North American Liver Fluke (*Metorchis conjunctus*) in a Canadian Aboriginal Population: A Submerging Human Pathogen?

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The North American Liver Fluke (*Metorchis conjunctus*) has long been recognized as an important cause of disease in fish-eating animals from Greenland to Alberta.[1,2] Various piscivores, such as bears and sled dogs, serve as definitive hosts, while the intermediate hosts are the aquatic snail *Amnicola limosa limosa* and several fish, including the white sucker *Catostomus commersoni*. In humans, asymptomatic excretion of *Metorchis* eggs has been described in native communities.[3,4] A 1975 survey of intestinal parasites in Sioux Lookout, Northwestern Ontario found a maximum *Metorchis* prevalence of 10/51 (20%) in Fort Hope.[5]

Symptomatic *M. conjunctus* illness in humans was unknown prior to 1993 when an outbreak occurred following consumption of raw sucker *C. commersoni* prepared as sashimi.[6] Because of this recent confirmation that *Metorchis* infection persists in local fish and also because serious disease (e.g., chronic biliary disease) is linked to infection with liver flukes, we performed a point-prevalence survey in Fort Hope in 1994-95 to determine whether significant carriage of *Metorchis* is still common.

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METHODS

The sampling frame for this seminomadic population was the 1994 nursing station census, which listed 1,602 residents. Excluding children under 18 and those on the census known to be deceased or living elsewhere left 492 eligible adults. A simple random sample of 70 individuals (to detect at least 5% prevalence with 5% precision at significance level of 0.05) was chosen by numbering all eligible individuals from 1 to 492; randomly generated numbers between 0 and 1 were multiplied by 492. Selected individuals were visited, and if in town, were invited to participate in English or Ojibway. After obtaining signed informed consent, a blood sample was drawn and two stool samples in sodium acetate-acetic acid-formalin preservative were requested. As well, 15 dog and 3 bear feces were collected for microscopy, and 6 fish were frozen for analysis.

Stools were processed with two types of sedimentation (formolethyl acetate and citric acid-Tween) as well as zinc sulfate flotation, and read with iodine staining. Serology was performed using an enzyme-linked immunosorbent assay (ELISA) for IgG antibodies against adult *Metorchis* antigens as previously described.[6] Positive controls were cases from the 1993 outbreak (n=19); negative control sera came from healthy lab personnel (n=22).

Statistical analysis employed the chi-square and Student's t-test to compare individuals who participated versus those not included in the study. The binomial method was used to generate 95% confidence intervals for point estimates.

RESULTS

Of 70 individuals selected for study, 46 (66%) were in town and agreed to participate; there were 11 refusals and 13 identified individuals who were out of town at the time of the study. The sex distribution of participants and those not included was the same (25/46 vs. 12/24 male sex, p = 0.84). Participants were slightly younger than non-participants (mean age 38.3 vs. 45.9) but the difference was not statistically significant (p = 0.11). Of the 46 participants, 37 of 46 (83%) provided both stool and serum samples, 1 provided stools and no serum, and 8 provided only serum.

Results of stool analysis of humans, dogs and bears are shown in Table I. *Metorchis* eggs were found in only one individual (1/38, 95% confidence interval: 0.1-13.8%), a well 24-year-old woman. This individual's stools were negative four months later, prior to treatment with praziquantel (75 mg/kg in 3 doses). Results of the serologic analysis indicated no results above 2 standard deviations of the negative controls (0/44, 95% confidence interval: 0-8.0%); relative optical density units for ELISA analysis had the following mean (± standard deviation) results for negative controls, outbreak cases and the present Fort Hope sample, respectively: 223 (±96), 432 (±368) and 177 (±65).

TABLE I
Occurrence of Parasites in Humans and Animals, Winter 1994-95, Fort Hope, Ontario

	Parasites Found	N Examined	N Positive
Humans	*Metorchis conjunctus*	38	1
	Giardia lamblia	38	1
	Entamoeba coli	38	9
	Endolimax nana	38	2
	Dientamoeba fragilis	38	1
	Blastocystis hominis	38	3
	Other Helminths	38	0
Dogs	*Metorchis conjunctus*	15	11
	Toxocara sp.	15	6
	Diphyllobothrium sp.	15	6
	Hookworm	15	8
	Trichuris sp.	15	1
Bears	*Metorchis conjunctus*	3	3
	Diphyllobothrium sp.	3	3
	Hookworm	3	1

Dog and bear samples were notable for the frequent presence of *Metorchis* and *Diphyllobothrium* eggs. Study of the local fish revealed 2 white sucker (*Catostomus commersoni*) with 43 and 11 metacercariae, 2 northern pike (*Esox lucius*) with 1 and 8 metacercariae, and 2 lake whitefish (*Coregonus clupeaformis*) free of infection.

DISCUSSION

We found that *M. conjunctus* is still enzootic in the Fort Hope region, but human infection currently appears to be rare. Since individuals who participated in this study were somewhat younger and by definition less likely to be out of town during the study period, it is possible that this result is a slight underestimate of the prevalence in the entire adult population of Fort Hope. As well, since children were specifically excluded from study, these results cannot be generalized to the pediatric population.

This low human prevalence can be explained by either a short duration of infection or low incidence of new infection. Auto-elimination of infection without therapeutic intervention has been demonstrated in an animal model of infection.[7] However, case reports have described prolonged shedding in individuals confined to tuberculosis sanitaria,[8] indicating the possibility of chronic infection. Alternatively, a reduced incidence of infection could be due to altered diet or food preparation. In fact, most individuals who participated in this study recalled having eaten smoked sucker as sustenance during long periods in the bush (hunting or trapping), but now in a settled community with 2 stores and an airstrip supplying external provisions, this practice appears to be greatly reduced. The dogs wandering about Fort Hope were observed consuming raw fish left over from the nets, which explains the high prevalence of fish-borne parasites, including *Metorchis* eggs, in the dog excrement. The bears were not studied, so the source of their infection (e.g., hunting of infected fish versus scavenging at the dump) is not known.

The lack of seropositivity in the Fort Hope participants supports the suggestion that incident human infection with *M. conjunctus* is currently infrequent in this community. While we have observed that serology can revert to negative within months of treatment of acute infection, the expected duration of seropositivity in untreated, presumably subclinical infection is unknown. The fact that both serology and stool microscopy were almost uniformly negative suggests a true low prevalence of infection rather than infection below the detection thresholds of these assays.

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