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### Programmed cardiac dysfunction due to prenatal exposure to maternal obesity vs. postnatal obesity

Loche E, Blackmore HL, Carpenter AA, Beeson JH, Pinnock A, Ashmore TJ, Aiken CE, de Almeida-Faria J, Schoonejans JM, Giussani DA, Fernandez-Twinn DS, Ozanne SE. Maternal diet-induced obesity programmes cardiac dysfunction in male mice independently of post-weaning diet. **Cardiovasc Res** 2018;114:1372-84. <http://doi.org/gddkvz>

During pregnancy, maternal obesity is associated with higher risk of developing obesity, metabolic disorders and cardiovascular diseases during postnatal life. This concept that the environment experienced by an individual during early life can shape its long-term health has been termed “developmental programming”. Experimental studies in animal models has shown that maternal over-nutrition during gestation increases the long-term risk of cardiovascular disorders in the offspring such as endothelial dysfunction, hypertension, left ventricular hypertrophy, fibrosis and left ventricular dysfunction, which are associated with metabolic conditions including hyperinsulinemia and increased glucose levels. These results were also confirmed by epidemiological studies which demonstrated that maternal body mass index during gestation positively correlates with premature death from cardiovascular events in the offspring. In addition, the offspring of obese mothers who underwent bariatric surgery have lower risk of developing cardiometabolic diseases compared to their siblings born before surgery. All this scientific evidence supports the idea that postnatal cardiovascular and metabolic risk may be programmed as a consequence of maternal environment during fetal life. However, the risk of developing these diseases also depends on the postnatal environment. Children born to obese women are more likely to be exposed to a family environment with obesogenic lifestyle which implies that the programmed cardiovascular risk may be further modified.

In this interesting study performed in mice, Loche et al. determined the consequences of combined exposure to a maternal and post-weaning obesogenic fat rich/fructose rich diet on offspring metabolism, blood pressure and cardiac structure and function. They used male offspring of obese mothers fed an

obesogenic diet during gestation and lactation, and another group of male offspring of mums fed normal diet. The offspring were divided into groups weaned onto obesogenic diet or normal diet for 8 weeks. The results show maternal obesity programmed offspring mice hypertension, abnormal remodeling of the left ventricle and ventricular dysfunction. These effects were mediated by the transcriptional re-activation of cardiac fetal genes as well as genes involved in the regulation of contractile function and matrix remodeling in the adult heart. A post-weaning obesogenic diet coupled with a maternal obesity worsened offspring hyperinsulinemia, hyperleptinemia, fat accretion, hypertension risk and cardiac fibrosis. In contrast, the post-weaning obesogenic diet caused cardiac dysfunction in control offspring but did not worsen the programmed cardiac dysfunction in the offspring of obese dams. Thus, obesity per se can act synergistically with maternal obesity to further increase circulating insulin and leptin levels, which may contribute to hypertension risk but not to additional loss of cardiac function.

*Obesity has reached epidemic levels worldwide and obese people exceed underweight people in number. Obesity is a risk factor for the development of cardiovascular diseases and, therefore, is one of the main causes of mortality. The progressive increase of obesity in women of childbearing age is a particularly alarming epidemiological finding. This concern is based on the fact that the increase in body weight is not only harmful to maternal health, predisposing mothers to obstetric complications (hypertension, gestational diabetes or abortion), but also to their offspring's health. An obese mother can compromise her offspring health in short term, with complications such as congenital defects or fetal death, or in the long term through developmental programming and the resulting predisposition to cardiometabolic conditions. Understanding the effects of maternal obesity on their offspring versus obesity induced by postnatal environment has important implications in terms of preventing obesity and its associated cardiovascular risk. The findings of this study suggest that the effect of obesity during pregnancy on cardiac dysfunction is similar to that of postnatal obesity; hence, this period is an important target for interventions aimed at reducing cardiovascular disease.*