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Human oesophagostomiasis: clinical presentations and subclinical colonic pathology

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CHAPTER 8

Natural progression of *Oesophagostomum bifurcum* pathology and infection in a rural community of northern Ghana

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ABSTRACT

An estimated 250,000 people in northern Ghana and Togo are infected with the intestinal helminthic parasite *Oesophagostomum bifurcum*, as detected by stool cultures. Clinical disease caused by *O. bifurcum* is responsible for approximately 50 cases per year at the region's central hospital, and presents as painful abdominal masses: inflammatory colonic nodules containing live juvenile stages of the helminth. In individuals living in villages highly endemic with *O. bifurcum* infection, colonic pathology visible by ultrasound is also highly prevalent. These nodules also contain *O. bifurcum* juvenile worms but are apparently asymptomatic.

Thus, *O. bifurcum* infection and asymptomatic colonic pathology are highly prevalent within this area, but clinical disease is relatively uncommon. The natural evolution and regression of the colonic pathology in an endemic community in northern Ghana and its distribution within the population is described.

28% of the 299 individuals in the study group had colonic pathology at recruitment in the late rainy season, which decreased with a half life of 3-4 months during the dry season. 28% of those negative at recruitment developed nodules during the year, the majority appearing at the end of the subsequent rainy season. Children developed more pathology than adults. 49% of the study group had colonic nodules at least once during the year, and 2% of these individuals presented with clinical disease to the local hospital during the mid rainy season.

INTRODUCTION

Oesophagostomum bifurcum is a highly prevalent human parasite in northern Ghana and Togo, where an estimated 250,000 individuals are infected⁴⁷⁻⁴⁹. The intestinal helminth is focally endemic, with infection prevalence ranging from 0% to 79% in villages within the same region (Chapter 5 and¹⁴⁶). The distribution of the parasite within the population is also uneven, with a few individuals harbouring the majority of worms.

Clinical disease caused by *O. bifurcum* accounts for 0.2% of out patients at the region's central hospital and 1% of major acute surgical procedures¹⁵². There are two distinct presentations of the disease¹⁵¹, both comprising granulomatous inflammatory lesions containing a live, white, juvenile stage of the parasite, approximately 12 mm long within thick yellow/green pus. Multinodular disease, in which the entire colon wall is studded with pea sized nodules presents with general abdominal pain, persistent diarrhoea and severe wasting. The Dapaong tumour presents as a painful 2 - 11 cm mass in the abdominal cavity or within the wall, often associated with fever.

Details of the *O. bifurcum* life cycle in humans are sparse, but transmission occurs during the rainy season⁵¹. In animal oesophagostomum infections, ingested larvae undergo an intestinal wall, histotropic, developmental stage surrounded by a nodule, before becoming lumen-dwelling, egg-laying adults. Larvae quickly pass through the nodule-dwelling stages of the life cycle: previously uninfected animals become stool positive a few weeks after infection³⁶. Arrested larval development has been described for animal *Oesophagostomum spp.*, where larvae remain as nodule-dwelling stages during harsh climatic conditions, but continue their development into lumen-dwelling egg-laying adults thereafter¹⁵⁴. The human life cycle of *O. bifurcum* is assumed to have similarities with the animal species.

Colonic anechogenic nodules visible by ultrasound are highly prevalent during the early dry season in apparently asymptomatic individuals from villages with a high prevalence of *O. bifurcum* positive stool cultures (Chapter 5). These nodules have been shown to contain a juvenile *O. bifurcum* of the same size and developmental stage as those seen in the clinical nodules (Chapter 6). No association at individual level is observed between stool and ultrasound positivity: many individuals are positive for stool but negative for ultrasound and vice versa (Chapter 5).

O. bifurcum infection detected by stool culture and colonic nodules visible by ultrasound

are therefore highly prevalent in this area, but clinical disease is comparatively uncommon: many stool positive people apparently tolerate the histotropic developmental stages of the life cycle. Whilst ultrasound nodules are pathological lesions, the proportion representing trapped stages or normal developmental stages of the *O. bifurcum* life cycle is unclear. This paper describes the natural evolution and regression of these lesions in an endemic community in northern Ghana.

METHODS

Study population

In November 1997, 399 people from Mangol, a village of some 500 people near the Ghana-Togo border 50km from Nalerigu, were examined by supine abdominal ultrasound, abdominal palpation and stool culture. Individuals volunteered to take part in the study after being informed of its design, and only individuals of five years or more were included. The Ghanaian Ministry of Health Ethics Committee agreed with the strategies and aims of this investigation. The volunteers were investigated a further three times during the course of the subsequent 12 months, in February, June and October of 1998. The four test times correspond to the early dry, late dry, mid rainy and late rainy seasons respectively. 299 people (44% males, ages ranging from 5 to 80 years, median 14) had results for all three parameters in all four tests, giving a completion rate of 75%. Distribution of the 299 people by sex and age group is shown in Figure 1. There were no significant age differences between males and females in the age groups.

During the study, treatments for minor illnesses were prescribed, and people with more serious conditions were transported to a local hospital. All the inhabitants of the village were treated with albendazole (Stat dose 10 mg / kg) at the end of the study.

Clinical and parasitological investigations

A Siemens LS portable ultrasound machine equipped with a 5Mz linear array transducer was used to investigate the entire abdominal wall and cavity, including an examination of the colon throughout its length. At each time point, the number of sonographically visible abdominal nodules and palpable abdominal masses per person suggestive of oesophagostomiasis were counted and measured. Also, duplicate 2 gram stool cultures^{43,53} from one stool sample were performed, and the number of third stage larvae present after seven days were counted. Stool culture is necessary because the eggs of *O. bifurcum* are morphologically identical to hookworm, but their third stage larvae are easily distinguishable.

Data analysis

The distribution of each of the 3 parameters of *O. bifurcum* was described by prevalence and intensity. Also, a cumulative prevalence (positive at least once during the year) was calculated for each parameter. Nodule sizes were described by 25th percentile values, as they did not show normal distribution following log transformation. Palpable mass sizes showed an approximate normal distribution and were described by their arithmetic mean and 95% confidence interval. An incidence percentage (becoming positive during the year after a negative test in November 1997) was calculated for the ultrasound test.

The Chi-square test was used to compare differences in prevalence and incidence, and the Mann-Whitney test was used to compare intensities and ages between the different groups. Seasonal variation in prevalence was tested with the Cochran Q and further analysed by the McNemar test. The seasonal intensities were analysed with the Friedman and Wilcoxon tests. Bonferroni correction was applied for all multiple comparison. $P<0.05$ was used to imply statistical significance for all the tests used.

RESULTS

At the survey in November 1997, 84 individuals (28%) had one or more colonic nodule visible by ultrasound, 25 individuals (8%) had one or more palpable abdominal mass, and 78 individuals (26%) had a positive stool culture. Figure 1 shows the age and gender distribution of ultrasound visible nodules and palpable masses. Both prevalence and intensity of ultrasound pathology tended to be higher in children (<20 years) as compared with adults ($P=0.06$), and in females of 40 years and above. Palpable masses were found to be significantly more frequent and numerous in children, while no palpable masses were found in males older than 20 years (Figure 1).

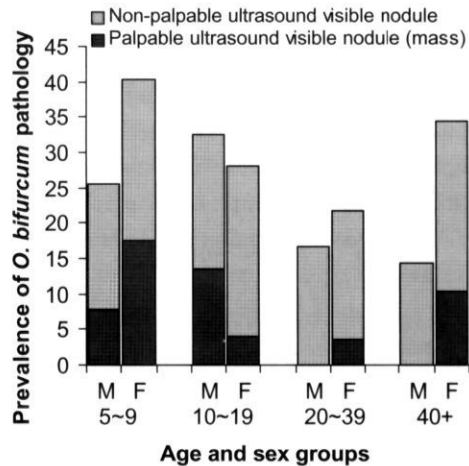


Figure 1: Demographic distribution of palpable and ultrasound visible pathology in November 1997. ($n=299$, in each group: 51, 57, 37, 25, 24, 55, 21, 29).

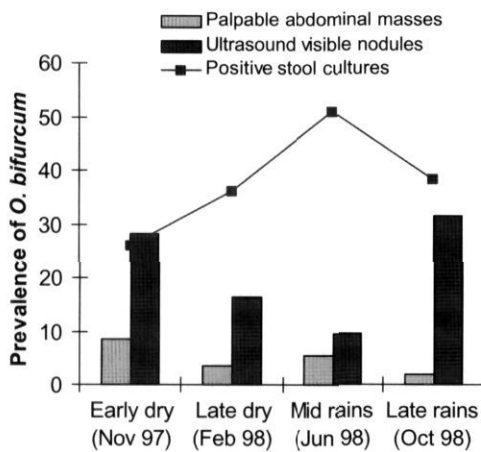


Figure 2: Seasonal prevalence of *O. bifurcum* infection, palpable masses and ultrasound visible nodules ($n = 299$).

Figure 2 shows the seasonal variation in the prevalence of *O. bifurcum* pathology and infection and Table 1 summarizes the number and sizes of observed nodules. Both the prevalence and intensity of ultrasound pathology varied significantly during the year. Levels were high during the early dry season, but decreased in February ($P < 0.001$) and June ($P < 0.001$), to reach their lowest level by the mid rains. In October, the prevalence and intensity of ultrasound pathology returned to levels similar to those found in November ($P > 0.38$).

The median number of nodules per person was 1 at all four test times. Five people had more than 9 nodules during the course of the study, notably one girl, with 53, 56, 17 and 3 nodules at the four time points respectively. The size of the 464 nodules measured throughout the study ranged from 7 - 57 mm with a median of 18 mm.

Table 1: Number of ultrasound nodules per person and average size of nodules by season ($n=299$ individuals).

Test date	No. nodules / person				No. nodules observed	No. nodules measured	Size of nodules (mm)		
	0	1	2~9	10+			25 th %tile	Median	75 th %tile
Nov 97	215	50	30	4	234	181	14	17	22
Feb 98	250	35	13	1	138	82	17	20	26
Jun 98	270	21	7	1	61	44	20	26	35
Oct 98	205	59	34	1	182	157	13	17	20

Also, the palpable abdominal mass prevalence varied significantly over the year, although this trend was less consistent than the trend seen for ultrasound nodules. Only a few individuals had more than one palpable mass. The abdominal masses were palpated in the path of the ascending and transverse sections of the colon. Their size ranges from 20 - 60 mm, with a mean of 28.6 mm (95% CI = 26.4 - 30.0).

The prevalence (Figure 2) and intensity (data not shown) of infection measured by stool cultures also varied significantly during the year. The infection prevalence increased during the late dry and early rainy seasons ($P<0.003$), while the intensity remained fairly stable during the first two time points and showed a sharp rise only after the rains began ($P<0.001$). In October, the infection prevalence and intensity decreased again ($P<0.001$) to a level similar to that measured in November and February. Thirty-one to 47% of the positive individuals showed 10 or more larvae during the different seasons. Approximately 20% of the cultures from the November stool test were infested by maggots, probably resulting in lower results for this test time.

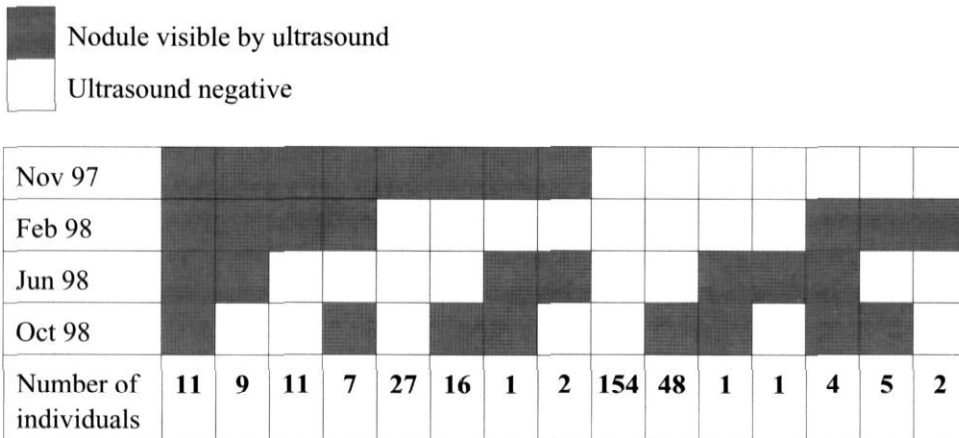


Figure 3: Seasonal emergence and regression patterns of ultrasound nodules at an individual level ($n = 299$).

The sharp increase in stool positivity in the period between February and June coincided with a decrease in nodule prevalence. However, only 10 of the 58 individuals commencing egg excretion between February and June had been ultrasound positive in

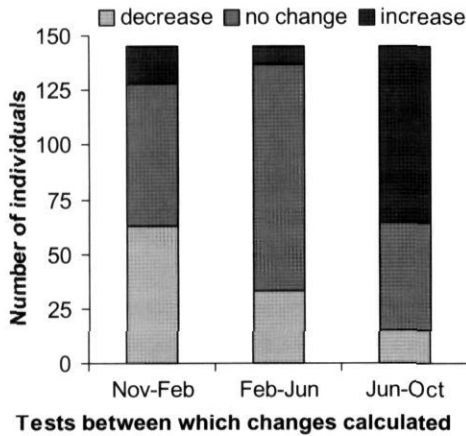


Figure 4: Seasonal changes in number of nodules per person, not including the 154 quadruple negatives (n=145).

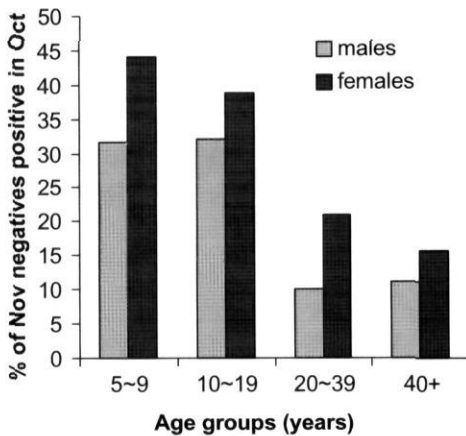


Figure 5: Incidence of ultrasound visible pathology, n = 215 (Numbers in each group: 38, 34, 25, 18, 20, 43, 18, 19).

February. The cumulative prevalence (positive once or more during the year) of ultrasound nodules, palpable masses and stool positivity were 49%, 13% and 68% respectively.

Figure 3 summarises the seasonal changes in ultrasound pathology at an individual level. In November, 215 people (72%) had no visible pathology. During the course of the year 61 individuals became positive at least once, giving an incidence of 28%. Few people developed ultrasound pathology during the dry and early rainy season, the largest number of new positives occurring between June and October. A similar trend was seen when looking at the number of nodules per person (Figure 4).

The 84 individuals who were ultrasound positive in November 1997 gradually became negative over the following months, as shown in Figure 3 and Table 2. The half life of the visibility by ultrasound of a nodule was 3 - 4 months.

A significant difference was seen in the age and gender distribution of new ultrasound pathology, as shown in Figure 5. Children (below 20 years old) developed more pathology than adults, and this held true when analysed separately for females and males ($P<0.01$), comparing boys with men, and girls with women.

Table 2: Half life of the visibility by ultrasound of a nodule
(n = 84 individuals with 234 nodules).

	Number of people remaining positive for ultrasound pathology (% of November positives)	Number of nodules observed in those people (% of November nodules)
Nov 97	84 (100)	234 (100)
Feb 98	38 (45)	127 (54)
Jun 98	20 (29)	51 (22)
Oct 98	11 (13)	21 (9)

Progression of *O. bifurcum* pathology to symptomatic clinical disease.

Three people from Mangol presented between July and September of 1998 to the weekly oesophagostomiasis clinic at Nalerigu hospital with symptomatic disease consistent with oesophagostomiasis. Two of the patients, 7 and 28 year old females, had palpable Dapaong tumours, adhered to the abdominal wall and locally painful in both cases. In the first case, the pathology had developed between July and September, and in the second case, the tumour had been present since November 1997, but asymptomatic. The third patient, a 25 year old male, presented with a two week history of severe lower right abdominal pain, which was now remitting. Since February 1998, there had been two nodules in the proximal ascending colon, and at the clinic in August, a resolving abscess in the right lower quadrant could be seen by ultrasound.

DISCUSSION

O. bifurcum infection has previously been shown to be more common in children, and more common in adult females as compared with adult males¹⁴⁶. The distribution of ultrasound nodules within the study group illustrates the propensity of children for developing *O. bifurcum* colonic pathology, but there is little difference in susceptibility between the genders. However, women have more abdominal wall adipose tissue than men which makes colonic viewing more difficult, whereas the thick abdominal wall musculature of men is an ideal ultrasound transmitting medium. It is therefore likely that women are under-represented for colonic pathology, and that the same pattern previously

found for stool infections is more pronouncedly true for colonic pathology than suggested by this data. The differences in abdominal wall thickness between the population groups must also detract from real age and sex related differences in the distribution of palpable masses.

Colonic pathology is a dynamic entity, as shown by its seasonal variation in prevalence and intensity, its incidence and the nodule half life. Emergence of a new nodule to visibility by ultrasound presumably implies a new infection with *O. bifurcum*. Ultrasound appears to be a reliable test for the detection of nodules, evidenced by the fact that few people developed them at deviant times during the year: in the middle of the dry season for example, when little transmission occurs.

The 1998 stool peak occurs before the 1998 nodule peak. It is therefore doubtful that the histotropic worms causing the nodule peak exited from their nodules to become the lumen dwelling egg-laying adults responsible for the earlier stool peak.

The nodules found in November 1997 (presumably from the 1997 rainy season) gradually disappeared from ultrasound visibility during the dry season and early rains of 1998. It is possible that some of these nodules contained arrested larvae which successfully completed their life cycle in the subsequent rains. However, two observations suggest that we do not see many of the luminal worm's developmental nodules: the fact that only one sixth of the people becoming stool positive at the start of the rains had previously had visible nodules, and secondly, the relatively low number of ultrasound nodules compared with the intensity of stool positivity. It seems probable that most of the nodules in which worms complete their life cycle are smaller than 7 mm (minimum ultrasound resolution; Chapters 6 & 7), and that most of those visible by ultrasound are therefore 'dead-end' nodules.

The average size of the nodules increased during the dry season, by which time the nodules had been in the colonic wall for several months. The actual size of the nodules may increase, or the small ones may be reabsorbed. The individuals developing clinical disease presented during the season when the nodules were at their biggest hinting that nodule size may be important in the development of symptoms. Our periodic presence in the village may have stimulated hospital presentation for an abdominal mass which might otherwise have been tolerated. Regression of clinical Dapaong tumours without intervention has been reported¹¹⁶.

49% of the population had colonic pathology visible by ultrasound during the year. Hospital presentation by 2% of these individuals is an appreciable rate of overt clinical manifestation, and illustrates that it is possible to detect the disease by ultrasound before the development of clinical symptoms. Colonic pathology was most commonly seen in children, they present most frequently with clinical oesophagostomiasis⁵⁷, and they are most commonly found to be infected by parasitological methods of *O. bifurcum* detection⁵⁰. Treatment to reduce the burden of disease and to prevent the development of clinical symptoms should therefore be aimed primarily at children, using doses of antihelminthics capable of killing the nodule dwelling worms.

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