Low maternal iodine consumption associated with impaired neurodevelopment of children

One of the most important things a pregnant woman can do to ensure the birth of a healthy child is eat nutrient-dense foods. Indeed, nutrient deficiencies during pregnancy can sometimes have severe outcomes for the baby. An example is iodine deficiency, which when severe can lead to the development of goiter (an enlarged thyroid gland) in the woman and permanent neurocognitive deficits (e.g., reduced IQ, or in the most severe form, cretinism) in the child. In fact, iodine deficiency during fetal development is considered the main cause of preventable brain damage globally. For this reason, substantial public health attention has been focused on preventing severe iodine deficiency around the world, with iodine supplements and fortified foods and other commodities (e.g., salt) often being deployed in this regard. However, much less is known about whether there are negative effects of less severe iodine deficiency during pregnancy. To help fill this research gap, Dr. Anne-Lise Brantsæter (Norwegian Institute of Public Health) and collaborators investigated this relation in an impressively large group of mother-child pairs living in Norway. Details about their study are published in the July 2017 issue of *The Journal of Nutrition*.

This study leveraged data collected from pregnant women and their children from 2002 and 2008; a total of 48,297 mother-child dyads were included. Maternal consumption of iodine from foods and beverages was estimated using a questionnaire administered during the first half of pregnancy. Selected neurodevelopmental milestones and markers were reported by the mothers when their children were 3 years old. This included information about language and communication skills, walking, gross and fine motor development, and behavior problems. The researchers then used sophisticated statistical analyses to investigate whether variation in maternal iodine intake was related to variation in these neurodevelopmental outcomes. Importantly, in the researchers mathematically controlled for a variety of potentially confounding variables such as maternal education, parental bilingualism, and intake of other nutrients such as folate and omega-3 fats.

Mothers who consumed the lowest amounts of iodine were at greatest risk of having children with language delays, behavior problems, and poor fine motor skills. Consuming iodine supplements did not appear to be related to improvements. The researchers concluded that their results “emphasize the urgent need for preventing inadequate iodine intake in women of childbearing age to secure optimal brain development in children.” They further posit that, with limited dietary sources of iodine and insufficient salt iodization, it is difficult to achieve the recommended intake of iodine even when adhering to current dietary guidelines. Because nationally-representative surveys also indicate
that pregnant American women are at risk of insufficient iodine intake, it is likely important that public health experts around the globe address this important health issue.

Reference

For More Information
To contact the corresponding author, Dr. Anne-Lise Brantsæter, please send an e-mail to annelise.brantsaeter@fhi.no.

Are pregnant women’s nighttime fasting habits related to neonatal growth?

Several decades of rigorous research have provided solid evidence that lifetime health and disease risks can be somewhat “programmed” into a child’s physiology during early life. This period of development, sometimes referred to as “the first 1000 days,” includes the time spanning pregnancy through a child’s 2nd birthday. For instance, lower-than-expected growth in utero (low birth weight) increases a newborn’s risk for cardiovascular disease later in life, and rapid weight gain in the first few months of life may predispose a child to increased risk of obesity. Maternal malnutrition during pregnancy is also thought to have long-lasting effects on a child’s health and well-being. Interestingly, emerging research suggests that babies born to moms engaged in nighttime shift-work (accompanied by alterations in habitual sleeping and eating patterns) are at higher risk of being born small. Whether this also translates into variation in obesity risk had not been investigated – that is until Dr. Fabian Yap (KK Women’s and Children’s Hospital, Duke-NUS Medical School, and Nanyang Technological University, Singapore) and colleagues studied it in a group of 384 pregnant women and their infants. Their results suggest that women’s night-fasting intervals are related to neonatal head circumference and body fat in girls, but not boys. The study is published in the July 2017 issue of *The Journal of Nutrition* and briefly described here.

To test their hypotheses, Yap and colleagues used data previously collected as part of the Growing Up in Singapore Towards healthy Outcomes (GUSTO), a study carried out in 2009 and 2010. Women were enrolled during their 2nd trimester of pregnancy and asked to complete detailed food records for 3 days as well as questionnaires concerning a multitude of lifestyle behaviors and health outcomes. Infants were carefully weighed and their head circumferences and lengths measured at birth. Each infant’s body fat was estimated using a mathematical equation and taking into account weight, sex, weeks gestation, and skinfold thickness. This information was then related to the mothers’ typical sleeping and eating patterns.

The researchers found that, on average, women experienced a ~10-hour nighttime period during which they did not eat. As the duration of this nighttime fasting increased so did head circumference and body fat of the babies; but this was only true for newborn girls, not boys. The relationship between moms’ nighttime fasting duration and girls’ head circumferences and body fat values could not be explained by differences in potentially confounding variables such as the mother’s age, ethnicity, education, employment status, eating frequency, and nighttime eating habits. Although the researchers admit that much work is needed to understand the physiologic basis of their findings, they hope their research will eventually lead to new approaches and recommendations related to optimizing maternal and infant health via paying attention to important variables such as length of nighttime fasting.

Reference

For More Information
To contact the corresponding author, Dr. Fabian Yap, please send an e-mail to fabian.yap.k.p@singhealth.com.sg.

Replacing refined sugars with egg protein and unsaturated fats may benefit heart health

Cardiovascular disease is the primary cause of death in the United States, and people who are at increased risk for heart disease and stroke often also suffer from obesity, inadequate blood sugar regulation, hypertension, and unhealthy blood lipid levels. As such, typical treatment regimens for cardiovascular disease often focus on practices and approaches that simultaneously foster weight loss while lowering blood pressure and helping regulate blood glucose. Central to many such approaches is the frequent recommendation to reduce or replace refined sugars – the simple sugars commonly added to food during processing that come in an extensive range of sweet products and beverages. However, one recent study suggests that replacing these sugars with a combination of egg protein and unsaturated fats may offer additional heart health benefits.

Reference
of these treatments is a healthy diet. But defining what “healthy” means in this context is more difficult than it sounds. Nonetheless, results from most well-controlled studies suggest that lowering refined carbohydrate intake may be helpful. Other studies point to a potential benefit of increasing protein, while still others advocate replacing saturated fats (e.g., animal fats and tropical oils) with unsaturated fats (e.g., vegetable oils and fish). However, few well-controlled dietary intervention studies have been conducted to substantiate these claims. The July 2017 issue of *The Journal of Nutrition*, however, features such a study.

This research was led by Dr. Kevin C. Maki (Midwest Biomedical Research: Center for Metabolic and Cardiovascular Health), and tested the hypothesis that substitution of refined starches and added sugars with a mix of protein and unsaturated fats would benefit glucose regulation and improve blood lipids. To test this, they enrolled 25 overweight or obese men and women with elevated blood triglyceride concentrations. None of the subjects had been diagnosed with diabetes, although most had insulin resistance. Each person participated in two dietary intervention periods. In one of them, they were provided a “control” diet providing ~60, 16, and 24% of calories from carbohydrates, protein, and fats, respectively. The other “experimental” diet provided ~44, 24, and 32% of calories from carbohydrates, protein, and fats, respectively. In this experimental diet, ~16% of energy from refined starches and added sugars in the control diet was replaced with egg protein and unsaturated fats from oils. Both diets provided enough calories to maintain body weight, and saturated fats were low (≤ 7%) in each. Each diet was consumed for 3 weeks, and their order was randomized among participants. Subjects were evaluated at the beginning of the study and at the end of each diet period for a variety of markers for cardiovascular risk.

The replacement of ~16% of energy from refined starches and added sugars with a combination of egg protein and unsaturated fats improved blood sugar regulation (insulin sensitivity) and altered several markers of cardiovascular health, including lowering triglycerides and increasing low-density lipoprotein (LDL, the “bad” form of cholesterol) particle size. The researchers remind us that their results are supportive of the recommendations put forth in the most recent version of the Dietary Guidelines for Americans.


**For More Information** To contact the corresponding author, Dr. Kevin Maki, please send an e-mail to kmaki@mbclinicalresearch.com.

---

**The Journal of Nutrition Editor's Picks**

- Studies to determine the benefit of vitamin D supplementation in older adults should focus on those with low serum concentrations
- Expression of placental iron and zinc transporters are impacted by maternal iron and zinc status
- The relative proportion of RRR-α-tocopherol in maternal plasma and milk are affected by the type of supplement used

**Studies to determine the benefit of vitamin D supplementation in older adults should focus on those with low serum concentrations**

The existing epidemiological literature suggests an inverse association exists between serum vitamin D concentration and mortality. These observations led to studies that assessed the impact of vitamin D supplementation on mortality, but few studies have considered baseline vitamin D [25(OH)D] levels when selecting subjects for the studies. As a result, those using subjects with adequate vitamin D levels has led to either no benefit being detected or even a negative impact on mortality being observed. Responses such as these suggest that inclusion of subjects with adequate vitamin D status may inhibit the identification of health benefits associated with vitamin D supplementation in those that do not have adequate vitamin D levels. Brenner and colleagues addressed this issue by conducting a study to explore the impact of experimental designs on the power of intervention studies and the resulting detected effect sizes. Their work is published in the July 2017 issue of *The Journal of Nutrition*.

Subjects (n=9579) in this study were enrolled in the German ESTHER study and were between 50 and 75 years old. Serum concentrations were determined...
at baseline and they were used to establish relationships with all cause mortality, or mortality from cardiovascular disease and cancer during the 12.4 year follow up period. Risks for each cause of mortality were estimated for defined increases in serum 25(OH)D across the full range of 25(OH)D concentrations or for those with 25(OH)D insufficiency or deficiency only. From these analyses, the authors were able to calculate the power of an intervention study to achieve specific effect sizes when the study did not discriminate on subject 25(OH)D levels or utilized only those with an insufficient or deficient 25(OH)D level.

There was an inverse association between mortality and serum 25(OH)D, but only for subjects in which the 25(OH)D levels were either insufficient or deficient. In fact, the strongest relationship was detected for those subjects with deficient serum 25(OH)D levels. Therefore, the power of the study to detect a benefit was higher when it targeted those individuals with low serum 25(OH)D instead of using an untargeted approach. If an untargeted intervention approach were used, it would be necessary to recruit much larger study populations to detect significant changes in mortality. The authors concluded that future studies using targeted supplementation approaches would identify much stronger effects with enhanced power.


For More Information To contact the corresponding author, Hermann Brenner, please send an email to h.brenner@dkfz.de.

Expression of placental iron and zinc transporters are impacted by maternal iron and zinc status

Deficiencies of iron and zinc are common in women of childbearing ages in sub-Saharan Africa. Deficiencies in iron and zinc are associated with poor pregnancy outcomes, such as low birthweight, being small for gestational age and being born premature. Many women in these areas also suffer from other micronutrient deficiencies, and as a result, supplementation strategies typically use supplements containing multiple micronutrients (MMN). Other approaches include a targeted iron and folic acid supplement (FeFol) or newer lipid-based nutrient supplements (LNS) that provide a potentially enhanced route of delivery. Little is currently known about the impact of maternal status and supplementation on placental iron and zinc transporters or fetal iron and zinc availability. To determine if supplementation is enhancing absorption of iron and zinc by the placenta and thus improving availability to the fetus, Jobarteh and colleagues evaluated the impact of MMN, FeFol and LNS supplements on placental expression of zinc and iron transporters as well as fetal cord blood iron and zinc concentrations. Results of their study are reported in the July 2017 issue of The Journal of Nutrition.

Subjects were those included in the prenatal arm of the Early Nutrition and Immune Development (ENID) trial conducted in Gambia, a randomized trial to determine the impact of supplements on infant immune development. The women (19-45 years old) included in this arm of the study were randomly assigned to receive supplements containing: 1) FeFol tablets, 2) MMN tablets, 3) protein and energy (PE) in an LNS, or 4) PE and MMN in an LNS (PE+MMN). Subjects underwent health assessments at enrollment, and at 20 and 30 weeks of gestation. The expression of zinc and iron transporter genes in placenta, iron levels in cord blood, and maternal plasma iron status were determined in 301 mother-infant pairs.

The PE and PE+MMN supplements resulted in 45 and 78% lower maternal plasma iron concentrations than the FeFol and MMN groups. Placental iron transporter gene expressions were 30-49% higher in the others receiving the PE and PE+MMN supplements than those receiving the FeFol supplement. Cord blood contained less of the iron storage/transport protein ferritin in those individuals receiving either of the LNS-based supplements. Zinc supplementation via the MMN supplements resulted in higher maternal plasma zinc concentrations. Use of the PE+MMN supplement led to reduced expression of zinc transporters, as compared to use of the non-zinc containing supplements. The authors concluded from these observations that placental expression of iron and zinc uptake proteins are upregulated when maternal iron levels are low and when zinc is not supplemented. They suggest this is occurring in an attempt to meet the demands by the fetus for these essential micronutrients when maternal supplies are low.

Reference Jobarteh ML, McArdle HJ, Holtrop G, Sise EA, Prentice AM, Moore SE. mRNA levels of placental iron and zinc transporter genes are upregulated in
The relative proportion of RRR-α-tocopherol in maternal plasma and milk are affected by the type of supplement used

Vitamin E deficiency is not a common occurrence, however, a deficiency in this micronutrient can contribute towards impairments in nervous system functioning. Newborns typically have low levels of α-tocopherol (the most abundant isomer of all vitamin E isomers), which means they are dependent upon colostrum, milk or infant formulas to meet their vitamin E requirements. A contributor to this low level of vitamin E in neonates is that most women in the United States do not consume the current estimated average requirement. Therefore, among women of childbearing age, supplementation is important in order to meet the daily requirements. Vitamin E in plant foods is made up of only the RRR-α-tocopherol stereoisomer, whereas chemically synthesized supplements (referred to as all-rac-α-tocopherol) contain a mixture of the 8 possible stereoisomers (RRR, RRS, RSR, RSS, SRR, SSR, SRS, and SSS). Only the RRR-α-tocopherol and 2R stereoisomers of all-rac-α-tocopherol are able to meet the vitamin E requirements in humans. Although studies have described the impact of α-tocopherol supplementation approaches on the level of total α-tocopherol in human milk, no work has been done to determine the impact of the stereoisomers in supplements on the distribution of stereoisomers in maternal plasma and milk. Gaur and colleagues addressed this void in our understanding of the impact of vitamin E supplementation on the availability of the essential isomers in milk and report the results of their study in the July 2017 issue of The Journal of Nutrition.

Subjects in this study were mothers (n=89) of singleton births within 4-6 weeks of giving birth prior to selection for the study, and who planned on continuing breastfeeding for 6 more weeks. Participants abstained from taking supplements containing lutein, DHA and -tocopherol for at least 10 days prior to starting the experiment and for the entire study. The mothers were assigned to receive the following supplements for 6 weeks: 1) 45.5 mg all-rac-α-tocopherol (ARAC), 2) 22.8 mg all-rac-α-tocopherol + 20.1 mg RRR-α-tocopherol (MIX), or 3) 40.2 mg RRR-α-tocopherol (RRR). Milk and blood samples were acquired before starting the supplements and at the end of the 6-week experiment.

RRR-α-tocopherol was the most abundant isomer in both maternal plasma and breast milk. The type of supplement influenced the α-tocopherol stereoisomer profile in milk and plasma. The RRR supplement led to an increase in the percentage of RRR-α-tocopherol in plasma and milk, whereas the percentage of RRR-α-tocopherol decreased when the ARAC and MIX supplements were used. The authors concluded that these observations indicate that the type of α-tocopherol supplementation strategy influences the availability of RRR-α-tocopherol in milk, which suggests the need for further research to explore the influence of differing maternal supplementation strategies on α-tocopherol status of breastfed infants.


For More Information To contact the corresponding author, Christina L. Sherry, please send an email to Christina.sherry@abbott.com.