

population. Furthermore, PCB concentrations in breast milk of women who ate Great Lakes fish were almost twice those of a control group (Fitzgerald et al. 1998, as cited in ATSDR 1999). PCB concentrations in blood were correlated with the number of years an individual had consumed Great Lakes fish. Individuals who consumed less than 6 pounds of fish per year had a geometric mean for PCB blood concentrations of 6.8 ppb, whereas those who consumed more than 24 pounds of Great Lake fish had mean blood PCB concentrations of 19 ppb (Hovinga 1993).

Phytoestrogens

Human and animal exposures to the phytoestrogens, particularly isoflavones, can be very high, because these compounds are found in many foods. Genistein, daidzein, formononetin, and equol are all present in clover. Infertility in sheep, "clover disease," has been traced to isoflavone concentrations as high as 5% of the dried weight of clover (Verdeal and Ryan 1979).

The recent practice of feeding infants soy-based formula has raised concerns with regard to the long-term health effects of exposure during development (Setchell et al. 1997; Irvine et al. 1998). For example, it has been recognized for some time that feeding infants soy-based formula was associated with goiter (thyroid enlargement associated with thyroid hormone deficiency) in animals and human infants (Shepard et al. 1960). One mechanism by which isoflavonoids, such as genistein, reduce thyroid hormone concentrations and result in goiter is by inhibiting thyroid peroxidase activity; this enzyme catalyzes thyroid hormone biosynthesis (Divi and Doerge 1996). The concentration of soy phytoestrogens that inhibited thyroid hormone biosynthesis are within the range of exposure of infants maintained on soy formula. Soy-based formulas contained isoflavones at 32-47 $\mu\text{g}/\text{mL}$, which corresponded to a daily exposure to total isoflavones of 4.5-8.0 mg/kg of body weight per day for a 4-month-old infant. That concentration is 6- to 11-fold higher than concentrations known to cause hormonal effects in adults. (Divi et al. 1997; Setchell et al. 1997). In a study by Irvine et al. (1998), the phytoestrogen content of soy-based formulas and cereals were compared with dairy-based formulas and human breast milk. Again, infants received approximately 3 mg/kg of body weight per day from the soy-based formula, but a single daily serving of infant cereal could increase the isoflavone intake by more than 25%. Dairy-based formula and human breast milk contained isoflavones below the limit of detection. Human breast milk had undetectable concentrations of phytoestrogens regardless of the diet of the mother, including women who were vegetarians and consumed greater than 50 g of soy products in a 48-hr period before sampling.

Potential exposure to plant estrogens found in wood has been assessed by various *in vitro* and *in vivo* bioassays. Wood-derived estrogens, such as beta-sitosterol, could represent environmental hormone exposures, particularly from pulp and paper mill effluents, downstream of wood-processing facilities. Mellanen et al. (1996) used two breast-cancer cell lines *in vitro* (MCF7 and T-47D) and expression of the vitellogenin gene in rainbow-trout livers to estimate estrogenic activity of wood-derived compounds. Some compounds, such as beta-sitosterol, were estrogenic in human and fish bioassays, but some phytoestrogens, such as betulin and pinosylvin, were estrogenic only in humans.