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Breast Cancer Incidence and Month of Birth: Evidence Against an Etiologic Association

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Abstract—*To investigate the potential relationship between month of birth and breast cancer risk, the authors examined the month of birth of* 14,289 *women with breast cancer and* 38,151 *women with cancer of sites other than the breast. All cases were newly diagnosed between* 1974 *and* 1984, *and were identified through the Cancer Surveillance System, one of* 10 *population-based cancer registries comprising the Surveillance, Epidemiology and End Results Program of the National Cancer Institute in the United States. Although breast cancer cases exhibited spring and fall peaks in their month of birth (confirming a previous report), the month of birth of non-breast cancer cases followed a similar distribution. Such patterns have also been reported from populations in other parts of the United States, western Europe, Japan and Australia. These findings suggest that the seasonal variation observed in month of birth of women who develop breast cancer is a reflection of the pattern of births in the underlying population, rather than a new variant in breast cancer epidemiology.*

INTRODUCTION

SEASONAL changes have long been known to affect animal behavior and to produce physiological responses in biological systems. The migratory habits of geese and the hibernation practices of various species of bats, rodents, amphibians and bear are familiar and simple examples of seasonal effects on animal behavior. Reproductive activity in many species is clearly a function of season [1].

In humans, biorhythms are known to exert regulatory activity on endocrine function. For example, melatonin production in the pineal gland is suppressed by daylight [2]. Pineal activity, in turn, can affect pituitary [3], ovarian [4] and adrenal [5] functions. Furthermore, seasonal changes may affect one's probability of encountering specific types of environmental exposures, particularly those to infectious agents.

Recently, Vassilaros *et al.* [6] suggested the possibility that biorhythm-induced endocrine imbalances might be etiologically related to the development of hormone-related malignancies; most specifically, breast cancer in females. To examine this possibility, they analyzed the distribution of month of birth of 1,165 women with breast cancer between the ages of 21–98 who were recorded in two cancer registries in Athens between 1975 and 1982. They found that women with breast cancer were significantly more likely to have been born in the early spring or in September. The authors suggested that, if their findings were not the result of a systematic bias in the selection of patients, they could reflect either a seasonal variation in biological activity related to the development of breast cancer or the effects of maternal and/or fetal factors expressed during the time of conception and gestation. We undertook the present investigation in an attempt to replicate their findings using population-based incidence data from the United States.

MATERIALS AND METHODS

Cancer patients in the present analysis were identified through the Cancer Surveillance System (CSS) of the Fred Hutchinson Cancer Research Center in Seattle, one of 10 population-based cancer registries operated as part of the Surveillance, Epidemiology and End Results (SEER) Progam of the National Cancer Institute. The CSS identifies approximately 98% of all incident cases of cancer occurring among residents of a 13-county area in northwestern Washington State. Case identification is accomplished through regular medical record

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Table 1. *Frequency distribution of female patients with cancer according to their month of birth, diagnosed from* 1974 *to* 1984

	Breast Cancer				Cancers other than breast			
Month	Total number observed	Observed number per 30 days	% of total	Observed/ expected	Total number observed	Observed number per 30 days	% of total	Observed/ expected
January	1197	1158.4	8.22	0.99	3120	3019.4	8.03	0.96
February	1142	1212.7	8.61	1.03	3020	3207.1	8.53	1.02
March	1263	1222.3	8.68	1.04	3301	3194.5	8.49	1.02
April	1176	1176.0	8.35	1.00	3144	3144.0	8.36	1.00
May	1168	1130.3	8.02	0.96	3282	3176.1	8.45	1.01
June	1151	1151.0	8.17	0.98	3047	3047.0	8.10	0.97
July	1192	1153.5	8.19	0.98	3280	3174.2	8.44	1.01
August	1171	1133.2	8.04	0.97	3301	3194.5	8.49	1.02
September	1293	1293.0	9.18	1.10	3305	3305.0	8.79	1.05
October	1233	1193.2	8.47	1.02	3300	3193.5	8.49	1.02
November	1120	1120.0	7.95	0.95	2988	2988.0	7.95	0.95
December	1183	1144.8	8.13	0.98	3063	2964.2	7.88	0.95

$\chi^2_{11} = 22.91, 0.01 < P < 0.025; \chi^2_{11} = 38.23, P < 0.001.$

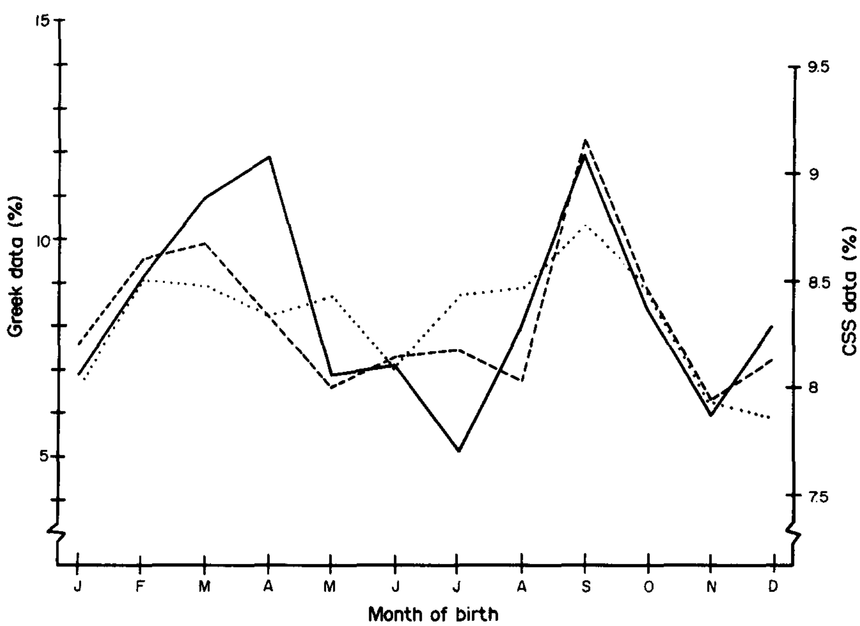

Fig. 1. *Frequency distributions of CSS female breast cancer patients, CSS female non-breast cancer patients and Greek female breast cancer patients by month of birth.* —— *Greek*; ----- *CSS female breast cancer*, ... *CSS female cancers other than breast.*

review in all 58 area hospitals, as well as routine surveillance of major pathology laboratories, private radiotherapy facilities and Washington State death certificates. Additional operational details of the SEER Program are published elsewhere [7].

We identified two groups of cancer patients for the present analysis: (1) females with breast cancer and (2) females with cancer of any site other than the breast. Eligible for inclusion were those women newly diagnosed with invasive cancer between 1 January 1974 and 31 December 1984 who were residents of the 13-county CSS reporting area at the time of diagnosis and were at least 20 years of age.

We utilized the statistical methods employed by Vassilaros *et al.* [6] to test the null hypothesis that the month of birth of cancer patients is distributed uniformly throughout the 12 months of the year. The observed number of cases each month (O_i) was computed with a correction made to a 30-day month. The expected number of cases each month (E_i) was simply the total number of observed cases during the entire time period divided by 12. In this context, an exact chi-square statistic with 11 degrees of freedom was calculated to test the null hypothesis. The test statistic was calculated as:

$$\chi^2 = \sum_{i=1}^{12} \frac{(O_i - E_i)^2}{E_i}.$$

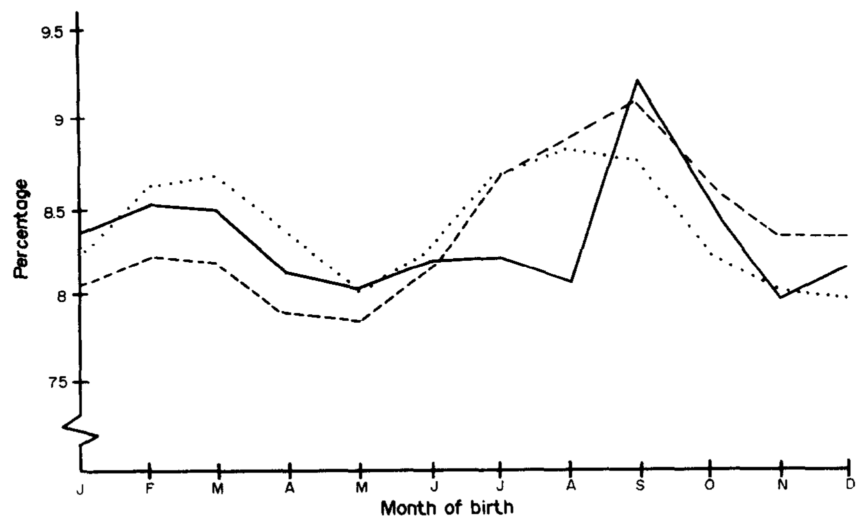

Fig. 2. Frequency distributions of births in the U.S. 1933–1939, *births in the U.S.* 1955–1963 *and CSS female breast cancer patients by months of birth.* —— *CSS female breast cancer;* ----- *U.S.* 1933–1939; ..... *U.S.* 1955–1963.

RESULTS

A total of 14,289 women with breast cancer and 38,151 women with cancer of sites other than the breast were identified. Table 1 shows the frequency distribution of these two groups according to their month of birth. Among women with breast cancer there is evidence of both a late winter/early spring peak and a September peak in monthly frequency of birth ($P < 0.05$). Women with cancer of sites other than the breast also tend to be born more frequently in the late winter/early spring and in September ($P < 0.001$). The similarity of the patterns of both breast and non-breast cancer occurrence in CSS women to the pattern of occurrence of breast cancer in Greek women is evident in Fig. 1.

To further explore this relationship, we stratified the breast cancer cases according to decade of birth. After examining each decade separately, we found that those patients born in each decade before 1930 demonstrated a spring and fall peak in month of birth. This pattern was significantly different from that expected assuming a uniform distribution of birth month ($P < 0.01$), and was quite similar to that seen among the Greek women with breast cancer without regard to decade of birth. In contrast, the month of birth distribution of breast cancer patients born in 1930 or later exhibited a fall peak but not a spring peak and, in fact, was not significantly different from a uniform monthly distribution ($P > 0.05$).

DISCUSSION

Our data confirm the results reported by Vassilaros *et al.* [6]. We found significant variation in the frequency distribution of month of birth of patients with breast cancer, with two peaks noted in early spring and September. This distribution was limited in our data to those patients born before 1930. These findings were observed among an unselected population-based group of incident cases of breast cancer diagnosed from 1974 to 1984 in the United States. Of primary concern in interpreting these results is whether they, indeed, reflect a biological characteristic of breast cancer, rather than simply a phenomenon that is not specific to this disease.

We found a similar pattern of month of birth among women diagnosed with other cancers from the same population base. This strongly argues against a relationship that is specific to breast cancer. In fact, several investigators have evaluated the frequency distribution of month of birth in various populations throughout the world. Such findings are particularly useful in placing the present results in proper perspective.

Based on national birth registration data collected by the National Center for Health Statistics, Rosenberg [8] examined the distribution of month of birth of babies born in the U.S. from 1933 to 1963. He found a pattern similar to that found for the CSS patients, with two peaks in early spring and fall (the highest point being in September). Figure 2, which is derived from Rosenberg's data, shows the month of birth of babies born in the U.S. during the periods 1933–1939 and 1955–1963. Spring and late summer/early fall peaks can be observed for both periods. The spring peak for the later born cohort is smaller than that for the earlier born one, which suggests that both the U.S. data and the CSS data are consistent with the hypothesis of a declining spring peak in month of birth for successive birth cohorts in the U.S.

Shimura *et al.* [9] have described the long-term variations of seasonal distribution of birth in Osaka City in Japan, the states of Massachusetts and

Missouri in the United States and Gorlitz City in East Germany. The births in Osaka exhibited a spring peak from 1871 to 1955, but no fall peak was observed. Data from the city of Gorlitz showed a spring and fall peak in births from 1675 to 1816. The United States data (from Massachusetts and Missouri) were remarkably similar to the CSS cancer data, with prominent spring and fall peaks occurring in births from 1881 to 1920. For 1931 and 1940, a much more uniform distribution of month of birth was observed.

Finally, Mathers and Harris [10] analyzed more than 2 million births from 1911 to 1940 and over 4 million births from 1962 to 1979 in Australia. These births represent more than 99% of the live births that occurred in Australia during these time periods. The data show two sharp peaks in the spring and fall for births from 1962 to 1979, and lesser peaks in the spring and fall for births from 1921 to 1940. No such pattern is seen in births from 1911 to 1920.

Collectively, these findings indicate that seasonal variation in month of birth is common. Of particular relevance is that seasonal patterns of birth similar to those seen among the CSS breast cancer cases have been observed in other population groups in the U.S., in Japan, in Western Europe and in Australia. It is interesting to note, however, that such seasonal variation in birth was not observed among Greek babies born during selected periods from 1921 to 1960 [6]. In this regard, the Greek breast cancer cases appear to exhibit different patterns of birth by season than the underlying Greek population as a whole, whereas the patterns observed within the CSS data appear consistent with existing evidence from the U.S. and other populations.

In conclusion, we find it difficult to accept the hypothesis that seasonal variation in month of birth is biologically related to the subsequent development of breast cancer in women. We propose instead that the seasonal fluctuations observed in month of birth among breast cancer patients in our data are simply representative of the seasonal fluctuations in the month of birth that naturally occur in the underlying population as a whole. There is little evidence to support the conclusion that seasonal variation in month of birth is a new variant in breast cancer epidemiology.

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REFERENCES

1. Villee CA, Walker WF, Smith FE. *General Zoology.* Philadelphia, Saunders, 1968, 715–717.
2. Carr DB, Axelrod L. The pineal gland, pineal dysfunction and cancer. *Rev Endocr Rel Cancer* 1981, **8**, 13–21.
3. Vaughan GM, Meyer GG, Reiter RJ. Evidence for a pineal–gonad relationship in the human. In: *Progress in Reproductive Biology: The Pineal and Reproduction,* 4. Reiter JJ, Hubinot PO, eds. Basel, Karger, 191–223.
4. MacPhee AA, Cole FE, Rice BF. The effect of melatonin on steroidogenesis by the human ovary *in vitro. J Clin Endocrinol Metab* 1981, **40**, 668–696.
5. Mori W. Melatonin in non-endocrinological pathology. In: *Advances in Biosciences* 29. Birau N, Schloot W, eds. Oxford, Pergamon Press, 329–355.
6. Vassilaros S, Tsiliakos S, Adamopoulos D *et al.* Seasonal variation in the frequency distribution of breast cancer in Greek women according to the month of their birth. *J Cancer Res Clin Oncol* 1985, **110**, 79–81.
7. Young JL, Percy CL, Asire AJ, eds. *Surveillance, Epidemiology, and End Results: Incidence and Mortality Data,* 1973–77. *Natl Cancer Inst Monogr* 57, 1981.
8. Rosenberg HM. *Seasonal Variation of Births—United States,* 1933–63. National Center for Health Statistics, 1986, PHS Publication No. 1000, Series 21, No. 9.
9. Shimura M, Richter J, Miura T. Geographical and secular changes in the seasonal distribution of birth. *Soc Sci Med* 1981, **15D**, 103–109.
10. Mathers CD, Harris RS. Seasonal distribution of births in Australia. *Int J Epidemiol* 1983, **12**, 326–331.