February 2017 Media Alert:
The Journal of Nutrition

The following articles are being published in the February 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.

Protein requirements likely higher than thought for PKU-affected children

Phenylketonuria (PKU) is an inherited disease caused by an inability to convert one amino acid (phenylalanine) to another (tyrosine), resulting in the build-up of phenylalanine in the blood and urine and a deficiency in tyrosine unless appropriate dietary changes are made. Because this can lead to impaired cognitive development, growth faltering, and other poor health outcomes, most infants born in the United States are tested for PKU in the first few days of life and, if found to have the condition, put on a strict low-phenylalanine diet with sufficient tyrosine. However, even when adhering to their special formulas and foods, these children often do not grow well, and many clinicians believe that this might be due to increased dietary protein requirements. Currently, whereas the recommended dietary allowance (RDA) for protein in healthy children is between 0.76 and 0.95 grams for every kilogram of body weight per day, children with PKU are advised to consume 1.14 to 1.33 grams of protein per kilogram body weight. In a paper published in the February 2017 issue of *The Journal of Nutrition*, a research team led by Dr. Rajavel Elango (British Columbia Children's Hospital Research Institute and the University of British Columbia) asked whether protein requirements for PKU-affected children might be even higher.

For their study, the researchers recruited 2 girls and 2 boys (9-18 years old) with PKU and mildly elevated circulating phenylalanine levels and asked them to participate in a series of controlled feeding regimens. Each time they were studied, the children were given highly-controlled standardized meals containing a predetermined amount of protein. Small amounts of stably-labeled amino acids were also given so that protein balance could be accurately assessed from breath and urine samples during the 8 hours following each test meal. In a nutshell, this method allows for the state-of-the-art determination of protein requirements by assessing at what dietary protein level the body switches from protein breakdown to protein synthesis.

The study team found that the average daily protein requirement for the four children was 1.85 grams per kilogram body weight, a value substantially higher than current recommendations. Additional studies are warranted to assess protein requirements for PKU-affected children with more severe forms of the disease.

Reference

Turki A, Ueda K, Cheng B, Giezen A, Salvarinova R, Stockler-Ipsiroglu S, Elango R. The indicator amino acid oxidation method using L-[1-13C] leucine suggests a higher than currently recommended protein

February 23. Scientific Sessions & Annual Meeting at EB early registration rate deadline.

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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requirement in children with phenylketonuria. *Journal of Nutrition* 2017;147:211-217.
For More Information To contact the corresponding author, Dr. Rajavel Elango, please send an e-mail to relango@cfri.ubc.ca

More evidence linking dairy to healthy blood pressure

Hypertension (high blood pressure) is an important risk factor for several of the world's leading causes of death, such as stroke and heart disease. Consequently, researchers and clinicians continue to investigate its causes and, perhaps even more important, ways to maintain healthy blood pressure throughout life. One of the most effective ways we currently know to prevent hypertension is consumption of the DASH (Dietary Approaches to Stop Hypertension) eating pattern, which emphasizes fruits, vegetables, low-fat or nonfat dairy foods, whole grains, lean meats, fish and poultry, nuts, and beans. The DASH diet is also high in fiber and follows national guidelines for sodium intake. How the DASH eating plan actually works to lower blood pressure is not known, but many believe that its emphasis on dairy foods might be important - perhaps, at least in part, via the role that calcium plays in maintaining cardiovascular health. Dairy foods are also excellent sources of high-quality protein, vitamins, and minerals - all of which likely work together to keep us healthy. Most studies designed to understand dairy's contribution to the health-promoting effects of the DASH diet, however, have been conducted in populations that typically consume relatively high amounts of dairy products. This fact makes it somewhat tricky to discern independent effects of calcium and dairy because almost all the former is obtained via consumption of the latter. To help fill this research gap, a team of scientists led by Drs. Mohammad Talaei and Woon-Puay Koh (National University of Singapore and Duke-NUS Medical School in Singapore) studied diet-health associations in ~37,000 Chinese men and women who historically have consumed relatively low amounts of dairy products. You can find details of their findings in the February 2017 issue of *The Journal of Nutrition*.

Participants in this study were recruited as part of the Singapore Chinese Health Study between 1993 and 1998 and were followed until ~2010. All the subjects were healthy with no history of hypertension or cardiovascular disease when they were enrolled, and typical dietary intake patterns were ascertained using a 165-item questionnaire. Occurrence of newly-diagnosed hypertension was diagnosed by physicians and documented twice during the study.

Consumption of dairy foods was inversely correlated with risk of becoming hypertensive during the follow-up period. Specifically, participants consuming the highest levels were 7% less likely to be diagnosed with hypertension than those consuming the least, and daily milk drinkers (mostly one glass per day) were 6% less likely than people consuming no milk. Whereas there was an overall association between higher calcium consumption from dairy and lower risk for hypertension, no such correlation was evidence when nondairy calcium was considered. These findings suggest that the effect of dairy foods on lowering blood pressure is likely not due simply to their calcium content.

Reference

Talaei M, Pan A, Yuan J-M, Koh W-P. Dairy food intake is inversely associated with risk of hypertension: The Singapore Chinese Health Study. *Journal of Nutrition* 2017;147:235-241.

For More Information To contact the corresponding authors, Drs. Mohammad Talaei and Woon-Puay Koh, please send e-mails to mohammad.talaei@u.nus.edu and woonpuay.koh@duke-nus.edu.sg, respectively.

New study finds evening out protein intake across the day may be important for adult muscle mass

Adequate amounts of dietary protein are needed throughout the lifespan, and requirements depend on a variety of factors including age, sex, physiologic state (e.g., pregnancy), and the amount of muscle mass a person has. However, not all proteins are similar in terms of their quality, with animal-source proteins having higher "values" than plant-source proteins. This is because animal-source foods, such as meat, dairy, and eggs, contain all the needed amino acids in the appropriate ratios, whereas their plant-source counterparts, such as wheat and soy, do not. As such, lower amounts of the former - as compared to the latter - may be sufficient to support optimal health. In addition, some evidence suggests that timing of protein intake throughout the day might impact its ability to be incorporated into muscles. Consequently, scientists continue to study protein quality, quantity, and daily distribution in their quest to understand better optimal protein intake throughout life. Helping to explore some of these research questions, Drs. Layne Norton and Donald Layman, both at the University of Illinois at Urbana-Champaign, conducted 2 studies in which adult rats were fed various types and timing of dietary protein. Their results, which are summarized below, can be found in the February 2017 issue of *The Journal of Nutrition*.

In the first study, rats were randomly assigned to consume experimental diets providing protein obtained from either dairy-source whey, egg white, soy, or wheat gluten. All diet types provided 16% of their calories from protein, but differed in their amino acid profiles. For instance, leucine contents were ~11, 9, 8, or 7%, respectively. Rats were trained to consume 3 meals per day, each one providing 4-6 grams of food and mimicking typical American eating habits. In the other study, all animals were fed a high-quality, whey-based diet, but some were provided with similar amounts of protein in each meal ("balanced" distribution) while others were given increasing amounts of protein from morning until evening ("unbalanced" distribution). Outcomes such as body composition and muscle protein synthesis were monitored in both studies.

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 Norton LE, Wilson GJ, Moulton CJ, Layman DK. Meal distribution of dietary protein and leucine influences long-term muscle mass and body composition in adult rats. *Journal of Nutrition* 2017;147:195-201.

For More Information To contact the corresponding authors, Drs. Layne Norton and Donald Layman, please send e-mails to biolaynellc@gmail.com and dlayman@illinois.edu, respectively.

The Journal of Nutrition: Editor's Picks

Protein synthesis is preferentially conserved in most mucin-producing gastrointestinal tissues during periods of threonine deficiency in infant piglets

Protein requirements for young growing animals and infants must be met in order to support the demands of multiple tissues, and those requirements change during growth and periods of stress, such as illness. Certain tissues preferentially use some amino acids, which means a deficient level of those amino acids may become even more limiting for tissues that do not have ready access to them. For example, between 60 and 90% of dietary threonine, an indispensible amino acid, is extracted for use by the small intestine, pancreas, spleen, and stomach. The threonine used by these epithelial tissues to synthesize proteins and mucins is preferentially derived from the dietary sources in the lumen of the intestine, instead of from arterial circulation. Therefore, during periods of threonine deficiency, other tissues would potentially receive even lower amounts of this amino acid. However, it is not known which tissues are most deprived during periods of limiting threonine supplies. This void in our understanding of amino acid metabolism was addressed in a paper published in the February issue of *The Journal of Nutrition* by Munasinghe and colleagues.

The study used 20 Yucatan miniature piglets that were 15 days of age (10 females and males) that were randomly assigned to receive a diet containing one of 20 threonine concentrations. The levels used ranged between 0.5 to 6.0 g/100 g total amino acids, which equate to 20-220% of their requirements. Whole body threonine requirement and protein synthesis rates in various tissues were determined.

Dietary threonine levels did not affect protein synthesis rates in the stomach, proximal jejunum, mid-jejunum or ileum. However, protein synthesis rates declined in all non-mucin producing tissues, as well as lung and colon as threonine levels declined. Whole body threonine requirement was estimated to be approximately 2.9 g/100 g total amino acids. The authors concluded that these data demonstrate threonine is preferentially utilized by the gastrointestinal tissues in piglets, and that the growth and function of other tissues are likely compromised when threonine levels are reduced in order to maintain the mucous layer in the intestine.

Reference

Munasinghe LL, Robinson JL, Harding SV, Brunton JA, Bertolo RF. Protein synthesis in mucin-producing tissues is conserved when dietary threonine is limiting in piglets. *Journal of Nutrition* 2017;147:202-210.

For More Information To contact the corresponding author, Robert F. Bertolo, please send an email to rbertolo@mun.ca.

The C-3a epimer of 25-hydroxycholecalciferol may have biological activity

Previous papers have described elevated levels of the C-3a epimer of 25-hydroxycholecalciferol (3-epi-25(OH)D3) during infancy, relative to the levels observed in adults. The existence of elevated levels during infancy suggests there could be functional relevance to this molecule. However, its origin, its metabolism and its biological activity are essentially unknown. The goals of Djekic-Ivankovic and colleagues were to determine if dietary cholecalciferol levels affected plasma levels of the epimer, and to explore the potential impact of 3-epi-25(OH)D3 on calcium metabolism and bone health in young rats. Their results are published in the February issue of *The Journal of Nutrition*.

To determine if the intake of cholecalciferol affected plasma levels of the C-3a epimer, young rats were provided diets containing 1, 2, or 4 IU of cholecalciferol/g diet. To determine if 3-epi-25(OH)D3 affected mineral metabolism or bone health, diets were formulated to contain either 0.5 IU/g of 25-hydroxycholecalciferol [25(OH)D3] or 0.5 or 1.0 IU/g of 3-epi-25(OH)D3. For both objectives, the diets were provided for 8 weeks and measurements were made at 0, 4, and 8 weeks.

The researchers found that levels of 3-epi-25(OH)D3 in the young rats were higher than those reported in adult rats. Increasing the content of cholecalciferol in the diet led to elevated levels of 3-epi-25(OH)D3 in plasma, which was more evident in females than in males. Including 3-epi-25(OH)D3 in the diet led to decreased plasma levels of 25(OH)D3 and 24,25(OH2)D3. In male rats, the increase in plasma 3-epi-25(OH)D3 led to reduced PTH levels. In this short term study, 3-epi-25(OH)D3, whether from the diet or endogenously produced, did not alter bone growth or mineral accretion. The authors conclude that these results support the hypothesis that 3-epi-25(OH)D3 is produced endogenously and has biological functions similar to 25(OH)D3. They recommend that further work needs to be conducted to explore the mechanisms involved to and to determine if similar responses are observed in humans.

Reference Djekic-Ivankovic M, Lavery P, Agellon S, Weiler HA. The C-3a epimer of 25-hydroxycholecalciferol from endogenous and exogenous sources supports normal growth and bone mineral density in weanling rats. *Journal of Nutrition* 2017;147:141-151.

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