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Breast Cancer in Greenland – Selected Epidemiological, Clinical, and Histological Features*

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Summary. Fifty-seven breast cancers were diagnosed among indigenous Greenlandic women from 1950 to 1974. An additional 22 cases registered between 1975 and 1979 represent a minimum number and were only used as basis for minimum incidence rates. Changes in age-adjusted rate, age-specific incidence pattern, and relative risk were consistent with an upward shift from a population of low risk between 1950 and 1969 to one of intermediate risk from 1970 onward, a finding that relates well to increased urbanization and westernization. The risk of breast cancer in Greenland may be associated with consumption of saturated fats but is seemingly not correlated to total fat intake which has always been on a par with high-risk Danish levels. An association with diet may in reality have been stronger than suggested but weakened by a counterbalancing effect of high fertility, especially in the youngest age groups. Evaluation of histological features and survival did not suggest differences which could favorably compare with findings in white population groups contrary to reported results from the population of Japan, also one of low risk and of mongoloid origin. Further studies should consider dietary intakes, endocrine variations, and breast fluid secretion with special attention to girls at the age of menarche.

Key words: Breast cancer – Eskimo – Greenland

Data on breast cancer have shown considerable international variation in the incidence of the disease (MacMahon et al. 1973a; Waterhouse et al. 1976) and have also pointed to differences in tumor histology and survival rates between countries or population groups (Morrison et al. 1973; Wynder et al. 1963). Incidence rates are 4–5 times higher in Northern Europe and North America than in most countries in Asia and Africa while intermediate rates prevail in Southern Europe and South America. Besides these differences variations also occur in the age pattern.

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In areas or populations of high risk the age-specific rates increase throughout life whereas in low-risk countries the rates increase until middle age and then decrease.

In the relatively homogenous population of Iceland a substantial increase in the overall incidence of breast cancer during the past 70 years was followed by a change in the age-specific rates from a low-risk pattern in the 1920s to a high-risk Western pattern in the 1950s (Bjarnason et al. 1974). It is of interest that the entire change could be explained solely by an increase in birth cohort specific incidence rates seemingly correlated to the marked westernization which occurred in the country during the same period. Studies of migrant populations as well have confirmed the importance of environmental factors in the etiology of breast cancer even though the gradual shift to the incidence of the host population sometimes seems to take more than one generation (Buell 1973; Dunn 1975).

Several risk factors have been demonstrated with relative consistency. They include nulliparity, late age at first full-term pregnancy, late menopause, family history, and previous breast cancer disease whereas evidence is less consistent with regard to factors like early menarche, low number of pregnancies, benign breast disease, premenstrual symptoms, obesity, and tall stature (Anderson 1971; Choi et al. 1978; Day et al. 1978; De Waard 1975, 1978; Henderson et al. 1974; Lewison and Neto 1971; MacMahon et al. 1970a; MacMahon et al. 1973a; Prior and Waterhouse 1978, Staszewski 1971; Trichopoulos et al. 1972, Tulinius et al. 1978; Wynder et al. 1978a, b; Yuasa and MacMahon 1970). Lactation, once believed to exert a protective influence, appears to have no effect on breast cancer risk (MacMahon et al. 1970b). However, even an extreme integration of the above mentioned variables cannot account for the magnitude of the world-wide variation in breast cancer incidence, which seems to be more explicable on the basis of dietary habits, particularly total fat intake. A number of population correlation studies and several case-control studies have supported a nutritional hypothesis and especially an association between breast cancer risk and a high fat diet (Armstrong and Doll 1975; Carroll et al. 1968; Hankin and Rawlings 1978; Hems 1978; Howell 1974; Miller et al. 1978; Nomura et al. 1978, Phillips 1975). Experimental data have further indicated that the high fat effect may possibly be mediated through increased levels of serum-prolactin (Chan and Cohen 1974; Chan et al. 1976).

International differences in breast cancer histology and survival rates are probably also predominantly caused by environmental influence although a genetic contribution seems difficult to rule out completely. Comparisons between Japan, a low-risk country, and high-risk Western countries have demonstrated a more frequent occurrence in Japan of histological features usually considered to be predictors of a more favorable prognosis (Chabon et al. 1974; MacMahon et al. 1973b). Also reported were higher Japanese survival rates which could neither be accounted for by the special histological characteristics nor by differences in age distribution, size and spread of primary lesion, or kinds of therapy (Morrison et al. 1973; Wynder et al. 1963).

Breast cancer has long been known to exist among indigenous Greenlanders, a population whose original diet contained a relatively large amount of fat. The first histologically verified case was published as early as 1904 (Bertelsen 1904) and Fibiger later reported five malignant breast tumors in a series of 11 cancers identified among Greenlandic women between 1911 and 1922 (Fibiger 1923). This

paper presents the incidence and some histological and clinical features of breast cancer in Greenland during the 25 years from 1950 to 1974, a period characterized by urbanization and westernization and by changes in life style including nutritional habits and reproductive patterns. To support some of the study results minimum incidence of the disease in 1975–1979 is also presented.

Material and Methods

Indigenous Greenlanders, the worlds largest single population of Eskimo descent, increased from 22,500 in 1950 to 40,000 in 1974 and reached 41,000 in 1979. The population structure and the medical facilities in Greenland have been described in previous publications (Nielsen et al. 1977, 1978). The country is divided into 16 medical districts each of which has a small hospital. In addition, a central referral hospital is located in the capital Nuuk (Godthåb), but all patients for radiotherapy have to be transferred to centers in Denmark, mainly in Copenhagen.

Records for all inpatients and outpatients at Greenland hospitals were examined for malignant disease and records of patients with breast cancer diagnosed during the 25-year period from 1950 to 1974 were reviewed for medical and demographic information. Supplementary data were obtained from files at referral centers in Denmark. Pathology and autopsy reports, death certificates, files at the Ministry for Greenland in Copenhagen, and data from the Danish Cancer Registry were reviewed as described in earlier studies (Nielsen et al. 1977, 1978). Data from Greenland parish registers on all women who gave birth between 1947 and 1960, available at the Statistical Office, Ministry for Greenland, in Copenhagen, were reviewed for supplementary information on age at first birth and total number of pregnancies. The Statistical Office supplied vital statistical data including the average age distribution of Greenlandic women during 5-year registration periods. An expected number of breast cancers was calculated for each 5-year period by applying age-specific incidence rates from Denmark (Clemmesen 1965, 1969, 1974, 1977) to the population of indigenous Greenlandic women. The deviation of observed-to-expected ratios from unity were tested for statistical significance (Bailar and Ederer 1964). Age-specific rates and incidence rates age adjusted to the "World Standard Population" (Doll 1976) were calculated for the three periods 1950–1959, 1960–1969, and 1970–1974. For statistical evaluation of incidence rates 95% confidence limit factors for estimates of Poisson-distributed variables were used according to Haenszel et al. (1962).

Data on size of tumor and metastatic spread at the time of diagnosis were sufficiently detailed in all cases to allow staging into three categories: (1) cases with localized tumor and no metastatic spread, (2) cases with metastatic spread to ipsilateral axillary nodes only, and (3) cases with distant metastases including spread to supraclavicular nodes. Primary tumors could be divided into those smaller or larger than 5 cm in diameter. A more refined staging was not possible. Malignancy diagnosed in the contralateral breast of a patient with previous breast cancer disease was excluded as a second primary tumor if distant metastases, positive supraclavicular nodes, or skin nodules were present either before or at the time of diagnosis of the second growth, or if fixed axillary nodes had been present at the time of the first tumor. Coincidental tumors diagnosed in both breasts at the same time or within 1 month of each other were regarded as one case.

Five-year survival rates based on follow-up to January 1, 1980, were calculated from determinate cases excluding patients dying from intercurrent disease and patients lost to follow-up. All cases histologically verified between 1960 and 1974 were reexamined and reclassified according to the criteria of WHO. Histological material was not available prior to 1960.

Although the main study covered only the period from 1950 to 1974 minimum incidence rates were added for 1975–1979 based on files at the Danish Cancer Registry and on reports from the pathology department at the Rigshospital, Copenhagen, which performs the major part of the histological service for Greenland. As the number of breast cancers obtained from these two sources cannot be considered complete the data have not yet been used for further analysis.

Results

Fifty-seven breast cancers were diagnosed among indigenous Greenlandic women in the 25-year period from 1950 to 1974 (Table 1). Fifty cases (88%) were histologi-

Table 1. Breast cancer among indigenous Greenlandic women between 1950 and 1974. Observed and expected[a] numbers for women of all ages and for women under the age of 40

Period	All ages			Ages under 40		
	Observed	Expected	O/E	Observed	Expected	O/E
1950–1954	8	15.7[b]	0.5[c]	2	2.0	1.0
1955–1959	7	17.1[b]	0.4[d]	2	2.0	1.0
1960–1964	10	20.8	0.5[c]	3	2.4	1.3
1965–1969	10	27.3	0.4[d]	2	3.3	0.6
1970–1974	22	33.8	0.7[c]	8	3.6	2.2
1950–1974	57	114.7	0.5[d]	17	13.3	1.3

[a] Based on the incidence in Denmark during the same period
[b] More than 10% of the population over 65 was of unknown exact age
[c] $P<0.05$
[d] $P<0.01$

cally verified. The remaining seven cases (12%), all diagnosed between 1950 and 1960, were based on unmistakable clinical evidence. Three additional malignancies diagnosed during the study period in the contralateral breast of patients with previous breast cancer disease could not be classified as second primaries and were excluded from the study.

The indirect comparison with incidence in Denmark (Table 1) showed a relative risk varying between 0.4 and 0.5 from 1950 to 1969 for all age groups combined but women under the age of 40 carried the same risk as Danish women. Between 1970 and 1974 the relative risk had increased to 0.7 and risk in women under 40 to more than twice the risk in Denmark. The latter ratio, however, was not statistically significant.

Age-specific incidence rates and age adjusted rates ("World Population") are given in Table 2. Between 1950 and 1959 the incidence reached a plateau in the age group 45–54 with a slight increase after the age of 65. From 1970 to 1974 rates had increased for all ages except for women aged 45–54. The increase was not only substantial in younger age groups but also pronounced and statistically significant in the age group 55–64, where the rate was comparable to recent rates in Denmark. The age-adjusted rate showed no alteration during the first 20 years, 18.2 between 1950 and 1959 and 18.1 between 1960 and 1969, but increased with statistical significance to 32.0 between 1970 and 1974. Minimum age-adjusted rate between 1975 and 1979 was 28.8, based on 22 cases.

Distribution by district, by town vs. settlement and by time period and age showed no significant gradients of frequency either in younger or in older age groups. From 1950 to 1974 a total of 40 patients came from district towns and 14 from settlements while two were patients at mental institutions in Denmark at the time of diagnosis. Information on residence was not available in one case.

The time from when the patients discovered the tumor until their hospitalization varied from an average of 7 months between 1950 and 1959 to 5 months between 1970 and 1974 (Table 3). The percentage of patients with localized tumor increased, however, from 13% between 1950 and 1959 to 64% between 1970 and 1974

Table 2. Breast cancer in Greenland between 1950 and 1979. Age-specific incidence rates and age-adjusted rates from 1950 to 1974. Minimum incidence rates from 1975 to 1979. Comparison with incidence in Denmark from 1968 to 1972

Age	Greenland 1950–1959	Greenland 1960–1969	Greenland 1970–1974	Denmark 1968–1972	Greenland 1975–1979 (minimum rates)
25–34	16.9	9.4	24.4	10.2	23.1
35–44	15.9	41.2[b]	58.6	66.9	68.9
45–54	52.5	35.4	30.4	139.2	75.1
55–64	50.8	34.9	142.4[b]	162.1	81.1
65–74	—	95.2	103.1	203.7	—
75+	64.9[a]	—	107.5	303.7	157.5
Age-adjusted rate (world population)	18.2	18.1	32.0	54.0	28.8
Number of cases	15	20	22	9599	22

[a] More than 10% of the population over 65 was of unknown exact age
[b] $P<0.05$

Table 3. Greenland 1950–1974. Distribution of breast cancers by stage of disease at the time of diagnosis. Size of tumor and average duration of symptoms prior to hospitalization

	1950–1959		1960–1969		1970–1974		1950–1974	
	No.	%	No.	%	No.	%	No.	%
Localized tumor	2	13	10	50	14	64	26	46
Axillary nodes involved	9	60	5	25	2	9	16	28
Distant metastases	3	20	5	25	6	27	14	24
Unknown	1	7	—	—	—	—	1	2
Total	15	100	20	100	22	100	57	100
Tumor < 5 cm	5	33	6	30	14	64	25	44
Duration of symptoms	7 months		6 months		5 months		6 months	

and the percentage with tumor under 5 cm in diameter increased from 33% to 64%. No difference in risk was found between the right and the left breast.

Of the 57 patients registered between 1950 and 1974, only 15 survived for 5 years or more, while 35 died of cancer, five of intercurrent disease, and two were lost to follow-up. Five-year survival rates by stage of disease and by age are presented in Table 4. At each stage survival rates were higher in patients under 55 than in patients aged 55 or more. The overall 5-year survival rate for patients with localized tumor was 48% and for all patients combined 32%. The highest survival rate, 83%, was found in patients under 55 with localized tumor diagnosed between 1970 and 1974.

Table 5 presents survival rates according to type of therapy during 1950–1974. The majority of the 42 operable patients with no distant metastases were treated

Table 4. Breast cancer among indigenous Greenlandic women between 1950 and 1974. Five-year survival rate by stage of disease and age. In parentheses number and survival rate of patients with localized tumor diagnosed between 1970 and 1974

Stage of disease	Under 55 years		55 years and more		All ages	
	No.	Survival rate	No.	Survival rate	No.	Survival rate
Localized	15 (7)	57 (83)	11 (7)	33 (20)	26 (14)	48 (55)
Axillary nodes involved	10	44	6	0	16	31
Distant metastases	8	13	6	0	14	7
All stages	33[a]	42	23	16	56[a]	32

[a] One patient with unknown stage of disease excluded

Table 5. Breast cancer among indigenous Greenlandic women between 1950 and 1974. Five-year survival rate by method of treatment

Treatment	Number	5-year Survival %
Radical mastectomy	14	39
Radical mastectomy with irradiation	1	100
Simple mastectomy	4	67
Simple mastectomy with irradiation	21	72
Extirpation of tumor	2	0
Palliative treatment (cases with distant metastases)	14	7
Total	56[a]	32

[a] One case with unknown treatment excluded

with either radical mastectomy (14 patients of whom five had localized tumor) or simple mastectomy with irradiation (21 patients of whom 16 had localized tumor). Five-year survival rates for these two groups were 39% and 72%, respectively.

Histological classification of 41 cases diagnosed between 1960 and 1974 (Table 6) showed a predominance of invasive ductal carcinomas, 75% of all types. Medullary carcinomas constituted 7.5% (three cases) and invasive lobular carcinomas 5% (two cases) while only one case was classified as mucinous carcinoma and one as intraductal carcinoma. Moderate or marked lymphocyte infiltration was only found in seven cases (18%) of invasive cancers including the three medullary carcinomas where lymphoid infiltrate is a diagnostic feature. Definite circumscription of tumor margin was found in 11 invasive tumors (28%) while severe or moderate fibrosis was present in 29 cases (74%). The three patients with medullary carcinoma were all alive after 5 years, while survival for patients with invasive duc-

Table 6. Breast cancer among indigenous Greenlandic women between 1960 and 1974. Number of cases by histologic characteristics. Five-year survival rates

Histological Type	Total		Moderate or marked lymphoid infiltration	Definite circum-scription of tumor margin	Moderate or severe fibrosis	5-year Survivl rate
	No.	(%)	No.	No.	No.	%
Invasive ductal carcinoma	31	(75)	3	8	24	18
Medullary carcinoma	3	(7.5)	3	2	1	100
Invasive lobular carcinoma	2	(5)	0	0	2	—
Mucinous carcinoma	1	(2.5)	1	1	1	0
Invasive ductal carcinoma with a predominant intraductal component	1	(2.5)	0	0	1	100
Intraductal carcinoma	1	(2.5)	–	–	–	100
Carcinosarcoma	1	(2.5)	0	0	0	0
Paget's disease	1	(2.5)	–	–	–	100
Total	41[a]	(100)	7	11	29	31

[a] One case, diagnosed in 1960, was not histologically verified

Table 7. The occurrence of risk factors in indigenous Greenlandic women with breast cancer diagnosed between 1950 and 1974. The number of patients for which information was not available is indicated in parentheses

	1950–1959 No.	1960–1969 No.	1970–1974 No.	1950–1974 No.
All patients	15	20	22	57
1st birth before 25	3 (8)	6 (7)	14 (0)	23 (15)
1st birth after 25	3 (8)	5 (7)	3 (0)	11 (15)
Nulliparity	1 (8)	2 (3)	5 (0)	8 (11)
Average no. of pregnancies	2 (9)	6.2 (3)	4.3 (0)	4.7 (12)
Average age at menarche (yr)	16 (10)	16 (11)	15 (0)	15 (21)
Average age at menopause (yr)	42 (10)	48 (3)	50 (0)	48 (13)

tal carcinoma was only 18%. The two patients with invasive lobular carcinoma both died of intercurrent disease.

Information regarding risk factors (Table 7) was only complete for patients from 1970 to 1974 with five nullipara (23%) and three (13%) with first full-term pregnancy after the age of 25. The number of pregnancies among these patients averaged 4.3 and the age at menarche 15 years, 1 year less than the average age (from obtainable information) during the previous 20 years. The age at menopause averaged 50 years between 1970 and 1974, higher than the average age (from obtainable information) between 1950 and 1969. No case was found with a family history of breast cancer but direct information regarding this aspect was only available in 38 cases (67%). One patient had a history of a primary cancer in the sigmoid colon histologically verified 1 year before the discovery of her breast tumor.

Discussion

As previously discussed (Nielsen and Hansen 1979), the possibility that cases of malignancy should have escaped medical attention in Greenland during the study period must be considered very slight. The number of breast cancers identified between 1950 and 1974 can be taken for the actual occurrence of the disease, but the results must be interpreted cautiously especially with regard to incidence and survival rates based as they are on small numbers. The deficit of cancers in comparison with Denmark (Table 1) is statistically significant during the whole study period and the significant increase in relative risk and age adjusted rate indicate an upward shift from a population of low risk during the first two decades to one of intermediate risk from 1970 onward. Age-adjusted rates from 1950 to 1969 are only slightly higher than recent rates in Japan (Waterhouse et al. 1976) and the age-specific incidence structure of this period resembles a low-risk pattern except for moderately elevated rates over age 65. Age-specific rates between 1970 and 1974, on the other hand, come closer to a Western pattern with highest rates found in all age groups over 55. The age-adjusted rate in this period, 32.0, ranks among the intermediate rates reported from, e.g., Finland and Spain (Waterhouse et al. 1976) and minimum age-adjusted incidence between 1975 and 1979 confirms the upward shift.

It is tempting to relate this change in Greenland breast cancer profile to an increased exposure to Western cultural influence in recent decades mediated primarily through an accelerated urbanization since World War II. One of the consequences has been a change in dietary habits as imported foods became more accessible, resulting among other things in an increased consumption of saturated fats. At the beginning of this century approximately half the calorical intake was covered by fats mainly of marine origin from seal, whale, and fish, rich in unsaturated fatty acids (Krogh and Krogh 1913). Partly owing to an increased admixture of imported nutriments Greenland foods have generally since 1930 been found to contain equal or slightly smaller amounts of fats and carbohydrates but more proteins than a Western diet (Bang et al. 1976). Imported fats constituted approximately 25% of total dietary fat in 1930–1933 (Bertelsen 1937), but had already increased to 46% in town populations in 1953, mainly consisting of butter and margarine of animal origin (Uhl 1955). In 1974, the average annual per capita consumption of butter was half of that in Denmark (Brenøe 1979) and the consumption of other dairy products somewhat lower; a recent analysis of settlement diet could still demonstrate a higher percentage of unsaturated fatty acids than in Danish foods, viz., 66% vs. 47% (Bang et al. 1976).

Studies from rodents have consistently demonstrated that unsaturated fats increased mammary tumorigenesis more than saturated fats (Carroll and Khor 1971; Rao and Abraham 1976). This has led to suggestions that an increased level of unsaturated fatty acids might inhibit immunological response to cancer (Mertin 1973) or make cell membranes more permeable to carcinogenic agents (Hopkins and West 1976). The present study does not support such experimental findings. Contrary to most international data, the present results do not indicate an association between breast cancer risk and intake of total fat, predominantly of unsaturated character and always on a par with high-risk Danish consumption. However, since

the magnitude of the potential breast cancer risk appears to be established for the major part already at menarche or during early reproductive years (MacMahon et al. 1973a), it cannot be excluded that the upward shift in Greenland risk from 1970 may reflect the increased consumption of saturated fats and associated variables such as cholesterol during the previous decades. Such an assumption would lend indirect support to a recent study which in humans has revealed significantly higher intakes of saturated (and total) fats than in controls, but little difference in the intake of several unsaturated fatty acids (Miller et al. 1978).

Indeed, a possible association between breast cancer and diet in Greenland may have been substantially stronger than suggested, but may have been weakened by a counterbalancing effect of high fertility which in young women aged 15–19 more than tripled from 1948 to 1965 (Ministry for Greenland 1971). The potential role of risk factors associated with reproductive life is difficult to evaluate in Greenland owing to small numbers, unavailability of complete information in many patients (Table 7), and unavailability of data on the overall occurrence of these risk factors in the general population. The relatively high proportion of nulliparous patients and patients with first birth after 25, in a population which almost doubled during the study period, suggests a higher risk in these two categories of women. The suggested tendency toward later age at menopause points in the expected direction of increased risk while the late menarche is consistent with a low-risk population (Wynder et al. 1963; Yuasa and MacMahon 1970). The suggested slight decrease in age at menarche may reflect changing nutritional status among adolescents (Frisch and McArthur 1974).

When considering a possible influence of pregnancy-related variables it must be emphasized, however, that not only do other female estrogen-dependent tumors, such as ovarian and endometrium cancers, exhibit a lower incidence in Greenland than in Western countries but clinical prostate cancer, also hormone-dependent and obviously not associated with reproductive life, is almost non-existent in Greenlandic men (Nielsen, unpubl. results).

The unstable 5-year survival rates, based on only 15 surviving patients, do not compare favorably with survivals reported from Denmark during the same period (Sørensen 1979). Better survival in patients under 55 is consistent with other findings but only two of the present survival rates are on a par with recent Danish rates (Clemmesen 1976), e.g., the very unstable rate of 83% in patients under 55 with localized tumor diagnosed between 1970 and 1974 and the rate of 72% in patients treated with simple mastectomy and irradiation (predominantly localized tumors).

Evaluation of histological features in Greenland breast cancers do not point in the direction of reported Japanese characteristics, although the Greenland population is also one of low-risk and of mongoloid origin. Comparative histological studies of breast cancer in the high-risk white population of the USA and in the low-risk population of Japan have demonstrated a significantly greater frequency of intraductal, medullary, and mucinous carcinomas in Japan (Mac Mahon et al. 1973b; Wynder et al. 1963), tumor types which are usually considered to have a better prognosis than invasive ductal carcinoma. The Japanese tumors furthermore appeared to have a less aggressive potentiality as indicated by more extensive lymphoid infiltration, sharper tumor circumscription and less fibrosis than in tumors from white patients (Chabon et al. 1974; MacMahon et al. 1973b).

In the present study the percentage of medullary, mucinous, and intraductal carcinomas and the degree of lymphoid infiltration were comparable to or lower than findings in white American and European population groups. The percentage of tumors with margin circumscription and with fibrosis were more on a level with Japanese findings, but the general significance of these two variables is not yet established.

A cohesive theory on the etiology of breast cancer is still lacking. Based on the well documented association with reproductive factors many studies have concentrated on serum levels and/or urinary excretions of the different estrogen fractions, of androgens, and of their metabolites and on a possible effect of diet exerted via the endocrine system (Wynder et al. 1978a). Investigations have been carried out in high- as well as low-risk populations, in pre-, peri-, and postmenopausal patients and controls, and in experimental animals, but a clear pattern has not evolved. The results have been somewhat inconsistent and conflicting possibly because data relating dietary factors to the synthesis and metabolism of hormones in healthy individuals in general are very sparse.

An association between breast cancer and cancer of the colon has given rise to the hypothesis that biliary steroids altered by gut bacteria could be common etiological factors (Hill et al. 1971; Howell 1976).

Also of interest are studies of prolactin, a pituitary peptide. In rats a high fat diet increases serum prolactin and promote mammary tumors but the promoting effect can be abolished by administering antiprolactin drugs (Chan and Cohen 1974). In humans change from a Western diet to a vegetarian diet has been shown to substantially reduce prolactin levels (Wynder et al. 1978a). Women with a family history of breast cancer exhibit higher serum levels of prolactin than the public in general (Henderson et al. 1975) and in vitro studies of isolated neoplastic mammary cells suggest that a high prolactin/estrogen ratio increases cell proliferation (Chan et al. 1976).

However, the effect of prolactin and other hormones may be only indirect or permissive as indicated by recent studies on human breast fluid secretion, (defined by nipple aspiration), in nonlactating women (Petrakis et al. 1975). This secretion appears to be genetically determined with variations in race and age which relate well to breast cancer risks. Exogenous substances such as technetium, products of cigarette smoking and other chemical substances are secreted rapidly into the fluid (Petrakis 1977) which otherwise normally contains lipids and associated metabolites seemingly dependent largely on diet. The effect of hormones on breast cancer risk could be one of duct cell stimulation only.

It is thus recommendable for future studies of breast cancer in Greenland that measurements be carried out of dietary intake, and of serum and urinary levels of selected hormones including prolactin. Such studies should consider healthy as well as diseased women, ideally separated into pre- and postmenopausal individuals, and should preferably include girls at the age of menarche and early reproductive years. Serum levels of prolactin should be determined at night when secretion is maximal (Wynder et al. 1978a). History of reproductive life and associated factors should be carefully recorded in every patient admitted to hospital and a survey carried out on the occurrence of these risk factors in the general population.

Of great interest would be determination in cases and controls of amount and composition of breast fluid secretion as obtained by nipple aspiration. Future trends in the occurrence of the disease should be followed carefully. If the recent change of incidence pattern, as in Iceland, is a cross-sectional result of increasing birth cohort specific rates, the size of which may have been established already at puberty, the overall incidence in Greenland is likely to increase considerably in coming years.

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