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Prospective Study of Dog Bite and Childhood Cancer[1]

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SUMMARY

Approximately 50,000 children who were bitten by dogs have been followed for 5 or more years to assess their risk of dying from cancer. An analysis was made that measured the immediate and continuing risk of death and also allowed for a latent period and an interval between onset and death. Total observed leukemia-lymphoma deaths were less than expected until 4 or more years after the bite. Standardized leukemia-lymphoma mortality ratios for the age group 10 to 14 rose to approximately 3-fold following an interval of 4 or more years after the bite, a result which is almost statistically significant at the 5% level. However, this finding was not consistent for other age groups.

These observations provide interesting but inconclusive epidemiological support for the hypothesis that dog bite is one type of initiating event in the occurrence of leukemia-lymphoma in children. Further inquiry is needed. The overall results of this study indicate that children bitten by dogs are not at substantial risk of developing leukemia-lymphoma.

INTRODUCTION

Interest in dogs and cats as possible primary hosts to an oncogenic virus that can produce human cancer has been stimulated by recent laboratory findings. Cats have been most suspect since the viral etiology of feline leukemia was established (7–9, 11) and its transmission to human embryonic living cells was achieved (6, 10, 12). An observation of feline leukemia virus has been made in the salivary glands of leukemic cats (5), which suggests that a bite or scratch could be a mode of transmission.

Evidence of virus-like particles has also been found in tumorous dogs (1), and there have been several case reports of human and canine leukemia related temporally and geographically (3, 14). Epidemiological evidence from two retrospective studies is negative, but inconclusive. Schneider *et al.* (13) found no significant association between human and canine cancer in the same household. Van Hoosier *et al.* (14) compared 2 groups of leukemic children: (*a*) those who had contact with dogs; and (*b*) those who were bitten by dogs, to nonleukemic controls. They found no significant association between childhood leukemia and previous dog bite or contact.

Presented here are the results of a prospective study of a large population of children bitten by dogs who have been followed for 5 or more years for deaths from cancer. A population of 6500 children bitten or scratched by cats has also been followed; however, this data base is too small to warrant a meaningful analysis. Two childhood leukemia deaths and 1 death from neuroblastoma have been observed in the cat bite/scratch population, which is close to expectation.

MATERIALS AND METHODS

The study population was formed from the animal bite reports received by the Los Angeles County Health Department from 1961 to 1963 and consisted of 49,239 children under 15 years old with a dog bite. The geographic area covered in the study included all of Los Angeles County, except Los Angeles City, Pasadena, and Long Beach. The estimated average population at ages 0 to 14 in this area at the time the study children were identified was 1,051,900.

The decedents in the study population were identified through California and reallocated death certificates for persons who died at ages 0 to 19 in years 1961 to 1968 with the underlying cause of death attributed to cancer (International Classification of Diseases, Nos. 140 to 204, 7th revision) and through a list with names and birth dates of persons who were born in California but died of cancer in other states at ages 0 to 14 in the years 1961 to 1966. The matching was facilitated by use of an alphabetical index of the bite victims and was carried out independently by 2 clerks who were trained for this task.

A match was considered definite if name, year of birth, and address agreed on the animal bite report and the death certificate. In some cases in which name and year of birth but not address matched on both records, a judgment of nonmatch was made if (*a*) the mother's or father's name was given on both records and was different or (*b*) the place and duration of residence of the cancer victim precluded his having lived in Los Angeles County at the time of the bite report.

In cases of a possible match in which the name was the same

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Table 1

Observed and expected deaths from leukemia-lymphoma and other forms of cancer in children who received a dog bite

The bite victims were identified in Los Angeles County health jurisdiction from 1961 to 1963.

Age	Immediate and continuing risk of death from cancer			3+-year interval between bite and death from cancer			4+-year interval between bite and death from cancer		
	Person years of experience	Observed/ expected[a]	SMR[b]/ 95% CL[c]	Person years of experience	Observed expected	SMR/ 95% CL	Person years of experience	Observed expected	SMR/ 95% CL
				Leukemia-lymphoma[d]					
0–19	317,133	8/13.10	0.61/0.26–1.20	169,434	6/6.64	0.90/0.33–1.96	120,202	5/4.65	1.08/0.35–2.52
0–4	28,800	1/1.39	0.72/0.02–4.00	984	0/0.05		56	0/0.00	
5–9	134,311	1/6.17	0.16/0.00–0.89	62,726	0/2.87	0/0.00–1.05	38,698	0/1.77	0/0.00–1.69
10–14	112,250	6/3.49	1.72/0.63–3.75	71,381	6/2.22	2.70/0.99–5.89	53,829	5/1.67	2.99/0.97–6.97
15–19	41,772	0/2.05	0/0.00–1.46	34,343	0/1.50	0/0.00–2.00	27,619	0/1.21	0/0.00–2.48
				Other cancer[e]					
0–19		5/10.79	0.46/0.15–1.07		4/5.80	0.69/0.19–1.77		2/4.13	0.48/0.06–1.73
0–4		1/1.04	0.96/0.02–5.35		0/0.03			0/0.00	
5–9		3/4.45	0.67/0.14–1.96		3/2.08	1.44/0.30–4.20		1/1.28	0.78/0.02–4.34
10–14		1/3.58	0.28/0.01–1.56		1/2.27	0.44/0.01–2.45		1/1.71	0.58/0.01–3.23
15–19		0/1.72	0/0.00–1.74		0/1.42	0/0.00–2.11		0/1.14	0/0.00–2.63

[a] Expected, if average, annual age-sex-cause specific mortality rates in Los Angeles County from 1961 to 1968 prevailed.
[b] Observed deaths/expected.
[c] Based on 95% confidence limits (CL) for the ratio of a Poisson variable to its expectation. Limits on the SMR are not shown where the expectation is less than 0.5.
[d] International Classification of Diseases, 7th revision (ICD-7th), Codes 200 to 205.
[e] ICD-7th, Codes 140 to 199.

or similar and the year of birth agreed ±1 year, but the address was different, a letter or phone call to the parents of either the cancer victim or the animal bite victim was used to solicit the information needed to determine a true or false match.

A total of 3816 in-state cancer deaths and 238 out-of-state cancer deaths were checked against the dog bite index; 68 deaths were considered to be at least possible matches and definitive information as to whether or not the death matched a child in the study population was secured for all but 12 (3 of 5 leukemia-lymphoma deaths and 3 of 7 other cancer deaths for which matches were not confirmed were for children who died outside of Los Angeles County).

Expected deaths by 5-year age groups and sex for leukemia-lymphoma and other cancer were computed with the use of the average, annual age-sex-cause specific mortality rates for Los Angeles County from 1961 to 1968. These rates were applied to the comparable number of exposure-years accumulated by dog bite victims in the study as observed through 1968. SMR's[2] were computed (observed no. of deaths/expected no.) and 95% confidence factors (2-tailed) for the ratio of a Poisson variable to its expectation (4) were used to compute confidence limits for the observed ratios.

The analysis was repeated with all but the 1st year of data, all but the 1st 2 years of data, etc., up to all but the 1st 5 years of data. This allowed for the possibility of a latent period between the dog bite and the onset of cancer and also for an interval between onset and death.

[2] The abbreviation used is: SMR, stardardized mortality ratio.

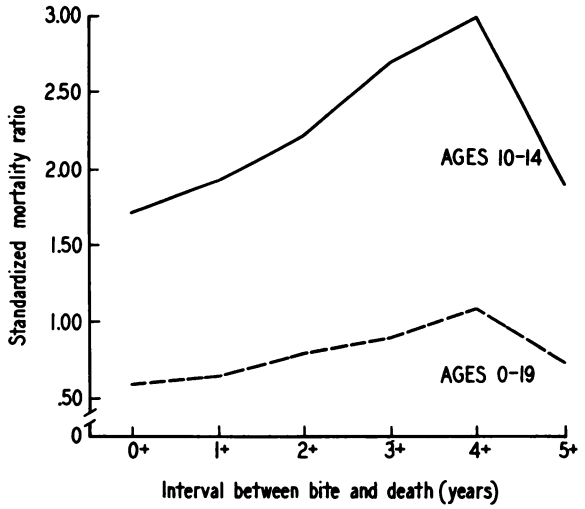

Chart 1. SMR's for leukemia-lymphoma among children bitten by dogs, according to time interval between bite and death.

RESULTS

Table 1 gives the results of the analysis under the assumptions of an immediate and continuing risk of death from cancer after a dog bite and with an interval of 3 or more years and 4 or more years between the animal bite and death.

The total number of leukemia-lymphoma deaths observed is less than expected until there has been a period of 4 or more years separating the bite and death, at which time the SMR for

ages 0 to 19 reaches unity. However, 6 of the 8 leukemia-lymphoma deaths observed were confined to the 10- to 14-year age group (actual ages 10 to 12); all 6 of these deaths occurred more than 3 years after the bite, and 5 of them more than 4 years after the bite. For this particular age group, the risk curve (Chart 1) for leukemia-lymphoma as exemplified by the SMR rises to approximately 3-fold at 4 or more years after the bite and declines at 5 or more years. The SMR's with 3 or more and 4 or more years of delay between the bite and death are almost significant at the 5% level ($p = 0.06$).

There is also an overall deficit of other cancer deaths; however, the SMR for the age group 5 to 9 is almost 1.5-fold at 3 or more years after the bite.

DISCUSSION

If cancer death occurs shortly after a child is bitten by a dog, the disease is not likely to be attributable to the bite. This is because an incubation or latent period of months or even years most likely precedes clinical onset and there is another interval between onset and death. For childhood leukemia, the survival period now averages about 1 year. Therefore, it is appropriate to postulate an interval of more than 1 year from the animal bite to cancer death in testing for an association between the 2 events.

This concept may also account for the deficit in cancer deaths observed over the entire follow-up period. A cancer death is generally preceded by a prolonged period of morbidity in which the patient is confined and his environment is under relatively strict control. Under these circumstances, it is less likely that children with cancer will be bitten than will children who are well and active. Thus, the population of children bitten in a given year would be expected to have a deficit of cancer deaths in the following 12 to 24 months because most chronically ill children are removed from risk of bite exposure.

Some brief speculation on the possible mechanisms whereby dog bite might lead to cancer is useful in putting the results of this study in the proper perspective. If the mechanism is one in which cancer is transferred from a cancerous animal to the child, it should not be expected that animal bites would raise the human cancer rate by more than the animal cancer rate. Dorn *et al.* (2) have reported that the average malignant lymphoma incidence is 24.0 per 100,000 for dogs; the leukemia-lymphoma annual incidence rate for children under 15 years of age is 4.2 per 100,000. Thus 100% transfer of disease by dog bite could lead to an almost 6-fold increase in rates among bitten humans. However, it is more likely that the transfer rate would be on the order of 10% or maybe much less, so that there would be only a small increase among bite victims.

Another possible mechanism, one for which this study is more reasonably suited, hypothesizes that cancers in humans result from a bite from a noncancerous dog, provided only that the animal harbors an agent capable of causing such cancers. The agent or virus would have to be one (or several) occurring with some fair frequency among dogs.

The finding in this study that children bitten in the age group 5 to 9 show a discrete latent period followed by a maximum occurrence of leukemia-lymphoma at ages 10 to 14 with subsequent decline is consistent with the hypothesis that a dog bite was the common initiating event. However, this finding has only borderline statistical significance, and it is weakened by the lack of consistency in other age groups.

Observed deaths are less than expected in age groups 5 to 9 and 15 to 19, with an interval of 4 or more years following the bite. The person years of experience at ages 5 to 9 with a 4+-year interval are contributed mainly by children bitten at ages 0 to 4 (93%), the youngest age group in the study population; similarly, most of the person years at ages 15 to 19 with a 4+-year interval are contributed by children bitten at ages 10 to 14 (84%), the oldest group. It is conceivable that the older children may have a better cancer defense mechanism, or they may simply have become more dispersed and for that reason harder to match with death data. Also, in this study, there is a low probability of detecting a statistically significant difference even if a 3-fold increase exists in the risk of leukemia-lymphoma with a 4+-year interval between bite and death.

The observations are provocative and should encourage further epidemiological study of the relationship between dog bite and childhood leukemia-lymphoma. The need is evident for a large study population and a 10-year follow-up, which would allow for an analysis that provides for a latency period.

The overall results of this study should be interpreted as indicating that children bitten by dogs do not incur an importantly increased risk of developing cancer.

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