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The Journal of Nutrition Media Alerts

The following articles are being published in the June 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.

- Genetics,lactose intolerance, and vitamin D status – how are they related?
- Can alteringthe texture of your foods and slow eating decrease calorie intake?
- Donorhuman milk for premature infants – what's the best way to pasteurize it?

Genetics,lactose intolerance, and vitamin D status – how are they related?

Dairyfoods are naturally rich in many essential nutrients, including high-qualityprotein, several of the B vitamins, and myriad minerals – particularly thoseimportant for bone health, such as calcium. Milk is often fortified withvitamin D, making dairy products a good source of this nutrient as well. However,in many populations (e.g., those living in much of East Asia and Africa) theability of the body to break down lactose disappears in childhood. Thisphenomenon is thought to be driven by genetic factors. Progressive inability tobreak down lactose also occurs in a subset of other populations that generallycontinue to drink milk into adulthood. When this condition (referred to aslactose intolerance) occurs, dairy consumption results in severegastrointestinal upset, bloating, and diarrhea. In response, people withlactose intolerance often simply stop consuming dairy products and subsequentlybecome at-risk for becoming deficient in calcium and vitamin D. As such, manyresearchers are interested in better understanding the connection betweengenetic predisposition for lactose intolerance, dietary intake, and nutritionalstatus around the globe. One such researcher is Dr. Ahmed El-Sohemy (Universityof Toronto) who along with Ohood Alharbi recently studied these relationshipsin 720 Canadians. Details about their study are published in the June 2017issue of *The Journal of Nutrition*.

El-Sohemyand Alharbi used a research technique called a "Mendelian randomization study"to determine which genetic variations were associated with lactose intolerancein their study participants. In particular, they focused on a previouslystudied, tiny variation in a gene called *LCT*.

Asexpected, they found that a large proportion of their study participants hadthe genotype typically associated with lactose intolerance, and people withthis genotype consumed the least dairy products – particularly skim milk. Theyalso had lower concentrations of vitamin D in their blood. As such, they didnot compensate by supplementing or eating other foods fortified with thisessential nutrient. For the first time, the researchers found that people withjust one, instead of two, copies of this genetic variant were also affected bylactose intolerance – albeit to a lesser degree – suggesting that clinicaldefinitions and genetic classifications of lactose intolerance could beexpanded to include this much larger group. The researchers also confirmedprevious findings that those who have the gene for lactose intolerance areslightly shorter than those who do not – suggesting insufficient intakes ofthese essential nutrients may limit bone growth. These findings emphasize theimportance of making sure people with lactose intolerance consume adequateamounts of vitamin D, and beg the question as to whether nondairy foods shouldalso be routinely fortified with this nutrient.

Reference AlharbiO, El-Sohemy A. Lactose intolerance (LCT-13910C>T) genotype is associated with plasma24-hydroxyvitamin D concentrations in Caucasians: A Mendelian randomizationstudy. *Journal of Nutrition* 147: 1063-1069.

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Can altering the texture of your foods and slow eating decrease calorie intake?

Researchershave long known that, in general, people will eat more if served largerportions of food. Dietary patterns that favor high-fat (energy-dense) foods arealso associated with increased calorie consumption. Conversely, when people areprompted to eat more slowly, they tend to eat less. But how do all of thesefactors contribute coordinately to unhealthy weight gain, and might we be ableto manipulate one of them to impact the others in terms of promoting weightloss? In a paper published in the June 2017 issue of *The Journal of*

Important Dates

Sept 18-20. Native American Nutrition Conference (Prior Lake, Minnesota)

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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Nutrition, researchers at the Singapore Institutefor Clinical Sciences and National University Health System devised two studiesto begin to experimentally test these questions. Their methods and findings aresummarized briefly here.

Theresearch team, led by Dr. Ciaran Forde, set out to test its hypothesis thatstudy participants would consume more calories during a meal if it was higherin energy density (more calories per gram) and served as a large portion, butthat both these effects would be reduced if the meal required more chewing, andthus took longer to eat. To do this, they conducted two experiments. In thefirst, they enrolled a group of healthy men and women, each of whom agreed toeat 4 breakfasts (in random order) consisting of a typical Singaporean meal:rice porridge made with chicken and broth, seasoned with green onions,shallots, sesame oil, and soy sauce. However, the breakfasts differed intexture (affecting eating rate) and energy density (calories/gram). In thesecond study, a different group of young women consumed similar breakfastsdiffering in texture and portion size.

Resultsindicate that, as hypothesized, increased energy density and portion sizeindependently boost calorie intake. When the porridge was thicker, however, itwas consumed more slowly – leading to an 11-13% reduction in food and energyintake. The research team concluded "an opportunity exists to use a combinationof energy-density dilution, smaller portions, and natural variations in foodtexture to design meals that promote reductions in energy intake whilemaintaining satiety." For instance, some forms of rice (e.g., brown rice) arechewier and, therefore, take longer to eat than others (e.g., polished whiterice). In addition, various cooking modalities can influence food texture.Paying attention to these differences might be valuable in helping people avoidunhealthy weight gain and promote weight loss when desirable.

Reference McCrickerd K, Lim CMH, Leong C, Chia EM, Forde CG. Texture-based differencesin eating rate reduce the impact of increased energy density and large portionson meal size in adults. *Journal ofNutrition* 147: 1208-1217.

For More Information To contact thecorresponding author, Dr. Forde, please send an e-mail to ciaran_forde@sics.a-star.edu.sg.

Donor human milk for premature infants - what's the best way to pasteurize it?

Breastfeeding provides optimal nutrition for almost all infants,particularly those living in difficult environments and those who are bornearly. In the case of the latter, however, mothers sometimes have difficultyproducing sufficient amounts of milk to feed to their infants. When thishappens, donor milk (often obtained from a milk bank) is often fed. However,some studies suggest that babies who get donor milk instead of their own mother'smilk grow more slowly and are more at-risk for illness. This may be because donormilk is heat treated (pasteurized) to kill potentially pathogenic bacteria, whereasmilk produced by an infant's own mother is not treated prior to feeding it. Expertshave proposed that, in addition to killing pathogenic microbes (a good thing),heat treatment destroys potentially important milk components, such as immunecells, enzymes, and immunomodulatory components. As such, there is greatinterest in finding alternative methods whereby the benefits of donor milk canbe preserved while making sure it doesn't contain potentially illness-causingmicrobes. In the June 2017 issue of *TheJournal of Nutrition*, a research team led by Drs. Yanqi Li and Per TorpSangild (University of Copenhagen) investigated if exposing milk to ultravioletlight, rather than heat, might be one such solution. Accompanying this manuscriptis an editorial by Dr. Douglas Burrin (Baylor College of Medicine) praising theresearchers on their elegant approaches to testing their hypotheses andhighlighting the importance of ramping up research in this important area.

Li, Sangild, and colleagues conducted two related studies, both of whichutilized a large pool (60 liters or about 16 gallons) of milk donated by 15healthy, breastfeeding women. The milk was divided into three smaller pools:one that remained untreated, another that was heat pasteurized, and a thirdsubjected to ultraviolet C irradiation. In the first study, these subfractionswere tested for their bacterial content and selected proteins, enzymes, milkbioactives and antioxidant capacity. In the second study, the milks were fed topiglets delivered early by cesarean section – mimicking premature infants.Piglets were studied to determine if feeding the different types of milkinfluenced their growth and gastrointestinal health.

As expected, both heating and irradiation killed the bacteria in themilk. Concentrations of many of the milk components studied were also betterpreserved in the irradiated versus heat-treated milk. And, importantly, the pigletsconsuming the irradiated milk grew more similarly to and had gastrointestinaltracts more resembling those fed the raw milk, as compared to those fed theheat-treated version. And fewer piglets fed the irradiated milk had bacteria intheir bone marrow, suggesting immunological benefits. The authors concludedthat ultraviolet treatment is better than heat treatment in preserving the bioactivefactors in human milk. Burrin concurs and, especially given the increasingincidence of premature births worldwide, urges the human nutrition researchcommunity to focus considerable effort toward understanding the safest andhealthiest nutrition possible for these at-risk infants.

References Li Y, Nguyen DN, de Waard M, Christensen L, Zhou P,Jiang P, Sun J, Bojesen AM, Lauridsen C, Lykkesfeldt J, Dalsgaard TK, BeringSB, Sangild PT. Pasteurization procedures for donor human milk affect bodygrowth, intestinal structure, and resistance against bacterial infections inpreterm pigs. *Journal of Nutrition* 147: 1121-1130.

Burrin DG.Preserving Mother Nature's best food for preterm infants. *Journal of Nutrition* 147: 1023-1024.

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The Journal of Nutrition Editor's Picks

- Liverprotein synthesis and gene expression changes induced by methionine restrictiondoes not require eukaryotic initiation factor 2 phosphorylation
- Zinc absorption increases during pregnancy and lactation tomeet predicted requirements, even when elevated phytate diets are consumed
- Human milk oligosaccharide-induced alterations in immune cell populations may reduce rotavirus infection susceptibility

Liver protein synthesis and gene expression changes induced by methionine restriction does not require eukaryotic initiation factor 2 phosphorylation

Methionine restriction may protect against metabolicdiseases and extend lifespans by reducing visceral fat, increasing insulinsensitivity and altering lipid metabolism. Insufficiency of amino acids initiates an integrated stress response(ISR) via pathways that involve the phosphorylation of eukaryotic initiationfactor 2 (p-eIF2) and general control nonderepressible 2 (GCN2) kinase. Outcomes of these changes include reducedprotein synthesis at the level of mRNA translation initiation, and reduced glutathionelevels. However, the existing literaturedoes not explain whether methionine restriction reduces body fat and regulatesprotein balance through the activation of ISR. Pettit and colleagues used a transgenic mouse model to explore the importanceof GCN2 in regulating the physiological responses to methionine restriction.The results of their study are published in the June 2017 issue of *The Journal of Nutrition*.

Male and female mice with whole body deletion of the GCN2gene (Gcn2) or liver-specific protein kinase R-like endoplasmic reticulumkinase (Perk) gene, as well as wild type mice and floxed control mice were usedin four studies. The mice were providedobesogenic diets containing either sufficient (0.86%) or restricted methionine(0.12%) levels. Metabolic phenotypingwas conducted at 4 weeks and body composition was measured throughout thestudies. Hepatic mRNA expression levelswere determined at 2 days and 5 weeks after starting the experimental diets, along with the activity of eIF2B and the level of p-eIF2.

After2 days, methionine restriction did not increase hepatic p-eIF2 or reduce eIF2Bactivity in the wild type or Gcn2 knockout mice, even though genestranscriptionally regulated by the ISR were altered in both strains. However, after 5 weeks of methioninerestriction p-eIF2 was increased and eIF2B activity was reduced in wild type, but not the Gcn2 knockout mice. Thegenes regulated by ISR were still altered similarly in both strains. Methionine restriction also reduced mixed andcytosolic protein synthesis, but not mitochondrial protein synthesis in theliver and skeletal muscle of both strains. There was no increase in energy expenditure or reduction in body fatwith methionine restriction in the Gcn2 knockout mice. The authors concluded that hepatic activationof ISR resulting from methionine restriction does not involve p-eIF2 and thatGcn2 status may influence body fat loss but not protein balance. They also concluded that the response tomethionine restriction is not only complex, but that it is dynamic over time.

Reference Pettit AP, Jonsson WO, Bargoud AR, Mirek ET, Peelor FF, Wang Y, Gettys TW, Kimball SR, Miller BF, Hamilton KL, Wek RC, Anthony TG. Dietary methioninerestriction regulates liver protein synthesis and gene expression independentlyof eukaryotic initiation factor 2 phosphorylation in mice. *Journalof Nutrition* 147:1031-1040, 2017.

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Zinc absorption increases during pregnancy and lactation to meet predicted requirements, even when elevated phytate diets are consumed

Even though zinc-restricted diets have a negative impact onreproduction in animal models, consistent adverse effects of apparently zincdeficient diets have not been reported for humans. Because of these observations, it has beenproposed that zinc absorption is upregulated during pregnancy and lactation. However, the effectiveness of increasedabsorption in meeting the increasing demands during these periods is unknown, especially in the context of a high phytate diet, which binds zinc and reducesits bioavailability. Outcomes from theresearch conducted by Hambidge and colleagues to address this question arereported in the June 2017 issue of *TheJournal of Nutrition*.

This prospective observational study was designed toevaluate zinc absorption in Guatemalan women at 8 and 34 weeks of gestation andagain at 2 and 6 months of lactation. The subjects were assigned to consume a typical diet containing maize(high in phytate, n = 8) or a similar diet containing low-phytate maize (n =14). Phytate and zinc contents of thediets were measured, and zinc absorption was determined and compared with theestimated physiological requirements.

Totalabsorbed zinc was greater in the women consuming the low phytate maize at alltime points, relative to the women consuming the higher phytate maize. Zinc absorption increased from 8 weeks ofgestation until 2 months of lactation and then dedined at 6 months oflactation. Absorption of zinc wasgreater than the amount predicted in samples collected after 8 weeks ofgestation. The high phytate diet did notprevent the increases in zinc absorption necessary during late pregnancy orduring lactation to meet the estimated requirements. The authors concluded the limited evidencefor severe zinc deficiency effects on pregnancy may result from the

mothersability to increase zinc absorption during these periods of pregnancy andlactation, even when consuming diets containing high levels phytate.

Reference Hambidge KM, Miller LV, Mazariegos M, Westcott J, SolomonsNW, Raboy V, Kemp JF, Das A, Goco N, Hartwell T, Wright L, Krebs NF. Upregulation of zinc absorption matchesincreases in physiologic requirements for zinc in women consuming high-ormoderate-phytate diets during late pregnancy and early lactation. *Journalof Nutrition* 147:1079-1085,2017.

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Human milk oligosaccharide-induced alterations in immunecell populations may reduce rotavirus infection susceptibility

Many children under 1 year of age requiring hospitalization tocombat diarrhea-associated disease test positive for rotavirus (46%) incountries where vaccination against the virus is not routine. The prevalence of such infections point tothe obvious need to identify other approaches to prevent or reduce the severityof rotavirus infections. Previous workhas demonstrated that breastfeeding reduces the incidence of rotavirus infections,yet a full understanding of the potential beneficial factors in breast milkcapable of fighting against infectious disease has not been described. Recent evidence suggests that in addition to theimmunoglobulins present in breast milk, there are potential immune benefitsderived from human milk oligosaccharides (HMOs). This theory was tested in an experimentconducted by Comstock and colleagues, which is reported in the June 2017 issueof *The Journal of Nutrition*.

Colostrum-deprived newborn piglets were used as a modelorganism for this work. They werepassively immunized through sow serum and the sows were vaccinated againststandard porcine diseases, but not to rotavirus. Piglets were fed a standard non-medicatedmilk replacer formula, a formula containing 4 g/L of HMOs, or a formulacontaining other prebiotic oligosaccharides. Ten days after birth, half of the piglets were challenged with an oralrotavirus containing solution. Samples ofperipheral blood mononuclear cell (PBMC), mesenteric lymph node (MLN), andileal Peyer's patch (IPP) immune cell populations were collected 5 days afterinfection.

Pigletsreceiving the rotavirus challenge had more natural killer cells, memoryeffector T cells, and major histocompatibility complex II cells. Providing HMOs in the diet, regardless ofinfection status, led to increases in PBMC natural killer cells and basophils,as well as more memory effector T cells in the MLN. The changes in immune cell populations withinfection were intermediate for piglets receiving the prebiotic containingformula. PBMCs from non-infected pigletsreceiving the HMO formula produced more IFN-g than those receiving the standard formula, whichmay have contributed to the reduction in duration of diarrhea reported inprevious studies. The changes in HMO-fednon-infected piglet MLN cell populations may be reflective of an improvedsurveillance capacity and ability to limit the clinical signs of rotavirusinfections. The authors concluded that HMOsare affecting infant immune development, which can improve their response toinfection challenges. They furtherpropose incorporation of HMO in infant formulas as an approach to reduce thenegative outcomes associated with rotavirus infections.

Reference ComstockSS, Li M, Wang M, Monaco MH, Kuhlenschmidt TB, Kuhlenschmidt MS, Donovan SM. Dietary human milk oligosaccharides but notprebiotic oligosaccharides increase circulating natural killer cell andmesenteric lymph node memory T cell populations in noninfected androtavirus-infected neonatal piglets. *Journal of Nutrition* 147:1041-1047, 2017.

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