Soyfoods for Infants, Children & Adolescents

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THE PUBLIC HEALTH BURDEN of diet-related chronic diseases has led to increasing emphasis on efforts to establish healthy eating habits as early in life as possible.[1] In part, this results from recognition that childhood eating habits track into adulthood and changing adult dietary behavior is difficult.[2-6]

Evidence also suggests that childhood and adolescent health behaviors affect the risk of developing certain chronic diseases later in life.[7-9] For example, obesity in childhood is associated with an increased mortality from cardiovascular disease in adulthood, independent of adult weight.[10] Early lifestyle factors are also known to affect the likelihood of developing breast cancer during adulthood.[11] These observations are important given that one in five U.S. children is overweight[12] and diseases once seen primarily only in adults, such as hypertension[13] and non-insulin dependent diabetes mellitus,[14] are increasingly common in childhood. It is also recognized that the beginning stages of chronic diseases, such as coronary heart disease, are already apparent in adolescents.[15]

Given the impact of early-life dietary behavior, it is important to understand how the nutritional attributes of soyfoods may impact the health of young people from infancy through the teenage years.

Soy Infant Formula

Although breast milk is the ideal food for infants,[16] about one-third of women choose not to breast feed for a variety of reasons. Of those who do, most switch to formula feeding at some point in the infant's first year.[17] Commercially-prepared, fortified infant formulas are appropriate to supplement or replace human milk for babies who are no longer breast fed during the first year of life. While most mothers initially choose a cow's milk-based formula, about 20 percent of infants are fed soy formula for some period of time.[18]

Milk allergy is one reason some mothers choose to switch to soy formula. There is evidence that soy formula is hypoallergenic relative to milk-based formulas,[19] although there is no consensus about when or whether to recommend that infants allergic to cow's milk should consume soy infant formula.[20, 21] Most recently however, an Australian panel of experts concluded that soy formula is an appropriate alternative for infants six months and older who demonstrate immediate food allergy to cow's milk and delayed reaction in the form of atopic eczema and other gastrointestinal syndromes.[22]

Isoflavones in Infant Diets

An estimated 20 million U.S. infants have consumed soy infant formula since it became commercially available in the 1960s.[18] With the exception of a few early cases of goiter[23-25] (an issue that was addressed in soy infant formula in the mid-1960s by iodine fortification), no problems related to soy formula consumption have been identified over this long history of use. Research shows that soy infant formula leads to normal short-term growth and development.[18, 20, 26-28]

Nevertheless, despite its widespread use over several decades, soy formula has become somewhat controversial in recent years due to the naturally high isoflavone content of soy protein.[29, 30] Isoflavones, which are often referred to as phytoestrogens, exhibit estrogen-like effects under certain experimental conditions.[31] However, research in adults shows that many biological measures affected by the hormone estrogen are not affected by isoflavones.[32-52] Thus, it is inappropriate to equate isoflavones with estrogen. Furthermore, there is no clinical evidence that soy formula consumption leads to adverse effects in infants.[26, 53, 54]

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The limited long-term data indicate no meaningful differences in a host of biological parameters between adults fed soy-based formula or cow's milk-based formula as infants.[55] Also, recent research has shown that young children fed soy formula as infants experienced no hormone-related abnormalities.[56]

According to the American Academy of Pediatrics, isolated soy protein-based formulas are safe and effective alternatives to breast milk or cow's milk-based formulas and provide appropriate nutrition for normal growth and development.

In fact, to the contrary, results from a small preliminary study found that girls fed soy formula as infants were 40 to 60 percent less likely to develop breast cancer as adults in comparison to women who, as infants, were fed breast milk, cow's milk formula or a combination of both.[57]

A comprehensive review published in 2004 summarized the situation regarding soy formula by stating, "The evidence from laboratories showing biological activities at doses or tissue concentrations relevant to soy-fed infants is difficult to reconcile with the long record of uneventful use of these formulas."[58]

As a high-quality protein, soyfoods can play an important role in a healthy and varied diet. And, most soyfoods are low in saturated fat.

Because it is not feasible to conduct some safety-related research in humans, animal studies are frequently cited despite the many physiological differences between animals and humans. It is important to note that animals, including rodents and monkeys, metabolize isoflavones very differently than humans.[59] Therefore, any extrapolation of findings in animals to humans should be done with caution.

In 2006, the National Toxicology Program Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) issued two comprehensive reports on the safety of soy formula and the isoflavone genistein.[60, 61] The expert panel that authored these reports reached the following two conclusions:

1) There is negligible concern for adverse effects in neonates and infants from genistein exposure as a result of consuming soy formula.

2) There are insufficient human or experimental animal data available to permit a determination of the developmental or reproductive toxicity of soy infant formula.

Thus, the NTP-CERHR panel concluded that soy formula is an appropriate choice for infants who are not breast fed during the first year of life.

Finally, soy formula may be contraindicated for infants with congenital hypothyroidism that use synthetic thyroid hormone.[62] There is some evidence that soy is one of a number of dietary components that may interfere with the absorption of medication in these infants.[63]

Soyfoods in the Diets of Children

As with adults,[64] clinical research shows that soy protein directly lowers serum cholesterol levels and improves other lipids in children.[65-69] In the most recent study, conducted over a 3-month period, when soy protein (average intake 0.5 g/kg body weight) was incorporated into the diet of children and adolescents (mean age, 8.8 years; range 4-18 years) with familial and polygenic hypercholesterolemia, low density lipoprotein cholesterol decreased by 6.4 percent beyond the 11 percent decrease that occurred in response to the adoption of standard low-saturated fat diet during the 3-month run-in period.[69] Thus, soy protein in combination with other dietary therapies may reduce cholesterol levels to target goals, although soy protein alone will not do so.[70]

Soy protein may also help to reduce the required dose of any hypocholesterolemic medication. Reducing medication would help to reduce or eliminate drug side effects. Maintaining normal cholesterol levels in children is important because the atherosclerotic process is already evident in some young people.[71]

Continued on page 3

Soy Protein Quality

Soyfoods provide high-quality protein and most come without high levels of saturated fat.[72] Because soy protein meets the nutritional needs of growing children, the U.S. Department of Agriculture (USDA) in 2000 removed previous limits on the amount of soy protein that can be used within the National School Lunch Program.[73]

For several reasons, access to healthful sources of protein without excessive saturated fat is important for children. Higher protein diets are associated with greater satiety and weight loss.[74] Also, recent evidence in young boys shows that consumption of protein above the recommended dietary allowance enhances the impact of physical activity on bone mineral density.[75]

Not surprisingly, because most soyfoods are relatively low in saturated fat, substituting them for more traditional sources of protein generally improves overall diet quality. Combining soy protein with either beef or pork proteins can lead to a decrease in the fat, saturated fat and calorie content for a total entree, as long as portion size stays the same.[76, 77] Similarly, combining cheese, eggs or meat with tofu leads to improved nutritional quality of entrees.[78]

In general, soyfoods help meet the USDA's Dietary Guidelines.[76, 78] Short-term studies show that soyfoods support the normal growth and development of children,[79] and improve growth when substituted for legumes in the diet of malnourished preschoolers.[80, 81] Thus, soyfoods can play an important part in a healthy and varied diet.

Acceptance of Soyfoods in Children's Diets

Studies show that soyfoods are generally quite acceptable to children.[78, 82, 83] For example, among preschool children aged 3 to 6 years old attending a Head Start program, children consumed soy-enhanced lunches as readily as those made with more traditional ingredients, as evidenced by the amounts eaten.[82]

Negative beliefs about soy's palatability persist among some populations, however. When non-vegetarian subjects are told that a product contained soy, they are more likely to rate is as "grainy, chalky, dry, and unappealing" even when, in fact, the product did not actually contain any soy ingredients.[84] However, foods containing soy are also generally thought by U.S. consumers to be more "healthy tasting."[84] Ratings are influenced primarily by the amount of soy consumed by a given individual.

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Soy Protein and Allergies

Essentially all food proteins have the potential to cause allergic reactions in some individuals. Although soy protein is one of the eight food proteins responsible for approximately 90 percent of all allergic reactions, the number of adults allergic to soy is extremely small.[85]

The relative number of children allergic to soy protein is almost certainly higher than adults because children are much more sensitive to dietary proteins than are adults.[86] Importantly, most children are thought to outgrow their soy allergies early on in life.[86] However, the pace at which children outgrow food allergies is a matter of some recent discussion.[87]

The FDA notes in the 2004 Food Allergen Labeling and Consumer Protection Act that highly refined oils, such as soybean oil, are non-allergenic because the protein that causes food allergy has been removed during processing.

Continued on page 4

Mounting evidence suggests that early life events greatly impact breast cancer risk:

Researchers from the National Cancer Institute reported that, in comparison to low-soy consumers, women who were classified as high-soy consumers during the ages of 5-11, 12-19, and 20+ years of age were 58, 21 and 29 percent less likely to develop breast cancer, respectively.

Isoflavones in Children's Diets

Recent preliminary data suggest that children absorb isoflavones to a greater extent than adults.[88]

While soyfoods have been consumed by Asian children for centuries without any apparent adverse effects, there is much interest in gaining insight into the biological effects of isoflavones in children.

Results of a recent Australian study which looked at effects of isoflavones on high-density lipoprotein (HDL) levels suggest that isoflavones do not exert estrogenic effects in teenage boys. HDL levels decrease in boys as they enter puberty whereas no such decrease occurs in girls — a difference that may be due to their higher estrogen levels. Isoflavones might be expected to lower HDL in pubescent boys if they exerted estrogenic effects, but in the Australian study, no such changes were seen.[89]

Finally, there are speculative although very intriguing data suggesting that soy intake during adolescence reduces breast cancer risk later in life.[90,91] The hypothesis that early soy intake reduces later risk of breast cancer is supported by both epidemiologic and animal data and is consistent with mounting evidence that early life events greatly impact breast cancer risk.[92] The first 20 years of life appear to be particularly important.[93]

Specifically with regard to soy, research from the University of Alabama has shown that when rats are given the primary isoflavone in soybeans for just a few weeks early in life followed by a typical laboratory diet, they develop 50 percent fewer tumors than rats not given this isoflavone.[90]

Consistent with these findings, women from Shanghai who consumed the equivalent of about 1½ servings of soyfoods daily when they were 13 to 15 years of age were 50 percent less likely to develop breast cancer as adults compared to Chinese women who consumed little soy during adolescence.[91]

More recently, researchers from the National Cancer Institute reported that, in comparison to low-soy consumers, women who were classified as high-soy consumers during the ages of 5-11, 12-19, and 20+ years of age were 58, 21 and 29 percent less likely to develop breast cancer, respectively.[94]

The potential public health benefit of modest soy consumption during childhood and adolescence can not be overstated.

Summary and Conclusions

Establishing good eating habits early in life is important. Childhood dietary intake may impact adult chronic disease risk and influence eating habits in adulthood. Soyfoods provide important options for improving the diets of young people, and research shows that these foods are accepted by children.

Therefore, soyfoods can be viewed as healthy additions to the diets of children and adolescents. Other than a relatively rare soy protein allergy, there is no clinical evidence that soyfoods exert any negative effects. To the contrary, there is evidence suggesting that exposure to soy during childhood and/or adolescence may reduce breast cancer risk later in life.

References

1. Ludwig DS. Childhood obesity--the shape of things to come. *N Engl J Med* 2007;357:2325-7.
2. Mikkila V, Rasanen L, Raitakari OT, Pietinen P, Viikari J. Consistent dietary patterns identified from childhood to adulthood: the cardiovascular risk in Young Finns Study. *Br J Nutr* 2005;93:923-31.
3. Mennella JA, Griffin CE, Beauchamp GK. Flavor programming during infancy. *Pediatrics* 2004;113:840-5.
4. Mennella JA, Beauchamp GK. Flavor experiences during formula feeding are related to preferences during childhood. *Early Hum Dev* 2002;68:71-82.
5. Birch LL. Development of food acceptance patterns in the first years of life. *Proc Nutr Soc* 1998;57:617-24.
6. Anonymous. Guidelines for school health programs to promote lifelong healthy eating. Centers for Disease Control and Prevention. *MMWR Recomm Rep* 1996;45:1-41.
7. Adair LS, Prentice AM. A critical evaluation of the fetal origins hypothesis and its implications for developing countries. *J Nutr* 2004;134:191-3.
8. McCormack VA, dos Santos Silva I, De Stavola BL, Mohsen R, Leon DA, Lithell HO. Fetal growth and subsequent risk of breast cancer: results from long term follow up of Swedish cohort. *BMJ* 2003;326:248.
9. Robinson R. The fetal origins of adult disease. *BMJ* 2001;322:375-6.
10. Must A, Jacques PF, Dallal GE, Bajema CJ, Dietz WH. Long-term morbidity and mortality of overweight adolescents. A follow-up of the Harvard Growth Study of 1922 to 1935. *N Engl J Med* 1992;327:1350-5.
11. Russo J, Lareef H, Tahin Q, Russo IH. Pathways of carcinogenesis and prevention in the human breast. *Eur J Cancer* 2002;38 Suppl 6:S31-2.
12. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA* 2006;295:1549-55.
13. Sorof JM. Prevalence and consequence of systolic hypertension in children. *Am J Hypertens* 2002;15:57S-60S.
14. Lipton RB. Incidence of diabetes in children and youth--tracking a moving target. *JAMA* 2007;297:2760-2.
15. Berenson GS, Srinivasan SR, Bao W, Newman WP, 3rd, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. *N Engl J Med* 1998;338:1650-6.
16. Breastfeeding and the use of human milk. American Academy of Pediatrics. Work Group on Breastfeeding. *Pediatrics* 1997;100:1035-9.
17. Ahluwalia IB, Morrow B, Hsia J, Grummer-Strawn LM. Who is breast-feeding? Recent trends from the pregnancy risk assessment and monitoring system. *J Pediatr* 2003;142:486-91.
18. Merritt RJ, Jenks BH. Safety of soy-based infant formulas containing isoflavones: the clinical evidence. *J Nutr* 2004;134:1220S-4S.
19. Osborn DA, Sinn J. Soy formula for prevention of allergy and food intolerance in infants. *Cochrane Database Syst Rev* 2006:CD003741.
20. American Academy of Pediatrics. Committee on Nutrition. Hypoallergenic infant formulas. *Pediatrics* 2000;106:346-9.
21. Agostoni C, Axelsson I, Goulet O, Koletzko B, Michaelsen KF, Puntis J, Rieu D, Rigo J, Shamir R, Szajewska H, Turck D. Soy Protein Infant Formulae and Follow-On Formulae: A Commentary by the ESPGHAN Committee on Nutrition. *J Pediatr Gastroenterol Nutr* 2006;42:352-61.
22. Kemp AS, Hill DJ, Allen KJ, Anderson K, Davidson GP, Day AS, Heine RG, Peake JE, Prescott SL, Shugg AW, Sinn JK. Guidelines for the use of infant formulas to treat cows milk protein allergy: an Australian consensus panel opinion. *Med J Aust* 2008;188:109-12.
23. Van Wyk JJ, Arnold MB, Wynn J, Pepper F. The effects of a soybean product on thyroid function in humans. *Pediatrics* 1959;24:752-60.
24. Shepard TH, Gordon EP, Kirschvink JF, McLean CM. Soybean goiter. *New Engl J Med* 1960;262:1099-103.
25. Pinchera A, MacGillivray H, Crawford JD, Freeman AG. Thyroid refractiveness in an athyreotic cretin fed soybean formula. *N Engl J Med* 1965;273:83-7.
26. Klein KO. Isoflavones, soy-based infant formulas, and relevance to endocrine function. *Nutr Rev* 1998;56:193-204.
27. Lasekan JB, Ostrom KM, Jacobs JR, Blatter MM, Ndife LI, Gooch WM, 3rd, Cho S. Growth of newborn, term infants fed soy formulas for 1 year. *Clin Pediatr* (Phila) 1999;38:563-71.
28. American Academy of Pediatrics. Committee on Nutrition. Soy protein-based formulas: recommendations for use in infant feeding. *Pediatrics* 1998;101:148-53.
29. Barrett JR. Soy and children's health: a formula for trouble. *Environ Health Perspect* 2002;110:A294-6.
30. Barrett JR. The science of soy: what do we really know? *Environ Health Perspect* 2006;114:A352-8.
31. Setchell KD, Zimmer-Nechemias L, Cai J, Heubi JE. Exposure of infants to phyto-oestrogens from soy-based infant formula. *Lancet* 1997;350:23-7.
32. Ho JY, Chen MJ, Sheu WH, Yi YC, Tsai AC, Guu HF, Ho ES. Differential effects of oral conjugated equine estrogen and transdermal estrogen on atherosclerotic vascular disease risk markers and endothelial function in healthy postmenopausal women. *Hum Reprod* 2006;21:2715-20.
33. Lakoski SG, Brosnihan B, Herrington DM. Hormone therapy, C-reactive protein, and progression of atherosclerosis: data from the Estrogen Replacement on Progression of Coronary Artery Atherosclerosis (ERA) trial. *Am Heart J* 2005;150:907-11.
34. Helgason S, Damber JE, Damber MG, von Schoultz B, Selstam G, Sodergard R. A comparative longitudinal study on sex hormone binding globulin capacity during estrogen replacement therapy. *Acta Obstet Gynecol Scand* 1982;61:97-100.
35. Serin IS, Ozcelik B, Basbug M, Aygen E, Kula M, Erez R. Long-term effects of continuous oral and transdermal estrogen replacement therapy on sex hormone binding globulin and free testosterone levels. *Eur J Obstet Gynecol Reprod Biol* 2001;99:222-5.
36. Reid IR, Eastell R, Fogelman I, Adachi JD, Rosen A, Netelenbos C, Watts NB, Seeman E, Ciaccia AV, Draper MW. A comparison of the effects of raloxifene and conjugated equine estrogen on bone and lipids in healthy postmenopausal women. *Arch Intern Med* 2004;164:871-9.
37. Shulman LP. Effects of progestins in different hormone replacement therapy formulations on estrogen-induced lipid changes in postmenopausal women. *Am J Cardiol* 2002;89:47E-54E; discussion E-5E.
38. Marqusee E, Braverman LE, Lawrence JE, Carroll JS, Seely EW. The effect of droloxifene and estrogen on thyroid function in postmenopausal women. *J Clin Endocrinol Metab* 2000;85:4407-10.
39. Abech DD, Moratelli HB, Leite SC, Oliveira MC. Effects of estrogen replacement therapy on pituitary size, prolactin and thyroid-stimulating hormone concentrations in menopausal women. *Gynecol Endocrinol* 2005;21:223-6.
40. Davies GC, Huster WJ, Shen W, Mitlak B, Plouffe L, Jr., Shah A, Cohen FJ. Endometrial response to raloxifene compared with placebo, cyclical hormone replacement therapy, and unopposed estrogen in postmenopausal women. *Menopause* 1999;6:188-95.
41. Meuwissen JH, van Langen H. Monitoring endometrial thickness during estrogen replacement therapy with vaginosonography. *Radiology* 1992;183:284.
42. Kaari C, Haidar MA, Junior JM, Nunes MG, Quadros LG, Kemp C, Stavale JN, Baracat EC. Randomized clinical trial comparing conjugated equine estrogens and isoflavones in postmenopausal women: a pilot study. *Maturitas* 2006;53:49-58.
43. Yildiz MF, Kumru S, Godekmerdan A, Kutlu S. Effects of raloxifene, hormone therapy, and soy isoflavone on serum high-sensitive C-reactive protein in postmenopausal women. *Int J Gynaecol Obstet* 2005;90:128-33.
44. D'Anna R, Baviera G, Corrado F, Cancellieri F, Crisafulli A, Squadrito F. The effect of the phytoestrogen genistein and hormone replacement therapy on homocysteine and C-reactive protein level in postmenopausal women. *Acta Obstet Gynecol Scand* 2005;84:474-7.
45. Garrido A, De la Maza MP, Hirsch S, Valladares L. Soy isoflavones affect platelet thromboxane A2 receptor density but not plasma lipids in menopausal women. *Maturitas* 2006;54:270-6.
46. Khaodhiar L, Ricciotti HA, Li L, et al. Daidzein-rich isoflavone aglycones are potentially effective in reducing hot flashes in menopausal women. *Menopause* 2008, 15:125-132.
47. Hall WL, Vafeiadou K, Hallund J, Bugel S, Reimann M, Koebnick C, Zunft HJ, Ferrari M, Branca F, Dadd T, Talbot D, Powell J, Minihane AM, Cassidy A, Nilsson M, Dahlman-Wright K, Gustafsson JA, Williams CM. Soy-isoflavone-enriched foods and markers of lipid and glucose metabolism in postmenopausal women: interactions with genotype and equol production. *Am J Clin Nutr* 2006;83:592-600.
48. Katz DL, Evans MA, Njike VY, Hoxley ML, Nawaz H, Comerford BP, Sarrel PM. Raloxifene, soy phytoestrogens and endothelial function in postmenopausal women. *Climacteric* 2007;10:500-7.
49. Cheng G, Wilczek B, Warner M, Gustafsson JA, Landgren BM. Isoflavone treatment for acute menopausal symptoms. *Menopause* 2007;14:468-73.
50. Bruce B, Messina M, Spiller GA. Isoflavone supplements do not affect thyroid function in iodine-replete postmenopausal women. *J Med Food* 2003;6:309-16.
51. Marini H, Minutoli L, Polito F, Bitto A, Altavilla D, Atteritano M, Gaudio A, Mazzaferro S, Frisina A, Frisina N, Lubrano C, Bonaiuto M, D'Anna R, Cannata ML, Corrado F, Adamo EB, Wilson S, Squadrito F. Effects of the phytoestrogen genistein on bone metabolism in osteopenic postmenopausal women: a randomized trial. *Ann Intern Med* 2007;146:839-47.
52. Sammartino A, Di Carlo C, Mandato VD, Bifulco G, Di Stefano M, Nappi C. Effects of genistein on the endometrium: ultrasonographic evaluation. *Gynecol Endocrinol* 2003;17:45-9.
53. Setchell KD. Assessing risks and benefits of genistein and soy. *Environ Health Perspect* 2006;114:A332-3.
54. Munro IC, Harwood M, Hlywka JJ, Stephen AM, Doull J, Flamm WG, Adlercreutz H. Soy isoflavones: a safety review. *Nutr Rev* 2003;61:1-33.
55. Strom BL, Schinnar R, Ziegler EE, Barnhart KT, Sammel MD, Macones GA, Stallings VA, Drulis JM, Nelson SE, Hanson SA. Exposure to soy-based formula in infancy and endocrinological and reproductive outcomes in young adulthood. *JAMA* 2001;286:807-14.

Continued on back page

References continued from inside page

56. Giampietro PG, Bruno G, Furcolo G, Casati A, Brunetti E, Spadoni GL, Galli E. Soy protein formulas in children: no hormonal effects in long-term feeding. *J Pediatr Endocrinol Metab* 2004;17:191-6.
57. Boucher BA, Cotterchio M, Kreiger N, Thompson LU. Soy Formula and Breast Cancer Risk. *Epidemiology* 2008;19:165-6.
58. Chen A, Rogan WJ. Isoflavones in soy infant formula: a review of evidence for endocrine and other activity in infants. *Annu Rev Nutr* 2004;24:33-54.
59. Gu L, House SE, Prior RL, Fang N, Ronis MJ, Clarkson TB, Wilson ME, Badger TM. Metabolic Phenotype of Isoflavones Differ among Female Rats, Pigs, Monkeys, and Women. *J Nutr* 2006;136:1215-21.
60. Rozman KK, Bhatia J, Calafat AM, Chambers C, Culty M, Etzel RA, Flaws JA, Hansen DK, Hoyer PB, Jeffery EH, Kesner JS, Marty S, Thomas JA, Umbach D. NTP-CERHR expert panel report on the reproductive and developmental toxicity of genistein. *Birth Defects Res B Dev Reprod Toxicol* 2006;77:485-638.
61. Rozman KK, Bhatia J, Calafat AM, Chambers C, Culty M, Etzel RA, Flaws JA, Hansen DK, Hoyer PB, Jeffery EH, Kesner JS, Marty S, Thomas JA, Umbach D. NTP-CERHR expert panel report on the reproductive and developmental toxicity of soy formula. *Birth Defects Res B Dev Reprod Toxicol* 2006;77:280-397.
62. Conrad SC, Chiu H, Silverman BL. Soy formula complicates management of congenital hypothyroidism. *Arch Dis Child* 2004;89:37-40.
63. Messina M, Redmond G. Effects of soy protein and soybean isoflavones on thyroid function in healthy adults and hypothyroid patients: a review of the relevant literature. *Thyroid* 2006;16:249-58.
64. Zhan S, Ho SC. Meta-analysis of the effects of soy protein containing isoflavones on the lipid profile. *Am J Clin Nutr* 2005;81:397-408.
65. Laurin D, Jacques H, Moorjani S, Steinke FH, Gagne C, Brun D, Lupien PJ. Effects of a soy-protein beverage on plasma lipoproteins in children with familial hypercholesterolemia. *Am J Clin Nutr* 1991;54:98-103.
66. Widhalm K, Brazda G, Schneider B, Kohl S. Effect of soy protein diet versus standard low fat, low cholesterol diet on lipid and lipoprotein levels in children with familial or polygenic hypercholesterolemia. *J Pediatr* 1993;123:30-4.
67. Gaddi A, Descovich GC, Noseda G, Fragiacomo C, Nicolini A, Montanari G, Vanetti G, Sirtori M, Gatti E, Sirtori CR. Hypercholesterolaemia treated by soybean protein diet. *Arch Dis Child* 1987;62:274-8.
68. Blumenschein S, Torres E, Kushmaul E, Crawford J, Fixler D. Effect of oat bran/soy protein in hypercholesterolemic children. *Ann N Y Acad Sci* 1991;623:413-5.
69. Weghuber D, Widhalm K. Effect of 3-month treatment of children and adolescents with familial and polygenic hypercholesterolaemia with a soya-substituted diet. *Br J Nutr* 2008;99:281-6.
70. Jenkins DJ, Kendall CW, Marchie A, Faulkner DA, Wong JM, de Souza R, Emam A, Parker TL, Vidgen E, Lapsley KG, Trautwein EA, Josse RG, Leiter LA, Connelly PW. Effects of a dietary portfolio of cholesterol-lowering foods vs lovastatin on serum lipids and C-reactive protein. *JAMA* 2003;290:502-10.
71. Charakida M, Deanfield JE, Halcox JP. Childhood origins of arterial disease. *Curr Opin Pediatr* 2007;19:538-45.
72. Rand WM, Pellett PL, Young VR. Meta-analysis of nitrogen balance studies for estimating protein requirements in healthy adults. *Am J Clin Nutr* 2003;77:109-27.
73. U.S. Department of Agriculture. Modification of the Vegetable Protein Products Requirements for the National School Lunch Program, School Breakfast Program, Summer Food Service Program and Child and Adult Care Food Program. *Fed Regist* 2000;7 CFR Parts 210, 215, 220, 225 and 226:12429-42.
74. Astrup A. The satiating power of protein--a key to obesity prevention? *Am J Clin Nutr* 2005;82:1-2.
75. Chevalley T, Bonjour JP, Ferrari S, Rizzoli R. High-Protein Intake Enhances the Positive Impact of Physical Activity on BMC in Prepubertal Boys. *J Bone Miner Res* 2008;23:131-42.
76. Thomas JM, Lutz SF. Soy protein lowers fat and saturated fat in school lunch beef and pork entrees. *J Am Diet Assoc* 2001;101:461-3.
77. McMindes MK. Applications of isolated soy protein in low-fat meal products. *Food Technology* 1991;45:61-4.
78. Ashraf HR, Schoeppel C, Nelson JA. Use of tofu in preschool meals. *J Am Diet Assoc* 1990;90:1114-6.
79. Egana JI, Fuentes A, Steinke FH, Uauy R. Protein quality comparison of a new isolated soy protein and milk in chilean preschool children. *Nutr Res* 1983;3:195-202.
80. Kay T, Ifeacho CL, Onowu G, Udenze V, Nnamani G, Anazonwu-Bello JN, Ifenu F, Modebe V, Emembolu M. Use of soya bean to improve the protein content of the diet in West Africa and thus prevent kwashiorkor. *J Trop Pediatr Environ Child Health* 1975;21:45-8.
81. Mathew A, Raut DS. Effect of soyamilk on the growth of malnourished children admitted to hospital wards. *Ind J Nutr Dietet* 1981;18:260-7.
82. Endres J, Barter S, Theodora P, Welch P. Soy-enhanced lunch acceptance by preschoolers. *J Am Diet Assoc* 2003;103:346-51.
83. Reilly JK, Lanou AJ, Barnard ND, Seidl K, Green AA. Acceptability of soymilk as a calcium-rich beverage in elementary school children. *J Am Diet Assoc* 2006;106:590-3.
84. Wansink B, Westgren R. Profiling taste-motivated segments. *Appetite* 2003;41:323-7.
85. Vierk KA, Koehler KM, Fein SB, Street DA. Prevalence of self-reported food allergy in American adults and use of food labels. *J Allergy Clin Immunol* 2007;119:1504-10.
86. Cordle CT. Soy protein allergy: incidence and relative severity. *J Nutr* 2004;134:1213S-9S.
87. Skripak JM, Matsui EC, Mudd K, Wood RA. The natural history of IgE-mediated cow's milk allergy. *J Allergy Clin Immunol* 2007;120:1172-7.
88. Halm BM, Ashburn LA, Franke AA. Isoflavones from soya foods are more bioavailable in children than adults. *Br J Nutr* 2007:1-8.
89. Dwyer T, Hynes KL, Fryer JL, Blizzard CL, Dalais FS. The lack of effect of isoflavones on high-density lipoprotein cholesterol concentrations in adolescent boys: a 6-week randomised trial. *Public Health Nutr* 2007:1-8.
90. Lamartiniere CA, Zhao YX, Fritz WA. Genistein: mammary cancer chemoprevention, in vivo mechanisms of action, potential for toxicity and bioavailability in rats. *J Women's Cancer* 2000;2:11-9.
91. Shu XO, Jin F, Dai Q, Wen W, Potter JD, Kushi LH, Ruan Z, Gao YT, Zheng W. Soyfood Intake during Adolescence and Subsequent Risk of Breast Cancer among Chinese Women. *Cancer Epidemiol Biomarkers Prev* 2001;10:483-8.
92. Russo J, Mailo D, Hu YF, Balogh G, Sheriff F, Russo IH. Breast differentiation and its implication in cancer prevention. *Clin Cancer Res* 2005;11:931s-6s.
93. Shimizu H, Ross RK, Bernstein L, Yatani R, Henderson BE, Mack TM. Cancers of the prostate and breast among Japanese and white immigrants in Los Angeles County. *Br J Cancer* 1991;63:963-6.
94. Korde LA, Wu AH, Fears T, Nomura AM, West DW, Kolonel LN, Pike MC, However RN, Ziegler RG. Childhood soy intake and breast cancer risk in Asian-American women. *Am Assoc Cancer Res Annual Meeting* (abstract - 06-AB-667-AACRCPR) 2006.

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