Cancer patterns in Inuit populations

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Inuit people inhabit the circumpolar region, with most living in Alaska, northwest Canada, and Greenland. Although malignant diseases were believed to be almost non-existent in Inuit populations during the beginning of the 20th century, the increasing life expectancy within these populations showed a distinct pattern, characterised by a high risk of Epstein-Barr virus-associated carcinomas of the nasopharynx and salivary glands, and a low risk of tumours common in white populations, including cancer of the prostate, testis, and haemopoietic system. Both genetic and environmental factors seem to be responsible for this pattern. During the second half of the 20th century, Inuit societies underwent major changes in lifestyle and living conditions, and the risk of lifestyle-associated tumours, especially cancers of the lung, colon, and breast, increased considerably after changes in smoking, diet, and reproductive factors. This Review will briefly summarise the current knowledge on cancer epidemiology in Inuit populations, with emphasis on the characteristic Inuit types of cancer.

Introduction

The Arctic region is inhabited by various indigenous people, including Inuit, Indians, Aleuts, Evenks, Nenets, and the Sami people.1 These populations each have a characteristic pattern of disease; however, the pattern of malignant diseases in Inuit is characterised by a unique presence of Epstein-Barr virus (EBV)-associated carcinomas and differs substantially from that in white populations. This Review will focus on malignant diseases in Inuit, with emphasis on the epidemiology and aetiology of the distinctive Inuit forms of cancer. The term Inuit refers to the group of people who were formerly referred to as Eskimo. The term Eskimo is no longer used in Greenland and Canada, although its use is still widespread in Alaska.

At the end of the 19th century, malignant diseases in Inuit were thought to be virtually non-existent. However, as life expectancy increased during the 20th century a distinct pattern of malignant diseases emerged, characterised by high frequencies of carcinomas of the nasopharynx, salivary glands, and oesophagus, and low frequencies of tumours common in white populations, such as cancers of the testis, prostate, breast, and haematological system. This disease pattern is believed to be the result of genetic heritage and indigenous lifestyle, but, changing living conditions, especially during the second half of the 20th century, have had a substantial effect on the occurrence of cancer in Inuit.

Inuit populations

The Inuit originate from East Asia and crossed the Bering Strait as part of a final wave of migration about 5000 years ago. Genetic markers in the present population show the Asian heritage.1 The present Inuit population constitutes an ethnic group of about 170 000 individuals in the circumpolar region (figure 1), with most living in Alaska, northern Canada, and Greenland.1 The Inuit populations are included in the general population census in Alaska, Canada, and Denmark, and in Alaska and Canada, information on ethnic affiliation can be registered. In Alaska, the term Alaska Natives encompasses Inuit, American Indians, and Aleuts, with Inuit being the largest group (52%).1 In Canada, most Inuit live in the Nunavut territory or the northern part of the Quebec province,1 and in Greenland, which has a home-rule government within the Danish kingdom, individuals of Inuit origin constitute about 90% of the population.1 The Inuit population in Siberia is small (about 1500 individuals), with most living on the coastline of the Chukotka peninsula. The incidence of cancer in this population has been reported, but besides indications of a high frequency of cancers of the oesophagus and stomach, numbers are too small for assessment.1

Changes in lifestyle and living conditions

During the second half of the 20th century, Inuit populations underwent major changes concerning a wide range of exposures. These changes included the establishment of larger urban communities, improvement of housing standards, and a transition from traditional fishing and hunting subsistence to a society where most people are employed in public administration, service, and trade.1 On an individual level, the Inuit have undergone noticeable dietary changes from a diet mainly based on fish and sea mammals towards a diet more dependent on imported food. A steep increase in tobacco consumption has also been noted, although this consumption seems to have decreased during the past...
The traditional Inuit diet contained few carbohydrates and little vegetable matter, but was rich in unsaturated fat, with most energy sources coming from protein and fat. In the modern Inuit diet, the main energy sources are fat and carbohydrate. The effect of the dietary changes on the risk of cancer is not straightforward. Although low in fresh vegetables and fruits, the traditional diet had a high content of nutrients hypothesised to protect against the development of several malignancies—eg, vitamin A and marine fatty acids. More importantly, the modern diet is associated with a considerable increase in the consumption of saturated fat, and this, combined with a more inactive lifestyle, has increased the frequency of obesity and diabetes considerably.1,4

Overall epidemiology
The Inuit cancer pattern, characterised by high frequencies of nasopharynx and salivary gland carcinomas, and low frequencies of cancer of the prostate, skin, breast, and the haematological system, has been a consistent finding in Arctic surveys (figure 2). During the second half of the 20th century, cancer incidence in the Arctic region increased steadily.5,11 Although age-standardised incidence rates in the 1950s and 1960s were below the corresponding national rates in the USA, Canada, and Denmark, overall rates now seem to be comparable. However, the increase has not been uniformly distributed over all cancer types, because the incidence of traditional Inuit cancers, such as cancer of the nasopharynx and salivary glands, has remained constant, whereas the incidence of lifestyle-associated cancers, especially cancer of the lung, breast, and colon, has increased (figure 3). These cancers now constitute the abundant forms of malignant disease in Inuit, and the increase in incidence of each of these three cancers is consistent with different aspects of the changing lifestyle of Inuit populations, symbolised by changes in smoking habits, reproductive factors, and dietary patterns.

Traditional Inuit cancers
Nasopharyngeal and salivary gland carcinoma
The worldwide distribution of nasopharyngeal carcinoma shows remarkable geographical and ethnic variation, with very low incidence rates in most populations, but high rates in areas of southern China, southeast Asia, north Africa, and in the Inuit population in the Arctic (table 1).20,21,24 Nasopharyngeal carcinoma is 25–40-times more frequent in Inuit populations than in white populations in the USA, Canada, and Denmark, and represents 4–7% of all malignancies in Inuit compared with less than 0.1% in white people.19 As in other high-incidence areas, most cases of nasopharyngeal carcinoma in Inuit are of the undifferentiated type. At least some of the factors important to the aetiology of this cancer are believed to be shared in the different high-risk populations. Thus, certain environmental factors have a role; in particular, infection with EBV affecting people who are genetically susceptible to nasopharyngeal carcinoma. The association between EBV and undifferentiated nasopharyngeal carcinoma is firmly established in Chinese populations,15 and much of the evidence that has formed the basis for causality has been reproduced in Inuit with this cancer; EBV DNA and proteins have been detected in tumour cells of nasopharyngeal carcinomas in Inuit;6,27 EBV has been detected in atypical nasopharyngeal lesions, suggesting that EBV infection of the epithelium is an early step in the pathogenesis;7 and increased EBV antibody titres have been noted in Inuit with nasopharyngeal carcinoma compared with controls.28 Specific EBV strains have been isolated in nasopharyngeal carcinomas from Inuit and other high-risk populations.8 The significance of this finding, however, remains unknown. The predominance of specific EBV variants in nasopharyngeal carcinoma could be associated with differences in the biological or molecular properties of the distinct forms of the virus, but also possible immune selection, because the selection of specific variants has been associated with certain types of human leucocyte antigen (HLA).29,30

The involvement of a hereditary component in the development of nasopharyngeal carcinoma is supported by reports of familial clustering, and an eight-times increased risk of nasopharyngeal carcinoma in first-degree relatives of Inuit with nasopharyngeal carcinoma has been reported.22,23 Although linkage studies in other high-risk populations have indicated a gene close to the HLA locus, and association studies have suggested many
candidate genes related to immunity, HLA alleles, cell-cycle regulation, detoxification, and EBV receptors, no conclusive genetic evidence exists. The food most consistently associated with this cancer has been Chinese salt-preserved fish, the carcinogenic potential of which has been supported by animal experiments, and salted and preserved meat and vegetables from north Africa have repeatedly been associated. Whether similar high-risk foods are associated with nasopharyngeal carcinoma in Inuit populations is unclear, but salted fish in the childhood diet has been found more frequently in Alaskan people with nasopharyngeal carcinoma than in controls, and a high content of nitrosamines has been identified in traditional dried fish, comparable with the high levels recorded in Chinese salted fish.

The incidence of nasopharyngeal carcinoma in other high-risk areas has shown a gradual decrease over the past few decades, which is suggested as being secondary to changes in lifestyle. Although recent data suggest a decreasing trend of nasopharyngeal carcinoma in Inuit, the change is not significant. While this non-significance might indicate a change in risk factors in a time period too recent to affect current rates, the small population needs a substantial time frame for changes to be obvious.

The incidence of nasopharyngeal carcinoma in other high-risk areas resembles that of nasopharyngeal carcinoma in Inuit, but the high risk of salivary gland carcinomas is unique to the Inuit population (table 1). Rare in most populations, the incidence of salivary gland carcinoma in Inuit is about 3–6 per 100 000, with the highest incidence noted in Canadian Inuit. In general, these tumours are 5–10 times more common in Inuit than in most other populations. Salivary gland carcinoma in Inuit shares many similarities with nasopharyngeal carcinoma. Undifferentiated salivary gland carcinomas are also associated with EBV infection, and histopathologically the tumour resembles a nasopharyngeal carcinoma.

The close relation between nasopharyngeal carcinoma and salivary gland carcinoma in Inuit is underlined by the finding of a substantially increased risk of salivary gland carcinomas in first-degree relatives of Inuit with nasopharyngeal carcinoma, which equals the increased risk of familial nasopharyngeal carcinoma. By contrast with nasopharyngeal carcinoma, salivary gland carcinomas are more frequent in females, but little is known about individual risk factors. However, in a study involving Greenlandic migrants in Denmark, the finding that the high risk of both nasopharyngeal carcinoma and salivary gland carcinoma is maintained in Inuit decades after migrating to a low-risk area suggests genetic risk factors or environmental risk factors acting early in life.

The high risk of EBV-associated carcinomas has stimulated investigations into the general EBV immune response in the Inuit population. Compared with white
children, Inuit children show a distinct EBV acquisition pattern characterised by early primary infection and remarkably high antibody titres.28 Furthermore, compared with Chinese and white populations, Inuit seem to harbour EBV in the nasopharyngeal epithelium more frequently. Additionally, EBV immunoglobulin A (IgA)-antibodies, proposed as a tumour marker for nasopharyngeal carcinoma in Chinese high-risk areas, are more often detected in the general Inuit population than in other populations.29,30 However, contrary to what has been noted in Chinese populations, EBV antibody titres do not seem to be increased in close family members of Inuit with nasopharyngeal carcinoma,29,31 and the significance of the general EBV immune response in the aetiology of EBV-associated carcinomas in Inuit remains unknown.

Oesophageal and stomach cancer
The incidence of oesophageal cancer shows considerable international variation, and high-incidence areas include those occupied by the Inuit, with incidence rates (age-standardised rate) of 6–22 per 100 000 person-years. Considerable geographical variation within the Arctic region is evident, with the incidence in Greenland being the highest.32 As opposed to the clear male predominance noted in other high-incidence areas, the risk of oesophageal cancer is more equally distributed between males and females in Inuit populations, with a male–female ratio of 1·2–2·0. Environmental factors have a central role in the aetiology of oesophageal carcinoma, with smoking and alcohol being established risk factors. However, the trends in the incidence rates of oesophageal carcinoma in Inuit have not paralleled the clear increase in lung-cancer rates, suggesting the presence of other risk factors. A low intake of fresh vegetables and fruits in the traditional diet, combined with a high content of nitrosamines in certain traditional foods might contribute to the high risk.25 Human papilloma virus (HPV) has been detected in a high proportion of oesophageal cancers in Alaska natives, which is interesting in view of the increased risk of HPV-associated carcinoma of the uterine cervix in Inuit populations.33

Although the overall incidence of oesophageal cancer in Inuit has remained stable, the incidence of stomach cancer has increased significantly over the past decades, clearly contrasting the decreasing global trends for this malignancy.8,9 This increase mainly involves males and is noted in both Greenland and Alaska. Reasons for the increase are unknown. Smoking is a risk factor for stomach cancer, but the substantial increase in stomach cancer in men aged 50–70 years in Greenland has not been followed by a parallel increase in the incidence of lung cancer in men (table 2). Non-cardia stomach cancer is associated with Helicobacter pylori infection, and the seroprevalence of Helicobacter pylori is high in the Arctic.10 A time series of the seroprevalence is not available, but the general sociocultural changes point against an increasing prevalence of Helicobacter pylori. Finally, the consumption of fresh vegetables and fruits, known to have a protective effect, has not decreased in recent decades.9

Populations in developed countries have witnessed a steep increase in the incidence of adenocarcinomas of the distal oesophagus and proximal stomach, proposed to be associated with the increase in obesity and diabetes. Data from Alaska natives do not support a change in the topographical distribution of gastric cancer during the past two decades,35 but data from Inuit cancer surveys are not routinely stratified for topography and histology.

Cancer of the liver and biliary system
Hepatocellular carcinoma is frequent in Inuit compared with their respective national populations in the USA,
Canada, and Denmark, with standardised-incidence ratios ranging between two and five. The risk is not equally distributed in the Arctic regions, and the Alaskan Inuit population seems to be at the highest risk. The main risk factors for the development of hepatocellular carcinoma are alcohol and hepatitis B virus (HBV), and the high risk of hepatocellular carcinoma in Inuit is consistent with a high prevalence of HBV. The prevalence of chronic HBV infection (HBsAg positive) in the general Inuit population ranges from 3–12%. However, the effect of HBV does not seem to be uniform, because the incidence of hepatocellular carcinoma in Inuit in Greenland is lower than in Alaska, despite a higher incidence of HBV infection. A possible explanation is an uneven distribution of virus genotypes, because HBV genotype F, which has been associated with the development of hepatocellular carcinoma in Alaska, is rare in Greenland. Prevention of HBV by routine vaccination in Alaska has clearly decreased the prevalence of HBV infection, and the effect on the subsequent risk of hepatocellular carcinoma is believed to be equal. The seroprevalence of hepatitis C virus infection in Inuit is generally low (<1%), although a higher prevalence has been shown in urban Alaskan areas. Cancer of the gall bladder is a relatively rare cancer in most populations and has been associated with various risk factors, including cholecystolithiasis, chronic infections of the gall bladder, obesity, reproductive factors, diet, and genetic susceptibility. A high risk of cancer of the gall bladder and biliary tract has traditionally been noted in Inuit populations. The Alaskan Inuit population has a 3–6-times increased risk compared with white populations, although the incidence seems to be decreasing. No specific risk factors in Inuit have been identified, but colorectal and gall-bladder cancers share dietary risk factors, including a high-fat, low-fibre diet, and the incidence of both cancers are highest in Alaskan Inuit. However, the temporal trends in incidence are conflicting, because colorectal cancer is increasing, whereas gall-bladder cancer is decreasing, suggesting that other factors are also important.

Gestational trophoblastic tumours
A high risk of gestational trophoblastic tumours, such as invasive mole and choriocarcinomas, has previously been reported in both Greenland and Alaskan Inuit women. Data on the development in incidence are not available, but the overall incidence is believed to decrease in parallel with the decreasing birth rate. The aetiology of gestational trophoblastic tumours is not well understood, but risk factors include a genetic predisposition, very low or very high reproductive ages, certain ABO blood groups, and use of oral contraceptives. The importance of these risk factors in the Arctic context is unknown.

Cancer of the uterine cervix
Cancer of the uterine cervix might not be considered a traditional Inuit cancer, and a low incidence was reported in the Arctic at the time of the first cancer surveys in the 1950s. In the following decades, the incidence increased greatly, and became five to six-times higher in Inuit populations compared with the national populations in the USA, Canada, and Denmark. Development of cancer of the uterine cervix is closely associated with genital human papilloma virus (HPV) infection, and early age at first intercourse, many sexual partners, and a high incidence of venereal diseases, were until recently prevalent in the Inuit populations. Although still high compared with national rates, the incidence of venereal diseases in Inuit has decreased considerably since the 1980s. This development, together with the introduction of organised cervical-cancer screening, has contributed to a significant decrease in the incidence of cervical cancer in the past two decades. However, despite a decreasing incidence, cancer of the uterine cervix remains two to three-times more common in Inuit populations than in the respective national populations, and the development of HPV vaccines constitutes an opportunity to further lower the risk in these populations.

Emerging cancers
The increase in overall cancer incidence in Inuit populations during recent decades is mainly explained by an increase in the lifestyle-associated cancers of the lung, breast, and colon (figure 3). These cancers now constitute most malignant diseases in Inuit in the Arctic and will continue to dominate the spectrum of malignant diseases in the decades to come.

Lung cancer
The incidence of lung cancer has increased remarkably in all Inuit populations over the past 40 years. The disease is now by far the most frequent malignancy in Inuit, and lung cancer constitutes about 20% of all cancers in Inuit. Compared with incidences worldwide, the incidences of lung cancer in Inuit men and women are within the highest range, and the incidence in women is probably the highest reported. Although the incidence of lung cancer in Inuit men seems to have reached a plateau in the past decade, the incidence in women continues to rise. The single most important risk factor for lung cancer is smoking, and the overall development in the incidence of lung cancer in Inuit is probably consistent with changes in smoking behaviour. The import of cigarettes to Greenland increased from 5-2 cigarettes per inhabitant per day in 1950 to 11-1 in 1980. Although recent surveys suggest a decreasing consumption, a latency period of several decades between smoking and cancer development implies that the lung-cancer epidemic, especially in Inuit women, might not have reached its peak.

Other factors are also known to affect the risk of lung cancer. A vegetable and fruit-rich diet has repeatedly been associated with a decreased risk of lung cancer, and the low intake of these foods in the traditional Inuit diet.
might contribute to an increased risk. But although dietary factors might be of some importance, the general development in dietary patterns in Inuit societies, combined with a steadily increasing incidence of lung cancer, suggest against a significant dietary effect.

The focus of attention has been on the possible effect of long-term radon exposure on the risk of lung cancer in Inuit. Radon is an inactive gas released from soils and rocks, and long-term exposure increases the risk of lung cancer. In Greenland, there is a considerable geographical variation in the proportion of houses exceeding the recommended radon levels, and although this factor might add to the increased risk locally, the overall contribution to lung-cancer development is probably small.

Cultural practices, especially before the smoking epidemic in the Arctic, could also have been a contributing factor. Lung cancer in Canadian Inuit in the 1950s was noted to be restricted to elderly women, and the inhalation of fumes and smudge from open-flame lamps, was proposed as a risk factor. However, the development in modern housing and lightning has eliminated this possible risk factor.

In conclusion, cigarette smoking is considered the prevailing cause of lung cancer in Inuit and with the avoidable nature of this exposure, campaigns to stop smoking in Inuit populations should have substantial beneficial effects on an otherwise concerning trend. In view of the marked effect of smoking on the incidence of lung cancer, the consistently low incidence of laryngeal cancer in Inuit populations is puzzling. The risk of laryngeal cancer is between one-tenth and one-fifth the risk in populations in the USA, Canada, and Denmark, a difference which remains unexplained.

Breast cancer

The incidence of breast cancer has traditionally been low in Inuit. However, recent decades have witnessed a considerable increase in incidence, and, although still lower, the incidence is now approaching incidences recorded in white populations. Diagnostic improvements during this period might contribute to the increase in incidence of breast cancer, but would be expected to affect the incidence in all age groups, whereas the increase seems to be most pronounced in postmenopausal women. Most of the ethnic and international differences in the risk of breast cancer can be explained by differences in environmental exposures and lifestyle, especially reproductive and hormonal factors. The birth rate in Inuit populations has been steadily decreasing, and the maternal mean age at first birth has increased. Both factors are known to increase the risk of breast cancer. Increased risk of breast cancer has also been associated with increased height, obesity after the menopause, and large weight gains after the age of 18 years. The increase in breast-cancer incidence is therefore consistent with the increasing prevalences of obesity and type-2 diabetes in Inuit populations. A contributing factor could be changes in the pattern of breastfeeding, because lengthened breastfeeding is associated with a decreased risk of breast cancer. Extended periods of breastfeeding, practically continued through the childbearing years, was common in Inuit populations during the beginning of the 20th century, but decreased throughout the century, and the pattern of breastfeeding is now similar to that seen in white populations. The traditional Inuit diet might also offer protection against breast cancer, because fatty acids originating from fish are suggested to have a protective effect.

In view of the considerable temporal changes in the incidence of breast cancer in Inuit, the contribution of environmental factors to breast-cancer development must be substantial. However, a recent study has shown a high proportion of BRCA1-mutation carriers in the general East Greenlandic Inuit population, suggesting a potential genetic effect on the risk of developing breast cancer in Inuit women.

Colorectal cancer

The global variation in the incidence of colorectal cancer is considerable, with high incidences noted in white populations and low incidences in Asian populations. The Inuit populations have shown a significant increase in the incidence of colorectal cancer over the past 30 years, and this cancer is now one of the most common malignancies in Inuit. Geographical differences are present in Inuit populations, and the incidence in Alaskan Inuit, especially women, has consistently been higher than in Inuit in Canada and Greenland. Although the incidence of colorectal cancer in Inuit in northern Canada and Greenland approaches that of the national populations in Canada and Denmark, the incidence in Alaskan Inuit exceeds that of white populations in the USA. The increased incidence of colorectal cancer in Alaska Native women and the finding of a larger proportion of proximal tumours in this population compared with in white populations, has raised speculations of an increased frequency of defective DNA mismatch repair in this Inuit population. However, the frequency was shown to be comparable with that in other populations. More likely, the rapid increase in the incidence of colorectal cancer in Inuit suggests the effect of environmental risk factors, with diet being the most important. Both an energy-dense diet rich in fat, refined carbohydrates, and animal protein, and a sedentary lifestyle increase the risk of colorectal cancer considerably. These factors probably affect colorectal carcinogenesis via insulin pathways, and a higher risk of disease has been noted in diabetics. Nowadays, the main part of the Inuit diet consists of imported food, and the incidence of obesity and diabetes is increasing. Thus, it seems likely that the dietary transition in Inuit populations, together with a less physically active lifestyle, has had a considerable effect on the incidence of colorectal cancer.
Rare cancers in Inuit people
A characteristic of the Inuit cancer pattern is the persistently low incidence of certain cancers common in white populations, such as cancer of the prostate, testis, skin, bladder, and haemopoietic system. Several factors are most likely to be responsible for these low risks.

Prostate cancer
The risk of prostate cancer in Inuit populations is one-tenth to one-fifth of the risk in their respective national white populations.10,60 The low incidence could indicate a paucity of detection, however, the proportion of Alaska Native patients diagnosed with localized disease is comparable with that in the general US population.10 Furthermore, the very low prevalence of prostate cancer in an autopsy study and the finding of a persistently low risk after migration to a high-incidence area, suggest a genuinely low risk in Inuit.27,60 Reasons for the low risk are unknown, but a possible genetic effect is supported by the finding of a lower frequency of high-activity polymorphisms of the 5-alpha-reductase type-2 enzyme and a lower androgen receptor activity in Greenlandic Inuit men compared with Swedish men, suggesting a lower genetically determined androgenicity.61 Environmental reasons have also been proposed, and because both selenium and omega-3 polyunsaturated fatty acids have been associated with a protective effect of prostate cancer, the high intake of these nutrients through the traditional diet could have a role.62-64 A high-calorie diet, obesity, and low physical activity are risk factors that are shared by colorectal and prostate cancer. An increasing incidence of prostate cancer has been noted in Alaskan Inuit, but not yet in the other Inuit populations, which is consistent with the higher incidence of colorectal cancer in Alaskan Inuit than in the other Inuit populations.60 Thus, an increasing incidence of prostate cancer over the next few decades should be anticipated in the other Inuit populations.

Bladder cancer
A consistently low risk of bladder cancer is noted in the Inuit populations, with incidences between one-fifth and one-third those in the national populations in the USA, Canada, and Denmark.65-68 Because smoking is a major risk factor for bladder cancer, the low incidence of bladder cancer in Inuit is surprising given the high prevalence of smoking and the corresponding high incidence of lung cancer. However, a note should be made that Inuit societies are devoid of several industrial exposures associated with bladder-cancer development, including rubber and painting industries. Specific protective factors in Inuit societies have not been identified, but the traditional diet, rich in vitamin A, might affect the risk, because vitamin A has been proposed as a protective factor for bladder cancer.69 A general low incidence of bladder cancer in Chinese populations could also suggest a common genetic protection.70

Cancer of the haemopoietic system
Cancers of the haemopoietic system are rare in Inuit populations compared with white populations and equal the low incidence noted in Chinese populations. Although the risk of leukaemia and non-Hodgkin lymphoma is about half the risk in white populations, the risk of Hodgkin’s lymphoma seems to be lower. A risk comparable with that in Chinese populations, the absence of temporal development in incidence, and the finding that the risk remains low after migration to high-incidence areas,27 suggest that genetic factors are influential in the aetiology.

Effect of environmental contaminants
The accumulation of heavy metals and organic pollutants in the Arctic food chain has attracted substantial attention in recent decades. The biomagnifying of contaminants up the food chain results in a large exposure for Inuit, and, consistent with a high intake of marine mammals, high levels of persistent organic pollutants (eg, polychlorinated biphenyls, pesticides, and dioxins) and heavy metals have been detected in Greenlandic and Canadian Inuit.69,71 There is considerable variation in the concentrations measured in the different Inuit populations, but concentrations are all above their respective national populations. The effect of these contaminants on cancer development in Inuit is difficult to assess. Although organic pollutants and heavy metals have shown mutagenic and carcinogenic properties in an abundance of experimental studies, evidence from observational studies is ambiguous. No increased risk of cancer has been noted in workers exposed to polychlorinated biphenyls,72 whereas other studies point to an association between polychlorinated biphenyls and breast cancer in conjunction with certain genetic polymorphisms involved in carcinogen activation.73 The sparse epidemiological data available suggest an increased risk of lung, kidney, and CNS cancers associated with heavy methyl mercury exposure.74 The effect of environmental contaminants on the increasing incidences of lung and breast cancer in Inuit is difficult to assess, because synchronous changes in smoking prevalence, diet, and the fertility pattern can explain a large part of the increase. The incidences of kidney and CNS cancers have remained stable in the Inuit populations, implying either a small effect of the contaminants or an induction period too long for the effect to be present in the available cancer statistics. Most studies addressing a possible association between modern lifestyle factors and the risk of cancer have been done in non-Inuit populations. Although most of the findings can probably be extrapolated to Inuit populations, at least to some extent, caution is needed, because studies of non-malignant diseases suggest that certain risk factors might act differently in Inuit and white populations. For example, although the metabolic effect of different levels of obesity in Inuit people increases in...
parallel with findings in Europeans, the effect at any level seems to be much less in Inuit populations, especially with respect to indicators such as high-density lipoprotein cholesterol and triglycerides. Thus, future studies on specific risk factors for cancer development in Inuit are important.

Conclusion
Inuit populations continue to show a unique distribution of malignant diseases. The genetic and environmental factors determining this pattern are still widely unknown, but the distinctive association between the EBV-associated carcinomas of the nasopharynx and salivary glands suggests risk factors specific for this population. Thus, research to identify factors affecting the risk of cancer in this specific population might provide new insight into cancer causality. Additionally, the effect of rapid introduction of lifestyle-associated risk factors in a population with a traditionally low risk of malignancies that are common in white populations also represents an area with clear potential for research and prevention. In view of the small size of the Inuit populations, collaborative studies that take advantage of pooling populations across the Arctic should be promoted.

Conflicts of interest
The authors declared no conflicts of interest.

References