March 2017 Media Alert:
The Journal of Nutrition

The following articles are being published in the March 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.

Higher circulating levels of some trans fatty acids may be associated with poor pregnancy outcomes

Trans fatty acids are a group of fats found naturally in dairy products and beef and in processed foods containing partially-hydrogenated oils, the latter constituting the majority of the *trans* fats found in most dietary patterns. Because higher consumption of industrially-produced *trans* fatty acids has been linked to greater risk of cardiovascular disease, many countries have recommended reducing intake and some have even begun to ban their use in commercial foods. Findings from a handful of studies have also suggested that high *trans* fat intake might lead to pregnancy complications, such as elevated blood pressure (pre-eclampsia), low birth weight, and premature delivery. However, these findings have been inconsistent. To shed more light on this important topic, a research team from the University Medical Centre Rotterdam (Netherlands) and led by Dr. Régine Steegers-Theunissen evaluated whether there was an association between circulating levels of a group of *trans* fatty acids referred to as "*trans* 18:1" and risk of pregnancy complications in a group of women living in the Netherlands. You can read more about this study and its findings in the March 2017 issue of *The Journal of Nutrition*.

This study, which included ~6700 women who were participants in the Generation R Study, took place between 2001 and 2006 - a period during which much of the Dutch food manufacturing industry began reducing the *trans* fatty acid from their processed products. Blood samples were obtained during the 2nd trimester of pregnancy and analyzed for *trans* 18:1 fatty acids, including both those contained naturally in dairy and beef and those coming from industrial sources. The researchers then explored whether circulating concentrations were statistically associated with a variety of pregnancy outcomes, such as birth weight, placental weight, and preeclampsia. They also investigated whether or not any of the relationships they uncovered changed over the course of the study.

Higher maternal plasma *trans* 18:1 concentration was indeed associated with lower birth weight and placental weights. In addition, women with the highest levels were more likely to develop pre-eclampsia. As expected, circulating levels of these fats decreased during the course of the study, likely due to their reduction in manufactured foods. Nonetheless, the relationships between circulating concentrations and birth outcomes remained. However, because not all *trans* 18:1 fatty acids have similar effects in the body with the naturally-occurring forms

March 31. Scientific Sessions & Annual Meeting at EB special meeting rate housing deadline. The ASN headquarters hotel is the Hilton Chicago.

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thought to be of much less concern, additional studies are needed to better discriminate which form(s) might be to blame. Alternatively, it is possible that other lifestyle choices (including diet) that coincide with a woman's decision to consume foods containing *trans* 18:1 fatty acids might actually explain these relations.

Reference

Grootendorst-van Mil NH, Tiemeier H, Steenweg-de Graaff J, Jaddoe VWV, Steegers EAP, Steegers-Theunissen RPM. Maternal midpregnancy plasma trans 18:1 fatty acid concentrations are positively associated with risk of maternal vascular complications and child low birth weight. *Journal of Nutrition* 147:398-403.

For More Information To contact the corresponding author, Dr. Régine Steegers-Theunissen, please send an e-mail to r.steegers@erasmusmc.nl.

Can we understand underlying biology of poor growth by looking at blood-borne proteins?

Chronic undernutrition can lead to growth faltering in childhood and short stature in adulthood. Although some may argue that this is a reasonable and protective response to living in conditions where food availability will be limited for a lifetime, childhood malnutrition leads to learning difficulties, greater risk for infection and illness, and long-term impairments in work capacity - all of which negatively impact quality of life. As such, being able to prevent and/or treat poor childhood growth remains an important target for nutrition researchers around the world. One such approach is measuring thousands of compounds, such as proteins and lipids, in the blood. These methods, collectively referred to as "omics" are initially used to discover which substances tend to be high or low in certain conditions. These findings are then used to help understand the condition itself and/or predict future risk for the condition of interest in subsequent, at-risk populations. In a paper published in the March 2017 issue of *The Journal of Nutrition*, Dr. Sun Eun Lee (Johns Hopkins Bloomberg School of Public Health) and colleagues report their findings that variation in circulating concentrations of myriad proteins - a "proteomics approach" - involved in nutrient transport, immunity, muscle synthesis, and neural development are all altered in undernourished school-aged children.

Information on growth and blood samples utilized for this study were obtained from a previously conducted investigation carried in a rural southeastern region of Nepal. A total of 500 children 6-8 years of age were studied, when blood samples were collected and analyzed for 982 proteins using state-of-the-art methodologies. Adequacy of growth was assessed in multiple ways including height, weight, body mass index, arm circumference, and skinfold measurements (to estimate body fat). The researchers uncovered several groupings of proteins that seemed to be associated with body growth and composition of children. For instance, variation in several proteins generally related to nutrient transport, activation of innate immunity, and bone mineralization was associated with age- and sex-adjusted height. And variation in 33 proteins, some of which are involved in muscle growth, neural development and ability to handle oxidative stress, was associated with age- and sex-adjusted body weight. The researchers concluded that these proteins might be valuable "biomarkers" of assessing adequacy of growth and nutritional status of children before measurable growth faltering is obvious.

Reference

Lee SE, Stewart CP, Schulze KJ, Cole RN, Wu LS-F, Yagr JD, Groopman JD, Khatry SK, Adhikari RK, Christian P, West KP. The plasma proteome is associated with anthropometric status of undernourished Nepalese school-aged children. *Journal of Nutrition* 147:304-313.

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Vitamin D supplements improve heart health in vitamin D-deficient diabetics

Vitamin D, sometimes called the "sunshine vitamin" because we can make it when our skin is exposed to sufficient amounts of sunlight, has long been known for its role in bone health. Also obtained from some

foods, particularly fatty fish, vitamin D has more recently been implicated in helping the body regulate blood sugar (glucose) levels, lower inflammation, and reduce the damaging effects of free radical oxidation in the body. Some studies have also provided evidence that low circulating vitamin D levels may be a risk factor for type 2 diabetes and cardiovascular disease. Published in the March 2017 issue of *The Journal of Nutrition*, results from a recently completed dietary intervention study suggest that high-dose, biweekly supplementation with vitamin D may be a beneficial strategy in treating at-risk individuals already diagnosed as having type 2 diabetes and coronary artery disease.

This study, conducted by a research team led by Dr. Zatollah Asemi (Kashan University of Medical Sciences), involved 60 overweight patients with type 2 diabetes, coronary artery disease, and low levels of circulating vitamin D. Half the participants consumed a placebo supplement every 2 weeks for 6 months, while the others took capsules containing 50,000 international units (IU) of vitamin D every 2 weeks for 6 months. To put this dosage into perspective, the Institute of Medicine recommends a daily vitamin D intake of 600 IU (8400 IU every 2 weeks), and a serving of salmon contains about 650 IU. Blood samples were collected before and after the supplementation period and analyzed for a panel of compounds related to blood glucose regulation, lipids, inflammation, and oxidative stress.

The researchers found that consumption of whey or egg protein increased muscle synthesis more than consumption of wheat or soy, and animals fed the gluten-based diet had 20% more body fat than those consuming soy, egg, or whey. In the second study, animals consuming the "balanced" distribution of protein over the course of the day had greater muscle mass than those consuming the "unbalanced" distribution. Collective results from these studies suggest that both meal distribution and amino acid content of the diet can influence muscle protein synthesis and long-term changes in muscle mass. Of course, follow-up studies will be required to determine if these effects are also seen in humans.

Reference

Farrokhian A, Raygen F, Bahmani F, Talari HR, Esfandiari R, Esmaillzadeh, Asemi Z. Long-term vitamin D supplementation affects metabolic status in vitamin D-deficient type 2 diabeteic patients with coronary artery disease. *Journal of Nutrition*147:384-389.

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The Journal of Nutrition: Editor's Picks

Pro-inflammatory dietary patterns are associated with colorectal cancer risk across race/ethnic groups

Chronic inflammation is associated with the onset and promotion of cancer, which partially explains why individuals with inflammatory bowel disease have a higher risk of developing colon cancer. Dietary patterns low in fruits, vegetables and whole grains and higher in fat and added sugars influence systemic inflammatory state, and are associated with elevated cancer risk and inflammation. Even though we have a general appreciation for the relationship between inflammation and colon cancer, the impact of diet on this relationship among diverse ethnic groups is not well known. To fill this void in our understanding, Harmon and colleagues evaluated the impact of diet on colon cancer in a large multi-ethnic study. Results of their work are published in the March issue of the *Journal of Nutrition*.

The Multiethnic Cohort is a prospective study involving 190,963 white, African-American, native Hawaiian, Japanese-American, and Latino men and women located in Hawaii and the Los Angeles area. Subjects were between 45 and 75 years of age at recruitment and were followed for

over 20 years. Subjects completed a questionnaire at entry that assessed usual intake patterns during the prior year. The food frequency questionnaire was validated for each race/ethnicity-sex group. From this information a dietary inflammatory index (DII) was calculated that also was adjusted for total energy intake. A higher DII suggests the dietary pattern is more pro-inflammatory and a lower DII suggests the dietary pattern is anti-inflammatory in nature.

A lower percentage of women (18%) than men (34%) had the most pro-inflammatory dietary pattern. The most pro-inflammatory diets were associated with an increased risk of colorectal cancer, with the most pronounced association occurring for men. When the data were stratified by race/ethnicity there were significant differences in the associations between groups of men, but not for women. The largest increase in risk for those consuming the most inflammatory dietary patterns, compared to the lowest, was observed for native Hawaiian women and Latino men. Increased risk was also observed for white men and Japanese-American men. The authors conclude that more pro-inflammatory dietary patterns are associated with elevated risk of developing colorectal cancers and that the association occurs across all racial/ethnic groups.

Reference

Harmon BE, Wirth MD, Boushey CJ, Wilkens LR, Draluck E, Shivappa N, Steck SE, Hofseth L, Haiman CA, Le Marchand L, Hébert JR. The dietary inflammatory index is associated with colorectal cancer risk in the Multiethnic Cohort. *Journal of Nutrition* 147:430-438, 2017.

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Adherence to cancer prevention guidelines results in elevated serum vitamin D metabolites

Lifestyle factors, including diet, physical activity, alcohol consumption and body weight are associated with the risk of developing cancer. Interestingly, some of these lifestyle factors are associated with elevated concentrations of vitamin D metabolites. Therefore, it is possible that adherence to current cancer risk reduction guidelines may also serve to increase vitamin D status. Kohler and colleagues conducted a study to explore the potential relationship between adherence to cancer prevention guidelines and serum levels of 25-hydroxycholecalciferol [25(OH)D] and 1α,25-dihyrdoxyvitamin D [1,25(OH)D]. Results from this study are published in the March issue of the *Journal of Nutrition*.

Data from two randomized, controlled, double-blind, Phase II clinical trials were used to perform the analyses. In one study subjects (n=503) were assigned to a low fiber diet or one containing a wheat bran fiber supplement. In the other study subjects (n=854) received a placebo or a supplement of ursodeoxycholic acid. Baseline body size, diet, physical activity and alcohol consumption were used to create an adherence score. Vitamin D metabolites were determined using serum samples collected at baseline.

Subjects with the greatest adherence score tended to be older, white and nonsmokers. Greater adherence was associated with elevated concentrations of both 25(OH)D and $1,25(OH)_2D$. For those with the greatest adherence, there was more than a 4-fold greater odds of attaining a sufficient status for 25(OH)D. The authors conclude from these results that by adhering to the cancer risk reduction guidelines, it is possible to achieve higher serum concentrations of both 25(OH)D and $1,25(OH)_2D$.

Reference

Kohler LN, Hibler EA, Harris RB, Oren E, Roe DJ, Jurutka PW, Jacobs ET. Greater adherence to cancer prevention guidelines is associated with higher circulating concentrations of vitamin D metabolites in a cross-sectional analysis of pooled participants from 2 chemoprevention trials. *Journal of Nutrition* 147:421-429, 2017.

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Mediterranean diets contribute to elevated plasma tryptophan and reduced risk of cardiovascular disease

Inflammation is recognized as an important contributor to cardiovascular

diseases. One molecule that regulates several pathways involved in inflammation through its role as a transcriptional regulator is interferon-γ. IFN-γ also activates an enzyme that regulates the conversion of tryptophan to kynurenine and other downstream products including kynurenic acid, 3-hydroxyanthranilic acid, and quinolinic acid. There are some existing studies suggesting an inverse relationship between tryptophan levels and cardiovascular disease. However, there have been no prospective studies evaluating the impact of diet on metabolites in the tryptophan/kynurenine pathway, and their association with risk of eventual cardiovascular disease. Yu and colleagues have addressed this question and the results of their work are published in the March issue of the
Journal of Nutrition.

The data for this work was collected from the Prevención con Dieta Mediterránea (PREDIMED) Study, which is a multicenter, randomized trial to determine the impact of a Mediterranean diet supplemented with either extra-virgin olive oil or nuts on cardiovascular disease. The study included 7,447 men and women at high risk of cardiovascular disease that were randomly assigned to be in a control group (advised to reduce fat intake), a Mediterranean diet supplemented with extra-virgin olive oil (1 liter/family each week) or 30 g of mixed nuts/day (walnuts, hazelnuts, and almonds). A selection of subjects from the main study (896 at baseline and 806 after 1 year) was used for measurement of tryptophan and its metabolites. A kynurenine risk score was created by combining the metabolites using a weighted coefficient for each metabolite's association with cardiovascular disease.

An increase in plasma tryptophan over the year each subject was monitored was associated with a lower risk of cardiovascular disease. The concentration of kynurenic acid at baseline was associated with a higher risk of myocardial infarction and coronary artery disease, but not the risk of stroke. Higher calculated kynurenine risk scores were more strongly associated with cardiovascular disease in the control group than it was in either of the two dietary treatment groups. The authors concluded these data support their hypothesis that by increasing plasma tryptophan it is possible to reduce the risk of cardiovascular disease. Moreover, they suggest that a Mediterranean diet may counteract the risk for cardiovascular disease predicted by high kynurenine risk scores.

Reference

Yu E, Ruiz-Canela M, Guasch-Ferré M, Zheng Y, Toledo E, Clish CB, Salas-Salvadó J, Liang L, Wang DD, Corella D, Fitó M, Gómez-Gracia E, Lapetra J, Estruch R, Ros E, Cofán M, Arós F, Romaguera D, Serra-Majem, L, Sorli JV, Hu FB, Martinez-Gonzalez MA. Increases in plasma tryptophan are inversely associated with incident cardiovascular disease in the Prevención con Dieta Mediterránea (PREDIMED) Study. *Journal of Nutrition* 147:314-322, 2017.

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