

RISK FACTOR INFORMATION FOR SELECTED CANCER TYPES

Breast Cancer

Breast cancer is the most frequently diagnosed cancer among women in both the United States and in Massachusetts. According to the North American Association of Central Cancer Registries, female breast cancer incidence in Massachusetts is the fifth highest among all states (Chen et al, 2000). Although during the 1980s breast cancer in the U.S. increased by about 4% per year, the incidence has leveled off to about 110.6 cases per 100,000 (ACS 2000). A similar trend occurred in Massachusetts and there was even a slight decrease in incidence (1%) between 1993 and 1997 (MCR 2000).

In the year 2005, approximately 211,240 women in the U.S. will be diagnosed with breast cancer (ACS 2005). Worldwide, female breast cancer incidence has increased, mainly among women in older age groups whose proportion of the population continues to increase as well (van Dijck, 1997). A woman's risk for developing breast cancer can change over time due to many factors, some of which are dependent upon the well-established risk factors for breast cancer. These include increased age, an early age at menarche (menstruation) and/or late age at menopause, late age at first full-term pregnancy, family history of breast cancer, and high levels of estrogen. Other risk factors that may contribute to a woman's risk include benign breast disease and lifestyle factors such as diet, body weight, lack of physical activity, consumption of alcohol, and exposure to cigarette smoke. Data on whether one's risk may be affected by exposure to environmental chemicals or radiation remains inconclusive. However, studies are continuing to investigate these factors and their relationship to breast cancer.

Family history of breast cancer does affect one's risk for developing the disease. Epidemiological studies have found that females who have a first-degree relative with premenopausal breast cancer experience a 3-fold greater risk. However, no increase in risk has been found for females with a first degree relative with postmenopausal breast cancer. If women have a first-degree relative with bilateral breast cancer (cancer in both breasts) at any age then their risk increases five-fold. Moreover, if a woman has a mother, sister or daughter with bilateral premenopausal breast cancer, their risk increases nine fold. (Broeders and Verbeek, 1997). In addition, twins have a higher risk of breast cancer compared to non-twins (Weiss et al, 1997).

A personal history of benign breast disease is also associated with development of invasive breast cancer. Chronic cystic or fibrocystic disease is the most commonly diagnosed benign breast disease. Women with cystic breast disease experience a 2-3 fold increase in risk for breast cancer (Henderson et al, 1996).

According to recent studies, approximately 10% of breast cancers can be attributed to inherited mutations in breast cancer related genes. Most of these mutations occur in the BRCA1 and BRCA2 genes. Approximately 50% to 60% of women who inherit BRCA1 or BRCA2 gene mutations will develop breast cancer by the age of 70 (ACS 2001).

Cumulative exposure of the breast tissue to estrogen and progesterone hormones may be one of the greatest contributors to risk for breast cancer (Henderson et al, 1996). Researchers suspect that early exposures to a high level of estrogen, even during fetal development, may add to one's risk of developing breast cancer later in life. Other studies have found that factors associated with increased levels of estrogen (i.e., neonatal jaundice, severe prematurity, and being a fraternal twin) may contribute to an elevated risk of developing breast cancer (Ekbom et al, 1997). Conversely, studies have revealed that women whose mothers experienced toxemia during pregnancy (a condition associated with low levels of estrogen) had a significantly reduced risk of developing breast cancer. Use of estrogen replacement therapy is another factor associated with increased

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hormone levels and it has been found to confer a modest (less than two-fold) elevation in risk when used for 10-15 years or longer (Kelsey, 1993). Similarly, more recent use of oral contraceptives or use for 12 years or longer seems to confer a modest increase in risk for bilateral breast cancer in premenopausal women (Ursin et al, 1998).

Cumulative lifetime exposure to estrogen may also be increased by certain reproductive events during one's life. Women who experience menarche at an early age (before age 12) have a 20% increase in risk compared to women who experience menarche at 14 years of age or older (Broeders and Verbeek, 1997; Harris et al, 1992). Women who experience menopause at a later age (after the age of 50) have a slightly elevated risk for developing the disease (ACS 2001). Furthermore, the increased cumulative exposure from the combined effect of early menarche and late menopause has been associated with elevated risk (Lipworth, 1995). In fact, women who have been actively menstruating for 40 or more years are thought to have twice the risk of developing breast cancer than women with 30 years or less of menstrual activity (Henderson et al, 1996). Other reproductive events have also shown a linear association with risk for breast cancer (Wohlfahrt, 2001). Specifically, women who gave birth for the first time before age 18 experience one-third the risk of women who have carried their first full-term pregnancy after age 30 (Boyle et al, 1988). The protective effect of earlier first full-term pregnancy appears to result from the reduced effect of circulating hormones on breast tissue after pregnancy (Kelsey, 1993).

Diet, and particularly fat intake, is another factor suggested to increase a woman's risk for breast cancer. Currently, a hypothesis exists that the type of fat in a woman's diet may be more important than her total fat intake (ACS 1998; Wynder et al, 1997). Monounsaturated fats (olive oil and canola oil) are associated with lower risk while polyunsaturated (corn oil, tub margarine) and saturated fats (from animal sources) are linked to an elevated risk. However, when factoring in a woman's weight with her dietary intake, the effect on risk becomes less clear (ACS 1998). Many studies indicate that a heavy body weight elevates the risk for breast cancer in postmenopausal women (Kelsey, 1993), probably due to fat tissue as the principal source of estrogen after menopause (McTiernan, 1997). Therefore, regular physical activity and a reduced body weight may decrease one's exposure to the hormones believed to play an important role in increasing breast cancer risk (Thune et al, 1997).

Aside from diet, regular alcohol consumption has also been associated with increased risk for breast cancer (Swanson et al, 1996; ACS 2001). Women who consumed one alcoholic beverage per day experienced a slight increase in risk (approximately 10%) compared to non-drinkers, however those who consumed 2 to 5 drinks per day experienced a 1.5 times increased risk (Ellison et al., 2001; ACS 2001). Despite this association, the effects of alcohol on estrogen metabolism have not been fully investigated (Swanson et al, 1996).

To date, no specific environmental factor, other than ionizing radiation, has been identified as a cause of breast cancer. The role of cigarette smoking in the development of breast cancer is unclear. Some studies suggest a relationship between passive smoking and increased risk for breast cancer; however, confirming this relationship has been difficult due to the lack of consistent results from studies investigating first-hand smoke exposure (Laden and Hunter, 1998).

Studies on exposure to high doses of ionizing radiation demonstrate a strong association with breast cancer risk. These studies have been conducted in atomic bomb survivors from Japan as well as patients that have been subjected to radiotherapy in treatments for other conditions (i.e., Hodgkin's Disease, non-Hodgkin's Lymphoma, tuberculosis, post-partum mastitis, and cervical cancer) (ACS 2001). However, it has not been shown that radiation exposures experienced by the

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general public or people living in areas of high radiation levels, from industrial accidents or nuclear activities, are related to an increase in breast cancer risk (Laden and Hunter, 1998). Investigations of electromagnetic field exposures in relation to breast cancer have been inconclusive as well.

Occupational exposures associated with increased risk for breast cancer have not been clearly identified. Experimental data suggests that exposure to certain organic solvents and other chemicals (e.g., benzene, trichloropropane, vinyl chloride, polycyclic aromatic hydrocarbons (PAHs)) causes the formation of breast tumors in animals and thus may contribute to such tumors in humans (Goldberg and Labreche, 1996). Particularly, a significantly elevated risk for breast cancer was found for young women employed in solvent-using industries (Hansen, 1999). Although risk for premenopausal breast cancer may be elevated in studies on the occupational exposure to a combination of chemicals, including benzene and PAHs, other studies on cigarette smoke (a source of both chemicals) and breast cancer have not shown an associated risk (Petralia et al, 1999). Hence, although study findings have yielded conflicting results, evidence does exist to warrant further investigation into the associations.

Other occupational and environmental exposures have been suggested to confer an increased risk for breast cancer in women, such as exposure to polychlorinated biphenyls (PCBs), chlorinated hydrocarbon pesticides (DDT and DDE), and other endocrine-disrupting chemicals. Because these compounds affect the body's estrogen production and metabolism, they can contribute to the development and growth of breast tumors (Davis et al, 1997; Holford et al, 2000; Laden and Hunter, 1998). However, studies on this association have yielded inconsistent results and follow-up studies are ongoing to further investigate any causal relationship (Safe, 2000).

When considering a possible relationship between any exposure and the development of cancer, it is important to consider the latency period. Latency refers to the time between exposure to a causative factor and the development of the disease outcome, in this case breast cancer. It has been reported that there is an 8 to 15 year latency period for breast cancer (Petralia 1999; Aschengrau 1998; Lewis-Michl 1996). That means that if an environmental exposure were related to breast cancer, it may take 8 to 15 years after exposure to a causative factor for breast cancer to develop.

Socioeconomic differences in breast cancer incidence may be a result of current screening participation rates. Currently, women of higher socioeconomic status (SES) have higher screening rates, which may result in more of the cases being detected in these women. However, women of higher SES may also have an increased risk for developing the disease due to different reproductive patterns (i.e., parity, age at first full-term birth, and age at menarche). Although women of lower SES show lower incidence rates of breast cancer in number, their cancers tend to be diagnosed at a later stage (Segnan, 1997). Hence, rates for their cancers may appear lower due to the lack of screening participation rather than a decreased risk for the disease. Moreover, it is likely that SES is not in itself the associated risk factor for breast cancer. Rather, SES probably represents different patterns of reproductive choices, occupational backgrounds, environmental exposures, and lifestyle factors (i.e., diet, physical activity, cultural practices) (Henderson et al, 1996).

Despite the vast number of studies on the causation of breast cancer, known factors are estimated to account for less than half of breast cancers in the general population (Madigan et al, 1995). Researchers are continuing to examine potential risks for developing breast cancer, especially environmental factors.

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