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Oesophagostomum bifurcum infection in man. A study on the taxonomy, diagnosis, epidemiology
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Chapter 1

GENERAL INTRODUCTION

Introduction

Representatives of the genus *Oesophagostomum* are small nematodes that occur in a wide range of animals. The first *Oesophagostomum* species were discovered in 1803 in cattle (*O. radiatum*) and pigs (*O. dentatum*). Later on, several other species were described, e.g. *O. quadrispinulatum* (pigs), *O. columbianum* and *O. venulosum* (sheep and goats) [1]. *O. aculeatum*, *O. stephanostomum* and *O. bifurcum* are species that have been recognized in monkeys [2-7]. The name of this nematode has its origin in the typical shape of the head, with an excretory pore clearly visible in the cephalic groove of the head (fig. 1).

The life cycle of *O. columbianum*, a common parasite of sheep causing serious disease and economic damage [8-10] has been studied extensively [11-13], and serves as an example for the life cycles of other *Oesophagostomum* sp.. Adult worms, living in the intestinal lumen of the sheep, produce eggs that leave the host with the faeces. Outside the host, the eggs develop into first-, second- and finally third-stage larvae (L-I, L-II and L-III larvae resp.). The development into the infectious L-III stages takes about 4 to 14 days, depending on temperature, humidity and other environmental factors, whereas the presence of toxins and acidity may influence the time required for development also. The L-III larvae are able to survive in the outside world for weeks or even months, depending on the climatic and geographical circumstances [14-16].

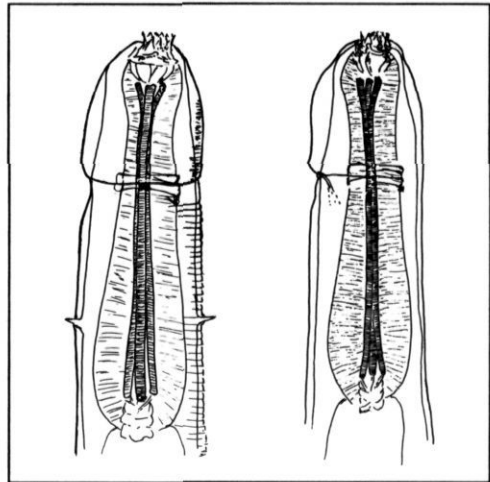


Figure 1. Head of *Oesophagostomum bifurcum*, showing the typical cephalic groove.

The infective larvae are swallowed by the host, where they penetrate into the intestinal wall of the small or large bowel. There, a small abscess is formed around the developing larvae, that enter the next, tissue dwelling stage. On some occasions, numerous nodules may cover the intestinal wall, and *Oesophagostomum* spp. are therefore also called 'nodular worms' [1, 17]. The pre-adult stages leave the nodule and re-enter the intestinal lumen, where they develop into adult worms and start producing eggs. The whole cycle takes approximately six to seven weeks [8, 18]. In some *Oesophagostomum* spp. the tissue-dwelling stages may enter a 'dormant phase': the development stops for a certain period, to continue much later. In *O. radiatum* for example, tissue dwelling stages do not fulfil the entire life-cycle until the same season of the following year [19]. In *O. columbianum*, too, larvae have been shown

to remain dormant for up to one year [20]. This postponed development offers certain advantages for the parasite. Firstly, the production of eggs will be highest during the season when the conditions for transmission are most favourable [19]. Secondly, the arrested larvae may be less sensitive to anthelmintics, because of the suppressed metabolism [21].

Table 1. Published cases of human oesophagostomiasis (for references see Chapter 5).

year	authors	cases	origin	notes
1905	Railliet & Henry	1	East-Africa	First human case
1910	Thomas	1	"	
1909/10	Railliet & Henry	1	Brazil	Same case as Thomas
1911	Leiper	1	Nigeria	First adult worms
1913	Johnson	8	Nigeria	
1920	Henry & Joyeux	1	Guinea	
1949/53	Lie Kian Joe	1	Indonesia	
1954	Elmes & McAdam	3	Uganda	Two European cases
1958	Chabaud	1	Ivory Coast	Classification of human <i>Oesophagostomum</i> species
1963	Adams & Seaton	1	Sudan	
1964	Jacques & Lynch	1	Sudan	
1964	Haaf & van Soest	9	Ghana	Bawku, near northern Togo
1966	Welchman	2	Uganda	No parasites isolated
1969	Marshall & Deneka	1	Uganda	
1969	Gordon <i>et al.</i>	1	Zimbabwe	
1972	Anthony & McAdam	34	Uganda	Three proven cases of <i>Oesophagostomum</i>
1977	Leoutsakos <i>et al.</i>	1	Ethiopia	
1977	Kaminsky <i>et al.</i>	1	Kenya	
1978	Barrowclough & Crome	1	Ghana	
1987	Gigase <i>et al.</i>	54	Togo	
1988	Pagès <i>et al.</i>	28	Togo	included in Gigase's series
1989	Ross <i>et al.</i>	1	Brunei	
1992	Karim & Yang	1	Malaysia	

Human oesophagostomiasis

In man, infection with *Oesophagostomum* has been described in only a limited number of cases (Table 1). The first description was published in 1905, by Railliet and Henry. They described six female immature worms that were found by Brumpt in 1902 when he performed autopsy on a 30-year old African man, who had been living near the River Omo, East-Africa [22,23]. They considered the parasites to be a new species, distinct from those found in other primates, and named the nematode after their discoverer: *Oesophagostomum brumpti*. In 1910, Thomas described the case of a native from Brazil, who died after three

days of dysentery. At autopsy, the ileum and colon were covered with nodules, each containing one single worm [24]. Railliet and Henry compared the specimens with the *O.stephanostomum* from gorillas, and called the species *O.stephanostomum* var.*Thomasi* because the species were not entirely identical [25].

In 1911, the first adult worms were described by Leiper [26]. Dr. Foy, a medical officer working in Nigeria, had sent him six adult specimens that had been isolated after treatment of a patient from Ibi, Mid-Nigeria. Leiper identified these nematodes as *O.apioistomum*. This nematode had been described in monkeys by Railliet and Henry, but Leiper remarked that the nematode they had called *O.brumpti*, showed several similarities with *O.apioistomum* [26]. Two years later, another medical officer, Johnson, who had been working with Dr. Foy, reported that out of 200 examined prisoners, eight appeared to be infected with *Oesophagostomum* [27]. It is not clear how he had diagnosed these infections, but since he states that diagnosis through identification of eggs is very difficult, this was probably based on isolation of the adult worms after treatment.

Thereafter, several reports were published from various parts of the world (Table 1). Elmes and McAdam described the occurrence of 'helminthoma', as they called it, in Uganda [28]. There, human oesophagostomiasis seems to be relatively common, but differs from former reports on oesophagostomiasis in that it frequently concerns one single helminthoma, caused by *O.stephanostomum*. In 1958, Chabaud and Larivière wrote a comprehensive paper on human oesophagostomiasis [29]. They divided the causative nematodes into three *Oesophagostomum* species: *O. bifurcum*, *O.aculeatum* and *O.stephanostomum*. Whereas *O. bifurcum* is frequently found in Africa, *O.aculeatum* occurs mainly in southeast Asia. *O.stephanostomum* has been identified in Brazil and Uganda.

***Oesophagostomum* infection in northern Togo and Ghana**

In spite of the number of reports, human oesophagostomiasis has always been considered to be a rare zoonosis, and completion of the life cycle in man was thought not to occur [10,17,28,29]. This changed through the publication of Gigase and others (1987), who presented a series of 54 cases of human *Oesophagostomum* infection in the northern region of Togo, West-Africa [30]. During the period 1980-1984, Dr. S. Baeta, the surgeon of Regional Hospital in Dapaong, noticed that many patients presented with a visible tumour in the abdominal wall. The tumours were variable in size, and they were often painful on palpation. Other patients were brought to the emergency ward because of an acute abdomen due to bowel obstruction or peritonitis. When Dr. Baeta operated upon these patients, it appeared that multiple nodules were found on the colon. Histological examination by

Prof. Gigase revealed that these nodules were in fact abscesses that contained an immature nematode, that could be identified as belonging to the genus *Oesophagostomum*.

The publication of Gigase and colleagues concerned the largest series of cases of human oesophagostomiasis. Another large series, however, had been published in 1964 by Haaf and Van Soest, who worked in Bawku, a Ghanaian city not far from Dapaong [31]. The large number of cases originating in this region suggested already that human oesophagostomiasis could be more than an accidental zoonosis.

Start of the research project

In 1986, Dr. Gigase, of the Tropical Institute of Antwerp, and Dr. Polderman, of the Laboratory for Parasitology of Leiden, travelled to northern Togo, to examine the possibilities for research on the occurrence of *Oesophagostomum* infection. The disease appeared to be known by the local population as 'Koun Koul', meaning 'turtle in the belly', and also as 'Tumeur de Dapaong'. Several stool samples of humans and of monkeys were collected and examined in Leiden. If man was a normal host for *Oesophagostomum*, it should be possible to find its eggs in the faeces. However, the eggs of *Oesophagostomum* are almost identical to hookworm eggs, and diagnosis of *Oesophagostomum* infection cannot be based on identification of the eggs [17]. Therefore, coprocultures were performed, to allow the eggs to develop into third-stage infective larvae, that can be differentiated easily from those of hookworm [32]. After one week of culturing, larvae of *Oesophagostomum* were isolated not only from stool samples of monkeys, but also from three Togolese persons, indicating that the parasite is able to develop into the adult, egg laying stage.

These findings were the onset of further research on the role of man in *Oesophagostomum* infection in northern Togo and Ghana. Because of the well organized structure of Togo and the continuous interest and support of the Togolese government, Dapaong was chosen as the centre of the research project, and a laboratory was established in the 'Centre Hospitalier de Dapaong'.

Questions to be answered

Human oesophagostomiasis has always been considered as an incidental zoonosis. Consequently, the occurrence, biology and life cycle of *Oesophagostomum* infection in man has never been investigated in depth. The object of this project was to examine

epidemiological, biological and medical aspects of *Oesophagostomum* infection in man, and it was attempted to gather answers to the following basic questions.

1. How can the infection be diagnosed, and how should a large scale-survey be carried out? Intestinal nematode infections are often diagnosed through identification of eggs in stool samples. In *Oesophagostomum* infections this is not feasible since its eggs are morphologically indistinguishable from those of hookworm. A differential diagnosis can be obtained through coproculture. With this procedure, the eggs are allowed to develop into third-stage infective larvae, which can be easily differentiated from hookworm [32].

Several coproculture methods can be applied in the differential diagnosis of nematode infections: the Haradi-Mori procedure, the charcoal-method, or modifications of these techniques. These methods are based on the creation of a favourable environment for egg development, including a sufficient humidity, temperature and aeration.

In Togo, a technique was sought that would not only be suitable for the research project, but also for daily practice in the local health care. In the petri-dish method, a mixture of ground charcoal and faeces is placed on an elevation in a petri-dish, where it is kept moist by a filter paper soaked in water (Figure 1). Eggs develop into third-stage larvae that migrate into the water. After sedimentation, they can be identified at low magnification. This procedure is simple, and the materials are cheap and readily available. It can be used in individual cases, and it should be possible to use it in large scale screening projects. In comparative trials, the petri-dish method appeared to have the highest sensitivity [unpublished results]. Therefore, this method was chosen as the diagnostic method in the research project in Togo and Ghana; its value in the diagnosis of *Oesophagostomum* infection in individual cases as well as the application in large scale surveys were to be evaluated in the research project.

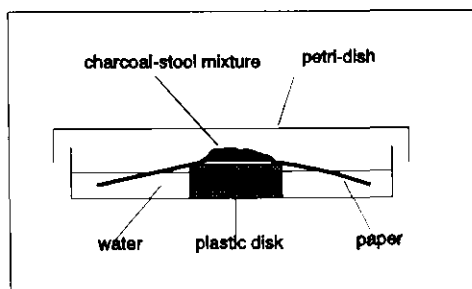


Figure 1. Schematic representation of the petri-dish coproculture method.

In animals, and presumably in man, intensive tissue contact exists between parasite and host during the tissue-dwelling stage which elicits a strong cellular and humoral immunoprotective reaction [33]. In this study, the possibility of a serological diagnosis of human *Oesophagostomum* infection and disease was to be examined.

2. Which is the *Oesophagostomum* species involved?

Species identification of nematodes is based on the description and classification of male and female adult specimens. In most publications on human oesophagostomiasis only immature, pre-adult specimens were found. Only three reports mention the finding of adult worms. Johnson [27] and Henry and Joyeux [34] do not describe them, but Leiper gives an accurate, though brief description [26]. He named the worms *O. apiostomum*, but hypothesized that they were of the same species as those found by Railliet and Henry, and referred to as *O. brumpti*. In 1958 Chabaud and Larivière distinguished three *Oesophagostomum* species occurring in humans: *O. stephanostomum*, *O. aculeatum* and *O. bifurcum* [29]. The latter was thought to be identical to *O. apiostomum*. However, this classification was based on relatively few descriptions of mainly pre-adult worms. The number of cases described by Gigase and colleagues surpassed the total number published in the world literature. They were 'tentatively assigned to *O. bifurcum*', but they emphasized that pre-adult stages are 'insufficient to arrive at a precise diagnosis'. It was, therefore, one of the objects of this study to give an accurate description of adult *Oesophagostomum* worms obtained from human hosts. At the same time, it was considered of relevance to investigate the presence of the parasite species in non-human hosts. In particular, the role of infections of monkeys was to be examined.

3. What is the prevalence of infection with *Oesophagostomum* in northern Togo and Ghana?

Most of the reports on human oesophagostomiasis concern cases that came to the attention of medical doctors because of their prominent clinical symptoms. It is probable that they represent only a small portion of the infected populations. These cases can be traced only by screening the population for the presence of *Oesophagostomum* infection, using coproculture on a large-scale basis. The distribution of *Oesophagostomum* infection in specific subgroups could identify certain risk groups. Sex- and age-related differences in the prevalence of nematode infections have been established in hookworm and *Ascaris* infection [35]. These differences are sometimes attributed to social and cultural habits, that may influence the risk of exposure. Similarly, belonging to certain tribes or religious groups, with special habits or traditions, may alter the prevalence of *Oesophagostomum* infection [36]. In summary, it is necessary to investigate the prevalence of *Oesophagostomum* infection in the study area's population as well as in specific subgroups, to determine the extent of the public health problem caused by *Oesophagostomum*, and to recognize certain risk factors for infection.

4. Is *Oesophagostomum* infection confined to this area? If so, what are the reasons for this?

Cases of human oesophagostomiasis have been reported from several parts of the world, but they concern mainly sporadic cases. One series, published by Anthony and McAdams, concerned 34 cases of helminthoma in Uganda, but in only eight the causative parasite was found; three cases were caused by *Oesophagostomum* [37]. It is possible that symptomatic

cases of human *Oesophagostomum* infection occur more frequently, but remain unrecognized because health workers are not familiar with its clinical picture. Also, if a person is infected with *Oesophagostomum* without any symptoms, its eggs will be identified as hookworm eggs unless coproculture is performed. It is possible that systematic screening will reveal a more common occurrence of *Oesophagostomum* infection in other areas.

If a high prevalence would appear to be limited to this particular area, what are the causes for this? Are there climatic or geographical conditions that prevent the parasite from spreading? Is the infection found in specific ethnic groups, or does religion play an important role? Is the prevalence higher near areas where monkeys are common?

5. What is the life-cycle of *Oesophagostomum*?

The life cycle of *Oesophagostomum* species that have been found in humans, is not known. Features of *Oesophagostomum* species occurring in animals include oral transmission, exsheathing of the infective larvae in the gastro-intestinal tract, entering a histiotrophic phase, and re-entering the intestinal lumen as pre-adult stages [1]. Arrested larval development has been described in some *Oesophagostomum* species [19] leading to a seasonal fluctuation of the infection rate and intensity of infection in a host population, a process which has also been described for *Ancylostoma duodenale* [38]. Is the life cycle of *Oesophagostomum* infection in man similar?

6. What is the relation between *Oesophagostomum* infection and disease?

The case histories of the series of Gigase and colleagues [30] and of Haaf and van Soest [31] give many details about the clinical presentation of human oesophagostomiasis. Their descriptions include painless abdominal tumours that may disappear or progress to a large painful abscess in the abdominal wall. This abscess sometimes bursts open into the abdominal cavity, causing peritonitis. In a later stage, the formation of scar tissue causes bowel obstruction by adhesions. However, those were patients in need of and in reach of medical attention. In infection with *O. columbianum* in sheep, the symptoms are the result of the degree of exposure, in combination with the development of a immune response by the host. Thus, after repeated infections with third-stage larvae, the host may have developed such a resistance that renewed infection may pass unnoticed. There are, however, less noticeable symptoms like weight loss, enteric protein loss and stunting of growth.

Does every infection with *Oesophagostomum* larvae lead to similar symptoms? Or is the majority of the infected population left unharmed by the parasite? Is every age group affected to the same degree, or are there age-dependent manifestations that could perhaps be explained by some degree of acquired immune-resistance? In view of the possible seasonal fluctuation

in egg production observed in other *Oesophagostomum* species, it would be important to record any seasonal variation in the incidence of symptoms.

7. What is the most effective treatment of Oesophagostomum infection?

Infection with *Oesophagostomum* may lead to serious complications, as shown by Gigase and colleagues [30]. In the Regional Hospital of Dapaong, a considerable expertise in the treatment of human oesophagostomiasis is present. Formerly, practically all patients with a 'Tumeur de Dapaong' were operated upon, but nowadays most patients are treated conservatively with antibiotics and anti-inflammatory drugs. Nevertheless, it has not been investigated in detail which approach gives the best results. Should anthelmintics be added, to kill the parasite more rapidly and thus removing the aetiological agent? Or will this lead to the release of more antigenic material, with a more intense inflammatory reaction as the result?

Furthermore, if the host is entirely without symptoms, should he be treated at all? If so, which anthelmintic should be used? If possible, the anthelmintics that are used in the treatment of animal infections with *Oesophagostomum*, should be tried in humans also. In addition, it is possible that anthelmintics currently used in the treatment of hookworm infection, might be effective against *Oesophagostomum* as well. Finally, in view of the hypothetical seasonal fluctuation, the most favourable period of treatment has to be established, by evaluating short-term as well as long-term follow-up studies.

During the research period it was attempted to find answer to these questions. The results obtained in this research project are presented in this thesis.

References

1. Levine ND, 1968. Nodular worms, bowel worms, gapeworms and kidney worms. In Levine, ed., 1968. *Nematode parasites of domestic animals and man.* : Burgess, 115-125.
2. Weinberg M, 1908. Oesophagostomose des anthropoïdes et des singes inférieures. *Archives de Parasitologie* 13:161-202.
3. Scheidegger S, Kreis HA, 1934. Über helminthiasis beim Schimpansen. *Zeitschrift für Parasitenkunde* 7:44-60.
4. Rousselot R, Pelissier A, 1952. III. Oesophagostomose nodulaire à Oesophagostomum stephanostomum du gorille et du chimpanzé. *Bulletin de la Société de Pathologie Exotique* 45:568-74.
5. Healy GR, Myers BJ, 1973. Intestinal helminths. In Bourne GH, ed., 1973. *The Chimpanzee. Vol. VI.* : Karger, Basel and University Park Press, 265-296.
6. Goldsmid JM, 1974. The Intestinal Helminthozoonoses of Primates in Rhodesia. *Annales de la Société Belge de la Médecine Tropicale* 54:87-101.
7. File SK, McGrew WC, Tutin CEG, 1976. The intestinal parasites of a community of feral chimpanzees, *Pan troglodytes schweinfurthii*. *Journal of Parasitology* 62:259-61.
8. Olsen OW, 1974. Oesophagostomum columbianum. In Olsen OW, ed., 1974. *Animal parasites. Their life cycles and ecology.* : Baltimore, University Park Press, 417-420.
9. Dobson C, 1966. Distribution of Oesophagostomum columbianum larvae along the alimentary tract of the sheep. *Australian Journal of Agricultural Research* 17:765-77.
10. Dooley JR, Neafie RC, 1976. Oesophagostomiasis. In Binford and others, eds., 1976. *Pathology of Tropical and Extraordinary Diseases.* : Armed Forces Institute, 440-445.
11. Dobson C, 1967. Changes in protein content of the serum and intestinal mucus of sheep with reference to the histology of the gut and immunological response to Oesophagostomum columbianum infections. *Parasitology* 57:201-19.
12. Dash KM, 1981. Development and distribution of Oesophagostomum columbianum in young lambs after oral or intraluminal infection. *Veterinary Parasitology* 9:145-9.

13. Dash KM, 1973. The life cycle of *Oesophagostomum columbianum* (Curtice, 1890) in sheep. *Internation Journal for Parasitology* 3:843-51.
14. Spindler LA, 1936. Effects of various physical factors on the survival of eggs and infective larvae of the swine nodular worm *Oesophagostomum dentatum*. *Parasitology* 22:529.
15. Rose JH, Small A, 1980. Observations on the development and survival of the free-living stages of *Oesophagostomum dentatum* both in their natural environment out-of-doors and under controlled conditions in the laboratory. *Parasitology* 81:507-17.
16. Barger LA, Lewis RJ, Brown GF, 1984. Survival of infective larvae of nematode parasites of cattle during drought. *Veterinary Parasitology* 14:143-52.
17. Beaver PC, Jung RC, Cupp EW, 1984. *Oesophagostomum* species. In Beaver and others, eds., 1984. *Clinical parasitology*. : Lea & Febiger, 287-288.
18. Lapage G, 1959. Genus *Oesophagostomum*. In Lapage G, ed., 1959. *Veterinary Helminthology and Entomology*. : Ballière, Tindall and Cox, 193-198.
19. Armour J, Duncan M, 1987. Arrested larval development in Cattle nematodes. *Parasitology Today* 3:171-6.
20. Taylor EL, Michel JF, 1953. The parasitological and pathological significance of arrested larval development in nematodes. *Journal of Helminthology* 27:199-205.
21. Coles G.C, 1986. Anthelmintics for Small Ruminants. *Veterinary Clinics of North America* 2:411-421.
22. Railliet A, Henry A, 1905. Encore un nouveau Sclérostomien (*Oesophagostomum Brumpti* nov.sp.) parasite de l'homme. *Comptes Rendues de la Société de Biologie* 58:643-5.
23. Brumpt E, 1947. Genre *Oesophagostomum* Molin, 1861. In Brumpt E, ed., 1947. *Précis de Parasitology* : Manson, 778-82.
24. Thomas HW, 1910. The pathological report of a case of oesophagostomiasis in man. *Annals of Tropical Medicine and Hygiene* 5:57-88.

25. Railliet A, Henry A, 1910. Etude zoologique de l'oesophagostome de Thomas. *Annals of Tropical Medicine and Parasitology* 4:89-64.
26. Leiper RT, 1911. The occurrence of Oesophagostomum apiostomum as an intestinal parasite of man in Nigeria. *Journal of Tropical Medicine and Hygiene*:116-8.
27. Johnson WB, 1913. Report on Entozoal Infection amongst Prisoners (in Zungeru Gaol, Northern Nigeria). *Tropical Diseases Bulletin* 2:190-2.
28. Elmes BGT, McAdam JWJ, 1954. Helminthic abscess, a surgical complication of oesophagostomes and hookworms. *Annals of Tropical Medicine and Parasitology* 48:1-7.
29. Chabaud AG, Larivière M, 1958. Sur les Oesophagostomes parasites de l'homme. *Bulletin de Société de Pathologie Exotique* 51:384-93.
30. Gigase P, Baeta S, Kumar V, Brandt J. 1987. Frequency of symptomatic human oesophagostomiasis (helminthoma) in Northern Togo. in Geerts and others, eds., 1987. *Helminth Zoonosis*.: Martinus Nijhoff, 223-236.
31. Haaf E, v Soest AH, 1964. Oesophagostomiasis in man in North Ghana. *Tropical and Geographical Medicine* 16:49-53.
32. Little MD, 1981. Differentiation of nematode larvae in coprocultures: Guidelines for routine practice in medical laboratories. *WHO Technical Reports Series No 666*:144-150.
33. Roberts FHS, Riek RF, Keith RK, 1963. Studies on resistance in calves to experimental infection with the nodular worm, Oesophagostomum radiatum. II. The role of the respective stages of the parasitic life cycle in the stimulation of resistance. *Australian Journal of Agricultural Research* 14:704-15.
34. Henry A, Joyeux Ch, 1920. Contribution à la faune helminthologique de la Haute-Guinée française. *Bulletin de Société de Pathologie Exotique* 13:176-82.
35. Pawlowski ZS, Arfaa F, 1985. Ascariasis. In Warren KS, Mahmoud AAF, eds., 1985. *Tropical and geographical medicine*. McGraw-Hill, 347-372.
36. Schad GA, Anderson RM, 1985. Predisposition to Hookworm infection in Humans. *Science* 230:1537-40.

37. Anthony PP, McAdam IWJ, 1972. Helmintic pseudotumours of the bowel: Thirty-four cases of helminthoma. *Gut* 13:8-16.
38. Maplestone PA, 1932. Further observations on seasonal variation in hookworm infection. *Indian Journal of Medical Research* 19:1145-51.