DOHaD 2026 ABSTRACT

In-Utero High-Saccharide Exposure Leads to Altered Fetal Heart Development and Can Program Cardiometabolic Dysfunction in Postnatal Life

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Background:
The heart is one of the first organs to develop and is highly sensitive to the *in-utero* environment. This study investigates the effect of maternal high-fructose or sucrose consumption on fetal heart development and whether these changes carry postnatal consequences for cardiac structure and function.

Methods:
Female C57BL6/J mice were allocated to a high-fructose, high-sucrose or matched control diet (AIN93G). After 5 weeks on their diet, mice were time mated.

In one cohort, gestation ceased at E17.5 to assess fetal development. Fetal body, heart and placental weight were measured, and underwent -omic profiling. In another cohort, pregnancies were carried to term, and the day after birth offspring either stayed on their maternal diet or switched diets. Offspring underwent cardiac and metabolic phenotyping over 30-weeks. Hearts were harvested at 30-weeks for -omic and histological analysis.

Results:
Fetal heart weights were significantly increased in response to both maternal high-fructose and sucrose diets compared to AIN93G.

At 30 weeks, male mice exposed to high-sucrose at any time point had significantly increased systolic and diastolic blood pressure (BP) compared to lifelong AIN93G, and males on lifelong high-fructose had significantly increased diastolic BP. In females, diastolic BP increased when mice were switched from AIN93G to high-sucrose. In males, E/e' ratio, indicating diastolic dysfunction, was increased when switched from *in-utero* sucrose to AIN93G. Fibrosis was increased in males on a diet switch compared to lifelong AIN93G.

Conclusions:
In-utero high-saccharide exposure alters fetal heart development, producing lasting changes in postnatal heart structure, systolic, and diastolic function.