

July 7, 1981

News

The University of Texas Health Science Center at Dallas
5323 Harry Hines Boulevard Dallas, Texas 75235 (214)688-3404

CONTACT: Ann Williams
Office: 214/688-3404
Home: 214/375-6043

* * * * * Non-diabetic parents of diabetic children have both vascular changes and a gene common in diabetics.

DALLAS -- Normal parents of children with diabetes have been found to have blood vessel changes commonly found in adults with diabetes. In addition, they have the gene for HLA antigen DR4, a protein important to the body's immune response, originally discovered in research on transplant rejection.

Results of the study at The University of Texas Health Science Center at Dallas were published in the June issue of "Diabetes."

HLA-DR4 has been known to be associated with diabetes. Now the "take-home message" from this study is "DR4 is also related to vascular changes," says Dr. James Marks, associate professor of Pediatrics.

Biopsies of the leg muscle were taken on 16 diabetic children, 20 of their unaffected siblings and 38 parents. The thickness of the capillary basement membrane (inside layer of the capillary wall) was measured using the electron microscope. A membrane thicker than 2000 angstroms (0.00002 centimeters) was found in 37 percent of the parents, in two of the patients (both age 19 or older) and in none of the siblings.

A high correlation was found between the thicker membranes, such as those found in adult diabetics, and the HLA-DR4 antigen.

Many factors may be related to the thickening of the capillary wall, says Marks. The traditional theory in treatment of diabetes has been that if the blood sugar could be kept within normal limits, there would be few circulatory complications such as blindness and kidney disease.

This new study, which has still to be confirmed by other centers, points to a genetic factor related to diabetes but possibly affecting capillaries in some other way than through high blood sugar.

Marks cautions that capillary changes in the leg may or may not parallel changes in the eyes, nerves and kidneys.

"I won't say as some physicians do, 'Take care of your blood sugar and you won't have trouble with your eyes and kidneys.' That's not fair. We don't know that," says Marks. "Some say, 'There's nothing you can do. It's genetic.' I'm somewhere in-between. But the position I take in management of diabetics is to control the blood sugar as much as I can since I clearly can't change the genetic factors."

-- over --

Several years ago there was no way to keep a diabetic's blood sugar in normal limits. The blood sugar decreases after an injection of insulin and then slowly increases until the next injection. Now with the new insulin infusion pumps it is possible to maintain a normal sugar level. The pump is currently being studied at the Dallas health science center by Dr. Philip Raskin, associate professor of Internal Medicine, and at other centers. "It will take years of study to know the effects of a normalized blood sugar in the patients using the pumps," says Marks. The longest period a patient has been on the pump now is two years. Further study will be needed to determine the effect of this therapy on muscle capillary walls as well as those of the eyes, nerves and kidneys.

On the genetic side, the HLA antigen system in white blood cells, used in tissue typing, was discovered in studying kidney transplants and the reasons for acceptance or rejection by the recipient. The antigens were designated A,B,C and D in order of their discovery. (DR means 'D-related'.)

The sixth chromosome carries the genetic code for making the HLA antigens including the DR antigen. Subjects in this study were tested for eight different DR antigens, and the only one that correlated with the thickened capillary membrane was DR4.

An individual has a pair of sixth chromosomes (one from the father and one from the mother) so he or she has the code for two DR antigens. Studies done in many centers in Western Europe and North America show the incidence of type I diabetes (juvenile-onset) to be closely linked to DR3 and DR4. A person with the DR3 antigen has three to four times the chance of developing type I diabetes as a person with neither DR3 nor DR4; a person with DR4 has four to 10 times the chance, and someone with both DR3 and DR4 has 33 to 44 times the chance of developing type I diabetes.

There has been no correlation shown between the DR antigens and type II (adult-onset) diabetes.

With diabetes there is a variety of susceptibility to vascular changes. Usually children who develop diabetes have complications later due to changes in the blood vessels, but some children never have vascular complications. Some adult diabetics develop vascular changes quickly; others, over a period of time.

This, too, indicates that high blood sugar may be only one of several factors involved in the thickening in the capillary walls. So identification and understanding of the genetic factor and possibly unknown factors are important in the on-going study of diabetes, says Marks.

Co-authors of the paper are Raskin and Dr. Peter Stastny, professor of Internal Medicine. The work was supported in part by grants from the American Diabetes Association and the National Institutes of Health.

##

DISTRIBUTION: AA,AB,AC,AF,AG,AH,AI,AK,SC,SL