March 2012 Media Alert: *The Journal of Nutrition*

The following articles are being published in the March 2012 issue of *The Journal of Nutrition (JN)*, 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.

Researchers find genetic variations in selenium-containing proteins related to effectiveness of body's antioxidant system

Arginine supplementation: impressive effects on pregnancy outcomes likely due to nitric oxide

World Health Organization growth standards reliably predict risk of child death

Researchers find genetic variations in selenium-containing proteins related to effectiveness of body's antioxidant system

Observational research has long suggested an association between higher selenium intake and lower risk for several chronic degenerative conditions, such as cancer and cardiovascular disease, known to be caused in part by oxidative stress. Indeed, selenium (a trace mineral found in a variety of foods, including grains, nuts, dairy products, meat, and seafood) is a component of several antioxidants collectively called selenoproteins. Among the most studied selenoproteins are selenoprotein P and a group of enzymes referred to as glutathione peroxidases (GPX). Consuming inadequate amounts of selenium can prevent these proteins from functioning, in turn increasing oxidative stress and its damaging effects on DNA, lipids, and proteins in the body. Limited research suggests that variations in the genes that code for these selenoproteins may also influence their effectiveness. Because understanding how nutritional status and genetic make-up can interactively work together to enhance or undermine selenoprotein activity, a research team led by Dr. Ulrike Peters (Fred Hutchinson Cancer Research Center) investigated whether variations in *GPX* genes might be correlated with the activities of the GPX proteins they code for. They also examined whether these genetic differences are related to measures of systemic oxidative stress in their subjects. You can read more about this study in the March 2012 issue of *The Journal of Nutrition*.

To test their hypotheses, the researchers obtained blood samples from a total of 195 participants (mean age: 64 years). White blood cells were used to determine the exact codes making up the *GPX* genes for each subject, and activities of GPX proteins were assessed in both white

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blood cells and plasma. Selenoprotein P was quantified in plasma samples. Two measures of oxidative stress (malondialdehyde and protein carbonyl content) were also quantified.

As anticipated, small alterations in the *GPX* genes were related to how well their resultant GPX proteins were able to exert antioxidant functions. Genetic variation in one of these genes was also related to how much selenoprotein P was in the plasma. Furthermore, genetic variation in the gene coding for selenoprotein P was associated with whole-body oxidative stress. Although they recognize their finding need to be confirmed in other populations, the authors concluded that common genetic variation in selenoproteins may affect their antioxidant activities. This finding may be particularly important in terms of public health recommendations regarding optimal dietary selenium intakes within a genetically-diverse population.

Reference Takata Y, King IB, Lampe JW, Burk RF, Hill KE, Santella RM, Kristal AR, Duggan DJ, Vaughan TL, Peters U. Genetic variation in *GPX1* is association with GPX1 activity in a comprehensive analysis of genetic variations in selenoenzyme genes and their activity and oxidative stress in humans. *Journal of Nutrition* 142:415-422, 2012.
For More Information To contact the corresponding author, Dr. Ulrike Peters, please send an e-mail to upeters@fhcrc.org.

Arginine supplementation: impressive effects on pregnancy outcomes likely due to nitric oxide

Arginine is a dietary amino acid that serves primarily as a building block for thousands of proteins needed by the body. However, it serves a myriad of other roles as well. For instance, arginine can be disassembled to produce nitric oxide (NO), a small substance that rapidly signals inflammation and engorgement. Likely best known for its role in penile erection (Viagra treats erectile dysfunction by enhancing the effects of NO), NO also helps redirect blood flow to areas that need it via a process called *angiogenesis*. Although scientists have long known that consumption of sufficient dietary arginine is important for many aspects of reproduction, how this occurs and whether these effects are all related to its conversion to NO are unknown. To help examine whether arginine's effects on pregnancy outcome may be acting through NO's effects on angiogenesis, researchers at Mississippi State University recently studied the effects of dietary arginine supplementation on pregnancy using a cleverly-designed, luminescent mouse model. Details of this study and its results are published in the March 2012 issue of *The Journal of Nutrition*.

The research team, directed by Dr. Peter Ryan, mated normal female mice with genetically-modified males possessing a gene coding for a protein that 'glows.' What makes this gene useful is that it can be linked to other genes of interest. In this case, the glowing gene was linked to another one coding for a protein (vascular endothelial growth factor receptor 2, Vegfr2) important for regulating angiogenesis. In this way, the amount of the 'glowing' protein detected using highly sensitive imaging equipment can be linked directly to how much Vegfr2 the animal is making. To test whether arginine (and, therefore, NO) might influence blood flow via increased Vegfr2 production, pregnant animals were fed a control diet, one with added arginine, or one with added alanine. Throughout pregnancy, luminescence of fetal and placental tissues was imaged repeatedly. Food intake, weight gain, and pregnancy outcomes (e.g., litter size, birth weight, pup growth) were assessed during pregnancy and for 3 weeks after birth.

The researchers found consistent positive effects of arginine supplementation on pregnancy outcomes. For instance, the pregnant mice consuming additional arginine gained significantly more weight and gave birth to almost twice as many pups. And as hypothesized, production of Vegfr2 was significantly higher in the arginine-supplemented group throughout pregnancy. The authors concluded that the beneficial effects of dietary arginine supplementation on mammalian reproduction are associated with enhanced Vegfr2 production by the tissues of the fetus and placenta, likely mediated by NO. Clearly, further research is needed to understand the practical implications of this discovery to both animal production and human health.

Reference Greene JM, Dunaway CW, Bowers SD, Rude BJ, Feugang JM, Ryan PL. Dietary L-arginine supplementation during gestation in mice enhances reproductive performance and *Vegfr2* transcription activity in the fetoplacental unit. *Journal of Nutrition* 142:452-456, 2012.

For More Information To contact the corresponding author, Dr. Peter Ryan, please send an e-mail to ryan@provost.msstate.edu.

World Health Organization growth standards reliably predict risk of child death

Although the risk of childhood malnutrition has dropped substantially over the past 2 decades, the World Health Organization estimates that malnutrition is still responsible for approximately one-third of child deaths during the first 5 years of life. Because measuring a child's actual nutritional status is difficult and expensive, health agencies typically rely on anthropometric measures of weight and height as proxies for overall level of nutrition. As such, these measures are often the best indices that a healthcare provider may have to determine a child's risk for nutrition-related illness and/or death. In response, the World Health Organization recently released new growth charts, which in addition to providing values for weight-for-age, length-for-age, and weight-for-length, also include previously unavailable reference values for body mass index (BMI) and weight gain velocity. Very little is known, however, about the relation between these new growth standards and risk for child death. To help fill this knowledge gap, an international collaboration of researchers from University College Cork (Ireland), the University of Tampere (Finland), and the University of Bergen (Norway) examined longitudinal health data collected from 2402 infants living in a rural area of the Democratic Republic of Congo. Details of this study are published in the March 2012 issue of *The Journal of Nutrition*.

Children under 5 years of age were enrolled in this study, which began in 1989 and ended 2 years later. All children who were under 2 years old (mean age: 8.7 months) were included in the portion of the study designed to assess risk for child death. At 3-month intervals, infants were weighed and measured by a well-trained clinician. For each child a score was calculated for BMI-for-age, weight-for-length, length-for-age, and weight gain velocity. The research team then statistically evaluated the relation between these anthropometric scores and risk of death during each 3-month interval.

During the period in which the study took place, a total of 57 of the subjects died. In general, the infants were found to have suboptimal growth, as evidenced by height-for-age, and weight gain velocities being well below those expected in a healthy population. Importantly, the infants with the lowest anthropometric values were at significantly

increased risk for death, with low BMI-for-age and weight-for-length being similarly predictive of impending demise. Very low weight gain velocity in the previous 3 months was found to be particularly predictive in this regard. The authors concluded that the World Health Organization's newest age-adjusted anthropometric growth standards, and especially weight gain velocity, are indeed useful predictors of child mortality in populations where malnutrition is endemic.

Reference O'Neill SM, Fitzgerald A, Briend A, Van den Broeck J. Child mortality as predicted by nutritional status and recent weight velocity in children under two in rural Africa. *Journal of Nutrition* 142:516-521, 2012.

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