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Opisthorchiasis in Western Siberia: Epidemiology and distribution in human, fish, snail, and animal populations

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ABSTRACT

Opisthorchiasis is a widespread helminth infection in Russia. The largest opisthorchiasis endemic focus in the world is the Ob river watershed in Western Siberia. The main causative agent of this condition is the liver fluke, *Opisthorchis felineus*. In addition, another liver fluke species in the Opisthorchiidae family, *Metorchis bilis,* causes a symptomatically similar disease, metorchiasis. Despite a long research history going back to 1927, opisthorchiasis remains a serious problem in Russia, and numerous questions related to the epidemiology of these liver fluke infections and their patterns of distribution in Western Siberia, the causes of high prevalence in different populations, and the prognosis of the epidemiological situation remain to be answered.

In this review, we first briefly describe the life cycle of *O. felineus* and then summarize the available published data on the epidemiological aspects of *O. felineus* infection among populations in Western Siberia. Additionally, the geographical distribution and rates of infection with the two major small liver flukes, *O. felineus* and *M. bilis,* in the intermediate (Bithyniidae snails and cyprinid fish) and definitive (humans, wild and domestic carnivorous animals and birds) hosts are described to assess their role in the transmission cycle. Moreover, species in the genus Opisthorchis and the genus Metorchis that have been reported in carnivorous mammals and birds in Western Siberia are listed and their potential to serve as the agents of opisthorchiasis transmission is discussed.

1. Introduction

Small liver flukes belonging to the family Opisthorchiidae (class Trematoda, phylum Platyhelminthes: Digenea) [1] can be transmitted via food (raw and undercooked Cypriniidae fish) to humans, domestic and wild piscivorous mammals and birds, resulting in adverse effects on their livers and bile ducts [2,3]. Currently, three liver fluke species, *Opisthorchis felineus* (Rivolta, 1894), *O. viverrini* (Poirier, 1886), and *Clonorchis sinensis* (Cobbold, 1875), are regarded as epidemiologically important in the aetiology of chronic hepatobiliary diseases and closely associated with cholangiocarcinoma. While *O. viverrini* is endemic to Southeast Asia, especially in the greater Mekong subregion, while *C. sinensis* is endemic to Far East Asia, and *O. felineus* is endemic to northern Eurasia [4–7]. In addition to the three major liver flukes that are causative agent of opisthorchiasis/clonorchiasis in humans, several liver flukes in the genus *Metorchis*, including *M. bilis* (Braun, 1890) in Eurasia [8–12], *M. conjunctus* (Cobbold, 1860) in North America [13], *M. orientalis* (Tanabe, 1921) in East Asia [14], and *Pseudoamhpistomum truncatum* (Rudolphi, 1819) in Eurasia [15] are known to cause human infections. It has been estimated that up to 40 million people are currently infected with small liver flukes worldwide, with a total of 600 million people at risk for infection [16].

The source of infection is the dietary consumption of fish by people, domestic animals (cats, pigs, dogs) and wild carnivores in endemic areas. Chronic infection with these liver flukes can lead to liver malfunction due to the development of various pathological and degenerative changes in tissues, such as cholangiolitis, cholecystitis, or even cholangiocarcinoma [7,8]. The magnitude of pathological changes in the liver is primarily determined by the burden of living worms and presence of resistance in affected hosts [5,7].

According to data reported by the World Health Organization, most patients with light infections are asymptomatic or scarcely symptomatic [17]. In Russia also the light degree infection with *O. felineus* was reported to be asymptomatic [8]. If the number of worms is significant (up to several thousand), the clinical features of the acute phase of *O. felineus* infection are much more severe than those of *O. viverini* or *C. sinensis* infections [17]. Some studies have shown that low levels of infection with *O. felineus* may be beneficial for the host (e.g., resulting in a reduction of cardiovascular risk and hypercholesterolemia) [18,19]. Such nuances should be considered when designing interventions for the control and prevention of *O. felineus* infection.

Opisthorchiasis is a widespread helminthiasis in the Russian Federation [20]; the main agent of opisthorchiasis is *O. felineus*, which is commonly known as the cat liver fluke or Siberian liver fluke [21]. According

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to data reported by the WHO and UN in 2005, 12.5 million people living in the former Soviet Union were at risk for infection with *O. felineus* [5]. The main opisthorchiasis-endemic foci are located in the basins and recognized by the names of large rivers. The largest *O. felineus* endemic area in Russia and, of course, the world is the Ob opisthorchiasis focus, which is located in basins of the Ob and Irtysh rivers in Western Siberia. This area covers 14 regions of the Russian Federation and four regions of Kazakhstan, potentially affecting a total population of approximately 15 million people [4,18,22–24]. Estimations of the prevalence of opisthorchiasis in Russia has been traditionally based on the stool or bile examinations. In this area, the highest prevalence of opisthorchiasis reported to date was 500 per 100,000 population. In the middle part of the Ob River, the prevalence of opisthorchiasis has been found to often reach 50–80% and even 100% in some villages [4,9]. In the European part of Russia, opisthorchiasis foci have been identified in the basins of the Volga and Kama Rivers (prevalence varying from 20 to 30%), Don and Dnieper Rivers (prevalence varying from 20 to 40% to 60–70%), Northern Dvina River (prevalence of 10–15%), Dniester and Neman Rivers (prevalence equal to or <10%), and other rivers [4]. Recently, the liver fluke distribution range has considerably expanded, and the prevalence of opisthorchiasis among humans in some regions has increased, which is considered to be associated with socioeconomic factors, such as migration of people between endemic and nonendemic areas [25–28]. Development of oil- and gas-bearing northern regions in Western Siberia has resulted in high opisthorchiasis infection among population in the Pur, Taz, and Nadym River basins, as populations in this territory widely practise shift work that leads to an increase of population [4,9] and infestation them by Opisthorchiidae parasite. For example, with beginning of the discovery of oil and gas deposits in Khanty-Mansiisk autonomous area the population increased by 10 times and prevalence of opisthorchiasis infection increased to 76.2% [10].

The consumption of raw, salted or undercooked freshwater cyprinid fish by the human population is thought to be the main factor linked to the high prevalence of infection. In this region, high level of infection with *O. felineus* in cyprinid fish have been reported [10] despite the absence of the first intermediate host, Bithyniidae snails, due to low water temperature [4,9]. Alternative snail host(s) should be identified in the future.

In this review, we summarize the available published data on the epidemiological aspects of opisthorchiasis among populations in Western Siberia, the geographical distribution of liver flukes, the life cycle of *O. felineus*, and the rates of infection with the Opisthorchiidae trematode parasite in intermediate (Bithyniidae snails and cyprinid fish) and definitive (humans, wild and domestic carnivorous mammals and birds) hosts. Potential measures that could be implemented for the control and prevention of the disease will be discussed.

2. General characteristics of Western Siberian aquatic bodies and watercourses

The area of Western Siberia is approximately 2.5 million km^2 [29]. This region is characterized by a developed network of river and lake systems. Thousands of rivers drain into the Western Siberian plain. The Ob River is one of the largest rivers in the world, with the area of its basin reaching almost 3 million km^2 and a length of 3676 km [30]. Characteristic of the Western Siberian rivers, including the largest ones, i.e., Ob and Irtysh, are small-angle slopes and a low flow speed (0.5 m/s), which result in large bogging areas. During the spring floods, rivers overflow and fill the river valleys. There are more than one million lakes with a total area of over 100,000 km^2 in the Western Siberian Plain. The ratio of lake surfaces to drainage areas varies from 1 to 1.5% in the southern region to 2% in the northern region, reaching 15–20% in some areas (i.e., the Surgut lowland) [31–33]. The aquatic bodies in arid areas (steppe and forest–steppe zones) are characterized by intra- and interannual fluctuations in water level that lead to fluctuations in the water-covered area and influence the hydrological and hydrochemical conditions and biota in both intra- and interannually.

An examination of the Ob opisthorchiasis focus suggests that the aquatic bodies and watercourses in this focus differ considerably from those other places in their hydroecological features and the characteristics of their hydrochemical and thermal regimes. In particular, this variation is associated with the specific features of different climatic zones. Three types of the opisthorchiasis foci have been distinguished: 1) *natural,* 2). *anthropic*, and 3) *mixed*. In natural foci, wild animals are involved in the transmission cycle [34]. In anthropic foci, opisthorchiasis is transmitted with the involvement of humans, whereas in mixed foci, transmission is associated with the involvement of both humans and domestic and wild animals [9]. In Western Siberia, all types of opisthorchiasis foci are associated with aquatic bodies lacking outflow and the Ob and Irtysh River floodplains. According to the hydrological and ecological features of affected aquatic bodies and watercourses, opisthorchiasis endemic foci that are associated with the tributaries of large rivers are categorized as *floodplain–river* foci, while foci associated with shallow lakes are associated with shallow lakes are categorized as *lake–interfluvial* foci [35–37]. The range and intensity of an opisthorchiasis focus may be estimated using statistical data on the prevalence of opisthorchiasis in the population, as reported by medical institutions [38–40]. The infection rates identified in Cyprinidae fish are also used for the estimation of the distribution and intensity of opisthorchiasis foci.

3. *Opisthorchis felineus* and its life cycle

O. felineus are hermaphrodite worms that, as adults, have a dorsoventrally flattened leaf-like shape, a body length of 13–18 mm and a width of 1–3.5 mm, and oral sucker at the anterior body end, ventral sucker in the anterior third of the body, and genital pore in the middle of the body [8]. The mouth is located at the bottom of the oral sucker and leads to the digestive tract, which comprises the pharynx, oesophagus, and two branches of the gut running along the sides of the body and blindly ending in the posterior part of the worm [4]. The life cycle of *O. felineus* in Prussia has been described in detail by Vogel [41], a German parasitologist. In Western Siberia, the biology of this parasite has been studied by several researchers [36]. The development of *O. felineus* includes sexual reproduction in the definitive hosts, which comprise carnivorous mammals, including humans, and piscivorous birds; asexual reproduction in the first intermediate host, which comprise snails of the family Bithyniidae; and development of the transmissible parasitic larvae, metacercariae, in the second intermediate host, which comprise fish of the family Cyprinidae (Fig. 1). Infection with Opisthorchiidae species (including *O. felineus)* has been detected in over 30 definitive host species [9].

Adult worms live in the intrahepatic bile ducts, gallbladder and more rarely in the extrahepatic pancreatic ducts of humans and carnivorous (domestic and wild) animals. Adult liver flukes can live in a human for 20 to 25 years [21]. The eggs laid by adult parasites through the genital pore enter the bile followed by the host's intestine, subsequently passing with the host's faecal material into environment. The eggs then continue to develop in freshwater. They can overwinter, thereby retaining their invasive ability. In the lake water at 0 to 5 °C, 42% of eggs could survive for up to 160 days [36]. Thus, at the bottom of the water reservoir, where the temperature is approximately 0 to 5 °C, the eggs can overwinter. *O. felineus* eggs can survive for up to 3 h at water temperatures ranging from −8 to −24 °C. The eggs may maintain viability for 10 h at temperatures ranging from −2 to 3 °C. In dried faeces, the eggs can survive for up to 3 days at 10 to 20 °C and up to 12 h at 2 °C. Although desiccation was found to completely kill eggs within 12 h, the eggs were found to remain viable for 16 to 18 days in incompletely dry faeces [42].

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