

Blood enzyme foretells heart attack threat

Elevated blood levels of a kidney-secreted enzyme may prove a potent predictor of heart attack risk among people with moderate hypertension, according to a new epidemiologic study. If further research confirms that finding, blood tests for the enzyme should help identify hypertensive people especially vulnerable to heart attack.

Years of high blood pressure can damage the heart and blood vessels. Some people with hypertension fall victim to a heart attack, while others escape that fate. Nearly 20 years ago, a retrospective study of hypertensive patients linked heart attack risk to the enzyme renin, but subsequent studies of similar patients showed no such association.

A research team in New York City has now reopened the case, adding significant weight to the renin/heart attack theory.

Renin "provides a powerful tool to identify [mild hypertensives] who are most likely to have a heart attack," says study coauthor Michael H. Alderman of the Albert Einstein College of Medicine. In the previous studies, investigators may have had trouble measuring the enzyme, he suggests.

Alderman and John H. Laragh of the Cornell University Medical College led a study of 1,717 men and women in New York City who belonged to various worker unions. All volunteers had a systolic (heart-pumping) blood pressure of at least 160 millimeters of mercury (mm Hg) and a diastolic (heart-resting) pressure of at least 95 mm Hg. (Hypertension is defined as systolic pressure of at least 140 and diastolic pressure of at least 90.) The researchers measured blood renin at the study's start, detecting high levels in 12 percent of the volunteers. All participants received antihypertensive drugs for the next eight years.

At the end of the study period, the researchers discovered a fivefold greater incidence of heart attack in the high-renin subgroup compared with the rest of the sample. And among volunteers who had no other known cardiovascular risk factors — such as smoking, diabetes or elevated blood cholesterol — those with high renin levels were seven times more likely to suffer a heart attack than were those with low to normal renin, the team reports in the April 18 *NEW ENGLAND JOURNAL OF MEDICINE*. Indeed, these data revealed an unexpected benefit of low renin levels: Hypertensives who had no other heart risk factors remained free of heart attacks throughout the eight-year study.

Laragh suspects a link between renin and cardiac risk not just among hypertensives but in the population at large. "I wouldn't want to have high renin, having seen what I've seen here," he says.

Laragh points out that renin converts a blood protein to angiotensin II, which helps regulate blood pressure by constricting the vessels, including the coronary arteries. He suggests that too much angiotensin may trigger ischemia, or reduced blood flow to the heart, which can lead to a heart attack.

The new findings hint that high-renin hypertensives may benefit from drug therapy to lower their blood levels of renin or angiotensin II, notes Victor J. Dzau of Stanford University School of Medicine, who wrote an editorial accompanying the research report. Such drugs include beta blockers and angiotensin-

converting-enzyme (ACE) inhibitors.

On the other hand, renin may prove merely a marker — rather than the cause — of heightened heart risk, warns Michael Horan, a cardiologist at the National Heart, Lung and Blood Institute in Bethesda, Md. "Right now, it would be too soon to say we ought to be changing our drug therapy of hypertensive patients," Horan says.

Alderman and Laragh add that beta blocker drugs did not appear to lower the risk of heart attack in their study. To establish whether beta blockers or ACE inhibitors can offer hypertensives any protection against heart attack, researchers need to conduct trials specifically designed to compare different drug regimens, they say. — *K.A. Fackelmann*

Toward laser control of chemical reactions

Chemists usually rely on relatively crude methods — such as adjusting the temperature or the concentrations of ingredients — to obtain the products they want. Now, researchers have demonstrated a much more subtle and direct means of controlling a chemical process. They use a pair of laser beams to alter the ionization rate of hydrogen chloride molecules in a predictable way, in effect telling individual molecules exactly what to do.

"What we're doing is so subtle that unless you look for it, you would never see it," says team leader Robert J. Gordon, a chemist with the University of Illinois at Chicago. The researchers manipulate the ionization rate simply by varying the phase relationship between two laser beams — in other words, by shifting the relative positions of the crests and troughs in two light waves.

This important step brings scientists closer to the long-standing goal of directly controlling the yield and distribution of products in a given chemical reaction. Gordon and his co-workers describe their work in a paper scheduled for the June 1 *JOURNAL OF CHEMICAL PHYSICS*.

The researchers apply a strategy first proposed by theorists Paul Brumer of the University of Toronto in Ontario and Moshe Shapiro of the Weizmann Institute of Science in Rehovot, Israel. The idea is to offer two alternative pathways for exciting a hydrogen chloride molecule to a specific energy level. One path involves excitation of the molecule by a single 112-nanometer photon of ultraviolet light. The alternative route requires three 336-nanometer photons to achieve the same result. In the final step, an excited molecule absorbs an additional 336-nanometer photon, which forces the ejection of an electron to produce ionized hydrogen chloride.

The Illinois team first generates two laser beams — one having exactly three times the wavelength of the other. "The

crucial thing is that because the 112-nanometer beam is manufactured from the 336-nanometer beam, there's a fixed, definite phase relationship between the two beams," Gordon says. "If we just took two lasers off the shelf and fired them, there would be absolutely no relation between the phases of the two beams."

The two beams travel together, passing through a chamber containing hydrogen or argon gas. By changing the gas pressure, the researchers can delay one laser beam relative to the other, altering the phase relationship between the two beams in a predictable, reproducible way.

When they focus the beams on a stream of hydrogen chloride molecules, they find that the rate at which the molecules become ionized depends on the phase relationship between the laser beams. According to quantum mechanics, this effect results from constructive and destructive interference between the two different ways of exciting hydrogen chloride molecules.

This method contrasts with technically much more complicated schemes for achieving control with extremely short, intense pulses of laser light (SN: 3/2/91, p.142). "The key theoretical contribution we made was to show that control has nothing to do with the time scale," Brumer says. "Such [short] pulses are totally unnecessary."

"We've demonstrated that the concept of quantum-mechanical control really works," Gordon adds. "It's not a little effect."

In principle, the same method used to control the ionization of hydrogen chloride molecules should also work for manipulating competing processes that generate different chemical products. "Our experiment is still only partway toward the ultimate goal," Gordon says. "We are now trying other molecules. We want to get two different sets of products and be able to control one product's [yield] at the expense of the other." — *I. Peterson*