

HERITABILITY OF OBESITY

Wardle J, Carnell S, Haworth CM, and Plomin R. Evidence for a strong genetic influence on childhood adiposity despite the force of the obesogenic environment. *Am J Clin Nutr* 2008;87:398–404.

The study of childhood obesity is complex, not only as a result of genetic variability among people (nature), but also as a result of multifaceted interpersonal and cultural factors (nurture). The contributions of nature and nurture in the development of adiposity remain essential questions in the study of obesity. Wardle et al. provide research on twins who were born after obesity rates increased sharply, to help distinguish genetic and environmental influences on adiposity.

Height, body weight, and waist circumference (WC) were measured in children enrolled in the Twins' Early Development Study (TEDS) from the 1994–1996 birth cohort (5092 pairs; ages 8–11 yrs). In comparison to 1990 norms, height, weight, and WC were higher in the present sample, but calculated BMIs were similar to 1990 levels. Dizygotic pairs had higher BMIs and WCs than monozygotic pairs. Twin correlations for BMI and WC were similar in monozygotic pairs and were higher than for dizygotic pairs, indicating a strong genetic influence. Heritability estimates for BMI (77%) and WC (76%) were higher than shared-environment effects (10% and 10%, respectively) and non-shared-environment effects (13% and 14%, respectively). The authors conclude that genetic influences are high in children born since the early 1990s, and that environment has a relatively small impact on adiposity in childhood.

Comment: Drs. Musani, Erickson, and Allison concur that the present study represents a major contribution to the study of pediatric obesity, and that a high heritability of obesity and overweight remains relevant even in light of rapidly increasing rates of obesity. Although they caution that environmental concerns must still play an important role in pediatric obesity, the basic genetic underpinnings of obesity continue to be significant contributors to this growing public health problem.

Musani SK, Erickson S, and Allison DB. Obesity – still highly heritable after all these years. *Am J Clin Nutr* 2008;87:275–276.

SERUM ANTIOXIDANTS AND FUNCTIONAL DECLINE

Bartali B, Frongillo EA, Guralnik JM, Stipanuk MH, Allore HG, Cherubini A, Bandinelli S, Ferrucci L, and

Gill TM. Serum micronutrient concentrations and decline in physical function among older persons. *JAMA* 2008;299:308–315.

The progressive decline seen frequently in aging deprives elders of their independence and remains an important public health concern. Disability in older people may be related, in part, to poor nutrient status, possibly through oxidative stress and inflammation. However, it is important to determine whether poor nutrition precedes disability, rather than nutritional status suffering as a consequence of impaired physical functioning. In the present study, Bartali et al. report on findings from the Invecchiare in Chianti (InCHIANTI) study, which is a population-based prospective study of risk factors that contribute to functional decline in aging.

Baseline and 3-year follow-up measures for cognitive function, physical performance, and serum micronutrient concentrations were measured in 698 (~54% women) free-living elders in the Tuscany region of Italy. Cognitive function and depressive symptoms were measured using the Mini-Mental State Examination (MMSE) and the Center for Epidemiological Studies-Depression Scale (CES-D). Physical function and performance was determined using Short Physical Performance Battery scores derived from 4-meter walking speed, repeated chair rises, and standing balance in various positions. Scores range from 0–12 with higher scores indicating better performance; decline was defined as at least a one-point loss in function at the 3-year follow up. Micronutrient analysis included folate, vitamins B6 and B12, vitamin E, 25-hydroxyvitamin D, and iron. Of all the nutrients analyzed, only low concentrations of vitamin E (<1.1 ug/ml) was linked to subsequent decline in physical performance. Cognitive and depressive scores did not vary as a function of the nutrients examined. The authors posit that vitamin E's antioxidant capabilities play an important role in the maintenance of physical function with aging, perhaps via prevention of DNA, neural, and muscle damage.

NUTRITION LABELING AND CONSUMER COMPREHENSION

Feunekes GI, Gortemaker IA, Willems AA, Lion R, and van den Kommer M. Front-of-pack nutrition labelling: testing effectiveness of different nutrition labelling

formats front-of-pack in four European countries. Appetite 2008;50:57–70.

Based on evidence linking certain dietary variables with chronic conditions such as cardiovascular disease, obesity, and diabetes, many countries require nutrition labels on packaged food. Nutrition labels on food packaging are intended to provide consumers with easily understandable information about nutrients and energy density, and in theory should allow consumers to make educated decisions regarding the “healthfulness” of a product. However so-called “back-of-pack” labels have come under criticism for failing to provide information that the average consumer can interpret, with lower-educated consumers particularly challenged. Newer “front-of-pack” labels and symbols are designed to rapidly convey health information to a wide range of consumers, thus enabling a broader range of the population to make healthier food choices. It is important to note that “healthy” choices in these cases are somewhat determined by what each country has mandated for labeling standards, but generally total energy value, sugars, fats, and sodium levels are included in this determination. Feunekes et al. studied different front-of-pack labels on European foodstuffs and evaluated their ability to help consumers distinguish between healthier and less-healthy food choices.

Labeling formats included a “healthier choice” check mark, a health-protection-factor “shield”, stars or smileys, a traffic light, and a “wheel of health”. The traffic light and “wheel of health” symbols are used in UK food labeling and indicate the levels of fat, sugar, sodium, and energy per serving of food. The other ratings, such as stars and smileys, were chosen since consumers are familiar with such rankings for restaurant and hotel quality. The study’s 1630 participants from the UK, Germany, Italy, and the Netherlands (ages 18–55 y) were recruited from Internet research panels, and testing was conducted online. Participants were shown nine pairs of products with front-of-pack labeling and were asked to rate the likeability, credibility, and perceived healthfulness of each product. Participants found all front-of-pack labels easy to understand and credible. The “wheel of health” and traffic lights were liked the most and stars/smileys were liked the least. However, stars and smileys were better differentiators for the healthfulness of a product. Additionally, participants with lower perceived nutritional knowledge were less able to use detailed information from symbols like the “wheel of health” than were more knowledgeable participants. Front-of-pack labeling is easily assimilated by consumers and enables shoppers to make healthier choices. Moreover, simple food ratings allow less-knowledgeable consumers to make relatively healthy choices within the context of food labeling.

POMEGRANATE AND ANTIOXIDANT FUNCTION

Guo C, Wei J, Yang J, Xu J, Pang W, and Jiang Y. Pomegranate juice is potentially better than apple juice in improving antioxidant function in elderly subjects. Nutr Res 2008;28:72–77.

A growing body of research suggests that long-term oxidative damage contributes to the aging process, and considerable research has been devoted to forging a link between antioxidant intake and improved functioning in older individuals. Fruits and vegetables are rich in polyphenols, vitamins, and minerals, and diets containing a variety of fruits and vegetables are associated with increased antioxidant capacity. However, certain varieties of fruits such as grapes, blueberries, and pomegranates have a higher profile of phenolic compounds than other fruits, such as apples, and certain fruits may be more efficacious in health-promoting effects than others. In the present study, Guo et al. compared pomegranate juice and apple juice for their ability to alter antioxidant functioning in elderly participants.

Twenty-six individuals (including six women) over the age of 60 from the People’s Republic of China were randomly assigned to one of two groups: pomegranate juice or apple juice (250 ml/d, consumed in the morning). Participants were instructed to maintain a balanced diet, as recommended by the Chinese Nutrition Society, for the duration of the study. Blood samples were collected at the beginning and end of the four-week study and analyzed for levels of ascorbic acid, vitamin E, antioxidant capacity, and activity of antioxidant enzymes. After four weeks of treatment, participants did not differ in plasma levels of ascorbic acid, vitamin E, or glutathione as a function of juice condition. Individuals drinking pomegranate juice showed increased antioxidant capacity and decreased plasma carbonyl content relative to those drinking apple juice. Pomegranates are higher in total phenolic compounds, flavonoids, and proanthocyanins than apples and the authors hypothesize that these compounds in pomegranates contribute significantly to antioxidant capacity following consumption. It is important to note that, in this study, the pomegranate juice was freshly made at the time of the study while the apple juice was purchased bottled. It is possible, that stored pomegranate juice may have a different antioxidant profile than fresh pomegranate juice. The researchers suggest that long-term studies with larger sample sizes will provide further information on the consumption of fruits rich in phenolic compounds and antioxidant functioning in elderly people.

GLYCEMIC INDEX AND POST-PARTUM DEPRESSION RISK

Murakami K, Miyake Y, Sasaki S, Tanaka K, Yokoyama T, Ohya Y, Fukushima W, Kiyohara C, Hirota Y, and The Osaka Maternal and Child Health Study Group. *Dietary glycemic index and load and the risk of postpartum depression in Japan: The Osaka Maternal and Child Health Study. J Affect Disord* 2008; [Epub ahead of print; doi:10.1016/j.jad.2007.12.230]

Post-partum depression is a frequent and troubling complication in new mothers, and is hypothesized to be related to decreases in central serotonin resulting from post-partum decreases in insulin levels. Cross-national observations of post-partum depression show the incidence is higher in nations following a relatively low glycemic index diet (such as the United States, the UK, and Australia) in comparison to nations following relatively high glycemic index diets. Murakami et al. present an intriguing hypothesis of an inverse relationship between dietary glycemic index and risk for post-partum depression. In this hypothesis, a high glycemic index diet would potentially keep both insulin and serotonin levels higher in the immediate post-natal period, thus reducing risk for depression.

Using data from the Osaka Maternal and Child Health Study (OMCHS), the authors investigated the dietary habits and outcome of post-partum depression in 865 Osakan women. Dietary intake patterns were estimated using a dietary history questionnaire. Dietary glycemic index (GI) was calculated by multiplying the contribution of each individual food to daily total intake of carbohydrate and then summing the products. Glycemic load (GL) was expressed by multiplying the dietary GI by total available dietary carbohydrate divided by 100. The authors acknowledge concerns about the utility of using GI for mixed meals and indicate that the use of GI gives an idea of carbohydrate quality in the diet while GL gives an indicator of both carbohydrate quality and quantity. Post-partum depression scores were determined using a 10-item scale rating the severity of depressive symptoms experienced within the most recent seven days (EPDS). Dietary GI and GL were then compared to EPDS scores. Fourteen percent of the participants were classified as having post-partum depression. When examined across quartiles, dietary GI in the third quartile was associated with less risk for post-partum depression than dietary GI in the lowest quartile; however, this relationship was not dose-dependent. Although this research study had some limitations, including collection of

dietary intake during pregnancy rather than at the time of depression rating, the relationship of dietary glycemic index to post-partum depression presents the opportunity to examine the role of dietary carbohydrate and mood during pregnancy and in the post-partum months.

SOY ISOFLAVONES AND BONE MINERAL DENSITY

Ma DF, Qin LQ, Wang PY, and Katoh R. *Soy isoflavone intake increases bone mineral density in the spine of menopausal women: meta-analysis of randomized controlled trials. Clin Nutr.* 2008;27:57-64.

In the first few years following menopause, women experience rapid bone loss that then becomes more gradual and sustained throughout the remainder of life if untreated. This loss of bone mass accompanies the decline of available estrogen in menopause, and long-term hormone-replacement remains an important preventive therapy for osteoporosis. Soy isoflavones and other phytoestrogens are gaining popularity as alternative menopausal therapies due to their actions at estrogen receptors. Several studies have addressed the efficacy of soy intake on maintaining bone mass in menopausal women, but the results have been mixed. Ma et al. identified nine randomized controlled trials examining soy isoflavone intake and bone metabolism and performed a meta-analysis on the outcomes of these studies.

To be included in the meta-analysis, each trial had to include measures of bone formation (serum bone-specific alkaline phosphatase [BAP]) and/or bone resorption (urinary deoxyypyridinoline [Dpyr]). Additionally, to be included, each trial needed to include a non-soy placebo condition, peri- or post-menopausal women, and intervention needed to last at least four weeks. Isoflavone intakes ranged from ~40 mg/day to ~118 mg/day and treatments lasted between 4 and 48 weeks. When data were pooled for meta-analysis, intake of soy isoflavones significantly decreased urinary Dpyr suggesting inhibition of bone resorption. This reduction in urinary Dpyr was not related to intake of isolated soy protein, and was seen with doses less than the recommended intake of 90 mg/day isoflavones. Isoflavone intake was associated with a significant increase in BAP, indicating a positive effect of isoflavones on bone formation. The authors suggest that isoflavones and phytoestrogens may alter bone metabolism via estrogen-mediated pathways.

KE D'Anci

SALT INTAKE AND SOFT DRINK CONSUMPTION IN CHILDREN

He FJ, Marrero NM, and MacGregor GA. Salt intake is related to soft drink consumption in children and adolescents. A link to obesity? *Hypertension*. 2008;51:629-634.

The link between salt intake and fluid intake is well characterized in adults. The World Health Organization has estimated that reducing daily salt intake by half, to ~5 g/d, would reduce fluid intake by about 350 mL/d per person. While intake of water is seldom of concern, much of the fluids consumed in developed nations contribute significant calories to the daily diet. Soft drink intake in children, in particular, is a concern due to the proposed link between intake of sweetened beverages and obesity. To determine a link between salt intake and soft drink consumption, He et al. analyzed data from the National Diet and Nutrition Survey for young people in Great Britain. The survey, conducted in 1997, provides a representative sample of young people between the ages of 4 and 18 years.

Data from 1688 participants (837 girls) were included in the analysis of He et al. Average salt intake (excluding that used in cooking or at the table) was ~4.6 g/d at age 4, and intake increased with age. By the age of 18, individuals were consuming ~6.8 g/d. Mean fluid intakes varied with age, with younger children consuming less than older children (range ~980-1300 mL/d). Approximately 30% of total fluid intake came from sugar-sweetened beverages. Salt intake was highly correlated with fluid intake, and regression analysis indicated that a 1 g/d reduction in salt intake would lead to a 100 g/d reduction in fluid intake. This study is the first to show a relationship between salt intake and fluid intake in children. Reduction of salt intake in general is a major public health goal, with the aim of reducing hypertension. The authors also posit that reduction of salt intake could potentially reduce obesity by limiting the amount of sweetened beverages children consume; however, this presumes that children will selectively reduce intake of sugar-sweetened beverages rather than reducing intake of beverages of all types.

Comment: Dr. Weinberger, in an accompanying editorial, addresses the conclusions drawn by He et al. Importantly, he notes that the relationship between sodium intake, caloric intake, and sweetened beverage consumption are not isolated variables in the recent rises in obesity in children and adolescents. Additionally, he observes that intake of sweetened beverages remains relatively constant, and he raises the point that salt intake may affect

hedonic preference for sweetened beverages, but that this has not been adequately explored.

Editorial Comment: Weinberger MH. Are children doomed by what they eat and drink? *Hypertension*. 2008;51:615-616.

VITAMIN K AND HIP FRACTURE

Yaegashi Y, Onoda T, Tanno K, Kuribayashi T, Sakata K, and Orimo H. Association of hip fracture incidence and intake of calcium, magnesium, vitamin D, and vitamin K. *Eur J Epidemiol*. 2008;23:219-225.

Hip fracture is a common and serious outcome of osteoporosis, which can lead to loss of independence and decreased quality of life in the elderly. Nutrients such as calcium, magnesium, and vitamins D and K are recognized for their importance in bone metabolism. Vitamin K has only recently gained attention for its proposed role in bone health, perhaps through positive effects on calcium balance. Yaegashi et al. explored national intake patterns of calcium, magnesium, and vitamins D and K and related intake levels to incidence of hip fracture in Japanese men and women.

The estimated number of hip fractures in 2002 was 211,600 (93,100 women), with different rates seen in different regions of the country. Fracture incidence was inversely correlated with regional intakes of vitamin K. In eastern Japan, high intake of vitamin K was associated with low incidence of hip fracture. In western areas of Japan, low vitamin K intake was associated with high incidence of hip fracture. It should be noted that the comparisons made in this study did not correlate intakes in individuals with or without hip fracture, but were made between national survey data. More research is needed to clearly establish the relationship between vitamin K and risk for hip fracture. The authors suggest that reconsidering the dietary reference intake of vitamin K from the perspective of osteoporosis is warranted.

HOMOCYSTEINE LOWERING AND PLASMA PHOSPHATIDYLCHOLINE

Crowe FL, Skeaff CM, McMahon JA, Williams SM, and Green TJ. Lowering plasma homocysteine concentrations of older men and women with folate, vitamin B-12, and vitamin B-6 does not affect the proportion of (n-3) long chain polyunsaturated fatty acids in plasma phosphatidylcholine. *J Nutr*. 2008;138:551-555.

High levels of circulating homocysteine are associated with increased risk of cardiovascular disease (CVD).

Although reasonable hypotheses have been made regarding the role of B vitamin deficiency in elevated homocysteine, and trials have examined the ability of homocysteine-lowering treatments to prevent CVD, these trials have not been overly successful at reducing CVD even in the presence of reduced homocysteine. It is likely, therefore, that these trials have been confounded by other, unmeasured risk factors. One proposed risk factor is plasma levels of n-3 long chain polyunsaturated fatty acids (n-3 PUFA). Some research shows that low folate status or high homocysteine can decrease the proportion of n-3 PUFA, and administration of folate can increase the proportion of n-3 PUFA. In humans, research on this relationship is limited, however. Crowe et al. report on data from a randomized controlled study examining the effect of folate, B₆, and B₁₂ on the fatty acid composition in plasma phosphatidylcholine in individuals 65 years of age or older.

Participants received either a capsule containing 1000 µg folate, 500 µg vitamin B₁₂, and 10 mg vitamin B₆ (*n* = 123), or placebo (*n* = 120) daily for 2 years. Fasting plasma samples were taken at baseline and at 6-month intervals. Plasma homocysteine was significantly reduced and plasma folate and B₁₂ were significantly elevated following intake of the supplement in comparison to placebo. The proportions of fatty acids in phosphatidylcholine were not affected by B vitamin intake. These data suggest that homocysteine or B vitamin intake may not affect the metabolism of n-3 PUFA. Although intake of the B vitamin supplement successfully lowered plasma homocysteine, plasma fatty acid proportions were not affected, providing one avenue to explore in the complex relationship among nutrient status, homocysteine, and CVD.

ANTIOXIDANT INTAKE AND DEMENTIA RISK

Gray SL, Anderson ML, Crane PK, Breitner JC, McCormick W, Bowen JD, Teri L, Larson E. Antioxidant vitamin supplement use and risk of dementia or Alzheimer's disease in older adults. *J Am Geriatr Soc.* 2008;56:291-295.

The antioxidant vitamins C and E have long been thought to play an important role in offsetting oxidative stress and subsequent disease. Epidemiological studies demonstrate a link between diets rich in antioxidants and reduced risk for Alzheimer's disease or vascular dementia. However, trials using supplements of vitamin C or vitamin E have shown no benefit in Alzheimer's disease risk. Gray et al. describe a prospective cohort study designed to examine the use of vitamins C and E, alone or in combination, and subsequent incidence of dementia or Alzheimer's disease.

Participants from the Adult Changes in Thought study were followed for an average of 5.5 years to identify dementia and Alzheimer's disease (*n* = 2969). Supplement use was determined by self-report of intake for at least 1 week in the month prior to baseline. During follow-up, 405 participants were diagnosed with dementia. Intake of vitamins C and E, alone or in combination, was not associated with a reduction in risk for developing dementia. A weakness of this study is the imprecise measurement of duration, frequency, and dose of antioxidant intake, and the reliance on participant self-report. For example, it is possible that as people progress into dementia, reports of supplement intake would become increasingly unreliable. Although many researchers propose a link between oxidative stress and the etiology of Alzheimer's disease and vascular dementias, hard evidence for the role of antioxidant supplements in preventing cognitive decline and onset of neuropathology remains elusive.

UTILITY OF GLUCOSAMINE SULFATE IN OSTEOARTHRITIS

Rozendaal RM, Koes BW, van Osch GJ, Uitterlinden EJ, Garling EH, Willemsen SP, Ginai AZ, Verhaar JA, Weinans H, and Bierma-Zeinstra SM. Effect of glucosamine sulfate on hip osteoarthritis: a randomized trial. *Ann Intern Med.* 2008;148:268-277.

Although widely used to treat symptoms of osteoarthritis, the efficacy of glucosamine sulfate in mediating pain and functioning in arthritis sufferers has not been established. Furthermore, many studies examine the effect of glucosamine in knee osteoarthritis, but its efficacy in hip osteoarthritis has not been reported. Rozendaal et al. conducted a 2-year randomized controlled trial comparing the effects of 1500 mg glucosamine sulfate and placebo on the progression of hip osteoarthritis.

Primary outcome measures included pain and function scores and joint space narrowing. A total of 207 individuals completed the 2-year trial (placebo *n* = 103, ~70% women; glucosamine *n* = 104, ~68% women). The results indicated glucosamine was not different from placebo in modifying the progression of hip osteoarthritis as determined by joint space narrowing or pain and function scores. The authors suggest that some studies show a benefit of glucosamine in the management of less severe osteoarthritis symptoms relative to more severe symptoms, although the severity of osteoarthritis in the present population was similar to that in other studies showing a benefit.

Comment: Glucosamine sulfate is thought to have its primary effect on preventing the loss of cartilage in osteoarthritis. Drs. Bijlsma and Lafeber suggest that the

progression of osteoarthritis in the Rozendaal et al. study may have been too slow to see positive effects of glucosamine sulfate. In the present study, they argue, the loss of cartilage did not proceed at a rate that could be realistically treated with glucosamine supplementation. They suggest that a similar trial in individuals with more advanced osteoarthritis, where cartilage loss occurs more

rapidly, would allow differences between glucosamine and placebo to be seen.

Editorial Comment: Bijlsma JW and Lafeber FP. Glucosamine sulfate in osteoarthritis: the jury is still out. Ann Intern Med. 2008;148:315–316.

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