Cancer Incidence in Thailand, 1988–19911

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Abstract

Results from three cancer registries (Chiang Mai, Khon Kaen, and Songkhla) in different regions of Thailand and from a cancer survey in the population of Bangkok during the years 1988–1991 are presented, together with an estimate of the incidence of cancer for the country as a whole. Overall, liver cancer is the most frequent malignancy, but there are large regional differences in incidence and in histological type, with very high rates of cholangiocarcinoma in the northeast (associated with endemic opisthorchiasis) but a more even distribution of hepatocellular carcinoma. Lung cancer is second in frequency, with the highest rates in northern Thailand, where the incidence in women (Age Standardized Rate, 37.4 per 100,000) is among the highest in the world. A link with tobacco smoking is suggested by similarly raised rates, especially in women, for cancers of the larynx and pancreas. Cervical cancer is the most common malignancy in women, with relatively little regional variation in risk, while the incidence of breast cancer is low. Other cancer sites showing moderately increased rates include the lip and oral cavity, particularly in females from the north and northeast, where the chewing of betel nut remains common among older generations, nasopharyngeal cancer, carcinoma of the esophagus in the southern region, and penile cancer, especially in the north and northeast. Previous studies which have investigated the etiological factors underlying these patterns are reviewed, and the implications for future research and for national cancer control policies are discussed.

Introduction

In Thailand, as in several other countries in Asia, rapid socioeconomic development and the control of noncommunicable disease have resulted in the emergence of cancer as the third most common cause of death after "heart disease" and accidents and poisoning (1). Although in the past some information on cancer patterns was available from hospital statistics, it was not until 1986 that the first population-based cancer registry was founded at Chiang Mai, in the northern region (2). This was followed in 1988 by the registry in Khon Kaen in the northeast (3), and in 1990 in Songkhla in the south. In 1991, it was decided that these three registries would produce a combined analysis of their results, including estimates for the country as a whole. Because there was no registry present in the densely populated central region, a population-based cancer survey was planned and carried out in Bangkok in 1992, with the objective of collecting data on residents of the metropolitan area diagnosed with cancer between 1988 and 1990.

This study is a summary of the full report on the project (4), which presents an overview of the cancer profile in the country as a whole, a comparison of regional differences, and a review of previous epidemiological studies. It thus provides a guide to future priorities for research into cancer cause and control.

Materials and Methods

Geography and Peoples

The Thai people almost certainly originated in southern China and migrated southwards to occupy what is now modern Thailand, Laos, and eastern Myanmar up to the 13th century AD. This population is culturally and religiously (almost entirely Buddhist) quite homogeneous, with regional differences but variations in the basic pattern. Subsequent migrations brought large numbers of Chinese. These were estimated to be 2.5 million in 1958, but migration virtually ceased in 1948; individuals of Chinese origin have taken Thai names and are now assimilated to varying degrees, making up about 10–14% of the population. Most Thais of Chinese origin live in central Thailand (especially Bangkok) or other urban centers. About 10% of the population is comprised of other ethnic groups, including some 500,000 hill tribe peoples of northern Thailand, most originating in southern China and migrating in the last 200 years, and the peoples of the southernmost seven provinces, who are of Malay origin and predominantly Muslim in religion.

Thailand is divided into 72 provinces grouped within 4 geographical regions: the northern, northeastern, southern, and central regions (Fig. 1). The northern region is mountainous with relatively cool winter temperatures and is the home of several minority tribes, some indigenous and others are more recent migrants. The northeast is a semi-arid plateau which, because it is the poorest part of the country, is attracting increasing industrial development. The population is culturally similar to that of neighboring Laos and speaks a distinct language (Isan) related to modern Lao. The central region is one of the most fertile rice-growing areas on earth and contains the densely populated Bangkok Metropolis (population, 5.8 million). The south is physically quite heterogeneous, with its long coastline and hilly interior given over to agriculture (fruit and rubber plantations), fishing, and tin mining.

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2 To whom requests for reprints should be addressed.
Sources of Cancer Data

Chiang Mai. A population-based registry was founded in 1986 in the University hospital. Data on cancer patients in this hospital and in 6 private and 29 community hospitals in the province of Chiang Mai (Fig. 1) are actively collected by the registry staff. Cases for the period 1988–1991 are included.

Khon Kaen. A population-based registration was started in 1987, with data collection from the registry of the University hospital, as well as from the regional hospital and other (27) public and private hospitals in the Khon Kaen province (Fig. 1). Cases for the period 1988–1991 are included.

Songkhla. This registry began operation in 1990, receiving data from the two hospital registries in the University city (Hat Yai), as well as one other major hospital in the provincial capital (Songkhla). Cases for the period 1989–1991 are included.

All three cancer registries use death certificates as an additional source of information on cancer cases, although there is some variation in the procedures for the follow-up of death certificate notifications. A certified cause of death is not very accurate in Thailand, with between 7 and 19% of certificates issued by nonmedical personnel. Cancer is clearly underenumerated, with many deaths recorded as "heart failure" or "old age." However, it is unlikely that there are many "false-positive" diagnoses; therefore, death certificates provide a useful check on probable cancer cases not identified during life.

Bangkok. Bangkok has no population-based registry. A cancer survey was carried out during 1991 to identify all cancer cases in the residents of Bangkok diagnosed in the 3-year period 1988 to 1990. Data were collected from all government and major private hospitals (with more than 100 beds) in the city and adjacent provinces. The three university hospitals and few medical center hospitals already had well-established hospital cancer registries. In the other government hospitals, data on cancer cases were collected via medical record departments (including in- and out-patients) and from the pathology departments. For private hospitals, most cases were identified from in-patient records. All death certificates for Bangkok residents who died during 1988–1990 and which mentioned cancer as a cause were compared with the file of registered cases, and unmatched deaths due to "cancer" were included as "death certificate only" cases, with no trace-back to the original source.

Population Denominators

The person-years at risk were calculated for the relevant periods in each registration area, based upon annual projections by age group and sex (5). The average annual populations of the four areas were: 1.33 million for Chiang Mai, 1.74 million for Khon Kaen, 1.17 million for Songkhla, and 5.78 million for Bangkok. Data from the 1990 census (6) were used in the estimation of incidence in the national population. The regional populations are: northern, 10.6 million; northeastern, 19.0 million; southern, 7.0 million; and central, 17.9 million.

Methods

Average annual incidence rates, per 100,000, were calculated with age standardization performed by the direct method using the "world standard population." ICD-O (7) was used by all centers to code cancer cases; this was converted to ICD-9 for reporting purposes.

The data quality in the different centers was evaluated by comparing the percentage of cases with histological verification of diagnosis and the percentage registered from information on the death certificate only (8).

To estimate cancer incidence in the national population in 1990, the average annual age- (5-year age group) and sex-specific incidence rates in the four registries (Chiang Mai, 1988–91; Khon Kaen, 1988–91; Songkhla, 1989–91; and Bangkok, 1988–90) were applied to the populations of the respective regions in 1990. The sum of these provides the estimated numbers of cancers by sex, site, and age group for the country as a whole, and the corresponding incidence rates are calculated using the 1990 census population.

Results

There were an estimated 29,950 new cancer cases in men and 29,517 in women in Thailand in 1990. Fig. 2 illustrates the percentage distribution of the 10 most common cancers in each sex. Tables 1 and 2 show, for males and females, respectively, the age-standardized incidence rates for the major cancers in each of the four registry areas and the estimate for Thailand as a whole. For comparison, age-standardized rates from the United States, Singapore, and Osaka (Japan) are also shown (8).
The proportion of cases registered with histological confirmation of diagnosis, or with no information other than that from the death certificate, is shown for the major cancer sites in Table 3.

Liver Cancer. The very high incidence of liver cancer in the northeastern region (which contains about 34.9% of the national population) results in this remaining the major cancer of men in the whole country, with an estimated 8000 new cases every year. Liver cancer is also the second most frequent cancer of women (12% of all cancers). Less than one-quarter of the liver cancer cases registered had been biopsied, but there were large regional differences in the histological type amongst those which had (Table 4). In Khon Kaen, 89% of liver cancers were cholangiocarcinomas, compared with only 2% in Songkhla in the south, where hepatocellular carcinoma predominates (96% of cases), as it does in Bangkok (71%). Although biopsy rates may not be identical for the different types of liver cancer, it is unlikely that cholangiocarcinomas are overrepresented in biopsy series, since diagnosis is relatively straightforward using ultrasound and needle biopsy is relatively hazardous.

Lung Cancer. Lung cancer is second in importance in males (15.6% of cancers) and fourth in women (8.8%). The incidence, in both sexes, is much higher in the north (Chiang Mai) than elsewhere in Thailand, and the incidence in females (ASR, 37.4/100,000) is very high, considerably above that in the United States, for example (Table 2). Fifty-one% of the lung cancers registered with a specified histology are adenocarcinomas (45% in males and 63% in females), with 33.7% squamous cell carcinomas (38% in males and 25% in females; Table 5). There was little geographical variation in this pattern.

Cervical and Breast Cancer. In women, the major cancer is cervical cancer (18.9% of cancers in women), almost twice as frequent overall as cancer of the breast (11.1%). Eighty-seven% of cervical cancer cases were squamous cell in type, with 11% adenocarcinomas; incidence rates were highest in Chiang Mai and lowest in Songkhla in the south. Breast cancer incidence is low, particularly so in the more rural northeast and south. Fig. 3 shows the age-specific rates for these two cancers. Cervical cancer incidence rises to a maximum in age group 55–59 and then declines, while for breast cancer, incidence rates increase until age 50–54, with almost no change with age thereafter.

Other cancer sites showing moderately increased rates include the lip (in Khon Kaen) and oral cavity, particularly in females, nasopharyngeal cancer, carcinoma of the esophagus in Songkhla, and cancer of the penis. Incidence rates for other cancers of the gastrointestinal tract (stomach, colon, rectum, and pancreas) are low, as are those for the kidney, bladder, and prostate.

Skin Cancer. Despite the fact that all of the registries recorded all diagnosed cases of skin cancer, the incidence rates are low. Of all skin cancer cases, 10.8% were melanomas, one-half of which were located on the lower limbs and one-quarter on the trunk. The distribution of nonmelanoma skin cancers by sex, histological type, and site is shown in Table 6. In men, squamous cell carcinomas are more common than basal cell; the reverse is true in women. In men, squamous cell carcinomas occur mainly on the lower limbs, while in women, the face is the most common site. Basal cell cancers are located mainly on

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Fig. 2. The ten leading cancers in Thailand, 1990, as a percentage of the total, by sex.
the face (63% in men, 82% in women), with 9.4% of cases on the trunk in men.

**Thyroid Cancer.** Thyroid cancer is three times more frequent in females than in males. In women, the highest incidence is observed in Khon Kaen, where the majority of tumors were follicular in type. The ratio of follicular to papillary carcinomas was 1.4, compared to an average of 0.46 elsewhere.

**Discussion**

There is quite a large difference in the incidence rates for cancer as a whole in the different registries. In particular, the overall incidence in Bangkok is low (ASR: 97.4 and 87.5 in men and women, respectively) compared with Chiang Mai (ASRs, 208.3 and 189.6) and Khon Kaen (ASRs, 196.9 and 154.4). In part, this reflects the quite different risks of different cancers with, for example, very high rates of liver cancer in Khon Kaen.

In consequence, it is likely that the data for incidence in Thailand are an underestimate of the true situation. The incidence rates for cancer at all sites (excluding skin; 149.6/100,000 for men and 125.2/100,000 for women) are about one-half those observed in Western countries but not very different from those elsewhere in the region. The estimated all-sites, age-standardized incidence rates (excluding other skin cancer) for southeastern Asia in 1985 are 122.1/100,000 in men and 137.7/100,000 in women (9).

The accuracy of the national estimates also depends upon how representative of their respective regions are the incidence patterns in the four registration areas. There are few data available with which to check this; however, the regional patterns from the national hospital registration scheme (10), which was estimated to cover 38% of hospital admissions in 1982, are broadly similar, although there are some exceptions. For example, lung cancer comprised only 9.2% of female hospital registrations in the northern region, compared to 18.6% of registrations in the Chiang Mai province (10).

**Cancer of the Oral Cavity.** Cancer of the oral cavity is common in Thailand with similar rates in the two sexes (in other parts of the world, males outnumber females by between two and ten to one). In the north (Chiang Mai) and northeast...
Nasopharyngeal Cancer. The incidence of nasopharyngeal cancer is intermediate between the very high rates observed in southern China and those of European populations. There is a strong genetic component to the risk of nasopharyngeal cancer (14), so that areas in which a significant proportion of the population has some Chinese ancestry, such as Thailand, might be expected to show an increase in risk (15). Consumption of salted fish is a well-known risk factor in Chinese populations (16). A case-control study by Srijamporn et al. (17) found that the consumption of sea-salted fish was a risk factor (OR, 2.5) in the population of northeast Thailand, as were agricultural occupations and wood-cutting (OR, 8.0).

Esophageal Cancer. The incidence of esophageal cancer is rather low in Thailand, except for Songkhla in the south, where rates in both sexes are moderately high (similar to Singapore Chinese). Chongsuvivatwong (18) found that tobacco smoking alone was not associated with a significantly elevated risk, but the risk for nonsmoking alcohol drinkers was 4.7 (nonsignificant because of small numbers). Subjects who both smoked and consumed alcohol were at a significantly higher risk (5.7) than smokers who abstained. Rubber-processing, an important local industry, did not appear to increase risk; in contrast, consumption of raw beans of Parkia speciosa ("Luk Rieng"), was found to be associated (OR, 8.0). Past consumption of two species of bean, Parkia timoriana and Parkia speciosa ("Luk Rieng"), was found to increase risk; in contrast, consumption of raw beans of Parkia speciosa ("Sataw") was found to be protective.

Gastrointestinal Cancers. The incidence of other gastrointestinal cancers, stomach and colorectal, is low in the Thai population. They have not been the subject of any epidemiological study at the time of this writing.
Cancer in Thailand

The incidence of liver cancer in Thailand is very high, and most of the marked regional variation is due to the very different risk of cholangiocarcinoma. This is normally a rather rare tumor comprising, for example, only 15% of liver cancers in the United States (22). High rates in Thailand have been convincingly linked to infestation with the liver fluke OV (23). The local habit of eating uncooked cypninoid fishes that are infected with OV is the source of the high prevalence in northeastern Thailand (24, 25); this dietary custom is sometimes practiced in the north but not at all in the south. The regional incidence of cholangiocarcinoma correlates well with the prevalence of OV infection (26), and there is a similar association at the local (district) level in the northeast (27). In a recent case-control study in subjects from northeastern Thailand, OV infection, as measured by an elevated titer of anti-OV antibodies, was strongly associated (OR, 5.0) with cholangiocarcinoma (28), and the percentage of cases attributable to opisthorchiasis was 72% in males and 62% in females. Various mechanisms have been proposed for the carcinogenic action of liver fluke infestation, including increased cellular proliferation in response to tissue damage, induction of nitric oxide synthetase by inflammatory cells, and increased activity of certain carcinogen-metabolizing cytochromes of the P450 group (23). Regular users of betel-nut (predominantly females) also had a high risk of cholangiocarcinoma (OR, 6.4; Ref. 28).

The incidence of hepatocellular carcinoma in Thailand is probably rather uniform between regions (29). A case-control study in residents in northeastern Thailand (30) has confirmed that chronic carriers of the hepatitis B surface antigen have a high relative risk (OR, 15.2). Hepatitis C infection appears to be rare (31).

In an early study, Shank et al. (32) found that estimated mortality rates from liver cancer in two areas were apparently related to exposure to aflatoxin-contaminated foodstuffs. However, although aflatoxin has been detected in a variety of market foods in Thailand (33-35), direct measurement of aflatoxin-albumin adducts in sera from human subjects suggests that intake is relatively low (36). This is consistent with the low prevalence of G to T mutations at codon 249 of the p53 gene in sera from Thai patients with hepatocellular carcinoma (37).

Pancreatic Cancer. The incidence of pancreatic cancer in Thailand is low, but there is a 3- to 5-fold variation in incidence by geographical region, with the highest rates noted in Chiang Mai. This may relate to the greater prevalence of smoking in the north; certainly, the incidence of both larynx cancer and lung cancer is also high in Chiang Mai, and the sex ratios (M:F) for all three cancers are strikingly low [1.0 (pancreas), 3.0 (larynx), and 1.3 (lung)] in comparison to the other centers and the comparison populations in Tables 2 and 3.

The high incidence of lung cancer in women in northern Thailand recalls the high rates found in Chinese females, in whom a high proportion of tumors are adenocarcinomas which,

Table 4 Distribution by center and histological type: liver cancer. Number of cases and percentage of known histological type

<table>
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<tr>
<th></th>
<th>Bangkok</th>
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<th></th>
<th></th>
<th>Chiang Mai</th>
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<th></th>
<th></th>
<th></th>
<th>Khon Kaen</th>
<th></th>
<th></th>
<th></th>
<th>Songkhla</th>
<th></th>
<th></th>
<th>Total</th>
<th></th>
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<tbody>
<tr>
<td>Hepatocellular carcinoma (8170)</td>
<td>259</td>
<td>70.8</td>
<td>135</td>
<td>47.9</td>
<td>23</td>
<td>7.6</td>
<td>47</td>
<td>95.9</td>
<td>464</td>
<td>46.5</td>
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<td>Cholangiocarcinoma (8140, 8141, 8160, 8161, and 8550)</td>
<td>86</td>
<td>23.5</td>
<td>128</td>
<td>45.4</td>
<td>268</td>
<td>89.0</td>
<td>1</td>
<td>2.0</td>
<td>483</td>
<td>48.4</td>
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<td></td>
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<tr>
<td>Other</td>
<td>21</td>
<td>5.7</td>
<td>19</td>
<td>6.7</td>
<td>10</td>
<td>3.3</td>
<td>1</td>
<td>2.0</td>
<td>51</td>
<td>5.1</td>
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<tr>
<td>Not specified (8000, 8001, 8002, 8003, 8004, and 9990)</td>
<td>362</td>
<td>480</td>
<td>2390</td>
<td>84</td>
<td>2341</td>
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<tr>
<td>Total</td>
<td>728</td>
<td>762</td>
<td>2691</td>
<td>133</td>
<td>4314</td>
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<td></td>
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</table>

Table 5 Distribution by histological type and sex: lung cancer

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th></th>
<th>Female</th>
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<tbody>
<tr>
<td>Squamous cell carcinoma (8070-8076)</td>
<td>453</td>
<td>19.4</td>
<td>38.1</td>
<td>147</td>
</tr>
<tr>
<td>Small cell carcinoma (8041-8043)</td>
<td>118</td>
<td>5.0</td>
<td>9.9</td>
<td>37</td>
</tr>
<tr>
<td>Adenocarcinoma (8250-8251, 8140-8231, 8260-8550, and 8570-8571)</td>
<td>535</td>
<td>22.9</td>
<td>45.0</td>
<td>372</td>
</tr>
<tr>
<td>Adenosquamous carcinoma (8560)</td>
<td>5</td>
<td>0.2</td>
<td>0.4</td>
<td>6</td>
</tr>
<tr>
<td>Other</td>
<td>78</td>
<td>3.3</td>
<td>6.6</td>
<td>32</td>
</tr>
<tr>
<td>Not specified (8000-8011, 8020-8022, and 9990)</td>
<td>1152</td>
<td>49.2</td>
<td>641</td>
<td>51.9</td>
</tr>
<tr>
<td>Total</td>
<td>2341</td>
<td>1235</td>
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</table>

*Percentage of those among the known histological cases only.

Fig. 3. Age-specific incidence rates per 100,000: cancers of the cervix uteri, and breast.
although associated with tobacco smoking, generally have lower relative risks than squamous and small cell cancers (38, 39). In a case-control study in Chiang Mai (12), smoking of cigarettes and “Khiyo” (long, indigenous cigars) was associated with nonsignificant elevated risks in both sexes, while chewing and smoking of miang (fermented wild tea leaves) was associated with an age-specific pattern typical of developing countries (15-49) ratio. This ratio is lowest in Bangkok (187.6), followed by Chiang Mai (386.0), Khon Kaen (476.8), and Songkhla (599.9), a ranking paralleling the incidence of breast cancer (except for Bangkok, where the low risk may be a consequence of previously high levels of fertility (early age at first pregnancy and multiple births) and low caloric intake (late menarche and low body mass). However, patterns of fertility and nutrition are changing fast in Thailand and have affected the regions of Thailand to different degrees, as shown by the child (0–4) per 1000 women (15–49) ratio. This ratio is lowest in Bangkok (187.6), followed by Chiang Mai (386.0), Khon Kaen (476.8), and Songkhla (599.9), a ranking paralleling the incidence of breast cancer (except for Bangkok, where the low ratio is a result of many young female immigrants, and the incidence of breast cancer is an underestimate).

**Cervical Cancer.** The high incidence of cervical cancer in Thailand (estimated national age-standardized incidence is 23.4/100,000) is quite typical of other developing countries in southern and southeastern Asia. In a case-control study in Bangkok, Wangsuphachart et al. (44) found trends of increasing risk with young age at first intercourse and number of sexual partners, although these were not statistically significant. However, very few women reported having more than one sexual partner (only 8% of controls). High parity has also been found to be an independent risk factor for cervical cancer in some high-fertility populations (45); this would be important in Thailand, where past fertility of older women is high, particularly in the more economically deprived areas such as the northeast. In the Bangkok study (44), women with high parity were at higher risk than nulliparous women, but there was no significant trend with increasing number of children. In other parts of the world where cervical cancer is frequent and where men have many sexual partners but women do not, as in Latin America (46), the effect of the sexual behavior of partners in disease risk has been demonstrated. This may be particularly relevant in Thailand.

**Penile Cancer.** A high frequency of penile cancer was noted in an earlier series based on histopathology data in Bangkok (1951–1956; Ref. 47), 6.3% of cancers in men, and in Chiang Mai (1966–1975; Ref. 48), 6.5% of cancers in men. Frequencies in the population-based data reported here are lower (2.9% in Songkhla and 1.6% in Chiang Mai), and this may correspond to a true decline in incidence. A similar dramatic decline in frequency has been reported for another population with pre-
Cancer in Thailand

Cancer in Thailand is already a major health problem in Thailand. Liver cancer is the most important neoplasm at present, and vaccination against hepatitis B virus and control of the liver fluke infestation by therapy and education to discourage the habit of eating raw fish are clearly priority areas. Tobacco-related cancers, which are already of importance (particularly in the north), are also an obvious target for prevention, and the reason for the high rates among females in this region is a priority area for research. Many of the cancers associated with Western life-styles (breast, colon, and rectum) are rare at present, but with the rapid changes occurring in the Thai population, they are likely to emerge as significant problems in the future.

Acknowledgments

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