

The legacy of hyperglycaemia in pregnancy

At the American Diabetes Association (ADA) 79th Scientific Sessions, both the maternal and paternal impacts on the metabolic health of children through intrauterine programming and epigenetic influence were the subject of intense interest and discussion. This topic was also briefly discussed during the British Society of Lifestyle Medicine conference in June. It is an exciting area where we, in primary care, may have the opportunity to influence the health of two generations with a single intervention, particularly through helping reduce the impact of over-nutrition in pregnancy on the child's metabolic health throughout life.

One out of every six births globally is now affected by hyperglycaemia during pregnancy, with nearly 90% of this related to gestational diabetes mellitus (GDM). Risks to both mother and baby from existing type 1 or type 2 diabetes, GDM or even high-normal glucose levels are explored in the International Federation of Gynecology and Obstetrics (FIGO) and International Diabetes Federation (IDF) joint statement on hyperglycaemia in pregnancy (Sadikot et al, 2018) and thought-provoking supporting articles. The 2018 Norbert Freinkel Award lecture, *Metabolic culprits in obese pregnancies and gestational diabetes mellitus: big babies, big twists, big picture*, was published recently in *Diabetes Care* (Barbour, 2019). In it, Linda Barbour reminded us that “fuel-mediated teratogenesis”, attributable not just to high glucose but also other nutrients, was described more than 40 years ago. In a recently published article in *Diabetologia*, an elegant record linkage study from Scotland demonstrates the association between maternal obesity at the beginning of pregnancy with increased incidence of type 2 diabetes in the offspring (Lahti-Pulkkinen et al, 2019). It is informative to explore both the short- and long-term impact of hyperglycaemia in pregnancy on mother and child.

From the mother's perspective, hyperglycaemia during pregnancy is associated with an increased risk of hypertension (including increased pre-eclampsia in GDM), obstructed labour, post-partum haemorrhage, infections, premature

delivery, large- and small-for-gestational-age babies, with an increased risk of stillbirths, congenital abnormalities (from pre-existing diabetes), neonatal deaths, hypoglycaemia and birth injuries (Mecacci et al, 2018). The stage of pregnancy when hyperglycaemia occurs and the level of hyperglycaemia both influence rates of complications. Interventions, such as increasing activity or changing diet during pregnancy, can reduce gestational weight gain, but this is likely to be too late to change pregnancy outcomes or ensure normal programming.

Rates of type 2 diabetes following GDM vary widely in different studies, with higher rates in the first 3–6 years and a 7-fold increased risk overall compared to women without GDM (Bellamy et al, 2009). Family history of diabetes, higher glucose levels, insulin required during pregnancy, older age, non-white ethnicity and additional pregnancies increase future type 2 diabetes risk.

Maternal hyperglycaemia, gestational diabetes (GDM), obesity and excessive weight gain during pregnancy can all contribute to macrosomia and excess adiposity in the infant, increasing longer-term risk of childhood overweight and obesity (Ma and Popkin, 2017). Longer term, children exposed to hyperglycaemia *in utero* are at increased risk of obesity, type 2 diabetes and cardiometabolic risk as a result of *in-utero* programming (Dabelea et al, 2008; Osgood et al, 2011; Armengaud et al, 2018). Birth weight <3000 g is associated with higher rates of GDM in adult life (Fabienke et al, 2018).

Maternal smoking, which is associated with *in-utero* under-nutrition and the increased risk of small-for-gestational-age babies, when combined with exposure to over-nutrition in later life, may also significantly increase cardiometabolic risk in the offspring.

Exposure to hyperglycaemia during pregnancy may be associated with neurodevelopmental problems, and increased risk of autism spectrum disorders has been associated with GDM diagnosed at <26 weeks' gestation (Xiang et al, 2015).

So, what can we do to lessen the impact? We need to code GDM, ensure we exclude type 2



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“Exposure to hyperglycaemia during pregnancy may be associated with neurodevelopmental problems.”

diabetes postnatally, and retest annually. We can help women understand their future risk of type 2 diabetes and the benefits of lifestyle interventions following pregnancy (Guo et al, 2016), including breast-feeding for at least 4 weeks and, ideally, >12 weeks. 4554 women with GDM in the Nurses' Health Study were followed to assess development of type 2 diabetes. Those who achieved at least 150 minutes of moderate-intensity physical activity per week reduced their risk of developing type 2 diabetes by 47% (Bao et al, 2014). If future pregnancies are planned, weight loss is more urgent, and benefits of optimising health and weight prior to conception should be shared. The ongoing LIPP (Lifestyle Intervention In Preparation for Pregnancy) study, discussed at the ADA meeting, will use a very low calorie meal replacement diet to help women achieve initial weight loss between pregnancies, and support them to maintain lower weight until conception and through the subsequent pregnancy, with the expectation that this will improve pregnancy outcomes and cardiometabolic risk of the offspring.

We can regularly track height, weight and BMI (with childhood BMI charts) in children of mothers with previous GDM and, where appropriate, discuss referral to agencies with expertise in managing obesity in children and young people. Since paternal programming also occurs via epigenetics, as well as postnatal paternal diet, lifestyle and environmental influences on the child, paternal pre-conception lifestyle advice may be an untapped area of influence. Most importantly, these are areas where brief interventions in primary care may make a difference to the health of both generations.

Journal update

We are excited to announce that, from the start of July, [registered readers](#) of *Diabetes & Primary Care* will receive fortnightly email updates of recently published content. In the first of these, we highlight a short article in which Rachel Pryke discusses [multimorbidity](#), and a comment piece by Peter Bagshaw in which he shares his thoughts on [dementia and diabetes](#).

Later this month, we will focus on nutrition, with the first part of Jane Diggle's guidance on diet in type 2 diabetes and *How to improve carbohydrate awareness*, reflecting the increasing interest from the ADA and other organisations

in the use of low-carbohydrate diets for weight loss and type 2 diabetes. In our *Breaking news* from the ADA meeting, we will include the results of REWIND (the cardiovascular outcome trial [CVOT] with dulaglutide), new cardiovascular data from CREDENCE (canagliflozin) and new data from DECLARE-TIMI 53 (dapagliflozin).

At the end of July, we'll share more from the meeting and provide guidance to help us incorporate the new findings in our practice. Our featured e-learning module will explore gastroenterological problems related to diabetes – our flyer will help you to see which aspects of the module would most inform your practice. On completion of the module and assessment, you will receive a certificate for your appraisal folder.

As part of a wider redesign of the Journal, we'll include shorter articles that reflect our need as busy clinicians for “information bites” that we can immediately use in our practice, rather than longer, time-consuming reads. Look out for our changes and, until then, enjoy your summer. ■

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