Comments on Isoflavones in Soy-Based Infant Formulas

Sir: A recent paper (Murphy et al., 1997) reporting the isoflavone content of soy-based infant formulas requires comment. First, the paper contains several factual errors, and, second, the authors' concluding statement, "it is likely that the potential health protective effects attributed to soy isoflavones may be an advantage to infants consuming soy formulas", requires a response.

The authors claim that soy-based formulas "have been fed to millions of infants with no evidence of harmful effects". The use of soy-based formulas became widespread in the United States about 40 years ago, but it is incorrect to state that there has been no evidence of harmful effects. Allergenic reactions aside, goiter and hypothyroidism were reported in infants fed soybean diets until the early 1960s (Shepherd, 1960). In fact, recent reports indicate that thyroid disorders may be attributable to feeding soy-based infant formulas (Fort et al., 1990). These findings appear consistent with the recently proposed mechanism by which soy isoflavones effect thyroid hormone synthesis (Divi et al., 1997).

Also, even if claims of no evidence of harmful effects were accurate, it would not equate to soy-based formulas being safe. This is because potential harmful effects of isoflavones have never been investigated and there is no certainty that harmful effects would have been obvious even if they did exist. Such an argument is presented by Sheehan (1998), who cites several examples including the case of DES. Treatment with this estrogenic drug continued for over 20 years before physicians fortuitously made the association between its use and the incidence of a rare type of malignancy in DES daughters. In terms of risk/benefit considerations, Sheehan likens soy products to herbal medicines and suggests that the confidence that soy products are safe appears to be based on belief rather than factual evidence. His conclusion is that there is no certainty that soy products are safe.

The authors report that the estrogenic activity of isoflavones is 100 000−500 000 times less than that of estradiol. In fact, the activity of genistein is approximately 1000 times less than that of estradiol (Markiewicz et al., 1993; Collins et al., 1997), and, hence, isoflavones are not very weak estrogens as some purport. Therefore, when they are consumed in sufficient amounts, soy isoflavones are biologically active in humans. Fukutake et al. (1997) report the daily intake by Japanese is 1.5−4.1 mg/person of genistein and 6.3−8.3 mg/person of genistin. This equates to a total genistein intake of between 5.4 and 9.3 mg/person/day, not 12 mg/day as reported by the authors (the sum of genistein and genistin does not equate to total genistein). This is relevant because it establishes that newborn infants fed soy-based formulas consume more genistein per day than Japanese adults. The maximum concentration of isoflavones in the breast milk of mothers consuming soy foods has been reported to be not greater than approximately 0.2 μM (Setchell et al., 1997), not 1−2 μM as stated by the authors. Therefore, infants fed soy-based formulas receive more than 2000 times the daily dose of isoflavones than breast-fed infants. The authors' suggestion that this may advantage soy-based-formula-fed infants (over breast-fed infants?) is bold indeed.

The first reported determination of isoflavone levels in soy-based infant formulas was by Setchell et al. (1987). Setchell had previously compared the exposure of infants to isoflavones in soy-based infant formulas with the exposure of sheep to isoflavones in clover (Setchell, 1985). This comparison was consistent with results from the previous four decades of research which showed that the isoflavones were potent disrupters of endocrine systems in a wide variety of animals.

In recent times there have been numerous claims that isoflavones prevent hormone-related diseases such as breast cancer. Under some conditions, genistein has been found to inhibit breast cancer cell growth (Hoffman, 1995). However, recent research by Dees et al. has shown that dietary concentrations of genistein may stimulate breast cells to enter the cell cycle; this finding led these authors to conclude that women should not consume soy products to prevent breast cancer (Dees et al., 1997).

Had the isoflavone content of soy-based infant formulas been determined during the early years of their development, it is doubtful that regulators would have permitted their inclusion in a diet that constitutes the exclusive source of nutrition for infants. Instead, infants fed soy-based formulas have been placed at risk in a "large, uncontrolled, and basically unmonitored human infant experiment" (Sheehan, 1997).

I conclude that the consumption of very high levels of isoflavones by infants fed soy-based formulas may be extremely disadvantageous. It is certain that the potential harmful effects of soy-based formulas on infants require urgent investigation.

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