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LACTATION AND A REDUCED RISK OF PREMENOPAUSAL BREAST CANCER

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Abstract *Background.* The evidence of an association of lactation with a reduction in the risk of breast cancer among women has been limited and inconsistent. The effect of lactation appears to be confined to premenopausal women with a history of long lactation, but most studies of this relation have been limited in statistical power. We conducted a multicenter, population-based, case–control study with a sample large enough for us to describe more precisely the association between lactation and the risk of breast cancer.

Methods. Patients less than 75 years old who had breast cancer were identified from statewide tumor registries in Wisconsin, Massachusetts, Maine, and New Hampshire. Controls were randomly selected from lists of licensed drivers if the case subjects were less than 65 years old, and from lists of Medicare beneficiaries if they were 65 through 74 years old. Information on lactation, reproductive history, and family and medical history was obtained by means of telephone interviews. After the exclusion of nulliparous women, 5878 case subjects and 8216 controls remained for analysis.

Results. After adjustment for parity, age at first delivery, and other risk factors for breast cancer, lactation was associated with a slight reduction in the risk of breast cancer among premenopausal women, as compared with the risk among women who were parous but had never lactated (relative risk, 0.78; 95 percent confidence interval, 0.66 to 0.91); the relative risk of breast cancer among postmenopausal women who had lactated, as compared with those who had not, was 1.04 (95 percent confidence interval, 0.95 to 1.14). With an increasing cumulative duration of lactation, there was a decreasing risk of breast cancer among premenopausal women (P for trend <0.001) but not among postmenopausal, parous women (P for trend = 0.51). A younger age at first lactation was significantly associated with a reduction in the risk of premenopausal breast cancer (P for trend = 0.003). As compared with parous women who did not lactate, the relative risk of breast cancer among women who first lactated at less than 20 years of age and breast-fed their infants for a total of six months was 0.54 (95 percent confidence interval, 0.36 to 0.82).

Conclusions. There is a reduction in the risk of breast cancer among premenopausal women who have lactated. No reduction in the risk of breast cancer occurred among postmenopausal women with a history of lactation. (N Engl J Med 1994;330:81-7.)

IN the search for practical methods to prevent breast cancer, lactation has a strong appeal as a potentially modifiable factor. Nonetheless, the association between lactation and the risk of breast cancer remains uncertain. In several recent case–control studies, lactation, particularly for relatively long periods, was associated with a small reduction in the risk of breast cancer.[1-11] This effect appeared to be limited to premenopausal women. In contrast, in a large cohort study,[12] as well as in several retrospective evaluations,[4,13-18] no association was seen. Since few of these studies included a large number of premenopausal women who had breast-fed for long periods, we conducted a multicenter case–control study to evaluate this potentially modifiable risk factor.

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METHODS

Identification of Case Subjects

All female residents of Wisconsin, western Massachusetts, Maine, and New Hampshire who were given a new diagnosis of breast cancer and who were less than 75 years of age were eligible for this study. Case subjects were identified by each state's cancer registry from April 1989 through December 1991, except for New Hampshire, where subjects were enrolled beginning in January 1990. Case subjects in whom breast cancer was diagnosed more than two years before the registry report were excluded from the

Table 1. Participation of Eligible Subjects with Breast Cancer and Controls in the Study, According to State.

CATEGORY	WISCONSIN		MAINE		NEW HAMPSHIRE		MASSACHUSETTS		TOTAL	
	CASE SUBJECTS	CONTROLS	CASE SUBJECTS	CONTROLS	CASE SUBJECTS	CONTROLS	CASE SUBJECTS	CONTROLS	CASE SUBJECTS	CONTROLS
No. eligible	4563	4445	920	1928	659	1119	2390	3837	8532	11,319
Reason for nonparticipation (%)										
Refusal by physician	8.3	—	9.2	—	1.5	—	9.8	—	8.3	—
Inability to locate subject	0.2	0.5	4.0	4.6	1.8	0.8	0.3	0.9	0.8	1.4
Refusal by subject	2.5	8.5	6.6	13.6	9.3	15.9	7.2	18.4	4.7	13.4
Death of subject	5.9	1.1	4.1	1.0	3.5	1.0	5.5	1.2	5.4	1.1
No. interviewed	3789	3999	699	1559	553	921	1847	3050	6888	9,529
% of eligible subjects	83.0	90.0	76.0	80.9	83.9	82.3	77.3	79.5	80.7	84.2

case group. Information was available from each state registry on cancer site, histologic features, extent of disease, demographic variables, and the name of the follow-up physician. According to a protocol approved by the institutional review board of each participating center, the physician of record for each eligible case subject was contacted by mail to obtain permission to interview the patient. Eligibility was limited to case subjects with listed telephone numbers, driver's licenses verified by self-report (if less than 65 years of age), and known dates of diagnosis. Of the 8532 eligible case subjects, physicians refused participation for 710 (8.3 percent), 463 (5.4 percent) had died, 66 (0.8 percent) could not be located, and 405 (4.7 percent) declined to participate (Table 1). Thus, data for 6888 women were available for analysis, for an overall response rate of 80.7 percent. Of these women, 98 percent had histologic confirmation of invasive breast carcinoma.

Identification of Controls

In each state, controls were randomly selected from the community in two ways: those under 65 years of age were selected from a list of licensed drivers, and those 65 through 74 years of age were selected from a roster of Medicare beneficiaries compiled by the Health Care Financing Administration. Computer files of potential controls were obtained annually. The randomly selected controls were intended to have an age distribution similar to that of the case subjects, but controls were oversampled among younger women in the New England states in order to increase the statistical power of the study. Controls were required to have no history of breast cancer and to have a listed telephone number. Of the 11,319 potential controls, 126 (1.1 percent) had died, 153 (1.4 percent) could not be located, and 1521 (13.4 percent) declined to participate. The overall rate of participation was 84.2 percent, and it varied somewhat among the study sites (Table 1).

Data Collection

Case subjects and controls were sent letters briefly describing the study before they were contacted by telephone. The 25-minute telephone interview elicited information on each woman's reproductive history, including, for each pregnancy, the duration of lactation, the reasons for stopping breast-feeding, and any medications used to inhibit lactation. The interview also covered the use of hormones, physical activity, alcohol use, selected dietary items, height and weight, medical history, and demographic factors. Information about the woman's personal and family history of breast cancer was obtained at the end of the interview to maintain blinding. The interviewers of 78 percent of the case subjects and 90 percent of the controls were unaware of the woman's case–control status until the end of the interview.

Statistical Analysis

Only lactation before an assigned reference date was included in this analysis. For case subjects this was the date of the diagnosis of breast cancer. For comparability, control subjects were assigned a reference date that corresponded to the average length of time from diagnosis to interview for the case group in each state (range, 8 to 21 months). Age was defined as the age at diagnosis or on the reference date. Parity was the number of full-term pregnancies (defined as pregnancies longer than six months resulting in a live birth or stillbirth). The women were defined as postmenopausal if they reported a natural menopause or a bilateral oophorectomy before the diagnosis or the reference date. Women who reported hysterectomy alone were classified as postmenopausal if their age at surgery was greater than or equal to the 90th percentile for age at natural menopause in the control group (54 years for smokers and 55 for nonsmokers). The women's menopausal status was considered unknown if they

Table 2. Selected Risk Factors among the Case Subjects and Controls Who Had Borne Children.

RISK FACTOR	CASE SUBJECTS (N = 5878)	CONTROLS (N = 8216)	RELATIVE RISK (95% CI)*
	no. of subjects		
Age at menarche (yr)†			
<11	297	407	1.00 (—)
11	756	1034	0.95 (0.80–1.14)
12	1330	1759	0.98 (0.83–1.17)
13	1683	2315	0.92 (0.78–1.09)
14	985	1456	0.83 (0.70–0.99)
≥15	750	1130	0.81 (0.68–0.98)
Age at birth of first child (yr)			
<20	886	1366	1.00 (—)
20–24	2697	4015	1.03 (0.93–1.14)
25–29	1637	2080	1.22 (1.09–1.36)
≥30	658	755	1.33 (1.15–1.53)
Parity			
1	772	981	1.00 (—)
2	1853	2479	0.92 (0.82–1.03)
3	1414	2102	0.80 (0.71–0.90)
≥4	1839	2654	0.76 (0.68–0.86)
Family history of breast cancer			
Absent	4669	7116	1.00 (—)
Present	1061	938	1.67 (1.52–1.85)
Unknown	148	162	1.40 (1.11–1.77)
Benign breast disease			
Absent	4871	7145	1.00 (—)
Present	891	964	1.35 (1.22–1.49)
Unknown	116	107	1.43 (1.09–1.88)
Body-mass index (quartile group)‡			
1 (<21.5)	1264	1981	1.00 (—)
2 (21.5–23.6)	1383	2078	1.03 (0.93–1.13)
3 (23.7–26.6)	1520	2058	1.08 (0.97–1.19)
4 (≥26.7)	1653	2036	1.16 (1.05–1.28)
Menopausal status			
Premenopausal	1201	2233	1.00 (—)
Postmenopausal	4428	5631	1.75 (1.50–2.04)
Unknown	249	352	1.22 (1.00–1.48)
Age at menopause (yr)§			
<45	605	1059	1.00 (—)
45–49	916	1208	1.36 (1.19–1.56)
50–54	1560	1834	1.58 (1.39–1.79)
≥55	481	618	1.43 (1.22–1.69)
Unknown	866	912	1.59 (1.38–1.83)

*Relative risks have been adjusted for age and state. CI denotes confidence interval.

†Excluding 192 women with missing values: 77 case subjects and 115 controls.

‡Excluding 121 women with missing values: 58 case subjects and 63 controls.

§Among women known to be postmenopausal.

Table 3. Relative Risk (RR) of Breast Cancer According to Lactation Experience, among the Case Subjects and Controls Who Had Borne Children.*

VARIABLE	PREMENOPAUSAL			POSTMENOPAUSAL			ALL		
	CASE SUBJECTS (N = 1180)	CONTROLS (N = 2185)	RR (95% CI)	CASE SUBJECTS (N = 4254)	CONTROLS (N = 5378)	RR (95% CI)	CASE SUBJECTS (N = 5434)	CONTROLS (N = 7563)	RR (95% CI)
	no. of subjects			*no. of subjects*			*no. of subjects*		
Lactation†									
No	602	1009	1.00 (—)	1774	2413	1.00 (—)	2376	3422	1.00 (—)
Yes	578	1176	0.78 (0.66–0.91)	2480	2965	1.04 (0.95–1.14)	3058	4141	0.97 (0.90–1.05)
Lifetime duration (mo)‡									
0	602	1009	1.00 (—)	1774	2413	1.00 (—)	2376	3422	1.00 (—)
≤3	203	375	0.85 (0.69–1.06)	1390	1704	1.03 (0.93–1.14)	1593	2079	0.98 (0.90–1.08)
4–12	195	390	0.78 (0.63–0.97)	681	760	1.07 (0.94–1.22)	876	1150	1.00 (0.89–1.11)
13–24	106	251	0.66 (0.50–0.87)	253	320	1.01 (0.83–1.21)	359	571	0.89 (0.77–1.04)
>24	74	160	0.72 (0.51–0.99)	156	181	1.04 (0.82–1.32)	230	341	0.95 (0.79–1.15)
P value for trend§		<0.001			0.51			0.30	

*Excluding 1097 women with missing values for body-mass index, age at menarche, duration of lactation, or menopausal status: 444 case subjects and 653 controls. Relative risks have been adjusted for age at first delivery, parity, personal history of benign breast disease, family history of breast cancer, body-mass index, and age at menarche. Those for postmenopausal women and all women have also been adjusted for age at menopause, and those for all women have been adjusted for menopausal status. CI denotes confidence interval.

†In the test for interaction of menopausal status and lactation, chi-square = 9.11, 1 df; P = 0.003.

‡In the test for overall interaction of menopausal status and lifetime duration of lactation, chi-square = 11.65, 2 df; P = 0.003.

§Includes women who never lactated.

had undergone hysterectomy without bilateral oophorectomy at 42 to 54 years of age for smokers or 42 to 55 years for nonsmokers. The lifetime duration of lactation was defined as the cumulative total of the periods of lactation after each live birth. The age at first lactation was the subject's age at the time of the first delivery after which breast-feeding was reported. Insufficient milk — a cause of the termination of lactation — was defined as an insufficient milk supply within the first three months after either of the first two pregnancies.

Odds ratios and 95 percent confidence intervals from logistic-regression models were used to evaluate relative risks. Conditional models stratified according to age (to intervals of approximately 0.10 year) and state were used to accommodate the different age distribution of the case subjects and the controls in each state.[19] Interactions involving the duration of lactation were evaluated with use of logarithmic transformation on a continuous scale, with the other factor also continuous (except for a personal history of benign breast disease, a family history of breast cancer, and menopausal status). Subjects with unknown values for any variables in the multivariate analyses were excluded unless they were incorporated as a separate category (as was the case for a personal history of benign breast disease, a family history of breast cancer, and age at menopause).

RESULTS

As compared with the controls, the women with breast cancer had a younger mean age at menarche, were older at the delivery of their first child, had lower parity, were more likely to have a family history of breast cancer or a history of benign breast disease, had a higher mean body-mass index (the weight in kilograms divided by the square of the height in meters), and were older at menopause (Table 2). These characteristics were also related to lactation, and we therefore controlled for them in all analyses. One thousand ten of the case subjects (15 percent) and 1313 of the controls (14 percent) either were nulliparous and therefore had never had the opportunity to lactate or could not provide a complete reproductive history. These women were excluded from all analyses, including that shown in Table 2.

Among all parous women who had ever lactated, the estimated relative risk of breast cancer was 0.97, as compared with that in women with children who had never lactated (Table 3). Among premenopausal women, however, a history of lactation was associated with a slight reduction in the risk of breast cancer (relative risk, 0.78). These estimates differed only slightly from estimates obtained after adjustment only for age and state (relative risk, 0.81) or for age, state, and parity (relative risk, 0.83), suggesting that confounding was unlikely to have introduced substantial bias. The total duration of lactation was also associated with a reduction in the risk of breast cancer, but only among premenopausal women. For premenopausal women with a cumulative total of more than 24 months of lactation, the relative risk of breast cancer was 0.72 as compared with that for women who had never lactated. When the women were divided into five groups according to the duration of lactation, with women who never lactated included as the group with the shortest duration (Table 3), an increasing duration of lactation was associated with a statistically significant trend toward a reduced risk of breast cancer ($P<0.001$). The exclusion of women who had never lactated resulted in a weaker trend ($P = 0.15$). Among models that included a single continuous term for the duration of lactation (linear, logarithmic, and square root), the logarithmic transformation provided the best fit to the data ($P<0.001$ for the comparison with the linear model) (Fig. 1). Among postmenopausal women, there was no association between the duration of lactation and the risk of breast cancer (P for trend = 0.51).

Age did not appear to modify the relation between the duration of lactation and the risk of breast cancer among premenopausal women ($P = 0.96$) or postmenopausal women ($P = 0.71$). Since the ages of the

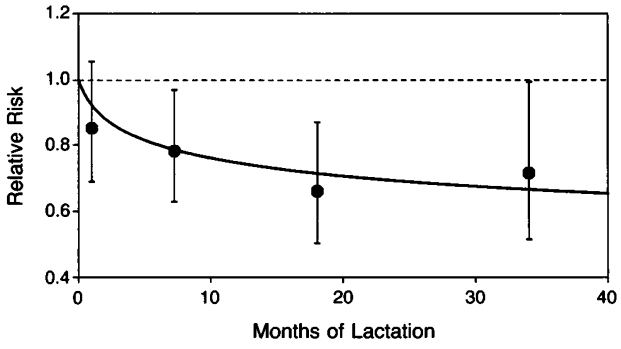

Figure 1. Relative Risk of Breast Cancer among Premenopausal Women According to the Cumulative Duration of Lactation.

Both log-transformed and categorical variables were used in analyzing the data. The curve shows the results of the logarithmic model, and the solid symbols those of the categorical model (plotted at the median value for the duration of lactation for the women in each category, as defined in Table 3). The bars represent the 95 percent confidence limits in the categorical model.

oldest premenopausal women overlapped the ages of the youngest postmenopausal women, these results suggest that the specificity of the association among premenopausal women is related to their menopausal status and is not a result of age. Among the smaller group of women 45 through 54 years of age, menopausal status still appeared to modify the effect of lactation on the incidence of breast cancer (P = 0.20).

Since the timing of exposure appears to be important in the development of breast cancer, we evaluated age at first lactation (Table 4). Younger ages at first lactation were associated with a decreased risk of breast cancer (P for trend = 0.003). Among women who were 20 years of age or younger when they first lactated, the risk of breast cancer was 0.54 for a total of six months of lactation, as compared with the risk among women who had never lactated. We considered the possibility that a residual association with the women's age at the first delivery was confounding this relation. Even after age at the first delivery was categorized in various ways, including by single years, however, the relation remained. The association with age at first lactation was not influenced by adjustment for the duration of lactation, nor did the risk vary according to the duration of lactation; therefore, we believe these two factors have independent relations to the risk of breast cancer.

An effect of early lactation may reflect the timing of exposure as well as the effect of latency. We evaluated latency by considering the effect of the length of time since the first episode of lactation and since the most recent episode. After adjustment for age at first lactation, neither the length of time since the first episode of lactation nor the length of time since the last episode was associated with the risk of breast cancer. Adjustment for these factors also did not alter the associations between both the duration of lactation and age at first lactation and breast cancer. The association between the total cumulative duration of lactation and age at first lactation did not vary according to age at the first delivery, age at menarche, parity, family history of breast cancer, or personal history of benign breast disease.

We considered the possibility that women who breast-fed for a short time may have been unable to breast-feed because of an insufficient milk supply. For women who reported insufficient milk within the first three months after the first or second delivery, as compared with women who lactated after the birth of the first or second child, but then stopped for reasons unrelated to the adequacy of the milk supply, the relative risk of premenopausal breast cancer was 0.99 (Table 5). Among postmenopausal women, the odds ratio was slightly, but significantly, reduced (relative risk = 0.86). The associations were not altered by adjustment for age, parity, or age at the first full-term pregnancy.

The use of hormones to inhibit the flow of milk after at least one pregnancy was reported by 43 percent of the controls and 44 percent of case subjects. The women were generally unable to identify the specific prepa-

Table 4. Relative Risk (RR) of Breast Cancer According to Age at First Lactation among the Case Subjects and Controls Who Had Borne Children.*

AGE (YR)†	PREMENOPAUSAL			POSTMENOPAUSAL			ALL		
	CASE SUBJECTS (N = 1180)	CONTROLS (N = 2185)	RR (95% CI)	CASE SUBJECTS (N = 4254)	CONTROLS (N = 5378)	RR (95% CI)	CASE SUBJECTS (N = 5434)	CONTROLS (N = 7563)	RR (95% CI)
	no. of subjects			*no. of subjects*			*no. of subjects*		
Never	602	1009	1.00 (—)	1774	2413	1.00 (—)	2376	3422	1.00 (—)
<20	48	133	0.54 (0.36–0.82)	337	423	1.01 (0.80–1.27)	385	556	0.88 (0.73–1.07)
20–24	209	453	0.73 (0.59–0.92)	1129	1444	1.06 (0.93–1.21)	1338	1897	0.97 (0.87–1.08)
25–29	189	399	0.76 (0.59–0.99)	747	797	1.07 (0.92–1.25)	936	1196	0.98 (0.86–1.11)
≥30	132	191	1.26 (0.89–1.80)	267	301	0.90 (0.73–1.12)	399	492	0.99 (0.83–1.19)
P value for trend‡		0.003			0.51			0.58	

*Excluding 1097 women with missing values for body-mass index, age at menarche, duration of lactation, or menopausal status: 444 case subjects and 653 controls. Relative risks have been adjusted for age at first delivery, parity, personal history of benign breast disease, family history of breast cancer, body-mass index, age at menarche, and the logarithm of the duration of lactation. Those for postmenopausal women and all women have also been adjusted for age at menopause, and those for all women for menopausal status. CI denotes confidence interval. The relative risks shown are estimates for women with a cumulative duration of lactation of six months.

†In the test for additional interaction of menopausal status and age at first lactation, chi-square = 5.68, 1 df; P = 0.02.

‡Among women who ever lactated.

Table 5. Relative Risk (RR) of Breast Cancer According to the Sufficiency of the Milk Supply and the Use of Hormones to Suppress Lactation.*

VARIABLE	PREMENOPAUSAL			POSTMENOPAUSAL		
	CASE SUBJECTS (N = 1180)	CONTROLS (N = 2185)	RR (95% CI)	CASE SUBJECTS (N = 4254)	CONTROLS (N = 5378)	RR (95% CI)
	no. of subjects			*no. of subjects*		
Sufficiency of milk†						
Sufficient	428	885	1.00 (—)	1260	1429	1.00 (—)
Insufficient	128	265	0.99 (0.76–1.29)	1343	1716	0.86 (0.77–0.96)
Never tried	622	1032	1.44 (1.17–1.76)	1631	2207	0.90 (0.79–1.02)
Use of hormones‡						
Never used	473	951	1.00 (—)	2401	2989	1.00 (—)
Ever used	645	1119	1.06 (0.86–1.30)	1515	1989	1.08 (0.97–1.19)
Once	255	467	1.06 (0.85–1.33)	688	820	1.16 (1.02–1.31)
More than once	390	652	1.06 (0.83–1.35)	827	1169	1.01 (0.89–1.14)

*Relative risks have been adjusted for age at first delivery, parity, personal history of benign breast disease, family history of breast cancer, body-mass index, age at menarche, the logarithm of the duration of lactation after the first two pregnancies, and age at first lactation. Those for postmenopausal women have also been adjusted for age at menopause. CI denotes confidence interval. The relative risks shown are estimates for women with an age at first lactation of 20 years.

†Excluding 5 premenopausal women (2 case subjects and 3 controls) and 46 postmenopausal women (20 case subjects and 26 controls) for whom sufficiency could not be determined. Included in the "sufficient" category are women who lactated and then stopped breast-feeding for other reasons. The determination of sufficiency refers only to the first two births.

‡Excluding 177 premenopausal women (62 case subjects and 115 controls) and 738 postmenopausal women (338 case subjects and 400 controls) with unknown hormone use.

rations used. Among postmenopausal women, hormone use after one pregnancy was associated with a small but statistically significant increase in the risk of breast cancer (relative risk, 1.16) (Table 5). A smaller increase, which was not statistically significant, was observed among premenopausal women. The risk associated with hormone use appeared to be similar for pills, injections, and unknown forms of lactation suppressants (data not shown).

Discussion

Overall, in this large study, lactation was not associated with the risk of breast cancer. Among premenopausal women, however, a slight inverse association was observed, and lactation at early ages and for long periods was associated with more substantial reductions in risk. Such relations were not found among postmenopausal women.

The relation between the risk of breast cancer and the duration of lactation among premenopausal women was similar to that in other reports,[1-3,5,7,9-11] though in those studies the duration of lactation necessary to achieve a significant reduction in the risk of breast cancer ranged from 4 to 12 months[2] to 6 to 8 years.[7] Previous studies demonstrating a protective effect of lactation included relatively high proportions of premenopausal women or carefully defined groups of premenopausal women.[1,2,10] We believe that the failure to examine the relation of lactation and the risk of breast cancer according to menopausal status may explain the null findings of MacMahon et al.[13] and other large case–control studies.[4,9,14,16] In our study, only 25 percent of the women were premenopausal; thus, as we observed, a relatively small effect in this smaller group of women could be obscured in an unstratified analysis.

Our findings appear to conflict with the results of two recent cohort studies.[12,18] Although both the cohorts in both these studies were large, the number of premenopausal women with breast cancer who had a history of long-term lactation was small; thus, the statistical power of the studies to assess the association of greatest interest was limited. In addition, the study of Kvåle and Heuch[12] reported results without considering a modifying effect of menopausal status, and premenopausal exposures were not updated over the 30 years of follow-up. Thus, it is likely that misclassification of lactation history occurred, particularly among the youngest members of the cohort. In the Nurses' Health Study,[18] data on most types of exposure were obtained prospectively, but lactation was assessed retrospectively. Also, because of their education level, few of these women were likely to have lactated at an early age, and it is in the group of women who were young at first lactation that we observed the strongest protective effect. Finally, women's employment profoundly affects factors related to breast-feeding, including the use of supplemental bottle feeding.[20,21] Although the proportion of women who ever lactated in the Nurses' Health Study was similar to that in our study, the use of supplemental feeding may have been more frequent among the nurses, and the return to regular menses correspondingly more rapid. Restricting our analysis to lifetime homemakers confirmed the protective association observed in the entire group of premenopausal women.

No previous studies have examined the relation between age at first lactation and the risk of breast cancer. Our finding of an association may be consistent with the observation that an early age at the first delivery reduces the risk of breast cancer.[13] In our data, however, age at first lactation is a stronger determinant of the risk of premenopausal breast cancer than any other reproductive factor. Since our investigation of the relation between breast cancer and age at first lactation was stimulated in part by post hoc findings, further studies will be necessary to confirm this association.

Byers et al., who reported a twofold increase in risk among women who reported that they had had insufficient milk, suggested that the inability to lactate, rather than lactation itself, might explain the difference in risk between women who lactate and those who do not.[1] We found no increased risk among women with insufficient milk, however, and other studies have also not found this effect.[9]

The use of hormones to suppress lactation was associated with a very small increase in risk among postmenopausal women only, though with no gradient of effect. Specific hormones were not identified. The use

of diethylstilbestrol during pregnancy has been associated with a modest increase in the risk of breast cancer among older women.[22-25]

Some limitations should be considered in interpreting our results. The response rates in this study (81 percent for case subjects, and 84 percent for controls) were high, which suggests that selection bias, if any, would be limited. We restricted this study to women who had a driver's license or were Medicare recipients and who had a listed telephone number; we do not believe the use of these criteria compromised the generalizability of our findings. Controls selected from the appropriate lists were similar in education and mean income to census estimates (Applied Population Laboratory, Department of Sociology, University of Wisconsin–Madison: unpublished data). However, nonwhites were underrepresented in both the control group and the case group, perhaps because we established eligibility through telephone directories. Finally, all information included in this analysis was based on reports by the case and control subjects themselves. For most subjects these well-defined events occurred many years before the interview, but reproductive histories tend to be reported with a high degree of accuracy.[26]

Lactation may reduce the risk of breast cancer simply by interrupting ovulation or by modifying pituitary and ovarian hormone secretion.[1,2,27,28] Direct physical changes in the breast that accompany milk production may also contribute to the protective effect.[2,28] In particular, in early reproductive life breast tissue may be favorably influenced by these changes.[29] Lactating rats and mice are relatively resistant to the effects of chemical carcinogens, as compared with nonlactating controls.[30-32] Such effects may reflect low rates of DNA synthesis during lactation[33,34] or increased elimination of the carcinogen by the secretory mammae.[30,32] Similar mechanisms could be important in breast cancer in premenopausal women, the risk factors for which appear to be somewhat different from those for postmenopausal disease.[8,35] We were not able to determine why lactation is associated with the risk of breast cancer only in premenopausal women.

If lactation, a potentially modifiable factor, indeed has a protective effect against premenopausal breast cancer, an important reduction in the incidence of this disease among women who have borne children could occur. If women who do not breast-feed or who breast-feed for less than 3 months were to do so for 4 to 12 months, breast cancer among parous premenopausal women could be reduced by 11 percent, judging from current rates. If all women with children lactated for 24 months or longer, however, then the incidence might be reduced by nearly 25 percent. This reduction would be even greater among women who first lactate at an early age.

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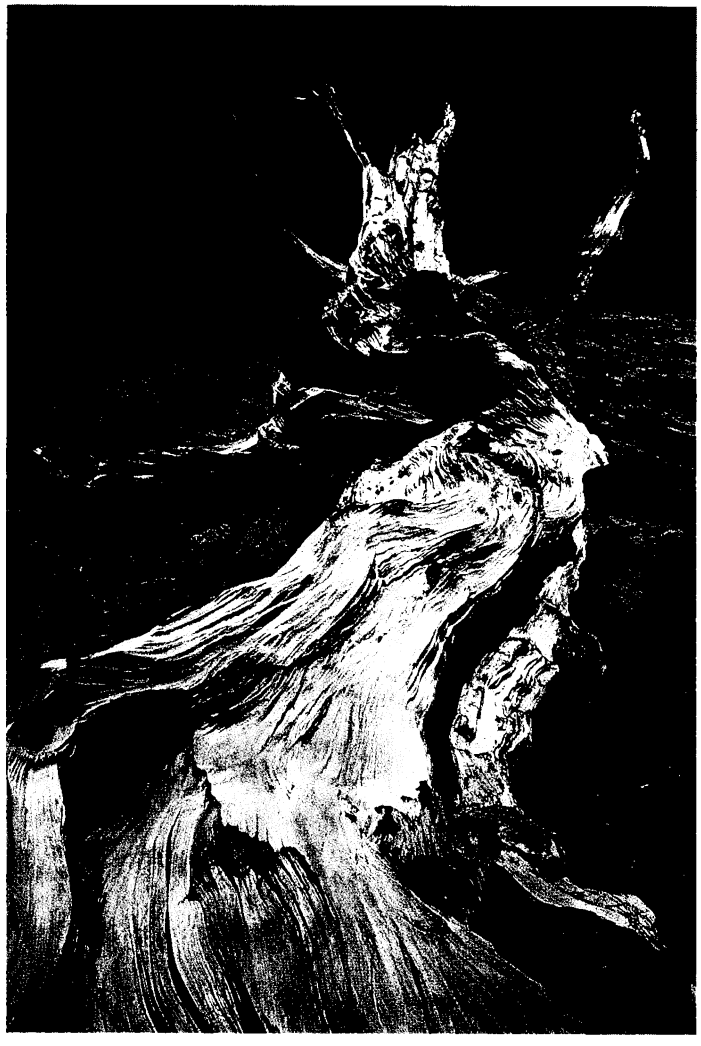

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