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Feature Articles

Cancer Registration and Incidence in Hawaii

Marc T. Goodman and Grant N. Stemmermann

INTRODUCTION

THE HAWAII Tumor Registry was established in 1960 by the Hawaii Medical Association, and developed as a collaborative effort between the Hawaii Medical Association, the Hawaii Department of Health and the local chapter of the American Cancer Society. In 1973, this registry provided the basis for a Hawaii component to the newly established Surveillance, Epidemiology, and End Results programme of the United States' National Cancer Institute [1].

The Hawaii Tumor Registry comprises a system of individual hospital tumour registries and a statewide central registry which participate in a programme to study cancer incidence and survival from neoplastic disease. Information concerning diagnostic procedures and findings, treatment, histology and staging is gathered to provide data on which to monitor trends and base patient management. Follow-up information is obtained annually. The registry uses a computer-linkage program adapted to the linguistic characteristics of the Asian and Polynesian groups that comprise the state's population. This facilitates checking for duplicate entries in the files.

Nearly all cancer epidemiology research and cancer control activities in Hawaii depend in a significant way on the database provided by the Hawaii Tumor Registry. The registry has several special features. It covers populations dispersed over a wide geographic area, encompassing several different islands in the Pacific Ocean. Yet, 75% of the cancer cases are registered by hospitals within a 3-mile radius of the central registry, leading to a close interaction of hospitals and central registry. Furthermore, because of the state's insular nature, the population is very much contained and outmigration rates are low, allowing for more efficient and complete follow-up.

The ethnic diversity of the population of approximately 1.1 million inhabitants covered by the registry creates a distinctive scientific resource. Only 24% of the population is white. Japanese comprise 23%, providing the largest concentration of Japanese in the Surveillance, Epidemiology, and End Results programme. Substantial numbers of Filipinos (11%) and Chinese (5%) are represented; growing numbers of Koreans (1%) and Samoans (1%) are present in the population; and the registry produces the only incidence and survival rates for Hawaiians (part-Hawaiians) (20%), a native American population. The mixed race group amounts to about 11% of the registry population. This ethnic diversity makes possible a variety of comparisons on incidence and survival that can contribute to the general understanding of cancer aetiology and responses to therapy.

With some exceptions, cancer rates in Hawaii are lower than rates for the mainland of the USA (Fig. 1), although the patterns of cancer incidence are similar. Lung cancer is the most common cancer among men, followed by cancers of the prostate and colon. Among women, cancers of the breast, colon and lung are the three most common sites.

Most descriptive and analytic epidemiology conducted in Hawaii has shown wide variation in the incidence and mortality for cancer and other diseases by ethnic group [2]. These data have been useful in generating hypotheses regarding cancer aetiology. In general, Asian-Americans experience lower rates than do whites and Hawaiians for many of the more common malignancies (Table 1). Dramatic shifts in the cancer rates among migrants in the parent country compared with those in the host country have shown that environmental factors, versus

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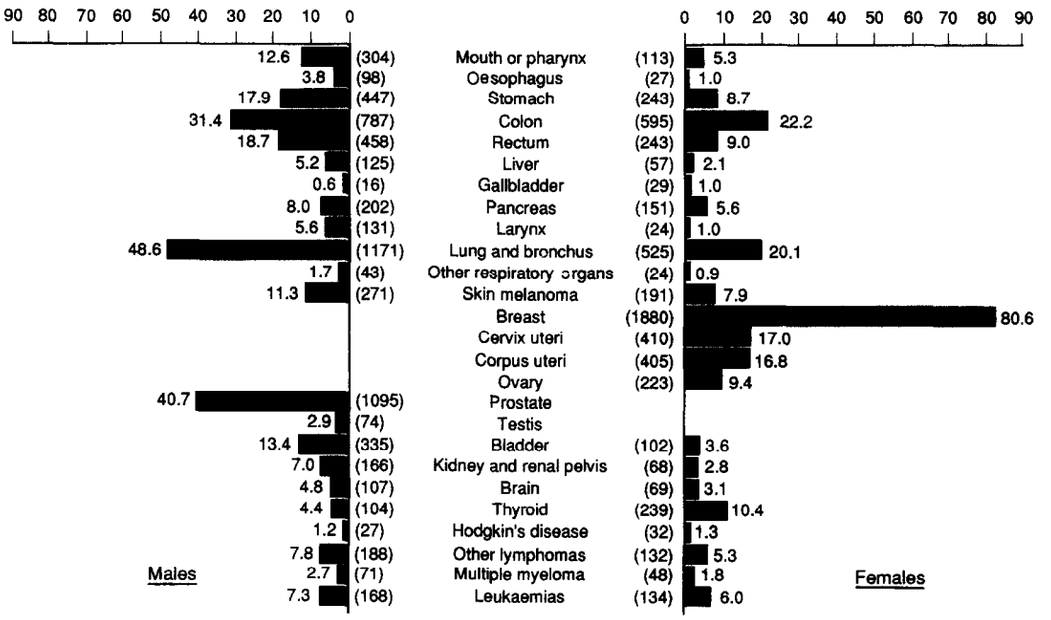

Fig. 1. Age-adjusted (world standard) incidence rates per 100 000 population for major cancer sites, Hawaii, 1983–1986. No. of registered cases is given in parentheses.

genetic background, are the main determinants of cancer incidence and, thus, must be largely responsible for ethnic differences in cancer rates [3–5].

GASTROINTESTINAL TRACT

Migrant data have provided some interesting clues to the aetiology of stomach cancer. US mainland whites have much lower rates of stomach cancer than whites migrating to or born in Hawaii, possibly because of the increased consumption of oriental foods [6] (Table 2). In turn, Japanese in Japan have much higher rates for stomach cancer than Japanese migrants to Hawaii [6]. Furthermore, the fact that Japanese migrants to Hawaii have a higher stomach cancer incidence than Japanese born in Hawaii suggests the importance of early-life exposures in the aetiology of this disease [6–8]. Second-generation migrants from Japan tend to acquire stomach cancer at rates approaching those of the USA. Registry follow-up data suggest that Hawaii–Japanese survival with stomach cancer is twice that of whites [9]. This can be attributed, only in part, to the larger percentage of Japanese patients with early stage lesions, since Japanese with stage 1 and stage 2 tumours show better survival than whites with similar stage cancers [10].

Besides the stomach, the colon is one of the few sites for which cancer rates are higher among Japanese men than white and US' black men (Table 1). The colon is also the only cancer site for which Hawaiians (of both genders) are at significantly lower risk compared with the other ethnic groups in Hawaii [2]. Japanese and Chinese men in Hawaii have higher rates of colorectal adenocarcinoma than do whites [11]. This contrasts with the observation of high colorectal cancer rates in countries which are predominantly white (Canada, USA, Denmark, New Zealand), and the low rates in Japan and among the Singapore Chinese [12]. The high rates among Hawaiian Orientals is mainly a result of the high incidence for cancer of the sigmoid colon, rectosigmoid and rectum. The age-adjusted rates for left-sided colon cancer have more than doubled among Hawaiian-Japanese men in the past 25 years [13], in contrast to stable rates among US whites and more modest increases in Japan itself [14] (Fig. 2).

Although breast and colorectal cancer incidence are highly correlated in most populations, Hawaiian women have a high rate for breast cancer, but a low rate for colorectal cancer (Table 1). Furthermore, compared with other ethnic groups in Hawaii, Hawaiian men and women had a higher proportion of their cancers located proximal to the sigmoid colon [11]. This finding is consistent with the observation that countries with a low risk of colon cancer have a low ratio of sigmoid colon to caecum-ascending colon.

Results of epidemiological and ecological studies of the role of fat and cholesterol in the aetiology of colon cancer are equivocal [13, 15, 16]. The dietary fat-colon cancer hypothesis is difficult to reconcile with the ethnic variation in incidence in Hawaii. Hawaiians who have a high-fat diet and Filipinos who consume a low-fat diet both have low rates for colon cancer (Table 1). Even though fat consumption is significantly different between first-generation and second-generation Japanese in Hawaii, their incidence for colon cancer are similar. Since most Japanese emigrated to Hawaii as adults, this observation would imply that changes in exposure to certain environmental factors in adulthood may have a major influence on the development of this cancer [17]. In contrast to Japanese, Filipino migrants to Hawaii do not experience an immediate increase in the rates for colon cancer, which is perhaps indicative of slower acculturation and adaptation to western lifestyle and diet [5].

LUNG CANCER

Hawaiians and blacks have the highest rates for lung cancer in the United States, followed by whites, Chinese, Filipinos, Japanese, New Mexico Hispanics, Puerto Ricans and American Indians [1]. Tobacco-smoking patterns are generally acknowledged to be closely related to risk patterns for lung cancer. However, although white men and women smoke more than Hawaiians (Table 3), Hawaiians have much higher rates for lung cancer [18]. Hawaiian and Japanese men have similar cigarette

Table 1. Age-adjusted (World Standard) incidence rates per 100 000 population by site and ethnicity, Hawaii, 1973–1986

Site or type of cancer	Ethnic group				
	Japanese	Chinese	Filipino	Hawaiian	White
Men					
All malignant neoplasms	240	212	214	297	363
Buccal cavity and pharynx	7	14	10	11	22
Oesophagus	4	3	5	11	3
Stomach	28	11	9	27	11
Colon	35	26	22	19	31
Rectum	21	16	20	15	16
Liver	5	8	7	8	3
Pancreas	8	8	7	8	9
Larynx	4	2	3	6	10
Lung and bronchus	37	34	32	83	67
Melanoma of skin	1	1	2	1	27
Prostate gland	33	29	34	35	59
Urinary bladder	10	11	6	7	25
Kidney and renal pelvis	6	4	4	6	10
Brain and CNS	3	3	4	3	8
Thyroid	5	8	8	6	3
Hodgkin's disease	1	1	2	1	3
Non-Hodgkin lymphomas	6	7	8	9	10
Leukaemias	7	8	8	9	9
Women					
All malignant neoplasms	205	230	206	313	360
Buccal cavity and pharynx	2	6	6	6	10
Oesophagus	1	1	2	2	2
Stomach	14	6	6	14	5
Colon	22	20	14	14	25
Rectum	9	9	8	7	11
Liver	2	3	3	3	1
Pancreas	5	7	4	7	7
Larynx	0	0	0	1	2
Lung and bronchus	10	18	18	39	32
Melanoma of skin	1	2	1	1	19
Breast	61	69	41	94	102
Cervix uteri	12	15	17	25	29
Corpus uteri	18	24	14	27	30
Ovary	8	8	9	11	12
Urinary bladder	3	2	4	5	6
Kidney and renal pelvis	2	2	2	3	4
Brain and CNS	2	3	1	4	4
Thyroid	6	8	23	12	7
Hodgkin's disease	0	2	1	1	2
Non-Hodgkin lymphomas	5	5	6	5	7
Leukaemias	5	6	7	6	7

use, yet Hawaiian men have an incidence of lung cancer that is twice that of the Japanese. Hawaiian, Filipino and white male smokers are at 121%, 53% and 46% greater risk for lung cancer than Japanese male smokers (L. Lemarchand, Personal Communication). These differences could have a genetic (e.g. aryl hydrocarbon hydroxylase activity, ability to activate procarcinogens in tobacco smoke) or environmental (e.g. dietary differences, passive smoking, exposure to cooking oil fumes, sex hormone differences) basis.

MELANOMA

The increased incidence of melanoma among whites in Hawaii supports the notion of a role for sunlight exposure in the aetiology of this disease [19, 20]. The much lower rates for this malignancy among the other major ethnic groups in Hawaii suggests that fair-skinned individuals are more susceptible to the effects of ultraviolet radiation.

BREAST CANCER

Ecological data have suggested that the large international variations in breast cancer occurrence are a result of differences in the level of consumption of animal fat or protein, or some other risk factor that is highly correlated with the consumption of animal products [21, 22]. On this basis, breast cancer incidence would be expected to be high among whites and Hawaiians whose diets are high in fats and animal protein, and correspond-

Table 2. Comparison of age-adjusted (World Standard) cancer incidence rates per 100 000 in Japan and Hawaii*

Site or type of cancer	Men					Women				
	JJ	HJ	HW	HJ:JJ	HJ:HW	JJ	HJ	HW	HJ:JJ	HJ:HN
Oesophagus	13.3	3.7	3.5	0.3	1.1	3.1	0.4	1.5	0.2	0.3
Stomach	79.6	28.4	11.8	0.4	2.4	36.0	14.1	6.0	0.4	2.4
Colon	9.8	34.1	28.1	3.5	1.2	9.4	22.0	21.2	2.3	1.0
Rectum	9.9	17.9	13.7	1.8	1.3	7.4	9.1	7.6	1.2	1.2
Liver	11.2	6.2	4.2	0.6	1.5	4.0	1.5	1.3	0.4	1.2
Lung and bronchus	29.6	36.0	66.2	1.2	0.5	8.7	10.3	32.7	1.2	0.3
Breast						22.0	50.1	84.4	2.3	0.6
Cervix uteri						10.0	6.4	8.1	0.6	0.8
Corpus uteri						2.8	15.5	23.4	5.5	0.7
Ovary						4.2	8.0	11.0	1.9	0.7
Testis	1.0	1.4	4.2	1.4	0.3					
Prostate	6.3	31.2	58.3	5.0	0.5					
Urinary bladder	6.4	9.6	24.9	1.5	0.4	1.9	3.8	6.0	2.0	0.6

* Age-adjusted to world population.
JJ = Japanese in Miyagi, Japan; HJ = Japanese in Hawaii; HW = whites in Hawaii. Source [12].

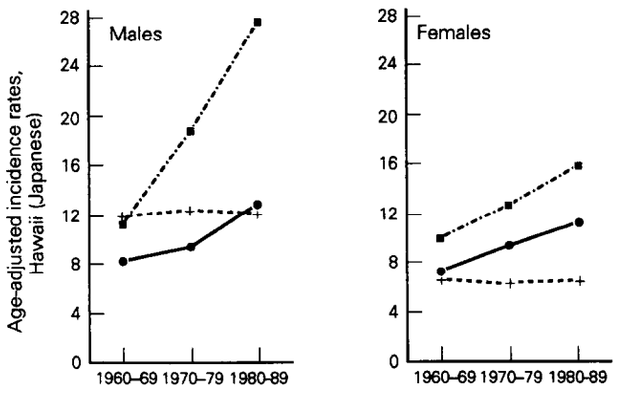

Fig. 2. Trends in cancer of the rectum and colonic subsites among Hawaii Japanese. ● = Right colon cancer (cecum, ascending, transverse); ■ = left colon cancer (descending, sigmoid); † = rectal cancer (rectosigmoid, rectum).

Table 3. Age-adjusted percentage of ever smokers by ethnic group and sex

	Men	Women
Japanese	52.8	26.1
Chinese	36.9	18.5
Filipino	48.0	28.5
Hawaiian	56.5	46.9
White	60.8	50.1

Reprinted from Kolonel [18], with permission from the author.

ingly lower for Chinese, Japanese and Filipinos whose consumption of calories from fat is more limited.

Studies have shown that the breast cancer rates for migrant Asian women shift from the rates prevailing in their country of origin toward the higher rates experienced in their host country [4, 24]. For example, women of Japanese ancestry in the USA have a 2–3 times higher risk of breast cancer than their counterparts in Japan, while the rate for Hawaii-Japanese women is almost one half that of Hawaii-white women (Table 2). This finding favours an environmental role in the aetiology of cancer of the breast. In view of the rapid increase in the incidence of breast cancer in first-generation migrants, early-life exposures to some carcinogens appear important [4, 23]. Differences in the proportions of *in situ* and invasive tumours among postmenopausal Japanese women compared with white women suggest a genetic influence on host response to induced breast cancer [24].

UROGENITAL TRACT

Asian-Americans in Hawaii have uniformly lower rates of bladder, kidney, cervix, endometrium, ovary and prostate cancer than do whites. Differences in the prevalence of tobacco smoking may explain part of the increased risk for cancers of the bladder, kidney, and perhaps cervix among whites. A greater proportion of white than Asian males and females have ever smoked (Table 3), and those who have smoked have tended to do so in greater amounts. Furthermore, white men report a higher consumption of coffee, a beverage that may be associated with an increased risk of bladder cancer, than men of other ethnic groups [2].

Prostate cancer incidence in Hawaii is highest among whites, followed by that of Hawaiians, Filipinos, Japanese and Chinese. Data from a large population-based cohort described by Kolonel *et al.* [25], showed that whites consume foods higher in fat and animal protein than do members of the other groups studied. Migrant data, comparing Japanese in Hawaii and Japanese in the Fukuoka prefecture in Japan, demonstrated a strong, positive correlation between dietary fat and protein intake and the incidence of prostate cancer [3]. A recent case-control study in Hawaii showed that, among men 70 years or older, consumption of saturated fat was positively associated with the risk for prostate cancer [26]. A prospective cohort study among Hawaii-Japanese men found no assocation of fat intake with the incidence for prostate cancer [27], although a positive association with lean body mass was reported [28].

The high rates for cervical cancer among Hawaiians and blacks in the USA may be a result of factors related to socioeconomic status, such as sexual practices, hygiene and access to

medical care [2]. It is noteworthy that Filipinos in Hawaii, who are also of low socioeconomic status, have lower rates of cervical and other cancers than Hawaiians. This may be attributable to other cultural (environmental) factors that are yet to be elucidated.

Similar to other reproductive cancers in women, ovarian cancer is more common in developed countries, with the notable exception of Japan [12]. The age-specific incidence rates in most countries suggest a bimodal peak in incidence with the first peak occurring sometime around the menopause [29]. There are little published data on ethnic variation in the incidence of ovarian cancer [30]. The highest rates occur among women in Europe and North America, while the rates in South America and Asia tend to be low [31]. Nathan *et al.* [32] observed that the rates for ovarian cancer are 2.5 times more common among Japanese in Hawaii than they are for Japanese in the Miyagi prefecture in Japan (Table 2). This appears to be due to an increase in the frequency of epithelial tumours in women of the menopausal and postmenopausal age groups. Germ cell tumours, which affect children and younger women, are less common in Hawaii than in Japan [32]. This trend is also evident for testicular tumours. However, the rates for ovarian cancer among Japanese and Chinese (and blacks) in the USA are still lower than those among US whites [1].

THYROID CANCER

There is modest international variation in the incidence of thyroid cancer, with certain exceptions like Hawaii, Iceland and Colombia [12]. Incidence rates for this malignancy in Hawaii are among the highest in the world [33]. Thyroid cancer accounted for 2.7% of all non-skin cancers in Hawaii between 1973 and 1977 compared with a national estimate of only 1.2% of all cancers for the USA [1]. Histological patterns of thyroid cancer appear to vary by ethnic group, with particularly high rates among Filipino women in Hawaii. Fukunaga and Yatani [34] examined the thyroid at autopsy by serial step sections of specimens from Canada, Japan, Poland, Colombia and Hawaii. They found that Japanese in Japan and Hawaii had significantly more occult papillary cancer than any other population. Spitz *et al.* [35] investigated ethnic patterns for thyroid cancer using SEER data for the period 1973–1981. The highest rates for papillary carcinoma were among Chinese, Japanese, Filipinos and Hawaiians of both sexes, with progressively lower rates for whites, hispanics and blacks. In general, populations with the highest incidence rates for thyroid cancer had the highest papillary-to-follicular ratio. A recent case-control study conducted in Hawaii supports the notion that a diet high in iodine increases the risk of thyroid cancer [36]. It has been suggested that high papillary-to-follicular ratios are found in areas with high iodine intake compared with areas with low iodine intake [37].

CONCLUSION

Descriptive studies in Hawaii have shown a tremendous ethnic diversity in cancer incidence and survival. This diversity is expressed not only in cancer rates, but also in culture and lifestyle, particularly dietary practices. Data from the Hawaii Tumor Registry have provided epidemiologists, clinicians, and laboratory scientists with a unique opportunity for aetiological and cancer control research. The objective of our crosscultural research has been to utilise effectively Hawaii's multiethnic population to identify factors of possible causal significance for cancer with the hope of using this information to reduce the cancer burden in our community.

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Genetics and Cancer*

W. K. Cavenee, B. Ponder and E. Solomon

INTRODUCTION

THE CURRENT issues of *Cancer Surveys* [1, 2] bring up to date our present knowledge on cancer and genetics.

The first issue of *Cancer Surveys* [3] was devoted to inherited susceptibility to cancer. In the years since then progress—and interest in the subject—has been enormous. It is interesting to reread the 1982 issue and see the major developments of the next few years already foreshadowed and particularly to note the title of the last paper in that volume, by Ray White: "DNA polymorphisms: New approaches to the genetics of cancer". The bar to progress in 1982 was that apart from a few candidates such as HLA, there were no real clues as to what the genes involved in cancer susceptibility might be; and the only way to make an empirical search for them by genetic linkage was frustrated by lack of linkage markers. Since then the use of DNA polymorphisms has allowed the rapid development of the human genome map; and it is no accident that the genetic loci for six of the inherited cancer syndromes were mapped for linkage in a single year (1987–1988) as the map reached a critical level of definition.

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*This is the second in our series of summaries from *Cancer Surveys*.

CANCER GENES

Exciting as these developments are they are only the very beginning. As several of the chapters in this volume show, moving from a genetic linkage for a cancer gene to the gene itself can be a slow and difficult business. Even when the gene itself has been identified—as in retinoblastoma, Wilms' tumour and neurofibromatosis type 1 (NF-1)—elucidation of the function of the normal gene and an explanation of the disease phenotype in terms of altered gene function remains a challenge. In NF-1, for example, it will be necessary to explain how the inherited inactivation of one copy of a gene which normally is apparently widely expressed and which probably is active as part of the *ras*-GTP signalling pathway can result in a huge range of possible phenotypic abnormalities in specific tissues, which range from a failure of development of a segment of one tibia (pseudoarthrosis) through melanocytic abnormalities (cafe au lait spots) to benign tumours of the optic nerve. The tools exist to provide a description of these genes at the level of the molecular biology of an individual cell: but how clearly this will point the way to an explanation in terms of the biology of a tissue or the whole organism is yet to be seen.

The predisposing genes that so far have been mapped are those for the so-called "inherited cancer syndromes" where the familial pattern of the disease is so clear-cut as to make genetic linkage easy. Numerically more important are the common cancers which tend to occur in familial clusters, such as breast, ovarian and colorectal cancers. An achievement of the past few years has been to set up large population-based studies of these cancers and to develop the statistical methods to analyse them.