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Experimental human infection with *Fibricola cratera* (Trematoda: Neodiplostomidae)

Wesley L. Shoop
Merck Institute for Therapeutic Research, P.O. Box 2000, Rahway, New Jersey 07065-0900, U.S.A.

Abstract: *Fibricola cratera* is a strigeoid trematode indigenous to North America that, heretofore, was known only to infect wild mammals. Herein, it is reported that an experimental inoculation of a human volunteer produced a patent infection that lasted 40 months. Symptoms of epigastric discomfort, loose stools and flatulence occurred over the first year of infection and ameliorated thereafter. Eggs per gram of stool were low (≤ 2) throughout the course of infection and were not detected by the standard technique of formalin-ether concentration. To monitor infection, the entire stool sample was examined each month after sieving through No. 10 (pore size 2 mm) and 100 (pore size 145 μm) sieves and collecting eggs on a No. 325 (pore size 45 μm) sieve. This is the first report of a North American strigeoid trematode capable of maturing in a human and is only the second species of strigeoid known to do so. The other species is *F. seoulensis* which has been implicated in 26 human infections in Korea.

Key words: *Fibricola cratera*, *F. seoulensis*, human, experimental infection

INTRODUCTION

Fibricola cratera is a strigeoid trematode indigenous to North America. Its life cycle includes a physid snail as first intermediate host, ranid frogs as second intermediate hosts, colubrid and viperid snakes as paratenic hosts and various species of wild mammals as definitive hosts(Hoffman, 1955; Ulmer, 1955; Turner, 1957; Shoop and Corkum, 1982; Cole and Shoop, 1987). The mammalian definitive host becomes infected by ingesting a metacercarial stage (neodiplostomulum) found either in the second intermediate or paratenic host. Because human infection by this species was thought to be remote, no medical significance has been accorded it. Recently, an Asian species reported as *Fibricola seoulensis* has been implicated in numerous human infections and is the only strigeoid trematode known to mature in this host (Seo *et al.*, 1982; Hong *et al.*, 1984 & 1986). Its life cycle is virtually identical to that of *F. cratera* (Seo *et al.*, 1988). Thus, the genealogical relationship and similarity of life cycle, ecology and morphology between *F. seoulensis* and *F. cratera* suggests that the latter may also have the potential to infect humans. The present study was designed to determine definitively whether *F. cratera* can mature in the human.

MATERIALS AND METHODS

Metacercariae of *F. cratera* were removed from the mesenteric fat deposits of cottonmouth snakes, *Agkistrodon piscivorus*, collected at Head-of-Island, Louisiana, USA. The fat de-

posits were placed in 0.7% saline and comminuted for 2 sec in a tissue blender. When the metacercariae had sedimented, the supernatant composed of lipid and lipocytes was decanted and fresh saline added. After several decantations, the supernatant was clear enough to view the helminths at the bottom of the vessel. The metacercariae of *F. cratera* were identified microscopically and separated from other helminths and tissue debris. One hundred of the metacercariae were isolated in sterile saline, concentrated in a single drop via a Pasteur pipette and inoculated into the back of the throat of a human volunteer on 14 March 1986. The volunteer was a 31 year old, caucasian male in good health and prior to inoculation had no helminth eggs in his stool.

After inoculation, a 1 g stool sample from the volunteer was examined for the presence of helminth eggs at weekly intervals for the first 6 weeks using the standard formalin-ether concentration method(Beaver *et al.*, 1984). Thereafter, the entire fecal sample was weighed and sieved through a No. 10 (pore size 2 mm) and 100 (pore size 145 μm) mesh screen and collected on a No. 325 (pore size 45 μm) mesh screen. The material was then backwashed into pilsner glasses, allowed to settle for 3 minutes, decanted and the entire sediment examined microscopically at monthly intervals for 3.5 years.

RESULTS

The first four weekly stool samples that were examined by the formalin-ether sedimentation method failed to detect any evidence of parasitism and the inoculation was believed to have been unsuccessful. However, beginning at 4 weeks post-inoculation, the volunteer began to experience epigastric discomfort, loose stools and flatulence. Formalin-ether samples up to 6 weeks post-inoculation contined to prove negative. At that point it was decided to examine the entire stool sample, and from the sievings were observed golden-brown, operculate eggs measuring 70 (65~75) μm wide and 125 (115~135) μm long. They were identified as *F. cratera* (Fig. 1). No other species of helminth egg or protozoan was ever observed from the stool samples.

At no time during the course of infection did the number of eggs in the feces ever exceed 2 eggs per gram. Notwithstanding low numbers, passage of eggs continued unabated for 40 months (Table 1). The aforementioned symptoms subsided, however, at approximately 12 months post-inoculation. At 41 months post-inoculation the passage of eggs ceased.

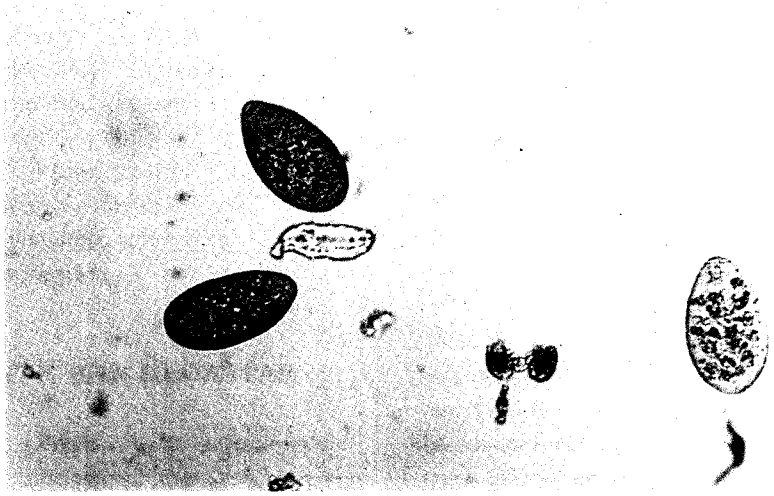

Fig. 1. Eggs of *Fibricola cratera* from the stool of an experimentally-infected human. Fggs measure 70 (65~75) μm wide by 125 (115~135) μm long.

Table 1. Stool data from a human experimentally-infected with 100 metacercariae of *Fibricola cratera* on 14 March, 1986

Date	Method	Eggs/gram
14 Mar. 1986	formalin/ether	0
21 Mar. 1986	formalin/ether	0
28 Mar. 1986	formalin/ether	0
5 Apr. 1986	formalin/ether	0
12 Apr. 1986	formalin/ether	0
19 Apr. 1986	formalin/ether	0
26 Apr. 1986	formalin/ether	0
26 Apr. 1986	total	2
14 May. 1986	formalin/ether	0
14 May. 1986	total	2
14 Jun. 1986	total	2
14 Jul. 1986	total	1
14 Aug. 1986	total	2
14 Sep. 1986	total	2
15 Oct. 1986	total	1
14 Nov. 1986	total	1
14 Dec. 1986	total	1
14 Jan. 1987	total	2
15 Feb. 1987	total	1
14 Mar. 1987	total	1
14 Apr. 1987	total	2
14 May. 1987	total	2
13 Jun. 1987	total	2
15 Jul. 1987	total	1
14 Aug. 1987	total	2
14 Sep. 1987	total	2
14 Oct. 1987	total	2
14 Nov. 1987	total	1
13 Dec. 1987	total	2
14 Jan. 1988	total	2
14 Feb. 1988	total	1
14 Mar. 1988	total	2
15 Apr. 1988	total	1
14 May. 1988	total	1
13 Jun. 1988	total	2
14 Jul. 1988	total	2
14 Aug. 1988	total	<1
15 Sep. 1988	total	<1
14 Oct. 1988	total	<1
14 Nov. 1988	total	<1
12 Dec. 1988	total	<1
14 Jan. 1989	total	<1
14 Mar. 1989	total	<1
14 Apr. 1989	total	<1
12 May. 1989	total	<1
13 Jun. 1989	total	<1
14 Jul. 1989	total	<1
21 Aug. 1989	total	<1
14 Sep. 1989	total	0

DISCUSSION

This study clearly demonstrates that *Fibricola cratera* is capable of infecting humans. This is the first North American strigeoid found to mature in a human and represents only the second strigeoid species ever reported to do so.

Egg production in the human volunteer was low and was initially missed by the standard concentration method for detecting trematode eggs, *i.e.* the formalin-ether method. Only upon examination of the entire stool sample were eggs observed. Low egg output is typical for this species of trematode (Turner, 1957) and in my experience with experimental and natural infections in a variety of definitive hosts there has never been more than six eggs in any one worm. It would appear then that natural human infections with *F. cratera* could easily be overlooked by standard methods.

Symptoms due to *F. cratera* and exhibited by the volunteer are typical of those reported for human infections with *F. seoulensis* (Seo *et al.*, 1982; Hong *et al.*, 1984 & 1986). Epigastric discomfort with hyperactive peristalsis, loose stools and flatulence are common. Both *F. seoulensis* and *F. cratera* inhabit the duodenum of the host and attach tenaciously to individual villi. In fact, the entire anterior end of these worms is scoop-shaped and fits securely on a villus (Lee *et al.*, 1985). In addition to the anterior end, the worms maintain their position in the intestine by attachment of the oral sucker, acetabulum, tribocytic organ and myriads of posteriorly-oriented spines located on the forebody. It is conjectured that these anchoring devices collectively contribute to the irritation of the intestinal tract and the symptoms that ensue.

The persistence of these infections is somewhat surprising. In reconstructing the epidemiology of *F. seoulensis* infection in Korean patients, Hong *et al.* (1984) concluded that the length of some infections appeared to be more than two years. The human infection reported

herein for *F. cratera* appears to confirm the fact that these organisms are long-lived and that even infections of over 3 years duration are possible.

Finally, the mode of *F. seoulensis* transmission to humans in Korea has been reported to be through ingestion of the metacercarial stages in raw or undercooked frogs and snakes. The muscle of frogs and snakes is ingested for nutritional benefits, but the viscera of snakes, in particular, is ingested raw because it is believed by some to have an effect on male virility (Hong *et al.*, 1984). Epidemiologically, this is important because it is in the snake viscera, particularly the fat bodies, that the metacercariae are concentrated. In North America, frog and, to a much lesser degree, snake flesh are consumed and considered a delicacy by many. However, ingestion of snake viscera as an enhancement for male virility has yet to become part of the cuisine. Thus, in North America the possibility of human infection with *F. cratera* is real, the probability is low, and methods for its detection at this time must be regarded as suspect.

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