Cancer in beluga whales from the St Lawrence Estuary, Quebec, Canada: A potential biomarker of environmental contamination[1]

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ABSTRACT

A population of approximately 500 white whales (*Delphinapterus leucas*) inhabits a short stretch of the St Lawrence Estuary which drains one of the most industrialised areas of the world. Over a 12-year period (1983-1994), 73 carcasses out of 175 beluga[2] whales reported stranded on the St Lawrence Estuary shoreline have been examined. Of these 73 carcasses, 14 (19%) were affected by 15 different malignant tumours (cancers), one animal being affected by two different types of cancer. Overall, 23% of necropsied sexually mature animals were affected by cancer. Forty percent of the 35 cancer cases reported world-wide in cetaceans occurred in this population. The estimated annual incidence rate (AIR) of cancer in St Lawrence beluga whales, a minimum figure of 233/100,000 animals, is much higher than that reported for any other population of cetaceans, and is similar to that of man, and of hospitalised cats and cattle. More specifically, the AIR of small intestinal cancers in the studied population, a minimum figure of 83/100,000 animals, is much higher than that observed in man and all animals, except in sheep in certain parts of the world, where an environmental carcinogen is believed to be etiologically involved.

KEYWORDS: POLLUTION-PAHS; WHITE WHALES; BIOMARKERS; DISEASE

INTRODUCTION

Despite the significant number of post-mortem examinations performed on cetaceans over the last 50 years, a relatively small number of cancers (malignant tumours) have been reported in these animals (e.g. Landy, 1980; Howard *et al.*, 1983; Geraci *et al.*, 1987). In a review of cetacean tumours, Geraci *et al.* (1987) examined the accuracy of diagnosis of reported neoplasms and concluded that no causal association could be identified between the reviewed tumours and environmental pollutants. Since that publication, most of the additional cases of cetacean cancers have been reported from the small (*ca* 500-1,000 animals; Kingsley, 1996) beluga whale population inhabiting the St Lawrence Estuary (Martineau *et al.*, 1988; 1995; Girard *et al.*, 1991; De Guise *et al.*, 1994). It has been

[1] A version of this paper was submitted to the IWC workshop on Chemical Pollution and Cetacean, March 1995, Bergen as SC/M95/P10.

[2] The official IWC common name for *Delphinapterus leucas* is the white whale. However, as the common name used in previous papers relating to this population is the alternative 'beluga whale', this has been retained for this paper.

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suggested that this high prevalence might be etiologically related to environmental contaminants (Martineau *et al.*, 1988; 1994; 1995; De Guise *et al.*, 1994). The purpose of this paper is to review reported cases of cancers in free-ranging cetaceans, and to compare the cancer prevalence found in St Lawrence beluga whales with that prevailing in other cetaceans, domestic animals and man. Two new cases of gastrointestinal cancer for cetaceans, a gastric adenocarcinoma and a small intestinal adenocarcinoma are also described.

MATERIALS AND METHODS

Previously reported cases

Published cases of cancers reported in free-ranging cetaceans and those listed in the Marine Mammal Database of the Registry of Comparative Pathology (Armed Forces Institute of Pathology (AFIP), Washington DC, 20306) were reviewed. The database includes tissue glands, glass slides, paraffin blocks and photographs from captive and free-ranging marine mammals affected by neoplasia, congenital conditions and diseases caused by parasites, bacteria and viruses. The samples are supplied from the USA and other countries on a voluntary basis by professionals (mostly biologists and veterinarians) involved with marine mammals. At the end of 1995, the database included reference to 834 diseased cetaceans (including 13 of the 14 St Lawrence white whales affected with cancer). Over 90% ($n = 774$) of the database examples originated from necropsies with the remainder ($n = 60$) from surgical submissions from live animals. In addition to the 13 white whales from St Lawrence a further 14 white whales affected by various diseases were included, all of which were captive. Of these, six were adults (10, 15, 19 and 26 years and two of unknown age but considered 'adults'), one was a new-born (4 days), a second was a juvenile (3 months) and the last was immature (3 years); the age of five animals was not reported. Samples from all of these whales were obtained from necropsies whilst three came from live diseased animals.

Biological sampling

Since January 1983, 175 beluga whale carcasses have been found drifting or stranded along the shoreline of the St Lawrence Estuary, Quebec, Canada. Some 42% ($n = 73$) were examined at the Faculté de Médecine Vétérinaire of Université de Montréal, of which 85% ($n = 62$) were sexually mature.

Cancer epidemiology in St Lawrence beluga whales

Assuming that the St Lawrence animals are a distinct population, the total incidence of cancers in the studied population during the study period can be expressed as:

$$\hat{N}_C = \frac{N_c}{M_A} \times M \text{ where:}$$

$\hat{N}_C$ = the estimated number of cancers in the population;
N_c = the number of autopsied animals with cancer;
M_A = the number of autopsied animals; and
M = the estimated minimum total mortality.

This assumes that the animals that are autopsied are representative of the total stranded 'population'. If it is assumed that all dead animals strand, then $M = M_s$, where $M_s =$ the number of stranded animals. However, weather conditions in the region mean that strandings can only be detected for 9 months of the year. If it is assumed that mortality is uniform throughout the year then;

$$M = M_s \times \frac{12}{9}$$

For other species, the parameter usually estimated is the annual incidence rate of cancers (AIR) expressed as the number of cancers per 100,000 individuals. Following Dorn and Priester (1987), for the study population this would be:

$$AIR = \frac{N_c}{T} \times \frac{100{,}000}{N_t}$$

where T is the study period in years and N_t is the estimated total population size. This assumes that N_t has been constant over the duration of the study.

The validity of the assumptions involved is discussed later in the paper. A crude sensitivity test is carried out by assuming different values for population size, N_t, and the correction factor for poor weather (see Tables 4 and 5). The scenarios tested have been termed: 'best' i.e. reflecting our view of the most likely values; 'optimistic' i.e. assumed values that lead to a lower AIR in the population and 'pessimistic'; i.e. assumed values that lead to a higher AIR.

RESULTS

Cancers reported in cetaceans

Malignant neoplasms that have been reported in free-ranging cetaceans are listed in Tables 1, 2 and 3. A total of only 35 cancers have been reported in two species of Mysticeti and nine species of Odontoceti.

High percentages of those cancers were found in the digestive (12/35 or 35%) and reproductive (9/35 or 26%) systems. The high number of ovarian cancers is probably explained by the emphasis put on the examination of the reproductive system during evaluation of the productivity of commercially exploited species (Geraci *et al.*, 1987).

Cancer incidence in the St Lawrence population

From equations (1) and (2) above and the parameter values listed in Table 5, the total incidence of animals with cancer in the studied population is about 45, translating to an AIR of about 750 animals per 100,000 for the 'best' scenario. The results of the sensitivity analysis are considered in the 'Discussion'.

Nature of the cancers in St Lawrence beluga whales

Two new gastrointestinal cancers

The carcass of an adult male beluga whale *(Dl-1-94)* was found drifting offshore near Tadoussac (48°7'N, 69°43'W) on 24 May 1994. The major finding of the necropsy was a large (9×7×2cm deep) ulcer present on the mucosa of the second gastric compartment. The ulcer was connected to the abdominal cavity by a 7mm-diameter perforation. Microscopic examination (performed in May 1995) revealed that the *tunica submucosa* and the *tunica muscularis* of the gastric wall adjacent to the ulcer were heavily infiltrated by large numbers

Table 1

Cancers reported in beluga whales from the St Lawrence Estuary (1983-1994).

Organ	Cancer type	Age (yrs)	Sex	Date of stranding	AFIP accession no.[1]	Reference
Urinary bladder	Transitional cell carcinoma	17	M	1983 (Dl-18-83)[2]		Martineau *et al.*, 1985
Intestine	Adenocarcinoma	29+	M	1989 (Dl-7-89)	2462295-3	De Guise *et al.*, 1994
Intestine	Adenocarcinoma	20+	M	1989 (Dl-8-89)	2462247-4	De Guise *et al.*, 1994
Intestine	Adenocarcinoma	25+	M	1993 (Dl-2-93)	2461200	Martineau *et al.*, 1995
Intestine	Adenocarcinoma	27+	M	1994 (Dl-2-94)	2464226-6	Martineau *et al.*, 1995
Intestine	Adenocarcinoma	27+	F	1994 (Dl-7-94)	2508083-900	This report
Stomach	Adenocarcinoma	21+	F	1988 (Dl-4-88)	2456949-3	De Guise *et al.*, 1994
Stomach	Adenocarcinoma	27+	M	1994 (Dl-1-94)	2508095-300	This report
Salivary gland	Adenocarcinoma	24	M	1986 (Dl-6-86)	2457053-3	Girard *et al.*, 1991
Liver	Adenocarcinoma	22+	F	1988 (Dl-9-88)[3]	2456952-7	De Guise *et al.*, 1994
Mammary gland	Adenocarcinoma					
Ovary	Granulosa cell tumour	24.5	F	1985 (Dl-2-85)	2519612	Martineau *et al.*, 1988
Ovary	Granulosa cell tumour	21+	F	1988 (Dl-13-88)	2462292-0	De Guise *et al.*, 1994
Ovary	Dysgerminoma[4]	25+	F	1989 (Dl-6-89)	2462229-2	De Guise *et al.*, 1994
Mediastinum	Poorly differentiated malignant neoplasm (cancer)[5]	18+	M	1990 (Dl-1-90)	2519747	De Guise *et al.*, 1994

[1]All cases have been submitted to the AFIP except Dl-18-83 which has been confirmed by Daniel Cowan, Department of Pathology, University of Texas Medical Branch, Galveston, Texas 77555-0588, USA. This case has also been confirmed in Geraci *et al.*, 1987. [2]Dl-18-83 is the 18th beluga examined in 1983. The same system was used for the classification of all carcasses. [3]Dl-9-88 was affected by two cancers. [4]Classified as Granulosa Cell Tumor in De Guise *et al.*, 1994. Reclassified as Dysgerminoma after consultation with AFIP. [5]Classified as metastatic poorly differentiated carcinoma in De Guise *et al.*, 1994. Reclassified as poorly differentiated neoplasm after consultation with AFIP.

of irregularly-shaped tubular glands separated by moderate amounts of connective tissue (Fig. 1). The tubular structures were lined by closely packed cuboidal cells that generally formed a single layer but occasionally piled up in a disorderly manner (Fig. 2). The tumour cells had varying amounts of eosinophilic cytoplasm and the generally round nuclei were hyperchromatic, often crowded, varied moderately in size and occupied a central position. Chromatin was finely to coarsely clumped and nucleoli could not be seen. The nucleus:cytoplasmic ratio was higher than one. Mitoses were rare. Multifocal aggregates of predominant macrophages were observed in the stroma with small numbers of plasmocytes and neutrophils. Accordingly, a gastric adenocarcinoma with a secondary perforating ulcer was diagnosed.

The carcass of a female beluga whale (*Dl-7-94)* was found at Saint-Paul du Nord (48°34'N, 69°15'W), on 25 December 1995. During the necropsy, it was found that the duodenal segment wall was diffusely thickened (3cm) over a length of 20cm at the junction with the stomach. The demarcation between the distal normal intestinal wall (1cm thick) and the thickened segment was abrupt. Microscopically, the intestinal wall was thickened by cellular nodules present mostly in the *tunica submucosa*. These nodules, separated by an abundant fibrous stroma, were composed of irregularly-sized and poorly-formed tubular glandular structures and nests of tumour cells that were separated by smaller amounts of stroma where single tumour cells were often present. Infiltrating tumour cells were also present in large numbers in the subjacent *tunica muscularis* where they formed small

Table 2

Cancers reported in free-ranging cetaceans, other than St Lawrence beluga whales.

Species	Organ	Cancer	Age	Sex	Sources	Reference
Bottlenose dolphin	Liver, lungs	Reticuloendotheliosis		F		Pers. comm. in Landy, 1980
Bottlenose dolphin	Pancreas	Carcinoma	Adult	M		Pers. comm. in Landy, 1980
Bottlenose dolphin	Spleen, lymph nodes	Lymphosarcoma	Adult	F		Pers. comm. in Landy, 1980
Pacific white-sided dolphin	Spleen, lymph nodes	Lymphosarcoma	Adult	M		Howard *et al.*, 1983
Pacific white-sided dolphin	Spleen, lymph nodes, liver, kidney	Eosinophilic leukemia	Adult	M		Howard *et al.*, 1983
Pilot whale	Ovary	Granulosa cell tumour	Adult	F		Bernischke and Marsh, 1984
Harbour porpoise	Unknown	Adenocarcinoma		F	British waters	Baker and Martin, 1992
Harbour porpoise	Stomach	Adenocarcinoma	Adult	F	Northern Wadden Sea	Breuer *et al.*, 1989
Amazon river dolphin	Lung	Squamous cell carcinoma	Adult	F		Geraci *et al.*, 1987
Blue whale	Ovary	Granulosa cell tumour	Adult	F	Antarctic	
Fin whale	Ovary	Granulosa cell tumour	Adult	F	Antarctic	Rewell and Willis, 1949
Fin whale	Ovary	Granulosa cell tumour	Adult	F	Antarctic	Rewell and Willis, 1949
Fin whale	Ovary	Carcinoma[1]	Adult	F	Antarctic	Stolk, 1952

[1]Reclassified as Granulosa cell tumour by Geraci *et al.*, 1987.

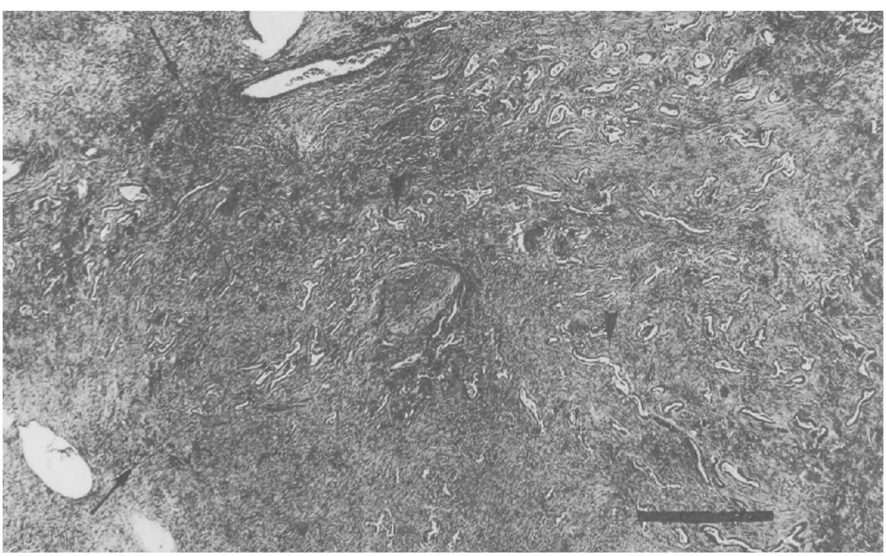

Fig. 1. Gastric adenocarcinoma in a beluga whale (DL-1-94). Numerous irregularly-shaped, tubular, gland-like structures (arrowheads) infiltrate the *tunica submucosa* of the second gastric compartment and are separated by a moderately abundant collagenous stroma. Arrows show the boundary between the normal *tunica submucosa* (left and right corners) and the infiltrating tumour cells (right). Bar: 0.5mm.

Table 3

Cetaceans affected by cancer listed in the Marine Mammal Database, AFIP (updated, December 1995).

Species	Status	Organ	Cancer type	Age	Sex	Sources	%[1]	Accession no.
Beluga	Captive	Brain	Carcinoma	19yrs	M	Arctic	7.1% (14)	2034441
Bottlenose dolphin	Wild	U[2]	Tubulopapillary adenocarcinoma	Adult	M	Gulf of Mexico	0.3% (384)	2304654
Bottlenose dolphin	Wild	Kidney	Renal cell carcinoma	Adult	F	Atlantic Ocean (S. Carolina)	0.3% (384)	2445679
Fin whale	Wild	Kidney	Lymphosarcoma	Adult	F	U	20% (5)	1470245
Killer whale	Captive	Liver, lymph node, spleen	Reticuloendotheliosis	Adult	F	U	5.3% (19)	162636
Killer whale	Captive	Lymph node	Hodgkin's disease-like[3]	Adult	M	Iceland	5.3% (19)	2337420
Pygmy sperm whale	U	Liver	Cholangiocarcinoma	U	U	U	1.7% (57)	1777514
Spotted dolphin	Wild	Testis, lymph nodes, adrenal glands	Malignant seminoma, Pheochromocytoma	Adult	M	Gulf of Mexico	16.7% (6)	2428264

[1](Number of animals affected by cancers of a given species) over (the total number of animals of this species) × 100; ( ): total number of animals that are listed in the Marine Mammal Database of the AFIP. [2]Unknown. [3]Yonezawa *et al.*, 1989.

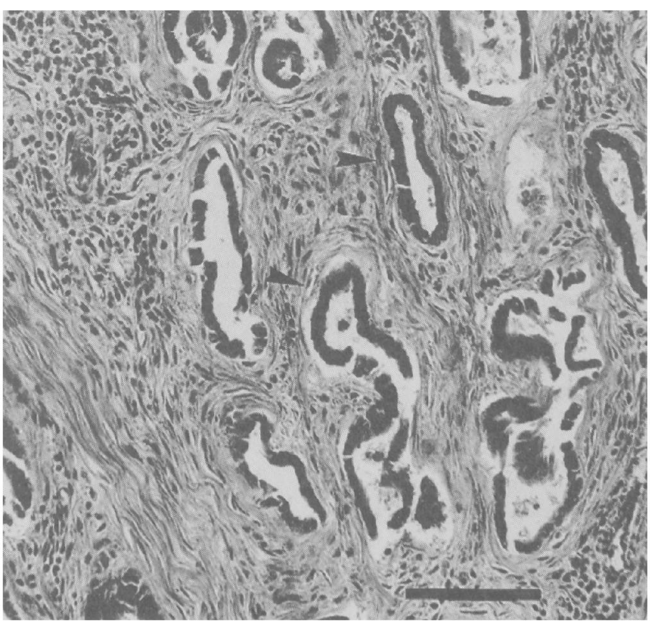

Fig. 2. Gastric adenocarcinoma in a beluga whale (DL-1-94). The glandular structures (arrowhead) are lined by a single layer of well differentiated cuboidal cells. The collagenous stroma contains several interspersed aggregates of mononuclear cells. The apparent detachment of tumour cells into the tubular lumen is due to autolysis. Bar: 100μm.

irregularly-shaped nests or poorly-formed acini with indistinct lumen (Fig. 3). In addition, single tumour cells were generally large, tended to be columnar, were irregularly-sized and shaped and showed loss of polarity. The cytoplasm was scarce, the nucleus:cytoplasm ratio was higher than one and the nuclei were large, variably-shaped and sized. A highly infiltrative small intestinal adenocarcinoma was diagnosed.

Summary of cancer types found

Fifteen cancers were diagnosed in 14 (19%) of the animals necropsied (Table 1). If only sexually mature adults are considered this rises to 23% (Martineau *et al.*, 1988; 1994; De Guise *et al.*, 1994). Some 60% of the malignant tumours originated from the epithelium lining the digestive system (adenocarcinomas of the intestine, stomach, liver and salivary gland) (Girard *et al.*, 1991; De Guise *et al.*, 1994; Martineau *et al.*, 1995). Four intestinal adenocarcinomas were close to the stomachs and one was closer to the anus (Martineau *et al.*, 1995).

DISCUSSION

Cancers previously reported in cetaceans

Limitations of the source material

The published material prior to this study does not comprise a systematic survey of cancer incidence in cetacean populations. Rather it reflects the interest of a relatively small number of scientists, particularly in earlier years. For example, only a tiny proportion of the baleen whales killed for commercial purposes this century, even those flensed with biologists present, were examined for cancer (or indeed any other diseases). This reflected the prevailing interest at that time, which was the estimation of population parameters, particularly with respect to reproduction. The same is true for catches of odontocetes. Thus, whilst the low number of reports might be taken as indicative of the relative rarity of cancer, it is impossible to quantify this in any way.

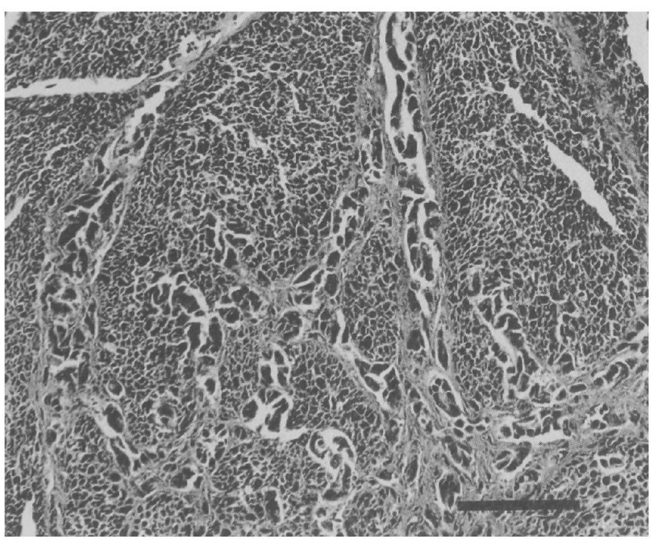

Fig. 3. Small intestinal (duodenal) adenocarcinoma in a beluga whale (DL-7-94). Multiple poorly-formed glandular structures and nests of epithelial cells infiltrate the duodenal *tunica muscularis* along fibrous septa. The empty spaces result from autolysis. Bar: 200μm.

However, there have been some relatively systematic studies. For example, a single cancer was found during the post-mortem examination of 301 cetaceans from British waters (J.R. Baker, University of Liverpool, pers. comm.), only one cancer was found by Geraci *et al.* (1987) in over 1,800 cetaceans examined and no tumours were found in approximately 50 beluga whales examined in the Arctic (D.J. St. Aubin, pers. comm. *in* De Guise *et al.*, 1994). In two other studies, neither Stroud and Roffe (1979) nor Howard *et al.* (1983) reported neoplasms from 21 stranded cetaceans and 65 stranded common dolphins (*Delphinus delphis*), respectively. Philo *et al.* (1993) reported that only one (apparently non-malignant) tumour had been found in 130 bowhead whales (*Balaena mysticetus*) examined between 1980 and 1989, but cautioned that the quality of the examinations were not consistent, depending on the personnel present and the prevailing conditions.

However, there are problems in quantitatively interpreting data from each of the above studies. For most, there is insufficient information available on the animals examined, in terms of how they were selected, associated biological data and their species and population identity. Interpretation of the Arctic beluga data is confounded by the fact that the ages of the animals are not known and, as discussed later, age may be a significant factor in cancer incidence.

The present review reveals that the St Lawrence population is the best studied cetacean population (as a proportion of the total population size) with respect to pathological studies.

The other major source of information was the AFIP database. This again clearly cannot be taken as providing a representative sample. It is by its nature confined to diseased animals submitted on a voluntary basis. Reasons for submission will be variable and unpredictable.

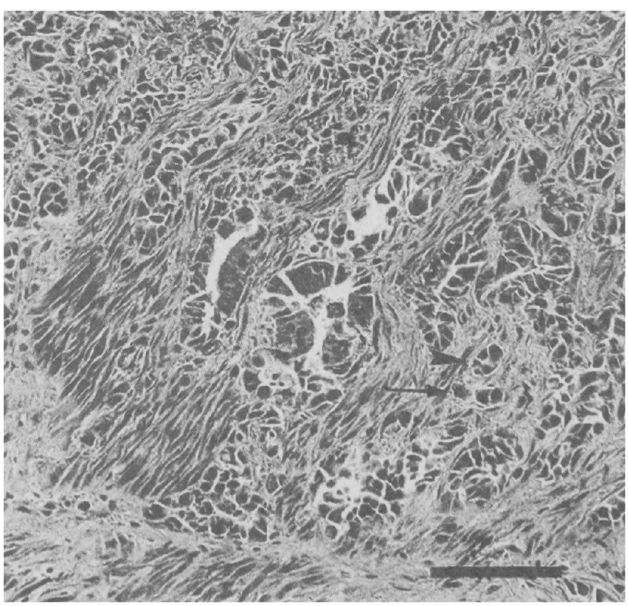

Fig. 4. Small intestinal (duodenal) adenocarcinoma in a beluga whale (DL-7-94). Tumour cells infiltrating the intestinal tunica muscularis tend to form glandular structures. Cellular nests (arrowhead) and individual tumour cells (arrow) are also observed. Note the loss of polarity of tumour cells and their markedly variable shape and size. Bar: 100μm.

Cases are usually sent to the AFIP in order to obtain the opinion of the AFIP's pathologists and/or because the cases are unusual or otherwise of interest. Samples will be biased towards captive animals (of which the number of species is limited and which may also include animals kept for most, if not all of their life in an artificial environment) and stranded animals, and probably the North American region. There are a number of well-known problems in the interpretation of such data. Age data will be of varying sophistication (as witnessed in Table 3 where only one animal is of known age). This is not to suggest that the data are of no value but rather to insert a note of caution into their interpretation.

Cancer incidence in the St Lawrence population

In the 'Materials and Methods' section, a number of assumptions were identified in the calculation of AIR. The validity of these is discussed below.

Can the St Lawrence animals be considered a separate population?

In veterinary, as in human epidemiology, the number of individuals at risk must be known precisely in order to determine the prevalence of disease. This requirement explains why there have been few epidemiological studies of cancer in wild mammals and especially in marine mammal populations, which are notoriously ill-defined and/or widespread.

However, the geographical isolation of the St Lawrence animals in a restricted, relatively small area at the southernmost range of the species means that they can be treated as a separate population (e.g. Bjørge *et al.*, 1994, pp.83-4). This population is believed to have declined from an estimated 5,000 to about 500-1,000 animals (*ibid.*, Table 9; Reeves and Mitchell, 1984), and is confined to a short stretch of the St Lawrence Estuary located downstream of a basin heavily contaminated by industrial pollutants. These whales have been the objects of numerous censuses, using a variety of techniques (Michaud *et al.*, 1990; Kingsley and Hammill, 1991; Michaud, 1993). All recent censuses have provided results within approximately the same range (see Table 4).

Are autopsied animals representative of the total population?

The only criterion used to determine whether a given carcass was autopsied was its state of preservation. Thus, it does not seem unreasonable to assume that the autopsied animals represent an unbiased sample of the total stranded animals.

It is assumed that all carcasses have equal chances of being recovered and are examined whatever the cause of death for the following reasons. Given the restricted range of this population and the fact that all carcasses have been found within that range or downstream as a result of drifting (Michaud *et al.*, 1990; Kingsley and Hammill, 1991; Michaud, 1993), apart from the winter period discussed above, it is probable that almost all deaths will result in detectable strandings. Thus, while some deaths may occasionally escape our attention, our

Table 4

Recent population estimates for the St Lawrence beluga population.

Year	Method	Estimate	SE	95%CI	Source
1988	Photo	491	69		Kingsley and Hammill, 1991
1990	Photo	606	308		Kingsley and Hammill, 1991
1992	Visual	490	n/a		Michaud, 1993
1992	Photo	525	71	410-725	Kingsley, 1996
1995	Photo	705	108	540-1035	Kingsley, 1996
	Average	563			

Table 5

Calculation of AIR for the St Lawrence beluga population, including a crude sensitivity test to some of the assumptions made (see text).

	Pessimistic	'Best'	Optimistic
No. of autopsied animals with cancer	14.00	14.00	14.00
No. of autopsied animals	73.00	73.00	73.00
No. of stranded animals	175.00	175.00	175.00
Correction for poor weather	1.50	1.33	1.00
Estimated total mortality	262.50	233.33	175.00
Estimated no. of cancers in the population	50.34	44.75	33.56
Study period in years	12.00	12.00	12.00
Annual estimated no. cancers	4.20	3.73	2.80
Estimated total population size	500.00	500.00	1,000.00
AIR	839.04	745.81	279.68

sampling is most likely representative of the population in terms of causes and extent of mortality (it is in practice a minimum total mortality). However, the correction used for poor weather may be biased downwards to an unknown degree in that it assumes equal mortality throughout the year, when in fact the poor weather may result in higher mortality during those months, as has been seen in some other odontocete species. The extreme ice and weather conditions found at that time of year effectively break down any carcasses into small pieces. Thus, the possibility that carcasses from animals that died during the winter period may still be available for detection, and thus allowed for twice, can be ruled out.

Sensitivity of the results to the assumptions made

Whilst the estimate of an AIR of about 750 per 100,000 individuals represents our best estimate, it is clear that this is assumption dependant. In order to examine the sensitivity of the estimate to the assumptions we have varied some of the parameter values used as shown in Table 4. The table shows that the AIR is heavily dependent on the assumptions made. The crude sensitivity analysis shown in the table (which only examines questions of weather correction and population size) gives a range of AIR values from about 280-840.

Comparison of St Lawrence Estuary beluga whales with other species/populations

Cetaceans

The present review has shown that 40% of the 35 cancers reported in cetaceans have been found in the St Lawrence beluga whale population. This dramatically high figure clearly needs to be interpreted with caution in view of the limitations of the source material discussed above. However, the cancer prevalence in this population is much higher than that observed in the albeit limited studies of other cetacean populations, including Arctic populations of the same species (D.J. St. Aubin, pers. comm. *in* De Guise *et al.*, 1994).

Cancer is generally a disease of old age and thus a longer life expectancy for St Lawrence beluga whales might explain their high rate of cancer. All animals with cancer in our study were over 16 years. A comparison of the age composition of the 135 stranded St Lawrence whales of known age with that of 412 harvested belugas from the Alaskan population (Burns and Seaman, 1985) shows that there are older animals in the Alaskan population (Fig. 5). However, as one might expect, the stranded population is bimodal, with a peak of newborns and then one of older animals in the 18-26 age group, in contrast to the harvested population which is skewed towards younger animals with a single peak at around 6-8 years followed

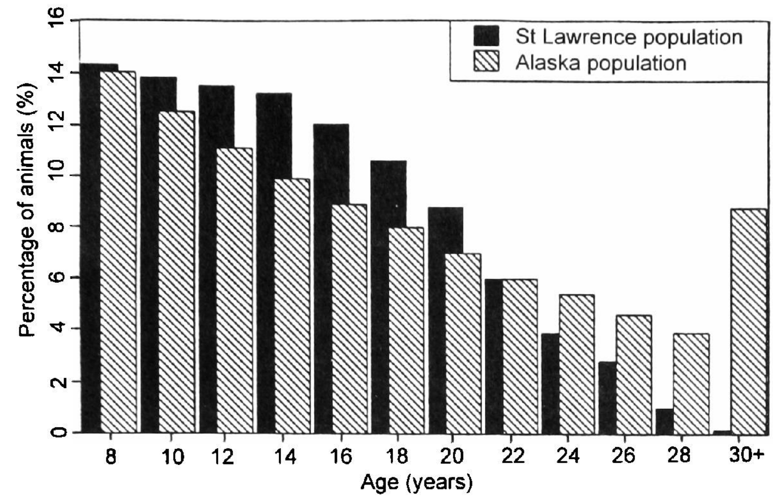

Fig. 5. Comparison of the age structure of the St Lawrence beluga whales (Béland *et al.*, 1988) with the Alaskan population (Burns and Seaman, 1985) according to published life tables.

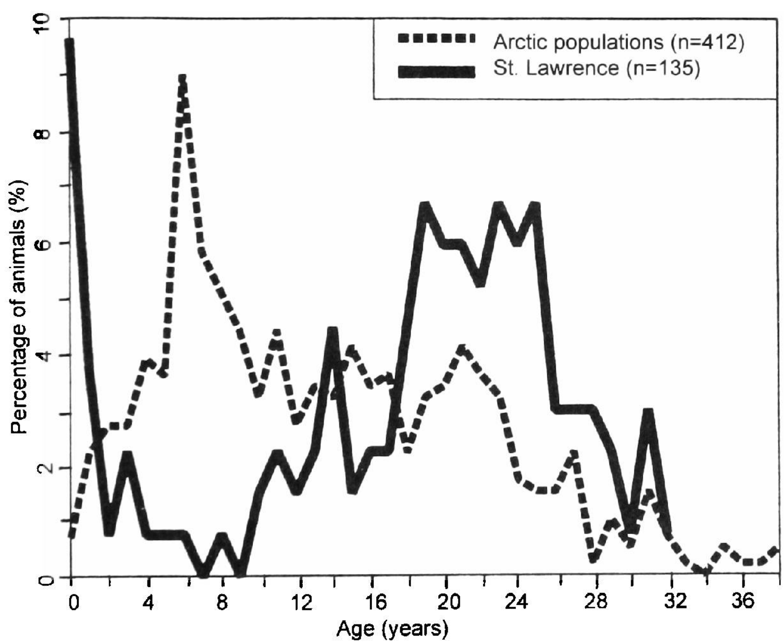

Fig. 6. Comparison of the age distribution of the St. Lawrence Estuary beluga whales found stranded (1983-1994) and the beluga whales sampled by aboriginal hunting in the Arctic (adapted from Burns and Seaman, 1985).

by a general decline (Fig.6). Without knowledge of the age structure of the Arctic population referred to (D.J. St Aubin pers. comm. in De Guise *et al.*, 1994) it is difficult to make a strict comparison of those data with the St Lawrence data that is not potentially confounded by age.

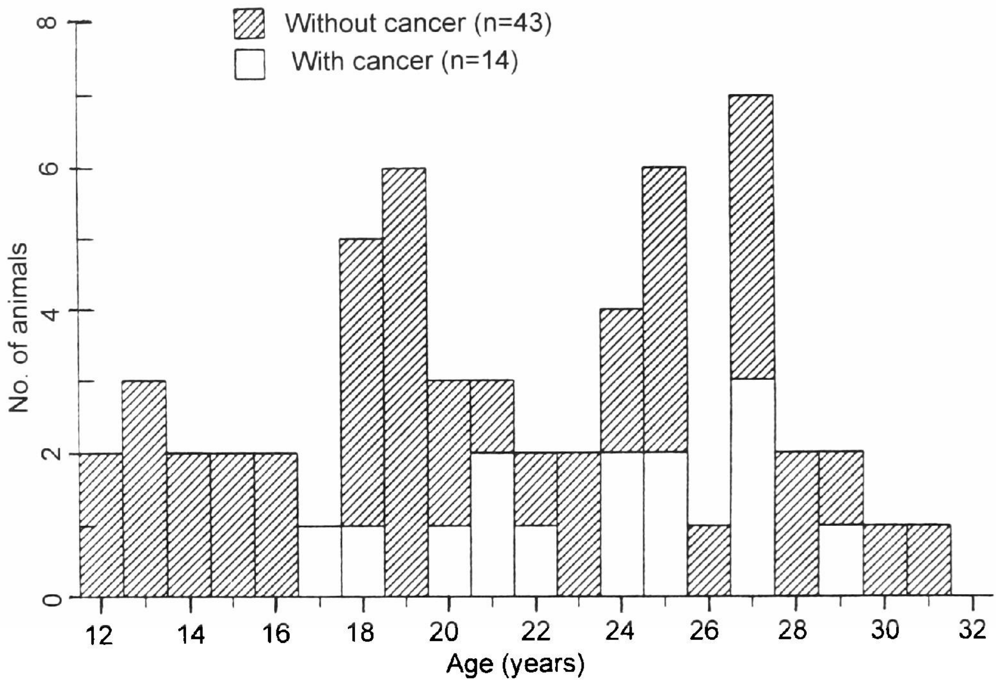

Fig. 7. Age distribution of stranded St Lawrence Estuary beluga whales with and without cancers and older than 12 years (1983-1994).

In mature whales (age 12 and older) with cancer and mature animals without cancers, the mean age of animals with cancer is 23.36 whereas that without is 20.84 (Fig.7). The difference is not significant at the $p > 0.10$ level.

Eight cases of cancers are reported among 834 cetaceans listed in the AFIP's Marine Mammal Database (1%) (Table 3). Whilst this is significantly lower (chi-square = 86.81;1df, $p < 0.01$) than the incidence in the St Lawrence population, the limitations of this database referred to earlier render such statistical tests difficult to interpret in anything more than a general way. It might seem more appropriate to compare the St Lawrence population with only the 14 beluga whales (11 necropsy cases with 1 cancer and 3 surgical biopsy cases with no cancers) included in the database. However, all of the animals were captive and from a variety of populations, and given the small sample size, the fact that there is no significant difference (chi-squared test) between the frequency of cancer (1/11) among the necropsied APIF beluga whales and those from the St Lawrence again does not allow one to reach any firm conclusions.

Other taxa

The populations of domestic species used in epidemiologic studies are animals that were examined at veterinary colleges (Priester and Mantel, 1971; Priester and McKay, 1980). These are probably under better medical care and include more sick animals than the general animal population. In addition, the older animals are more numerous in the pet animal population owing to curative and preventative improvement in veterinary medicine (Dorn and Priester, 1987).

Free-ranging animals generally have a shorter life span than captives because of predation, harsh environmental conditions and malnutrition. Since the risk of developing cancer increases with age, it is reasonable that cancer rates in pet, zoo and aquarium animals would be higher than in free-ranging mammals (Fowler, 1987). Yet, for all cancer types, our 'best' AIR estimate for St Lawrence belugas is much higher than that observed in horses and cats, is slightly lower than the rate observed in dogs and is twice that of man. Even if the 'optimistic' scenario is chosen, the value is comparable with that of cats and horses and close to that of man.

In addition, the rate of gastrointestinal cancers affecting St Lawrence belugas appears much higher than the rate observed in man and domestic species, with the exception of sheep in certain parts of the world. Thus, not only does this whale population appear to have a high prevalence of cancer, but this is particularly marked with regard to adenocarcinomas of the gastrointestinal tract (intestine, stomach and salivary glands); such tumours accounted for half of the malignant tumours found (Table 6).

Table 6

Frequency of cancer in St Lawrence estuary beluga whales over 12 years (1983-1994) compared to that of man and domestic animals. Estimated annual incidence rate of cancer per 100,000 animals (AIR).

	Total cancer	Epithelial cancer of the small intestine	Epithelial cancer of the gastrointestinal tract[1]
Beluga	233 (750)[2]	83 (266)[7] 67 (212)[8]	117 (327)
Man[3]	363.4	0.8	55.6
Cattle[4]	177.2	2.78	2.78
Dog[5]	828.3	6.87[9]	24.3
Cat[5]	257.4	26	29.2
Horse[5]	256.3	0	7.7
Sheep[6]	0.03	up to 2,000	ND

[1]Gastrointestinal tract: glandular stomach, small and large intestine combined. [2]( ): AAIR: adjusted AIR accounting for mortality in winter months and for total mortality. [3]Man (Anonymous, 1991; Anonymous, 1992). [4]Cattle (Priester and Mantel, 1971; Priester and McKay, 1980; Bristol *et al.*, 1994). [5]Dog, cat, horse (Priester and Mantel, 1971; Priester and McKay, 1980). [6]Sheep (Georgsson and Vigfusson, 1973). [7]Five cancers of the small intestine (if the most distal intestinal adenocarcinoma is considered as affecting the small intestine). [8]Four cancers of the small intestine (if the most distal intestinal adenocarcinoma is considered as affecting the large, instead of the small intestine, Martineau *et al.*, 1995). [9]Sum of epithelial cancers listed under 'small intestine' and 'intestine not otherwise specified' in Priester and McKay, 1980.

Several etiologies for the high prevalence of a specific cancer cell type in such a small population can be envisaged.

In cattle, small intestinal cancer results from an interaction between exogenous carcinogens and viruses. Bovine papillomavirus type-4 causes papillomas in the bovine upper digestive tract. In cattle infected with that virus and fed with bracken fern, a plant that contains powerful carcinogens, these benign tumours become malignant and are accompanied by intestinal adenomas and adenocarcinomas that do not contain viral DNA (Campo *et al.*, 1994). thus, viral infection alone does not cause cancer. A similar interplay might be at work in St Lawrence belugas since gastric papillomatosis has been observed in a significant number of carcasses and particles consistent with papillomaviruses have been visualised in papillomas (Martineau *et al.*, 1988; De Guise *et al.*, 1994).

In contrast to their rarity in other animals, high prevalences (0.2-1.58%) of intestinal adenocarcinomas are observed in sheep in some regions of Australia and New Zealand.

Ingestion of environmental carcinogens, particularly phenoxy and picolinic acid herbicides, are thought to be major etiological factors of these endemic cancers (e.g. Dodd, 1960; Webster, 1966; Cordes and Shortridge, 1971; Georgsson and Vigfusson, 1973). Carcinogens are also present in the environment of St Lawrence belugas and are probably ingested by these animals. The Saguenay River is part of the St Lawrence belugas' habitat. Its sediments contain 500-4,500ppb of total polycyclic aromatic hydrocarbons (PAH) (dry weight) (Martel *et al.*, 1986). Benzopyrene DNA adducts were detected in St Lawrence beluga tissues, and were absent from the brain and liver of four Arctic whales (Mackenzie Estuary) (Shugart *et al.*, 1990). Beluga whales, unique among odontoceti in that regard, are known to feed in significant amounts on bottom invertebrates (Vladykov, 1944; 1946). They dive comfortably down to 400 meters (Ridgway *et al.*, 1984). In addition, field observations suggest that these whales dig into sediments (Dalcourt *et al.*, 1992). Considered together, these observations suggest that St Lawrence belugas ingest carcinogenic compounds, which might explain the high rate of digestive tract cancers seen in this population.

This situation would not be without precedent. In bottom-dwelling fish, labial papilloma and liver cancer are strongly associated with chemical contamination of sediments (Harshbarger and Clark, 1990). Interestingly, in humans, gastric cancers and the rare epithelial cancers of small intestines have been associated with the ingestion of smoked food, which are contaminated with benzopyrene (Chow *et al.*, 1993).

That small intestinal cancer might be a feature of beluga whales as a species appears unlikely; the presence of only a single case of cancer (not intestinal) among the 17 beluga whales listed in the Marine Mammal Database and the absence of this condition in the literature do not support this hypothesis.

Inbreeding has led to some degree of genetic homogeneity in St Lawrence belugas (Patenaude *et al.*, 1994). Cancers have not been reported in genetically highly homogenous wild animals such as free-ranging cheetahs and Florida panthers (O'Brien, 1994). In man, rare forms of cancers are known to be inherited (Cotran *et al.*, 1994). However, in free-ranging animal populations there are no reports which document genetic susceptibility to certain types of cancers, although some reports do suggest that such susceptibility concerns free-ranging animals that have been kept in captivity for months or years (Carpenter *et al.*, 1981).

CONCLUSION

This paper has highlighted the limited amount of data available on cancer in cetaceans that can be used in a rigorous quantitative manner. Despite this, it is clear from examining the available data from cetaceans and other mammals, that there appears to be an unusually high incidence of cancer in the St Lawrence beluga population. There is evidence to suggest that this may be related to chemical pollutants but the difficulties of establishing such a cause-effect relationship are well-known and will require a major dedicated research programme (see Reijnders *et al.*, 1999).

Convincing statistics would require much larger numbers of whales and/or the follow-up of St Lawrence belugas for many more decades. These are drawbacks that have long been recognised by cancer epidemiologists and that have been partly solved by studying large numbers of bottom-dwelling fish (Harshbarger and Clark, 1990) or small numbers of dogs in well designed epidemiological studies using age, breed and sex-matched controls. In the latter studies, cancer specific types have been associated with exposure to asbestos and insecticides (e.g. Glickman *et al.*, 1983; 1989; Hayes *et al.*, 1991).

The observation of high cancer prevalences in other populations of marine mammals similarly exposed to carcinogens would strengthen an etiological relation with chemical carcinogenesis (Fox, 1991). Such observations have recently been made; 65 cases of metastatic carcinomas have been reported in 370 California sea lions stranded alive from 1979 to 1994 along the Californian coast (7.6% of necropsied animals) (Gulland *et al.*, 1996) and in eight adult sea lions out of 82 (9.7% of necropsied animals) in 1993-94 (Holshuh *et al.*, 1995). In both instances, exogenous carcinogens have been considered as possible etiological agents.

The etiological role of contaminants in cancer of marine mammals would be supported by the absence of tumours in stranded animals from non-exposed populations and by the detection of specific, identical mutations in genes such as *ras* or p53 in tumours. The possible contribution of other factors to the etiology of cancer in St Lawrence belugas such as genetic homogeneity and viruses should also be examined.

Acknowledgments

We wish to thank Bruce Williams from the Department of Veterinary Pathology, AFIP, for his help, B. Clausen from the Environmental Investigation Agency, the Ministry of Environment, Government of Denmark and Greg Donovan of the International Whaling Commission for reviewing the manuscript and providing useful comments.

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