICAL REVIEW LETTERS

Colorized images show the condensate's absorption of laser light at 590 nanokelvins (a) and at 100 nanokelvins (b). Diffracted light produces the blue halo around the condensate.

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