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A review of the heterophyid flukes in man

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The heterophyid flukes are intestinal parasites of birds and mammals. Infestations with these flukes are acquired by consuming raw fish containing metacercariae, the infective stage of the flukes. To date, about 21 species have been naturally and experimentally reported in man; pathological effects, geographic distributions, and life cycles are reviewed.

จิตรา ไวกกุล. พยาธิใบไม้ตระกูลเฮตเทอโรไฟอิดที่พบในคน. จุฬาลงกรณ์เวชสาร 2528 ตุลาคม; 29(10) : 1131-1138

พยาธิใบไม้ตระกูลเฮตเทอโรไฟอิดี้ โดยปกติอาศัยในลำไส้เล็กของสัตว์ปีกและสัตว์เลี้ยงลูกด้วยนม ติดต่อกันได้โดยการกินปลาดิบซึ่งมีตัวอ่อนระยะติดต่อก่อน, เมตตาเซอคาเรีย, ของพยาธิตระกูลนี้เข้าไป ถึงปัจจุบันนี้มีผู้รายงานพบพยาธิตระกูลนี้ในคนแล้ว 21 ชนิด พยาธิสภาพ การแพร่กระจาย และวงจรชีวิตของพยาธิในตระกูลนี้ได้รวบรวมไว้ในบทความนี้

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The family Heterophyidae comprises a number of small flukes, parasitic mostly in the small intestine of birds and mammals. The heterophyids differ from flukes in other families in having a peculiar structure at the genital pore, the gonotyl, that forms the basis of the classification of the family Heterophyidae. The heterophyids are small, usually less than 5 mm. in length, the body usually covered with scale-like spines; oral sucker and pharynx are present, the caeca tubular, the ventral sucker well developed or modified, the gonotyl present or absent, the testes globular or lobed, usually two with well developed seminal vesicle, the ovary pretesticular; the egg small containing miracidium.^(1,2) Members of this family are of great interest as they are common parasites in man and domestic animals; infections by some species were believed to have been fatal in the Philippines.⁽³⁾

Species Reported In Man

The heterophyids in man have been reviewed by a number of authors.^(1,4,5,6) To date, about 21 species have been reported in man, both natural and experimental infections, scientific names and localities recorded are listed in Table 1. In North America, infection with *Apophallus venustus* has been inferred from the presence of trematode eggs in human faeces,^(7,8) there being no other fish-borne trematode whose eggs were morphologically similar in that area. Although infection with *Metagonimus romanicus* has been considered to occur in man, in Spain,⁽⁹⁾ the differential diagnosis between the two species based on egg morphology alone can not be certain as the heterophyid egg is similar to eggs of trematodes in many families such as the

opisthorchids, the microphallids and the plagiorchids. *Heterophyes dispar* and *Heterophyes aequalis* were reported by Witenberg⁽⁵⁾ without detail. Human infection with *Cornatrium perpendiculum* was quoted by Price⁽¹⁾ but not in the original report of Onji & Nishio.⁽¹⁰⁾ The species mentioned above are not listed here as heterophyids in man. Infection with *Procerovum varium*, *Centrocestus formosanus*, *Metagonimus minutus* and *Apophallus donicus* has been established experimentally in man. Some localities recorded are not listed here, such as *Procerovum calderoni*, reported in China by Chen⁽¹¹⁾ and Hsu⁽¹²⁾ but thought to be *Procerovum varium* by Pearson.⁽¹³⁾ Faust,⁽¹⁴⁾ who considered *Heterophyes nocens* to be a synonym for *Heterophyes heterophyes*, reported *H. heterophyes* in Japan and China where it had not yet been found.

In Thailand, *Haplorchis taichui* was reported in 1 and *Haplorchis yokogawai* in 2 of 21 autopsies at Udomthani provincial hospital.⁽¹⁵⁾ Klicks and Tantachamrun⁽¹⁶⁾ initially reported a case of *Stellantchasmus falcatus* in Chaingmai, but added 3 more cases⁽¹⁷⁾ found in surgical sections of the terminal ileum. Radomyos, Bunnag and Harinasuta⁽¹⁸⁾ found 301 *Haplorchis pumilio* adults in 12 of 411 faecal materials from patients taking antihelminthic drug. To date, only 4 species of heterophyids have been reported in Thai people, from the subfamily Haplorchinae, *Haplorchis*-group which was described in detail by Pearson and Ow-Yang.⁽¹⁹⁾

The incidence of heterophyid flukes in man depends on the culinary habits of the area where fish is an important source of protein. High incidence can be expected where raw fish is preferred; on the other

hand infection take place accidentally by hand or by food and water contamination with the metacercariae.

Pathology

Symptom of this infection vary from case to case, light infection with *Metagonimus yokogawai* in 154 adults were reported as asymptomatic, but heavy infection in 17,560 adults, were characterized by mild chronic diarrhoea.⁽²⁰⁾ An infection with 204 metacercariae of *M. Yokogawai* given orally produced a gastro-intestinal allergy characterized by pyrexia, headache, nausea, muscular and abdominal pain and diarrhoea.⁽²¹⁾ Mild necrosis of the intestinal mucosa at the attachment sites of the worms was observed by Khalil.⁽²²⁾ An adult *Heterophyes* was removed from a cerebral cyst in a native of Morocco while the eggs were discovered as subcutaneous and muscular cysts.⁽²³⁾ Neurological symptoms and abnormalities of the cerebrospinal fluid were also reported.⁽²⁴⁾ A tumour was reported in the abdomen of a Japanese patient and eggs found in the tumour were identified as *Heterophyes nocens*.⁽²⁵⁾ This identification was entirely based on eggs and thus may be inaccurate. In the Philippines Africa, De Leon & Garcia^(26,27,28,3) reported several species of heterophid flukes, in more than thirty autopsies at the Manila city morgue. In thirteen of those, where deaths were diagnosed as heart failure, eggs were found in organs such as brain, heart, spinal cord, liver lung and spleen, reaching their destination presumably via the circulatory system.

Life Cycle

The known life-cycles of heterophyids follow a pattern common to the superfamily Opisthorchioidea. Eggs are ingested by a

gastropod, the first intermediate host; miracidia hatch in its small intestine and penetrate the intestinal wall where sporocysts develop in the outer layer, Cercariae leave the rediae when they are not fully grown and develop freely inside the snail to emerge when fully grown by penetrating its skin; they swim in the water until they contact a fish, the second intermediate host, which they penetrate to encyst as metacercariae in various parts such as the muscle, gill, fin ray, outer intestinal wall, the membrane of the brain, the liver, heart and under the scales; some species also encyst in amphibians. The infection of the definitive host occur with the ingestion of the metacercariae in the second intermediate host.

Cable⁽²⁾ proposed the name 'opisthorchioid' for all types of cercariae in the superfamily Opisthorchioidea which are similar in morphology, including those of the Heterophyidae. The common features of cercariae are as follows^(2,29) : small body usually pigmented with a pair of eyespots, covered with spines, oral sucker, armed typically with three transverse rows of per-oral spines, pharynx being present, caeca rudimentary or absent, penetration glands usually seven in pairs with ducts opening to four groups of 3-4-4-3, cystogenous glands numerous dorso-laterally, ventral sucker and genital primordium rudimentary, excretory bladder epithelial variable in shape from saccate to v-shaped, tail longer than body typically with a dorso-ventral finfold.

The cyst of metacercaria is usually small and ovoid. The wall is composed of a thin transparent layer of hyaline material secreted by the cercarial body and usually covered with a thick layer of

Table 1 Species and localities records of heterophyid flukes in man

Species	Localities Record in man	Authority
<i>Apophallus donicus</i>	Oregon	(30)
<i>Centrocestus armatus</i>	Japan	(31)
	Egypt	(32)
<i>C. cuspidatus</i>	Formosa	(33)
<i>C. formosanus</i>	Formosa	(34)
<i>C. longus</i>	Formosa	(35)
<i>Cryptocotyle lingua</i>	Greenland	(5)
<i>Haplorchis pumilio</i>	Formosa	(34)
	Egypt	(22)
	Philippines	(3)
	Thailand	(18)
<i>H. taichui</i>	Philippines	(36)
	Pakistan	(37)
	Formosa	(34)
	Thailand	(15)
<i>H. vanissimus</i>	Philippines	(36)
<i>H. yokogawai</i>	Formosa	(38)
	Philippines	(39)
	Indonesia	(40)
	Thailand	(15)
<i>Heterophyes heterophyes</i>	Egypt	(41)
	Israel	(42)
	Turkey	(43)
<i>H. katuradai</i>	Japan	(44)
<i>H. nocens</i>	Japan	(45)
<i>Heterophyopsis continus</i>	Japan	(35)
<i>Metagonimus minutus</i>	Formosa	(46)
<i>M. yokogawai</i>	Formosa	(47)
	Japan, Korea	
	Philippines	
	China, Spain	
	Ukraine	
	Rumania	
	East Indies	
<i>Procerovum calderoni</i>	Philippines	(3)
<i>P. varium</i>	Japan	(48)
<i>Pygidiopsis summa</i>	Japan	(49)
<i>Stellantchasmus falcatus</i>	Hawaii	(50)
	Japan	(51)
	Formosa	(38)
	Philippines	(3)
	Thailand	(16)
<i>Stictodora fuscata</i>	Japan	(52)

host reaction tissue. The fully grown heterophyid metacercariae look like young non-ovigerous adults, that is, almost sexually mature.

Most of the heterophyids in man are also found in birds and other mammals but *Heterophyes nocens*, *Metagonimus minutus*, *Procerovum calderoni*, *Procerovum varium* and *Stictodora fuscata* have to date been reported in mammals only. Common bird definitive hosts are *Milvus migrans*, *Nycticorax nycticorax*, *Egretta intermedia*, *Larus argentatus*, *Pelecanus*

onocrotalus and *Sterna hirundo* which probably are the most easily collected fish-eating birds. The snail host of the heterophyid flukes commonly belongs to the families Thiaridae, Pleuroceridae, Littorinidae and Potamidae. Heterophyid metacercariae are usually found encysted in many families of fish such as Cobitidae, Cottidae, Cyprinidae, Gobiidae, Mugilidae, Ophicephalidae, Percidae, Pleglossidae and Siluridae. These snails and fishes belong to both freshwater and marine species.

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