Early Life Exposures and Bone Health and Body Composition

This session was started by Prof Cyrus Cooper who discussed effects of maternal vitamin D supplementation on offspring bone mass. vitamin D supplementation (100U/day) trial resulted in a seasonal effect, where vitamin D increased BMD and BMC and bone area in offspring of mothers treated in winter. Furthermore, the supplementation also prevented decreases in maternal vitamin D loss normally seen in winter and spring. Prof Lisa Miclesfield discussed some preliminary findings from the Birth to 20 cohort in young South African adults using pQCT, which assesses volumetric BMD and bone geometry rather than the 2D areal density obtained from DXA. Cortical densities were found to be high at the radius and tibia in females compared to males. Sex significant associations were present, and it seems that early growth as well as current body size determine bone size and density in this cohort. Dr Karin Montz discussed the effects of alcohol consumption on offspring development. Very high rates of drinking in have been observed in young Australian women (who drink an average of 7 drinks a day at age 18-24), and the average consumption is 2-3 drinks per day for women. Most pregnancies in this population are unplanned (50%) and high rates of drinking and high rates of fetal alcohol exposure have been observed in Australia. Karin wanted to understand whether exposure to alcohol around the time of conception can program metabolism. The rat study conducted showed that alcohol intake up until the time of conception caused lower growth rates, insulin resistance, increased body fat and decreased lean mass in offspring. She now aims to start looking at mechanisms, epigenetics, and mother's biology such as factors in utero that could cause these problems. Prof Susan Carton discussed maternal DHA supplementation to assess whether maternal vitamin D supplementation trial resulted in a seasonal effect, where vitamin D increased BMD and BMC and bone area in offspring of mothers treated in winter. There are also significant benefits of maternal vitamin D supplementation on offspring bone mass. Less sleep was associated with higher BMI. Hazel cautioned against interventions at this point, as the full effects on body composition are still not well understood. Dr Caroline Childs discussed the effects of maternal Vitamin B status during pregnancy on offspring adiposity at 6 years. Low vitamin B2, B12, and B6 in pregnancy was related to higher adiposity at 6 years. Fat free mass also increased in this group. No effect was observed for fat mass. But B9 was not associated. Further work is being done looking at potential confounders and causal mechanisms. Dr Robert Levitan looked at the effects of maternal sensitivity (how a mother responds to infant signals) and child BMI. The 7 repeat DRD4 (dopamine 4 receptor gene) allele and plasticity effects of this gene were examined by looking at the MAVIDA study in Canada and the Generation R study in Europe. Greater effects of sensitivity on BMI in girls who have the gene have been observed in the Generation R study, but in the MAVAN study they only found this effect for boys. Low maternal sensitivity was associated with high BMI in girls in both cohorts, but further modifications were seen after considering the DRD4 gene. Dr Albert Koulman discussed lipid metabolism in infants and has shown differences in breast fed vs lipid fed offspring where high triglycerides in the mother's milk lead to high small dense LDL particles and high triglycerides in the infant. Therefore lipid composition of breast milk affects how infants process lipids. Dr Arend Van Deutekom presented on how to measure associations between birth weight and infant growth with energy balance behaviours (such as energy intake, eating behaviours, physical activity and sedentary behaviours). Generally, there was insufficient evidence for the association of infant growth with energy related behaviours. He suggested that a shift in focus from birth weight to infant growth should occur, and shift focus from physical activity measurements to sedentary behaviours. Lastly, Simon Scherbuchner looked at ethnic differences in pubertal bone accrual in Birth to 20 adults using pQCT. Simon wanted to understand if ethnic differences in bone accrual due to differences in puberty timing. Using STAR curves to model his data, males were found to have a 9 month difference in age at peak height velocity. Site specific differences were found even after adjusting for pubertal maturation. They therefore compared skeletal development should take differences in ethnicity and maturity into account.
DOHaD and Nutrition: Are we doing enough to improve birth and long term outcomes through maternal nutrition?

During this session, an overview of the current evidence on the role of nutrition in optimising short and long term infant outcomes was provided and key gaps in the research were identified for future prioritisation in this area. Maternal micronutrient supplementation has well-documented effects on fetal growth and birth outcomes; however, each intervention (balanced protein-energy, iron-folate and multiple micronutrient supplementation) addresses individual nutritional causes of fetal growth restriction. It is important to start considering interventions in combination, rather than as independent pathways, which are commonly found in undernourished settings where they present as multiple, rather than single deficiencies. By doing so, we may begin to see the additive effects of providing a comprehensive package of interventions to vulnerable pregnant women, rather than the beneficial, but perhaps limited, effects of isolated interventions.

Additionally, and particularly relevant for DOHaD, evidence for the medium/long term health benefits of early life micronutrient interventions in humans is limited and existing follow-up studies have focused on periods of the human life-cycle that have been identified as particularly mutable and developmentally plastic. For example, the rainy season. This would possibly create a greater gene risk across the life course, preconception and antenatal interventions need more and longer term follow-up, particularly in low-middle income undernourished and transitioning populations.

DOHaD and Translating Public Health Nutrition Policy into Action: Reaching the Hard to Reach

The DOHaD message has centered on intercepting negative trajectories from as early as conception. This session explored how the research evidence brought forth by DOHaD can be taken up by governments, translate into policy and application of interventions in order to change negative behaviour.

Research done in the UK Southampton Women’s Survey has shown that maternal diet has an impact on infant growth and health. Increased fat (FB) and lower IQ at age four resulted from poor maternal diet. Panel members from the University of Southampton demonstrated how the in the UK they have translated research into action through the Life-Lab intervention, which aims to change negative behaviors in teenagers such as poor diet choice, unhealthy life among other things. The theory behind Life-Lab is that negative behavior (poor diet choice) is much easier to change pre-pregnancy than during or post-pregnancy. The Life-Lab intervention is termed as “the educational intervention” because the teens are first taught in a classroom the theories of how poor health choices have adverse effects later on in life, then the students are allowed to come to the lab to scientifically tests those theories. It was shown that teenagers who took part in terms of healthy choices as opposed to teenagers that did not attend the Life-Lab. Another intervention that was tested and proven to be effective in changing female diet choices in Southwark, was changing the way which practitioners communicated the message of healthy nutrition, it was found that this changes behavior.

Evidence from Denmark showed that targeting and concentrating government resources on risk populations proved to be effective in changing behaviors. It is important for governments to address health inequities as a form of social policy, as mainly of low socioeconomic status population, the government partnered with schools & day-care institutions, media and supermarkets in order to drive the message of healthy eating. The last WHO policy change in guidance for nutritional supplementation of pregnant women was in 1968, namely the use of iron-folic acid supplementation during pregnancy to prevent and treat gestational anaemia. The Cochrane review published on 1 November 2015 is set to change this as the reviewers reported a strong bias in the evidence on the replacement of iron, folic acid with multiple-micronutrient supplements for pregnant women in low- and middle-income countries.

At this meeting, Parul Christian of John Hopkins reported that the benefits of multiple-micronutrient supplementation are over and above those seen with iron-folic acid use. A further recommendation was that in food insecure settings where maternal iron deficiency (DMI) and low birth weight prevalence is high, balanced protein energy supplementation is needed.

However, we have little data on the use of nutritional supplements during pregnancy as statistics are available from just 28 countries. Mean coverage of iron/folic acid supplementation is only 29%.

Phillip James reports that in The Gambia, nutritional status varies considerably between the dry and rainy season. Maternal pre-conception concentrations of folate, B2, bethaine and the SAM:SAH and the BET:DMG ratios were higher in the rainy season. An increase in these concentrations would possibly create a greater gene methylation potential.

DOHaD and Cardiovascular Disease

Various aspects of cardiovascular disease in childhood in animal and human studies were covered extensively in the Early life factors and cardiometabolism session. Despite having over 12 presentations in this session that spanned almost all continents, the time restrictions prevented the presenters from moving away from the standard of the papers or the high quality research that was presented. The main thematic areas of focus in this section was fetal growth and growth restriction; metabolic disease; hypertension and heart and vessel imaging.

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Early life exposures and later outcomes

The principles of DOHaD describe how early life exposures in conception, pregnancy, infancy and childhood can have a significant impact on health and diseases risk in later life. The presenters in this session sought to answer the above question by highlighting how early life environments affect children’s developmental outcomes such as body composition, cognition and cardiometabolism.

These were some of the findings reported by the speakers:

- Among indicators of physical development at birth, only head-circumference was the most prominent predictor of intelligence as measured by IQ in 1 year olds.
- It was reported that maternal HIV status was not associated with any outcomes. However, the higher maternal cognitive ability improved cognition to some extent. Further research is needed to investigate the role of maternal dietary patterns affect rates of asthma in the offspring, focusing on oily fish, vegetables and Vitamin D. Consumption of oily fish and Vitamin D were protective against asthma in the offspring.
- Lung development starts in utero and continues up to about 20 years of age and therefore disruptions at that period could potentially lead to a decrease in lung function on an earlier age. A Finnish study to investigate the effect of preterm birth on adult lung function indicated an independent effect of preterm birth and fetal life on lung function not explained or mediated by childhood obesity, current lifestyle or manifestation of obstructive airways disease. In the long term, fetal life may lead to increased lower body obesity.
- Around 60% of women of child-bearing age are obese in America and maternal obesity is a risk factor for offspring obesity in later life. In line with this the US Institute of Medicine has guidelines for weight gain in pregnancy. Using data from two US birth cohorts, the 60% investigators set out to assess the impact of exceeding current weight gain guidelines on the risk of obesity in offspring by age 40. According to Lauren Houghton the study showed that exceeding the guidelines tripled the risk of daughters being overweight/obese in midlife. Obesity in the offspring was seen even in girls who were not obese in childhood and further obesity was noted to be linked to a higher risk of hypertension that were born naturally.
- In the New Delhi Cohort it was found that mother-child versus father-child associations were stronger predictors of cardiometabolic risk, of which they postulated it to be an intergenerational transfare through intra-uterine programming.

Can we optimise maternal nutrition to minimize epigenetic errors?

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