SUMMARY
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In 1986, following the discovery that Oesophagostomum eggs are excreted by people living in northern Ghana and Togo, Polderman and Gigase concluded that Oesophagostomum worms are able to complete their life cycle in humans, and that the helminth causes considerable disease in this area.

There have been many cases of clinical oesophagostomiasis reported in the literature over the last century, but diagnosis has usually been based on a pathology specimen and clinical details have been sparse. We therefore amassed a cohort of 156 patients presenting to Nalerigu hospital in northern Ghana, and identified two distinct clinical presentations of the disease, Dapaong tumour and multinodular disease, described in Chapter 2. Multinodular disease (13% of the cases) results from hundreds of pea sized nodules within the colon wall and other intra-abdominal structures, and presents with general abdominal pain, persistent diarrhoea and weight loss. Dapaong tumour (87%) presents as an abdominal inflammatory mass often associated with fever. The tumour is usually painful, well-delineated, smooth, spherical, 3 - 6 cm, 'wooden', periumbilical, and adhered to the abdominal wall. Oesophagostomiasis accounted for 0.2% of the out patient department new presentations (approximately 1 patient per week), and 1% (16) of the major acute surgical cases.

Children between 5 and 9 years were most commonly affected, typically presenting during the late rains and early dry season. Transmission-dependent explanations for the biphasic distribution of the number of nodules found in Dapaong tumour and multinodular disease were not apparent. There was no difference between the size of the worms from Dapaong tumour and multinodular disease, despite the dissimilarity in nodule size. They were sexually developed juveniles designated L5, 7 - 13 mm long, and none of the females contained eggs.

Due to the vague, poorly localising signs and symptoms of oesophagostomiasis, many of the previously reported cases were suspected but not confirmed until exploratory laparotomy. Chapter 3 describes the ultrasound appearance of oesophagostomiasis: the nodules are pus filled and therefore appear as echo free ovoid abdominal lesions. Multinodular disease gives a nodular ‘Target’ appearance to the colon. The advantage of a pre-surgical diagnosis of acute oesophagostomiasis in terms of pre-operative chemotherapy, anaesthetic and incision type cannot be underestimated.

During the last decade at Nalerigu hospital, oesophagostomiasis has become recognised as a significant disease entity and it represents an important health problem for northern
Ghana. Now that its symptoms and signs have been described and the presentations classified, prompt, consistent and reliable clinical diagnosis can be made, as presentation pattern recognition is possible.

There was some economy of effort by clinicians in always performing exploratory laparotomy, as management was invariably by colectomy. But in CHAPTER 4, 10mg/kg albendazole for 5 days is used to effectively manage a chronic case of multinodular disease. The advantage of albendazole treatment over colectomy is clear. It is possible because multinodular disease can now be reliably diagnosed without the need for exploratory surgery, and remission of the colonic inflammation can be monitored using ultrasound.

In CHAPTER 5, it was discovered that in villages highly infected with *O. bifurcum* by stool culture methods of detection, colonic pathology can be visualised by ultrasound: anechogenic colonic lesions with posterior wall enhancement were observed in 54.2% and 24.5% of individuals from two endemic villages, but were not seen in a stool negative village outside the endemic area. These lesions are described as *O. bifurcum* induced nodules, on the basis of their association at a population level with stool prevalence, their expected ultrasound appearance and distribution from surgical experience of oesophagostomiasis, and the lack of a convincing differential diagnosis. There is no correlation between stool culture results and ultrasound observations at an individual level, which is to be expected, because ultrasound observes the tissue-living juvenile stages of *O. bifurcum*, whereas stool cultures detect a later stage of the infection, the presence of lumen dwelling egg-laying adults. Confirmation that the lesions are induced by *O. bifurcum* is obtained in CHAPTER 6, when during surgery following visualisation of a colonic lesion, an *O. bifurcum* juvenile is obtained from a colonic nodule. A pre-clinical diagnosis of *O. bifurcum* induced colonic pathology is therefore possible with ultrasound.

In contrast to other imaging techniques, ultrasound of the abdomen can be considerably handicapped by observer bias. To estimate its reliability for the detection of *O. bifurcum* induced colonic wall pathology, three studies to assess the intra- and inter-observer variation of the technique were performed, as described in CHAPTER 7. For both prevalence and intensity observations, only a small degree of intra- and inter-observer variation was found, and we therefore felt confident to use ultrasound for diagnosis of *O. bifurcum* induced colonic pathology. Nodules can be measured to within an accuracy of approximately 5 mm.
O. bifurcum infection and asymptomatic colonic pathology are highly prevalent within northern Ghana, but clinical disease is relatively uncommon. The natural evolution and regression of the colonic pathology in an endemic community in northern Ghana is therefore described in Chapter 8, together with its distribution within the population. 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, with children developing 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. Progression of this pathology into clinical disease is doubtless influenced by mechanical, anatomical, genetic and immunological factors.

Albendazole has effectively been used for the treatment of hospital cases of oesophagostomiasis, presumably acting by killing the histotropic juvenile worms. In Chapter 9, 54 ultrasound positive children living in a heavily infected community were each given 5 days of treatment with albendazole (10 mg/kg.day) early in the dry season, and the response to treatment was compared with a group of 55 untreated ultrasound positive children. Treatment reduced the prevalence, number, size and half-life of the ultrasound visible nodules, stopped the excretion of O. bifurcum eggs, and reduced the development of clinical oesophagostomiasis during the subsequent 8 months. However, the treatment had no impact on the new infections that occurred during the following rainy season, and no impact on nodule prevalence by the end of that rainy season.

Previously, when the parameters of infection and disease were limited to parasitological investigations and clinical observations, there was a clear cut distinction between infection and disease. But now, with the discovery that asymptomatic individuals have tissue living stages of O. bifurcum within their colon wall resulting in colonic pathology visible by ultrasound, the accuracy of this delineation is diminished. A person stool culture positive for O. bifurcum with or without the symptoms or signs attributable to the parasite can be described as having ‘Oesophagostomum infection’. A patient presenting to the medical profession with symptoms characteristic of O. bifurcum has ‘clinical oesophagostomiasis’. ‘Subclinical oesophagostomiasis’ can be used to describe people in whom signs of O. bifurcum can be found by the medical profession without a history of associated symptoms: eg. those in whom distinctive abdominal pathology can be seen by ultrasound without its related symptoms. A
limited but important number of cases of subclinical oesophagostomiasis are in fact ‘preclinical oesophagostomiasis’.

Our current hypothesis regarding the *O. bifurcum* life cycle and the nature of the subclinical nodules visible by ultrasound is as follows. The development of L3 into lumen-dwelling egg-laying adults in humans occurs within a couple of weeks. During harsh environmental conditions, L4 remain encysted in nodules - arrested larval development - emerging when conditions are more conducive to transmission. We are unable to visualise nodules containing L4 stages, as they are too small. However, some L4 nodule dwelling juveniles become trapped within their nodules (‘dead-end life cycles’) and these granulomas enlarge to become visible by ultrasound, the L4 continuing their development into L5 immature adults. A few of these ultrasound visible nodules progress to clinical disease, and the remainder are eventually reabsorbed during the dry season, following worm death. Completed and uncompleted life cycles occur simultaneously from one infective dose of L3.

In conclusion, clinical oesophagostomiasis and *O. bifurcum* induced colonic pathology represent a serious and common problem in northern Ghana. There is much still to be elucidated regarding its life cycle and control in this area of the world. The presence of human *O. bifurcum* infection in other countries is an intriguing possibility. To this end, may I request a few moments of your time to complete and return the questionnaire in Appendix 5.