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The Incidence of Breast Cancer: Analysis of the Age Dependence

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Abstract. *The incidence of female breast cancer was studied as a function of age in 71 different populations throughout the world. Incidence data was normalized for differences in frequency of occurrence. Median normalized incidence increased exponentially from age 20 to 45. After age 45 the rate of incidence decreased, and we suggest that menopause may be responsible for the rate reduction.*

Populations were not randomly distributed about the total population median normalized incidence at the various age intervals. Populations were classified according to their age-incidence patterns in 3 groups: Group 1 (with median % incidence after age 69=50); Group 2 (with median % incidence after age 69=47), and Group 3 (with median % incidence after age 69=31). At most age intervals, the normalized incidence in Group 1 populations was less than the total median, while the normalized incidence in Group 3 populations was greater than the total median. Although we cannot exclude the possibility that the variation in age-incidence patterns among the population groups is an artifact of tumor registration errors, evidence suggests that such an artifact is unlikely. Breast cancer occurs more frequently in Group 1 populations than it does in Group 3 populations. We suggest that Group 3 populations may share an element of protection from, or that Group 1 populations may share an element of risk for, breast cancer.

The incidence of most human tumors increases continuously with advancing age of the host (1-9). We have found that when incidence data is normalized for differences in frequency of tumor occurrence, the vast majority of human tumors exhibit very similar age-incidence patterns which can be described by an equation of the form,

$$\log I = mt + b$$

where I = incidence of tumors, t = age, m is a small positive constant, and b is a small negative constant (7-9). We wished to compare the age-incidence pattern for female breast cancer among different populations. In order to avoid being distracted by differences among the populations in frequency of breast cancer occurrence, we normalized incidence data for variation in frequency of tumor occurrence. The normalized age-incidence patterns for female breast cancer are unusual. In addition, differences exist in the normalized age-incidence patterns among the populations studied. These differences permitted the populations to be divided into three groups according to the percentage of total breast cancer incidence which occurred in elderly relative to young and middle aged subjects.

Materials and Methods

Age-specific incidence rates (number of tumors per 100,000 females at each age interval per year) for malignant tumors of the female breast were obtained from a published report (10). All populations reporting more than 100 total cases of breast cancer were included in this study. These populations are listed in Table I. We normalized the age-specific incidence rates as described previously (7). For each population, the average annual incidence per 100,000 females at each age was summed over all ages to give total incidence. The percentage of this total incidence which occurred at each age was then calculated.

The significance of differences between medians was determined by the «median test» (11) as follows: 1) The common median for two groups combined was computed. 2) The number of observations in each group which existed above and below the common median was determined. 3) A 2×2 contingency table was prepared. 4) The chi-square test was performed with one degree of freedom.

Results

The percentage incidence which occurred at each age interval was calculated for each population studied. The median percentage incidence at each age interval for all populations studied is listed in Table II and displayed on a logarithmic incidence scale in Fig. 1. The difference between the data in Fig. 1 and the least squares straight line is insignificant ($P > .90$) between ages 20 and 45 according to the chi-square test. We conclude that between ages 20 and 45, the incidence of

Key Words: Breast cancer, age dependence.

TABLE I. *Populations grouped according to their age-incidence patterns for female breast cancer.*

Group 1 (median % incidence after age 69 = 50)	Group 2 (median % incidence after age 69 = 47)	Group 3 (median % incidence after age 69 = 31)
California: Alameda, White 1969-73	Brazil: Perñambuco, Recife 1968-71	Brazil: Sao Paulo 1969
California: San Francisco White 1969-73	California: Alameda, Black 1969-73	Columbia: Cali 1967-71
Canada: Alberta 1969-72	California: San Francisco Black 1969-73	England: Sheffield 1967-70
Canada: British Columbia 1969-72	Canada: Manitoba 1969-72	England: South-West 1966-70
Canada: Maritime Provinces 1969-72	Canada: Newfoundland 1969-72	Hawaii: Caucasian 1968-72
Connecticut 1968-72	Canada: Quebec 1969-72	Hawaii: Havaiian 1968-72
Cuba 1968-72	Canada: Saskatchewan 1969-72	Hawaii: Japanese 1968-72
Denmark 1963-67	England and Wales: Liverpool 1968-72	Hungary: Szabolcs-Szatmar 1969-71
England: Birmingham 1968-72	Federal Republic Germany Hamburg 1969-72	Hungary: Vas 1968-72
England: Oxford 1968-72	German Democratic Republic 1969-72	Israel: All Jews 1967-71
England: South Metropolitan 1963-66	Iceland 1964-72	Israel: Jews born in Africa or Asia 1967-71
England: South Metropolitan 1967-71	India: Bombay 1968-72	Israel: Jews born in Europe or America 1967-71
Federal Republic Germany, Saarland 1968-72	Malta, 1969-72	Israel: Jews born in Israel, 1967-71
Finland 1966-70	Michigan: Detroit, Black 1969-71	Jamaica: Kingston and St. Andrew 1967-72
Lowa 1969-71	New Zealand: Non-Maori, 1968-71	Japan: Miyagi 1968-71
Michigan: Detroit, White, 1969-71	Poland: Katowice 1970-72	Japan: Okayama, 1969
New York State (less N.Y. City), 1969-71	Poland: Warsaw City, 1968-72	Japan: Osaka 1970-71
New Zealand: Maori, 1968-72	Romania: Timis, 1970-72	New Mexico: Spanish, 1969-72
Norway, 1968-72	Scotland: Ayrshire 1970-72	New Mexico: White, 1969-72
Norway: Rural, 1968-72	Texas: El Paso, White 1968-70	Nigeria: Ibadan, 1960-69
Norway: Urban, 1968-72	Yugoslavia: Slovenia 1968-72	Poland: Cieszyn and Nowy, Sacz 1968-72
Sweden 1966-70		Poland: Cracow, 1968-72
Switzerland: Geneva, 1970-72		Poland: Warsaw Rural, 1968-72
Utah, 1966-70		Puerto Rico, 1968-72
		Singapore: Chinese, 1968-72
		Spain: Zaragoza, 1968-72

female breast cancer can be described by the least squares equation:

$$\log \% \text{ incidence} = 0.075 \text{ (age)} - 2.29.$$

After age 45, the data deviate from this equation (Fig. 1).

We wished to understand whether the distribution of populations about the total median percentage incidence at the various age intervals was random or ordered. If the distribution was random, the number of age intervals in which the percentage incidence exceeded the total median should equal the number of age intervals in which the percentage incidence was less than the total median in each population. We therefore graded each population according to the fraction of age intervals in which percentage incidence exceeded, equaled, or was less than the total median. Three groups of populations were recognized. Group 1 populations were less than the total median percentage incidence in most age intervals. In each group 1 population, the number of age intervals in which percentage incidence was less than the total median exceeded the number of age intervals in which percentage incidence was equal to or greater than the total median by a factor of at least 2.5. Group 3 populations exceeded the total median percentage incidence in most age intervals. In each group 3 population, the number of age intervals in which per-

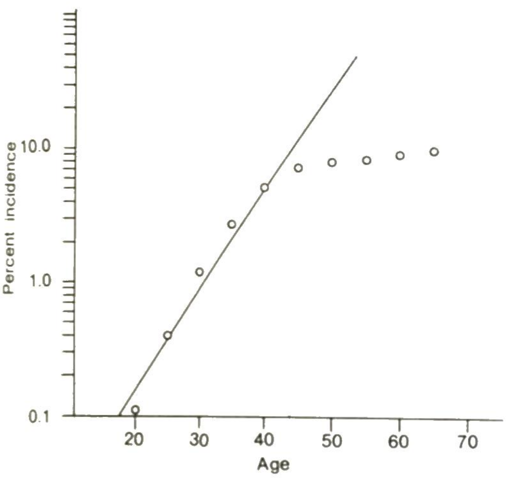

Fig. 1 *Median percentage incidence of female breast cancer among all populations studied as a function of age.*

TABLE II. *Median percentage incidence of breast cancer at various ages.*

Age	Population: Total	Group 1		Group 2		Group 3
20-24	0.1%	0.1%		0.1%		0.1%
25-29	0.4%	0.3%	$P<.02$	0.4%	$P>.05$	0.5%
30-34	1.2%	1.0%	$P<.01$	1.3%	$P<.01$	1.8%
35-39	2.8%	2.3%	$P<.01$	2.9%	$P<.01$	3.5%
40-44	5.2%	4.7%	$P<.01$	5.1%	$P<.01$	6.6%
45-49	7.4%	7.2%	$P>.05$	7.3%	$P<.01$	10.0%
50-54	8.3%	7.2%	$P<.01$	7.9%	$P<.01$	9.9%
55-59	8.7%	8.2%	$P>.05$	8.7%	$P<.01$	10.5%
60-64	9.7%	9.1%	$P>.05$	9.4%	$P<.01$	12.5%
65-69	10.2%	9.8%	$P<.01$	10.2%	$P<.01$	13.4%
70 +	46.7%	50.0%	$P<.02$	47.0%	$P<.01$	30.5%

P is the probability of same difference occurring by chance as determined by the «median test».

centage incidence was greater than the total median exceeded the number of age intervals in which percentage incidence was equal to or less than the total median by a factor of at least 3.0. Group 2 populations resembled a random distribution about the total median. In each group 2 population, the number of age intervals in which percentage incidence was greater than the total median exceeded the number of age intervals in which percentage incidence was equal to or less than the total median by no more than a factor of 2.0, and the number of age intervals in which percentage incidence was less than the total median exceeded the number of age intervals in which percentage incidence was equal to or greater than the total median by no more than a factor of 2.0. These population groups are described in Table I and identified in Fig. 2.

The median percentage incidence which occurred at each age interval was calculated within each group of populations. These within group medians are listed in Table II. Differences between group medians are significant at most age intervals. We conclude that the distribution of populations about the median percentage incidence is ordered at all age intervals.

In order to compare the quality of tumor registration in the three groups of populations, we calculated the average mortality/morbidity ratios (Table III) and the average percentage of cases confirmed histologically (Table IV) for the three population groups. The differences in average mortality/morbidity ratios for the three groups of populations are not significant (Table III). A smaller percentage of cases registered is confirmed histologically in elderly patients than in young and middle aged patients. This difference is greater in Group 3 than it is in Groups 1 and 2 (Table IV).

TABLE III. *Mortality/morbidity ratios: Female deaths from all tumours as a percentage of female tumors registered (from data in Table 6.7, pp 100-101 of reference 10).*

	Population: Group 1		Group 2		Group 3
Average for ages 25-69	41	$P>0.1$	43	$P>0.1$	47
			$P>.05$		
Average for ages >69	70	$P>0.1$	73	$P>0.1$	71
			$P>0.1$		
Difference	29	$P>0.1$	30	$P>0.1$	24
			$P>.05$		

P is the probability of same difference occurring by chance according to the t test.

TABLE IV. *Percentage of all female tumors confirmed histologically (from data in Table 6.2 pp 68-69 of reference 10).*

	Population: Group 1		Group 2		Group 3
Average for ages 25-69	91		82		78
Average for ages >69	74		61		49
Difference	17	$P>0.1$	21	$P<.05$	29
			$P<.001$		

P is the probability of same difference occurring by chance according to the t test.

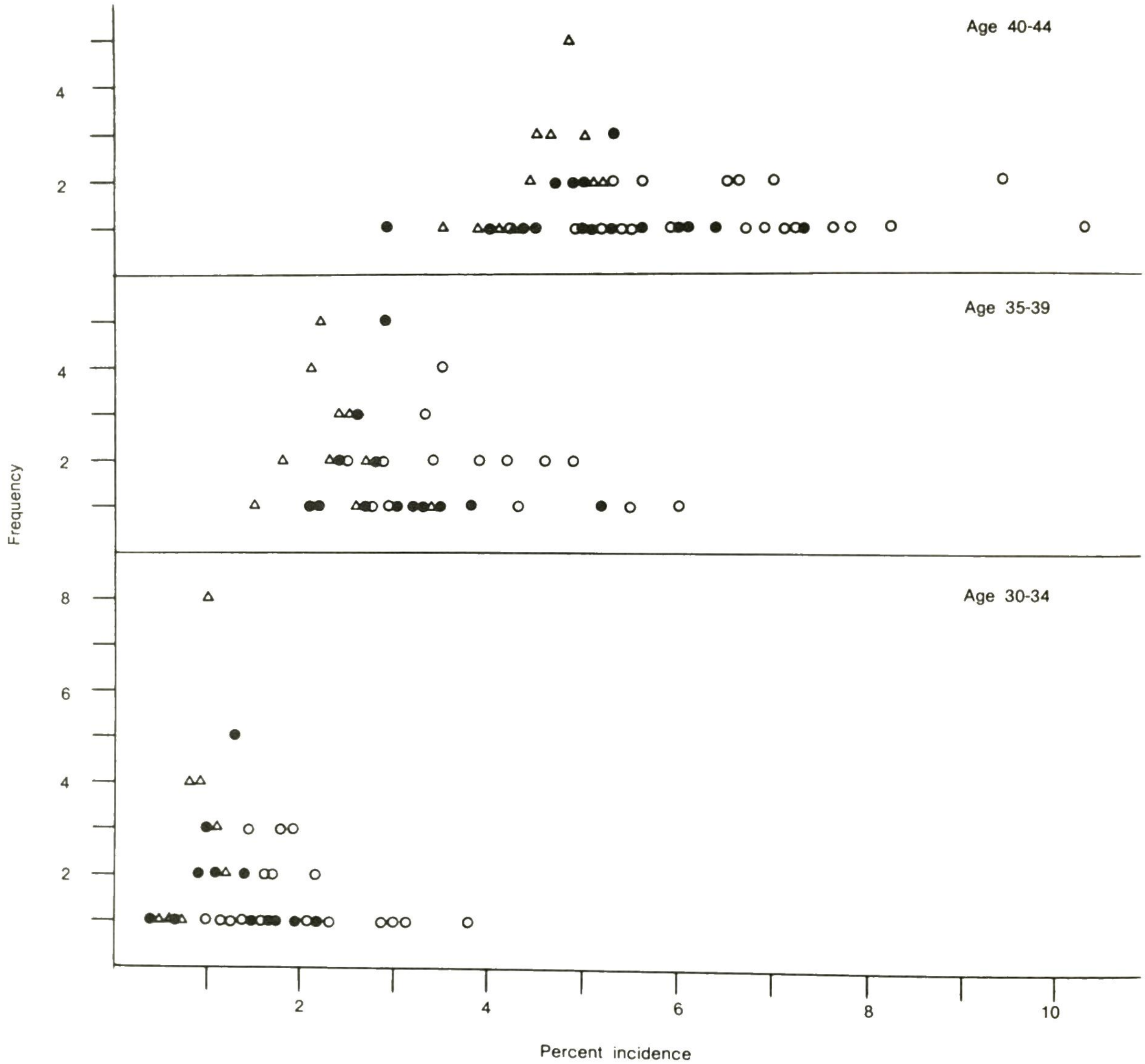

Fig. 2. *Frequency distribution of percentage incidence of female breast cancer for all populations studied at three different age intervals. Each population is identified by group: Group 1 (△) Group 2 (●), and Group 3 (○).*

The relationship between age-incidence pattern and frequency of tumor occurrence is described in Table V. Breast cancer is more common in Group 1 than it is in Groups 2 and 3.

Discussion

The results raise two questions: 1) Why does normalized incidence deviate from a simple exponential pattern after age 45? 2) Why are there differences in age-incidence patterns among the different groups of populations?

Most tumors obey a simple exponential age-incidence equation throughout life (7-9). For female breast cancer this equation applies only before age 45. The most outstanding change in female physiology which occurs near age 45 is menopause. We suggest that menopause may reduce the incidence rate of breast cancer (12).

The most obvious explanation for the variation in age-incidence patterns among the population groups is an artifact of registration. An impairment in registration of breast cancer in the elderly would artificially increase percentage incidence in young and middle

TABLE V. *Relationship between crude incidence rate for female breast cancer (average «all ages» rate from Table 7.1 of reference 10) and polulation group.*

Group 1		Group 2		Group 3
71.1	$P < .01$	51.1	$P > .05$	37.7
		$P < .001$		

P is the probability of same difference occurring by chance according to the t test.

aged subjects. The possibility of this artifact is important and cannot be ignored. However, two pieces of evidence argue against it. First, the insignificant differences among the three groups of populations in mortality/morbidity ratios (Table III) suggest no difference in completeness of registration for elderly relative to young and middle aged subjects among the three groups of populations. Second, the percentage of cases histologically confirmed (Table IV) suggests that incidence in elderly subjects is more likely to be overestimated in Group 3 than in Groups 1 and 2. Histological confirmation minimizes false incidence. The higher the percentage of cases confirmed histologically, the less likely that incidence is overestimated. A lower percentage of cases are confirmed histologically in elderly subjects than in young and middle aged subjects. Thus incidence in the elderly is more likely to be overestimated than incidence in the young and middle aged subjects. The difference in percentage histological confirmation between elderly and young-middle aged subjects is greater in Group 3 than it is in Groups 1 and 2 (Table IV). Thus incidence in the elderly is more likely to be overestimated in Group 3 than in Groups 1 and 2. An overestimation of incidence in the elderly would artificially decrease percentage incidence in the young and middle aged subjects. Since percentage incidence among young and middle aged subjects is greater in Group 3 than it is in Groups 1 and 2, we conclude that this effect is unlikely to be due to an artifact of registration.

The correlation between age-incidence pattern and frequency of breast cancer occurrence (Table V) suggests that the populations in Group 3 may share a common element of greater protection from, or that the populations in Group 1 may share a common element of greater risk for, breast cancer.

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