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 altering the texture of your foods and slow eating decrease calorie intake?
- Donor human milk for premature infants – what’s the best way to pasteurize it?

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

Dairy foods are naturally rich in many essential nutrients, including high-quality protein, several of the B vitamins, and myriad minerals – particularly those important for bone health, such as calcium. Milk is often fortified with vitamin 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) the ability of the body to break down lactose disappears in childhood. This phenomenon is thought to be driven by genetic factors. Progressive inability to break down lactose also occurs in a subset of other populations that generally continue to drink milk into adulthood. When this condition (referred to as lactose intolerance) occurs, dairy consumption results in severe gastrointestinal upset, bloating, and diarrhea. In response, people with lactose intolerance often simply stop consuming dairy products and subsequently become at-risk for becoming deficient in calcium and vitamin D. As such, many researchers are interested in better understanding the connection between genetic predisposition for lactose intolerance, dietary intake, and nutritional status around the globe. One such researcher is Dr. Ahmed El-Sohemy (University of Toronto) who along with Ohood Alharbi recently studied these relationships in 720 Canadians. Details about their study are published in the June 2017 issue of *The Journal of Nutrition*.

El-Sohemy and Alharbi used a research technique called a “Mendelian randomization study” to determine which genetic variations were associated with lactose intolerance in their study participants. In particular, they focused on a previously studied, tiny variation in a gene called LCT.

As expected, they found that a large proportion of their study participants had the genotype typically associated with lactose intolerance, and people with this genotype consumed the least dairy products – particularly skim milk. They also had lower concentrations of vitamin D in their blood. As such, they did not consume or eat other foods fortified with this essential nutrient.

For the first time, the researchers found that people with this one, instead of two, copies of this genetic variant were also affected by lactose intolerance – albeit to a lesser degree — suggesting that clinical definitions and genetic classifications of lactose intolerance could be expanded to include this much larger group. The researchers also confirmed previous findings that those who have the gene for lactose intolerance are slightly shorter than those who do not — suggesting insufficient intakes of these essential nutrients may limit bone growth. These findings emphasize the importance of making sure people with lactose intolerance consume adequate amounts of vitamin D, and begged the question as to whether nondairy foods should also be routinely fortified with this essential nutrient. For the first time, the researchers found that people with just one, instead of two copies of the genotype typically associated with lactose intolerance, and people with this genotype consumed the least dairy products — particularly skim milk. They also had lower concentrations of vitamin D in their blood. As such, they did not consume or eat other foods fortified with this essential nutrient.


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

Researchers have long known that, in general, people will eat more if served larger portions of food. Dietary patterns that favor high-fat (energy-dense) foods are also associated with increased calorie consumption. Conversely, when people are prompted to eat more slowly, they tend to eat less. But how do all of these factors contribute to unhealthy weight gain, and might we be able manipulate one of them to impact the others in terms of promoting weight loss? In a paper published in the June 2017 issue of *The Journal of Nutrition*, researchers prompted people to eat more slowly, and found that they ate less. But how do all of these factors contribute to unhealthy weight gain, and might we be able to manipulate one of them to impact the others in terms of promoting weight loss? In a paper published in the June 2017 issue of *The Journal of Nutrition*, researchers prompted people to eat more slowly, and found that they ate less.
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Nutrition, researchers at the Singapore Institute for Clinical Sciences and National University System devised two studies to begin to experimentally test these questions. Their methods and findings are summarized briefly here.

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

Results indicate that, as hypothesized, increased energy density and portion size independently boost calorie intake. When the porridge was thicker, however, it was consumed more slowly — leading to an 11-13% reduction in food and energy intake. The research team concluded "an opportunity exists to use a combination of energy density, smaller portions, and natural variations in food texture to design meals that promote reductions in energy intake without maintaining satiety." For instance, some forms of rice (e.g., brown rice) are chewier and, therefore, take longer to eat than others (e.g., polished white rice). In addition, various cooking modalities can influence food texture. Paying attention to these differences might be valuable in helping people avoid unhealthy weight gain and promote weight loss when desirable.


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 born prematurely. In the case of the latter, however, mothers sometimes have difficulty producing sufficient amounts of milk to feed their infants. When this happens, 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’s milk grow more slowly and are more at-risk for illness. This may be because donor milk is heat treated (pasteurized) to kill potentially pathogenic bacteria, whereas milk produced by an infant’s own mother is not treated prior to feeding it. Experts have proposed that, in addition to killing pathogenic microbes (a good thing), heat treatment destroys potentially important milk components, such as immunoglobulins, enzymes, and immunomodulatory components. As such, there is great interest in finding alternative methods whereby the benefits of donor milk can be preserved while making sure it doesn’t contain potentially illness-causing microbes. In the June 2017 issue of *The Journal of Nutrition*, a research team led by Drs. Yanqi Li and Per Torp Sangild (University of Copenhagen) investigated if exposing milk to ultraviolet light, rather than heat, might be one such solution. Accompanying this manuscript is an editorial by Dr. Douglas Burrin (Baylor College of Medicine) praising the researchers on their elegant approaches to testing their hypotheses and highlighting the importance of ramping up research in this important area.

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

As expected, both heating and irradiation killed the bacteria in the milk. Concentrations of many of the milk components studied were also better preserved in the irradiated versus heat-treated milk. And, importantly, the piglets consuming the irradiated milk grew more similarly to and had gastrointestinal tracts more resembling those fed the raw milk, as compared to those fed the heat-treated version. And fewer piglets fed the irradiated milk had bacteria in their bone marrow, suggesting immunological benefits. The authors concluded that ultraviolet treatment is better than heat treatment in preserving the bioactive factors in human milk. Burrin concurs and, especially given the increasing incidence of premature births worldwide, urges the human nutrition research community to focus considerable effort toward understanding the safest and healthiest nutrition possible for these at-risk infants.


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

Methionine restriction may protect against metabolic diseases and extend lifespan by reducing visceral fat, increasing insulin sensitivity and altering lipid metabolism. Insufficiency of amino acids initiates an integrated stress response (ISR) via pathways that involve the phosphorylation of eukaryotic initiation factor 2 (p-eIF2) and general control nonderepressible 2 (GCN2) kinase. Outcomes of these changes include reduced protein synthesis at the level of mRNA translation initiation, and reduced glutathione levels. However, the existing literature does not explain whether methionine restriction reduces body fat and regulates protein synthesis through the activation of ISR. Pettit and colleagues used a transgenic mouse model to explore the importance of 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 GCN2 gene (Gcn2) or liver-specific protein kinase R-like endoplasmic reticulum kinase (Perk) gene, as well as wild type mice and mixed control mice were used in four studies. The mice were provided obesogenic diets containing either sufficient (0.86%) or restricted methionine (0.12%) levels. Metabolic phenotyping was conducted at 4 weeks and body composition was measured throughout the studies. Hepatic mRNA expression levels were determined at 2 days and 5 weeks after starting the experimental diets, along with the activity of eIF2B and the level of p-eIF2.

After 2 days, methionine restriction did not increase hepatic p-eIF2 or reduce eIF2B activity in the wild type or Gcn2 knockout mice, even though genetrasnationally regulated liver protein synthesis was reduced in both strains. However, after 5 weeks of methionine restriction p-eIF2 was increased and eIF2B activity was reduced in wild type, but not the Gcn2 knockout mice. The genes regulated by ISR were still altered similarly in both strains. Methionine restriction also reduced mixed cytosolic protein synthesis, but not mitochondrial protein synthesis in the liver and skeletal muscle of both strains. There was no increase in energy expenditure or reduction in body fat with methionine restriction in the Gcn2 knockout mice. The authors concluded that hepatic activation of ISR resulting from methionine restriction does not involve p-eIF2 and that Gcn2 may influence body fat loss but not protein balance. They also concluded that the response to methionine restriction is not only complex, but that it is dynamic over time.


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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 on reproduction in animal models, consistent adverse effects of apparently zinc-deficient diets have not been reported for humans. Because of these observations, it has been proposed that zinc absorption is upregulated during pregnancy and lactation. However, the effectiveness of increased absorption in meeting the increasing demands during these periods is unknown, especially in the context of a high phytate diet, which binds zinc and reduces its bioavailability. Outcomes from research conducted by Pettit and colleagues to address this question are reported in the June 2017 issue of *The Journal of Nutrition*.

This prospective observational study was designed to evaluate zinc absorption in Guatemalan women at 8 and 34 weeks of gestation and again 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 the diets were measured, and zinc absorption was determined and compared with the estimated physiological requirements.

Total absorbed zinc was greater in the women consuming the low phytate maize at all time points, relative to the women consuming the higher phytate maize. Zinc absorption increased from 8 weeks of gestation until 2 months of lactation and then declined at 6 months of lactation. Absorption of zinc was greater than the amount predicted in samples collected at 8 weeks of gestation. The high phytate diet did not increase in zinc absorption necessary during late pregnancy or during lactation to meet the estimated requirements. The authors concluded the limited evidence for severe zinc deficiency effects on pregnancy may result from the...
mothers’ ability to increase zinc absorption during these periods of pregnancy and lactation, even when consuming diets containing high levels of phytate.


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

Many children under 1 year of age requiring hospitalization to combat diarrhea-associated disease test positive for rotavirus (46%) in countries where vaccination against the virus is not routine. The prevalence of such infections points to the obvious need to identify other approaches to prevent or reduce the severity of rotavirus infections. Previous work has demonstrated that breastfeeding reduces the incidence of rotavirus infections; yet, a full understanding of the potential beneficial factors in breast milk capable of fighting against infectious disease has not been described. Recent evidence suggests that in addition to their immunoglobulins, there are potential immune benefits derived from human milk oligosaccharides (HMOs). This theory was tested in an experiment conducted by Comstock and colleagues, which is reported in the June 2017 issue of *The Journal of Nutrition*.

Colostrum-deprived newborn piglets were used as a model organism for this work. They were passively immunized through sow serum and the sows were vaccinated against standard porcine diseases, but not to rotavirus. Piglets were fed a standard non-medicated milk replacer formula, a formula containing 4 g/L of HMOs, or a formula containing other prebiotic oligosaccharides. Ten days after birth, half of the piglets were challenged with an oral rotavirus containing solution. Samples of peripheral blood mononuclear cell (PBMC), mesenteric lymph node (MLN), and ileal Peyer’s patch (IPP) immune cell populations were collected 5 days after infection.

Piglets receiving the rotavirus challenge had more natural killer cells, memory effector T cells, and major histocompatibility complex II cells. Providing HMOs in the diet, regardless of infection 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 within the infection status were intermediary for piglets receiving the prebiotic containing formula. PBMCs from non-infected piglets receiving the HMO formula produced more IFN-γ than those receiving the standard formula, which may have contributed to the reduction in duration of diarrhea reported in previous studies. The changes in HMO-fed non-infected piglet MLN cell populations may be reflective of an improved surveillance capacity and ability to limit the clinical signs of rotavirus infections. The authors concluded that HMOs are affecting infant immune development, which can improve their response to infection challenges. They further propose incorporation of HMO in infant formulas as an approach to reduce the negative outcomes associated with rotavirus infections.


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