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**STUDY FINDS TYPE 1 INCIDENCE IN U.S. MAY
BE HIGHER THAN THOUGHT**

A new research study estimates that about 15,000 children and adolescents in the United States are diagnosed with type 1 diabetes every year, a number higher than the incidence reported by previous U.S. childhood diabetes registries.

SEARCH for Diabetes in Youth, a multi-center study of childhood diabetes in racially and ethnically diverse populations, is the largest surveillance effort of diabetes among people under the age of 20 conducted in the U.S. to date. The study includes 10 locations across the country where about 5.5 million children live.

“For the first time from medical researchers, we have an accurate estimate of the incidence of diabetes in youth in the United States, including numbers from minority groups,” said Marie Nierras, JDRF’s Director of Partnerships and Consortia. “The data show that the incidence of diabetes is rising, and has enormous health policy implications, both nationally and for every state.”

In a report in the *Journal of the American Medical Association*, study investigators identified 2,435 youth who were diagnosed with type 1 and type 2 diabetes in 2002 and 2003. Extrapolating that over the U.S. population, they note that the estimated overall incidence of diabetes in youth is 24.3 per 100,000 per year.

The study also found that, contrary to conventional wisdom increasingly portrayed in the media, the vast majority of people under 20 with diabetes have type 1, not type 2, diabetes.

In children under 10, regardless of their race or ethnicity, most patients with diabetes had type 1 diabetes, previously known as juvenile or insulin-dependent diabetes. Among non-Hispanic white children ages 5-9, the incidence was 28.1 per 100,000 per year; for ages 10-14, the rate was 32.9. This incidence is higher than previously believed and confirms the perception among researchers that the incidence of type 1 diabetes is increasing.

Even among older youth ages 10-14, type 1 diabetes was frequent among non-Hispanic white (32.0 per 100,000 per year), African-American (19.2 per 100,000) and Hispanic adolescents (19.2 per

100,000 per year), but was much less common among Asian Pacific Islander (8.3 per 100,000 per year) and Native American youth (7.1 per 100,000 per year). In all age groups, the highest rates of type 1 diabetes were observed in non-Hispanic white boys and girls.

The study was funded by the Centers for Disease Control and Prevention (CDC) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), a part of the National Institutes of Health (NIH). Resources from the NIH Special Funding Program for Type 1 Diabetes Research supported the study. The program provides \$150 million a year in medical research support for type 1 diabetes but is set to expire at the end of next year unless reauthorized by Congress.

SEARCH investigators will continue to track the incidence of diabetes in youth in all of the various population groups through 2009.

“Continuing this surveillance effort is essential to document temporal trends in the incidence of diabetes among various racial and ethnic groups and accurately assess the future health care burden of diabetes and its complications in the U.S. pediatric and young adult population,” said lead author Dana Dabelea, M.D., Ph.D., an Associate Professor of Preventive Medicine at the University of Colorado at Denver and Health Sciences Center’s School of Medicine, and SEARCH principal investigator (PI) for the Colorado site.

**MOUSE SKIN CELLS REPROGRAMMED TO
EMBRYONIC STATE**

Three research teams have shown that ordinary skin cells in mice can be reprogrammed to an embryonic state that is virtually indistinguishable from embryonic stem cells.

The advance underscores the potential for scientists to use the technique to generate a replenishable source of genetically matched, mature insulin-producing beta cells to replace those destroyed by type 1 diabetes.

In studies published in the journals *Nature* and *Cell-Stem Cell*, researchers found that by injecting four genes into normal fetal mouse skin cells, they could reprogram the cells to an embryonic state. These cells became, in effect, embryonic stem cells, capable of developing into many of the body’s major tissues.

Scientists will now focus on trying to apply the procedure to human cells to achieve the same results. If they are successful, then researchers might ultimately be able to use a patient’s skin cells to generate new cells—such as insulin-producing beta cells or heart cells—that could potentially be transplanted into the

patient without fear of being rejected by the immune system. In a treatment of type 1 diabetes, the autoimmune attack would still need to be blocked.

Although the new studies offer hope for further advances, it remains unclear if the procedure will work in human cells. “These results are preliminary and proof of principle,” said Rudolf Jaenisch, an MIT professor who led one of the research teams, in a press release. “It will be a while before we know if this can ever be done in humans.”

An important implication of this research is that it could provide an additional pathway to create “customized” or host-matched embryonic stem cells. Currently, the only way to convert mouse adult cells to embryonic form has been by nuclear transfer – a method in which researchers insert an adult cell’s nucleus into an egg whose own nucleus has been removed. The egg reprograms the nucleus back to an embryonic state, and the cell begins developing to a stage at which embryonic stem cells can be derived.

There are several serious barriers that must be addressed before the technique can prove useful with human cells— for example, the technique must be applied to adult mouse cells. And two of the genes used by the scientists can cause cancer. For this reason, current research into human embryonic stem cells continues to be crucial, said Dr. Jaenisch. “Human embryonic stem cells remain the gold standard for pluripotent cells, and it is a necessity to continue studying embryonic stem cells through traditional means.”

POWERFUL RESEARCH METHOD FINDS FOUR NEW TYPE 1 DIABETES GENETIC REGIONS

Researchers have identified four new genetic regions that can determine risk for type 1 diabetes. This finding, made through a powerful new tool called genome wide association (GWA) should help scientists better understand the disease pathway and could someday provide a profile of individual risk.

The GWA approach looks for small differences in genetic markers spread throughout the entire genome, comparing the markers present in people with the disease against those who are unaffected. This method was used by Wellcome Trust Case Control Consortium (WTCCC), a collaboration of 24 geneticists in the United Kingdom, to examine the genetics behind many common diseases. As part of this large study, the WTCCC identified six chromosomal regions that they suspect are related to type 1 diabetes.

JDRF researchers at the Juvenile Diabetes Research Foundation/Wellcome Trust Diabetes and Inflammation Laboratory in Cambridge followed up these findings by examining those regions using a large set of DNA samples. They confirmed that four of the regions are associated with type 1 risk, increasing the number of genetic regions identified as diabetes-related from six to 10. The finding is published in the journal *Nature Genetics*.

“The Wellcome Trust study provides valuable new insight into the genetic origins of type 1 diabetes. This brings us one big step closer to understanding the genetic basis of disease and provides insights that may lead to preventing and/or curing it,” said Dr. Richard Insel, Executive Vice President of Research for JDRF.

In one genetic region, the study pinned the location down to a specific gene, PTPN2, which also is associated with risk for Crohn’s disease, another autoimmune affliction. This is the first time a genetic link has been identified between these two diseases. Detection of unsuspected genes such as this is one of the payoffs of the GWA approach.

Professor John Todd, co-director of the laboratory, said, “We know that the causes of diabetes are complex and that the genes almost certainly interact with environmental factors, such as diet, low levels of vitamin D, and viral infections, to trigger the disease. But this is the first time that we have seen a link between type 1 diabetes and Crohn’s disease.”

“The link between the two diseases is clearly a very promising avenue for us to understand how they occur,” Todd said. “The pathways that lead to Crohn’s disease are increasingly well understood, particularly when enhanced by these new findings. We hope that progress in treating Crohn’s disease will give us clues on how to treat type 1 diabetes.”

In addition to PTPN2, the researchers identified three other new type 1 genetic regions: KIAA0350, SH2B3, and ERBB3. Finally, the scientists also validated six other previously known type 1 genes. The WTCCC paper is published in *Nature*.

Studies Converge to Yield Disease Clues

GWA studies became feasible only recently, due partly to technological advances that have made genome scanning faster and cheaper. Researchers are able to draw on data compiled for the Human Genome Project and the Haplotype Map, which indexed common patterns of human genetic variation.

The WTCCC involves 50 leading research groups and over 200 scientists in the field of human genetics from dozens of institutions. The consortium analyzed 17,000 DNA samples taken from people in the U.K.—2,000 patients for each disease and 3,000 control samples—to identify common genetic variations for each affliction. The type 1 diabetes samples came from the Juvenile Diabetes Research Foundation/Wellcome Trust Diabetes and Inflammation Laboratory

The GWA study by the WTCCC searched for genetic links to seven common diseases: type 1 and type 2 diabetes, rheumatoid arthritis, Crohn’s disease, bipolar disorder, and hypertension. The study was a proof-of-principle experiment for the validity of the GWA approach to finding disease genes. The type 1-related findings were published in *Nature Genetics* as a complement to this work.