By Lois Baker

# Perpetuating Obesity

## In utero "malprogramming" of appetite center

**If findings by UB metabolic researchers** are taken into account, the adage "You are what you eat" should be rephrased to include "and so are your children."

Long-term studies by the UB scientists have shown that rat pups raised artificially on a high-carbohydrate milk formula identical in calories to mother's milk developed changes in pancreatic islets, resulting in overproduction of insulin and obesity in adulthood.

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Progeny of these high-carbohydrate (HC) mothers raised naturally also develop the same maladjustments, they found.

In recent studies, the researchers now have shown that this metabolic "malprogramming" is permanent and occurs in utero, resulting in the next generation born to HC mothers carrying the HC phenotype. Rat fetuses had increased plasma insulin levels, increased mRNA levels of preproinsulin, a precursor of insulin, and increased insulin in the pancreas, without an increase in body weight, plasma glucose level or a change in islet structure.

They also found changes in the hypothalamus, the brain's center of appetite regulation, that result in appetite stimulation.

While these studies were done with rats, Mulchand Patel, PhD, UB distinguished professor of biochemistry and first author on the study, speculates that there is good reason to think the mechanism could be similar in humans.

"Obesity can be perpetuated via the maternal intrauterine environment," says Patel, who reported the findings at the 2005 Experimental Biology meeting held in San Diego in early April.

"Our earlier studies looked at progeny in the post-weaning period, so we didn't know how early this malprogramming occurred. Now we know it occurs in utero. We predicted that this could be the case, and our present findings support this prediction."

Plasma levels of rat pups (2-HC) born to HC mothers returned to normal during the suckling period, results showed, but islets from 12-day-old suckling 2-HC rats showed a capacity for insulin oversecretion when maintained in culture medium containing high glucose levels. By the 28th day, approximately 4 days after weaning to rat chow, 2-HC rats once again had high insulin levels and showed a higher capacity for insulin secretion to a glucose stimulus. Even on rat chow, body weight began to increase around day 55, and 2-HC rats were obese by postnatal day 100.

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Malathi Srinivasan, PhD, Suhad Shbeir-El Dika, Ravikumar Aalinkeel, PhD, Fei Song, PhD, Lioudmila Pliss, PhD, and Paul Mitrani from Patel's lab, along with Roberta Pentney, PhD, from the UB Department of Pathology and Anatomical Sciences, contributed to the study, as well as Shanthie Damodaran, PhD, and Sherin Devaskar, MD, from the Department of Pediatrics at UCLA, and Brenda Strutt and David Hill PhD, from the Lawson Research Institute in London, Ontario.

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