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The Journal of Nutrition Media Alerts

The following articles are being published in the July 2017 issue of *The Journal of Nutrition*, a publication of the American Society for Nutrition. Summaries of the selected articles appear below; the full text of each article is available by clicking on the links listed. Manuscripts published in *The Journal of Nutrition* are embargoed until the article appears online either as in press (Articles in Press) or as a final version. The embargoes for the following articles have expired.

- Lowmaternal iodine consumption associated with impaired neurodevelopment ofchildren
- Are pregnantwomen's nighttime fasting habits related to neonatal growth?
- Replacing refinedsugars with egg protein and unsaturated fats may benefit heart health

Lowmaternal iodine consumption associated with impaired neurodevelopment ofchildren

One ofthe most important things a pregnant woman can do to ensure the birth of ahealthy child is eat nutrient-dense foods. Indeed, nutrient deficiencies duringpregnancy can sometimes have severe outcomes for the baby. An example is iodinedeficiency, which when severe can lead to the development of goiter (anenlarged thyroid gland) in the woman and permanent neurocognitive deficits(e.g., reduced IQ, or in the most severe form, cretinism) in the child. Infact, iodine deficiency during fetal development is considered the main causeof preventable brain damage globally. For this reason, substantial publichealth attention has been focused on preventing severe iodine deficiency aroundthe world, with iodine supplements and fortified foods and other commodities(e.g., salt) often being deployed in this regard. However, much less is knownabout whether there are negative effects of less severe iodine deficiencyduring pregnancy. To help fill this research gap, Dr. Anne-Lise Brantsæter(Norwegian Institute of Public Health) and collaborators investigated thisrelation 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*.

Thisstudy leveraged data collected from pregnant women and their children from 2002and 2008; a total of 48,297 mother-child dyads were included. Maternalconsumption of iodine from foods and beverages was estimated using aquestionnaire administered during the first half of pregnancy. Selectedneurodevelopmental milestones and markers were reported by the mothers whentheir children were 3 years old. This included information about language andcommunication skills, walking, gross and fine motor development, and behaviorproblems. The researchers then used sophisticated statistical analyses toinvestigate whether variation in maternal iodine intake was related tovariation in these neurodevelopmental outcomes. Importantly, in the researchersmathematically controlled for a variety of potentially confounding variables suchas maternal education, parental bilingualism, and intake of other nutrientssuch as folate and omega-3 fats.

Motherswho consumed the lowest amounts of iodine were at greatest risk of havingchildren with language delays, behavior problems, and poor fine motor skills.Consuming iodine supplements did not appear to be related to improvements. Theresearchers concluded that their results "emphasize the urgent need forpreventing inadequate iodine intake in women of childbearing age to secureoptimal brain development in children." They further posit that, with limiteddietary sources of iodine and insufficient salt iodization, it is difficult toachieve the recommended intake of iodine even when adhering to current dietaryguidelines. Because nationally-representative surveys also indicate

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Oct 15-20. IUNS-ICN Meeting (Buenos Aires)

June 9-12, 2018. Nutrition 2018, ASN's nutrition focused conference, debuts in Boston.

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thatpregnant American women are at risk of insufficient iodine intake, it is likelyimportant that public health experts around the globe address this importanthealth issue.

Reference Abel MH, Caspersen IH, Meltzer HM, Haugen M, Brandlistuen RE, Aase H,Alexander J, Torheim LE, Brantsæter A-L. Suboptimal maternal iodine intake isassociated with impaired child neurodevelopment at 3 years of age in theNorwegian Mother and Child Cohort Study. *Journalof Nutrition* 147:1314-1324.
ForMore Information Tocontact the corresponding author, Dr. Anne-Lise Brantsæter, please send ane-mail to annelise.brantsaeter@fhi.no.

Are pregnantwomen's nighttime fasting habits related to neonatal growth?

Severaldecades of rigorous research have provided solid evidence that lifetime healthand disease risks can be somewhat "programmed" into a child's physiology duringearly life. This period of development, sometimes referred to as "the first1000 days," includes the time spanning pregnancy through a child's 2ndbirthday. For instance, lower-than-expected growth *in utero* (low birth weight) increases a newborn's risk forcardiovascular disease later in life, and rapid weight gain in the first fewmonths of life may predispose a child to increased risk of obesity. Maternalmalnutrition during pregnancy is also thought to have long-lasting effects on achild's health and well-being. Interestingly, emerging research suggests thatbabies born to moms engaged in nighttime shift-work (accompanied byalternations in habitual sleeping and eating patterns) are at higher risk ofbeing born small. Whether this also translates into variation in obesity riskhad not been investigated – that is until Dr. Fabian Yap (KK Women's andChildren's Hospital, Duke-NUS Medical School, and Nanyang TechnologicalUniversity, Singapore) and colleagues studied it in a group of 384 pregnantwomen and their infants. Their results suggest that women's night-fastingintervals are related to neonatal head circumference and body fat in girls, butnot boys. The study is published in the July 2017 issue of *The Journal of Nutrition* and briefly described here.

To testtheir hypotheses, Yap and colleagues used data previously collected as part ofthe Growing Up in Singapore Towards healthy Outcomes (GUSTO), a study carriedout in 2009 and 2010. Women were enrolled during their 2nd trimesterof pregnancy and asked to complete detailed food records for 3 days as well asquestionnaires concerning a multitude of lifestyle behaviors and healthoutcomes. Infants were carefully weighed and their head circumferences andlengths measured at birth. Each infant's body fat was estimated using amathematical equation and taking into account weight, sex, weeks gestation, andskinfold thickness. This information was then related to the mothers' typicalsleeping and eating patterns.

Theresearchers found that, on average, women experienced a ~10-hour nighttimeperiod during which they did not eat. As the duration of this nighttime fastingincreased so did head circumference and body fat of the babies; but this wasonly true for newborn girls, not boys. The relationship between moms' nighttimefasting duration and girls' head circumferences and body fat values could notbe explained by differences in potentially confounding variables such as themother's age, ethnicity, education, employment status, eating frequency, andnighttime eating habits. Although the researchers admit that much work isneeded to understand the physiologic basis of their findings, they hope theirresearch will eventually lead to new approaches and recommendations related tooptimizing maternal and infant health via paying attention to importantvariables such as length of nighttime fasting.

Reference Loy SL, Wee PH, Colega MT, et al. Maternal night-fasting interval duringpregnancy is directly associated with neonatal head circumference and adiposityin girls but not boys. *Journal ofNutrition* 147:1384-1391.
ForMore Information Tocontact the corresponding author, Dr. Fabian Yap, please send an e-mail tofabian.yap.k.p@singhealth.com.sg

Replacingrefined sugars with egg protein and unsaturated fats may benefit heart health

Cardiovasculardisease is the primary cause of death in the United States, and people who areat increased risk for heart disease and stroke often also suffer from obesity,inadequate blood sugar regulation, hypertension, and unhealthy blood lipidlevels. As such, typical treatment regimens for cardiovascular disease oftenfocus on practices and approaches that simultaneously foster weight loss whilelowering blood pressure and helping regulate blood glucose. Central to many

Contact ASN

9211 Corporate Blvd.
Suite 300
Rockville, MD 20850

info@nutrition.org

(240) 428-3650

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

Thisresearch was led by Dr. Kevin C. Maki (Midwest Biomedical Research: Center forMetabolic and Cardiovascular Health), and tested the hypothesis thatsubstitution of refined starches and added sugars with a mix of protein and unsaturatedfats would benefit glucose regulation and improve blood lipids. To test this,they enrolled 25 overweight or obese men and women with elevated bloodtriglyceride concentrations. None of the subjects had been diagnosed withdiabetes, although most had insulin resistance. Each person participated in two dietary intervention periods. In one ofthem, they were provided a “control” diet providing ~60, 16, and 24% ofcalories 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 fromrefined starches and added sugars in the control diet was replaced with eggprotein and unsaturated fats from oils. Both diets provided enough calories tomaintain body weight, and saturated fats were low (≤ 7%) in each. Each diet wasconsumed for 3 weeks, and their order was randomized among participants.Subjects were evaluated at the beginning of the study and at the end of eachdiet period for a variety of markers for cardiovascular risk.

Thereplacement of ~16% of energy from refined starches and added sugars with acombination 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 thattheir results are supportive of the recommendations put forth in the mostrecent version of the Dietary Guidelines for Americans.

Reference Maki KC, Palacios OM, Lindner E, Nieman KM, Bell M, Sorce J. Replacementof refined starches and added sugars with egg protein and unsaturated fatsincreases insulin sensitivity and lowers triglycerides in overweight or obeseadults with elevated triglycerides. *Journalof Nutrition* 147:1267-1274.
For More Information To contact thecorresponding author, Dr. Kevin Maki, please send an e-mail tokmaki@mbdinicalresearch.com.

The Journal of Nutrition Editor's Picks

- Studies to determine the benefit of vitamin Dsupplementation in older adults should focus on those with low serumconcentrations
- Expression of placental iron and zinc transporters areimpacted by material iron and zinc status
- The relative proportion of *RRR*-α-tocopherol inmaternal plasma and milk are affected by the type of supplement used

Studies to determine the benefit of vitamin Dsupplementation in older adults should focus on those with low serumconcentrations

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

Subjects (n=9579) in this study were enrolled in the GermanESTHER study and were between 50 and 75 years old. Serum concentrations were determined

atbaseline and they were used to establish relationships with all causemortality, or mortality from cardiovascular disease and cancer during the 12.4year follow up period. Risks for eachcause of mortality were estimated for defined increases in serum 25(OH)D acrossthe full range of 25(OH)D concentrations or for those with 25(OH)Dinsufficiency or deficiency only. Fromthese analyses, the authors were able to calculate the power of an interventionstudy to achieve specific effect sizes when the study did not discriminate onsubject 25(OH)D levels or utilized only those with an insufficient or deficient25(OH)D level.

Therewas an inverse association between mortality and serum 25(OH)D, but only forsubjects in which the 25(OH)D levels were either insufficient ordeficient. In fact the strongestrelationship was detected for those subjects with deficient serum 25(OH)Dlevels. Therefore, the power of thestudy to detect a benefit was higher when it targeted those individuals withlow serum 25(OH)D instead of using an untargeted approach. If an untargeted intervention approach wereused, it would be necessary to recruit much larger study populations to detectsignificant changes in mortality. Theauthors concluded that future studies using targeted supplementation approacheswould identify much stronger effects with enhanced power.

Reference Brenner H, Jansen L, Saum K-U, Holleczek B, Schöttker B. Vitamin D Supplementation trials aimed atreducing mortality have much higher power when focusing on people with lowserum 25-hydroxyvitamin D concentrations.*Journal of Nutrition* 147:1325-1333, 2017.
For More Information To contact the corresponding author, HermannBrenner, please send an email to h.brenner@dkfz.de.

Expression of placental iron and zinc transporters areimpacted by material iron and zinc status

Deficiencies of iron and zinc are common in women of childbearingages in sub-Saharan Africa. Deficienciesin 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 fromother micronutrient deficiencies, and as a result, supplementation strategiestypically use supplements containing multiple micronutrients (MMN). Other approaches include a targeted iron andfolic 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 ofmaternal status and supplementation on placental iron and zinc transporters orfetal iron and zinc availability. Todetermine if supplementation is enhancing absorption of iron and zinc by the placentaand thus improving availability to the fetus, Jobarteh and colleagues evaluatedthe impact of MMN, FeFol and LNS supplements on placental expression of zincand iron transporters as well as fetal cord blood iron and zinc concentrations. Results of their study are reported in the July2017 issue of *The Journal of Nutrition*.

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

The PEand PE+MMN supplements resulted in 45 and 78% lower maternal plasma ironconcentrations than the FeFol and MMN groups. Placental iron transporter gene expressions were 30-49% higher in themothers receiving the PE and PE+MMN supplements than those receiving the FeFolsupplement. Cord blood contained less ofthe iron storage/transport protein ferritin in those individuals receivingeither of the LNS-based supplements. Zinc supplementation via the MMN supplements resulted in higher maternalplasma zinc concentrations. Use of thePE+MMN supplement led to reduced expression of zinc transporters, as comparedto use of the non-zinc containing supplements. The authors concluded from these observations that placental expressionof iron and zinc uptake proteins are upregulated when maternal iron levels arelow and when zinc is not supplemented. They suggest this is occurring in an attempt to meet the demands by thefetus 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 ironand zinc transporter genes are upregulated in

Gambian women with low iron andzinc status. *Journal of Nutrition* 147:1401-1409, 2017.
ForMore Information To contact the corresponding author, Sophie E. Moore, pleasesend an email to sophie.moore@kcl.ac.uk.

The relative proportion of *RRR*-α-tocopherol inmaternal plasma and milk are affected by the type of supplement used

Vitamin E deficiency is not a common occurrence, however, adeficiency in this micronutrient can contribute towards impairments in nervoussystem functioning. Newborns typicallyhave low levels of -tocopherol (themost abundant isomer of all vitamin E isomers), which means they are dependentupon colostrum, milk or infant formulas to meet their vitamin E requirements. A contributor to this low level of vitamin Ein neonates is that most women in the United States do not consume the currentestimated average requirement. Therefore, among women of childbearing age, supplementation is importantin order to meet the daily requirements. Vitamin E in plant foods is made up of only the *RRR*-α-tocopherolstereoisomer, 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-tocopheroland 2R stereoisomers of *all-rac*-α-tocopherol are able to meet the vitamin Erequirements in humans. Although studieshave described the impact of α-tocopherolsupplementation approaches on the level of total α-tocopherolin human milk, no work has been done to determine the impact of thestereoisomers in supplements on the distribution of stereoisomers in maternal plasmaand milk. Gaur and colleagues addressedthis void in our understanding of the impact of vitamin E supplementation onavailability of the essential isomers in milk and report the results of theirstudy in the July 2017 issue of *TheJournal of Nutrition*.

Subjects in this study were mothers (n=89) of singletonbirths within 4-6 weeks of giving birth prior to selection for the study, and whoplanned on continuing breastfeeding for at least 6 more weeks. Participants abstained from takingsupplements containing lutein, DHA and -tocopherolfor at least 10 days prior to starting the experiment and for the entirestudy. The mothers were assigned to receivethe 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). Milkand blood samples were acquired before starting the supplements and at the endof the 6-week experiment.

RRR-α-tocopherolwas the most abundant isomer in both maternal plasma and breast milk. Thetype of supplement influenced the α-tocopherol stereoisomer profile in milk andplasma. The RRR supplement led to anincrease in the percentage of *RRR*-α-tocopherolin plasma and milk, whereas the percentage of *RRR*-α-tocopheroldecreased when the ARAC and MIX supplements were used. The authors concluded that these observationsindicate that the type of α-tocopherolsupplementation strategy influences the availability of *RRR*-α-tocopherolin milk, which suggests the need for further research to explore the influenceof differing maternal supplementation strategies on α-tocopherolstatus of breastfed infants.

Reference Gaur S, Kuchan MJ, Lai C-S, Jensen SK, Sherry CL. Supplementation with RRR- or all-rac-α-tocopherol differentially affects the a -tocopherol stereoisomer profile in the milkand plasma of lactating women. *Journal of Nutrition* 147:1301-1307, 2017.
ForMore Information To contact the corresponding author, Christina L. Sherry, pleasesend an email to Christina.sherry@abbott.com.
