Molecular Basis of Milk Allergy
Wesley Burks, Duke University

The spectrum of food allergic diseases will be discussed along with the most recent studies related to the development and loss of milk allergy in children. Sequential epitopes have been identified on the bovine alpha(s2)-casein cow’s milk that bind human IgE from milk-allergic patients. Additional studies have compared conformational and linear IgE-binding epitopes in the milk proteins. Patients who have persistently milk allergic typically have increased milk-specific IgE binding to the linear epitopes in these proteins, possibly indicating a different immune response in those patients who are less likely to outgrow their milk allergy. More recent studies have identified specific types of milk-specific regulatory T cells that develop in children who outgrow their milk allergy. Further studies have shown that milk-specific IgE, if followed over time, the rate of decrease of IgE may correlate with the development of tolerance. New studies are underway to develop allergen-specific immunotherapy for patients who will not outgrow their milk allergy.

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Introduction to Dairy Vernacular
Harry Farrell, USDA/ARS (Emeritus)

The virtual image of milk, which would be constructed by most people, is that of a creamy white fluid. The lubricity and taste of milk are related to this perception and are based upon three unique biological structures: the colloidal calcium-protein complexes (the casein micelles), the milk fat globules and their limiting membrane, and the milk sugar lactose. The complexity of these structures is necessitated by the fact that milk is predominately water. It is the accommodation of these ingredients to an aqueous environment that forms the basis for the structure of milk at the molecular level and calls for a unique secretory process. Finally, this nutritionally valuable fluid presents a myriad of challenges and opportunities to the dairy industry.

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How Soon Will The “ics” Affect Animal Production and Human Health and Nutrition?
Bruce German, UC-Davis

Vitamin D has classically been associated with calcium and bone, and the deficiency disease associated with inadequate vitamin D intake is rickets (in children) and osteomalacia (in adults). There is no epidemic of rickets or osteomalacia today.

However, there is an emerging consensus that vitamin D acts in a number of different ways and affects many organs and systems other than bone. The Food and Nutrition Board of the Institute of Medicine defined serum 25(OH)D as the functional indicator of vitamin D status, and as experience with measuring this indicator has grown, it has become clear that most adults in N. America have undesirably low values. Recent studies have shown that Ca absorption improves substantially, and both fall frequency and actual osteoporotic fracture risk decline as serum 25(OH)D level is raised. Additionally, it is now recognized that vitamin D acts in cell cycle regulation, altogether apart from any role it may play in the Ca economy, and that some fraction of the disease burden of epithelial cancers and various autoimmune disorders (ranging from diabetes mellitus to multiple sclerosis) can likely be attributed to widespread vitamin D inadequacy. Given the prevalence of these disorders in N. America, one can truly say that a vitamin D deficiency epidemic does exist. Fortunately the methods needed to treat it are readily available.

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Calcium, Vitamin D, and Bone Health
Karl Insogna, Yale University

The role of calcium and vitamin D in skeletal health has been an area of intense investigative interest for nearly 100 years, yet areas of controversy and uncertainty remain. It is clear that extreme, long-standing deficiency of either calcium or vitamin D has profoundly negative effects on both skeletal accrual and on the health of the mature skeleton. What remains uncertain is pretty much everything else. While the majority of evidence supports the notion that there is a threshold for optimal calcium intake during childhood and adolescence, the impact of maintaining an intake at or above this threshold during the period of skeletal accrual, on adult bone mass and metabolism remains unclear.

It is clear that even moderate calcium insufficiency in adulthood (often due to impaired absorption and poor dietary habits) leads to accelerated bone loss particularly in women after menopause. It is also clear that correcting calcium insufficiency slows the rate of skeletal resorption. Surprisingly, available evidence does not consistently support the conclusion that calcium alone reduces the rate of fragility fracture.

As it is the case with calcium, subtle vitamin D insufficiency has become a major area of clinical concern and investigation. In the last three decades the “optimal” serum 25-hydroxyvitamin D level has risen from \( \geq 5 \text{ ng/ml} \) to \( \geq 20 \text{ ng/ml} \) to “somewhere around 30 ng/ml.” This reflects a growing appreciation for the broad spectrum of skeletal and non-skeletal effects of the vitamin D endocrine system. The evidence that correcting deficits in vitamin D stores improves skeletal health is compelling. Most studies show that vitamin D supplementation in populations at risk for vitamin D-insufficiency reduces the risk of fracture. This robust effect likely is due to the multiple salutary effects of vitamin D on skeletal homeostasis including correcting secondary hyperparathyroidism by improving intestinal calcium absorption, correcting subclinical mineralization defects, and improving muscle function.

Conversely vitamin D insufficiency and calcium insufficiency may interact in a negative way with the latter increasing catabolism of already marginal 25-hydroxyvitamin D stores.

The fact that obesity, at least in Caucasians, is associated with lower serum levels of 25-hydroxyvitamin D and that the same hepatic enzyme system that detoxifies xenobiotics also accelerates vitamin D catabolism, represent emerging challenges to ensuring vitamin D sufficiency in the general population.

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Milk composition analysis and interest in research is heavily influenced by current nutritional and commercial needs that go far beyond the traditional nutrient and commodity view. Under the scrutiny of new tools and focusing on biological activity of its components, it is becoming clear that milk contains components that are important regardless their relative low chemical concentration in milk. Oligosaccharides, peptides, glycoproteins, some minerals and lipids, have potential biological activities at low concentrations. Furthermore, it seems very likely that their activity is not only linked to their nature, but also to other components and their relative concentration of surrounding components at the time of ingestion. This complexity in components from milk is exemplified in the milk fat/lipid globule membrane. This material is complex, containing oligosaccharides, phospholipids, glycolipids, glycoproteins, and other compounds with proven biological activity in terms of human health. These components are functionally important as food emulsifiers or agents in liposomes, and sources of highly active phospholipids, complex glycoproteins and lipids that regulate cell communication such as sphingomyelin. This presentation aims to present the challenge to harness the potential in the MFGM, and exemplifies an approach by a particular processing and formulation strategy.

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Minor Milk Components in Novel Formulations
Rafael Jiménez-Flores, California Polytechnic University DPTC

Role of Vitamin D in Older Adults
Mary Ann Johnson, University of Georgia, Athens
Professor of Foods and Nutrition and Faculty of Gerontology

About 1 million people will turn 65 each year during the next 50 years in the US. The number of people 65 and older will increase from 36 million in 2003 to about 86 million in 2050. Among the older adult population, 59% are aged 65 to 74 and 41% are aged 75 and older. The majority is white (83.6%) and the predominant ethnic/racial groups are black (8.1%) and Hispanic (5.0%). More than 96% of older adults live in the community rather than in long term care facilities. The 65 year old of today can expect to live at least 16 years more years and the 85 year old for more than 6 additional years (Federal Interagency Forum on Aging and Related Statistics, 2004; US Census Bureau, 2004).

The 2005 Dietary Guidelines for Americans recommends that older adults consume 1000 IU (25 μg) daily of vitamin D, which is a substantial increase above the Adequate Intake (50 to 70 years: 400 IU; > 70 years: 600 IU, IOM, 1997). Adequate vitamin D status is needed for optimal calcium absorption, while poor vitamin D status has been linked to numerous health problems including osteoporosis, falls, poor immune function, and risk for some types of cancer and heart disease. There is evidence from randomized control trials that vitamin D and/or calcium supplements improves bone mineral density and decreases the risk of falls and bone fractures (Chapuy et al., 1992; Bischoff-Ferrari et al., 2004; Dawson-Hughes et al., 1997; Papadimitropoulos et al., 2002; Shea et al., 2004).

Vitamin D comes from foods, supplements, and synthesis in the skin. Older adults, as well as people with dark pigmented skin or people who use sunscreen properly, have low synthesis of vitamin D-precursors in the skin, even in sunny areas of the US such as southern Florida (Levis et al., 2005; Park and Johnson, 2005). Those exposed to little sunlight, such as homebound individuals, also have increased risk of low serum concentrations of 25-hydroxyvitamin D. People living at higher latitudes in the northern US are particularly at risk for vitamin D deficiency. In addition to low skin synthesis, darker skinned ethnic/racial groups may be at increased risk of poor vitamin D status because of lower intakes of vitamin D-fortified dairy foods and vitamin-D containing supplements, as well as from obesity which may lead to less time spent in the sun or sequestration of vitamin D in the fat mass. The best marker of vitamin D status from oral intake and skin synthesis is serum 25-hydroxyvitamin D. Optimal serum 25-hydroxyvitamin D may be as high as 80 nmol/L based on randomized control trials of vitamin D supplementation and bone fractures and minimization of parathyroid hormone (Dawson-Hughes, 2004). Depending on the biochemical cutoff used, between 5 and 70% of older adults may have poor vitamin D status (Looker et al., 2002).

Older people consume only about 200 IU of vitamin D from foods (Calvo et al., 2005). It is very difficult to meet vitamin D recommendations from foods alone, even when consuming several servings of vitamin D-fortified dairy foods such as milk (100 IU/cup). Commonly eaten fish such as salmon has about 324 to 624 IU vitamin D per 100 grams and canned tuna has 236 IU vitamin D per 100 grams, while the average vitamin D content of 26 fish products was about 300 IU per 100 grams (USDA, 2004).

Vitamin D supplements are needed to meet the new recommendation of 1000 IU daily. The amount of supplement needed will depend on the dietary intake of vitamin D. The Upper Level of vitamin D is 2,000 IU daily, so older adults should carefully read the labels on supplements to ensure staying below the Upper Level. This will be particularly important if the supplement industry markets higher potency vitamin D supplements than those currently available.

There are also opportunities for the food and dairy industries to fortify foods with vitamin D, especially those foods consumed by people at high risk for vitamin D deficiency.

Various Ways to Consume 1,000 IU of Vitamin D Daily

<table>
<thead>
<tr>
<th>Per serving</th>
<th>IU/day</th>
<th>IU/day</th>
<th>IU/day</th>
<th>IU/day</th>
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<tbody>
<tr>
<td>Milk and/or yogurt fortified with vitamin D, 1 cup.</td>
<td>100</td>
<td>300</td>
<td>300</td>
<td>0</td>
</tr>
<tr>
<td>Orange juice fortified with vitamin D and calcium, ½ cup.</td>
<td>75</td>
<td>75</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Breakfast cereal fortified with vitamin D, ½ to 1 cup or about 1 ounce.</td>
<td>40</td>
<td>40</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fish and shellfish, 8 ounces per week.</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Eggs. 3 medium per week</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vitamin-D containing supplements with or without calcium</td>
<td>100 to 400</td>
<td>400</td>
<td>700</td>
<td>700</td>
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</tbody>
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Total | 1015 | 1000 | 1015 | 1000 |

Selected References:


How Serious Is Our Present Health Condition? Is There Hope for the Future?
Milch Kanter, Ph.D.
Cargill, Inc.
Food Technology Development Center

Development of the central nervous system (CNS) takes place during the gestational period and continues throughout the first two years of life or longer. A major portion of the brain is comprised of fats which are provided by the maternal supply and circulation during pregnancy and by breastfeeding and/or formula after birth, followed by weaning foods and then table foods for the toddler. Dairy foods are a good source of many nutrients during all of these periods, including fats/lipids required for brain growth and probably cognitive development.

The fats of dairy foods are relatively unexplored in terms of their potential benefits for CNS development. Additionally, novel fats that have potential developmental and/or protective benefits for the CNS are currently being discovered and dairy foods should be investigated as sources of these novel lipid moieties. An example of these are the endocannabinoids which are lipid and lipid-like molecules; endocannabinoids may protect cells of the CNS.

To define the role of dairy fats in infant brain development, there is a need to turn to the behavioralists and their methodologies. The path has been paved by the scientists who are defining the developmental advantages to the developing infant of the n-3 polyunsaturated long chain fatty acid, DHA, which is found in cold-water marine fish. For example, the potential benefit of cholesterol after birth could be investigated by assessing the infant’s vision, ability to solve a simple problem-solving exercise, or resistance to distraction while playing. These and similar approaches, coupled with the biochemical data and dietary information, can provide the evidence for linking dairy fats with development.

There is also potential for engineering functional dairy foods, changing the content of dairy foods with fats that are being shown to provide neurological advantages.

Information about the benefits of dairy foods for brain development will be instrumental in laying the foundation for nutrition public policy and recommendations for women of child-bearing age and their infants and toddlers. Approaches that enhance cognitive development hold the potential for improving the school readiness of our children.

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Roles of Branched-Chain Amino Acids in Blood Glucose Control
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Glucose intolerance and hyperinsulinemia are metabolic characteristics common to the epidemic increase in obesity and type 2 diabetes. Currently, most researchers have focused errors in peripheral glucose uptake or insulin signaling. Contrary to this approach, we think that the error lies in an excess of carbohydrate fuels available in an environment of limited muscle metabolic activity. We have elected an alternative approach to re-balance the macronutrient ratios of the diet to reduce the requirement for peripheral disposal of large boluses of dietary carbohydrates. Our research with diets containing increased levels of high quality protein (>1.4 g kg\(^{-1} \cdot d^{-1}\)) and reduced carbohydrates (100 to 160 g/d) appear to enhance weight loss due to increased loss of body fat and reduced loss of lean body mass. Short-term studies using moderate protein diets have found beneficial effects including increased satiety, increased thermogenesis, sparing of muscle protein during weight loss and enhanced glycemic control. The total benefits of a moderate protein diet are likely derived from the combined effects of lower carbohydrates resulting in lower post-prandial increase in blood glucose and lower insulin response and increased protein providing increased branched-chain amino acid (BCAA) leucine and gluconeogenic substrates. Leucine and the BCAA, which are unusually high in dairy proteins, exerts unique regulatory actions on muscle protein synthesis, modulation of
Innovation is the key to product development. As the industry developed beyond home consumption, distribution created new challenges in terms of shelf-life and food safety.

Innovation doesn’t just happen – it is a solution to a problem or the creation of a new opportunity. As the industry developed beyond home consumption, distribution created new challenges in terms of shelf-life and food safety. Thus, methods for pasteurization were created and dairy grew markets beyond local town and, eventually, state borders. Eventually the industry became large enough to support marketing, research and nutrition education activities. Early on it was evident that milk held tremendous nutritional benefits but in the early 20th century, the field of nutrition was just getting started. As it grew, the American dairy industry was quick to jump in promoting dairy as part of a balanced diet. They also invested in research to support this belief.
As we know, innovation isn’t exclusive to one industry over another. Innovation on the part of the competition found that chemical hydrogenation of vegetable oils could produce hard fats to compete with milkfat/butter at lower cost. Soon after that the whole cholesterol issue came forward and the fledging margarine industry invested heavily in research and promotion to take advantage of the issue. They went further to show how saturated fat (a chemical term) caused heart disease. What was not considered in the ensuing definition of saturated fat was that butter contained significant levels of short chain saturated fats that were metabolized very differently than the longer chain varieties. This oversight or lack of understanding was a serious marketing tool for dairy and misleading to consumers. The dairy industry was not prepared to collectively invest in the research, education and marketing now required in the new food business. That all changed in 1984 with the creation of the National Dairy Promotion & Research Board (NDPRB).

Since that time, the NDPRB, backed by dairy check-off dollars and significant leadership, has worked diligently to bring the dairy industry back into competition in the food marketplace. In the meantime, the story on cholesterol has radically changed as has that of saturated fats. Calcium became the nutritional superstar and now we are looking at how dairy products play a role in weight management. The next area for innovation will be in bioactive components, put into milk by nature to promote health, being discovered and then playing a role in food formulation. Also, new research to understand the relationship between milk and beneficial bacteria will lead to new markets for fermented dairy products. The industry, through innovation, is even addressing environmental stewardship as a means of ensuring consumer confidence. With innovation leading the way – milk and milk products are clearly back in the game.


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**Lactose Intolerance: Myth or Reality?**

Dennis Savaiano, PhD

Purdue University

Dairy foods provide many essential nutrients including approximately 75% of the calcium available in the American diet. One potential barrier to the consumption of dairy foods is a somewhat limited capacity to digest the carbohydrate lactose found in milk. Approximately 75% of the World’s population loses the majority of their intestinal capacity to digest milk sugar (lactose) sometime in early childhood. This is a normal biological phenomenon that exists among all mammals. These ‘lactose maldigesters’ make up approximately 25% of the US population, including approximately half of the Hispanic population, 70% of the African American population and nearly all of the Asian American population. These ‘lactose maldigesters’ are often inappropriately called ‘lactose intolerant’ even though many, if not most of these individuals do not limit their consumption of dairy foods and do not suffer from intolerance symptoms.

Research over the past 30 years clearly demonstrates that ‘lactose intolerant’ individuals, including African-Americans, Hispanics and Asian Americans, can enjoy dairy foods without symptoms of intolerance if simple dietary guidelines are followed. Yet many individuals avoid dairy foods and the excellent nutrition they provide.

Guidelines for inclusion of dairy foods include:

1) Consume fluid milk with meals, not on an empty stomach. This approach slows intestinal transit, allowing a greater digestion of lactose and limiting lactose transit into the colon where symptoms can occur. 2) Limit consumption of fluid milk to one serving per meal. Lactose maldigesters who consume only 12 grams of lactose (the amount found in 8 ounces of milk), or less, at a meal rarely have symptoms. 3) Enjoy cheeses and other dairy foods that are low in lactose. Lactose is water soluble and becomes part of the whey rather than the curds in cheese production. 4) Eat yogurts, which are well tolerated due to a unique ability of yogurt to assist in the digest of lactose in the intestine. 5) Eat dairy foods daily to keep the intestinal bacteria adapted to maximize tolerance. The intestinal bacteria are highly adapted to the nutrients that reach the colon. Regular metabolism of milk sugar by the colon bacteria increases the efficiency of digestion, limiting the possibility for symptoms.

Using these guidelines, lactose maldigesters can consume 3 or more servings of dairy daily and remain symptom-free. Thus, to label individuals who have a limited capacity to digest milk sugar as ‘lactose intolerant’ is a myth. These individuals should be encouraged to enjoy the nutritional benefits of dairy foods, especially for the high levels of calcium, protein and B vitamins found in dairy foods.

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**Milk-derived Sphingolipids and their Role in Cancer Prevention**

Eva M. Schmelz, Wayne State University

Tremendous research efforts have been focussed on the prevention and treatment of cancer, and although some attempts were successful, the incidence and mortality of other cancers have remained essentially unchanged. The development of new strategies for cancer prevention, detection and treatment is therefore indispensable. Compounds found in foods with proven anti-cancer properties have received increased attention in the last decades. Sphingolipids are an important group of compounds in this category because as lipid second messengers they regulate cell growth, differentiation and cell death- all events that are dysregulated in cancer cells. Sphingolipids can be found in most foods, but are especially rich in milk and milk products, meat and soy. Intestinal cells are constantly exposed to bioactive sphingolipid metabolites after the hydrolysis of complex dietary sphingolipids, suggesting that transformed cells in the colon may be directly targeted for regulation by orally administered sphingolipids. Accordingly, adding sphingolipids to the diet of mice reduced significantly early and late stages of colon cancer without causing toxic side effects. Early results indicate that this effect may not be restricted to the colon but that cancer of other organs such as breast can also be targeted by orally administered sphingolipids.

The convenient route of administration and their apparent lack of side effects are important criteria for establishing sphingolipids as chemopreventive agents that may have to be administered to high-risk groups for a prolonged period of time. The determination of the mechanisms of how sphingolipids suppress tumor formation and progression in amounts that could be reached in the human diet and the identification of cellular markers for sphingolipid efficacy is therefore important for the development of a cancer prevention strategy using orally administered sphingolipids.

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**Milk as a Tool to Battle the Obesity Epidemic**

Marta D. Van Loan, Ph.D., FACSM

USDA, ARS, Western Human Nutrition Research Center

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The problem addressed in this presentation is the use of milk and other dairy foods and/or products as tools to counter the rise in obesity in the American public. Obesity is a major public health issue facing the nation and has numerous consequences including diabetes, hypertension, and heart disease, to name a few. Additionally, the cost for health care to combat these illnesses is rising dramatically.

In this presentation a review is given that encompasses research results from animal models, epidemiological evidence and clinical trials that used a variety of dairy foods or the constituents thereof. Animal research using, conjugated linoleic acid (CLA) have provided promising results for reductions in fat mass in rodents and possible increases in metabolic rate. Results from in vivo studies with human research volunteers have not been as promising; there appears to be little or no effect of CLA on...
body fat changes in obese humans during weight reduction. However, CLA did increase muscle size and strength gains in body builders. Conflicting findings with the use of CLA may be the result of different concentrations of CLA and different isomer composition used between studies. The role of calcium or dairy foods is a different scenario. Animal research has suggested a mechanism by which increased Ca intake may increase intracellular Ca and function in the regulation of lipolysis and lipogenesis. Epidemiological evidence has shown inverse relationships between calcium intake and/or dairy intake and body weight, relative risk for obesity, and body fat gain. These findings have been supported by positive findings in clinical trials using both calcium supplementation and dairy foods. Some research studies have shown changes in body weight and composition with Ca supplements, however, more recent results have demonstrated greater losses in body weight, body fat, and trunk fat with dairy foods.

In summary, the use of dairy foods to battle the obesity epidemic is promising. Furthermore improvements in the American diet that may be beneficial to reducing obesity and its associated co-morbidities will also reduce the burden placed on health care costs; thereby having major implications for the health of the nation both medically and financially.

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**Latest Thinking on Milk Fat – Friend or Foe?**

Bruce Watkins, Purdue University

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**Basis for 3 Daily Servings of Milk in the 2005 Dietary Guidelines**

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