Eating habits early in life may impact adult chronic diseases. This fact sheet will explore soyfoods’ beneficial role in the diets of infants, children and adolescents.

Introduction

Establishing healthful eating habits early in life is important for at least two reasons. The first being childhood eating habits track into adulthood, and changing adult dietary behavior is difficult. In fact, recent research shows that dietary habits established during infancy track into mid-childhood. The second reason is that evidence suggests healthful behaviors during childhood and adolescence can affect the risk of developing certain chronic diseases later in life. For example, early lifestyle factors are thought to affect the likelihood of developing breast cancer. Additionally, childhood obesity is associated with increased mortality from cardiovascular disease in adulthood, independent of adult weight. This observation is especially important given that 36 percent of U.S. children are overweight.

Diseases once seen primarily in adults, such as hypertension and Type 2 diabetes mellitus, are increasingly common in childhood.

Evidence indicates it isn’t just that chronic diseases begin early in life, but that programming during fetal life and infancy permanently affects the 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. Programming is not just limited to the in-utero environment but extends into childhood, where different organs and systems continue to adapt to various cues.

Another acknowledgement is that the beginning stages of chronic diseases such as coronary heart disease are already apparent in adolescents.\(^{17,18}\) Importantly, there is an emerging epidemic of non-alcoholic fatty liver disease (NAFLD) estimated to affect millions of obese children\(^{19,20}\) and one out of every four adults globally.\(^{21}\) Autopsy findings show that 9.6% of the U.S. population, age 2–19 years and 38% of the obese individuals within this age range have NAFLD.\(^{22}\) NAFLD can progress to non-alcoholic steatohepatitis, which is characterized by oxidative stress, inflammation, apoptosis and fibrogenesis.\(^{23}\) Some animal\(^{24-27}\) and epidemiologic\(^{28}\) data suggests soy may help to prevent the development of NAFLD.

**Soy Infant Formula**

Although breast milk is the ideal food for infants, about one-third of U.S. women are unable to breastfeed or choose not to do so.\(^{29}\) Of those who choose breastfeeding, most switch to formula feeding at some point in the infant’s first year.\(^{30}\) Commercially-prepared, fortified infant formulas are appropriate to supplement or replace human milk during the first year of life. Soy infant formula (SIF) is fortified with iodine, iron, methionine, carnitine and taurine, and contains 20 percent more calcium and phosphorous than cow’s milk formulas.

There are various estimates for the prevalence of SIF. A recent 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 percent of infants who were fed formula or regular
milk, 12 percent consumed SIF. The percentage of infants consuming SIF was significantly higher (P < 0.05) among those from higher income groups compared with the lowest income group.

An allergy to milk protein is among the most common reasons for placing an infant on SIF. Although there is evidence that SIF is hypoallergenic and relative to cow’s milk formula,\(^3\) an estimated 10–14 percent of infants who are allergic to cow’s milk formula are also allergic to SIF. As a result, the American Academy of Pediatrics (AAP) suggests that infants with documented cow’s milk protein allergy (CMA) should be switched directly to a hydrolyzed-protein formula.\(^3\) It should be noted that soybean-specific immunoglobulin E (IgE) titers are not an effective predictor of a positive response to the food challenge test.\(^4\)

In contrast to the AAP, an Australian panel of experts concluded that SIF 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.\(^3\) The French Society of Pediatrics holds a similar position but with the caveat that tolerance to soy protein should first be established by clinical challenge.\(^3\) Importantly, U.K. research found that of the 60% of all infants with CMA initially fed SIF, only 9% remained symptomatic.\(^3\) 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 SIF formula may have advantages over hydrolyzed formulas.\(^3\)

A systematic review and meta-analysis, which included 40 studies that evaluated the prevalence of IgE-mediated soy allergies in infants and children, concluded that recommendations to postpone the introduction of SIF in infants with IgE-CMA during the first six months of life were based on the concern for an increased risk of allergy to soy and are not warranted.\(^3\) More recently, Vandenplas\(^4\) concluded that cow-milk based extensive hydrolysates are the first option for the treatment of CMA for the majority of patients, while amino acid formulas are reserved for the most severe cases, whereas rice hydrolysates and SIF are second choice options.
Isoflavones in Diets of Infants Fed Soy Formula

An estimated 20 million people in the U.S. consumed SIF during infancy since it first became commercially available in the 1960s.\textsuperscript{41} Despite its long history of use, SIF has become controversial in recent years due to its naturally high isoflavone content.\textsuperscript{42,43} In the mid-1960s, several cases of goiter were identified in infants using SIF.\textsuperscript{44-46} Soon after, iodine was added to the formula: since fortification began, no thyroid problems attributed to SIF use have been identified in healthy infants, and research shows that infants fed SIF grow and develop normally.\textsuperscript{41,47-50} SIF may be contraindicated for infants with congenital hypothyroidism who require synthetic thyroid hormone,\textsuperscript{51} not because the formula contains isoflavones, but because of evidence suggesting soy protein is one of a number of factors that may interfere with the absorption of thyroid medication.\textsuperscript{52}

In 2006, the National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction evaluated the safety of SIF. Although their initial conclusions supported the safety of SIF, no final report was issued.\textsuperscript{53,54} In 2009, the NTP again took up this issue. The conclusion of the 14-member panel of independent scientists was that there was “minimal concern” (the five levels of concern are negligible concern, minimal concern, some concern, concern and serious concern) about the safety of SIF.\textsuperscript{55} In response to the NTP report, the AAP submitted a formal letter to the NTP, in which they stated their position that there is negligible concern about the safety of SIF. The current position of the AAP is that “…isolated soy protein–based formulas may be used to provide nutrition for normal growth and development ...”\textsuperscript{53}

In 2014, the first published systematic review and meta-analysis to focus on the safety of SIF concluded that in normal full-term infants – even during the most rapid phase of growth – SIF produces normal anthropometric growth, adequate protein status, bone mineralization and normal immune development.\textsuperscript{56} More recently, a small Israeli study found SIF use wasn’t associated with puberty onset in boys or girls.\textsuperscript{57} Despite all the research, there continues to be controversy surrounding SIF.

Contributing to this controversy are the results of an epidemiologic study by Adgent et al.\textsuperscript{58} published in 2018 which suggest that SIF may exert modest estrogenic effects in infant girls but not boys. This study garnered considerable media attention. However, as described below, a subsequently published study not involving SIF should give considerable pause about drawing any long-term conclusions about the health effects of SIF based on studies in infants.\textsuperscript{59}
The study Adgent et al. enrolled 410 infants born in Philadelphia-area hospitals between 2010 and 2014 that were exclusively fed SIF, cow-milk formula or breast milk throughout the study (birth to 28 or 36 weeks for boys and girls, respectively). Maternal demographics did not differ between cow-milk fed and SIF-fed infants but did differ markedly between formula fed and breastfed infants. Vaginal-cell maturation index (a marker of estrogen exposure) trended higher and uterine volume decreased more slowly in SIF-fed girls compared with cow-milk formula-fed girls; however, their trajectories of breast-bud diameter and hormone concentrations did not differ. The authors concluded that SIF “demonstrated tissue- and organ-level developmental trajectories consistent with response to exogenous estrogen exposure” but readily acknowledged that the long-term implications of these differences, if any, are unknown.

This study makes an important contribution to the literature. However, because it is an epidemiologic study rather than a randomized controlled trial, it is important to recognize its inherent limitations. Furthermore, the effects in girls contrast with results from the Beginnings study, which have shown SIF does not produce estrogenic effects in girls or boys in comparison to infants fed cow-milk formula or breast milk. Interestingly, at four months of age, the ovarian volume of the cow-milk formula-fed infants was statistically significantly larger than that of infants in the other two groups, which is suggestive of an estrogenic effect. However, by five years of age this difference in ovarian size was no longer evident. Thus, the impact of cow’s milk formula was transient.

The transient effect of cow-milk formula on ovarian volume is consistent with the results of a recent study Fledermann et al. The Belgrade-Munich infant milk trial found there were no long-term effects resulting from marked differences in growth patterns up to four months of age due to differences in formula feeding, on anthropometry at four years of age. This study was a randomized controlled trial in which healthy term infants received either a protein-reduced infant formula or a standard formula. Non-randomized breastfed infants were used as a reference group. The increase in weight and length z-scores between one and four months of age was higher for low-protein formula-fed infants than for the standard-formula-fed infants. However, after four months of age, a significantly lower increase in z-scores (for weight and length) was observed in the infants fed the low-protein formula compared with the infants fed the standard formula. Consequently, there were no differences at four years of age.

The transient effects in infants resulting from differences in dietary intake in the Beginnings study and the Belgrade-Munich infant milk study should give considerable pause about drawing conclusions about the long-term health implications of formula feeding based on differences observed in infants. Insights about infant feeding patterns may need to come from long-term prospective studies or carefully controlled retrospective studies.
Isoflavones in Diet of Children

Young Asians have consumed soyfoods for centuries without any apparent adverse effects. Nevertheless, there is interest in gaining a better understanding of the effects of isoflavones in children. Preliminary data indicates that children absorb isoflavones to a greater extent than adults do.63

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.70,71 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.72,73 Xenoestrogen exposure, which includes phytoestrogens such as isoflavones, has been proposed as another factor leading to earlier puberty onset. 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.74,75 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 and nutrition, maternal menarcheal age, body mass index and maternal age at birth were variables that appear to influence AOM in Korean girls.76 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,74,75 a prospective study involving 1,239 U.S. girls aged 6–8 who were followed for seven years found no relationship between pubertal development and urinary isoflavone excretion.77 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.78 Nevertheless, this finding agrees with the results of a German longitudinal study.79

Relatively little soy or isoflavone-related research has been conducted in children but as noted below, that which has, does not suggest isoflavones exert hormonal effects:

1. An Australian study found that isoflavones have no effect on high-density lipoprotein cholesterol (HDL-C) levels in teenage boys, which suggests isoflavones don’t exert estrogenic effects.44 HDL-C 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 hypothesized that isoflavone exposure would raise HDL-C.

2. A small Israeli 12-week cross-over study found isoflavone supplements (0, 16 and 48 mg/d) had no effect on blood reproductive hormone levels in young boys and girls.45

3. A pilot U.S. study involving 17 girls found that the consumption of approximately one serving of soyfoods daily (average isoflavone intake, ~27 mg) had no effect on urinary sex steroid levels.44
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 (<2 mg/d).

In the study involving boys, puberty onset as judged by first appearance of pubic hair in high-soy-consumers (>20 mg/d isoflavones) was found to be well within the normal range for U.S. children.81

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 epidemiologic83-86 and animal87-89 data, indicating that soy intake when young reduces breast cancer risk later in life.

Two U.S. cross-sectional studies provide more meaningful insight into whether soy intake impacts pubertal development. One study involved Seventh-day Adventist (SDA) girls (N=327; age range 12 to 18; mean age, 15)80 and the other study involved SDA boys.81 Approximately 40 percent of SDAs are vegetarians so their soy consumption is much higher than the general U.S. population. The authors of these studies assumed that current soy intake reflected past intake, an assumption that is supported by the literature.82

The average number of servings of soyfoods among the adolescent girls was 12.9 per week and 21.1 percent of the girls consumed soyfoods ≥4x/week. 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.80
### Sources of Soy Protein

<table>
<thead>
<tr>
<th>SOYFOOD</th>
<th>SERVING SIZE</th>
<th>GRAMS OF SOY PROTEIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fortified Soymilk</td>
<td>1 cup</td>
<td>6-7</td>
</tr>
<tr>
<td>Soy Cereal</td>
<td>1 ¼ cup</td>
<td>7</td>
</tr>
<tr>
<td>Soy Yogurt, Vanilla</td>
<td>1 cup</td>
<td>6</td>
</tr>
<tr>
<td>Soy Breakfast Patty</td>
<td>2 patties</td>
<td>11</td>
</tr>
<tr>
<td>Soy Bar</td>
<td>1 bar</td>
<td>14</td>
</tr>
<tr>
<td>Soy Chips</td>
<td>1 bag</td>
<td>7</td>
</tr>
<tr>
<td>Soynut Butter</td>
<td>2 tbsp</td>
<td>7</td>
</tr>
<tr>
<td>Soynuts, Roasted, Unsalted</td>
<td>¼ cup</td>
<td>11</td>
</tr>
<tr>
<td>Tofu</td>
<td>½ cup</td>
<td>10</td>
</tr>
<tr>
<td>Edamame</td>
<td>½ cup</td>
<td>11</td>
</tr>
<tr>
<td>Soy Burger</td>
<td>1 patty</td>
<td>13-14</td>
</tr>
<tr>
<td>Soy Pasta</td>
<td>½ cup (cooked)</td>
<td>13</td>
</tr>
<tr>
<td>Soy Pudding</td>
<td>½ cup</td>
<td>6</td>
</tr>
</tbody>
</table>

Source: United States Department of Agriculture Nutrient Database.

### 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 (NSLP). To qualify as an alternate protein product in the NSLP requires that a protein have a protein digestibility corrected amino acid score of at least 80 percent of that of casein; soy protein easily meets this standard. 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. Evidence in young boys, although limited, 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 percent 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. Furthermore, according to a recent clinical trial involving Australian children...
by age 10.\textsuperscript{116} The higher the baseline soy-specific serum IgE levels, the longer it takes to occur. Data suggest that by age 10, only about one out of approximately every 1,000 children are allergic to soy protein.

### Acceptance of Soyfoods by Children

Research shows that soyfoods are generally well accepted by children.\textsuperscript{108,117,118} 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.\textsuperscript{147}

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.\textsuperscript{119} Foods containing soy are also generally thought by U.S. consumers to be more “healthy tasting.”\textsuperscript{119} 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 uncommon allergic reactions to soy protein, there is no clinical evidence that soyfoods exert any adverse effects in children. To the contrary, there is evidence suggesting that exposure to soy during childhood and adolescence reduces breast cancer risk later in life.

For more information visit SoyConnection.com or contact info@soyconnection.com

Soy Connection, on behalf of the United Soybean Board (USB), is a collaboration of health, nutrition and food industry experts with U.S. soybean farmers to educate on the benefits of U.S.-grown soy, including heart-healthy soybean oil and soyfoods. USB’s 73 farmer-directors work on behalf of all U.S. soybean farmers to achieve maximum value for their soy checkoff investments. These volunteers invest and leverage checkoff funds in programs and partnerships to drive soybean innovation beyond the bushel and increase preference for U.S. soy. That preference is based on U.S. soybean meal and oil quality and the sustainability of U.S. soybean farmers. As stipulated in the federal Soybean Promotion, Research and Consumer Information Act, the USDA Agricultural Marketing Service has oversight responsibilities for USB and the soy checkoff.