

## JOURNAL CLUB

**Maternal nutritional history predicts obesity in adult offspring independent of postnatal diet**Margie H. Davenport<sup>1</sup> and Marta Rodriguez Cabrero<sup>2</sup><sup>1</sup>R. Samuel McLaughlin Foundation Exercise and Pregnancy Lab, School of Kinesiology, The University of Western Ontario, London, Ontario, Canada, N6A 3K7<sup>2</sup>Department of Health and Human Performance, Faculty of Physical Activity and Sport Sciences – INEF, Universidad Politecnica de Madrid, Ciudad Universitaria, Madrid 28040, Spain

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In the mid-1980s, Dr David Barker began a new field of work examining the impact of events that occurred during pregnancy on the long-term health of the fetus. This work led to the theory of Developmental Origins of Health and Disease (DOHaD). Since that time, researchers have found robust epidemiological links between fetal environment and long-term health. Much of the original research into DOHaD centred around the effects of under-nutrition. With the rising prevalence of maternal obesity and the hypercaloric environment of most developed countries, more recent studies have examined the effects of overnutrition on the development of diabetes, cardiovascular disease and obesity. Studies in humans have shown that the offspring of obese mothers are also more likely to be obese (Gale *et al.* 2007). However, the mechanism for this transfer of risk from mother to child is currently unknown. The relatively quick rise in the obesity epidemic suggests that environmental and/or epigenetic influences are at the root of the problem rather than a major shift in the genome in keeping with DOHaD.

In a recent issue of *The Journal of Physiology*, Howie *et al.* (2009) examined the long-term impact of a moderately high fat diet during preconception and/or pregnancy and lactation on postnatal growth and metabolism of the offspring

from birth to adulthood. After weaning, the authors assigned 24 weight-matched virgin Wistar rats to one of three groups: (1) controls (Cont) where dams were fed a standard chow diet throughout life; (2) maternal high fat (MHF) where dams were fed a high fat diet throughout life; or (3) pregnancy and lactation high fat (PLHF) where dams were fed a chow diet from weaning to conception and a high fat diet during pregnancy and lactation. At post-natal day 110, the dams underwent dual energy X-ray absorptiometry (DEXA) to assess body fat. Ten days later they were mated. Throughout gestation and lactation, the dams were weighed and food intake was measured on a daily basis. After delivery, the litter size was culled to eight pups (4 male and 4 female) who were weighed every 3 days until weaning. After weaning, plasma insulin and leptin levels were measured in the dams following an overnight fast. After weaning, the offspring were randomly assigned to a high fat or chow diet *ad libitum*. On day 150 body composition was assessed via DEXA in the offspring. Ten days later the offspring were killed to measure leptin, glucose and insulin concentrations.

This study is the first to examine the effect of a maternal high fat diet on critical time points during fetal development and post-weaning on long-term obesity in the offspring. The major findings of this study were: (1) the offspring of dams fed a high fat diet during pregnancy and lactation had significantly smaller pups; (2) a post-weaning high fat diet increased adiposity in all groups but the offspring whose dams were fed a high fat diet during pregnancy and lactation (MHF and PLHF) had elevated adiposity compared to Cont regardless of post-weaning diet; (3) this increased adiposity was accompanied by hyperinsulinaemia and hyperleptinaemia; and (4) maternal pre-conceptual diet did not impact offspring adiposity.

The authors suggest that it is the diet in pregnancy and lactation, not pre-conception, that is the important influence on the long-term health of the offspring. Recently Bayol *et al.* (2008) examined the impact of a 'junk food' diet during pregnancy and lactation on adiposity of the offspring. These authors found that a maternal junk food diet increased adiposity in the offspring (at 70 days post delivery).

They found that the adiposity that occurs as a result of a maternal junk food diet is not reversed when the offspring are fed a chow diet after weaning. The combined results of these two studies could have major implications for prevention of childhood obesity. Lifestyle interventions that begin during pregnancy which emphasize healthy eating may be able to break the trans-generational risk of obese mothers raising obese children. However, in order to more conclusively demonstrate the importance of a healthy diet during pregnancy and lactation, a fourth group should be added to the study by Howie *et al.* (2009). This potential fourth group would be placed on a high fat pre-conceptual diet followed by a chow diet during pregnancy and lactation. If offspring adiposity is unchanged from the Cont group or lower than the MHF and PLHF groups, this would lend strong support to dietary interventions in the pregnancy and lactation period to prevent childhood obesity.

It was unfortunate that maternal glucose was not measured during pregnancy (Howie *et al.* 2009). Although the authors suggest that gestational diabetes can be ruled out in the MHF and PLHF groups since the offspring were not macrosomic, it has been shown in human populations that pregnancies affected by gestational diabetes can result in growth-restricted infants. In addition, maternal obesity *per se* has been found to adversely affect glucose metabolism in the offspring (Chen *et al.* 2008). Although glucose levels were not different for offspring groups in adulthood, glucose levels were not measured immediately after delivery (Howie *et al.* 2009). Alternatively, the finding of smaller offspring could be a reflection of the composition (fat, protein and carbohydrate) of the maternal diet. A diet that is high in fat means that it is lower in carbohydrates and/or protein. Studies examining the effects of a low protein maternal diet indicate that the offspring are of a lower birth weight than those whose mothers ate sufficient protein during pregnancy. Since the composition of the high fat maternal diet was not reported, this possibility cannot be ruled out.

Leptin and insulin resistance is a common phenotype of diet-induced obesity. Leptin works with insulin to directly affect the

hypothalamic regulation of appetite (Chen *et al.* 2008). The adult offspring of MHF and PLHF dams in the present study were both hyperinsulinaemic and hyperleptinaemic indicating resistance to these hormones (Howie *et al.* 2009). However, 2 days after delivery the offspring of MHF and PLHF dams exhibited suppressed leptin and insulin. Although these findings are of interest, they do not provide insight into the role that leptin and insulin may play in the development of adiposity in the offspring. The authors note that they are currently investigating this relationship; however, Chen *et al.* (2008) examined the effect of a maternal high fat diet on offspring appetite regulation and metabolism at 20 days after delivery. These authors found that maternal obesity caused programming *in utero* of the brain appetite centres via increases in neuropeptide Y and decreases in proopiomelanocortin (POMC) potentially through regulation via leptin. Offspring appetite is set within weeks after delivery and low levels of leptin can programme the brain appetite centres to increase appetite throughout life. Bouret *et al.* (2004) demonstrated that administration of leptin soon after delivery could prevent the programming of increased appetite; however, administration in adulthood had no effect. These results indicate that there are critical periods during offspring development (pregnancy and the early post-

partum period) for the development of appetite regulation.

Howie *et al.* (2009) found that the relative pregnancy weight gain was not different between the three groups. As a result they suggest that it is the composition of the maternal diet rather than excess caloric intake resulting in an elevated pregnancy weight gain that affects offspring obesity. However, in humans there are guidelines for maternal weight gain set by the Institute of Medicine in 1990 which recommends a decreased maternal weight gain with increasing BMI. Since dams who were fed a high fat diet before conception started pregnancy at a higher body mass, it could be suggested that these dams should have gained less weight during pregnancy and the finding that they gained the same amount of weight was actually detrimental. The authors' suggestion that composition (fat, protein and carbohydrate) of the maternal diet is more important than maternal weight gain in determining offspring obesity requires further investigation. Future studies examining the effect of a maternal hypercaloric, normal fat diet compared to a normal caloric, high fat diet on offspring obesity during adulthood would be interesting.

In summary, the authors are to be commended for their investigation of the influence of a maternal high fat diet on the long-term outcome of the offspring.

This information suggests that dietary interventions that begin after conception could have a profound impact on the long-term health of the offspring.

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