

Rare pregnancy condition programs babies to become overweight in later life

June 24 2013

Babies born to mothers who suffer from a rare metabolic complication during pregnancy are programmed to be overweight, according to a study published today in the *Journal of Clinical Investigation*.

The study is the first to look at the long term effects on babies born to mothers with intrahepatic cholestasis of pregnancy (ICP), also called obstetric cholestasis, a rare [complication of pregnancy](#) characterised by the build-up of [bile acids](#) in the bloodstream.

The findings add to the strong evidence that the environment that babies are exposed to in the womb is a major cause of [metabolic diseases](#) in adults.

ICP can affect up to one in 50 pregnant women in different populations. It is caused by disruption in the flow of bile, a fluid produced by the liver to help with the digestion of fats. This can result in some leakage of bile, and in particular bile salts, into the bloodstream leading to symptoms including persistent itching and complications for both mother and baby.

The researchers looked at a cohort of babies born in Northern Finland between 1985 and 1986 and identified 45 babies who were born to mothers with ICP who were of healthy weight and had no other known diseases or complications, such as diabetes.

Although there were no differences in the birth weights of these babies

compared with infants born during the same period from normal pregnancies, the team found that by age sixteen, boys born from cholestatic pregnancies had a much higher [body mass index](#), by up to four points. They also had higher levels of the [hormone insulin](#) after a period of fasting, a symptom of [type 2 diabetes](#). Whilst the effect in girls was smaller, waist measurements from girls of the same age born to mothers with cholestasis were increased by up to 9cm and hip measurements by up to 5cm compared with girls born from normal pregnancies.

To further investigate the effects of cholestasis during pregnancy on the health of the offspring, the researchers created a mouse model of the disease by supplementing the diet of normal mice with cholic acid, a type of bile acid. Mice born from these pregnancies were also more prone to obesity and diabetes, confirming the findings from the human studies.

Dr Georgia Papacleovoulou, first author of the study from Imperial College London, explains: "This is the first evidence that cholestasis during pregnancy can have long-term effects on the health of the baby as it grows into adulthood."

Both the human and mouse studies revealed an increase in fats and excessive cholesterol transport in placentas from mothers with cholestasis compared with healthy mothers, consistent with a disruption in the metabolism of fats. The researchers propose that this shift in the nutrients supplied by the mother is likely to affect the energy balance in the unborn baby, something that could continue after the baby is born, resulting in an altered metabolism in adult life that could give rise to diseases such as obesity and diabetes.

Using another [mouse model](#), the researchers showed that feeding bile salts to mice during [pregnancy](#) resulted in chemical changes to the DNA

of the offspring, or epigenetic changes.

Professor Catherine Williamson, lead author of the study from Imperial College London and King's College London, said: "We don't yet know the exact mechanisms of how the increase in bile salts in the mothers' blood programs the unborn baby towards metabolic disease but it seems likely that epigenetics plays a role. We need to do more experiments to work out how these chemical changes to the DNA of the baby affect its ability to metabolise fats."

Dr Alison Cave, Head of Cellular, Developmental and Physiological Sciences at the Wellcome Trust, said: "We're in the grips of an epidemic of obesity and diabetes and this study adds to the increasing evidence which suggests that it may not be explained by unhealthy diets and lack of exercise alone. We know that the environment that babies are exposed to before they are born can have a huge impact on their health in later life. Studies like this are important to help us develop interventions that might be able to prevent these diseases arising in young adults."

More information: G. Papacleovoulou et al. Maternal cholestasis during pregnancy programs metabolic disease in offspring. *Journal of Clinical Investigation*, 2013. [epub ahead of print]

Provided by Wellcome Trust

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