

Transplant drug a clue to hypertension?

By studying kidney transplant patients, scientists at the University of Alabama at Birmingham hope to understand essential hypertension, which is high blood pressure of unknown cause. Most of the estimated 60 million U.S. cases of high blood pressure fit into this category, which carries a higher risk of heart, kidney and blood vessel disease. An explanation of why the drug cyclosporine can increase blood pressure should give information on the basic biological mechanisms involved in developing hypertension.

Since it received federal approval in 1983, cyclosporine has significantly improved transplant survival through its suppression of the immune system. Clinicians, however, have noted an increased incidence of high blood pressure in cyclosporine-treated animals and humans. For example, among cardiac transplant patients on the drug, the incidence of hypertension rises from about 10 percent to 90 percent or more. In high doses it is known to be toxic to the kidneys, which are thought to help maintain blood pressure and salt levels. To piece together the picture of hypertension, John L. Curtis and his co-workers in Birmingham have been studying patients receiving transplanted kidneys and various immunosuppressive drugs, including cyclosporine.

Although the 25,000 kidney transplants done annually in the United States could account for only a small percentage of people with hypertension, Curtis said last week that kidney transplant patients treated with cyclosporine may serve as models of high blood pressure.

By giving kidney recipients fluctuating amounts of salt, Curtis has been able to measure changes in blood flow and pressure in their kidneys. When comparing cyclosporine-treated patients with those not receiving the drug, says Curtis, "it is clear that [cyclosporine] does have acute [blood flow] effects, most of which are reversible." In describing this new form of drug-induced hypertension, Curtis says it is "compressed in time," quickly appearing and disappearing with drug administration and withdrawal. When 14 patients stopped taking cyclosporine, their renal vascular resistance (a measure of pressure in the kidneys related to blood vessel size) dropped by about 36 percent, says Curtis. Because these results suggest that lowering the dose might alleviate the hypertension problem, he is currently testing the effects on blood pressure of different doses of cyclosporine.

Slave-ship hypothesis of hypertension

Conditions on slave ships traversing the Atlantic Ocean during a 350-year period beginning in the 16th century may be responsible for the increased prevalence of high blood pressure among blacks in the United States, according to a hypothesis by Clarence E. Grim of the Charles R. Drew University of Medicine and Science in Los Angeles. After studying rates of hypertension among blacks on both sides of the Atlantic, as well as historical data about the slave trade, Grim concludes that voyages on the ships could have resulted in "survival of the fittest," with those better able to retain salt more likely to live through the lack of food and water and the dehydrating seasickness and diarrhea. This more efficient use of salt, however, has subsequently caused problems among slave descendants with salt-rich diets, suggests Grim.

The unproven hypothesis depends partly on the complicated question about which factors influence a person's high blood pressure. Studies conducted by various groups on twins and adopted children indicate that blood pressure is largely set by genetics—data that Grim calls "very powerful evidence that your blood pressure is set by something other than your environment."

He says his earlier studies among blacks in Indiana also

showed that blood pressure levels and the ability to excrete sodium are "strongly inherited." For example, when black patients were given salt, they had a faster rise in blood pressure at a lower level of salt than did white patients. On the basis of these results and his ongoing study of black twins in the Los Angeles area, Grim concludes that 60 to 80 percent of the variability in blood pressure seen among individuals is related to heritable factors, with the remainder due to environmental factors like stress and diet.

Grim's conclusions conflict with other theories that higher blood pressure among U.S. blacks is primarily caused by stress, or that their African ancestors retained more salt and water in order to survive hot, humid weather. But Grim says several comparisons show that blacks in the United States, Jamaica and Belize have consistently higher blood pressure than those in Africa, indicating changes occurred after slaves were removed from Africa. He also discounts the possibility that living conditions after the slaves were sold would be a major evolutionary factor, saying such conditions were too inconsistent to account for such widespread hypertension.

In order to prove his hypothesis, Grim says he will expand his studies to include African blacks matched with U.S. blacks on the basis of economics, education and other characteristics. Also included will be studies of blood pressure patterns among black families whose ancestors arrived after the slave period. Among the health benefits of confirming that high blood pressure is an inherited condition among blacks could be the identification of a genetic marker, says Grim. He suggests that such a marker should alert physicians and lead to earlier changes in diet as a preventive measure.

Stroke effects compounded by depression

Because strokes are the third leading cause of death in the United States, the public eye ordinarily focuses on mortality associated with the condition, which is caused by inadequate oxygen supply to the brain. More researchers and clinicians, however, are looking at the quality of life among stroke survivors, a group that includes nearly 2 million in the United States alone. Calling the condition of patients following a stroke "an underappreciated problem in health," Thomas R. Price of the University of Maryland School of Medicine in Baltimore says a new combination of psychiatry and post-stroke care should help change the attitude that mental impairment can be inevitable in elderly stroke victims.

Work by Price's group and others shows that strokes are followed by major depression in roughly 50 to 60 percent of patients. This depression goes beyond "feeling blue," says Price. Studies by the Maryland group indicate that mental capability is significantly impaired among depressed patients, causing signs of dementia for a year or longer. Presence of this depression-linked dementia seems to be dictated by the location of brain damage, says Price. Computed tomography scans used to find brain lesions show that the appearance of depression is most often associated with lesions in the left forward side of the brain. The researchers currently are looking for the biological cause of the depression, using animal studies and imaging methods that detect chemical changes in the brain.

Although both depressed and nondepressed stroke patients ordinarily improve with time, Price says depressed patients do not improve as quickly. Many are unaware how common this depression is following strokes, according to Price, who says that "[physicians] don't diagnose it . . . and don't really expect it." Instead, physicians and families wait for the patient to get better, eventually losing hope. But drug treatments for depression can improve a patient's prognosis, says Price.