Sushi Delights and Parasites: The Risk of Fishborne and Foodborne Parasitic Zoonoses in Asia

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Because of the worldwide popularization of Japanese cuisine, the traditional Japanese fish dishes sushi and sashimi that are served in Japanese restaurants and sushi bars have been suspected of causing fishborne parasitic zoonoses, especially anisakiasis. In addition, an array of freshwater and brackish-water fish and wild animal meats, which are important sources of infection with zoonotic parasites, are served as sushi and sashimi in rural areas of Japan. Such fishborne and foodborne parasitic zoonoses are also endemic in many Asian countries that have related traditional cooking styles. Despite the recent increase in the number of travelers to areas where these zoonoses are endemic, travelers and even infectious disease specialists are unaware of the risk of infection associated with eating exotic ethnic dishes. The aim of this review is to provide practical background information regarding representative fishborne and foodborne parasitic zoonoses endemic in Asian countries.

Sushi and sashimi are traditional Japanese dishes known worldwide. In Japanese restaurants and sushi bars, they are preferentially, although not exclusively, prepared from relatively expensive marine fish such as tuna, yellow tail, red snapper, salmon, and flatfish/flounder. Among those fish, salmon is an important intermediate host for the fish tapeworm *Diphyllobothrium latum.* Although various marine fish species harbor *Anisakis* larvae, fish that are preferentially served in Japanese restaurants and sushi bars are less contaminated or are even free of *Anisakis* larvae. In contrast, other popular and cheap marine fish, such as cod, herring, mackerel, and squid tend to be heavily infected with *Anisakis* larvae and are mainly consumed at home or at local restaurants. Except for *Anisakis* and *D. latum,* marine fish usually only transmit few parasite species that infect humans. Thus, the risk of infection with fishborne parasites by dining in the Japanese restaurants and sushi bars is not as significant as is generally feared.

In rural areas in Japan, freshwater or brackish-water fish are consumed as sushi and sashimi. Moreover, various wild animals like frogs, land snails, snakes, backyard chicken, and wild boar are also served as sushi and sashimi, especially in the mountainous areas. They are also consumed raw or undercooked in a variety of ethnic dishes in many Asian countries as well. Because of this, an array of zoonotic parasites are transmitted to humans (table 1). Thus, travelers dining in local restaurants or street shops can be expected to have much higher risks of infections with various parasites. The aim of this review is to provide practical information on fishborne and foodborne parasitic diseases from Asia, which are less well-known among travelers and physicians in Western countries.

ANISAKIASIS

Anisakiasis is primarily an acute gastrointestinal disease caused by infection with either the herring worm *(Anisakis* species) or the cod worm *(Pseudoterranova decipiens).* The larvae reside in the muscles and the visceral organs of marine fish, with the intensity of infection varying among fish species. Human infection occurs by ingesting raw or undercooked fish. The apparent increase in anisakiasis cases in Japan and other developed countries is more related to advances in diagnostic techniques, such as endoscopy, than to an actual increase in the number of infections among sushi consumers [1].

The larvae usually penetrate the gastric wall causing acute abdominal pain, nausea, and vomiting within a few minutes to several hours (gastric anisakiasis). Immediate diagnosis can

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Table 1. Fishborne and other foodborne parasites.

Parasite	Source of human infection	Area with endemicity	Site(s) of infection	
			Usual	Occasional
Anisakis simplex	Marine fish (herring and mackerel)	Cosmopolitan regions	Stomach	Intestine and peritoneal cavity
Pseudoterranova decipiens	Marine fish (cod and squid)	Cosmopolitan regions	Stomach	…
Diphyllobothrium latum[a]	Lake trout	Cosmopolitan regions	Intestine	…
Gnathostoma sp.	Freshwater fish and snakes	Asia, Latin America, and Africa	Skin	Eyes and CNS
Capillaria philippinensis	Freshwater and brackish-water fish	The Philippines and Thailand	Intestine	…
Clonorchis sinensis	Freshwater and brackish-water fish	East Asia	Liver	…
Opistorchis viverrini	Freshwater fish	Indochina	Liver	…
Minute intestinal flukes				
Metagonimus yokogawai	Freshwater fish	Japan and Korea	Intestine	…
Others	Freshwater fish, frogs, and snakes	Asia	Intestine	…
Paragonimus species	Freshwater crabs, crayfish, and wild boar	East Asia	Lung	Skin and CNS
Angiostrongylus cantonensis	Snails, slugs, and green vegetables	Pacific Islands, Taiwan, and China	CNS	…
Spirometra erinaceieuropaei	Snakes, frogs, and backyard chicken	Cosmopolitan regions (mainly in Asia)	Skin	…
Fasciola hepatica[b]	Aquatic plants and bovine liver	Cosmopolitan regions	Liver	…
Fasciolopsis buski	Aquatic plants	China, Indochina, and India	Intestine	…

[a] The species endemic in Japan is classified as *Diphyllobothrium nihonkaienze,* and the major source of infection is an ocean trout.
[b] The species endemic in Asia is classified as *Fasciola gigantica*.

be confirmed by direct detection and extirpation of the parasite by upper gastrointestinal endoscopic examination.

Although the frequency is low, larvae may invade the intestinal mucosa (intestinal anisakiasis). Severe local pain occurs and inflammatory reaction often results in reactive intestinal obstruction. Radiological findings include irregular thickening and mucosal edema of the gastrointestinal tract, luminal narrowing, and dilatation. *Anisakis* larvae only survive for a few days in the intestinal tract of humans. Thus, empirical treatment using decompression with nasogastric tubing is recommended.

Anisakis larvae occasionally penetrate into the peritoneal cavity or other visceral organs (extragastrointestinal anisakiasis) [2] to cause eosinophilic granuloma, which is often suspected of being neoplasia. Pleurisy due to migration of *Anisakis* has been reported rarely in Japan [3]. Allergic reactions, such as angiedema, urticaria, or even systemic anaphylaxis, may accompany or dominate the clinical picture [4].

Peripheral blood eosinophilia may be absent in the acute stage of the disease, but the eosinophil count increases gradually with time. An antigen-capture ELISA with a reported sensitivity and specificity near 100% appears to be a very appropriate test for serodiagnosis of anisakiasis [5]. The appropriate drug treatment for anisakiasis has not been established. However, albendazole (dosage, 400 or 800 mg for 6–21 days) was shown to be effective in case reports [6, 7].

DIPHYLLOBOTHRIASIS

Diphyllobothriasis is an intestinal infection caused by the fish tapeworm *D. latum*. Infective larvae (plerocercoid) of *D. latum* reside in the muscles of trout, salmon, pike, and sea bass. After being ingested, the plerocercoids attach to the mucosa of the small intestine, where they become adult worms of ∼5–10 m in length. Its tail end (mature proglottids) often protrudes from the anus of a patient to cause an alarming surprise. The disease is regularly observed in cold climate areas, such as northern Europe and northern America. In Japan, salmon and trout have been commonly served as sushi and sashimi, and >100 cases are now recorded annually in the northern part of the country. Together with the development of a chilled transportation system, this disease is spreading all over Japan [8].

Infection with *D. latum* is mostly oligosymptomatic. Although diphyllobothriasis is known to cause reduced serum levels of vitamin B12 and subsequent anemia, such findings have never been recorded in Japanese patients. This may be related to the biological difference between the causative pathogens. In Japan, *Diphyllobothrium nihonkaiense*, which is different from *D. latum* in morphology [9] and molecular taxonomy [10], is responsible for some, if not all infections. The diagnosis is mainly based on the detection of ova or proglottids in the feces. The treatment of choice is a single dose of praziquantel (10–20 mg/kg).

GNATHOSTOMIASIS

Gnathostomiasis is primarily a disease of the skin caused by migration of the larvae of a *Gnatostoma* nematode. Of the 12 distinctive *Gnatostoma* species, *Gnatostoma spinigerum* is widely distributed in Asia and has been considered to be the only species with human pathogenicity. Infected patients are mainly found in Thailand and Japan. Recently, *Gnatostoma hispidum, Gnatostoma doloresi,* and *Gnatostoma nipponicum* have all been found in patients in Japan [11], and the recent outbreak of gnathostomiasis in Latin America was caused by *Gnatostoma binucleatum* [12]. Various fish harbor the parasites: snakehead *(G. spinigerum),* catfish *(G. spinigerum),* loach *(G. hispidum* and *G. nipponicum),* brook trout *(G. doloresi),* and tilapia *(G. binucleatum).* A few cases of infection after ingesting sashimi of terrestrial snakes have also been reported in Japan [13]. Snake meat is believed to have special tonic effects [14].

Nonspecific prodromal symptoms, such as malaise, fever, urticaria, and nausea, may be observed shortly after ingestion of larvae. Eosinophilia occurs by the time a skin lesion begins to develop. Dermatologic symptoms and their duration vary according to the causative species [16]. In *G. spinigerum* and *G. binucleatum* infections, the symptoms include the episodic appearance of migrating erythema, usually on the peripheral parts of the body. The symptoms may last for a few days to several years. In contrast, in *G. hispidum, G. nipponicum,* and *G. doloresi* infections, the larvae tend to migrate into the surface skin to form a serpiginous eruption on the trunk, and the lesion spontaneously disappears within 3 months after onset.

The occasional instance in which *Gnathostoma* larvae migrate into vital organs results in a serious, sometimes fatal illness. Involvement of the CNS may present as meningoencephalitis, cranial nerve palsy, myelitis, radiculitis, or subarachnoidal bleeding [15]. It is commonly associated with pleocytosis and eosinophilia (15%–90% of the nucleated cells) in the CSF [15]. MRI may reveal high intensity signals [16, 17]. Involvement of other organs and systems (e.g., lungs, intestines, genital organs, ear, and nose) is less frequently reported.

Diagnosis is based on the patient's memory of consuming undercooked fish in a region where gnathostomiasis is endemic, the clinical picture, eosinophilia in the peripheral blood and/or the CSF, serologic test results, and histological examination results. Skin lesions similar to those associated with gnathostomiasis are caused by other parasites. Creeping serpiginous eruptions are caused by dog or cat hookworm larvae or by *Spirurina* type X larvae. *Spirurina* infection in humans occurs after ingestion of sashimi of the tiny squid *Watasenia scintillans* [18] and has been reported only in Japan. Migratory edema and erythema can be seen in cases of cutaneous migration of *Paragonimus* species or *Spirometra* species (see below). Diagnosis can only be established by identification of the worms by biopsy, but immunoserological testing, in combination with obtaining a suggestive history, may be helpful in the absence of biopsies.

Treatment with albendazole at a dosage of 400 mg daily or twice daily for 21 days has been effective against cutaneous gnathostomiasis [19]. A comparable cure rate can be achieved by with a single dose of ivermectin (0.2 mg/kg) [20]. For CNS infection, a combination of treatment with albendazole at a dosage of 400 mg twice daily and corticosteroids was successful among infected tourists [16, 17]

INTESTINAL CAPILLARIASIS

This famous parasitic disease is caused by the nematode *Capillaria philippinensis.* Fish-eating birds appear to be the natural final host, and freshwater or brackish-water fish are the intermediate hosts. Human infection occurs after ingestion of raw fish. It is endemic in restricted areas of The Philippines and Thailand [21]. Sporadic cases have been reported in Japan, Korea, Taiwan, India, and Iran [22]. Recently, this disease was reported to be emerging in Egypt [23, 24]. One Italian [25] and 1 Korean [26] traveler have acquired this parasite in Indonesia, and 1 case has been discovered in Indonesia [27].

In the human intestine, adult female worms produce fertilized eggs and larvae. The latter can cause internal autoinfection. Patients experience diarrhea and abdominal pain, and, if the infection goes untreated, the symptoms get worse with progressive weight loss, weakness, malaise, anorexia, edema, and cachexia and often can result in death. Diagnosis is made by identifying the characteristic eggs in stool samples. Treatment with albendazole at a dosage of 200 mg daily (adult dose) for 10 days is standard.

PARAGONIMIASIS

Paragonimiasis is caused by infection with *Paragonimus* lung flukes. *Paragonimus westermani* is the most common species in Asia and is the major source of human infection. In addition, *Paragonimus scrjabini* in China, *Paragonimus heterotremus* in Indochina, *Paragonimus uterobilateralis* in Africa, and *Paragonimus mexicanus* in Latin America are known to cause human disease. Infective larvae (metacercariae) reside encysted in freshwater crabs, which may be included in ethnic dishes and ingested. Larvae penetrate the peritoneal cavity and move across the diaphragm into the pleural cavity. Abdominal symptoms may be observed during the migratory phase. Finally, the parasites migrate into the lung parenchyma, where they reach maturity and form solid worm cysts. Typical clinical manifestations are fever, chest pain, and chronic cough with hemoptysis (rusty-colored sputum). Radiographic findings are characterized by infiltrative, nodular, and cavitating lesions (figure 1) .

Diagnosis is confirmed by either detection of ova in sputum,

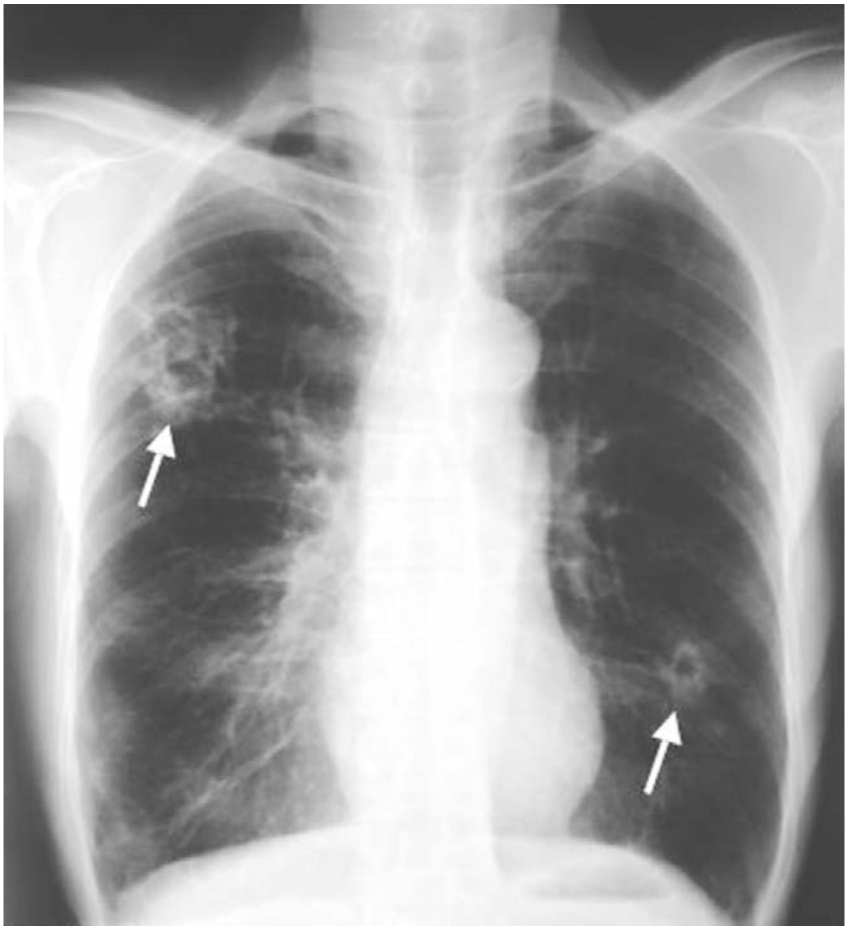

Figure 1. Chest radiograph showing typical cavitating lesions caused by *Paragonimus westermani* infection. The patient ate sashimi of wild boar meat ∼2 months before onset of the disease.

stool, or gastric aspirate specimens or serological test results [28]. Because of the complexity of the parasite's migration route within the host, cases of extrapulmonary paragonimiasis have occurred. Of those cases, cutaneous and cerebral paragonimiasis are the classic known forms of ectopic infection. Although paragonimiasis is still endemic in Japan and 30–50 new cases have been discovered annually, cerebral cases are extremely rare, although cutaneous cases are still occasionally recorded. This may be related to low density of infection [28].

Regardless of the causative species and the sites affected, patients can be treated with praziquantel at a dosage of 75 mg/kg per day for 3 days. Pleural effusion should be extensively drained off before the medication is given.

LIVER FLUKE INFECTIONS

Two species of liver flukes, *Clonorchis sinensis* and *Opistorchis viverrini*, are known to cause hepatobiliary disease. *C. sinensis* is widely distributed in Southeast Asia. The nationwide survey conducted in China in 1988–1992 estimated the total number of cases of clonorchiasis to be 4.12 million [29], and in 1974–1982, the number of cases in Korea was estimated to be >2 million [30]. Although Japan was a heavily infected area until around the 1960s, the number of infected patients drastically decreased with industrialization [31]. *O. viverrini* infection occurs in parts of northern Indochina. The mean prevalence of opistorchiasis in all of Thailand in 1992 was 15.2%, with the highest prevalence being in the northeast (24.1%) and second highest prevalence being in the north (22.8%) [32].

Human infection occurs after ingesting raw freshwater or brackish-water fish carrying infective larvae (metacercariae). Larvae migrate to bile ducts, where they develop into adult worms. Patients infected with only a few parasites are usually asymptomatic. A heavy infection may lead to obstructive jaundice and eventually to liver cirrhosis and cholangiocellular carcinoma, which is a serious public health issue in Thailand [33]. The infection is diagnosed by detection of ova in feces specimens, with the aid of radiographic or ultrasound findings (intraductal echoes and biliary dilatation). Because treatment with praziquantel (75 mg/kg per day for 2 days) is highly effective, early diagnosis and treatment are crucial to prevent long-term damage.

Another important hepatotropic fluke, *Fasciola hepatica,* is not a fishborne parasite. Infection occurs by ingesting aquatic plants. It does, however, have an unusual route: infection can occur by ingesting raw or undercooked bovine liver contaminated with juvenile worms [34]. Sashimi of bovine liver is served in "Yakitori" bars in Japan. Unlike its effectiveness in treating other fluke (trematode) infections, praziquantel is ineffective for the treatment of fascioliasis. Instead, a single dose of triclabendazole (10–20 mg/kg) is the treatment of choice [35, 36].

MINUTE INTESTINAL FLUKE INFECTIONS

Globally, ~70 species of intestinal flukes (trematodes) are known to infect humans [37]. Of those, 31 species belong to the *Heterophyidae* family, and 21 belong to the *Echinostomatidae* family; both are well-known families of fishborne parasites, many of which are distributed widely in Asia and are human pathogens. Infections with other species can occur by ingesting snails, frogs, snakes, and even aquatic plants. Nationwide epidemiological surveys have been conducted in Korea and Thailand; 17 indigenous species have been recorded in Korea [38], and 23 indigenous species have been recorded in Thailand [39]. In Japan, infection with *Metagonimus yokogawai* is still prevalent because people prefer to eat sushi and sashimi of the locally famous freshwater fish "Ayu" *(Plecoglossus altivelis). M. yokogawai* is the most frequently (10%–20%) detected parasite by examination of stool samples for parasite eggs at Mitsui Memorial Hospital in Tokyo, Japan [40].

Minute intestinal flukes are usually harmless, but heavy infections occasionally cause serious gastrointestinal symptoms. Regardless of the causative species, clinical features of intestinal fluke infections are similar. Because of the morphological similarities between species, species-specific diagnosis by identification of eggs in stool samples is almost impossible. Differential diagnosis can only be established by distinguishing adult worms purged in stool after treatment. Treatment with a single dose of praziquantel (10–50 mg/kg, depending on the parasite species) is effective for the treatment of minute intestinal fluke infections [38].

ANGIOSTRONGYLIASIS

Angiostrongyliasis is an acute or subacute infectious disease of the CNS caused by the larval stage of the nematode *Angiostrongylus cantonensis.* The parasite is distributed throughout tropical and subtropical countries between Madagascar and Tahiti, although the majority of human cases have been reported in the south Pacific islands and in Southeast Asia, especially in Taiwan [41] and Thailand [42]. Recently, an outbreak of the disease was reported in the southern coastal area of the Chinese mainland [43].

This nematode naturally parasitizes the pulmonary artery of wild rats. Human infection occurs after ingestion of raw or undercooked snails or slugs, which are the intermediate hosts. Recently, however, outbreaks of this disease associated with drinking vegetable juice [44] or eating green salad [45] were reported in Taiwan and Japan, respectively. Larvae usually migrate into the CNS via the bloodstream, causing eosinophilic meningoencephalitis. Infected patients present with a variety of symptoms, including from asymptomatic to transient meningitis, coma, and even death [41, 42]. The common clinical features include severe headache, neck stiffness, nausea, and vomiting. Patients frequently experienced visual disturbance or diplopia after experiencing headache. Various types of paresthesia were also noted in many patients. Ocular migration of larvae has been reported in countries where *A. cantonensis* is endemic [41–43, 45]. Analysis of CSF samples obtained from infected patients has revealed pleocytosis with eosinophilia [41–43]. Antibodies can be detected in serum samples from most patients [41–43]. Detection of antibodies in the CSF is helpful [41–43].

The treatment of angiostrongyliasis is still controversial. Albendazole may cause the clinical course to deteriorate, possibly because of an inflammatory reaction to the dead worms causing damage to brain tissues. Generally, steroid use is recommended for patients with elevated intracranial pressure. Recently, however, Chotmongkol et al. [46] recommended a combination of albendazole and corticosteroid for the treatment of this disease.

SPARGANOSIS (SPIROMETOROSIS)

Spirometra erinacei-europaei is a tapeworm found in dogs and cats. Its larva (plerocercoid), also called *Sparganum mansoni,* looks like a white tape of about 10–20 cm (up to 70 cm) in length and resides in the connective tissues, muscles, or viscera of various amphibians, reptiles, birds, and mammals. Infection in humans occurs by ingesting raw or undercooked meat of those animals. In Japan, sashimi of frogs, snakes, and backyard chicken are the major sources of human infection. Approximately 500 cases have been reported in Japan [47], but the realistic figures are certainly higher.

In the human body, larvae usually appear in the subcutaneous tissues of the anterior chest, the abdominal wall, or the inguinal region and form slow-growing migratory nodular lesions without causing pain or redness. Larvae may occasionally migrate into unexpected parts of the body, such as the pleural cavity [48] or the CNS [49], causing unusual or even fatal manifestations. A total of 11 cases of cerebral sparganosis have

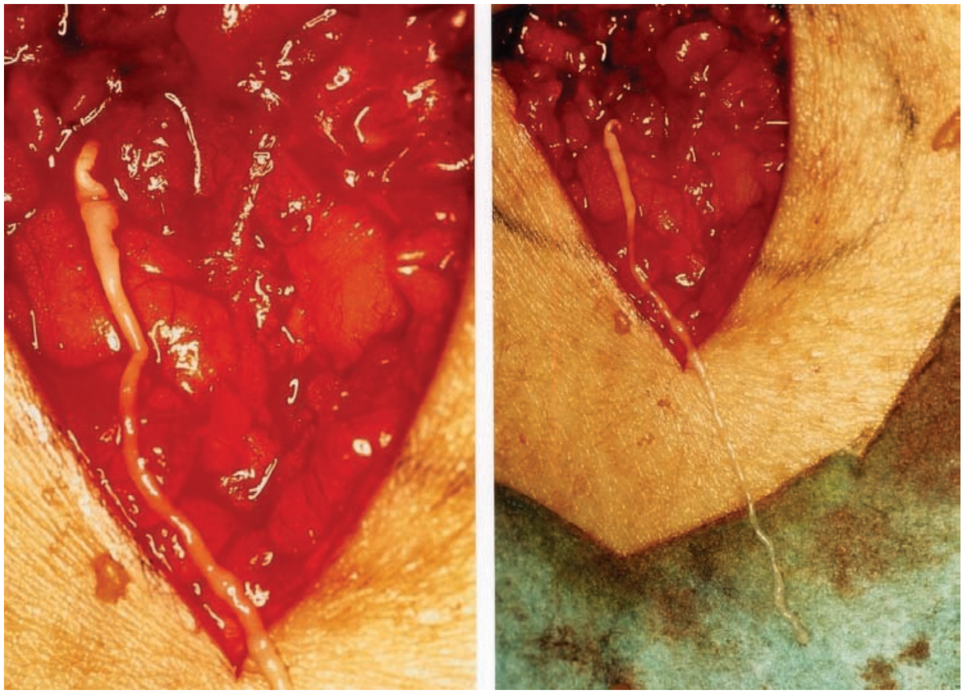

Figure 2. Surgical extirpation of *Spirometra erinacei-europaei* from the nodular lesion on a patient's thigh. Although the actual source of infection was not identified, the patient often ate sashimi of backyard chicken meat, which was believed to be the source of infection.

been reported in Japan [49]. The diagnosis is based on histological identification of the worm or serologic test results.

Surgical removal of the worm (figure 2) is the first choice of treatment. Attention must be paid to ensure that the worm is removed completely, because the worms can regenerate from the residual head and neck portions. Because cases of pleural sparganosis have been successfully treated by oral administration of praziquantel at a dosage of 75 mg/kg per day for 3 days [48], this protocol could be applied to other forms of this disease.

CONCLUSIONS

Sushi and sashimi prepared from expensive marine fish harbor a low risk of infection with zoonotic parasites. In particular, the US Food and Drug Administration recommends preserving fish for raw consumption by storing it at less than −35°C for 15 h or at less than −20°C for 7 days. Similarly, according to the European Union–Hazard Analysis and Critical Control Points, marine fish for raw consumption should be frozen at less than −20°C for more than 24 h. Therefore, sushi and sashimi served in sushi bars and Japanese restaurants in those areas are safe. The risk of infection by eating sushi and sashimi is higher in countries where such legal regulations have not been implemented.

More attention is necessary regarding local ethnic dishes prepared from local freshwater or brackish-water fish and wild animal meats, which are consumed as sashimi or some other special dishes, following a belief that consuming them will result in mysterious tonic effects. They serve as intermediate or reservoir hosts for various zoonotic parasites, which are not common in Western countries. Taking fishborne and other foodborne parasites into consideration, zoonotic parasites cause an unacceptable burden of morbidity and mortality and lead to serious damage in aquaculture, which is a valuable source of food and employment in developing countries [50].

Travelers and physicians in Western countries should be informed about the risk and possible symptoms of such infections caused by eating ethnic dishes. The majority of human cases of fishborne or other foodborne parasitic infections can, generally, be easily be treated by anthelmintic drugs after an accurate and early diagnosis has been established.

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