ACE inhibitor protects diabetics' kidneys

People with insulin-dependent (juvenile-onset) diabetes – a disease that interferes with the metabolism of sugar – run about a 35 percent risk of getting kidney disease, or nephropathy.

Nephropathy, a progressive condition, can lead to complete kidney failure within 10 years. Diabetics with this complication are nine times more likely to die prematurely than diabetics without it.

However, a new study shows that a drug commonly used to control high blood pressure may also offer some protection against nephropathy.

Edmund J. Lewis, a physician at Rush-Presbyterian-St. Luke's Medical Center in Chicago, and his colleagues report that captopril – a type of angiotensin-converting-enzyme (ACE) inhibitor – "protects renal function in insulin-dependent diabetic nephropathy and is significantly more effective than blood-pressure control alone." Their report appears in the Nov. 11 NEW ENGLAND JOURNAL OF MEDICINE.

"We were struck by how positive the study's results are," Lewis says. "We found that ACE inhibitors retard kidney disease at all stages studied. The fact that there was a positive effect in patients with the most advanced disease was a surprise. Most people believe that once kidney disease has gone far, there's no stopping it."

The researchers studied 409 diabetics between December 1987 and October 1990. The patients, 18 to 49 years old, had insulin-dependent diabetes for at least seven years, with an onset before age 30, plus kidney disease, measured by protein excretions in their urine and elevated concentrations of serum creatinine, indications of kidney damage. In the double-blind study, 207 patients took 25 milligrams of captopril three times a day, while 202 patients received placebo pills.

A total of 301 patients completed the study as planned; 58 patients required additional follow-up or were removed from the study for health reasons; and 50 underwent kidney dialysis, had a kidney transplant, or died.

Among the conclusions: "We found that captopril significantly retarded the rate of loss of renal function in this group of patients with diabetic nephropathy. In the captopril group, the risk of a doubling of the serum creatinine concentration was reduced by almost one-half, as was the combined risk of death, dialysis, and transplantation," the researchers state. And captopril's protective mechanism appears "independent of its antihypertensive properties."

The researchers believe that captopril, like other ACE inhibitors, eases the pressure within the kidneys' many small filters, called glomeruli. "The blood vessels draining these filters, for unknown reasons, constrict in the diabetic state," Lewis says. "This constriction causes the glomeruli's internal pressure to rise, which seems to cause scarring that leads to progressive renal failure."

A hormone produced in the kidney, called angiotensin II, controls this renal constriction, says Lewis. Captopril inhibits the hormone's production, thus allowing the pressure within the glomeruli to fall. Whether other ACE inhibitors will perform equally well remains an open question, he adds, "but the rationale behind the study suggests they could. We studied captopril because we'd had the most experience with it, but we don't know yet how other ACE inhibitors will do."

These findings could affect the treatment of the 14 million U.S. diabetics and the 100 to 150 million worldwide, says Sara King of the Juvenile Diabetes Foundation. About 10 percent of diabetics develop insulin-dependent diabetes, usually in childhood; the rest develop non-insulin-dependent diabetes, she notes. Although this study focused on juvenile-onset diabetics, Lewis believes captopril may benefit adult-onset patients as well.

"It's possible that diabetic nephropathy is now a preventable disease," says Neil Kurtzman, president of the National Kidney Foundation, "provided we start treatment early enough." – *R. Lipkin*

Questioning a galactic star-forming model

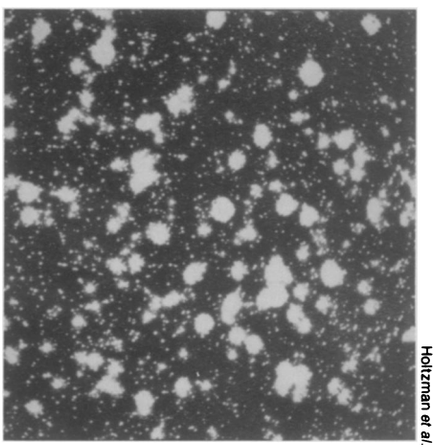
Like the two halves of a watermelon, concentrations of stars and gas sit above and below the disk of our galaxy. Astronomers have long believed that this dense central bulge, which makes up about one-fifth of the Milky Way's visible mass, contains many of the oldest stars in the galaxy. But a new study suggests that a significant number of stars in the bulge are not elderly, just middle-aged.

This finding, along with observations of three neighboring galaxies, flies in the face of conventional wisdom, which holds that the densest parts of a galaxy make most of their stars before other regions begin the process. The finding may force astronomers to revise the standard model of how and when galactic bulges make stars, says Jon A. Holtzman of Lowell Observatory in Flagstaff, Ariz.

Holtzman and his colleagues used the Hubble Space Telescope's wide-field camera to peer through a relatively dust-free pathway, known as Baade's Window, into the galactic bulge. The camera recorded stars 10 times fainter than those previously seen in the bulge. Relying on the principle that massive stars shine more brightly but die out more quickly than less massive ones, the researchers inferred an age range for the bulge stars by determining the luminosity at which the number of stars abruptly decreases.

The team estimates that a substantial number of stars in the bulge are 6 to 10 billion years old, rather than the 10 to 15 billion years previously suggested by researchers. Astronomers had thought that all bulge stars were related to and roughly the same age as those in the Milky Way's globular clusters, ancient star-packed groupings surrounding the disk of the galaxy. Holtzman and his coworkers describe their study in the November ASTRONOMICAL JOURNAL.

Holtzman cites three difficulties that make the results of the Hubble study somewhat tentative: the telescope's flawed optics, incomplete mapping of the amount of light-obscuring dust in Baade's Window, and uncertainties about the distance to the bulge.



Holtzman *et al.*

Stars in the Milky Way's bulge.

However, several recent ground-based studies reveal that bulge stars in nearby galaxies are also younger than once thought. For example, in Andromeda, the nearest galaxy similar to our own, stars in the bulge appear to be younger than those in that galaxy's oldest globular clusters. R. Michael Rich of Columbia University in New York City, Jeremy R. Mould of the California Institute of Technology in Pasadena, and James R. Graham of the University of California, Berkeley, will report the Andromeda study in the December ASTRONOMICAL JOURNAL. Other astronomers have reported similar age estimates for the bulge of M32, a satellite of Andromeda, and for the galaxy M33.

Astronomers have proposed that a galactic merger or collision may explain why many stars in the bulge don't form until well after other parts of a galaxy have had their first glimmers of starbirth. In these models, notes Rich, a violent encounter later in the life of a galaxy would drive gas into the core, where it would trigger a burst of star formation and eventually thicken into a bulge. – *R. Cowen*