ADIPS ANNUAL SCIENTIFIC MEETING 2007

Christchurch, NZ

The plenary lecturer for the 2007 Christchurch meeting was Sylvie Hauguel-de Mouzon. Sylvie's current positions are as Professor of Reproductive Biology at Case Western Reserve University, Cleveland, USA and Director of the OBGYN Research Division at MetroHealth Medical Center. She was awarded her PhD at the University of Paris. Her long-term research interest has been on placenta physiology and molecular biology. Her most recent focus is on the mechanisms of in utero metabolic programming in diabetes and obesity. She has always been very committed to enhancing the quality of basic and clinical research in the field of diabetes in pregnancy as is evident in her current Chairs of the Diabetes in Pregnancy Council of the American Diabetes Association and the European Diabetes in Pregnancy Study Group (DPSG). Sylvie's contribution to the Christchurch meeting was as expected, excellent. It was a great pleasure to have her attend.

Sylvie presented two different, but related, lectures on the placenta in maternal obesity and diabetes with some focus on the potential relevance of placental dysfunction on fetal development. The first was titled "Diabetes, adipocytokines and the fetal origin of obesity". The second was "Placental inflammation: an early determinant of prenatal obesity". From both lectures, it was clearly evident that both maternal diabetes and obesity have major effects on placental function, including effects on placental adipocytokine production and placental inflammation. A vast amount of non-pregnancy metabolic research in obesity has now shown inflammatory activity in adipose tissue and altered adipocytokine production from fat that have major roles in causing insulin resistance and the metabolic syndrome. The key messages from Sylvie's lectures were that increased inflammation and altered adipocytokine metabolism are also evident in the placenta in diabetes and obesity and that these changes most likely have both short and long term implications for the health of the neonate.

In the first lecture, the focus was on maternal diabetes and matters relating to leptin, tumour necrosis factor alpha (TNF-α) and adiponectin. Maternal plasma leptin is known to increase in normal pregnancy, but it is overproduced from the placenta in diabetic pregnancy and this is at least partly at the transcriptional level as placental leptin mRNA is increased. Leptin may have a physiological role in altering maternal metabolism late in pregnancy, including the enhancement of maternal fatty acid oxidation and this would favour sparing of maternal glucose for the fetus. In the placenta, there are leptin receptors on the maternal, but not the fetal side. Leptin action on placenta appears to promote mitogenesis causing placental growth and to stimulate fatty acid uptake. The latter may be potentiated in the presence of elevated glucose. Neonates of mothers with diabetes have higher cord leptin levels that are associated with fetal adiposity. Leptin has now been shown to have effects on the development of the hypothalamic appetite and weight control centres. It has been proposed that abnormal fetal leptin metabolism may have detrimental effects on programming of the hypothamic set-point for weight control.

TNF-α expression and content of placental tissues is also increased in diabetes and obesity. It almost certainly acts locally, as TNF-α is not released into the maternal or fetal circulations to any substantial degree. TNF-α is undoubtedly involved in the increased inflammation in diabetic placenta. Interestingly, TNF-α can increase the expression of leptin and also promote its own expression. Both TNF-α and leptin increase the activity of phospholipase A2 (PLA2) in placenta, and increased PLA2 increases levels of many polyunsaturated fatty acid moities (including the eiconasoids) within the placenta. These fatty acids can be involved in altering cellular membrane properties, various cellular signalling processes (many involved in inflammation) and are also provided to the fetus.

Adiponectin is the only adipocytokine that is reduced when fat mass is increased. It is present in large amounts in plasma and it is negatively associated with insulin resistance and parameters of the metabolic syndrome. It is very well established that plasma adiponectin is reduced when insulin resistance is high. In normal pregnancy, plasma adiponectin levels fall by about 30% and this is associated with about a 70% reduction in adiponectin mRNA in maternal fat tissue. This is probably related in some way to the physiological insulin resistance of pregnancy. In obesity and GDM, maternal adiponectin levels are usually lower again. Although there are some reports of adiponectin being produced by placental tissues, this is almost certainly not correct. Adiponectin can be detected by Western blot in placenta- because it is present within the fetal circulation. Adiponectin is present in fetal circulation at approximately 3 fold the levels found in the maternal circulation and this is derived from fetal fat tissue.

Interestingly, circulating fetal adiponectin and TNF-α correlate poorly with fetal adiposity. The correlations of fetal leptin with fetal adiposity, however, are very strong. Considering the recent discovery of important windows of time for leptin signaling for correct establishment of neural networks within the appetite/weight control centres of the hypothalamus, this may prove to be very important for future understanding of the fetal origins of childhood and adult obesity.

The second lecture expanded on the findings of increased inflammation within the placenta in obese mothers. Sylvie showed some very new and strong data with respect to placental macrophages. The number of placental stromal macrophages is dramatically increased in obese women. Further research is being directed to determine the origins of these macrophages with the assumption that they are probably from maternal origins and somehow associated with the increased numbers of macrophages in maternal adipose tissue of obese women. It seems less likely that they are from fetal origins. Following on from her first talk, the associated increased cytokines released by the macrophages are likely to alter placental function and may be particularly important in resulting in adipogenic signals for the developing fetus.

Both lectures demonstrated the importance of improved understanding of placenta from the basic science point of view in the maternal conditions of diabetes and obesity. We look forward to hearing the future outcomes of Sylvie's research.

Chris Nolan