OBSTETRICS

Rat maternal obesity and high-fat diet program offspring metabolic syndrome

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OBJECTIVE: We determined the potential programming effects of maternal obesity and high-fat (HF) diet during pregnancy and/or lactation on offspring metabolic syndrome.

STUDY DESIGN: A rat model of maternal obesity was created using an HF diet prior to and throughout pregnancy and lactation. At birth, pups were cross-fostered, thereby generating 4 paradigms of maternal diets during pregnancy/lactation: (1) control (Con) diet during pregnancy and lactation (Con/Con), (2) HF during pregnancy and lactation (HF/HF), (3) HF during pregnancy alone (HF/Con), and (4) HF during lactation alone (Con/HF).

RESULTS: Maternal phenotype during pregnancy and the end of lactation evidenced markedly elevated body fat and plasma corticosterone levels in HF dams. In the offspring, the maternal HF diet during pregnancy alone programmed increased offspring adiposity, although with normal body weight, whereas the maternal HF diet during lactation increased both body weight and adiposity. Metabolic disturbances, particularly that of hyperglycemia, were apparent in all groups exposed to the maternal HF diet (during pregnancy and/or lactation), although differences were apparent in the manifestation of insulin resistant vs insulin-deficient phenotypes. Elevated systolic blood pressure was manifest in all groups, implying that exposure to an obese/HF environment is disadvantageous for offspring health, regardless of pregnancy or lactation periods. Nonetheless, the underlying mechanism may differ because offspring that experienced in utero HF exposure had increased corticosterone levels.

CONCLUSION: Maternal obesity/HF diet has a marked impact on offspring body composition and the risk of metabolic syndrome was dependent on the period of exposure during pregnancy and/or lactation.

Key words: hypertension, impaired glucose tolerance, lactation, obesity, pregnancy, rat

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An epidemic of metabolic syndrome is well recognized within the United States. Currently 65% of adult Americans are overweight and 30% obese, although a marked increase in obesity is apparent from childhood through adolescence.[1] Notably, prepregnancy obesity prevalence continues to increase as well.[2,3] Among women presenting for prenatal care, the incidence of obesity has doubled since 1980.[4] Not only do women begin pregnancy at a higher body mass index, but women also gain excess gestational weight.[5] Thus, clinicians caring for pregnant women are increasingly caring for women who are overweight or obese.

It is well established in human studies and animal models that maternal nutritional factors during pregnancy may have marked effects on fetal growth and ultimately influence the offspring's predisposition to obesity.[6,7] Studies that have examined the developmental origins of adult obesity have demonstrated that maternal obesity, weight gain during pregnancy, and/or the presence of gestational diabetes are each associated with an increased risk of the offspring becoming obese during childhood and/or as adults.

Recent human studies have demonstrated that among these factors, maternal prepregnancy weight may be the most predictive of offspring obesity.[8,9] Animal studies have begun to examine the mechanisms of fetal programming, with evidence that maternal obesity and a Western high-fat (HF) diet program fetal adipose tissue to promote increased adipogenesis and hypothalamic neural pathways to promote appetite as compared with satiety.[10-12]

Breast-feeding has been strongly encouraged for postpartum women in the United States, with evidence suggesting significant benefits in newborn immune function, nutrition, maternal weight loss, and maternal-newborn bonding.[13,14]

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TABLE 1
Nutrient composition of diets

Variable	Purified diet 58Y2, 10% k/cal fat	Purified diet 58Y1, 60% k/cal fat
Nutrients, %		
Carbohydrates	67.4	25.9
Protein	17.3	23.1
Fat	4.3	34.9
Lard	1.9	31.7
Soybean oil	2.4	3.2
Fat type, %		
Saturated	25	37
Monounsaturated	35	46
Polyunsaturated	40	17

Nutrient values are percentage per 100 g food, and fat type is percentage of total fat.

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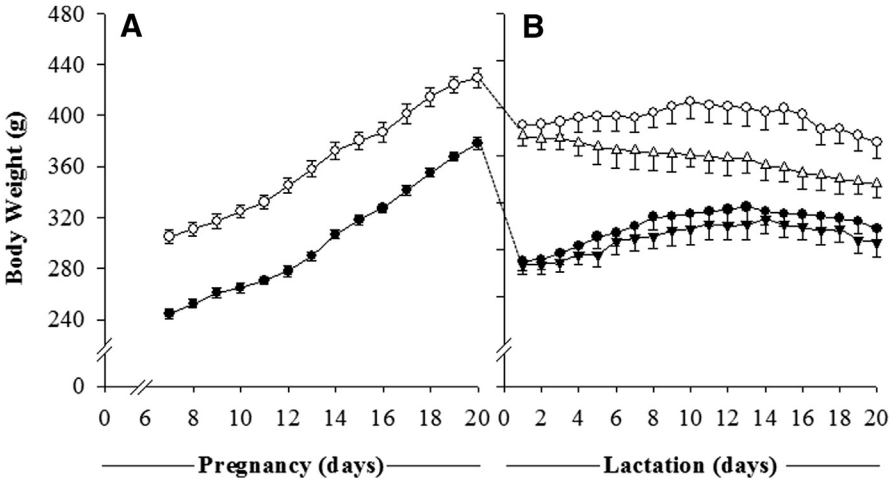
However, it is recognized that maternal breast milk reflects in part, the maternal diet, and maternal obesity and the HF Western diet may contribute to higher fat content in breast milk.[15] Thus, maternal obesity may affect breast milk–induced newborn programming, independent of the maternal obesity effects on fetal programming.

In view of the potential programming effects of maternal obesity during both pregnancy and lactation, we sought to examine the effects of each of these periods on programmed metabolic syndrome in rats. We hypothesized that offspring exposed to maternal obesity during both pregnancy and lactation would be more obese and exhibit a greater degree of metabolic abnormalities.

FIGURE 1
Maternal body weights during pregnancy and lactation



A, Daily maternal body weight during pregnancy (e8–e20) of Con (*filled circles*) and HF dams (*open circles*). **B,** Daily maternal body weight during lactation (day 2–20) of Con dams nursing Con pups (*filled circles*), HF dams nursing HF pups (*open circles*), Con dams nursing HF pups (*filled triangles*), and HF dams nursing Con pups (*open triangles*). Values are mean ± SE of 16 dams per group during pregnancy and 8 dams per group during lactation.

Con, control; *HF*, high-fat.

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Materials and Methods

Maternal diet and studies

A rat model of maternal obesity was created using a HF diet prior to and through pregnancy and lactation was utilized. Studies were approved by the Animal Research Committee of Harbor-UCLA Medical Research and Education Institute and were in accordance with the American Association for Accreditation of Laboratory Care and National Institutes of Health guidelines.

Sprague Dawley rats (Charles River Laboratories, Inc, Hollister, CA) were housed in a facility with constant temperature and humidity and on a controlled 12 hour light–12 hour dark cycle. Beginning as weanlings, female rats were fed a HF (60% k/cal fat; Purified Diet 58Y1, New Brunswick, NJ; n = 16) or control (Con; 10% k/cal fat, Purified Diet 58Y2; n = 16) diet. The nutrient composition is given in Table 1. At 11 weeks of age, the rats were mated and continued on their respective diets during pregnancy and lactation.

Maternal body weights and their food intake were recorded daily. In addition, maternal blood was obtained via a tail bleed at term (gestational age embryonic day [e] 20) and at the end of lactation (21 days postpartum) for glucose, lipid, and hormonal analysis (details are given in the following text). The food was removed 1 hour prior to the blood sampling. Furthermore, at the end of lactation, dams underwent a noninvasive dual-energy x-ray absorptiometry (DEXA) scan (details are given in the following text) for evaluating percentage body fat and lean body mass.

The offspring

At birth, pups were culled to 8 per litter (4 males and 4 females) to normalize rearing and were cross-fostered, thereby generating 4 paradigms of maternal diets