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Integrated parasite management: path to sustainable control of fishborne trematodes in aquaculture

Jesper H. Clausen[1], Henry Madsen[1], Phan Thi Van[2], Anders Dalsgaard[1], and K. Darwin Murrell[1]

[1] Faculty of Health and Medical Sciences, Department of Veterinary Disease Biology, University of Copenhagen, Denmark
[2] Research Institute for Aquaculture Number 1 (RIA1), Bac Ninh, Viet Nam

Fishborne zoonotic trematodes (FZT) are an emerging problem and there is now a consensus that, in addition to wild-caught fish, fish produced in aquaculture present a major food safety risk, especially in Southeast Asia where aquaculture is important economically. Current control programs target communities at risk through mass drug administration. However, we argue that treatment alone will not reduce the risk from eating infected fish and that sustainable effective control must adopt an integrated FZT control approach based on education, infrastructure improvements, and management practices that target critical control points in the aquaculture production cycle identified from a thorough understanding of FZT and host biology and epidemiology. We present recommendations for an integrated parasite management (IPM) program for aquaculture farms.

The problem of fishborne parasites in aquaculture

Recent global health assessments have identified FZT (see Glossary) as among the most important (and neglected) parasitic zoonotic diseases [1–7]. Along with bacteria and viruses, FZT can be important causes of illnesses in humans, ranging from mild gastroenteritis to life-threatening disease [8]. These infections occur in humans and other reservoir hosts as a result of ingesting raw or improperly cooked fish that are infected with the metacercaria stage of the zoonotic trematodes (or flukes). The liver flukes *Opisthorchis viverrini, O. felineus*, and *Clonorchis sinensis* are notable for causing chronic inflammation of the hepatobiliary system, which in chronic infections may lead to cholangiocarcinoma [9]. Infections with intestinal FZT (mainly species of Heterophyidae such as *Haplorchis* spp.) and Echinostomatidae (e.g., *Echinochasmus* spp.) may cause intestinal inflammation, diarrhea, and invasion of the heart, brain, and spinal cord by parasite eggs [10,11]. Other important intestinal flukes are *Metagonimus* spp., *Centrocestus* spp., *Stellantchasmus falcatus*, and *Procerovum varium* [11].

In many countries, wild-caught fish are important sources of FZT, and the increase in aquaculture production in Asia has been proposed as increasing the risk for human cases of fishborne trematodiasis in that region [1,2,4,12,13]; research is needed to clarify the relative risk from these sources of fish. The growth in aquaculture has been remarkable over the past few decades, especially in the People's Republic of China, India, and several countries in Southeast Asia. The increase in production is driven by growing demands in both national and global markets, as well as by technological advances and improved efficiency in the aquaculture sector [14,15]. Fish cultured in Asia now account for 85% of world aquaculture production, and

Glossary

Catchment area: the area from which rainfall flows into a single basin (e.g., pond, reservoir, lake, or river).
Cercaria: a larval trematode that develops in a molluscan host from a redia or sporocyst and emerges as a tailed swimming form that seeks out a host (e.g., fish) in which it invades and develops to the metacercaria stage (usually encysted).
Cholangiocarcinoma: a cancer of the biliary system of humans, which has been associated with chronic infections of the liver flukes *Opisthorchis* spp and *Clonorchis sinensis*.
Fish fry: fish larvae that have developed to the age that they are capable of feeding themselves.
Fishborne zoonotic trematodes (FZT): these are transmitted to humans as metacercariae that have encysted in fish.
Host: most trematodes have a life cycle requiring at least two hosts: the definitive or primary host (a vertebrate) in which the flukes sexually reproduce, and an intermediate host (a mollusk), in which asexual reproduction occurs, producing a cercaria, the agent of transmission to other hosts.
Integrated parasite management (IPM): the inclusion of prevention and control actions that are identified through HACCP analysis as critical points for risk of infection, and may include education, management and infrastructure changes, and use of drug treatment of definitive hosts when appropriate.
Juvenile fish: fish fry that morphologically resemble the adult (e.g., possess scales and working fins) but are sexually immature and are not full-grown.
Metacercaria: a tailless encysted (e.g., in the tissues of a fish) late larva of a trematode that is usually the stage that is infective for the definitive host.
Semi-intensive aquaculture systems: semi-intensive culture systems which depend at least partially on natural food that can be increased over baseline levels by fertilization (often in the form of human and animal fecal waste) and/or use of supplementary feed to complement natural food.
Reservoir host: definitive host (for a parasite to reproduce sexually) that can serve as a source of infection for other hosts, independently of human hosts in the case of zoonotic trematodes.
Trematoda: trematodes (flukes) represent a class of mostly hermaphroditic, dorso-ventrally flattened worms in the phylum Platyhelminthes that internally parasitize molluscs and vertebrates.
VAC system: a semi-intensive fish culture system named after the Vietnamese words for garden (*Vuon*), pond (*Ao*), and livestock housing (*Chuong*, pigsty).

Corresponding author: Murrell, K.D. (kdmurrell@comcast.net).
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many species are globally traded and consumed. With this global increase in aquaculture production, the potential for contamination of aquaculture products with biological and chemical agents has also grown [1,3,6,16]. The prevalence of FZT in humans and cultured fish in Asia is often very high, up to 50–70% for both hosts [1,4,9,11,12,17–23]. Current control strategies for dealing with this food safety risk at the pre-harvest stage of aquaculture production are either lacking or ineffective. This paper discusses recent progress in the effort to develop a sustainable and practical FZT control program for aquaculture that reduces the risk of infection for both fish and people, and highlights future research needs into prevention and control that could minimize the risk from FZT in fish and humans.

The biology and epidemiology of FZT in aquaculture

The life cycles of FZT are complicated and begin with the contamination of the aquatic environment by infected host feces containing parasite eggs and their subsequent ingestion by a suitable aquatic snail intermediate host (Figure 1). This initiates the stages of trematode asexual multiplication that leads to infection of fish by cercariae and the subsequent development of the metacercariae, the infective stage for humans and a wide range of reservoir hosts, especially cats, dogs, and pigs [11]. Typically, infected humans and reservoir hosts harbor multiple species of FZT, frequently both liver and intestinal flukes [24–28]. Importantly, fish-eating birds may serve as a reservoir host for the intestinal species of FZT. The snail intermediate hosts are species of the family Bithynidae (for both liver flukes and intestinal flukes) or the family Thiaridae (intestinal flukes and possibly liver flukes) (Figure 2). Numerous species of fresh- and brackish-water fish may serve as second intermediate hosts for both liver and intestinal flukes, and mixed infections in both cultured and wild fish are common [21,23,29–39]. In some areas of Southeast Asia, wild fish are important sources of FZT infection.

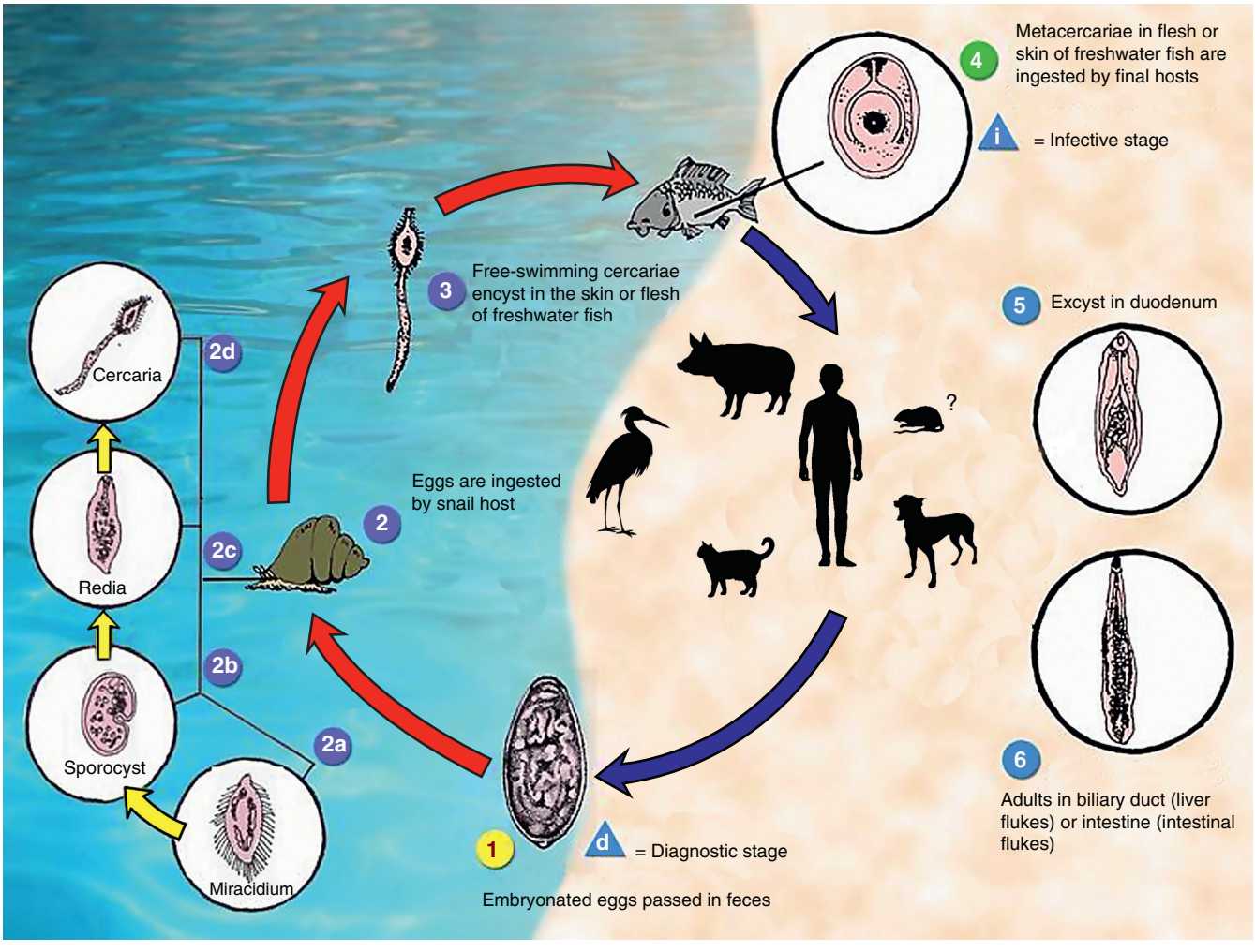

Figure 1. The basic life cycle of the fishborne liver and intestinal flukes is illustrated. These parasites are members of the superfamily Opisthorchoidea and have very similar life cycles. However, the liver flukes belong to the family Opisthorchiidae, and utilize snail intermediate host species that differ from that of the intestinal flukes, most of which belong to the family Heteropyhidae. As their common names indicate, the majority of opisthorchid adults parasitize the liver, bile ducts, and gall bladder of mammals and birds. Most adult heterophyids, by contrast, parasitize the intestine of fish-eating birds and mammals (a few species inhabit fish as adult worms). Infected hosts shed fluke eggs in their feces and, if the eggs reach water, they can be ingested by an appropriate snail species. In the snail, the parasite emerges from the egg and undergoes several stages of asexual multiplication before emerging from the snail as swimming cercaria. Fish movements attract cercariae which, on contact with the fish, penetrate various tissues, including under scales, and develop into encysted metacercaria. This stage is infective to mammals (and birds in the case of the intestinal flukes) and is transmitted to them when the fish is ingested improperly prepared (i.e., inadequately cooked, frozen, or pickled [1]).