DIPHYLLOBOTHRIASIS: UPDATE ON HUMAN CASES, FOCI, PATTERNS AND SOURCES OF HUMAN INFECTIONS AND FUTURE CONSIDERATIONS

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Abstract. Diphylobothriasis is a well documented disease of humans. On a world scale new infections are reported regularly, especially from Russia and parts of Japan. Globally, new species have been discovered and the etiology of the disease may be changing. Human infections appear to be in decline but it is not clear if the sources of infection are also in decline or if public health awareness has improved. In North America there has been a decline in human cases while in South America an increase in reports from fish, especially salmonids suggests high levels in these fish species. The history of human infections of *Diphyllobothrium latum* is primarily associated with the consumption of the northern circumpolar distributed pike and percids and is often considered a parasite of humans only. Indeed some researchers believe that *D. latum* was introduced to North America by northern European immigrants. The more benign human infections of *D. dendriticum* appears to be primarily associated with salmonids and coregonid fishes and fish eating birds. Although the early cases of diphyllobothriasis in the 1930s in North America came from fish originating in Lake Winnipeg, Manitoba, there was general belief that it was declining in fish populations and therefore of little significance to humans in the area. However, high levels of a plerocercoid in the flesh of walleyes and pike led to rejection of commercially harvested walleye and pike in Manitoba and northern Ontario, Canada, and a financial loss to Aboriginal fishers. *D. latum* is widely distributed in fishes of Manitoba and is infective to humans where it is not pathogenic and has a life span up to 4.5 years. The distribution and potential infection routes has not changed in a century and is still well established in natural hosts in the boreal regions of North America. Evidence is building for an old pre-European presence in North America, involving the Beringian land bridge and later involvement of susceptible hosts (northern European immigrants).

INTRODUCTION

Diphyllobothriasis is caused by intestinal infections of the adults of certain species of the pseudophyllidean tapeworm *Diphyllobothrium*. The main species associated with this condition is the broad-tapeworm, *Diphyllobothrium latum*. Humans become infected by ingesting the larval stages (plerocerocoids) in raw or insufficiently cooked fish. During the past century of research into *Diphyllobothrium* spp, it has become clear that several other species can also infect humans (Table 1). Worldwide, these include *Diphyllobothrium dendriticum*, a widely distributed parasite primarily of fish-eating birds such as gulls, *D. dalliae*, a parasite of gulls and dogs in Alaska, *D. klebanovskii* from humans along the Amur River drainage in far eastern Siberia, and *D. nihonkaiense* from humans in coastal Japan. Numerous other species of *Diphyllobothrium* have been described from fish eating birds and mammals in the north-temperate and Arctic regions (Table 1), in both freshwater and marine environments, and this has led to a considerable amount of taxonomic confusion regarding the distribution and host-associations of the primary human cause of diphyllobothriasis, *D. latum*. The presence of *D. latum* in North America has also been the subject of long-standing controversy. Early researchers such as Vergeer (1928, 1929a,b) and Magath (1933,1937) were of the opinion that *D. latum* was introduced into North America by northern European immigrants, while others such as Bajkov (1933) argued strongly against that view. Bajkov's contention that *D. latum* was already present in North America before European immigration was supported by Wardle (1935) and later by Lubinsky and Loch (1979). A combination of survey work and experimental infections carried out during the early half of the 20th century, in Manitoba, by Wardle and his colleagues (Lubinsky and Loch, 1979; Wardle, 1932, 1935; Wardle and McLeod, 1952), suggested that plerocercoids of *D. latum* were found in the musculature of only the following species of fish: pike (*Esox lucius*), yellow perch (*Perca flavescens*), walleye (*Stizostedion vitreum*) and sauger (*S. canadense*); plerocercoids in burbot (*Lota lota*) were considered to be a different species. However, the decades of survey work after that saw *D. latum* reported from salmonid fishes in North America, particularly along the Pacific coast (Margolis and Arthur, 1979; Hoffman, 1999 and comments therein). In Europe and northern Asia (Siberia), the main hosts of *D. latum* have been considered to be: pike (*E. lucius*), perch

Table 1
Species of *Diphyllobothrium* encountered in freshwaters of North America and Eurasia (and of importance to humans).

Species	Distribution	Fish hosts	Definitive host
D. latum	Holarctic	Pike, some percids	Humans, dogs, bears
D. ditremum	Holarctic	Salmonids	Fish-eating birds
D. dendriticum	Holarctic	Salmonids	Fish-eating birds
D. dalliae	Alaska	*Dallia pectoralis*	Gull, dog
D. ursi[a]	Alaska	Salmonines	Bears
D. alascense[b]	Alaska	Salmonines	Dogs (atypical)
D. vogeli	Eurasia	Salmonids	Fish-eating birds
D. klebanovskii[b]	Amur River	Salmonines	Humans (atypical[b])
D. nihonkaiense[b]	Japan	Salmonines	Humans (atypical[b])

[a] Considered a synonym of *D. dendriticum* by some (Hoffman, 1999) but not by others (Rausch and Adams, 2000).
[b] Likely or possibly a marine species.

(*P. fluviatilis*), ruffe (*Acerina cernua*) and burbot (*Lota lota*) (Dubinina, 1987) but salmonids (salmonines and coregonines) have been and continue to be reported as hosts of this tapeworm. Generally, there has been a drastic decline in reports of *D. latum* in North America and northwestern Europe (Scandinavia) over the last 100 years, a change brought about by the increased awareness of the disease and transmission, resulting in a stricter monitoring of food fish and possibly a change of eating habits, and higher standards of public hygiene. Reports of human *D. latum* infections in formerly endemic areas such as Manitoba have virtually become a thing of the past but there has been reports of infections in fish from local areas (Dick and Poole,1985; deVos and Dick, 1989). Despite this, our study will show that the parasite is still widely distributed in Manitoba, reopening the still unsettled issue of the origins of North American *D. latum* and its natural transmission. As human reports in North America have generally declined, new foci of infections have been reported, such as in south-temperate South America (Argentina and Chile), through the introduction of salmonids and foci of endemicity continue to exist in many parts of the former Soviet Union, in European and Asian regions.

The first objective of this study is to review some of the controversies and problems surrounding *D. latum* infections in humans, the persistence of the parasite without human involvement, emerging cases worldwide, its reported introduction and presence outside the holarctic region and future challenges and directions. The second objective is to show that although human infections are in decline that *D. latum* is still widely distributed in fish hosts and infective experimentally to humans near the center of its range in North America *ie*, Manitoba, Canada.

MATERIALS AND METHODS

Literature

Literature relating to reports of *D. latum* in humans was obtained from the following abstracting sources: Biological Abstracts, CAB Helminthological Abstracts, Medline, and Zoological Record, as well as from books and from citations in published papers. For a summary of records in North American freshwater fishes, we used Margolis and Arthur (1979), McDonald and Margolis (1995) and for summaries from the former Soviet Union, Dubinina (1987). For this review, we have concentrated mainly on published records of *D. latum* in humans, *ie* only cases where a specific identification has been made. Given the large body of literature relating to the well-documented presence of *D. latum* in Siberia, the Baltic region and European Russia (von Bonsdorff, 1977), we have decided instead to list new and emerging cases in hitherto unknown areas, particularly in the period between 1975-2000 (Table 2). While we have attempted to provide a thorough list of human infections in North and South America (Table 3), and the distribution of *D. latum* in

Table 2
Records of *D. latum* in humans in North America and South America.

Year	Location	Host	Reference
1879	North America	Swedish immigrant	von Bonsdorff (1977)
1901	Montreal, Canada	French Canadian	(Hamilton in Cushing and Bacal, 1934)
1932	New York City	3 cases	Waters and O'Connor (1932)
1932	Oklahoma, USA	Immigrant Finn	Canavan (1932)
1932	New York City	Jewish residents (21)	Plotz (1932)
1936	Ely, Minnesota	Residents	Thompson (1936)
1937	Syracuse, NY	1 human	Mueller (1937)
1939	Indiana, US	1 native resident	Headlee *et al* (1939)
1943	Florida, US	3 children (+ family dog)	Summers and Weinstein (1943)
1947	USA	11 cases	Sandweiss and Sugarman (1947)
1947	Canada	95 cases to date	Sandweiss and Sugarman (1947)
1947	USA	309 cases to date	Sandweiss and Sugarman (1947)
1950-1953	New York City	13 cases	Rosenberg *et al* (1955)
1950	Chile	1 case	Neghme *et al* (1950a)
1950	Chile	12 cases to date	Neghme *et al* (1950b)
1951	Chile	22 cases to date	Neghme and Bertin (1951)
1955	Chile	2 cases	Neghme *et al* (1955)
1949-1970	Alaska, USA	Native cases	Rausch and Hilliard (1970)
1961-1971	Chile	0.3% of 51,010	Reyes *et al* (1972)
1973	Quebec, Canada	2 of 500 Chinese	Seah (1973)
1974	Ontario, Canada	9 native cases	Turgeon (1974)
1974	Louisiana, USA	4 children	Christian and Perret (1974)
1979	Canada	Human fecal samples	Croll and Gyorkos (1979)
1932	Yellowstone, US	Black bears	Rush (1932)

other mammals and fish in North America, we have been more selective in listing reports of human infections from other regions. We recognize that there may be many other records of "*Diphyllobothrium*" in humans but those records are outside the scope of this review. Many such records are from inaccessible Russian literature, and many are from regional and local periodicals.

Survey work in Manitoba and the Whiteshell Area

Pike (*Esox lucius*), walleye (*Stizostedion vitreum*), and yellow perch (*Perca flavescens*) were collected from lakes in Manitoba and the Whiteshell region (Figs 1, 2, 3) using gillnets, transported to the laboratory fresh on ice. Whole fish were eviscerated, the carcasse filleted and then thin slices were made perpendicular to the longitudinal axis of the fillet at 0.5 cm intervals. The total number of plerocercoids per fish were recorded and a prevalence determined.

Experimental Infections

Experimental infections were done using plerocercoids recovered from pike collected during February, 1994. Plerocercoids were removed intact

Table 3
Reports and publications on human infections of *D. latum* in chronological order (1975-1997).

1976	*D. latum* reviewed in Finland. Prevalence dropped in the last 20 years (1956 - 1976) from 20% to 2% over the whole country, and from 100% to 10% in eastern areas.
1977	Eastern Taimyr, Khatangskii region (Russia). Human infections: *D. latum* dominates in upper reaches of the Khatanga (where people eat *Lota lota* and *E. lucius*) while *D. dendriticum* dominates the lower Khatanga region where people eat mainly coregonids.
1975	Perm region, Russia. *D. latum* mainly in housewives (get infected by tasting minced raw fish while preparing fish balls etc).
1979	Hawaii. Man infected from eating raw fish while in Alaska.
1979	Okayama Prefecture, Japan. 5 cases in humans.
1979	Chiba Prefecture, Japan. Human infections.
1979	Kyubishev Reservoir, Russia. Focus of *D. latum* .
1980	Pakistan, Karachi. Human infection.
1982	Novosibirsk region (Russia, Siberia), *D.latum* known in humans.
1983	Southern Sukhon River (Russia, SFSR), *D. latum* focus.
1983	Southern Chile. New cases of *D. latum* in humans.
1984	Finland. *D. latum* in 1-4 % of the population. Some geographical variability in prevalence. .
1984	Experimental infection of Japanese men with *D. latum* of Finnish origin. Pathogenic effects due to the parasitism.
1985	Amur River basin (eastern Siberia). *D. latum*: 4.2% among natives, 0.34% among newcomers (settlers). Fish hosts: *Oncorhynchus keta* and *O. gorbuscha*. This species later became *D. klebanovskii* (see later, for 1988).
1985	European part of Russian SFSR. In humans, pike, perch and ruffe (*Acerina cernua* or *Gymnocephalus cernua*, a perch-like percid).
1986	Kremenchug Reservoir, Russia. Focus of *D. latum*. Fish hosts: *E. lucius* and *P. fluviatilis*. Human hosts not mentioned.
1986	Vanzetur settlement. Lower Ob' river. Siberia. Khanty, Mansi and Komi aboriginals. *D. latum* in 34.3% of the northern natives, 20.2% of the Russian residents (settlers).
1986	Sao Paulo, Brazil. Eggs identified as *D. latum* in sand on beaches.
1986	Korea, Seoul. *D. latum* eggs in human stool samples.
1987	Japan. 3 cases of *D. latum* treated between 1970-1974 at the Dept of Medical Zoology, Prefectural University of Medicine.
1987	Iraq. First record of *D. latum* in fishes in Iraq.
1988	Amur River, Siberia. Lower reaches of the river. '*D. latum*' described as a new species, *D. klebanovskii*, with *Oncorhynchus* as the fish intermediate host.
1988	Okhostsk Sea, coastal areas. *D. latum* in humans (1%).
1988	Sverdlovsk region, Russia. *D. latum*: Human infections.
1989	Korea: 7 cases of *D. latum* in humans. From eating marine fish.
1990	Cuba. First case of *D. latum* in man (proglottides recovered).
1991	Jordan. *D. latum* in dog feces.
1992	Czech Republic. Czech man returned from 6-month stay in Finland infected with *D. latum*.
1993	Finland. Low levels of *D. latum* still detected in humans.
1994	Korea. Claimed to be 'first record' in humans in Korea (but see 1986).
1996	Pakistan. Faislabad. *D.latum* in dogs.
1996	Upper Pur River basin, Russia. (Yamal-Neto Autonomous district). *D. latum* in humans.
1997	Korea. 5 cases of '*D. latum*' in humans from eating raw *Liza haematocheilus*.

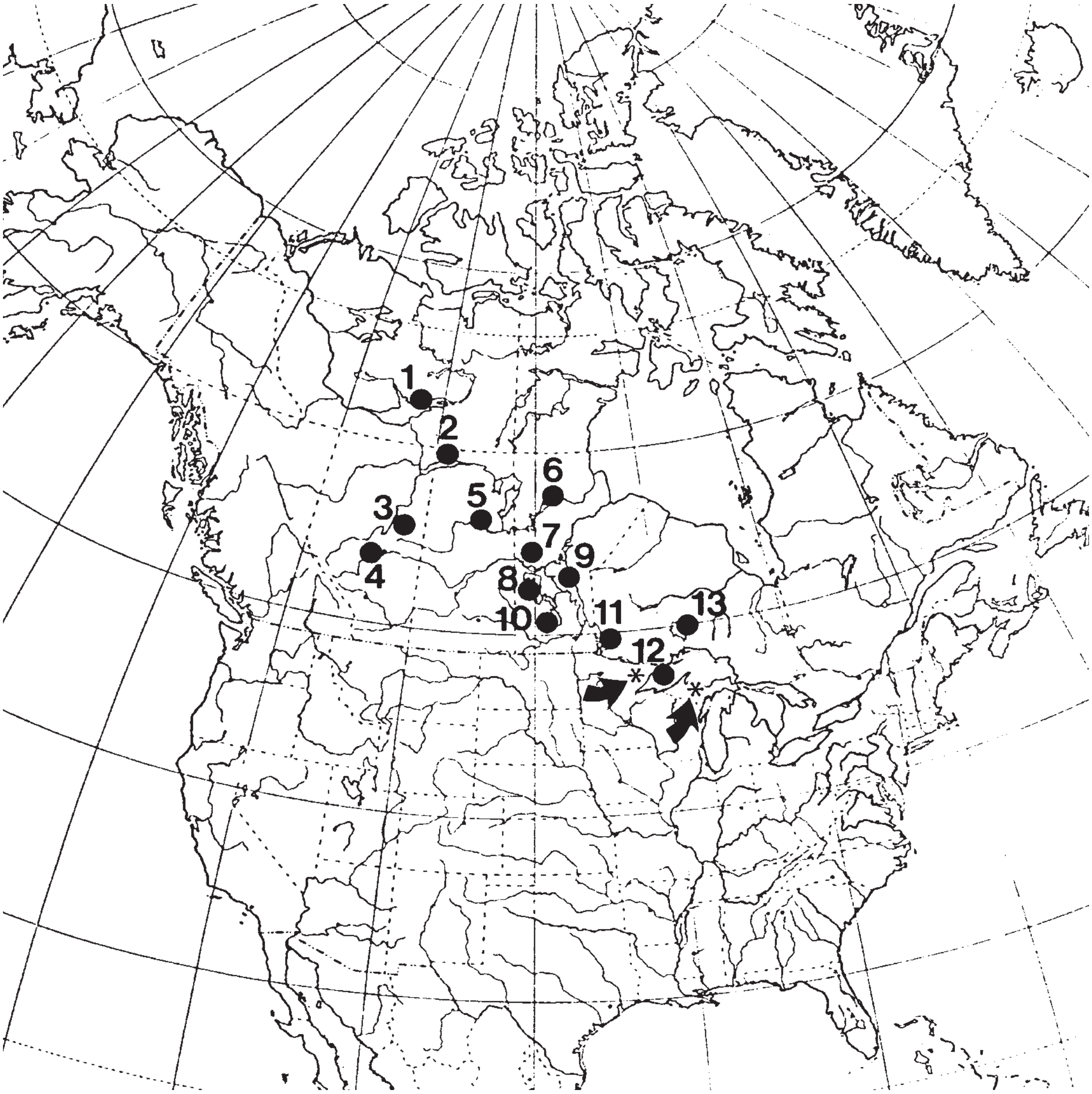

Fig 1- Map of North America showing the major drainages, waterbodies and areas where *Diphyllobothrium latum* has been reported in fish. 1. Greater Slave Lake (Mackenzie River drainage), 2. Lake Athabasca (Mackenzie/Churchill River drainage), 3. Lac LaBiche (Athabasca River drainage), 4. Lac Ste. Anne (North Saskatchewan River drainage), 5. Lac La Ronge (Churchill River drainage), 6. Southern Indian Lake (Churchill River drainage), 7. Lakes of the Pas, 8. Lake Winnipegosis, 9. Lake Winnipeg, 10. Lake Manitoba, 11. Whiteshell area and Lake of the Woods (Winnipeg River drainage), 12. Lake Superior (Laurentian Great Lakes drainage) and 13. Lake Nipigon. Heavy arrows point to location (asterisks) in northern Minnesota and Michigan where *D. latum* have been reported in pike and/or percids (perch and walleye).

Symbols are as follows for Figs 2 and 3: solid circles: pike (*E. lucius*), solid squares: walleye (*S. vitreum*), solid triangles: yellow perch (*P. flavescens*), star: sauger (*S. canadense*).

These records are from one or more of the following fish species: northern pike, perch, walleye and sauger. Records in salmonids are considered dubious (see Margolis and Arthur, 1979) and have been excluded.

from the muscle and washed several times in sterile saline (0.85%) and then quaffed in a small amount of water or chocolate milk by three volunteers (the authors); two individuals were given two plerocerocoids each and one individual was given three plerocercoids. Feces were collected and using the floatation method eggs were recovered from stool samples. One subject was treated with the drug at 4 months and at 2 and 4 months post-infection serum samples were collected and stored for testing against a *Diphyllobothrium* antigen (DA). The DA was prepared as follows: Segments of tapeworm passed in the feces by one of the infected individuals was collected in saline, washed 3 times in sterile saline and stored in 1.5 ml microcentrifuge tubes at -70˚C. These frozen samples were ground frozen into a fine powder with a microcentrifuge pestel, then 0.5 ml PBS was added and the solution was placed in a 12-14,000 molecular weight cut-off dialysis tubing and dialysed against PBS for 48 hours with 3 changes of the buffer. The antigen protein concentration was determined by the Lowry method. The ELISA was done as follows: microtiter plates were coated with antigen at protein concentration of 1 μg/100 μl, blocked with 3 % BSA in PBS, then added diluted human serum and goat anti-human IgG (Fc specific) and goat anti-human IgA (alpha-chain specific).

RESULTS AND DISCUSSION

Human cases of *D. latum* in North America

Earlier reports of human *D. latum* infections were summarized by von Bonsdorff (1977). It is clear that some of the reports of *Diphyllobothrium* from humans are in fact of *D. dendriticum*, not *D. latum*. This seems particularly true for the higher latitudes and the Aleut (Eskimo) population (discussion by von Bonsdorff, 1977), where the primary fish eaten is arctic charr (*Salvelinus alpinus*). Bona fide reports of *D. latum* in humans in the endemic areas include the reports in Manitoba, Ontario and northern Minnesota as well as the reports from Alaska (Rausch and Hilliard, 1970). At present, human diphyllobothriasis does not appear to be a mandatory reportable disease in Canada or the US. Consequently, it is difficult to ascertain whether the sharp decline in reports reflects a real phenomenon or an artifact of monitoring. Nevertheless, it does seem that *D. latum* infections in human infections have become relatively infrequent (Table 3), due largely to increased public awareness, public-health monitoring, as well as modern sanitation and hygiene. Following the early work of Vergeer, Magath, Nicholson, Bajkov, Wardle and others, in Manitoba, Michigan and Minnesota, and the pioneering work of Hilliard and Rausch in Alaska, human reports of *D. latum* declined sharply in the 1960s and 1970s (von Bonsdorff, 1977). An analysis of 414,820 fecal samples examined by State and Territorial laboratories in the US showed only 25 positive cases of *D. latum*. The last 2 decades have seen very few published reports of *D. latum* in humans in North America (*eg* Kingston and Kilbourne, 1989). Notable cases that deserve mention involve locations outside the known 'endemic' areas. Examination of stool samples of 452 children in Baton Rouge, Louisiana, revealed a 1% prevalence of what was identified as *D. latum* (Christian and Perret, 1974) and *D. latum* has also been reported from humans (mainly children) in Florida (Summers and Weinstein, 1943). In addition, *D. latum* has also been reported from the islands of Hawaii, where the infection was acquired by eating raw fish in Alaska (Ho *et al*, 1979), and from Cuba (Bouza-Suarez *et al*, 1990).

North American *D. latum*: Native or introduced

Much of the early pioneering work on *D. latum* in North America was focused in Manitoba, Canada, following the discovery that the large lakes of Manitoba, particularly Lake Winnipeg, were important foci of *D. latum* infections. This and the fact that human infections in distant places such as New York were a result of eating infected fish, mainly pike and some percids, that originated in the Manitoba 'great lakes' generated intensive research efforts in the region. The major researchers investigating the biology of the parasite at the time were either based in Manitoba (Bajkov, Wardle) or worked with material from Manitoba (Magath, Vergeer) at some phase or another (Lubinsky and Loch, 1979). These and other researchers invested a considerable portion of their time in an effort to understand the biology of this parasite. Wardle (1933) reported that 500 sled dogs in vicinity of Lake Winnipeg examined by Bajkov (1933) had a prevalence of 85%. Another study in the southern area of Lake Winnipeg found *D. latum* in 85% for pike (*Esox lucius*), 7% in sauger (*Stizostedion canadense*), and 28% in yellow perch (*Perca flavescens)*, walleye (*Stizostedion vitreum)*, and burbot (*Lota lota).* Wardle (1933) also reported the absence of pathology around the plerocercoid in the fish flesh and noted that the plerocercoid may extend into adjacent myotomes. This was also seen by Dick and Poole (1985). Interestingly very little pathology is associated with the *D. latum* from Manitoba but Davydov (1978) found considerable pathology around the worm in pike and burbot with capsules being located in the liver and striated muscles. It was noted that the distribution of *D. latum* did not coincide precisely with immigrants from European tapeworm areas and that the tapeworm was common in Eskimos and Indians before the beginning of such immigration (Wardle, 1933). The final host were considered to be man, bear, mink, cats, dogs, particularly the husky dog of the Eskimo, Indian and immigrant fisher folk (Wardle, 1933).

It is important to note that the investigations of these early researchers had certain advantages over similar work done in Europe. First, the intermediate fish hosts were established early on and quite clearly as being pike, yellow perch, walleye and sauger. In addition, the burbot has also been reported as a host although Wardle was not certain about its specific identity. These hosts are either identical or closely related to fish hosts eventually determined to be the typical of *D. latum* sensu stricto in Europe and Siberia. The situation in Manitoba is not complicated by reports in salmonids as has been the case in Europe, and coregonines which are common in Manitoba waters are definitely not hosts of *D. latum*. Experimental infections, done time and again, in dogs (Vergeer also infected 2 black bears) using plerocercoids from these pike and percid hosts clearly demonstrates the identity of this parasite in this region. The fact that only plerocercoids from these fish hosts were used precludes confusion with other *Diphyllobothrium* spp. Numerous studies on fish parasites in Manitoba over the years, including work done in the laboratory of the senior author (Lubinsky and Loch, 1979; McDonald and Margolis, 1995) clearly demonstrate that plerocercoids of *D. latum* do not occur in any other species of fish. The only salmonine in Manitoba waters within areas relevant to the distribution of *D. latum* is the lake trout, *Salvelinus namaycush*, inhabiting deeper oligotrophic lakes and it is not known to be a host of *D. latum*. In addition to *D. latum*, two other diphyllobothriids, *D. ditremum* and *D. dendriticum*, are common and widespread in Manitoba. Both species are parasites of coregonines in this region and mature in fish-eating birds. Of these two species, *D. dendriticum* is capable of infecting humans for a short while but not *D. ditremum*. Finally, it has been stated that reports of *D. latum* from salmonids in North America are doubtful (Freeman in Margolis and Arthur, 1979; see also comments by Hoffman, 1999).

From the early investigations in North America emerged two opposing views regarding the origin of *D. latum* in North America, giving rise to a long-standing and largely unresolved controversy. One position was that all *D. latum* in North America was introduced by northern Europeans (Vergeer, 1928, 1929a; Magath, 1933; Magath and Essex, 1931) particularly Finns, a theory reiterated by von Bonsdorff (1977). The contrary position, advocated by Bajkov (1933) and Wardle (1932) was that the parasite was already present before European immigration, a position also taken by Lubinsky and Loch (1979) who provide an excellent review of the early work and circumstances surrounding this controversy. As pointed out by these authors, even Vergeer (1929b) stated:

"Fish in the smaller lakes far distant from towns were moderately infested with broad tapeworm. This immediately suggests the possibility of wild carnivores as a source of infestation and again raises the problem whether the white man or the tapeworm was first in North America".

Despite his own evidence to the contrary, Vergeer concluded that *D. latum* was introduced by European immigrants. Bajkov (1933) in particular was emphatic in his position that "… the American *Diphyllobothrium* has not been introduced from Europe, but is a native form". He also stated that "Canadian Indians along the shores of Lake Winnipeg knew and observed *Diphyllobothrium latum* in connection with their dogs a long time before it was discovered by white man" and concluded that the tapeworm was "very abundant in all eastern and western tributaries of Lake Winnipeg, in the Nelson River, also practically all lakes of northern Manitoba" (Bajkov, 1933). Our study also shows that, even today, *D. latum* is widely distributed in lakes of various sizes in the forested Whiteshell Area of Manitoba.

In addition to the wide geographic range of *D. latum* in North America, one of the major stumbling blocks to the theory that the tapeworm was introduced by European immigrants is the presence of this parasite in more western regions of the continent such as Alaska (Rausch and Hilliard, 1970). Von Bonsdorff (1977) attempted to explain the problem by invoking visits by Finns and Lapps serving on Russian ships during the period when Alaska was a Russian territory. The evidence of Rausch and Hilliard (1970) remains convincing and unless it can be demonstrated that the *D. latum* reported by them is in fact distinct from the *D. latum* of more interior North American boreal regions, the theory that this species existed prior to European immigration must be considered. Two possibilities exist: first, that *D. latum* in North America is an original parasite of this continent, and second, that relatively rare introductions by European immigrants has been superimposed upon an already existing distribution of a much older population of *D. latum* (Cameron, 1945). The first possibility raises the question: if there was an older existing *D. latum* population in North America, as Bajkov and Wardle argued, what is (are) the natural definitive host(s)? According to these researchers, *D. latum* is capable of maturing in dogs, bears, cats and mink, thereby providing ample opportunity for a natural cycle of this parasite to be maintained in the wild. As with the fish hosts, these mammalian hosts also have close relatives in Eurasia capable of being or actually known (dogs, foxes) as hosts of this parasite. The relatively high prevalences in certain areas and the wide distribution of this parasite in the Whiteshell Area of Manitoba even today (this study) is evidence that the life cycle can indeed be maintained without the participation of human hosts. Both black bears (*Ursus americanus*) and dogs are common in this area. This brings us to the central question of whether or not *D. latum* is originally a human parasite or whether humans are accidental participants in what is really a life cycle involving some wild fish-eating carnivore. A consideration of the historical biogeography of this parasite may provide a clue to these questions.

South America

According to von Bonsdorff (1977), *D. latum* has been known to be present in humans and dogs in Chile since 1919. Early research established that *D. latum* was localized in the southern part of the country, associated with a number of lakes, Colico, Villarria, Panguipulli, Rinihue and Ranco, where dogs and humans were infected with adult worms and introduced rainbow trout (*Oncorhynchus mykiss*) and brown trout (*Salmo trutta*) harbor the plerocercoids (Neghme *et al*, 1950a, b; Neghme and Bertin, 1951a, b; Neghme, 1953). Neghme and Bertin (1951b) concluded that the rainbow trout was the main fish host in practically all the rivers and lakes in the Lake Colico area where such fish were introduced. Humans, dogs and even cats were found infected with this tapeworm (Neghme and Bertin, 1951b, 1953). Faust *et al* (1951) reported infections in humans and dogs along the lakes at approximately 40˚S and rainbow trout appeared to be the only fish incriminated and infections were established in experimentally infected dogs. Infections of humans in other parts of Chile could be traced back to this southern endemic focus in the Lake Colico area (Faigenbaum and Donckaster, 1955). Over a decade later, an examination of 51,010 people in Santiago, Chile led to the diagnosis of *D. latum* in 0.3% cases (Reyes *et al*, 1972). Several years later no *D. latum* eggs were found in an examination of 60 people living by Lake Colico, leading the authors (Ramirez *et al*, 1977) to conclude that humans were not involved in the life cycle of the parasite in the lake. A subsequent investigation of 5 lakes in this endemic region revealed that two, not one, species of *Diphyllobothrium* infected rainbow trout, *D. dendriticum* which comprised the greater proportion (87.2%) of the plerocercoids, with *D. latum* comprising the rest. The focus of *D. latum* may also have shifted slightly since plerocercoids were found mainly in Lakes Rinihue and Panguipulli (Torres *et al*, 1983). Humans were still found infected with *D. latum* but in addition a dog was found infected with *D. pacificum*. Follow-up studies by Torres *et al* (1989a, b) found *D. latum* in rainbow trout and brown trout in lakes and rivers of the Valdivia River basin and in humans (1.2%) and dogs (5.3% and 9.8%) in two of the six districts surveyed. Monitoring of *D. latum* has continued in this region and 15 new cases have been reported from humans between 1981-1991 although the incidence of infections have remained relatively constant over this period (Torres *et al*, 1993). The transmission at present involves rainbow trout, humans and dogs (Torres *et al*, 1998).

In 1952, Szidat and Soria reported *Diphyllobothrium* sp plerocercoids in introduced rainbow trout ("*Salmo irideus*" = *O. mykiss*) from Lake Nahuel Huapi at 41˚S latitude near the Argentina-Chile border, close to the endemic focus in Chile. More detailed examination in the Nahuel Huapi National Park and Reserve revealed that two distinct types of plerocercoids were involved, that of *D. dendriticum* and *D. latum* (Revenga and Semenas, 1991), both of which were confirmed by experimental infections in golden hamsters (Revenga and Semnas, 1991; Revenga, 1993). All three introduced salmonids, rainbow trout, brown trout and brook trout (*Salvelinus fontinalis*) were hosts of *Diphyllobothrium* spp although the rainbow trout was considered the most important host for both tapeworm species. For the first time in South America, a native fish species, *Percichthys* sp, was also found infected with *D. latum*. Apart from this latter observation, the situation in Argentina appears to mirror the situation in Chile, with similar host-parasite associations involving mainly rainbow trout, humans and dogs.

The situation in South America raises some important issues. First, there is the question of the source of the introductions. The fish species playing the major role as intermediate host, *O. mykiss*, was introduced from North America, not Europe as von Bonsdorff (1977) supposed. Pacific salmonids (*Oncorhynchus* spp) may host a number of diphyllobothriids but *D. latum* is not one of them. Brook trout were also introduced from North America but this fish is not a natural host of *D. latum* either. It is somewhat puzzling that immigrant Europeans introduced a parasite that has as its main intermediate host a fish species, rainbow trout, that is not naturally a host of *D. latum* in North America. In fact, it is very doubtful if there are any bona fide records of *D. latum* in salmonid hosts in North America (see comments in Margolis and Arthur, 1979; Hoffman, 2000). Over a hundred years of research and survey work has shown quite unambiguously that in the holarctic region, the main fish hosts of *D. latum* are: the pike, the North American and Eurasian perches, the North Amercian and Eurasian pike-perches, the ruffe (*Acerina cernua*) which has no counterpart in North America, and possibly the burbot. Neither the amphi-Atlantic trouts (*Salmo* spp), nor the amphi-Pacific trouts (*Oncorhynchus* spp) or the charrs (*Salvelinus* spp) can be considered significant natural hosts of *D. latum*, scattered and often unsubstantiated records of them as such notwithstanding. Furthermore, it has been shown recently that species thought to be *D. latum* in Pacific trouts (*eg Oncorhynchus masou*) causing diphyllobothriasis in Japan is in fact a distinct species, *D. nihonkaiense*. A species infecting humans in the Amur basin with plerocercoids in *Oncorhynchus* spp has also been recognized as a distinct species, *D. klebanovskii*. Furthermore, reports of the dwarf human tapeworm, "*D. latum parvum*" also cause taxonomic problems. In view of these biological facts, particularly the predominance of non-salmonid hosts (pike and some percids) in the transmission of *D. latum* sensu stricto, the identity of the "*D. latum*" in humans and salmonids in South America needs to be re-examined. The species requires a careful comparison with European and North Amercian *D. latum*, preferably using a combination of biological characterization and enzyme/molecular techniques. We should not be surprised if this species is in fact one of the lesser known diphyllobothriids of Pacific salmonids.

Diphyllobothrium latum in Eurasia

Siberia: Historically, most of the published information and distributional data left the impression that *D. latum* was a predominantly European parasite, with occasional introductions into distant locations (as in North America). However, numerous studies showed that the tapeworm is in fact very common east of the Urals in Asian Siberia. Major foci of infection involving humans and dogs were initially reported from the Ob and later the Yenisei River drainages. Later studies showed that the parasite is also very widespread in all major drainages further east, such as those of the Lena, Kolyma and Indigirka Rivers (Suvorina and Simonova, 1993). In addition to *D. latum*, Suvorina and Simonova (1993) were also able to identify *D. dendriticum*, *D. ditremum* and *D. strictum* in fishes of these river basins. Human infections of *D. latum* were also prevalent in eastern Taimyr (Khatangskii region), particularly along the Khatanga and Khata Rivers, where the favorite food fishes were pike (*E. lucius*) and burbot (*L. lota*) (Klebanovskii *et al*, 1977). *Diphyllobrothrium latum* was also reported as a human parasite in the Amur River basin (Muratov, 1985), with plerocercoids in *Oncorhynchus* spp, but this was later shown to be a distinct, likely marine, species, *D. klebanovskii* (Muratov and Semenova, 1986; Muratov and Posokhov, 1988). The natural defintive host of *D. klebanovskii* is thought to be some, as yet undetermined, marine mammal. *Diphyllobothrium latum* and *D. dendriticum* have also been identified from the far eastern (Okhotsk) regions of Russia using morphological criteria of plerocercoids and experimental self-infections (Dovgalev *et al*, 1991). However, the "F" type plerocercoid (unencapsulated in salmonids) reported from the Okhotsk region and identified as *D. latum* (Dovgalev, 1988; Dovgalev *et al*, 1991) is also the type of plerocercoid in the case of *D. klebanovskii* and it is possible that this "*D. latum*" in salmonids is actually *D. klebanovskii*. In addition, *D. dendriticum* also infects humans in eastern Siberia. It is clear that if we are to gain a deeper understanding of the origins and biogeography of this parasite, its biology and distribution in eastern Siberia needs to be thoroughly understood and that region must become the focus of future studies.

Japan: Von Bonsdorff (1977) was very critical of the state of confusion that surrounded the information concerning the purported presence of *D. latum* in Japan up until the time of writing his book. It would appear that the name *D. latum* was widely used for human diphyllobthriid infections in Japan without critical evaluation, making it very difficult to determine with any degree of certainty whether reported *D. latum* infections were in fact due to that parasite. Aspects of the biology and distribution of "*D. latum*" in Japan were clarified by the pioneering works of Eguchi (1973). The widely held view that the parasite was acquired by eating sashimi of Pacific salmonids and other marine fishes should have provided the first clue that it was likely not *D. latum*. However, given the long-standing confusion surrounding the fish intermediate hosts of *D. latum* even in regions where extensive studies had been carried out, *eg* Europe, this was understandable. Human diphyllobothriasis was reported from various locations in Japan such as Okayama (Tomita *et al*, 1979), Chiba (Yokogawa *et al*, 1979) and possibly Kochi prefectures. The differences between the Japanese "*D. latum*" and the true *D. latum* were eventually recognized by Yamane *et al* (1988) with the description of *D. nihonkaiense* and a revised taxonomy for Japanese *Diphyllobothrium* spp. Subsequent studies using immunoelectrophoresis (Fukumoto *et al*, 1988), isozyme patterns and soluble protein profiles (Fukumoto *et al*, 1990) and restriction fragment length polymorphisms of rDNA (Matsuura *et al*, 1992) showed the *D. nihonkaiense* was indeed distinct from *D. latum*. More recently, "diphyllobothriasis *latum*" has been used as a synonym of "diphyllobothriasis *nihonkaiense*" in Japan (Nishiyama, 1994), likely in recognition of the fact that *D. nihonkaiense* has been commonly misidentified as *D. latum*. In view of the work of Yamane *et al* (1988, 1989) on *D. nihonkaiense*, Hatsushika *et al* (1995) proposed that Japanese *D. latum* be regarded as *D. nihonkaiense*. However, *D. latum* continues to be reported in humans in Japan (Nishiyama, 1994;

Hatsushika *et al*, 1997; Yamaguchi *et al*, 1997), often along with *D. nihonkaiense*, and infections are apparently acquired by eating raw fish such as salmonid sashimi. The results of experimental infections of 2 Japanese men with *D. latum* of Finnish origin (Yazaki *et al*, 1984) resulted in general fatigue, epigastric pain, fever and diarrhea, increased eosinophilia, as well as hypochromatic anemia in one man; these symptoms and pathology are not associated with "*D. latum*" infections acquired indigenously in Japan. This is further evidence that biologically, Japanese "*D. latum*" is not the same as the European species. The presence of other diphyllobothriids in the region, particularly marine species such as *D. yonagoensis*, *D. cordatum*, *Diplogonoporus* spp., and possibly others (*D. dendriticum* and *D. ursi*) complicates species identification. Eguchi (1973) found "*D. latum*" to be prevalent in brown bears *Ursus arctos vesoensis*, which feed on migratory salmonids, and considered dogs and humans accidental hosts. It is possible that these brown bears are the hosts of *D. nihonkaiense* or that "*D. latum*" in bears is in fact *D. ursi* or even mixed infections with *D. dendriticum*. Clearly, future work in this region will have to incorporate molecular techniques and careful observations on biological characteristics to identify and distinguish the various diphyllobothriids (Seki, 1975; Hotta *et al*, 1978) in salmonids, marine non-salmonids and mammals in the region.

Korea: Outside of Japan, "*D. latum*" has been most frequently reported in neighboring Korea. Human infections of diphyllobthriids in Korea (Moon, 1976; Min, 1990) are not surprising, given the proximity to Japan and the similar customs of eating raw salmonids and marine fishes (sashimi). The earliest reported case appears to be by Cho *et al* (1974), followed by a report of a human case of *D. latum* infection in Kangwon Do (Cho *et al*, 1974). An examination of 5,251 human fecal samples in the Seoul area between 1985-1986 revealed a prevalence of 0.2% (Min *et al*, 1987) prevalence of *D. latum*. Seven new cases were reported by Lee *et al* (1989), bringing the total number of cases in Korea to 28. A second larger study of 52,552 human fecal samples from the Seoul Park Hospital between 1984-1992 revealed a low prevalence by 0.004% (Lee *et al*, 1994a). The most definitive report of a diphyllobothriid in Korea is the recovery of the "dwarf-type" of *D. latum*, namely *D. latum parvum* (Lee *et al*, 1994b) from a human case. More recently, five cases of human *D. latum* infections have been reported in Korea from the consumption of the redlip mullet, *Liza haematocheila* (Chung *et al*, 1997). Given the fish host involved, it is unlikely that this involves *D. latum* and it is more probable that a different, possibly marine diphyllobothriid is the cause. As was done in Japan, much careful work needs to be done to sort out the taxonomy of diphyllobothriids in Korea.

Subtropical and tropical Asia: Two human cases of "*D. latum*" have been reported recently from China (Fan *et al*, 1995; Zhang *et al*, 1996) but diphyllobothriasis appears to be rare in that country. Given the presence of diphyllobothriids in the Amur River basin, a river that forms a common border between China and Russia in the north, diphyllobothriasis may occur in Chinese citizens inhabiting that region. Mar *et al* (1999) reported *D. latum* in 1% each of 96 stray dogs and 95 stray cats in Taipei, Taiwan, but these could have been confused with other diphyllobothriids, particularly *Spirometra* spp.

More surprising are reports of *D. latum* from the Indian subcontinent. A human case was reported from southern India (Pancharatnam *et al*, 1998). A human case was also reported in Karachi, Pakistan (Bilqees *et al*, 1984) and *D. latum* was reported from 1.2% of 756 dogs examined in Faislabad (Maqbool *et al*, 1995). In India, *D. latum* has been reported from dogs in Kerala (Jacob *et al*, 1991), from a clouded leopard in Alipore Zoo, Calcutta (Sengupta, 1974), and from a necropsy of a tiger in Nehru Zoological Park, Hyderabad (Rao and Singh, 1998). It is very likely that these are misidentifications of other diphyllobothriids, such as *Spirometra* spp, which are found in 'cats' and dogs and are definitely more typical of felids than *Diphyllobothrium* spp.

Diphyllobothrium latum has also been reported from 1.5% of 756 dog fecal deposits collected from 5 governorates in Jordan (Abo-Shehada and Ziyadeh, 1991). Again, given the absence of appropriate fish intermediate hosts, it is highly doubtful that these are records of true *D. latum*. Given the geographical location of the Sefid Rud river drainage (Caspian basin) in Iran, the record of "*D. latum*" from those locations (Mokhayer, 1981) cannot be dismissed as misidentifications and certainly warrant further investigation. Plerocercoids identified as those of *D. latum* from a cyprinid, *Acanthobrama centisquama*, in Iraq (Ali *et al*, 1987) and in *Harpodon nehereus* in Bangladesh (Uddin *et al*, 1980) are most certainly misidentifications.

Diphyllobothrium in fish hosts

The areas sampled in central North America where *D. latum* plerocercoids were recovered from fish are illustrated in Fig 1 and the distribution in province of Manitoba (Fig 2) and in the Whiteshell area are given in Fig 3. While pike seems to be the most frequently infected fish host it is also common in walleye and perch (Tables 4, 5). Other lakes where pike were found to be infected with *D. latum* include Hawnek, Sheep and Rae. McLaren and Reindeer lakes are commercially fished for walleye and the prevalences in walleye were greater than 50%. Fish from these lakes were rejected for human consumption. McLaren is a relatively small lake of a few square miles while Reindeer is a very large lake in northern Manitoba. It can been seen from Table 4 that walleye are usually not this heavily infected so the reason for the higher prevalences was investigated. McLaren Lake is isolated with no permanent human settlements and only an occasionally fisher or sport fisherman on the lake. Upon questioning, the fishers revealed that at McLaren Lake fish remains were left on shore and they noted a lot of feeding activity by wolves and foxes on these remains. In the case of Reindeer Lake there are several sections on the lake where fishing effort is concentrated. One of these areas is isolated but near a large island where dogs are held during the summer and these dogs are fed whole fish and fish remains. These two examples indicate a natural cycle involving canids where local transmission is amplified by human activities.

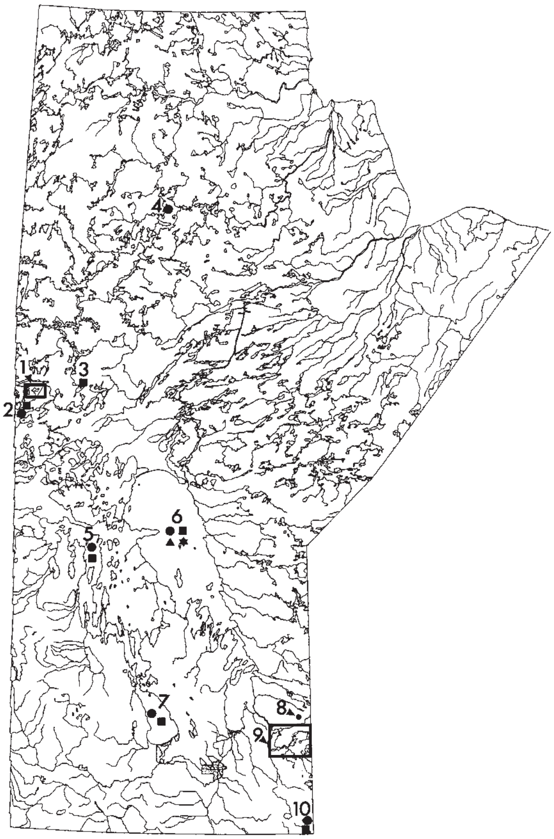

Fig 2- Map of Manitoba showing waterbodies where *D. latum* has been reported in fish. 1. Heming Lakes study area, 2. Other lakes of the Pas, 3. Lake Snow, 4. Southern Indian lake, 5. Lake Winnipegosis, 6. Lake Winnipeg, 7. Lake Manitoba, 8. Lake Manigotagan, 9. Whiteshell lakes, 10. Lake of the Woods. Boxed areas (locations 1 and 9) are enlarged in Fig 3. Location 9 represents the area investigated in this study.

Experimental human infections

All three experimental subjects were infected as determined by either the presence of eggs in the feces and/or the presence or expulsion in the stool. During the prepatent stage on 23 to 25 days there were few clinical signs. These consisted of mild indigestion, some gas in the digestive tract, and a general mild nausea. No diarrhea nor severe cramps were noted during the early stages of establishment of the infection or later in the infection. The most dramatic aspect of the infections was the appearance of large sections of strobila, up to 30 inches in length, hanging from the anus during a bowel movement. This was most pronounced in one individual who also tended to pass sections of the worm after eating a hot curry or had soft stools, the other individual passed segments only rarely (once in 2 years and 11 months). A second individual, exhibited constipation regularly, and passed strobila on 4 and 7 months (at 7 months the strobila were much smaller measuring less than cm in width. This same individual did not have eggs in the feces. Only 2 individual passed eggs in the feces on regular basis. There was no evidence for an immune response as determined by an ELISA. The drug praziqantel eliminated the *Diphyllobothrium* in one individual and stools tested up to 2 years 11 months post infection were negative. The two untreated individuals self cured, one in 7 months and the other in 4.5 years.

The distribution of *Diphyllobothrium* infective to humans in the Whiteshell region of Manitoba, Canada is wide spread in pike, walleye and yellow perch. Prevalences are higher in smaller lakes than in larger bodies of water. The tapeworm is definitely *D. latum* based on its ability to infect humans, the size of the proglottids shed in the feces of humans, the morphology of the gravid proglottids, and the longevity of the infection. Infections of *D. dendriticum* are known from humans but usually are not of long duration. There is a widely held belief that *Diphyllobothrium* infections in North America must have originated from humans infections. However, the situation is less clear in parts of Canada as pointed out by Dick and Poole (1985) where infections in hamsters from plerocercoids recovered from pike from northern Manitoba were clearly *D. latum*, based on the criteria of Andersen *et al* (1987). Further as pointed out by Dick and Poole

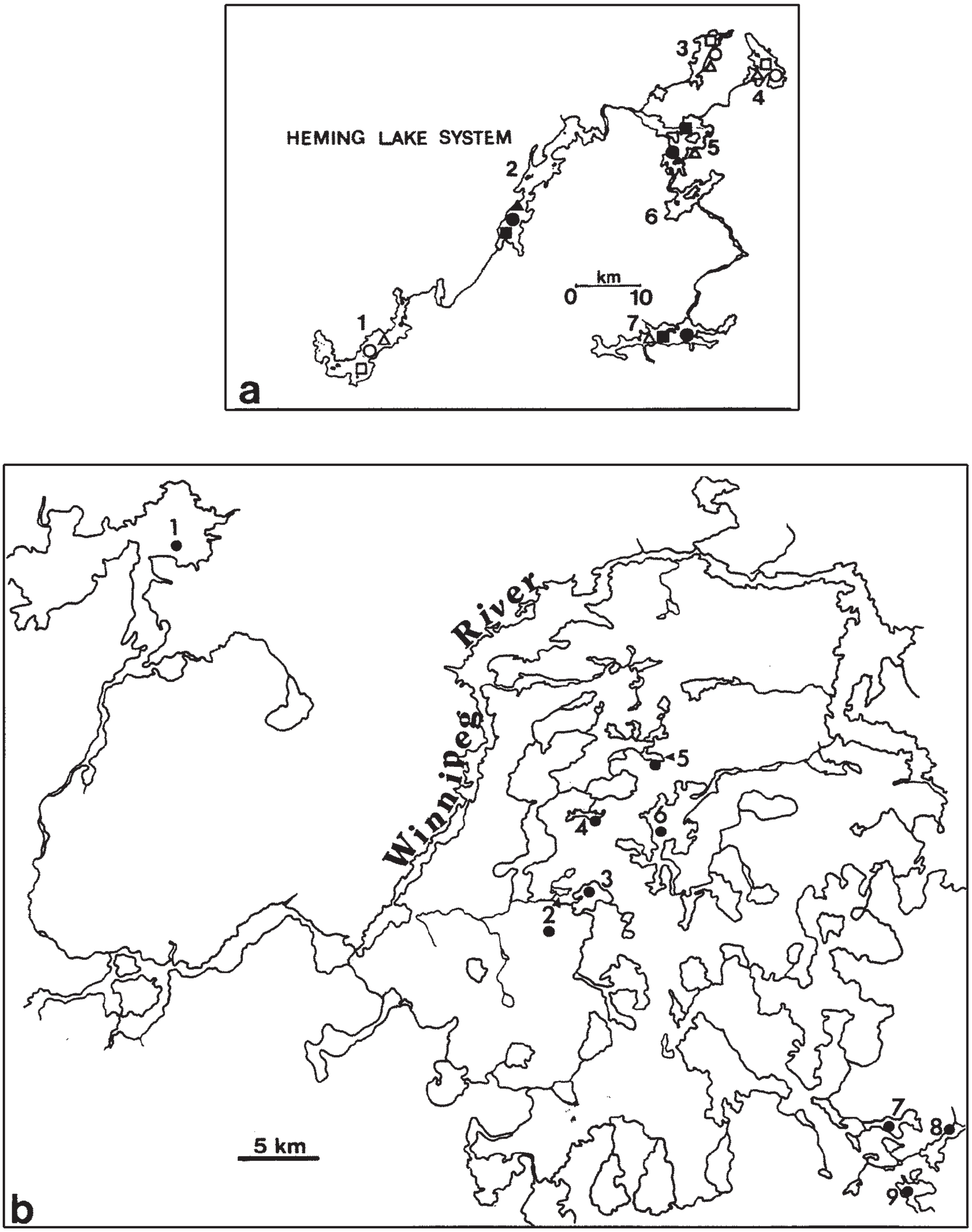

Fig 3- Enlarged maps of boxed areas in Fig 2 representing locations 1 and 9. Symbols are as in Fig 2.

3a. Heming lakes study area. 1. Wapun Lake, 2. Heming Lake, 3. Unger Lake, 4. Martin Lake, 5. Home Lake, 6. DeMarch Lake, 7. Quigly Lake. Open symbols indicate the absence of *D. latum* in samples of those species.

3b. Whiteshell study area. 1. Lac DuBonnet, 2. Beck Lake, 3. North Sailing Lake, 4. Boon Lake, 5. Boatfield Lake, 6. Echo Lake. 7. Sheep Lake, 8. Jadel Lake and 9. Mantario Lake.

Table 4
Diphyllobothrium latum in fishes from Manitoba lakes.

Lake	*Esox lucius*	*Stizostedion vitreum*	*Perca flavescens*
Heming	P (187)	P (48)	0.5 (201)
Home	P (75)	P (75)	1.3 (78)
Demarch	P (75)	2.5 (76)	0 (40)
Quigly	46.9 (33)	51 (78)	0 (11)
South Indian	54.8 (444)	NS	NS
North Sailing	70 (30)	NS	50 (42)
Echo	28.5 (32)	50 (28)	6.25 (16)

P = Present, NS = No sample, Prevalence (sample size)

Table 5
Diphyllobothrium latum in pike: eastern region of Manitoba.

Lake	No	Prevalence
Lac Du Bonnet	18	0
Quesnel/ Manigatogan	30	10
Beck	7	55
Boatfield	3	66.7
Boon	5	60
Johnstone	10	20
Falcon	55	100
Horse Shoe	38	50

(1985) Quigly Lake had no human habitation other than an occasional itinerant trapper and even these visits were years apart. Our experimental infections with plerocercoids of *D. latum* again support the contention that a definitive host, other than humans is important in the transmission of *D. latum* in the boreal region of Canada and this seems to be better established in small lakes. Although two otters were necropsied by the authors and the feces of several more were examined by the floatation method no strobila or eggs of *D. latum* were recovered. Consequently we still do not have a clear-cut answer on the natural definitive host in this part of North American. However, we are certain that plerocercoids, common in pike, produce a long-lived *D. latum* tapeworm infection in humans and that this parasite is widely distributed in fish and not in decline.

CONCLUSIONS

There is no doubt that *D. latum* in central Canada is infective to humans and is widely distributed in pike and to a lesser extent in walleye and yellow perch. It is also apparent that there is little change in its distribution from nearly a century ago and likely little change in its distribution even prior to immigrants arriving in this part of North America.

Evidence is building for an old pre-European presence in North America, involving the Beringian land bridge and later involvement of susceptible hosts (northern European immigrants). Old and new populations of *D. latum* were likely superimposed in Manitoba during the late 1800 and early 1900s as immigrants brought the European form to North America but the main source of infection today is sylvatic. There is need for a comparison of *D. latum* from remote areas in North America with that from northern European and eastern Siberian populations and at the species level for phylogenetic systematics of *Diphyllobothrium* to understand origins and distribution of *D. latum*.

We speculate that the original North American *D. latum* genotype will be more closely related (as distinct from more similar) to the northeastern Siberian genotype than to European *D. latum* genotype. Clearly, what is now needed is a phylogenetic analysis of the diphyllobothriids and a focus on the taxonomy and biology of diphyllobothriids in Alaska and Siberia (as in Rausch and Adams, 2000), incorporating molecular tools of differentiation.

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