Some Epidemiologic Variables in Ovarian Carcinoma

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THE age-adjusted mortality rate from carcinoma of the ovary (primary) (175, International Classification of Diseases, 1955 revision) in the United States has increased from 3.1 to 7.6 per 100,000 population for the years 1930–67, partially because of improved diagnostic facilities and increased awareness of the disease (*1, 2*). The end results data of the National Cancer Institute show that the 5-year survival rate has increased from approximately 24 percent for 1940–49 to 30 percent for 1955–59 for all stages (*3, 4*). Thus, despite a slight increase in relative survival rates, ovarian cancer mortality continues to rise. This rise must mean that there is an increased incidence of ovarian carcinoma throughout the United States, perhaps indicating some genetic or environmental changes in the population at risk.

The increase of ovarian cancer among Japanese immigrants to the United States has been suggested by Wynder and co-workers (*2*) as indicative of the role the environment plays in general as a cause of ovarian cancer. Schenker and co-workers (*5*) have also shown that genetic or environmental influences play a role in ovarian cancer because among Israeli Jews, ovarian cancer was three times higher in women of European-American origin than in women of Asian-African origin.

Haenszel (*6*), however, in examining comparative data on national origin has found no evidence that suggests an environmental influence in the causation of ovarian cancer, implying that the distribution of the disease is influenced by physiological and hormonal aspects of the female reproductive cycle.

Several epidemiologic variables taken from appropriate California data relating to ovarian cancer incidence and mortality rates will be examined in this paper.

Materials and Methods

Appropriate data from the California Tumor Registry for the years 1942–69 were examined with the cooperation of the California Tumor Registry staff. The California Tumor Registry is maintained cooperatively by 58 California hospitals and the California State Department of Public Health. By combining the data of many hospitals, a larger and more representative series of cases was obtained. The registry has collected data on more than 390,000 cases of cancer, and about 20,000 are being added each year. Details on methodology are elaborated on in previous publications (*7–9*).

Data on incidence rates were based upon material generated by the Alameda County Cancer Registry, a unit of the California Tumor Registry (*8*). Data from the California Tumor Registry for the years 1942–56 were examined to compare county hospi-

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tals with private hospitals to obtain a relative index of socioeconomic differences among patients with ovarian cancer. To obtain a further index of socioeconomic status, California counties were ranked by an index developed by the California State Department of Public Health and then correlated with age-adjusted ovarian cancer mortality rates as derived from the recent study by the registry for the California Regional Medical Program (*9*).

In addition, the following countywide variables were examined in relation to ovarian cancer mortality; urban compared with rural residence, geographic distribution, percentage of county residents with Spanish surnames, percentage of families with preschool children under age 6, and the median population per household.

Results and Discussions

Histological confirmation. Ninety-eight percent of the cases termed "primary ovarian carcinoma" listed in the California and Alameda County registeries were histologically confirmed. The ovarian cancer referred to in this paper is primary rather than metastatic. Eighty-three percent of these tumors were epithelial in origin. Discrepancies in histological confirmation might have accounted for the increase of ovarian cancer among Japanese immigrants noted by Haenszel and Kurihara (*10*); only 54 percent of the cases were histologically confirmed in Japan in 1962 compared with 91 percent in the United States in 1962 as noted by Doll and co-workers (*11*). Increased histological confirmations, that is increased diagnostic factors, might have artificially accounted for the increase in recorded cases of ovarian cancer diagnosed in Japanese immigrants in the United States.

Age and race distribution. The distribution of ovarian cancer by age and race for Alameda County are shown in table 1.

Using California Tumor Registry prevalence data on ovarian cancer, the median age for women for all stages of disease was 56.7 years, and for localized cases, the median age was 52.9 years. These data compare with other prevalence data. For all stages of ovarian cancer, other authors noted patients' median ages of 52 (*2*), 48.5 (*12*), and 58.9 (*13*) years for primary epithelial tumors.

The average annual cancer incidence rates per 100,000 population for Alameda County for 1960–64 by race follow:

Race	*Rate*
Whites	13.9
Negroes	11.3
Chinese	[1]2.9
Japanese	—
Total	13.3

[1] Based on 5 or fewer cases.

SOURCE: Reference 8.

In the Alameda County incidence data (table 1), the deficiency of ovarian cancer cases among Negroes in the age group 55–64 years relative to whites and an excess of Negro patients relative to whites in the age group 65–74 years are noteworthy. This postmenopausal delay in ovarian cancer incidence in the Negro race certainly deserves further epidemiologic investigation. The delay may indicate differential Negro susceptibility or exposure to some factor or factors experienced by the white population, such as cyclical exposure to sunlight or susceptibility to viral disease.

Comparative mortality rates. It should be noted that histological confirmation is more than 80 percent for all countries compared in this paper, making dilutional effects because of diagnostic differences unlikely. The higher mortality rates for Denmark, Norway, and Sweden (table 2) where there is increased cyclical (seasonal) variation in sunlight, suggest an interesting avenue for further epidemiologic investigation. Because Finland has a somewhat lower mortality rate, dietary, social, economic, and occupational differences in addition to latitudinal effects require further investigation.

Wilson reported adenocarcinoma in 17 of 19 chickens after maintaining them constantly in a stressful environment with 12 hours of fluorescent lighting daily (*14*). Thus, the role stress plays

Table 1. Ovarian cancer average annual incidence rates by age and race, Alameda County, Calif., 1960–64

Age (years)	Whites	Negroes	Total (N=7,656 cases)
Under 15	...	...	...
15–24	1.7	4.4	2.0
25–34	5.8	4.7	5.1
35–44	9.4	3.9	8.6
45–54	32.6	31.3	31.7
55–64	40.9	9.2	36.9
65–74	44.9	61.9	45.5
75–84	59.3	26.2	57.2
85 and over	51.7	32.6	56.1

SOURCE: Alameda County Tumor Registry staff.

in causing ovarian cancer also might be investigated, as none of the control hens kept under normal conditions with seasonal variation developed ovarian tumors.

Socioeconomic factors. Data in table 3 show a definite lack of a relationship between socioeconomic class (as measured by differential county hospitalization compared with private hospitalization experiences) and ovarian cancer.

Standardized relative frequencies and their method of calculation are described in a California Tumor Registry publication (*7a*). As a further test, however, the 58 counties in California were ranked by quartiles according to a socioeconomic index developed by the California State Department of Health. A complex scaling of income criteria, education, and employment described in a previous publication was used (*15*), and there was a direct association ($P<0.05$, $r=+0.37$) with ovarian cancer mortality, age adjusted by county for 1960. The data failed, however, to show any significant geographic or urban-rural distribution of ovarian cancer cases by patients' residence in any of California's eight regional medical program regions or 58 counties ($P>0.10$). Thus, this study confirms those of Cohart (*16*), Wynder and co-workers (*2*), Graham and co-workers (*17*), and the Registrar General of Great Britain (*18*), indicating a direct relationship between higher socioeconomic ranking and ovarian cancer.

The survey of Dorn and Cutler (*19*) showed no socioeconomic differences for ovarian cancer. The standard cancer ratios for cancer of the ovary by socioeconomic class follow:

Socioeconomic class	*58 California counties (1960)*
I(highest)	110
II	107
III	98
IV(lowest)	87

SOURCE: Calculated from data in references 9 and 15.

Clustering and ovarian cancer. There was a positive association ($r = +0.13$ at $P=+0.06$) between the age-adjusted mortality rates for ovarian cancer in 58 California counties and the population per household of those counties. Thus crowding as one measure of stress was associated but not to a statistically significant degree with ovarian cancer mortality in this study.

Future studies comparing incidence data with the population per household are warranted, however, because mortality data becomes more limited in its epidemiologic application to ovarian cancer as the survival rates improve.

There was a surprising association ($r = +0.26$ at $P = 0.04$) between the age-adjusted mortality rate for ovarian cancer in 1960 and those counties with 25 percent or more families with children under age 6. If ovarian cancer is common in counties with more young children, hypothetically then the women who are at the age when they are susceptible to ovarian cancer will be exposed to more infectious childhood diseases.

In an attempt to determine some of the factors or intervening variables responsible for this isolated statistical association, studies based on replies to questionnaires are in progress. Wynder and co-workers (*2*) have shown that there were no differences in ovarian cancer incidence rates among married or single women,

Table 3. Standardized relative frequencies of cases of ovarian cancer by type of hospital, California, 1942–56

Type of hospital	Number
Observed:	
County	671
Private	2,038
Expected:	
County	724
Private	1,985
Standardized relative frequency:	
County	93
Private	103

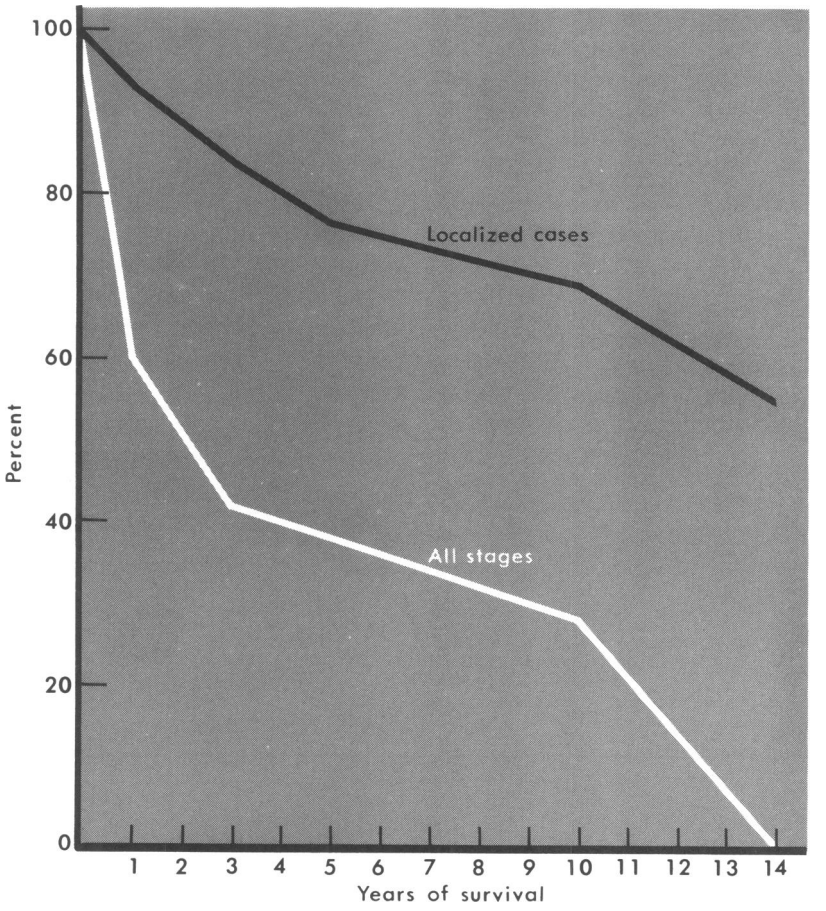
SOURCE: Reference 7.

Table 2. Comparative mortality and incidence rates for selected areas and countries for ovarian cancer (175, ICD)

Country or area	Age-adjusted mortality rates per 100,000 (1960–64 average)[1]	Age-adjusted incidence rates per 100,000 (1962)[2]
Denmark	11.0	13.1
Sweden	8.7	13.1
Finland	7.0	9.0
West Germany	..	17.6
Iceland	..	13.1
England and Wales	8.0	10.5
Norway	8.4	11.5
Yugoslavia	..	8.1
New Zealand	7.9	12.5
Hawaii (whites)	..	11.4
Connecticut (USA)	7.6	14.1
California (Alameda County)	8.2	13.5

[1] Reference 2 (Wynder after Segi, 1966).
[2] Reference 11.

Relative survival rates for ovarian cancer from time of first diagnosis, 1955–69



SOURCE: California Tumor Registry staff (1970)

and they noted in a survey of the literature that ovarian cancer was more common in single women and the nulliparous.

Thus, the discovery of an excess of ovarian cancer in counties where households had large numbers of preschool children per household suggests that exposure to childhood diseases might be related. West has suggested that having mumps may protect women against ovarian cancer (*20*). Certainly the susceptibility to ovarian cancer of women who have contact with children harboring viruses deserves further investigation.

Percentage with Spanish surnames. There was a direct association ($r = +0.24$) between California counties having 15 percent or more residents with Spanish surnames and the age-adjusted mortality rates for ovarian cancer for those counties. This association was statistically significant ($P = 0.05$). Newill (*21*) has shown that Jews and Protestants in New York City have a higher mortality from ovarian cancer than do Catholics. Thus, the possibility is remote that the difference noted is caused by an excessive number of Catholics among persons with Spanish surnames.

Unfortunately, there is no good way to get accurate data on religion by county in California. There are also no published rates in the literature for ovarian cancer incidence or mortality among Mexican-Americans, and the possibility exists that these persons may have a higher rate of ovarian cancer than the native-born white population, independent of their religious preference.

Survival data. Surgery was performed on 35 percent of the 7,656 women listed as having ovarian cancer in the California Tumor Registry for the period 1942–69. Thirty-one percent of these women had had adjuvant radiation, and 12 percent had had radiation only. The relative 5-year survivals for all stages of the disease and localized cases from 1955 to 1969 are shown in the accompanying chart. Fifty-eight percent had distant spread (metastases formation) at first diagnosis.

At first diagnosis only 26 percent of the ovarian cancers were localized and 14 percent of these showed regional spread to adjacent lymph nodes, which accounted for the poor survival rates. Nonetheless, the large number of women surviving with localized ovarian cancer contributed to the great difference between incidence and mortality rates in Alameda County (table 2).

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KRAIN, LAWRENCE STIRLING (University of California, Los Angeles Medical Center): *Some epidemiologic variables in ovarian carcinoma. HSMHA Health Reports, Vol. 87, January 1972, pp. 56–60.*

Appropriate data from the California and Alameda County Tumor Registries were analyzed with specific reference to ovarian cancer (175, International Classification of Diseases, 1955 revision). The deficiency of incident ovarian cancer cases in Negroes ages 55–64 years relative to whites and an excess of Negro patients with ovarian cancer relative to whites in the age group 65–74 years were noteworthy. Prevalence data from the California Tumor Registry revealed that the median age for women with ovarian cancer was 56.7 years for all stages.

There was a direct association of the age-adjusted death rate for ovarian cancer in California counties to certain population characteristics in the county, such as a high socioeconomic ranking ($r = +0.37$), a high percentage of children under age 6 in the family ($r = +0.26$), and a high percentage of residents with Spanish surnames ($r = +0.24$).

All associations were statistically significant ($P<0.05$). There was no statistically significant difference between ovarian cancer mortality and its geographic or urban-rural distribution in any of California's eight regional medical program regions or 58 counties ($P>0.10$). The large difference between incidence and mortality rates in Alameda County, Calif., is due to the 5-year relative survival rate of 36 percent for all stages of disease. Surgery was performed on 35 percent and surgery plus adjuvant radiation was used on 31 percent of the 7,656 women with ovarian cancer recorded in the California Tumor Registry from 1942–69.

Further areas that require investigation include the relationship between incidence data for ovarian cancer and the population per household and the relationship of exposure to childhood diseases to incidence of and mortality from ovarian cancer.