

CANCER BREAST

Essay

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By

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**TO MY WIFE
AND
DAUGHTER**



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INTRODUCTION

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Breast cancer is the most common form of malignancy in women, and despite advances in diagnosis and therapy of this condition, there has been little change in the prognosis over the past 30 years. The disease affects 7% of all women in North American and Europe, and remains one of the most significant problems currently facing modern medicine. Over 33,000 women died from breast cancer in the United States alone in 1980 and as mentioned above despite improvement in diagnosis and initial treatment two of every 3 patients will eventually require treatment for metastatic disease.

As regard to surgical treatment of breast cancer Kinne in 1984 reported that modified radical mastectomy is considered the standard approach for patients with primary operable or potentially curable breast cancer, but certain carefully selected cases with smaller tumors are being treated in some centers with a breast-sparing operation, usually with some type of axillary dissection, followed by radical

radiation therapy. According to the American college of surgeons, whereas in 1972 only 26% of primary breast operation were modified radical mastectomy, in 1977 that operation comprised 58% of all procedures.

Hawkins, (1980) reported that in advanced breast cancer 54% of patients with estrogen receptor positive tumors responded to the antiestrogen tamoxifen (Nolvadex), whereas only 14% of patients with estrogen receptor negative tumors responded. Also Smith et al., reported that aminoglutethimide produced an increased response rate in bone metastases by suppression of prostaglandin synthesis by direct action and possibly secondary to estrogen suppression.

KaWitha et al., (1984) reported that 53% of their patients whose disease progressed while on CMFVP combination therapy responded to the ADM (adriamycin, dibromodulcitol and mitomycin) combination, suggesting that there was no crossresistance between these two regimens.

AETIOLOGY

ETIOLOGY OF BREAST CANCER

1. Sex:

Breast cancer is very rare in males. Malness is not a complete protection, However; there is one carcinoma of the breast in men for every 100 Carcinoma of the breast in women. (Cowan et al., 1981).

2. Age:

Breast cancer manifests itself chiefly from menopause years and increases in frequency throughout the entire-life span. Nearly 85% of breast cancer are clinically detected in persons over the age of 40 years and 87% are detected after age 50. Less than 1.5% occur in persons under the age of 30 years, and in those under 21 breast cancer is a medical curiosity (Lilienfeld et al., 1975).

3. Reproductive factors:

The importance of having born children is emphasized by the relative increased incidence of breast cancer in nuns (Fraumeni et al., 1969). It

was found also that women with multiple births (5 or more) had a slightly diminished risk. (0.8) after adjustment for individual ages at first livebirth (Brinton et al., 1983). The risk of breast cancer increases with advancing age at first livebirth, with women having the first livebirth after the age of thirty showing 4 - 5 fold excess risk compared to those having the first birth prior to age 18 (Brinton et al., 1983). The protective effect of an early pregnancy is dependent on its continuing to fullterm, with no protection being associated with occurrence of miscarriage (Mac Mahon et al., 1970; Choi et al., 1978).

However, the excess risk is restricted to women with multiple miscarriages (Brinton et al., 1983) a condition that may relate to progesterone deficiency (Shearman, 1980). Also progesterone deficiency is responsible for the increased incidence of breast cancer in cases of infertility (Henderson et al., 1974, Bain et al., 1981).

4. Previous benign breast disease:

It is certain that the frequency of microscopically observed fibrocystic disease is greater in cancerous than in the non cancerous breast, but histologic evidence is lacking that the malignant tumour arise from the benign lesions (Ackerman and del Regato, 1977).

Black et al., (1972) have reported that the types of fibrocystic disease that seem to play a role in the development of breast cancer are the proliferative lesions of duct epithelial hyperplasia with atypia and apocrine metaplasia with atypia. They call these lesions "pre-cancerous mastopathy" and reported that a woman with ductular atypia is subject to a five time greater risk of developing breast cancer than is a woman with no evidence of atypical changes found in the biopsy of benign lesion.

Haagensen, (1971) also considered the gross cystic type of fibrocystic disease to be precancerous based on his findings of a fourfold increased

incidence of breast cancer in a series of 1.693 patients with gross cystic disease studied by him between 1930 and 1968.

5. Previous cancer in one breast:

There is no question that the remaining breast after the first has been removed for cancer is an organ at risk. The risk of developing second primary cancer in it, is about 5 times greater than the risk of initial breast cancer in the general population (Bedwink et al., 1981). Furthermore there is a group of patient at even higher risk of developing cancer in the remaining breast, including :

- 1) Those with noninvasive cancers,
- 2) Those with invasive cancers that are not prone to metastasize,
- 3) Those with stage 0 or stage I cancers.
- 4) Those with familial history of breast cancer.
- 5) Those in whom random biopsy of the other breast showed precancerous mastopathy.

- 6) Those under 50 years of age at the time of the first breast cancer. (Greer, 1976).

6. Genetic predisposition:

From various sources, attention has been called to the remarkably greater occurrence of cancer of the breast among the female members of some families. The fact has been observed that in such families, the tumours seem to occur at an earlier age in succeeding generation (Keller, 1976) and also that there is a greater frequency of bilaterality (Working party 1976).

There seems to be an interrelationship of benign breast disease and malignant tumours in mothers and daughters that suggest a possible role of breast feeding (Graig, et al., 1974 and Morgan, et al., 1974).

7. Hormonal factors:

The endocrine control of the breast is extremely complex and involves many hormones, including

estrogens, progesterone, prolactin, the growth hormone, the corticosteroids, the glucocorticoids and thyroxine. Of these estrogens seem to be the most important in the etiology of breast cancer, probably acting as powerful potentiators or promoters rather than a true carcinogens. (Adams, 1977).

It is hypothesized that prolonged exposure to normal level of ovarian estrogens and cyclic progesterone resulting from early menarche and late menopause, and primarily willful nulliparity and late childbearing, act as an early stage in the developing of breast cancer by promoting excessive proliferation of normal epithelial stem cells. Excess endogenous or exogenous estrogens can enhance risk by stimulating proliferation of epithelial cells that have undergone partial malignant transformation (Thomas 1984). However, no clear-cut pattern of either abnormal estrogen and progesterone production or milieu has been found in women with carcinoma of the breast (Gambrell, 1981).

Other hermones: The is an evidence that hypothyroidism is somehow conductive to the development and progress of mammary carcinoma (Edelstyn and Welbounn, 1958; Black Winkel and Jackson, 1984; Papaioannou, 1974 and Leis 1976).

Kapdi and Walfe (1976) referred to several investigators who have proposed a linkage between thyroid gland dysfunction in breast cancer and to others who claimed that thyroid hormones are important in the preventation and treatement of breast cancer. They raised the question of whether the increased incidence of breast cancer in patients with hypothyroidism is due to thyroid gland dysfunction or to prolonged intake of thyroid supplements, (Leis 1978).

8. Oral contraceptives: -----

Jick et al., (1981) suggested that recent oral contraceptive use might be hazardous in premenopausal women aged 46 - 55 ys., While Pike et al., (1981), and Harris et al., (1982) found an increased risk