Section on Environmental Health Policy

ENVIRONMENTAL AND OCCUPATIONAL POLLUTANTS ARE AVOIDABLE CAUSES OF BREAST CANCER

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For over three decades, evidence has accumulated relating avoidable exposures to environmental and occupational carcinogens to the escalating incidence of breast cancer in the United States and other major industrialized nations. This evidence has until very recently been totally ignored by the cancer establishment, the National Cancer Institute, and the American Cancer Society, despite expenditures of over $1 billion on breast cancer research. Recognition of these environmental and occupational risk factors should lead to the belated development of public health policies directed to the primary prevention of breast cancer. Their recognition should also lend urgency to the need for radical reforms in the priorities and leadership of the cancer establishment.

Breast cancer is a complex and heterogeneous group of malignancies that encompass distinct clinical entities, pathologies, and etiologies. Nevertheless, three major classes of overall risk factors for breast cancers have been and still are conventionally recognized. The first is a familial history of breast cancer, particularly early age at onset. The second is reproductive or "estrogen-window" factors: early menarche; nulliparity; late menopause; and exogenous hormones including prolonged use of oral contraceptives from an early age, injectable Depo-provera contraceptives, long-term postmenopausal estrogen replacement therapy, especially when combined with progestogens, and diethylstilbestrol (1–4). The third is a high-fat diet. However, as confirmed by a series of recent case control and cohort studies, evidence for the role of dietary fat per se is at best inconsistent and tenuous (2). The role of these risk factors in the aggregate has been incriminated in only 20 to 30 percent of all breast cancers (5, 6). Furthermore, they cannot account for the escalating incidence of breast cancer, particularly in postmenopausal women, in the United States and other major industrialized nations; incidence rates in white women in the United States from 1950 to 1989 increased by 53 percent, or by over 1 percent annually (7). These trends are real and, in large measure, cannot be explained away by the relatively

International Journal of Health Services, Volume 24, Number 1, Pages 145–150, 1994

doi: 10.2190/5GM4-HW92-QE9K-RK37
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recent large-scale use of mammography screening (8, 9). However, these trends are not unique as they are paralelled or even sharply exceeded by those for a wide range of other cancers (7, 8, 10).

Not one of the heavily funded U.S. and other nutritional studies on the relation between dietary fat and breast cancer has investigated, let alone even considered, the role of carcinogenic dietary contaminants (10). However, it has been known since the late 1960s that carcinogenic organochlorine pesticides that concentrate in animal and human fat, such as aldrin, dieldrin, chlordane, and heptachlor, induce breast cancer in rodents (11–14). This creates the strong presumption for a causal role of such contaminants in human breast cancer, as the sites of cancer induced by carcinogens in experimental animals and humans are generally similar (15). Furthermore, DDT promotes breast cancer induced in male rodents by the unrelated carcinogen acetamidophenanthrene (16). The authors of the latter study concluded that: "Because of their fat-solubility and tendency toward long-term deposition in body fat, particularly in the female breast, and the apparent ability of DDT to promote tumors in the mammary gland of the male rat, such agents might be considered possible contributors to the high incidence of breast cancer among women."

Further evidence for the role of organochlorine carcinogens is provided by findings that DDT and polychlorinated biphenyls (PCBs) concentrate in human breast cancer itself in contrast to adjacent non-neoplastic tissue (17). These organochlorines also concentrate in breasts with cancer in contrast to those with fibrocystic disease (18). Additionally, the pesticide hexachlorocyclohexane concentrates in breasts with cancer in contrast to normal breasts (19). Other and unique supportive evidence comes from reports that, in spite of increasing fat consumption and decreasing parity, breast cancer mortality in premenopausal Israeli women declined by 30 percent following strong representations by this author (20) and subsequent regulations, opposed by the Israeli cancer establishment, reducing the high levels of hexachlorocyclohexane and DDT in dairy products (21). The mechanism of action of organochlorine carcinogens in relation to breast cancer probably involves their estrogenic properties, well known for decades, reflecting their potent induction of cytochrome P-450 mixed-function oxidases, stimulation of estrogen metabolism, and binding to human estrogen receptors (21); such properties reflect the recent belated recognition of these organochlorines as xeno-estrogens (22).

Atrazine, a carcinogenic chlorinated triazine, has been and still is one of the most heavily used herbicides in the world (23). In view of its mobility in soil and its aquatic stability, it is one of the commonest carcinogenic pollutants in European and U.S. surface waters, often exceeding the U.S. Health Advisory Level of 3 parts per billion. Atrazine exerts hormonal effects on the hypothalamic-pituitary-gonadal axis, with marked inhibition of 5-alpha steroid reductase, and induces breast and other reproductive tumors in rats (23). It has also been incriminated in human ovarian cancer and lymphohematopoietic

malignancies (24). Nevertheless, the role of atrazine in human breast cancer has still not been investigated. Still also ignored is the role of other carcinogenic and estrogenic chlorinated pesticides such as endosulfan and the DDT-contaminated Dicofol.

Estrogens are another important class of dietary contaminants, resulting from their virtually unregulated use as growth-promoting feed additives for cattle, hogs, and poultry (25). In view of the known carcinogenicity of exogenous estrogens, lifelong exposure to these contaminants is clearly a risk factor for breast cancer, as emphasized by Roy Hertz, the National Cancer Institute's former leading authority on endocrine cancer (26). Furthermore, estrogens are known to synergize the carcinogenic effects of radiation of the breast (27, 28), thus possibly further increasing risks of mammography (10). Estrogens also synergize the carcinogenic effects in the breast of polynuclear hydrocarbon carcinogens (29). More recent concerns on estrogenic dietary contaminants are provided by findings of increased breast cancer risk among women with prenatal exposure to elevated estrogen levels (30). This also raises the possibility of similar effects of prenatal exposure to maternal residues of organochlorine carcinogens.

Proximity of residence to hazardous waste sites has been associated with major increased risks of breast and other cancers (31). Most recently, the high increase in breast cancer incidence and mortality in Connecticut and suburban New York counties, especially Nassau and Suffolk, has been associated with consumption of milk and water contaminated over the last two decades with nuclear fission products, the short-lived radioactive iodine and the long-lived bone-seeking strontium-90, from the Millstone and Indian Point civilian nuclear reactors (32). An additional environmental risk factor in Nassau and Suffolk Counties may reflect past exposure from extensive agricultural use of carcinogenic soil fumigant pesticides, the organochlorine dichloropropane and the highly potent organohalogens ethylene dibromide and dibromochloropropane, all of which induce breast cancer in rodents (33–37).

A variety of occupational exposures has been incriminated as risk factors for breast cancer. Excess incidence and mortality have been reported among women exposed to dioxin, the most potent known inducer of P-450 enzymes, in a German pesticide plant (38), among women exposed to petroleum products including chlorinated organic solvents (39), among professional chemists (40), and among hairdressers, as well as users of hair dyes (41).

Not surprising is the recent conclusion "that there has been no progress in preventing the disease," despite U.S. expenditure of over $1 billion on breast cancer over the last two decades (5). More surprising, however, is the persisting failure of the U.S. cancer establishment, the National Cancer Institute, and the American Cancer Society, to have recognized and investigated longstanding evidence on the role of a wide range of avoidable environmental and occupational risk factors for breast cancer besides for a wide range of other cancers (10). Their

recognition should result in the belated development of public health policies directed to primary prevention of breast and other cancers, and should also further reinforce recommendations for major reforms in the priorities and leadership of the cancer establishment (10).

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