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Lactation and Reproductive Histories of Breast Cancer Patients in Tokyo, Japan*

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Epidemiological characteristics of breast cancer have been studied in Tokyo, an area of relatively low breast cancer rates, as part of an international collaborative study. Breast feeding of infants is customary for Japanese women, but even very prolonged lactation did not appear to be associated with a reduction in breast cancer risk. Late age at menarche and early age at first pregnancy were both associated with reduced breast cancer risk. The protective effect of early pregnancy seems much greater than has previously been recognized, and may indeed be greater in Japan than in other areas. However, the average age at first pregnancy is not lower in Tokyo than in areas where breast cancer rates are high.

The low rate of breast cancer in Japan, relative to North America and northern Europe, constitutes one of the most intriguing epidemiological features of this disease. The known association of breast cancer with low fertility, and the hypothesis, long suggested, of the influence of lactation in reducing breast cancer risk, invite comparison of the reproductive histories of women in Japan with those in Europe and North America, to determine how much, if any, of the difference in breast cancer risk can be explained by differences in reproductive and lactation experiences. Therefore, as part of an international collaborative study we have attempted to assemble a large and representative series of Japanese breast cancer patients and controls to examine the epidemiological characteristics of the disease in Japan.

MATERIAL AND METHOD

The cases

Arrangements were made to interview breast cancer patients in 25 of the largest hospitals in Tokyo. The intention was to interview all female residents of the prefecture of Tokyo (*Tokyo-to*) who were admitted during the study period (1 April 1965–31 March 1967) for a hospital stay during which an initial diagnosis of breast cancer was made. A total of 861 eligible patients was identified and all but 12 were interviewed. Altogether, 409 of the 861 came from the two largest, specialized cancer hospitals; the remainder came from 23 general hospitals.

In most of the centres in the international study, an attempt was made to identify all new cases occurring in a geographically defined population. The purpose of this was (1) to allow estimates of incidence in the study centres to be made, and (2) to ensure that the interviewed patients would be representative. The need for a large series of Japanese patients dictated the selection of Tokyo as the study centre, but the great size of the city, which has more than 500 hospitals and in-patient facilities, precluded the identification of all new cases. Estimates of the incidence of breast cancer in the city as a whole cannot therefore be given. However, it is believed that the inclusion of cases from a wide variety of hospitals gives reasonable assurance of the representative nature of the series. By applying the age-specific breast cancer incidence rates reported for the cities of Hiroshima and Nagasaki (Harada et al., 1963) to the female population of *Tokyo-to*, we estimate that about 1700 new cases occurred in *Tokyo-to* during the study period. The series of 861 patients therefore represents about 50% of the total incident cases of breast cancer.

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In 757 of the 861 cases, a histological preparation was sent to the co-ordinating centre of the international study and was confirmed by the central pathologist as cancer. For the remaining patients, a histological diagnosis of cancer was made by the individual hospital pathologist, but no preparation was available to the pathologist at the co-ordinating centre.

The controls

For each breast cancer patient interviewed, 3 controls were selected from patients in the same hospital. They were to be the 3 eligible patients in the beds closest to the breast cancer patients at the time of the interview. Eligibility required that they were resident of the study area, never having had a diagnosis of breast cancer and, if the breast cancer patient was 35 years of age or older, also being 35 years or older. If the breast cancer patient was under 35 years of age, the control patients were required to be within 2 years of that age. If 3 eligible controls could not be obtained, the case was closed with whatever number was available. A total of 2268 eligible controls was identified, and all but 18 were interviewed.

The interviews

The interviews were conducted by 7 paramedical college graduates and 1 physician. In nearly all instances the same interviewer interviewed a " set " of 1 case and the 3 corresponding controls. At the end of the interview, the interviewer rated the respondent as " reliable ", " doubtful " or " unreliable ". No case and only 1 control was rated as unreliable; 1 case and 12 controls were rated as doubtful. To conform with procedures in the other centres, the 1 " unreliable " patient was excluded but those rated " doubtful " were retained.

The interviewers recorded the beginning and ending times of each interview, and the durations were computed subsequently. The means and standard deviations of these durations were 14.2 minutes$\pm$7.8 minutes and 14.7 minutes$\pm$8.2 minutes in the cases and controls, respectively.

Analysis

Although, except with breast cancer patients under 35 years of age, the control patients were not age-matched in the process of selection, the over-all distributions of patients and controls by age were similar, the means and standard deviations for the 2 groups being 49.8 years$\pm$11.5 years and 51.2 years $\pm$11.9 years, respectively. Nevertheless, to compensate for fluctuations between age-groups in the ratio of cases to controls, the observed numbers of patients with specified characteristics have been compared with age-adjusted expected values derived from the control series. The expected values were computed by applying to the total number of cases in each 10-year age-group the probabilities observed in the control series in the same age-group and summing over all age-groups. All the expected values shown are adjusted for age in this way. Some of the expected values have been adjusted for both age and parity, using the same method, as indicated in the footnotes to the tables.

The relative risk associated with any specified characteristic is computed from the usual formula ad/bc, where a and b are observed and expected values, respectively, for women with the characteristic, and c and d are the corresponding values for women without the characteristic. The χ^2 tests for statistical significance are shown as summary χ^2 values with 1 degree of freedom as described by Mantel & Haenszel (1959) and Mantel (1963).

RESULTS

Residence

All but 15 of the patients and 27 of the controls were born in Japan. Table 1 shows a significant difference in the length of residence in the study area; women resident in Tokyo for 10 years or more had a breast cancer risk almost 50% higher than those resident for less than 10 years.

Socio-economic status

The measure of socio-economic status most clearly related to breast cancer risk was duration of schooling (Table 2). The breast cancer risk for patients with schooling of 12 years or more, relative to those with less than 8 years schooling, was 1.53. Classification of the husband's occupation according to the classification of the US Bureau of the Census revealed no difference between the observed and expected distributions, perhaps because of the unsuitability of this classification for the Japanese situation.

Duration of schooling and length of residence in Tokyo are correlated. However, the direction of the correlation is such as to reduce the correlation of each of the 2 variables with breast cancer, that is, patients with long residence in Tokyo tended to have a shorter duration of schooling than recent migrants. With respect to breast cancer risk, duration of schooling seems to be the more directly

TABLE 1

OBSERVED AND EXPECTED NUMBERS OF CASES, AND ESTIMATES OF RELATIVE RISK, BY DURATION OF RESIDENCE IN THE STUDY AREA

Duration of residence (years)[a]	No. of cases		Relative risk[b]
	Observed	Expected	
0–4	28	40.2	1.00
5–9	33	47.6	1.00
10–19	129	126.6	1.46
⩾20	656	631.5	1.49
Total	846	845.9	—

$\chi^2 = 6.0$, $P \simeq 0.015$

[a] The duration of residence was unknown for 3 cases and 10 controls.

[b] Relative to a risk of 1.00 for women resident for less than 5 years.

TABLE 2

OBSERVED AND EXPECTED NUMBER OF CASES BY DURATION OF SCHOOLING OF PATIENT AND HUSBAND

	Duration of schooling (years)[a]				Total
	<8	8-11	12-15	⩾16	
Patient:					
Observed	153	539	145	9	846
Expected	184.8	540.0	108.8	12.4	846.0
Husband:					
Observed	80	353	134	180	747
Expected	98.7	357.8	109.2	181.3	747.0

Patient's schooling: $\chi^2 = 56.6$, $P < 0.001$

Husband's schooling: $\chi^2 = 27.6$, $P < 0.001$

[a] Patient's schooling was not recorded for 3 patients and 3 controls. Numbers of ever-married women for whom husband's schooling was not recorded are 36 and 97, respectively.

relevant of the 2 variables. After adjustment for duration of schooling, the relative risk of 1.49 associated with residence of 10 years or more remained unchanged. The relative risk of 1.53 associated with schooling of 12 years or more was increased to 1.70 by adjustment for length of residence in Tokyo.

Marital status

Altogether, 66 of the patients had never been married, in comparison with the 45.6 expected on the basis of the control series. The relative risk for the single compared with the ever-married women is 1.49.

Reproductive history

The analysis of reproductive history was restricted to the 783 patients and 2131 controls who had ever been married.

The usual inverse relationship between parity (expressed as the number of full-term births) and breast cancer risk is shown in Table 3. Women

TABLE 3

OBSERVED AND EXPECTED NUMBERS OF CASES, AND ESTIMATES OF RELATIVE RISK, BY PARITY (FULL-TERM BIRTHS); EVER-MARRIED WOMEN ONLY

Parity[a]	No. of cases		Relative risk[b]
	Observed	Expected	
0	158	109.3	1.00
1	136	111.9	0.84
2	187	157.0	0.82
3	117	138.7	0.58
4	98	107.6	0.63
⩾5	87	158.6	0.38
Total	783	783.1	—

[a] Parity was unknown for 1 married control.

[b] Relative to a risk of 1.00 for non-parous, married women.

who had had 5 or more births had only 38% of the risk experienced by nulliparous women. Among the 1766 full-term children born to patients there were 77 stillbirths observed and 73.7 expected; the difference is not significant ($\chi^2 = 0.1$, $P \simeq 0.8$). Observed and expected distributions by the number of abortions reported are given in Table 4. There was a significant excess of cases reporting 1 or more abortions (relative risk 1.24) but there was no trend in risk according to the number of abortions reported.

In Table 5 the observed and expected distributions of cases with respect to age at first pregnancy are compared. The data suggest that the breast cancer risk for women first becoming pregnant under 20 years of age is only a little over one-quarter of

TABLE 4

OBSERVED AND EXPECTED NUMBERS OF CASES, BY NUMBER OF ABORTIONS REPORTED; EVER-MARRIED WOMEN ONLY

	No. of abortions reported					Total
	0	1	2	3	⩾4	
Observed	437	158	107	46	34	782
Expected [a]	478.2	155.4	73.2	43.7	31.4	781.9

$\chi^2 = 8.10$, $P \simeq 0.004$

[a] Expected values in this table are based on distributions specific for both age and parity.

that for women first pregnant when over 35 years of age. The comparisons are shown for individual parities because of the correlation of parity with age at first pregnancy. That the association of breast cancer risk with age at first pregnancy is not merely a consequence of the low parity of the breast cancer cases is shown by the consistent differences within each parity group, and by the difference between the total observed distribution and the expected distribution adjusted for both age and parity.

Lactation

Analysis of lactation was restricted to the 610 married patients and 1818 married controls who had had at least 1 liveborn child. The observed and expected distributions of cases were compared with respect to the four following measures of lactation experience:

(1) the number of women with liveborn children who never lactated;

(2) the number of liveborn children who were not breast fed;

(3) among children who were breast fed, the mean duration of lactation per child;

(4) the number of women who lactated for an extended length of time (shown in Tables 6 and 7 as more than 60 months).

TABLE 5

OBSERVED AND EXPECTED NUMBERS OF CASES, AND ESTIMATES OF RELATIVE RISK, BY PARITY AND AGE AT FIRST PREGNANCY; EVER-MARRIED PAROUS PATIENTS ONLY

Parity	Age at first pregnancy (years) [a]					Total
	<20	20–24	25–29	30–34	⩾35	
1: Observed	6	35	42	30	23	136
Expected	8.7	46.5	49.9	21.9	9.7	136.0
2: Observed	3	70	82	25	7	187
Expected	8.4	81.7	71.8	20.4	4.7	187.0
3: Observed	3	57	49	7	0	116
Expected	8.1	62.1	38.0	7.0	0.8	116.0
4: Observed	8	40	41	8	1	98
Expected	6.5	57.7	30.1	3.7	0.0	98.0
⩾5: Observed	5	60	20	1	0	87
Expected	14.1	53.5	16.4	1.5	0.4	85.9
All parities: [b]						
Observed	25	262	234	71	31	623
Expected	45.9	301.5	206.2	53.8	15.6	623.0
Relative risk [c]	1.0	1.6	2.1	2.4	3.6	—

$\chi^2 = 27.3$, $P < 0.001$

[a] Age at first pregnancy was unknown for 2 patients and 2 comparison patients.
[b] Adjusted for both age and parity.
[c] Relative to a risk of 1.0 for women with first births at age of 20 years or under.

TABLE 6

SELECTED LACTATION CHARACTERISTICS FOR MARRIED WOMEN WHO HAD AT LEAST 1 FULL-TERM PREGNANCY; BY AGE

Characteristic	Age (years)						All ages [a]	χ^2 [b]
	20–39	40–49	50–59	60–69	70–79	⩾80		
No. of cases with liveborn children	109	208	163	93	33	4	610	
No. who never lactated:								
Observed	15	14	5	0	2	0	36	
Expected	12.5	10.7	8.7	5.7	0.6	0.0	38.2	0.01
No. of liveborn children	201	517	506	306	146	14	1 690	
No. who were not breast fed:								
Observed	39	40	26	20	6	0	131	
Expected	32.9	33.8	31.7	18.0	3.3	0.8	120.6	0.86
No. of children breast fed	162	472	470	278	133	14	1 529 [c]	
Mean duration of lactation (months):								
Observed	8.8	13.4	15.9	19.4	16.8	24.0	15.2	
Expected	10.6	13.7	15.9	17.5	19.1	14.8	15.2	0.10
No. of cases who lactated	94	190	155	89	28	4	560 [d]	
No. who lactated for more than 60 months:								
Observed	2	29	46	33	16	1	127	
Expected	2.0	25.1	46.9	37.2	17.8	1.3	130.3	0.30

[a] The expected values are adjusted for both age at interview and parity.

[b] Summary χ^2 with 1 degree of freedom, based on observations for all ages. For P = 0.05, χ^2 = 3.84.

[c] Excludes 30 children known to have been breast fed, but for an unknown duration.

[d] Excludes 14 women who were known to have lactated, but for an unknown duration.

In view of the fact that Kamoi (1960) found no difference in the lactation experience of breast cancer patients and controls under the age of 40 years, but a significant difference over that age, these characteristics have been examined separately by age (Table 6). In view of the importance of parity as a determinant of lactation experience, the data are also given by parity (Table 7). The summary values for all age-groups and parities combined are adjusted to allow for differences between cases and controls with respect to both age and parity. In all of these summary comparisons, the observed values are very close to the expected. No statistically significant differences are seen, nor is there evidence of any consistent or substantial differences in any specific age- or parity-groups.

The tables show the numbers of women lactating for a total of more than 60 months—an arbitrary limit which identifies about one-fifth of the patients and controls with liveborn children. However, the over-all distributions for total months of lactation, with adjustments for age and parity, have also been compared. The observed and expected distributions were similar ($\chi^2 = 0.14$, $P \simeq 0.8$). Finally, taking a very unusual group of women, namely, those with total lactation experience of more than 120 months, the observed number of cases was 24 and the expected 23.0.

These findings suggest that lactation, even when very prolonged, is not associated with decreased breast cancer risk.

Menstrual history

The modal age at menarche reported both by patients and by controls was 14 years. However, there was a highly significant difference in the 2 distributions, that for the cases being shifted towards the younger ages (Table 8). The relative risks indicate that the breast cancer risk for women reporting menarche prior to the age of 13 years

TABLE 7

SELECTED LACTATION CHARACTERISTICS FOR MARRIED WOMEN WHO HAD AT LEAST 1 FULL-TERM PREGNANCY; BY PARITY

Characteristic	Parity					All parities [a]
	1	2	3	4	⩾5	
No. of cases with liveborn children	124	185	117	98	86	610
No. who never lactated:						
Observed	15	15	4	1	1	36
Expected	20.3	10.5	3.1	2.2	2.2	38.2
No. of liveborn children	124	361	337	372	496	1 690
No. who were not breast fed:						
Observed	15	44	31	12	29	131
Expected	19.5	34.7	16.3	23.1	27.0	120.6
No. of children breast fed	109	314	305	355	446	1 529 [b]
Mean duration of lactation per child (months):						
Observed	15.3	12.4	15.0	15.8	16.7	15.2
Expected	15.4	13.1	14.9	16.0	16.3	15.2
No. of cases who lactated	109	168	112	94	77	560 [c]
No. who lactated for more than 60 months:						
Observed	2	9	18	37	61	127
Expected	1.3	10.7	21.9	37.1	59.3	130.3

[a] The expected values are adjusted by both age and parity and are therefore identical to the values for " All ages " given in Table 6.

[b] Excludes 30 children known to have been breast fed, but for an unknown duration.

[c] Excludes 14 women who were known to have lactated, but for an unknown duration.

TABLE 8

OBSERVED AND EXPECTED NUMBERS OF CASES, AND ESTIMATES OF RELATIVE RISK, BY AGE AT MENARCHE

	Age at menarche [a]						Total
	<13	13	14	15	16	⩾17	
Observed	68	146	224	185	129	95	847
Expected	39.0	129.8	215.8	189.0	152.0	121.3	846.9
Relative risk [b]	2.2	1.4	1.3	1.3	1.1	1.0	—

$\chi^2 = 17.6$, $P < 0.001$

[a] Age at menarche was unknown for 2 patients and 9 comparison patients.

[b] Relative to a risk of 1.0 for women with menarche at 17 years of age or more.

was twice as high as that for those with menarche occurring after 16 years of age.

The great majority of patients reported that their menstrual periods were regular at intervals of 25–30 days (observed 674, expected 667.7) and there were no significant differences between observed and expected numbers reporting regular periods at longer or shorter intervals, or irregular periods.

In all, 34 patients (expected 42.5) reported having had a surgical menopause and 2 (expected 5.5) reported having had radiological menopause. In 10 of these 36 patients (expected 12.6), the artificial menopause was induced prior to the age of 40 years. Menopauses induced for the present disease, or within 2 years of the current hospitalization, are excluded from these numbers. The differences between observed and expected values are in the same direction as those from previous studies in which breast cancer patients have been found to have fewer artificial menopauses than controls have (Lilienfeld, 1956; MacMahon & Feinleib, 1960; Hirayama & Wynder, 1962), but the numbers in our study are too small to be interpreted as supporting the previous work.

Restricting attention to women aged 55 years or more who had a natural menopause, Table 9 gives the distribution by reported age at menopause. The relative risk for women reporting menopause at 50 years of age or over, relative to those reporting it prior to 50 years, was 1.40; the difference is on the border of statistical significance.

TABLE 9

OBSERVED AND EXPECTED NUMBER OF CASES BY AGE AT NATURAL MENOPAUSE [a]

Age at menopause (years)	No. of cases		Relative risk [b]
	Observed	Expected	
<40	6	6.5	1.0
40–44	31	37.7	
45–49	77	90.0	1.0
50–54	118	97.7	1.4
⩾55	10	10.2	1.2
Total	242	242.1	—

$x^2 = 3.84$, $P \simeq 0.05$

[a] The table is restricted to women 55 years of age or more who reported having had a natural menopause. It excludes 2 patients and 4 controls reported to be still menstruating at the age 55 years or more, and 1 patient and 4 controls for whom age at menopause was not recorded.

[b] Relative to a risk of 1.0 for women whose menopause occurred before the age of 45 years.

DISCUSSION

There have been two previous studies in Japan with which the results of this investigation may be compared. First, the Committee for Epidemiologic Study on Cancer (CESC) carried out an investigation throughout Japan during 1953–55 covering several cancer sites (Segi et al., 1957). Altogether, 45 university hospitals, 1 cancer hospital and 1 national general hospital were asked to complete a questionnaire concerning patients admitted during the study period. Among 32 000 cancer patients reported, there were 2197 females with cancer of the breast. For 644 of these patients, detailed epidemiological information was obtained by the individual hospitals. The controls were patients in local health centres, matched to the cancer patients by age and sex. With respect to cancer of the breast, the findings of this study were (1) a higher percentage of single women among the cancer cases, (2) a later mean age at first marriage among the patients than among the controls (21.9 and 20.8 years, respectively), (3) a higher age at first delivery among the patients (23.8 and 22.6 years, respectively), (4) a lower total parity for the patients, (5) significantly earlier mean age at menarche for the patients (14.7 years) than for the controls (15.1 years), (6) a higher rate of both spontaneous and artificial interruption of pregnancy among the patients and (7) a lower proportion of breast-fed children among the patients. Certain other observations were made for which no comparable data are available in the present study. Kamoi (1960) extended the analysis of these data with respect to the lactation issue specifically, adding additional cases and assembling a series of 811 patients and 1239 controls who had at least 1 live-born child. He found that there was no difference in the lactation experience of controls and women with breast cancer under the age of 40 years but that women in whom the disease developed after that age had significantly shorter lactation experiences than did controls of comparable age. He concluded that differences in the number of deliveries and in the duration of lactation may be a reason for the lower breast cancer rate in Japan than in Europe and North America.

The second study is that of Wynder, Bross & Hirayama (1960) based on 116 breast cancer patients

and 116 control patients from several hospitals in Tokyo. In this study, relative to the controls, the patients had more education, a higher proportion of single women, later marriage, later first pregnancy, more abortions and shorter and less frequent lactation. The mean durations of lactation per child were 17 and 24 months, respectively, in the patients and controls. There was no significant difference between patients and controls in the mean age at menarche, the values being 15.3 years and 15.4 years, respectively.

Certain discrepancies exist between the findings in these previous studies and those reported in the present paper. One is the fact that the study of Wynder, Bross & Hirayama (1960) revealed no difference between patients and controls in age at menarche. In view of the consistency of this finding in the two larger studies, namely, that of Segi et al. (1957) and the present study, we are inclined to attribute this discrepancy to the relatively small numbers in the Wynder, Bross & Hirayama series. Actually there is a small difference between cases and controls in the Wynder, Bross & Hirayama series—in the same direction as that in the other two—but it is small and not significant. The average age at menarche reported by the controls in Wynder, Bross & Hirayama series (15.4 years) is somewhat higher than that in either the CESC series (15.1 years) or the present data (14.9 years).

The other discrepancy is in the findings with respect to lactation experience. In this respect, the negative findings in the present study are at variance with the two previous reports. A possible explanation of this discrepancy is that the differences between patients and controls in socio-economic status were greater in previous studies than in the material of the present study. Duration of breast feeding is highly correlated with socio-economic status. For example, from the present data, among 420 control patients with less than 8 years of schooling, 39.6% lactated for more than 60 months; among 215 controls with 12 or more years of schooling only 7.8% fell into this category. That the difference between patients and controls in socio-economic status may be smaller in this than in previous studies may result from (1) the partial matching on this variable which occurred in the present study because controls were selected from the same hospitals and, in most instances, the same wards as the cancer patients, and (2) the possibility that in earlier studies controls were selected from lower socio-economic strata than those from which the cancer patients came. Wynder, Bross & Hirayama (1960) gave data on the duration of schooling of their patients. They stated "71% of the controls and 38% of the cancer patients attended grammar school; 25% and 60% respectively attended high school". These percentages would indicate a risk of breast cancer in high school graduates 4.5 times as high as that in grammar school graduates ($60 \times 71/38 \times 25$). Taking as "high school graduates" those with 12 or more years of education, the present data (Table 2) show much lower relative risks—namely, 1.3 relative to those with 8–11 years of schooling and 1.5 relative to those with less than 8 years of schooling. It is clear, therefore, that the socio-economic differences between patients and controls are much greater in the Wynder, Bross & Hirayama data than in the present series. Whether or not this is the correct explanation of the discrepancy between the present findings and those of others on the effect of lactation, support for our negative conclusion comes from other centres in this study, in several of which very prolonged lactation is also common (MacMahon et al., 1970).

On the other hand, there seems to be agreement between the three studies in Japan on the association of breast cancer risk with age at first pregnancy, although this association has not previously been shown to exist independently of parity. Neither has the extent of the risk associated with this variable been recognized previously. For example, the difference between the mean age at first delivery of the patients and controls in the CESC series (1.2 years), although statistically significant, does not convey the impression, seen in Table 5, that there is an almost 4-fold difference in breast cancer risk associated with the range of this variable. The CESC report includes a table from which relative risks comparable to those in Table 5 may be computed, although without adjustment for age or parity. These data are given in Table 10. The similarity of the trend to that seen in the present data is remarkable. The association of breast cancer risk with age at first pregnancy has been observed in other centres of this international study (Valaoras et al., 1969; Salber, Trichopoulos & MacMahon, 1969), and will be explored in greater detail in another publication, using the data from all centres.[1] Among the centres included in the international study, the trend was

[1] MacMahon, B., Cole, P., Lin, T. M., Lowe, C. R., Mirra, A. P., Ravnihar, B., Salber, E. J., Valaoras, V. G. & Yuasa, S., *Age at first birth and breast cancer risk* (in preparation).

TABLE 10
RELATIVE RISK BY AGE AT FIRST DELIVERY, ESTIMATED FROM THE DATA OF SEGI ET AL. (1957) AND THE PRESENT STUDY

Age at first delivery (years)	Segi et al.		Relative risk	
	No. of cases	No. of controls	Segi et al.	Present study
<20	58	32	1.0	1.0
20–24	226	995	1.3	1.6
25–29	108	322	1.9	2.1
30–34	25	55	2.5	2.4
⩾35	15	20	4.2	3.6
Total	432	1 713	—	—

most marked in Tokyo. The similarity of the Tokyo data and the previously reported CESC data in this respect suggests that it may indeed be true that the protective effect of early pregnancy is particularly strong in Japan.

It should be noted, however, that the association of breast cancer risk with age at first birth does not account for the low frequency of this disease in Japan. Thus, in the Boston component of this same international study (Salber, Trichopoulos & MacMahon, 1969), the distribution of controls by age at first pregnancy was quite similar to that in Tokyo. The modal age at first pregnancy was 22 years in Boston and 23 in Tokyo. The percentage of first pregnancies under 20 years of age was 11.4 in Boston and 7.4 in Tokyo. These differences are not such as to introduce appreciable differences in breast cancer risk between the centres, despite the strong relationship of breast cancer risk with age at first pregnancy, and, in any event, are in the wrong direction to explain a higher breast cancer rate in Boston than in Tokyo.

There is also agreement between all three studies to the effect that Japanese breast cancer patients report a history of abortions more frequently than do controls. There is agreement between our data and that of Wynder, Bross & Hirayama (1960) with respect to the high socio-economic status of breast cancer patients, and the lack of association with regularity and other characteristics of the menstrual cycle. These matters were not examined in the CESC study. Menopausal characteristics also were not examined in the CESC study, and no conclusions in this area were reached by Wynder, Bross & Hirayama (1960) because of the large proportion of their patients and controls who were still menstruating at the time of interview. The present findings on this question therefore cannot be compared with other Japanese data.

In regard both to the strength of the relationships noted and their consistency with experimental and clinical observations, the epidemiological characteristics noted above that seem likely to be of greatest significance are the relationships with age at menarche and age at first pregnancy. These two observations strengthen the growing evidence that early reproductive life is an important period in the genesis of human mammary cancer (Cole & MacMahon, 1969).

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RÉSUMÉ

ANTÉCÉDENTS, EN MATIÈRE DE LACTATION ET DE REPRODUCTION, DE PATIENTES ATTEINTES DE CANCER DU SEIN À TOKYO, JAPON

On a interrogé toutes les femmes admises dans 25 hôpitaux de Tokyo (Japon), avec le diagnostic (récemment posé) de cancer du sein, entre le 1er avril 1965 et le 31 mars 1967. L'entretien a surtout porté sur les antécédents relatifs à la lactation, la reproduction et la menstruation. Aux fins de comparaison, on a recueilli, pour chaque cas de cancer du sein, des données analogues auprès de trois malades hospitalisées dans le même établissement de soins pour d'autres raisons. Au total, l'enquête a porté sur 849 malades atteintes de cancer du sein et sur 2250 malades témoins.

Par rapport aux malades témoins, les malades souffrant de cancer du sein comptaient une plus forte proportion de femmes habitant Tokyo depuis plus de 10 ans, davantage de femmes ayant fréquenté un établissement d'enseignement pendant 12 ans et plus, et un plus grand nombre de célibataires. Elles signalaient un nombre relativement moins élevé de grossesses menées à terme, mais on dénombrait parmi elles davantage de femmes ayant eu une ou plusieurs fausses-couches. On a constaté une forte corrélation entre le risque de cancer du sein et l'âge de la femme au moment de la première grossesse, le risque auquel sont exposées les femmes qui ont eu leur premier enfant avant l'âge de 20 ans ne représentant que le quart environ du risque couru par les femmes enceintes pour la première fois après l'âge de 35 ans. Cette relation ne s'est pas démentie après qu'on ait opéré les corrections rendues nécessaires par le faible taux d'accouchement des femmes atteintes de cancer du sein.

On n'a relevé aucune différence notable entre les malades atteintes de cancer du sein et les malades témoins sous le rapport de la durée de la lactation, évaluée selon divers critères. Parmi les premières, 127 avaient allaité pendant une durée totale de 5 ans ou plus et 24 pendant 10 ans ou plus. En regard de ces valeurs observées, les valeurs escomptées, basées sur les taux relevés dans le groupe témoin, étaient respectivement de 130,3 et de 23,0.

Les renseignements recueillis au sujet de l'âge de la puberté ont fait ressortir des différences significatives entre les deux groupes de malades. Ils semblent indiquer que pour les femmes qui ont eu leur première menstruation avant l'âge de 13 ans le risque de cancer du sein est deux fois plus élevé que pour les femmes chez lesquelles la puberté est apparue après l'âge de 16 ans. Il y avait parmi les patientes atteintes de cancer du sein une plus forte proportion de femmes chez lesquelles la ménopause s'était installée après l'âge de 50 ans. Aucune différence n'a été constatée entre les deux groupes de malades en ce qui regarde la fréquence et la régularité des cycles menstruels.

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