Undernourishment in pregnant, lactating females found key to next generation's disease

June 13 2011

A new study published by the American Physiological Society offers the strongest evidence yet that vulnerability to type 2 diabetes can begin in the womb, giving new insight into the mechanisms that underlie a potentially devastating disease at the center of a worldwide epidemic. The study, conducted in baboon primates, finds that when mothers are even moderately undernourished while pregnant and breastfeeding, their offspring are consistently found to be prediabetic before adolescence. It is the first time that diabetes has been shown to have prenatal origins in a primate model.

According to Peter W. Nathanielsz, senior author of the study, "We pass more biological milestones before we are born and in the early weeks of life than at any other time." Poor maternal nutrition, which translates to less sustenance for growing fetuses, is a stubborn problem in parts of the U.S. and the developing world, Nathanielsz said. Thus, "Poor nutrition at critical periods of development can hinder growth of essential organs such as the pancreas, which sees a significantly decrease in its ability to secrete insulin. Our study is the first to show in a primate that poor nutrition during fetal and early life can damage the pancreas and predispose one to type 2 diabetes."

The study, "Emergence of insulin resistance in juvenile baboon offspring of mothers exposed to moderate maternal nutrient reduction" was conducted by Nathanielsz and colleagues Jaehyek Choi, Cun Li, and

Thomas J. McDonald of the School of Medicine at the University of Texas Health Science Center at San Antonio, and Anthony Comuzzie and Vicki Mattern of the Texas Biomedical Research Institute in San Antonio. The study was funded by the National Institute of Diabetes and Digestive and Kidney Diseases. It is published in the online edition of the American Journal of Physiology—*Regulatory, Integrative and Comparative Physiology*.

Background

Type 2 diabetes occurs when the body develops resistance to insulin, a hormone that regulates blood sugar. Although the body may initially compensate by secreting more insulin, eventually the pancreas cannot produce enough of the hormone to keep blood sugar from rising. In poorly controlled diabetes, elevated blood sugar severely damages the heart, blood vessels, eyes, kidneys and nerves. The consequences can be fatal and include heart disease, stroke, amputations, blindness and kidney failure.

Worldwide, diabetes is an escalating public health crisis. According to estimates from the World Health Organization (WHO), 366 million people will be diabetic by the 2030, up from 171 million in 2000. This is a 114 percent projected increase.

Formerly called "adult-onset diabetes," type 2 diabetes is seen increasingly in children at earlier and earlier ages. Excess body weight and physical inactivity are known causes, but Nathanielsz and his collaborators have long been interested in whether some individuals might be predisposed to diabetes from birth, or even earlier. Nathanielsz conducts research on this and similar topics through the Center for Pregnancy and Newborn Research in the UT Health Science Center's Department of Obstetrics and Gynecology.

The Study

For this study, to avoid the complication of influences from genes, researchers selected 18 female baboons similar in age and other observable characteristics and housed them with a fertile male baboon. All females became pregnant. From 30 days of gestation, 12 females were randomly assigned to be fed an appropriate diet for their weight. The other six received 70 percent of the chow given to control females on a weight-adjusted basis. The female baboons continued on their respective diets through delivery and the weaning of their offspring. Once the young baboons were weaned, they were fed normal diets.

Just before they reached puberty, the six young baboons from nutritionally restricted mothers showed increases in fasting glucose, fasting insulin and other hallmarks of prediabetes. The 12 young baboons whose mothers received adequate nutrition displayed none of these traits.

The central importance of this observation is that the mothers' food intake was only moderately restricted – similar to the decrease faced in the United State by many people living with food insecurity. There are 925 million undernourished people worldwide, including 19 million in developed countries, according to the Food and Agriculture Organization of the United Nations.

The researchers conclude that even moderate nutrient deficiencies during pregnancy result in offspring predisposed to type 2 diabetes, particularly if they are exposed to other risk factors in later life, such as a Western diet and physical inactivity leading to obesity. A fetus may also receive fewer nutrients due to teenage pregnancy, where the growing mother competes with her offspring for resources; in pregnancies complicated by maternal vascular disease, which may occur in women who become pregnant later in their reproductive life; and

when placental problems exist. The decrease in fetal growth observed in the newborn baboons was only about 10 percent, very similar to many human babies born growth restricted.

Next Steps

According to Dr. Nathanielsz, the next step is separating the effect of nutrient deficiencies experienced during pregnancy from those that occur during breastfeeding.

More information: Emergence of insulin resistance in juvenile baboon offspring of mothers exposed to moderate maternal nutrient reduction, Published online before print June 2011, doi: 10.1152/ajpregu.00051.2011

Provided by American Physiological Society