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Heterophyiasis, an intestinal fluke infection of man and vertebrates transmitted by euryhaline gastropods and fish

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ABSTRACT: *Heterophyes heterophyes,* agent of human heterophyiasis in the Near East, is transmitted in marine lagoons and saline inland waters, where the euryhaline intermediate hosts are abundant. In Egypt, mullets, the predominant second intermediate hosts, are customarily consumed raw; thus man becomes infected easily. Symptoms of human infections are usually considered mild. Mullets do not seem to be affected by the metacercariae encysted in the muscles, whereas the growth of the snail host *Pirenella conica* was found to be enhanced due to the infestation by the trematodes. In laboratory experiments, the flukes were found to be well developed in dogs, foxes and cats, but failed to reach sexual maturity in several other potentially piscivorous mammals and birds. In nature, dogs probably serve as the major reservoir hosts. Heterophyiasis is most prevalent in the Nile Delta, a huge brackish water area which is densely populated by humans and, consequently, also by dogs and cats. In the Far East, besides *Heterophyes nocens,* several other heterophyids with marine or fresh-water life-cycles are known to infect humans.

INTRODUCTION

At least 14 species of heterophyid trematodes are known from the human intestine. Humans as definitive hosts are affected accidentally, or on a large scale where fish is consumed raw, salted, or insufficiently cooked (chiefly in East Asia and in South-East Asia).

As these 'human' heterophyids are transmitted by prosobranch gastropods of the families Potamididae, Melaniidae, Pleuroceridae and Littorinidae – and subsequently by fish with a similar habitat preference – several species are encountered along the coasts. Still, *Cryptocotyle lingua,* which was shown to parasitize 6 % of the investigated Eskimos on Greenland (Babbot et al., 1961), is the only species marine biologists have paid attention to adequately.

Among the heterophyids with medical relevance the species most frequently reported from humans are listed in Table 1. As heterophyid eggs of different species may be very similar to each other, infections can often be diagnosed to the species level only, by medical expulsion of the flukes or by autopsy. Only such reports are listed in Table 1.

Mullets, *Mugil cephalus* for instance, act as the most important second intermediate hosts of *Heterophyes* spp., *Pygidiopsis summa* and *Stellantchasmus falcatus* (Table 1). *Metagonimus* spp. and *Haplorchis yokogawai* encyst in fresh water fish. As mullets may

Table 1. Heterophyidae most frequently reported from the human intestine

Fluke species	Snail hosts	Human cases reported from	Recent reports or reviews, remarks
Heterophyes heterophyes (v. Siebold) Stiles & Hassal	Near East: *Pirenella conica* (Potamididae)	Near East	v. Siebold (1852); Looss (1902); Khalil (1937); Kuntz & Chandler (1956a)
H. nocens Onji & Nishio	*Cerithidea cingulata (= Tympanotonus micropterus)* (Potamididae)	East Asia	Ito (1964); Yokogawa et al. (1965); Seo et al. (1981). Often *H. nocens* is considered a subspecies of *H. heterophyes*
Pygidiopsis summa Onji & Nishio	*Cerithidea cingulata*	East Asia	Ito (1964); Yokogawa et al. (1965); Seo et al. (1981)
Metagonimus yokogawai Katsurada	*Semisulcospira libertina* (Pleuroceridae)	Asia	Ito (1964); Yokogawa et al. (1965); Seo et al. (1981). Ito (1964): "The incidence of *Metagonimus* in the human body (in Japan) is considered to be ca 1 %, and yet in certain local areas the incidence of tens percent is exhibited."
M. takahashii Suzuki	*Semisulcospira libertina*	East Asia	Sakai (1962); Ito (1964). In recent years generally accepted as a species different from *M. yokogawai* (Saito, 1973)
Stellantchasmus falcatus Onji & Nishio	*Tarebia granifera* and other melaniid snails	Asia, Oceania	Ito (1964); Kagei et al. (1964); Tantachamrum & Kliks (1978)
Haplorchis yokogawai Katsuta	*Melanoides tuberculatus* and other melaniid snails	Asia	Ito (1964); Manning & Lertprasert (1970); Manning et al. (1971). Africa (1938): ". . . not only the most frequently encountered in man in this country (Philippines) but also the most frequently associated with cardiac failure."

freely migrate between the sea and fresh water, metacercariae of the 'coastal species' may be carried into fresh water as well.

The aim of this paper is to summarize the information on the biology and ecology of *Heterophyes heterophyes* (Fig. 1), the agent of human heterophyiasis.

HOST RECORDS

Definitive hosts

Heterophyes heterophyes was found in Egypt in the human intestine for the first time in 1851 (v. Siebold, 1852). Later on, the number of autopsies mentioned is only

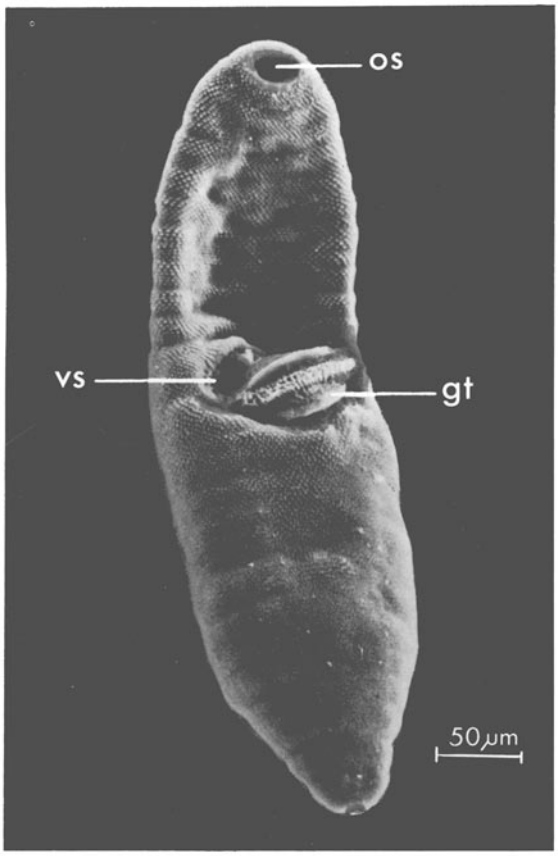

Fig. 1. *Heterophyes heterophyes* from intestine of a cat taken by a scanning electron microscope. os = oral sucker; vs = ventral sucker; gt = gonotyl (genital sucker)

scarce (Looss, 1902; Khalil, 1937). However, the fluke has been frequently diagnosed by coprological diagnosis (Khalil, 1937; Wells & Blagg, 1956; Nagathy & Khalil, 1964; Coble et al., 1968; Sheir & El-Shabrawy Aboul-Enein, 1970; Rifaat et al., 1980). As the prevalence of other heterophyids in the area in question is lower than that of *H. heterophyes* (Taraschewski, 1984), in Egypt this diagnosis can be accepted as fairly reliable.

Positive dissections of dogs (Abdel Azim, 1938; Kuntz & Chandler, 1956a; Wells & Randall, 1956; Fahmy & Selim, 1959) and cats (Kuntz & Chandler, 1956a; Wells & Randall, 1956) have shown that this parasite is not specific to humans.

A few wild mammals and birds were also found to be infected: *Vulpes vulpes, Canis aureus, Felis chaus, Milvus migrans* (Wells & Randall, 1956); *Pelecanus onocrotalus* (Looss, 1902).

Outside Egypt, the fluke has been recorded, in recent years*, only in dogs and to a lesser extent in cats. Mediterranean area: Witenberg (1929); Balozet & Callot (1939);

* Witenberg (1932) also reported human cases from Palestine (Israel).

Mimioglu et al. (1959); Deiana (1961); Himonas (1964, 1968, 1977); Jemen: Kuntz & Chandler (1956a); Iran: Massoud et al. (1982); India, Sri Lanka: Rao & Ayyar (1932); Maplestone & Bhaduri (1940); Dissanaike (1961); Sen (1965); Rao & Anantaraman (1967); Rajasekariah et al. (1974); in India *H. heterophyes* is considered an extremely rare parasite of man (Maplestone & Bhaduri, 1940); South-East Asia: Segal et al. (1968).

As the taxonomical status of *Heterophyes nocens* is not sufficiently solved yet, *H. heterophyes* is sometimes recorded from East Asia also. Whenever descriptions of the flukes in question are available, however, it becomes clear that *H. nocens* is meant.

Second intermediate hosts

Khalil (1923) detected that mullets serve as the second intermediate hosts of *H. heterophyes*. Several species of Mugilidae have been found infected since then (data only from Egypt and Israel available). Paperna & Overstreet (1981) listed: *Mugil cephalus, M. capito, M. auratus, M. saliens,* and *M. chelo* as being naturally infected. Mature metacercariae of *H. heterophyes* were also obtained experimentally from *Liza subviridis* and *L. ramada* (Taraschewski & Paperna, 1981).

In addition to these Mugilidae, many species of other euryhaline and marine fishes were recorded as intermediate hosts: *Epinephelus enaeus* (Serranidae), *Tilapia (Sarotherodon) simonis* (Cichlidae), *Lichia amia, L. glauca* (Carangidae), *Barbus canis* (Cyprinidae) (Witenberg, 1929), *Tilapia (Sarotherodon) nilotica, T. zillii, Solea solea* (Soleidae), *Sciaena aquilla* (Sciaenidae) (Wells & Randall, 1956).

Heterophyid metacercariae, obviously of *H. heterophyes,* were also found in *Dicentrarchus labrax, D. punctatus, Sparus auratus, Argyrosoma regius* (Paperna & Overstreet, 1981). Non-mugilid fishes were also described as being susceptible to experimental infections: *Gambusia affinis* (Poecilioidae) (Khalil, 1937), *Fundulus parvipinnis* (Cyprinodontidae) (Kuntz & Chandler, 1956a) and *Tilapia (Sarotherodon) mossambica* (Taraschewski, 1984).

Usually mullets show the highest intensities of *Heterophyes* infections (Khalil, 1937; Wells & Randall, 1956; Paperna & Overstreet, 1981). As yet, there is no information available on whether Mugilidae are most susceptible or whether it is the habitat preference of these fish which makes them the predominant intermediate hosts.

First intermediate host

Khalil (1937) found the mud snail *Pirenella conica* Blainville to be the first intermediate host of *H. heterophyes*. Since then *P. conica* naturally infected with *H. heterophyes* have been mentioned by Martin & Kuntz (1955); Kuntz & Chandler (1956a); Martin (1959); Taraschewski & Paperna (1981, 1982). Quantitative data on specific prevalence of this fluke in different snail populations have been collected by Taraschewski (Fig. 2, Table 2). Contrary to the distribution of the second intermediate hosts, distribution of *P. conica* is limited to the eastern and southern Mediterranean, Red Sea and the Persian Gulf (Taraschewski & Paperna, 1981). As no other potamidid gastropod is known from the Mediterranean, it can be concluded that this species acts as the only snail host in the Mediterranean. In India, however, *Cerithidea cingulata* (syn. *Tympanotonus micropterus*), the host of *H. (heterophyes) nocens* in East Asia (Asada, 1928)

probably is the first intermediate host. According to Evans et al. (1973), both potamidid snails occur in the Persian Gulf. Thus in this area too, further investigation into the intramolluscan part of the life cycle is desired.

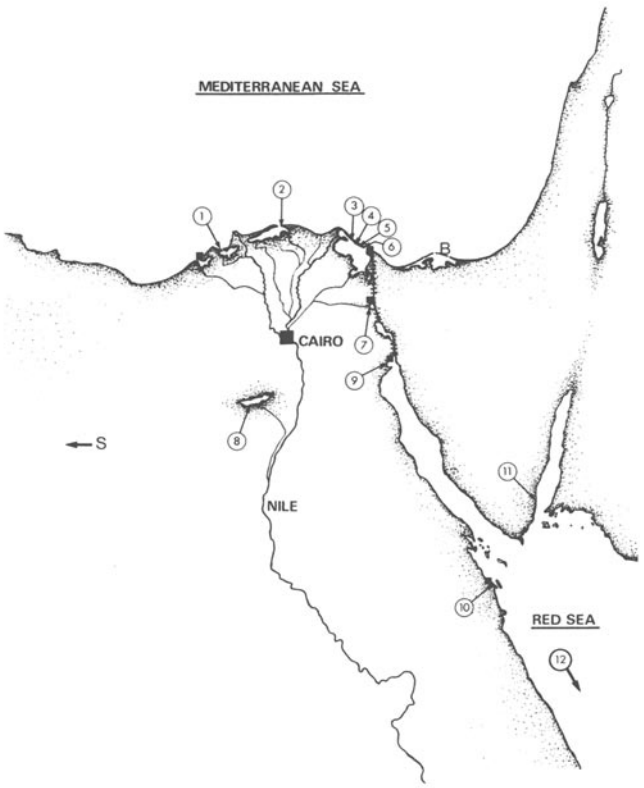

Fig. 2. Populations of *Pirenella conica* examined for prevalence of *Heterophyes heterophyes*. For explanations see Table 2. B = Bardawil Lagoon; S = Siwa Oasis

ENVIRONMENT OF TRANSMISSION

As shown by Seo et al. (1981), in Korea prevalence of *Heterophyes nocens* and *Pygidiopsis summa* in humans is concentrated along the coast, where *Cerithidea cingulata* thrives in lagoons and estuaries, while *Metagonimus yokogawai* is the dominant heterophyid inland. According to Vohra (1970), *C. cingulata* occurs in a variety of wave sheltered (subsequently soft sediment) habitats 'from brackish water to supersalted fishponds with a salinity range of 15–45 ‰', usually in high population densities. In Japan, environmental conditions such as these are chiefly found around the 'Inland Sea' between the major islands, where prevalence of H. nocens in that country is accordingly highest (Ito, 1964).

Pirenella conica is also adapted to lagoon environment (Fig. 3) (Taraschewski & Paperna, 1981, 1982); however, salinity tolerance also includes the hypersaline range,

Table 2. Prevalence rate of *Heterophyes heterophyes* in *Pirenella conica* in Egypt and Sudan

Sampling site	Site No. (see Fig. 2)	Date of sampling	No. of snails examined	No. of snails shedding *H. heterophyes*	Prevalence rate (%)	Habitat type
Lake Idku	1	April 1982	400	27	7	brackish water lake; rural environment; 10 km east of Alexandria
Lake Burullus	2	April 1982	150	57	38	huge brackish water lake; sampling station on black mud off a small town; prevalence of other trematodes in *P. conica* very low
Lake Menzaleh	3	Sept. 1981	295	10	3	huge brackish water lake; important fishery ground; distance to the city of Port Said decreasing from Station 3 to Station 6; Station 6 at the outskirts of the city
	4	Sept. 1981	225	10	4	
	5	Sept. 1981	200	27	14	
	6	Sept. 1981	500	~80	16	
Lake Timsah	7	Sept. 1981	375	1	0.3	saline inland lake in the Suez Canal; only one population of *P. conica* on the bathing beach of Ismaelia
Lake Qarun	8	April 1982	650	15	2	saline inland lake; rural environment; only few populations of *P. conica*
Suez beach	9	Sept. 1981	250	1	0.4	northern end of Gulf of Suez; dense population of *P. conica* on black mud; high prevalence of other heterophyids
	9	April 1982	540	~10	2	
Hurghada harbor	10	April 1982	623	~12	2	fishery harbor of Hurghada; only a few human settlements in vicinity; high prevalence of other heterophyids
Sinai Mangrove	11	April 1980	500	–	–	marine lagoon fringed by a mangrove thicket; no human settlements in vicinity; abundance of water birds; high prevalence of *Heterophyes aequalis* and other heterophyids
	11	April 1981	630	~3	0.5	
	11	Febr. 1982	200	1	0.5	
Sudan Mangrove	12	Dec. 1980	400	–	–	mangrove thicket on uninhabited island near Suakin; abundance of water birds; other heterophyids very prevalent

Fig. 3. *Pirenella conica* (dark dots) on intertidal mud flat (after Taraschewski & Paperna, 1981)

obviously due to the arid climate of the Near East. It has been shown by field observations and laboratory experiments that this gastropod was able to tolerate a salinity range of 15–80 ‰. *P. conica* also occurs in saline inland waters with an athalassiohalinic ion composition such as Lake Qarun and lakes of the Siwa Oasis (Fig. 2) (Taraschewski & Paperna, 1981).

Along the Mediterranean Coast, the Nile Delta is the major centre of abundance of *P. conica;* dense populations are found in each of the great brackish water lakes (Fig. 2).

Numerous dense populations of *P. conica* also exist along the sheltered shore of the northern Red Sea. In the Nile Delta, however, the accumulation of first and second intermediate hosts and definitive hosts creates a unique epidemiological situation. The eutrophic lakes serve as nursery and feeding grounds for mullets and other fishes of commercial importance (e.g. *Tilapia [Sarotherodon] nilotica*) (Khalil, 1937; Paperna & Overstreet, 1981). Most of the present-day 43 million Egyptians live in the delta surrounded by large numbers of stray dogs and cats. In addition, – contrary to other Mediterranean countries like Tunisia, where it is unusual to consume raw fish (Balozet & Callot, 1939) – fresh salted mullet 'fessikh' is considered a delicacy by many Egyptians (Khalil, 1937; Rifaat et al., 1980) and is thus probably the most important source of infection to man. According to Khalil (1937), metacercariae inside mullet put on ice

(2–4 °C) were found still alive and infective after 13 days, in salted fish for a maximum of 7 days.

PREVALENCE OF INFECTION

Snails

A survey of different habitats of *Pirenella conica* in Egypt and Sudan (Taraschewski, 1984) (Fig. 2) revealed, that prevalence of *Heterophyes heterophyes* was highest in the Nile Delta (Table 2). At Lake Burullus, 38 % of the snails examined* shed cercariae of *H. heterophyes***. At Lake Menzaleh on the outskirts of Port Said, about 16 % infection was noted. Prevalence rates decreased with increasing distance to the city of Port Said (Fig. 2, Table 2). At the inland saline lakes Qarun and Timsah, prevalence rates were lower than in the Delta, also on the scarcely populated coast of the Red Sea, where only a few snails were found infected by *H. heterophyes*. At the Red Sea two other *Heterophyes* spp. *(H. aequalis, H. dispar),* which have a more sylvatic cycle are abundant (Taraschewski, 1984).

Fish

Second intermediate hosts are heavily parasitized by metacercariae of *H. heterophyes* throughout the Delta and the surrounding Sea (Khalil, 1937; Wells & Randall, 1956; Paperna & Overstreet, 1981). In the 1950s, prevalence rates of *Mugil cephalus* and *M. capito* of Lake Menzaleh (Fig. 2) were found to be 100 % or almost 100 % (Wells & Randall, 1956); these authors reported similarly high prevalence rates of *H. heterophyes* in fish from the inland Lake Qarun (Fig. 2), where only a few snails were found to be infected in 1982 (Table 2).

As to the intensity, there is only one report available from Bardawil lagoon (Fig. 2), east of the Suez Canal. About 10 years ago, up to 6000 heterophyid metacercariae were recorded per gramm of muscle in *Mugil capito* and up to about 1000 in *M. cephalus* (Paperna & Overstreet, 1981). Probably, these enormous parasite burdens were obtained in the adjacent Nile Delta, as the environment of Bardawil lagoon is almost uninhabited. This assumption is supported by the fact that young fish of the lagoon were predominantly infected by *Heterophyes aequalis* and *Stictodora sawakinensis,* both of which are shown to be transmitted in a sylvatic kind of environment (Taraschewski, in prep.) such as that at Bardawil lagoon. According to recent spot checks by Paperna (pers. comm.) and by Taraschewski (unpubl.), it seems that the intensity of infection in mullet of that lagoon has been decreasing. East of Bardawil lagoon, on the Israeli coast, where only one epidemiologically isolated population of *P. conica* exists, *H. heterophyes* is also sometimes found in large mullets (Paperna & Overstreet, 1981), which probably became infected in the Nile Delta. Heterophyid infections in young-of-the-year mullet mostly consisted of *Stellantchasmus falcatus* (Paperna & Overstreet, 1981). Cercariae of this species were shown to have the best viability at salinities ranging from 4.5–9.0 ‰ S (Lee

* Only snails > 6 mm in length were collected, as no infection was noted in snails below that minimal size (Taraschewski & Paperna, 1981, 1982).

** Actual prevalence was probably higher, as not all infected snails will have released cercariae after experimental treatment.

& Cheng, 1970). So these infections, obtained in the low salinity estuaries of the Israeli coast, could be autochthonous.

Definitive hosts

As to the definitive hosts, the first quantitative data on human infections became available in 1937. At that time, up to 90 % of the school children investigated and 22 % of the adults near Lake Menzaleh (Fig. 2) defecated '*Heterophyes* eggs' (Khalil, 1937) (Fig. 4). Wells & Blagg (1956) found *Heterophyes* eggs in the stools of 36 % of the school children of Baltim at Lake Burullus (Fig. 2). Nagathy & Khalil (1964) reported about 10 % of the persons investigated near Lake Menzaleh to be infected. Finally Rifaat et al. (1980) found an average of 2.5 % infection in the same area. Thus, like other intestinal helminth diseases of humans the prevalence of heterophyiasis seems to be declining.

From the area of the saline inland lakes, snails of which have been examined by Taraschewski (Fig. 2, Table 2), and the Red Sea, nothing is known about the prevalence of *H. heterophyes* in humans. From the Siwa Oasis, however, about 300 km inside the Libyan Desert (Egypt), of 42 persons investigated, one defecated *Heterophyes* eggs (Coble et al., 1968). Although two populations of *P. conica* have been reported from the Siwa Depression (Crawford, 1948; Ibrahim, 1975), it is uncertain whether the case reported by Coble et al. can be considered autochthonous.

Concerning the other vertebrate hosts in Egypt, all quantitative data are older than 25 years. In addition, either the three Egyptian *Heterophyes* spp. are not treated separately and data of different geographical origin are pooled (Wells & Randall, 1956), or statements are very general (Kuntz & Chandler, 1956a). Proportionally large numbers

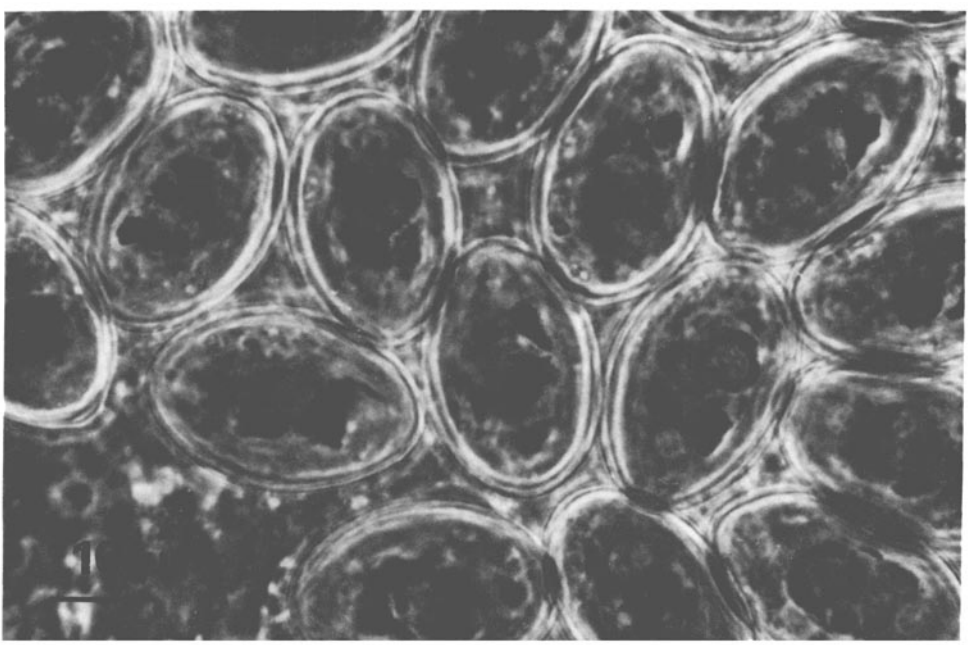

Fig. 4. Embryonated eggs of *Heterophyes heterophyes* inside the uterus of a fluke

of the cat and dog population were infected. According to recent reports from Greece (Himonas, 1968, 1977), 16 % (n: 186) of the examined stray dogs and 6 % (n: 123) of stray cats of the city of Thessaloniki were found to be infected by *H. heterophyes*.

CONCLUSIONS

Laboratory experiments with 16 different definitive hosts (Taraschewski, in prep.) have shown (Table 3) that (besides humans) probably only Canidae and cats are susceptible to *Heterophyes* infection; in these animals the flukes reach a life span of

Table 3. Susceptibility of different definitive hosts to infection by *Heterophyes heterophyes*

Hosts	No. of animals sacrificed	Flukes reach sexual maturity	Days of life span	Recovery rates (%) (3–25 d p.i.)
Macaca irus	2	–	< 12	0–15
Rattus norvegicus	5	–	< 16	0–94
R. tiomanicus	7	–	< 18	0–71
R. rattus	5	–	< 8	0–29
Canis familiaris	5	+	~ 60	61–83
Alopex lagopus	4	+	> 23	66–93
Vulpes vulpes	7	+	~ 60	55–91
Felis catus	14	+	60–120	32–81
Meles meles	1	–	< 6	0
Mustela putorius furo	4	–	< 3	0
Martes foina	1	–	< 6	1
Sus scrofa	2	–	< 14	0–12
Egretta gularis	2	–	< 3	0
Ardeola ibis × *Nycticorax nycticorax*	1	–	< 9	0
Larus argentatus	4	–	< 9	0–30
L. ridibundus	3	–	< 3	0

about 2 to 4 months. Considering the larger size and greater amount of uterine eggs, Canidae turned out to be better hosts than cats. In all the other hosts uterine eggs did not become embryonated and life span did not exceed 14 days.

As flukes from the human intestine were found to have a similar size to those from dogs (Kuntz & Chandler, 1956a), humans can be considered suitable hosts.

Besides dogs and cats, *Canis aureus, Vulpes vulpes, Felis chaus* and *Milvus migrans* may also act as reservoir hosts (these species besides dogs and cats were found naturally infected by Wells & Randall, 1956). However, probably only dogs serve as important reservoir hosts. Cats do not defecate on wet substrate and, as the Egyptian human population rapidly increases, wild animals are becoming rare.

According to Ito (1964), in Japan *Metagonimus yokogawai* is found more frequently in dogs than in humans. For *H. heterophyes* this observation can be confirmed in respect to the prevalence of this fluke in India or in Greece for instance. In Egypt, however, it is uncertain whether dogs or humans act as the predominant definitive hosts.

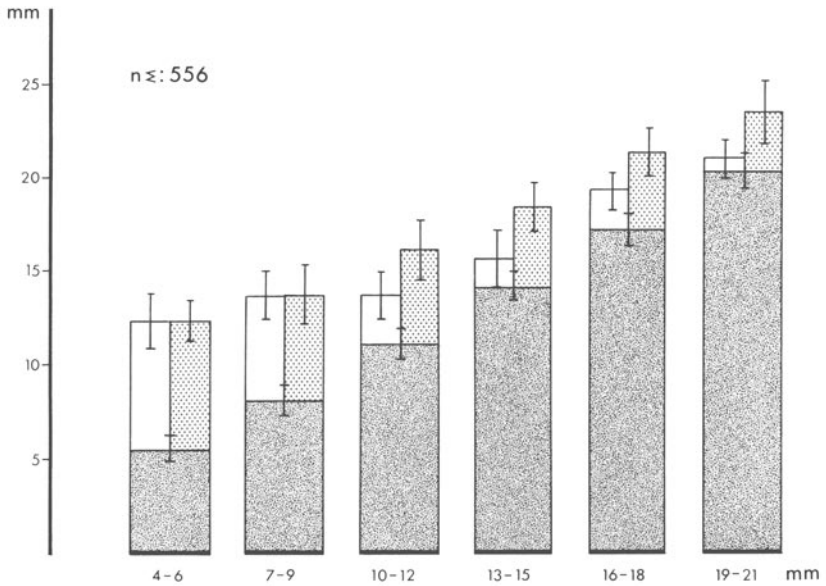

Fig. 5. Growth of *P. conica* naturally infected by heterophyids *(H. heterophyes, H. aequalis, Stictodora sawakinensis)* within 2 months. Ordinate: snail length in mm; abscissa: initial length of snails in mm; base column: initial length; undotted column: growth of uninfected snails (Σn: 297); dotted column: growth of infected snails (Σn: 259)

Host-parasite relations

Little investigation has been conducted on the question of how intermediate and definitive hosts of *H. heterophyes* are affected by the fluke.

Snails

After the snails have ingested the fluke eggs, the embryonic development of *H. heterophyes* is presumably similar to that of *H. aequalis,* described by Kuntz & Chandler (1956b). Rediae, producing cercariae, were found inside the digestive glands (Taraschewski & Paperna, 1981). From growth experiments with snails naturally infected with heterophyids (*H. heterophyes, H. aequalis, Stictodora sawakinensis*), it becomes conspicuous that below 10 mm initial size, growth of infected and of uninfected specimens was about the same (Fig. 5). Above 10 mm initial length, infected snails showed enhanced growth when compared to the uninfected snails (Taraschewski, 1980). Thus it can be suspected that heterophyid trematodes have some detrimental influence on reproduction of *Pirenella conica,* as was shown in other relationships between snails and flukes.

Fish

Nothing is known about the pathogenicity of *H. heterophyes* inside the second intermediate hosts. There is only one investigation available on *Stellantchasmus falcatus* infections in *Mugil cephalus* (Lee & Cheng, 1970). These authors reported that "the presence of the parasite, even when unencysted, results in the necrotic degeneration of

the surrounding muscle cells, especially those situated at the anterior or posterior ends of the parasite. Large, vacuolated fat cells . . . are usually found filling the spaces vacated by necrotic muscle cells" (Lee & Cheng, 1970).

As those mullets highly infected with *Heterophyes* metacercariae, reported by Paperna & Overstreet (1981), were still found alive, one may conclude that the viability of mullets is not much affected by the presence of the *Heterophyes* metacercariae in their muscles. Still, investigation on the pathogenicity of *Heterophyes heterophyes* in different fish hosts is needed.

Metacercariae in experimentally infected *Gambusia affinis* (Khalil, 1937) and *Tilapia (Sarotherodon) mossambica* (Taraschewski, 1984) became infective about 20 days post infectionem.

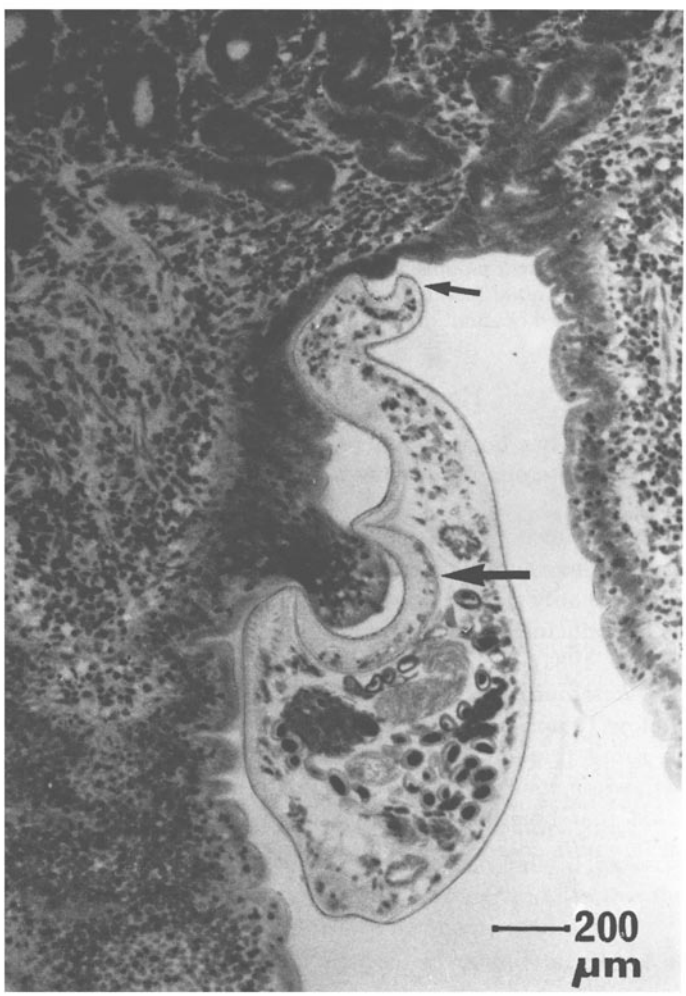

Fig. 6. *Heterophyes* spec. in small intestine of a cat. Big arrow: ventral sucker clinging to host mucosa; small arrow: oral sucker feeding on host tissue

Definitive hosts

Inside experimentally infected definitive hosts, metacercariae of *H. heterophyes* were shown (dogs: Khalil, 1937; cats: Taraschewski, 1984) to excyst about 4 h after oral application. Excystment took place in the upper small intestine (Taraschewski, 1984) or in the duodenum (Khalil, 1937). From *H. heterophyes* (Hamdy & Nicola, 1981), *Metagonimus yokogawai* (Ito, 1964) and *Haplorchis yokogawai* (Africa et al., 1940) it has been described that after excystment, the juvenile flukes penetrate into the intestinal glands or into the tissue of the mucosa. After a few days they normally return to the intestinal lumen, where they adhere to the mucosa by their ventral sucker (Fig. 6). By means of their oral sucker they feed on the host's mucosal tissue (Fig. 6).

From the data on *H. heterophyes*, it seems that the place of primary attachment to the mucosa is in the same part of the small intestine as the place of excystment where the flukes are still found one or two months later (in suitable hosts) (Taraschewski, 1984). When the site of attachment of juvenile flukes 3 d p.i. (days post infectionem) is compared to that of sexually mature flukes 10–120 d p.i. it appears that – due to the intestinal motility – they are just passively carried slightly backwards (Fig. 7). Independent of the species of host, *H. heterophyes* generally prefers the middle part of the small intestine (Fig. 7).

In some cases, sexually mature heterophyids were found stuck in the intestinal wall, from where their eggs could be infiltrated into different organs by way of the blood stream or lymphatic system (see review by Ito, 1964). In Japan, where *Metagonimus yokogawai* is the most prevalent heterophyid species, nothing is known about fatal human cases due to such eggs (Ito, 1964). In the Philippines, however, where *Haplorchis yokogawai* is the most prevalent species in humans, Africa et al. (1940) estimated that 15 % of the fatal heart cases resulted from heterophyid myocarditis. In a series of papers,

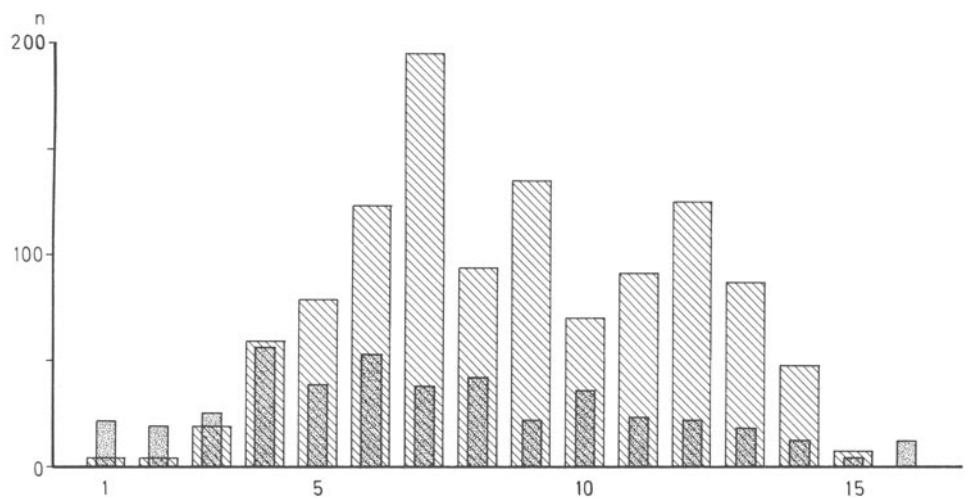

Fig. 7. Distribution of juvenile and mature *Heterophyes heterophyes* throughout the small intestine of experimentally infected definitive hosts. Ordinate: n flukes; abscissa: 16 segments of small intestine. Narrow striped bars = Juvenile flukes (3 d p.i., n: 358 from 9 cats and 3 foxes). Broad dotted bars = Mature flukes (10–120 d p.i., n: 862 from 9 cats and 3 foxes)

summarized in 1940, these authors reported many findings of heterophyid eggs in the tissues of human beings autopsied in the Philippines.

Only in two cases were eggs, assigned to *H. heterophyes,* found encapsulated in the human brain (Collomb et al., 1960). In another case, an egg attributed to *H. nocens* was detected inside a tumor of an inflamed appendix (Ito, 1964).

Symptoms of intestinal heterophyiasis seem to be – as usual – dependent on the intensity of infection. Heavy infections, according to Khalil (1937), are accompanied by abdominal discomfort, nausea, headache, vomiting, diarrhea, and sometimes dysentery. Similar symptoms are described for human infections by *Metagonimus yokogawai,* where the literature is much more comprehensive (Ito, 1964).

Experimentally infected dogs started defecating eggs (Fig. 4) of *H. heterophyes* 8 d p.i. (Witenberg, 1929); experimentally infected cats on day 9 (Khalil, 1937). Assumably the prepatent period also in humans will be about 7 days, while flukes may have a life span of 1 to 4 months, as shown from infected Canidae and cats (Table 3).

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