Maternal diabetes has direct effect on childhood kidney disease

"...one in 400 live births were likely to develop childhood CKD, but that this risk was increased by 69% for children whose mothers had diabetes before they fell pregnant."

A recent study by a group from the University of Washington, USA has uncovered a link between maternal diabetes and the subsequent development of childhood kidney disorders in offspring.

The group studied more than 4000 patients with childhood chronic kidney disease (CKD) who were diagnosed before the age of 21 years, and more than 20,000 healthy children in order to identify a possible relationship between diabetes and obesity during pregnancy and the risk of developing childhood CKD.

It was found that approximately one in 400 live births were likely to develop childhood CKD, but that this risk was increased by 69% for children whose mothers had diabetes before they fell pregnant. Similarly a 28% increased risk was observed for children whose mothers developed diabetes during their pregnancy. Interestingly, they also found that obesity during pregnancy resulted in a 22% increased risk for children.

As well as assessing the relationship between CKD diagnosis and diabetes during pregnancy, the research group also examined kidney-related birth defects, such as renal aplasia or dysplasia. Lead author of the study Christine W Hsu explains, "Developmental abnormalities of the kidney and urinary tract are the most common cause of childhood CKD." They observed a nearly 700% increase in the risk of kidney-related birth defects in the children of mothers who had diabetes prior to their pregnancy. Increases in risk were also observed for the children of mothers who developed gestational diabetes, were obese during their pregnancy and even for mothers who were overweight but not classified as obese.

Hsu points out that "previous studies have demonstrated that maternal diabetes is associated with an increased risk of general congenital abnormalities," adding that "Our research shows that childhood CKD is modestly associated with maternal diabetes and maternal overweight or obesity, with the strongest association between abnormal kidney development and maternal diabetes."

These results suggest that stricter weight control and diabetes management during pregnancy could lead to a decrease in children's risk of developing CKD. This could also have a knock-on effect on the risk of the child developing diabetes and other complications later in life as CKD in adults is often associated with diabetes and high blood pressure.

The study was somewhat limited by the fact that it was only able to identify those children who had been admitted to hospital as a result of their CKD, as well as the use of a broad definition of CKD. However, the relationships observed in this study has paved the way for future research into this area and further studies are already underway using a stricter definition of CKD.

Source: Hsu CW, Yamamoto K, Henry R, Symons J, de Roos A: Prenatal risk factors for childhood chronic kidney disease. Presented at: *American Society of Nephrology's 43rd Annual Meeting and Scientific Exposition*. Denver, CO, USA, 16-21 November 2010.

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Synthetic proteins could lead to new treatments for diabetes

Based on research started in 2009 a group from The Scripps Research Institute in Florida, USA has discovered a synthetic activator of two proteins that have key roles in both metabolic and immune functions.

In 2009, study director Tom Burris, professor in the Department of Molecular Therapeutics at Scripps Florida and his group, identified a high affinity synthetic inverse agonist of a pair of retinoid-related orphan (ROR) nuclear receptors. Using this initial compound, known as T1317, as a scaffold they synthesized a range of further compounds whose activities were then measured against an array of receptors, including the ROR nuclear receptors RORα and RORγ.

One particular compound was found to display a unique pharmacological profile which indicated a high potential for use as a chemical probe for assessing ROR receptor function. This compound, termed SR1078, functioned as a ROR agonist and was subsequently demonstrated to increased RORα transcription as well as RORγ dependent transcription in cell culture studies. This upregulation of transcription resulted in a significant increase in ROR receptor production.

The discovery of SR1078 represents the first synthetic ligand that functions as an agonist of both RORα and RORγ. These nuclear receptors have been implicated in the progress of some cancers and have recently become the drug development targets for metabolic diseases such as Type 2 diabetes and atherosclerosis. Studies using animal models have demonstrated that a loss of RORγ is associated with resistance to certain autoimmune diseases, whereas loss of RORα is associated with resistance to weight gain.

Burris and his group have used animal models to demonstrate that activation of RORα can stimulate secretion of FGF21 from the liver, which can have positive effects as a treatment for diabetes.

Whilst the full significance of the discovery of SR1078 is yet to be discovered, the findings by the group at The Scripps Research Institute demonstrate that it is selective for certain receptors and it works *in vivo*. Burris concludes that "these two properties give it significant potential as a possible therapeutic compound."

Source: Wang Y, Kumar N, Nuhant P *et al.*: Identification of SR1078, a synthetic agonist for the orphan nuclear receptors RORa and RORg. *ACS Chem. Biol.* DOI: 10.1021/cb100223d (2010) (Epub ahead of print).

Key role for dietitians in the management of diabetes

A recent study lead by Marion J Franz, a nutrition consultant, has reviewed nutrition practice guidelines for diabetes management, highlighting the essential role played by dietitians in aiding patients' self management of their diabetes.

Following their review of research literature, the group presented 29 key nutrition practice guidelines, which they believe will best help dietitians to support diabetes patients. The guidelines include recommendations for patient assessment, intervention selection and the subsequent monitoring and evaluation of patients' treatment. Franz notes that "The evidence is strong that medical nutrition therapy provided by dietitians is an effective and essential therapy in the management of diabetes."

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The guidelines include the major nutrition therapy factors: carbohydrates, including intake, glycemic index, sugars and sweeteners; protein intake; cardiovascular disease and weight management. The study aims to provide dietitians with a standardized outline for patient management and provides six key recommendations including consistent day-to-day carbohydrate intake for Type 2 diabetes patients, adjustment of insulin dose to match carbohydrate intake for Type 1 diabetes patients and the use of self glucose monitoring to enable patients to determine whether or not they are meeting their goals.

Franz's team provide evidence that proper nutrition therapy is essential for the successful management of both Type 1 and Type 2 diabetes and they hope that their guidelines can help dietitians to play a key role in the healthcare management of patients.

Source: Franz MJ, Powerse MA, Leontos C *et al.*: The evidence for medical nutrition therapy for Type 1 and Type 2 diabetes in adults. *J. Am. Diet Assoc.* 110(12), 1852–1889 (2010).

Computer program shows response of fat cells to exercise

Researchers develop method to assess cellular response to mechanical stresses.

Recent research at Tel Aviv University, Israel has lead to the development of a computer model for assessing the effects of mechanical stresses on fat cells.

Fat cells are responsible for the production of fat within our bodies. Lead author of the study Professor Amit Gefen hopes that by recreating fat cell structure using a computer model they will uncover methods to control the amount of fat produced by fat cells.

The idea behind the research is that fat cells are influenced by mechanical loads, that is, the amount of force placed on an area occupied by these cells. Applying mechanical loads to tissues has an effect on many different cells within the body. For example, bones and muscles at zero gravity are weakened due to the lack of mechanical load placed on them. As a result, many astronauts are often confined to a wheelchair for a short period following their return from prolonged space flight.

The team at Tel Aviv, hope that their model will enable them to determine how much mechanical load fat cells can tolerate before they begin to disintegrate.

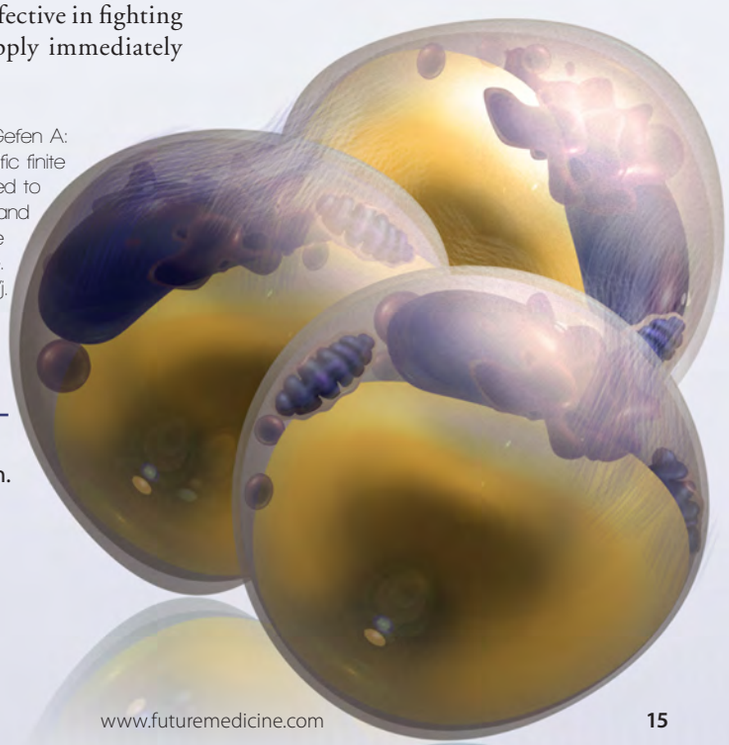
The computer model uses laser confocal microscopy images of tissue slices to reconstruct a virtual version of individual cells. The virtual cells can then be subjected to different mechanical loads and the outcome evaluated. Professor Gefen explains, "We use these computer models to see how cells function under mechanical loading, much like simulations in structural engineering are used to test the strength of bridges or machines."

Initial results have demonstrated that fat cells reach a point where the mechanical load placed on them causes them to disintegrate, and a separate point where they are able to resist disintegration. The team hope that their results will lead to better weight control methods, such as 'ab vibrators', through the ability to tailor the mechanical stresses applied to the fat cells.

The group now need to determine the specific loads and frequencies associated with the results they have observed so that they are able to predict how a fat cell will respond to particular levels of force. The hope is that this will lead to a better understanding of how to use mechanical loads to control fat production, which could have a big impact on rising obesity levels and consequent obesity related disease such as diabetes. Professor Gefen explains that "any treatment that would be effective in fighting obesity would also apply immediately to diabetes."

"The team at Tel Aviv, hope that their model will enable them to determine how much mechanical load fat cells can tolerate before they begin to disintegrate."

Source: Or-Tzadikarios, Gefen A: Confocal-based cell-specific finite element modelling extended to study variable cell shapes and intracellular structures: the example of the adipocyte. *J. Biomech.* DOI: 10.1016/j.jbiomech.2010.09.012 (2010) (Epub ahead of print).



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