BIOCHEMISTRY

Genes Affect Transplants

The discovery of a rejection mechanism dependent on genetic factors rather than antigen-antibody reactions was hailed as an advance in transplant research—By Faye Marley

➤ GENETIC FACTORS account for the acceptance or rejection of transplants, a husband and wife team from the Karolinska Institutet, Stockholm, Sweden, said in New York at the Seventh International Transplantation Conference. Their report was hailed as a breakthrough in the long search for knowledge of mechanisms involved in tissue and organ transplants.

Drs. Ingegerd Hellstrom and Karl Erik Hellstrom reported the existence of a rejection mechanism that does not depend upon antigen-antibody reactions.

An antigen is any foreign substance, which when introduced into the body, leads to the formation of antibodies. Antibodies have been believed to produce immunity to transplants as they do to any specific germ, virus or foreign substance.

They told the meeting, which was sponsored jointly by the New York Academy of Sciences and the New York University Medical Center, that similar or homozygous tumor cells in mice survive and multiply without difficulty when transplanted to other mice with identical genes.

Mouse tumor cells are homozygous when each cell contains a certain pair of genes, both of which carry the same formula for a chemical called an isoantigen.

Mouse recipients of transplants are called "syngeneic" when the corresponding pair of genes in each host cell are identical with those of the homozygous tumor cells.

If mouse hosts are only semi-syngeneic the homozygous mouse tumor cells transplanted do not multiply and survive readily. Each cell of the semi-syngeneic host contains one isoantigen formula gene like those in the tumor cells. The other gene of the pair carries a different formula. The inhibition of tumor cell growth in the semi-syngeneic host is called allogeneic inhibition. "Allo" is a prefix meaning other.

The researchers told of several experiments designed to uncover the mechanism of allogeneic inhibition.

"The findings support the previously advanced hypothesis that allogeneic inhibition is nonimmunological, and due to a direct growth inhibition of cells with an isoantigen equipment that differs from the surrounding tissues," they said.

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PHARMACOLOGY

Headache Drug Harmful

➤ BAD NEWS for migraine headache sufferers—a drug called Sansert, licensed in 1963 by the U.S. Food and Drug Administration, can cause growth of fibrous tissue, and physicians are being warned to be on the lookout for harmful effects.

A group of Harvard physicians, who previously had praised the drug as the best for prevention of vascular migraine headaches, have reported trouble in 27 patients using it.

Their research was aided not only by the Headache Research Foundation, but by the drug's producer, Sandoz Chemical Company of Hanover, N.J., and others. The chemical name of Sansert is methysergide.

Sandoz has warned doctors not to give the drug more than six months at a time when symptoms occur. This period should be followed by a drug-free interval of three or four weeks. The company also informed the U.S. Food and Drug Administration of the possible relationship of Sansert to fibrosis, in spite of the fact that 150 cases had been recorded in the medical literature before this drug was developed.

FDA officials told SCIENCE SERVICE that representatives of the agency are actively pursuing the effects of methysergide to find the extent of its harm.

Dr. John Graham and his colleagues reported in the New England Journal of Medicine, 274:359, 1966, that during the past five years about 1,000 patients in Harvard medical complex hospitals have taken methysergide.

"They tend to be patients with unusually severe headache, and some have taken higher doses of the drug than are currently recommended," the group stated.

Although the high dosage may have a bearing on the harmful effects, patients have taken the drug for varying periods, some for only a few days or weeks, and some for months or years.

Methysergide belongs to the ergot family, and many of these patients had used ergotamine tartrate as treatment for their headaches before and during methysergide therapy. Apparently all members of the ergot family thus come under suspicion and should be given only with the greatest caution to patients who have been shown to have growth of fibrous tissue behind the lining of the abdominal and pelvic cavities. This growth is technically known as retroperitoneal fibrosis.

One case is that of a 53-year-old married woman who began to take four milligrams of methysergide daily about six years ago. She later took 14 to 16 milligrams a day after suffering more pain and some complications. An examination to determine the cause of pain following an appendectomy revealed growth of fibrous tissue involving both ureters. Surgery, more drugs, including steroid hormones, and dilatations were used. The surgery showed that function of the right kidney had been largely destroyed.

After stopping all drugs then being used, the woman began to feel better.

Observation of suspected relationship of the drug to heart murmurs and fibrosis of the aorta, heart valves and lung tissue was reported, but the researchers say further confirmation is needed to prove the connection.

Disturbances in the connective tissues around joints and arteries are also linked to methysergide and new precautions are being added to treatment of migraine when these collagen diseases develop.

Collaborating with Dr. Graham in this study were Drs. Howard I. Suby, Philip R. LeCompte and Norman L. Sadowsky, all of the Harvard Medical School.

Another case of retroperitoneal fibrosis was reported in Washington, D.C., which was associated with the use of methysergide maleate. A 38-year-old man had been taking four tablets of the drug daily for approximately three years to control his headaches. The pain of fibrosis was relieved by continuous uretal catheter drainage and oral steroid therapy, and four months later he appeared to be normal.

Dr. Donald A. Johnson, a Washington neurologist, and Dr. William M. Ballinger of Georgetown University School of Medicine reported the case in Medical Annals of D.C., 35:75, 1966.

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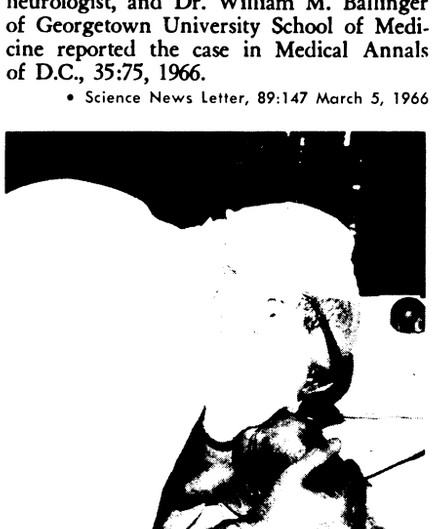

Smith Kline & French Laboratories

THE BREATH OF LIFE—A newborn Cameroon baby receives the breath of life through mouth-to-mouth resuscitation applied by Robert Suskind of the University of Pennsylvania School of Medicine. Mr. Suskind, who is serving in the Cameroons on a Smith Kline & French international fellowship, had delivered the infant just seconds before.