Reply to KN Litwak and S Levin

Dear Sir:

We agree with Litwak and Levin that clinical trials are the best way to determine human health effects of dietary components. However, nonhuman primates offer experimental control and an anatomically and physiologically representative animal model and have inherent value in translational research. Details regarding study methodology are available on request, as they were at the time of review. Studies were conducted appropriately with regard to animal selection, known caloric intakes, and comparable dietary volume (our Table 1: caloric density was only 5% different). Species were not collapsed in any statistical analyses, because study 1 was conducted in cynomolgus macaques and study 2 in African green monkeys. Both species showed liver pathology with consumption of the same diet, which upholds the commonality in primate physiology that imparts value to dietary studies in monkeys. We believe that our results indicate that microbial translocation is an understudied factor in the epidemic of fatty liver and that the role of fructose deserves further investigation.

None of the authors had any conflicts of interest with respect to the work presented.

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Study examining effects of poor nutrition during pregnancy and lactation in a primate lacks translatability

Dear Sir:

The recent article by Keenan et al (1) intends to describe, in a nonhuman primate, the effects of poor nutrition during pregnancy and lactation on future neurodevelopment of the offspring. Certainly, this is a relevant topic to study because many epidemiologic studies have associated insufficient intakes of calories, proteins, and micronutrients by the mother with poor developmental outcomes in the child. However, beyond the ethical issues with regard to the use of animals for questions better answered in human investigations, there are important scientific flaws in the study design, which contains multiple confounding variables that have not been adequately described and likely have a significant effect on the outcomes, interpretation, and utility of the data.

Prenatal characteristics

The maternal nutrient restriction (MNR) diet was based on consumption of the control monkeys at the time of pregnancy assessment. Thus, the amount of food that was consumed by the MNR group, as a percentage of their baseline consumption, could have been quite variable. In fact, as described previously by this group (2), using the control group to set the diet of the restricted group resulted in a 41% decrease in calories offered. Because the weight of the monkeys was determined frequently and they were fed individually, it should have been possible to better control the caloric value of the diet. Although the diet was certainly restricted from baseline levels, it is unclear if the decrease represents undernutrition. Pursuant to that point, data previously published by this group describe minor weight loss (<10% of baseline) in nutrient-restricted females but no fetal size difference compared with controls. Finally, the pregnant females were housed in 2 groups of up to 16. Maternal social status and associated stress play a significant role in fetal development and have been shown to have long-term effects on the neonate (3).

Postpartum description

The authors’ Table 1 describes the morphologic characteristics of the MNR and control offspring. Whereas there appears to be a difference in weight between groups (MNR compared with control: 0.74 ± 0.05 compared with 0.88 ± 0.04 kg), both are within the normal range of baboon birth weights (4). The authors describe the juveniles being moved in cohorts of 5–7 over a period of 9 mo to a different facility, where they were singly housed. However, there is no description of when juveniles were removed from their mother and their initial age at the time of single housing, both of which could have had a much greater effect on neurodevelopmental outcomes than gestational nutrition. In fact, many studies have shown the deleterious effects of social impoverishment on physiologic and behavioral processes (5). Finally, there was no mention of other studies to which the juvenile monkeys were exposed over the intervening time between separation from their mother and conduct of the current study.

Diet

The term “poor nutrition” defines a broad category of nutritionally incomplete diets. In the context of this study, it was used to define a lack of calories; however, the term can also be used for overly high-calorie diets, high-fat diets, diets lacking in nutrients, etc. Use of the appropriate descriptive terms will help readers assess the value of the data. Because no data were presented on the weights of the mothers during pregnancy, it is impossible to assess if the amount of diet consumed by the mothers was lacking in calories, the central tenet of the article.

The authors state that in all human studies poor nutrition occurs in the context of psychosocial stressors and genetic risk factors. They then state that a controlled study in a well-established