EATING HABITS EARLY IN LIFE MAY IMPACT ADULT CHRONIC DISEASES. THIS FACT SHEET WILL EXPLORE SOYFOODS' SAFE AND BENEFICIAL ROLE IN THE DIETS OF INFANTS, CHILDREN AND ADOLESCENTS.

INTRODUCTION

Establishing healthful eating habits early in life is important for two reasons. First, childhood eating habits track into adulthood, and changing adult dietary behavior is difficult. Second, evidence suggests that healthful behaviors during childhood and adolescence can affect the risk of developing certain chronic diseases later in life. For example, childhood obesity is associated with increased mortality from cardiovascular disease in adulthood, independent of adult weight. Early lifestyle factors are also thought to affect the likelihood of developing breast cancer during adulthood. These observations are important given that 20% of U.S. children are obese and diseases once seen primarily in adults, such as hypertension and Type 2 diabetes mellitus, are increasingly common in childhood. Evidence indicates that it isn’t just that chronic diseases begin early in life but that programming during fetal life and infancy permanently affects risk of developing non-communicable diseases in adult life. Programming refers to permanent changes in the body’s structure, physiology, and metabolism, which influences health throughout life. It is not just limited to the in utero environment, but extends into childhood, where different organs and systems continue to adapt to various cues.

It is also recognized that the beginning stages of chronic diseases, such as coronary heart disease, are already apparent in adolescents. In addition, there is an emerging epidemic of non-alcoholic fatty liver disease (NAFLD) estimated to affect millions of obese children. A recently published autopsy study found that 9.6% of the U.S. population, age 2-19 years old, and 38% of the obese individuals within this age range have NAFLD. NAFLD can progress to non-alcoholic steatohepatitis, which is characterized by oxidative stress, inflammation, apoptosis and fibrogenesis. Some animal data suggest soy may help to prevent the development of NAFLD.

Given the importance of early-life dietary behavior, it is essential 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, about one-third of women are unable to breastfeed or choose not to do so. Of those who choose breastfeeding, most switch to formula feeding at some point in the infant’s first year. Commercially-prepared, fortified infant formulas are appropriate to supplement or replace human milk during the first year of life. Various estimates for the prevalence of soy infant formula use exist. One older review noted not surprisingly that cow’s milk formula is the most commonly used product, but that about 13% of infants are fed soy infant formula (SF) for some period of time. More recently, a survey of a nationally representative sample of 1,864 infants, 0 to 12 months old, from the National Health and Nutrition Examination Survey, 2003-2010, found that among the 81% of infants who were fed formula or regular milk, 69% consumed cow’s milk formula, 12% consumed SF, 5% consumed gentle/lactose-reduced formulas, 6% consumed specialty formulas, and 13% consumed regular milk products. The percentage of children consuming SF was significantly higher (P < .05) among infants from higher income groups compared with the lower income group.

An allergy to milk protein is among the most common reasons for placing an infant on SF. There is evidence that SF is hypoallergenic relative to cow’s milk formulas. However, because according to some estimates 10-14% of infants who are allergic to cow’s milk formula are also allergic to SF, the American Academy of Pediatrics (AAP) suggests that many infants with documented cow’s milk protein allergy (CMA) should be switched directly to a hydrolyzed protein formula. It should be noted that soybean-specific IgE titers are not an effective predictor of a positive response to the food challenge test.

In contrast to the AAP, an Australian panel of experts concluded that SF is an appropriate alternative for infants over six months old who demonstrate immediate food allergy to cow’s milk and delayed reaction in the form of atopic eczema and other gastrointestinal syndromes. The French Society of Paediatrics holds a similar position but with the caveat that tolerance to soy protein should first be established by clinical challenge. Importantly, UK research found that of the 60% of all infants with CMA initially fed SF, only 9% remained symptomatic. In contrast, of the 18% of patients consuming extensively hydrolyzed formula, 29% remained symptomatic. The results from a small retrospective study from Portugal, which evaluated children with persistent CMA, also suggest that SF formula may have advantages over hydrolyzed formulas.

Finally, there are the conclusions of a newly published systematic review and meta-analysis, the first of its kind, which included 40 studies that evaluated the prevalence of IgE-mediated soy allergies in infants and children. According to the authors, their findings do not substantiate recommendations to postpone the introduction of SF in infants with IgE-CMA during the first six months of life based on the concern for an increased risk of allergy to soy.
ISOFLAVONES IN DIETS OF INFANTS FED SOY FORMULA

An estimated 20 million people in the United States consumed SF during infancy since it first became commercially available in the 1960s. Several cases of goiter were identified in the mid-1960s in infants using SF but this problem was eliminated soon thereafter when iodine was added to the formula. Since then, no thyroid problems attributed to SF use have been identified in healthy infants, and research shows that infants fed SF grow and develop normally.

In addition to iodine, all SF is fortified with iron, methionine, carnitine and taurine, and contains 20% more calcium and phosphorous than cow’s milk formulas. However, SF may be contraindicated for infants with congenital hypothyroidism who require synthetic thyroid hormone. This contraindication is because of evidence suggesting soy protein is one of a number of factors that may interfere with the absorption of thyroid medication.

Despite its long history of use, SF has become controversial in recent years due to its naturally high isoflavone content. Isoflavones, which are classified as phytoestrogens, exhibit estrogen-like effects under certain experimental conditions. However, isoflavones are very different from the hormone estrogen. The literature is replete with clinical examples demonstrating that isoflavones and estrogen affect a variety of health outcomes differently. Furthermore, isolated soy protein, which is the protein source in SF, should not be equated with isoflavones. There is no evidence from clinical studies that SF consumption leads to adverse effects in infants.

Especially important insight into the health effects of SF comes from a unique study underway at the Arkansas Children’s Nutrition Center, University of Arkansas for Medical Sciences. In this study, breast buds, uterus, ovaries, prostate and testicular volumes were assessed by ultrasonography at four months of age in 40 breast-fed infants, 41 infants fed cow’s milk formula and 39 infants fed SF. In all cases, SF-fed infants were similar to breast-fed or milk formula-fed infants whereas, unexpectedly, milk formula-fed infants had greater mean ovarian volume and greater numbers of ovarian cysts per ovary than did breast-fed infants. At this point the clinical relevance of these findings is unclear. Additional data from this research group continues to show that for a variety of health outcomes, infants fed SF fall well within the normal ranges.

Long-term data are limited, but in one retrospective study no meaningful differences in a host of biological parameters between adults who had consumed SF or cow’s milk formula as infants were noted. Interestingly, results from a very small and very preliminary study found that girls fed SF as infants were 40-60% less likely to develop breast cancer as adults compared to women who were fed breast milk, cow’s milk formula or a combination of both.
A comprehensive review published in 2004 summarized views on the isoflavone content of SF with this statement: “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.” This sentiment is similar to the current position of the AAP, which was issued in 2008: “…although studied by numerous investigators in various species, there is no conclusive evidence from animal, adult human, or infant populations that dietary soy isoflavones may adversely affect human development, reproduction, or endocrine function.”

An older Puerto Rican epidemiologic study found an association between SF use (along with several other factors) and premature breast development, but no such association was identified in a more recently published Israeli study. Because the types of safety-related research that can be conducted in humans are limited, animal studies are frequently cited in support of potential adverse effects of SF. Results of these studies are of questionable value due to the many physiological differences between animals and humans. Furthermore, many animals, including rodents and monkeys, metabolize isoflavones very differently than humans. For a review of some of the key issues see reference. In 2006, the National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction evaluated the safety of SF. Although their initial conclusions supported the safety of soy formula use, no final report was issued.
ISOFLAVONES IN CHILDREN’S DIETS

There is interest in gaining a better understanding of the effects of isoflavones in children although it is recognized that soyfoods have been consumed by young Asians for centuries without any apparent adverse effects. This interest is based on preliminary data indicating that children absorb isoflavones to a greater extent than adults and that relatively little research involving children has been conducted.

Three clinical studies were designed to determine whether isoflavones or soyfoods exert hormonal effects in children and/or adolescents:

- An Australian study found that isoflavones have no effect on high-density lipoprotein cholesterol (HDLC) levels in teenage boys, which suggests isoflavones don’t exert estrogenic effects. HDLC levels decrease in boys as they enter puberty whereas no such decrease occurs in girls, a difference that may be due to the higher estrogen levels in females. It was therefore hypothesized that isoflavone exposure would raise HDLC levels in boys.

- A small Israeli 12-week cross-over study found isoflavone supplements (0, 16 and 48mg/d) had no effect on blood reproductive hormone levels in young boys and girls.

- A pilot U.S. study involving 17 girls found that the consumption of approximately one serving of soyfoods daily (average isoflavone intake, ~27mg) had no effect on urinary sex steroid levels.

The lack of hormonal effects in these clinical trials involving children is consistent with research in adults showing that isoflavone exposure from soyfoods or supplements has no effects on circulating testosterone in men or estrogen levels in men or women.

There is increasing interest in understanding the impact of diet on pubertal development because pubertal characteristics are occurring at an earlier age in U.S. girls. Many factors likely contribute to this trend such as increasing adiposity. Epidemiologic studies have found that both total protein and animal protein intake is associated with earlier menarche and the development of early pubertal characteristics. Xenoestrogen exposure, which includes phytoestrogens such as isoflavones, has been proposed as another factor. For this reason, there is interest in determining whether soy intake affects pubertal development.

Two small Korean epidemiologic studies found that urinary isoflavones in children with precocious puberty were higher than in children serving as controls. Age of menarche (AOM) has been declining (i.e., occurring at a young age) in Korea but an analysis found that in addition to diet/nutrition, maternal menarcheal age, body mass index and maternal age at birth were variables that appear to influence AOM in Korean girls. It is important to note the AOM is generally declining throughout the world including in countries where soyfoods are not consumed.
In contrast to the Korean studies, a prospective study involving 1,239 U.S. girls aged six to eight who were followed for seven years found no relationship between pubertal development and urinary isoflavone excretion. In fact, another U.S. study found isoflavone exposure was associated with delayed breast development, although this study was small and utilized a cross-sectional design. Nevertheless, this finding agrees with the results of a German longitudinal study. However, epidemiologic studies conducted outside of Asia involving the general population are of questionable utility for understanding the health effects of soy consumption because isoflavone intake is so low (<2mg/d).

One U.S. cross-sectional study that does provide meaningful insight into whether soy intake impacts pubertal development involved Seventh-day Adventist (SDA) girls (N=327; age range 12 to 18; mean age, 15). Approximately 40% of SDAs are vegetarians so their soy consumption is much higher than the general U.S. population. The authors of this study assumed that current soy intake reflected past intake. There is research to support this assumption. A study involving a diverse population of children ages 9-18 years, in which dietary intake patterns were assessed five years apart, found intake to be stable over time.

The mean number of servings of soyfoods among the adolescent girls was 12.9 per week and 21.1% of the girls consumed soyfoods ≥4x/week. These findings confirm the higher soy intake among SDA compared with the general population. The results showed that the consumption of total soyfoods and the intake of three specific soyfoods was not significantly associated with AOM or with the odds for early- or late-AOM.

One adverse effect associated with earlier puberty in girls is an increased risk of developing breast cancer later in life. While the effect of soy on puberty has been studied to only a very limited extent, there is an impressive body of research, consisting of both epidemiologic and animal data, indicating that soy intake when young reduces breast cancer risk later in life. This evidence is consistent with mounting data that early life events greatly impact breast cancer risk. The first 20 years of life appear to be particularly important. In fact, a recent commentary concluded that there is growing evidence linking childhood and adolescent lifestyle and environmental exposures with subsequent risk of a range of cancers arising in adulthood.
EFFECTS OF SOY PROTEIN ON CHOLESTEROL LEVELS IN CHILDREN

As with adults, clinical research in children shows that soy protein favorably affects lipid levels. In the most recent study, when soy protein (average intake 0.5g/kg body weight) was incorporated into the diets 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% beyond the 11% decrease that occurred in response to the adoption of a standard low-saturated fat diet during the three-month run-in period. Therefore, soy protein used in combination with other dietary therapies can help to reduce cholesterol levels to target goals. Soy protein may also serve as an adjunct to therapy in children taking medication for lowering cholesterol, thereby reducing the required medication dose, which may help to minimize or eliminate side effects.

Research has shown that when rats are given genistein, the primary isoflavone in soybeans, for just a few weeks early in life and then put on a typical laboratory diet, they develop 50% fewer chemically induced mammary tumors than rats not given this isoflavone. Isoflavone exposure causes mammary cells to be transformed in a way that makes them permanently less likely to develop into cancer cells later in life. The effect of isoflavones may be similar in some ways to that of early pregnancy, which is protective against breast cancer. Several mechanisms for the hypothesized protective effects of isoflavones have been proposed including increases in cell differentiation, BRCA1 gene expression and estrogen receptor-β expression.

The epidemiologic data suggest that quite modest amounts (perhaps just one serving daily) of soy during the early years are likely sufficient to reduce breast cancer risk. The period of exposure to soy that is theoretically most protective against breast cancer is unclear. Although most studies focused on the teenage years, the results of a small study by Korde et al. suggest soy consumption during childhood may be most protective.
SOY PROTEIN QUALITY

Soyfoods provide high-quality protein and are generally low in saturated fat. Soy protein can meet the protein needs of growing children. In 2000, the U.S. Department of Agriculture removed limits on the amount of soy protein that can be used in the National School Lunch Program.

Providing healthful sources of protein without excessive saturated fat content is important for children. Higher-protein diets are associated with greater satiety and weight loss. Also, recent evidence in young boys shows that consumption of protein above the recommended dietary allowance enhances the favorable impact of physical activity on bone mineral density. Additionally, evidence indicates that the protein requirements of children may be 50% higher than the current recommended dietary allowance.

Many protein-rich foods in children’s diets are high in saturated fat. Substituting soyfoods for more traditional sources of protein generally improves overall diet quality. Even substituting soy protein for part of the beef or pork protein in a recipe can lead to a decrease in the fat, saturated fat and calorie content for the total entree, as long as portion size stays the same. Similarly, combining cheese, eggs or meat with tofu leads to improved nutritional quality of entrees.

In general, soyfoods help children meet the Dietary Guidelines. Short-term studies show that soyfoods support the normal growth and development of children and improve growth when substituted for legumes in the diets of malnourished preschoolers. Also, according to a recent clinical trial involving Australian children 18 to 114 months old, soymilk may help to alleviate chronic functional constipation (CFC), which is defined as having one bowel motion every three to 15 days. CFC occurs commonly in children and among those children attending a consultation with a pediatrician, the prevalence may be as high as 36 percent.

Collectively, the evidence shows soyfoods can play an important part in a healthful and varied diet.

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% of all allergic reactions, these eight foods are not equally allergenic. The number of adults allergic to soy is quite small. In fact, a recent survey found that cow’s milk allergy was 40-fold more common than allergy to soy protein.

The relative number of children allergic to soy protein is almost certainly higher than the number of adults because children are much more sensitive to dietary proteins in general. Nevertheless, according to a new systematic review, even among infants and children, the prevalence of soy allergies among the general population ranges from 0 to only 0.5 percent.

Most children are thought to outgrow their soy allergies early on in life, although the pace at which this occurs is a matter of some recent discussion. One study reported that more than 80% of infants outgrew their soy allergy by two years of age although a more recent study found that 70% of children outgrow their soy allergies by age 10. The higher the baseline soy-specific serum IgE levels, the longer it takes for this to occur. Data suggest that by age 10, only about one out of every 1000 children are allergic to soy protein.
Eosinophilic esophagitis (EoE) is a chronic inflammatory disorder of the esophagus that is being diagnosed with increased frequency in both children and adults and which is related to allergies. Clinical symptoms in children range from food aversion and malnutrition in infants and toddlers, to vomiting in preschoolers and abdominal pain in preteenagers. The immune-mediated esophageal inflammation is triggered by a food antigen in most children and adults.

A sixfold elimination diet (SFED) excluding cow’s milk, soy, wheat, egg, peanuts/tree nuts, and seafood has been shown to induce remission in a majority of children with EoE. However, in a recent study, it was shown that of 36 of 46 children (mean age, 7.6 years) were initially successfully treated with SFED.152

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**ACCEPTANCE OF SOYFOODS IN CHILDREN’S DIETS**

Research shows that soyfoods are generally well accepted by children.141, 153, 154 For example, among preschool children, three to six years old, who attended a Head Start program, soy-enhanced lunches were as readily consumed as those made with more traditional ingredients, as evidenced by the amounts eaten.153

Negative beliefs about soy’s palatability persist among some populations. When non-vegetarian study participants were told that a product contained soy, they were more likely to rate it as “grainy, chalky, dry, and unappealing” even though the product did not actually contain any soy ingredients.155 Foods containing soy are also generally thought by U.S. consumers to be more “healthy tasting”.155 Ratings reflect the amount of soy consumed by a given individual.
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 and enjoyed by children.

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


