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CANCER IN CIRCUMPOLAR INUIT 1969–1988

A summary

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The results of an international, collaborative study of cancer in Circumpolar Inuit in Greenland, Canada, Alaska and Russia are summarized. A total of 3 255 incident cancers were diagnosed from 1969 to 1988 among 85 000–110 000 individuals. Indirect standardization (SIR) based on comparison populations in Connecticut (USA), Canada and Denmark showed excess risk of cancer of the lung, nasopharynx, salivary glands, gallbladder and extrahepatic bile ducts in both sexes, of liver and stomach cancer in men, and renal and cervical cancer in women. Low risk was observed for cancer of the bladder, breast, endometrium and prostate, and for non-Hodgkin lymphoma, Hodgkin's disease, leukaemia, multiple myeloma and melanoma. Age-standardized incidence rates (ASRs) of cancer of lung, cervix, nasopharynx and salivary glands among Inuit were among the world's highest as were rates in women of oesophageal and renal cancer. Regional differences in ASRs within the Circumpolar area were observed for cancer of the cervix, lung, colon and rectum, liver, gallbladder and breast. The differences in the Inuit cancer incidence pattern to some extent reflect known variations in lifestyle, diet and other exposures, as well as implementation of cancer control measures. Future research addressing possible individual differences are needed to evaluate environmental and genetic factors in etiology and evaluate intervention studies.

The present paper summarizes the results of an international, collaborative study analysing 20 years of cancer incidence data in Circumpolar Inuit living in Arctic regions of Greenland, Canada, Alaska and Russia. Publications from this study appearing earlier in this volume have dealt with risk factors in the various Inuit population groups (1–4), the definitions, methods and data sources used in the study (5) and site-specific results for cancers of the buccal cavity and pharynx (6), digestive system (7), respiratory system (8), breast (9), female genital tract (10), male genital tract (11), urinary system (12), lymphatic and haematopoietic system (13) and skin, bone, connective tissues, brain, eye, thyroid and other specified and unspecified sites (14).

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Statistical summary

A total of 3 255 incident cancers were diagnosed among 85 000–110 000 Circumpolar Inuit during the 20 years 1969–1988; of these 1 413 (43.4%) were reported from Greenland, 1 141 (35.1%) from Alaska, 661 (20.3%) from Canada (Table 1), and 40 (1.2%) from Russia (1). These data exclude non-melanoma skin cancers which were incompletely reported from some regions. Further, the cases reported from Russian Siberia (Chukotka) (1) have been excluded from most incidence calculations since the age distribution of that small population is unknown during the study period. Overall, 85% of cancers were microscopically verified while 5% were based on death certificates only (Table 2).

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Table 1

Cancer in Circumpolar Inuit 1969–1988 by site (ICD 9). Total number of cases, crude-, age standardized (ASR world)-and cumulative (Cum 64) incidence rates by sex, region and 5-year time period. Standardized incidence ratios (SIR) and 95% confidence interval (95% CI) compared with Connecticut, Denmark and Canada

All sites excl. other skin			Total No.	Crude rate	ASR world	Cum 64	Connecticut		Denmark		Canada	
							SIR	95% CI	SIR	95% CI	SIR	95% CI
Males	1969–88	Circumpolar	1518	153.7	270.9	15.4	0.9	0.8–0.9	1.0	1.0–1.1	0.9	0.9–1.0
		Alaska	585	174.0	278.1	14.9	0.9	0.8–0.9	1.0	0.9–1.1	0.9	0.9–1.0
		Greenland	600	143.7	249.5	14.8	0.8	0.8–0.9	1.0	0.9–1.0	0.9	0.8–1.0
		Canada	333	142.5	296.5	17.6	1.0	0.9–1.1	1.1	1.0–1.3	1.1	0.9–1.2
	1969–73	Circumpolar	276	128.4	249.7	14.6	0.9	0.8–1.0	1.1	0.9–1.2	1.1	1.0–1.2
		Alaska	113	159.1	299.3	16.3	1.0	0.8–1.2	1.2	1.0–1.4	1.2	1.0–1.5
		Greenland	112	115.1	227.8	14.0	0.8	0.7–1.0	1.0	0.8–1.2	1.0	0.9–1.2
		Canada	51	109.5	206.9	13.2	0.8	0.6–1.1	1.0	0.7–1.3	1.1	0.8–1.4
	1974–78	Circumpolar	291	123.1	222.1	12.1	0.7	0.6–0.8	0.9	0.8–1.0	0.8	0.7–0.9
		Alaska	119	150.6	241.9	11.8	0.8	0.6–0.9	0.9	0.8–1.1	0.9	0.7–1.1
		Greenland	119	116.4	209.6	11.9	0.7	0.6–0.8	0.8	0.7–1.0	0.8	0.7–1.0
		Canada	53	96.1	203.6	13.1	0.7	0.5–0.9	0.8	0.6–1.0	0.8	0.6–1.0
	1979–83	Circumpolar	427	166.9	287.4	16.2	0.9	0.8–1.0	1.1	1.0–1.2	0.9	0.9–1.0
		Alaska	163	187.3	291.4	15.7	0.9	0.7–1.0	1.0	0.9–1.2	0.9	0.8–1.1
		Greenland	165	156.3	260.7	15.5	0.8	0.7–1.0	1.0	0.8–1.1	0.9	0.7–1.0
		Canada	99	156.5	331.0	19.0	1.1	0.9–1.3	1.3	1.0–1.5	1.1	0.9–1.4
	1984–88	Circumpolar	524	187.0	309.0	17.8	0.9	0.9–1.0	1.1	1.0–1.2	0.9	0.9–1.0
		Alaska	190	191.7	289.8	15.8	0.9	0.8–1.0	1.0	0.9–1.2	0.9	0.8–1.0
		Greenland	204	181.6	286.6	17.3	0.9	0.8–1.0	1.0	0.9–1.2	0.9	0.8–1.0
		Canada	130	189.2	390.3	22.2	1.2	1.0–1.4	1.3	1.1–1.6	1.2	1.0–1.4
Females	1969–88	Circumpolar	1697	176.9	268.8	17.5	1.0	1.0–1.1	1.1	1.1–1.2	1.0	0.9–1.0
		Alaska	556	169.7	261.8	14.9	1.0	0.9–1.1	1.1	1.0–1.1	0.9	0.8–1.0
		Greenland	813	200.0	268.7	18.4	1.0	1.0–1.1	1.1	1.0–1.2	1.0	0.9–1.1
		Canada	328	145.7	287.4	20.2	1.1	1.0–1.2	1.1	1.0–1.3	1.0	0.9–1.1
	1969–73	Circumpolar	296	140.1	236.9	15.6	1.0	0.9–1.1	1.1	1.0–1.2	1.0	0.9–1.1
		Alaska	81	115.9	195.6	13.4	0.8	0.7–1.1	0.9	0.7–1.1	0.8	0.7–1.0
		Greenland	171	175.9	273.3	17.9	1.2	1.0–1.3	1.2	1.1–1.4	1.1	1.0–1.3
		Canada	44	99.6	215.1	15.5	0.8	0.6–1.1	0.9	0.7–1.2	0.8	0.6–1.1
	1974–78	Circumpolar	346	150.9	240.5	15.9	0.9	0.8–1.0	1.0	0.9–1.1	0.9	0.8–1.0
		Alaska	114	148.4	246.9	12.8	0.9	0.8–1.1	1.0	0.8–1.2	0.9	0.7–1.1
		Greenland	169	169.6	239.0	17.0	0.9	0.8–1.1	1.0	0.9–1.2	0.9	0.8–1.1
		Canada	63	119.3	245.1	18.8	0.9	0.7–1.2	1.0	0.8–1.3	0.9	0.7–1.1
	1979–83	Circumpolar	478	194.1	288.1	18.7	1.1	1.0–1.2	1.2	1.1–1.3	1.0	0.9–1.1
		Alaska	151	180.4	272.7	15.0	1.0	0.8–1.2	1.1	0.9–1.3	0.9	0.8–1.1
		Greenland	231	227.1	291.1	19.8	1.1	1.0–1.2	1.2	1.0–1.3	1.0	0.9–1.2
		Canada	96	157.7	327.1	23.4	1.2	1.0–1.4	1.3	1.0–1.5	1.0	0.8–1.3
	1984–88	Circumpolar	577	211.8	293.1	18.9	1.1	1.0–1.1	1.1	1.1–1.2	1.0	0.9–1.1
		Alaska	210	215.9	299.7	17.5	1.1	0.9–1.2	1.2	1.0–1.3	1.0	0.9–1.2
		Greenland	242	224.2	275.5	19.1	1.0	0.9–1.1	1.1	0.9–1.2	0.9	0.8–1.1
		Canada	125	185.8	333.8	21.3	1.2	1.0–1.4	1.3	1.1–1.5	1.1	0.9–1.3

While the number of cancers reported almost doubled, from 572 in 1969–1973 to 1 101 in 1984–1988, age-standardized rates increased less rapidly, by 22% for men and 24% for women, due to the ageing of the Inuit population (Table 1) (2–5). Further, incidence of cancer among Inuit as measured by the SIRs did not deviate significantly from rates in any of the three comparison populations of Denmark, Canada and Connecticut (USA) in any time period.

The four top-ranking cancer sites in each sex constituted half of all cancers diagnosed during the period: among men, these were lung (28.3%), colon (8.1%), stomach (7.0%) and nasopharynx (6.5%); among women, these were cervix (17.6%), lung (13.7%), breast (11.4%) and colon (9.6%). For details of single sites the reader is referred to the previous publications (6–14).

Considerable site-specific differences were found in Inuit when compared to the three populations of Connecticut, Canada and Denmark, respectively (Figs. 1, 2). Cancers with excess risk in both sexes—and relative to all three comparison populations—were lung (8), nasopharynx, salivary glands (6), oesophagus and gallbladder and extrahepatic bile ducts (7). Among men, increased risk was

Table 2

Cancer in Circumpolar Inuit 1969–1988. Total number of cases and verification of diagnosis (% of total) by site (ICD 9) and region.

		Total No.	DCO[1] %	HV[2] %	OTH[3] %
All sites excl. other skin	Circumpolar	3215	5	85	10
	Alaska	1141	0	94	6
	Greenland	1413	7	80	13
	Canada	661	10	82	8

[1]DCO = Death certificate only.
[2]HV = Histologically verified. [3]OTH = Other.

found also for cancer of the liver and stomach (7), and among women for cervical and renal cancer (10, 12).

Low risks were observed in both sexes for bladder cancer (12), non-Hodgkin lymphoma and Hodgkin's disease, leukaemia (particularly chronic lymphatic leukaemia), multiple myeloma (13), melanoma of skin and other skin cancers (14). Inuit men experienced low risks of rectal cancer (7), laryngeal cancer (8) and tumors of the brain and central nervous system (14). Consistently low risk was found also for prostate cancer (11), female breast cancer (9) and cancer of the endometrium (10).

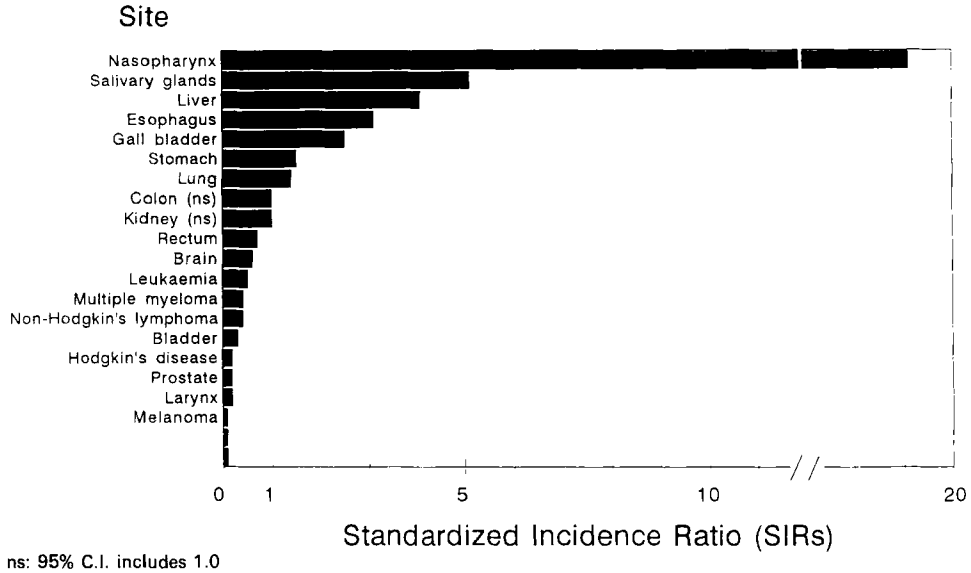

Fig. 1. Standardized Incidence Ratios. Cancer in Circumpolar Inuit Men 1969–1988.

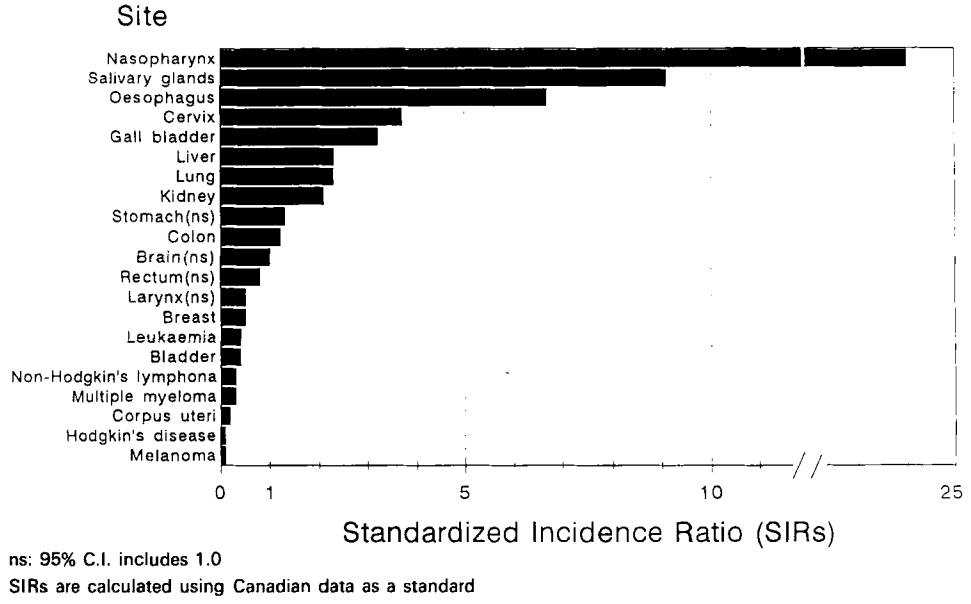

Fig. 2. Standardized Incidence Ratios. Cancer in Circumpolar Inuit Women 1969–1988.

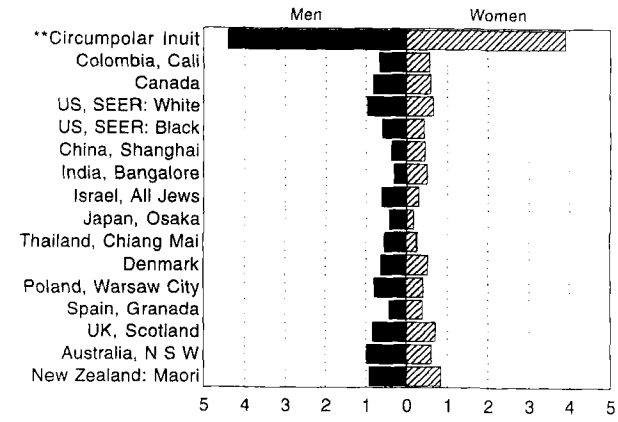

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Fig. 3. Age-standardized Incidence Rates (World): International variation of Cancer, Salivary Glands.

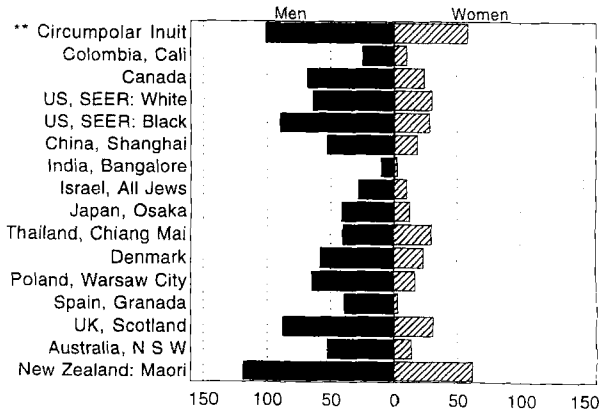

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Fig. 6. Age-standardized Incidence Rates (World): International variation of Cancer, Bronchus, lung.

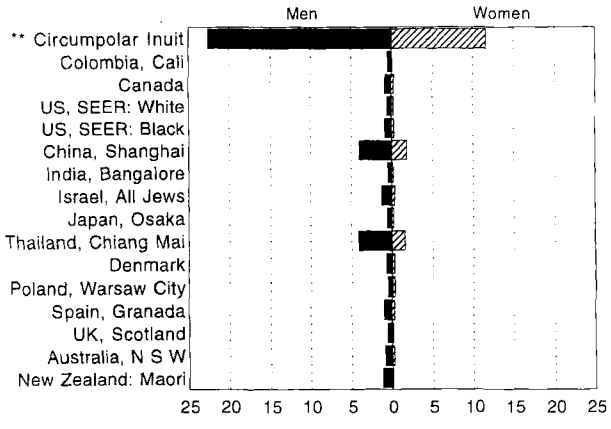

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Fig. 4. Age-standardized Incidence Rates (World): International variation of Cancer, Nasopharynx.

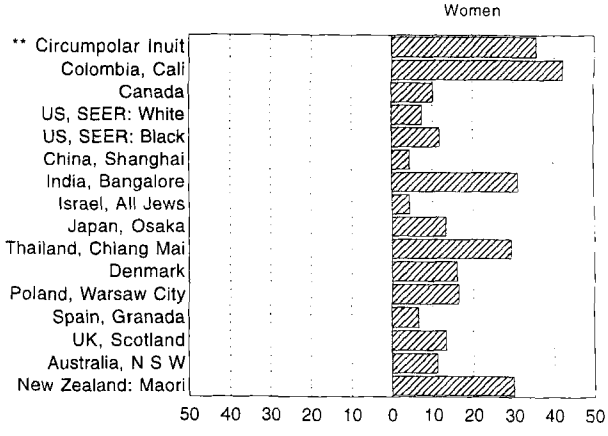

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Fig. 7. Age-standardized Incidence Rates (World): International variation of Cancer, Cervix Uteri.

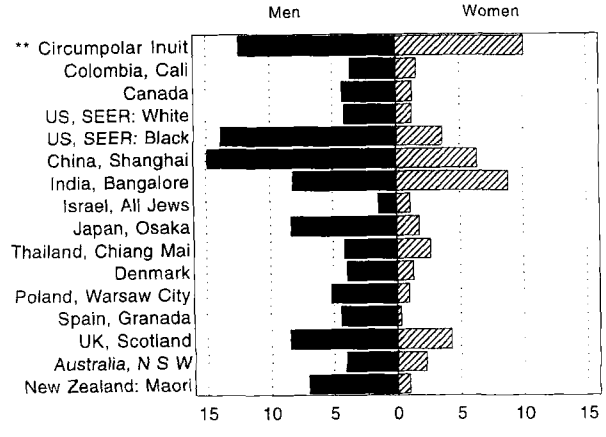

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Fig. 5. Age-standardized Incidence Rates (World): International variation of Cancer, Oesophagus.

Cancers of a secondary or unspecified nature accounted for 7% of all cancers in the Inuit (14), a rate 2–3 times more frequent than in the comparison populations. These findings point to differences in health care access and in the availability of diagnostic facilities for the Inuit populations. They also indicate a need for caution in interpreting some of the low rates recorded among the Inuit, particularly in sites with small numbers of cancers. However, the more strikingly low incidence rates are unlikely to be artefactual since the SIRs for these sites were uni-formly reduced for all Inuit populations in all 5-year time periods.

Some Inuit age-standardized cancer rates (ASRs) were among the world's highest (15) (Figs. 3–7), and were generally significantly higher than those for the comparison populations. The high rates of salivary gland cancer are unique for Inuit (6), while very high rates were also found for nasopharyngeal and lung cancer in both sexes (6, 8) and

for cancers of the cervix (10), oesophagus (7) and kidney (12) in women. For specific Inuit populations, the rates for cancers of the gallbladder and extrahepatic bile duct cancer, colon and the combined rate of colo-rectal cancer in Alaskan Inuit (7) were at the high end of the world rates as was the rate of invasive cervical cancer in Greenlandic Inuit (10). The excessively high rates of lung cancer in Canadian Inuit were higher than any reported in the world (8).

Some Inuit ASRs were among the lowest reported worldwide, in particular the low breast cancer rates among Canadian Inuit women (9).

The present analysis highlights the potential importance of both environmental and genetic factors in cancer etiology. These include influences of tobacco and alcohol consumption, traditional as well as western diet, environmental contaminants, endogenous hormones, reproductive factors, sexual behaviour, viruses and genetically determined host responses (1–4).

Tobacco and alcohol consumption

Tobacco consumption is causally associated world-wide not only with lung cancer but also with cancers of the upper respiratory tract (lip, oral cavity, pharynx, larynx), upper digestive tract (oesophagus), pancreas, urinary bladder and kidney. Alcohol increases the risk for developing cancer of the oral cavity, pharynx, larynx, oesophagus and liver and the risk for these cancers are multiplied in people who also smoke (16, 17).

Inuit men and women have been exposed to high levels of both tobacco and alcohol for several decades (2–4). By the mid-1950s, cigarette consumption in Greenland exceeded that in Denmark and soon reached one of the highest consumption levels in the world. Women contributed to this level as much as men did (18), while smoking rates for Canadian Inuit women exceeded that of Inuit men (4).

Tobacco-related cancers as listed above accounted for 36% of all Inuit cancers during the study period, although risk patterns varied by site. Lung cancer incidence rose sharply with time in both sexes in all areas, compatible with the emergence of a tobacco-associated epidemic (8). However, the increasing lung cancer rates contrasted markedly to the more uniform temporal rates of other tobacco and alcohol-related cancers. Oesophageal cancer rates were consistently high throughout the 20-year period (7), as were the rates of female renal cancer (12). In sharp contrast, rates of bladder and laryngeal cancers were consistently low (8, 12), while rates for cancers of the pancreas (7), of the oral cavity and pharynx (excluding nasopharynx) (6), and of kidney (among males) (12) were similar to those in the comparison populations. Such findings could reflect different states of carcinogenesis affected by tobacco and alcohol for each site, different latency periods between exposure and cancer development for the various cancers, or the operation of other factors of environmental or genetic origin with an enhancing or protective effect.

Dietary components

Extensive data indicate that diet can influence the process of human carcinogenesis (19–21). Associations have been reported between a high consumption of fat—particularly saturated fat of animal origin—and an increased risk of colorectal cancer and cancers of the breast, endometrium, ovary, prostate, and pancreas. Complex carbohydrates and salted foods have been positively associated with stomach cancer, and high total caloric intake with cancers of the breast, colon and rectum, and of the gallbladder and biliary tract. Various N-nitroso compounds have been correlated with a higher risk of cancers of the stomach, oesophagus, oral cavity and urinary bladder.

Fresh fruits and vegetables, dietary fibre, beta-carotene, vitamins C and E, selenium and calcium have been reported as protective against carcinogenesis in a variety of sites such as larynx, lung, oesophagus, stomach, colon, rectum, breast and cervix. A positive value of omega-3 fatty acids in reducing the risk of breast cancer has been suggested (22).

The traditional Inuit diet, based on fish and marine mammals, is rich in omega-3 fatty acids and high in total fat, protein, and total calories, in cholesterol, and in vitamin A (23–29). It also contains some amounts of N-nitrosodimethylamine or precursors (30, 31), but is low in vitamin C and E, in selenium, calcium and beta-carotene, and almost totally devoid of fresh fruit and vegetables, and of fibres and carbohydrates. Today, a more westernized diet based on imported foods prevails in many families, but the ratio of traditional diet versus imported food still varies from household to household (24, 32–35).

Such dietary variations might explain at least some of the deviations from expected rates in incidence of certain cancers among Inuit, in particular the lower than expected rates for breast, prostate and endometrial cancers, and the higher than expected rates for colorectal, stomach and oesophageal cancers. Dietary differences may also be implicated as co-factors in some of the risk differences between the various national Inuit population groups such as the very high risk of lung cancer among Canadian Inuit compared to their Alaskan and Greenlandic counterparts (8), and the high risk of gallbladder and colorectal cancer found only among Alaskan Inuit (7). Of particular interest are the rates of colorectal cancer in Alaskan Inuit women which almost doubled during the study period, while rates in Greenland decreased to one fifth of the Alaskan rates. While differences in diagnostic procedures among the areas must be considered, they cannot readily explain such marked variations. Nor have dietary surveys so far revealed important inter-regional differences in Inuit diets, and at present we have no explanation for the observed differences.

Endogenous hormones and reproductive factors

Various aspects of reproductive behaviour influence cancer risk (20, 36). Thus, the risk of cancers of the breast, ovary and endometrium is influenced by reproductive factors associated with ovarian activity. For breast cancer, such risk factors include early menarche, late menopause, low parity, late age at first birth and absence of lactation. Cancers of the endometrium and ovary share several of these risk factors with breast cancer, while low parity also appears to play a role for female colon cancer. Such risk factors point to the existence of some hormonal determinants not yet fully understood.

Among men, fewer associations have been noted between a possible hormonal influence and cancer. Prostate cancer has been related to increased sexual activity and hormonal stimulation (estrogen and testosterone) but convincing evidence is lacking.

The pattern of low rates of Inuit breast and endometrial cancer was to be expected when considering the different risk factors involved (2–4). However, ovarian cancer occurred in Inuit at rates more similar to rates in the comparison populations (10). And while rates for endometrial, breast and prostate cancer were lower than expected, the occurrence of colon cancer in Inuit women was surprisingly higher than expected, particularly in Alaska (7). The possible influence of endogenous hormones is puzzling based on these observations.

Viruses and sexual behaviour

The present study clarifies the potential importance of viruses in Inuit carcinogenesis. High rates of the traditional Inuit cancers of the salivary gland and nasopharynx may well be causally associated with the Epstein-Barr virus (EBV), with a possible concomitant influence from genetic factors and environmental co-factors (6).

The differences in liver cancer rates, including age-specific rates, between Alaska, Greenland and Canada, and particularly among men (7), suggest different relative risks associated with carriers of the hepatitis B virus (HBV). Patterns of transmission of HBV or genetic factors influencing host response to HBV may be involved (37–39).

The incidence of cancer of the cervix, which is often inversely associated with the incidence of breast, endometrial and ovarian cancer, is normally closely associated with factors relating to sexual activity such as early first intercourse and multiple partners suggesting, in part, a viral-related etiology. The incidence of this particular cancer was high among the Inuit populations and it might be assumed that this indicates high prevalence of human papilloma virus (HPV) genital infections in the Inuit female population. However, studies from Greenland have demonstrated that this link may not always be straight forward (10). Worldwide there is now substantial laboratory and epidemiological evidence confirming the role of genital HPVs, which are transmitted sexually, as the central etiological factor in cervical cancer (40–45). Earlier studies with conflicting results were often limited by variation in laboratory methods used, with different levels of sensitivity and specificity. Other sexually transmitted diseases and smoking have been suggested as either independent risk factors for cervical cancer or cofactors promoting the carcinogenicity of HPV (45–48). Whether the high level of such factors in Inuit women could partially explain their excess risk of cervical cancer remains speculative.

Penile cancer, which is believed to share some etiological factors with cervical cancer, was at elevated risk among Inuit (11) although not as much as expected from the cervix cancer incidence.

Genetic factors

Genetic markers have demonstrated that the Inuit are of Asiatic origin (49–51). Cancer patterns among Inuit in many ways resemble patterns reported from China as well as from Chinese population groups located elsewhere, and particularly in southeast Asia (15). Inuit and Chinese populations share high risks for cancer of the nasopharynx, oesophagus, liver and lung, and low risks for cancer of the breast, endometrium, prostate, urinary bladder and larynx and for melanoma of skin. Common low risks are also found for lymphomas, multiple myeloma and leukaemia, particularly for Hodgkin's disease and chronic lymphatic leukaemia.

Although probably largely induced by environmental agents, risks for several of these cancers may well be modified by genetically determined host factors, e.g., genetic polymorphisms involved in carcinogen activation or detoxification.

The familial clusterings of nasopharyngeal and salivary gland cancer (6) suggest polygenic susceptibility which may affect a substantial segment of the Inuit population.

Prevention and early detection

The present study has identified some aspects of cancer in the Inuit where cancer control strategies could be developed or improved. Emphasis should be placed on health promotion, especially reduction or elimination of tobacco (both smoking and chewing) and alcohol. Coordinated government intervention by legislation—e.g. smokefree environment, restrictions of import, taxation/pricing policies—should be followed by health promotion and health care delivery programs aimed at individual behaviour modifications and education. Dietary recommendations should emphasize the benefit of the traditional diet of fish, marine mammals, and caribou instead of fat or meat of commercial origin. The importance of a daily consumption of fruits, vegetables and whole grain should be recognized. Primary prevention should also include information and

education relevant to prevention of sexually transmitted diseases and consideration of vaccination against hepatitis B as a preventive measure for cancer of the liver. Such recommendations and control programs should be implemented starting early in life, as it seems likely that the high risk factors for a number of malignancies exert much of their future effect in the young.

As part of general health care, relevant education on cancer symptoms is needed to increase awareness of the problem of cancer and encourage early detection and compliance with screening programs, e.g., PAP smear and breast self-examination. More effective screening programs for cancer of the cervix should be implemented, particularly in Greenland where a nationwide program is badly needed (52).

Some health promotion procedures have been implemented in several areas. Legal restrictions against the importation and/or sale of alcohol are now locally imposed in approximately half of all Alaskan communities (53). In Greenland, government intervention by legislation, taxation and education has reduced tobacco consumption by 10% (54). Extensive dietary surveys among Siberian Chukotka and Alaska Native adults have resulted in promotion of food consumption practices along the guidelines delineated above (34, 55). In Canada, organized cervical cancer screening has been implemented in the Northwest Territories and northern Quebec, smoke-free environments are increasingly encouraged in Northern communities and sex education provides some information relevant to prevention of sexually transmitted diseases (4). Immunization programs against hepatitis B were initiated in Alaska in 1983 (56) and are now in place in the Canadian Northwest Territories (4).

Future priorities for research

The complex pattern of cancer in the Inuit and its differences from the comparison populations suggest a number of directions for research, including evaluation of both environmental and genetic factors in etiology, as well as evaluation of intervention studies related to cancer control measures. The environmental factors include viruses, smoking, alcohol, environmental contaminants, the influence of traditional as well as modern diet and traditional cooking practices. Evaluation of genetic predisposition should include biomarkers expressing metabolic/detoxification genotypes, DNA repair genes of relevance to cancer induction and the contribution of other candidate genes, e.g. within the HLA-system. The major sites of interest are the high risk sites of lung, nasopharynx, salivary glands, oesophagus, colon, rectum, liver, gallbladder and bile duct, kidney and cervix, and the low risk sites of breast, endometrium, prostate and lymphomas. A combined case-control investigation which simultaneously evaluated a number of etiological factors and several cancer sites seems likely to be the most efficient approach in this small and widely scattered population. This would permit intercancer comparisons as well as ensure maximal utilization of the controls. For some aspects of research into viruses and genetic factors, randomly selected population-based samples may need to be identified.

Detailed tabular material by 5-year calendar periods 1969–1988 is available upon request. Please contact the Danish Cancer Registry, Danish Cancer Society, Strandboulevarden 49, DK-2100 Copenhagen, Denmark.

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