# Mom's obesity during conception phase may set the stage for offspring's obesity risk

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The number of overweight and obese Americans continues to grow rapidly. Today, 50 percent of adults are overweight and up to 20 percent are obese. While the number of overweight/obese children is at an all time high, the steady increase of overweight infants -- individuals under 11 months old -- is alarming.

Research studies have found that pregnant women who are overweight/obese are more likely to give birth to heavier babies, and the risk of overweight children becoming obese adults is nearly nine times greater than for children who are not overweight. Studies also show that greater body-weight at birth and weight gain early in life increases the risk of becoming overweight or obese as an adult. Inheritance studies show that a child's body mass index (BMI) correlates more closely with the mother's BMI than with it's father's, suggesting that an interaction of both genetic and intrauterine influences, may contribute to later-life obesity risk in the offspring.

Armed with these and other data, a team of researchers from the USDA-Arkansas Children's Nutrition Center has examined whether the subtle effects of fetal exposure to the mother's obesity can have a latent effect on the offspring. In a new report, investigators studied whether fetal exposure to gestational obesity leads to a self-reinforcing viscious cycle of excessive weight gain and body fat which passes from mother to child. The results of the new study suggest they do.

**The Study**

The study is entitled, "Maternal Obesity at Conception Programs Obesity in the Offspring." It was conducted by the research team of Kartik Shankar, Amanda Harrell, Xiaoli Liu, Janet M. Gilchrist, Martin J.J. Ronis and Thomas M. Badger, all of the Arkansas Children's Nutrition Center, Little Rock, AR. Their findings appear in the online edition of the American Journal of Physiology -- Regulatory, Integrative and Comparative Physiology (doi:10.1152/ajpregu.00316.2007). The journal is one of 11 published each month by the American Physiological Society (APS; http://www.the-aps.org/ ).

To test the theory that obesity in adulthood may be subject to programming during fetal development, the researchers developed an overfeeding model which was used in rats. The model allowed the investigators to replicate many of the metabolic and hormonal features of overweight human individuals. They were also able to exclude parental genetic influences, match gestational weight gain, limit the exposure of maternal obesity in utero, and control lactation efficiency, all of which can be difficult confounding variables in studies with human subjects.

**Summary of Methodology**

Virgin female rats were fed liquid diets via enteral nutrition at one of two caloric levels: (1) the caloric level recommended by the National Research Council (187 kcal/kg3/4/day) or (2) a level of 15 percent overfeeding (220 kcal/kg3/4/day). In the preliminary experiments, the rats consuming the normal caloric intake had weight gains similar to controls while those being fed the obesegenic diet had become substantially overweight. Body weights were monitored three times a week and body composition was analyzed non-invasively on a regular basis.

To examine the long-term gestational effects of maternal obesity on the offspring, lean (n=7) and obese (n=15) rats were allowed to mate with normal (lean) male rats for a period of one week. Following mating, all female rats (lean and obese) received respective diets at 15 percent excess calories per day in order to ensure adequate caloric intake for pregnancy. Maternal body weights were monitored three times a week and all rats gave birth naturally. Offspring born to lean or obese rats

were raised by surrogates who were fed regular rodent diets to ascertain the pups' obesity exposure was limited only during gestation.

The male offspring from each group were weaned from the surrogate mother at 21 days after birth and fed (by giving unlimited access to) either a normal diet or a high-fat diet. The pups' body weight, body composition and other factors were analyzed for 130 days. At day 130 additional samples were taken and analyzed, to include organ weights, glucose and triglyceride levels, fat cell size, body composition and hormones.

**Key Findings**

The researchers found the following:

- at birth, the weight of the offspring from both groups was similar. The number and size of pups and the ratio of males to females did not differ significantly.

- the amount of calories the pups consumed (relative to their body-weight) at the 60- and 120-day mark suggested that both groups consumed the same amount of calories, indicating no effect of maternal obesity on the offspring's food intake.

- when both the lean and obese offspring were fed a control diet, their body weights remained similar. However, when both groups were fed a high-fat diet, the obese offspring gained remarkably more weight, suggesting that exposure to maternal obesity led to programming of increased susceptibility to obesity in the offspring, which was revealed following an obesegenic challenge despite a normal birth weight.

- when both groups were fed a control diet, obese offspring had a ~ 1.6 times greater fat ratio compared to their lean offspring counterparts. Further, obese offspring fed a high-fat diet had a 26 percent greater percent fat ratio and a 60 percent increase in subcutaneous fat mass vs. lean offspring.

- high fat feeding significantly increased serum glucose, triglyceride, insulin and leptin levels in both groups. Strikingly, the serum insulin and leptin levels increased by 2.2 and 2.3 fold in obese offspring compared to lean offspring fed the same diet.

**Conclusions**

These findings add to the existing body of evidence showing that both maternal obesity and genetic background influence offspring's susceptibility to obesity. It goes further, to highlight the role of post-natal obesegenic diet as a determinant in revealing subtle programming imposed by maternal obesity. The results also demonstrate that high levels of adiposity (body fat) occur in the offspring of obese mothers despite consuming similar calories as their lean-offspring counterparts and that offspring obesity is associated with insulin resistance.

The "programming" of susceptibility to obesity occurs in the absence of changes in birth weights and other fetal outcomes.

According to Dr. Kartik Shankar of the Arkansas Children's Nutrition Center, "The mother's body composition at conception has important implications for the metabolism and risk of obesity in the offspring in later years. Not only do these findings help us appreciate the reasons for the rapid rise in obesity, this novel model will allow us to understand the underlying mechanisms and should provide fertile opportunity for translational type research."

Source: American Physiological Society