

Diabetic Mouse Studied

A mouse with hereditary diabetes that can be used for the first time in the study of human diabetes has been discovered

► **DISCOVERY** of a laboratory animal with hereditary diabetes resembling the human disease was reported in *Science*, 153:1127, 1966, by three scientists at The Jackson Laboratory, Bar Harbor, Maine.

The discovery is important news to researchers, who up to now have lacked a suitable animal model of human diabetes for investigation. Already 300 diabetic mice make up The Jackson Laboratory colony, and as soon as the colony is large enough, specimens will be shipped out on request.

Drs. Katharine P. Hummel and Margaret M. Dickie, with Dr. Douglas L. Coleman, all of The Jackson Laboratory, reported the research, which is being expanded to accommodate the numerous scientists doing basic research as well as those seeking a cause and cure of the disease.

To have diabetes in full form, the mice must inherit the gene from both parents. Such mice are infertile, and a special ovary-transplantation technique has to be carried out to keep the line from dying out.

The diabetic female's egg cells carry the diabetes gene, and so her ovaries are transplanted to a healthy female that

is then mated with a male that is fertile because he carries only one diabetes gene. About half the mice born of such matings carry two diabetes genes and consequently develop the disease.

At first the mutant mice appear to be normal but soon get fat. In spite of fasting and losing weight, with lowered blood sugar, they soon regain weight and blood sugar levels after plenty of food is restored. Attempts to control weight by restriction of food, as has been successful with the obese, have failed.

Commenting on the research, Dr. Hummel said that later as the disease becomes rampant, the mice lose weight drastically as happens with human diabetics. Between three months and six months of age the animals enter a terminal phase and usually die.

Other ways in which the animal disease parallels that in humans include sensitivity to stress, excretion of large amounts of sugar in the urine, and strikingly abnormal changes in a part of the pancreas.

Some of the diabetic mice have responded to insulin treatment but the proper dosage remains to be worked out.



THE JACKSON LABORATORY

DIABETIC MOUSE—An abnormal tendency to obesity is shown by an adult mouse with diabetes (right) in comparison to a normal mouse (left). A new strain of diabetic animals, discovered at The Jackson Laboratory, Bar Harbor, Maine, carries hereditary diabetes similar to that found in humans.

Dystrophy Noncarrier Not 100% Traceable

► **MOST FEMALE** carriers of the gene for Duchenne muscular dystrophy—a severe progressive muscle-wasting disease that attacks young boys—can be identified by an enzyme test. There is, however, no 100% accurate way to detect a noncarrier.

This causes a problem in genetic counseling, Dr. Margaret W. Thompson and Phyllis J. McAlpine of Toronto, Canada, told the Third International Congress of Human Genetics meeting in Chicago.

Not every suspected carrier will have a son affected by this type of muscular dystrophy. Until positive identification of all carriers can be demonstrated, however, the only known way to be sure of reducing the incidence of the disease is for female relatives of such patients to avoid pregnancy.

Duchenne muscular dystrophy is inherited by an X-linked mutant gene transmitted by clinically normal carrier females.

The enzyme test for creatine kinase activity in the blood was first developed in France and is now used in many research centers. The Toronto researchers applied it to 200 female relatives of affected boys who attend the muscular dystrophy clinic of the Hospital for Sick Children in Toronto.

They found that high creatine kinase activity identified a woman as a carrier, but normal activity is only 75% to 90% accurate as evidence that she is a noncarrier. About two-thirds of mothers who were known to be carriers had raised enzyme levels, but the rest of them had normal levels.

Among possible carriers—mainly sisters of affected boys and mothers of isolated cases—there are also, apparently, some who have the Duchenne gene but have an enzyme level in the normal range, the researchers believe.

The enzyme test is more accurate in younger than in older women. The number of sisters and cousins of patients who had elevated creatine kinase activity was in close agreement with the genetic expectation. However, in older age groups it is believed that, as in the known carriers, only about two-thirds of the carrier women will have a high enzyme level.

Women who have an affected son but no other relatives with the disease have about one chance in two of being carriers, and thus being capable of having other affected sons and carrier daughters.

Dr. Thompson is an associate professor in the department of pediatrics, University of Toronto, and Miss McAlpine is a research assistant in the department of genetics, Hospital for Sick Children.