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Controlling human Oesophagostomiasis in Northern Ghana

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-Summary-

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Following discovery, about 3 decades ago, that human oesophagostomiasis was focally endemic in parts of northern Ghana and in northern Togo; the *Oesophagostomum* Research Project was initiated in this region in the late 1980s by Dr. A. M. Polderman. The research project made extensive studies of aspects of the biology and transmission of this worm and related helminth infections, the epidemiology of infection in Ghana and Togo and the clinical and laboratory diagnosis of infections and associated pathology. Over the years, it gradually became apparent that human oesophagostomiasis had assumed public health dimensions in this area. This has led to the design of a research proposal within the frame-work of the *Oesophagostomum* research project to determine the possibilities of controlling human oesophagostomiasis using mass drug treatment. This study was carried out over the past 5 years and has led to the present thesis.

Chapter 1 of the thesis describes the background and rationale of the study. Our hypothesis concerning human *Oesophagostomum* infections and related morbidity postulates that repeated mass drug treatment with albendazole could disrupt the life-cycle of *Oesophagostomum* infections resulting in transmission and disease control. A similar approach had been employed in the control of other soil transmitted helminth infections such as hookworm. Control efforts in such infections were often frustrated by rapid re-infections due to the presence of large reservoir of infections. In literature, no experience has been reported on efforts to control human *Oesophagostomum* infections. We assume, however, that there are two important reasons why this approach might be successful: the focal distribution of human *Oesophagostomum* infections and the parasite's poor adaptation to the human host. Initially, an important reason for carrying out this study was to develop good strategies to be replicated for area-wide control of human oesophagostomiasis in this endemic focus, but in the course of executing the study, much of northern Ghana and northern Togo including our research area were covered with mass drug treatment using albendazole plus ivermectin by the Lymphatic Filariasis Elimination Programme (LFEP). We therefore expanded our study objectives to include evaluation of the prospects of control of infection over a wider area..

Chapters 2 and 3 give a detailed epidemiological description of *Oesophagostomum* and hookworm infections in the study area. We focus on both infection and the morbidity marker of infection (*Oesophagostomum*-induced nodular pathology) in the study area before the start of mass treatment. The patterns of infection in relation to age, gender and geographical location have been outlined. The results in chapter 2 show that third stage larvae of *O. bifurcum* and hookworm were detected in 53.0% and 86.9% of subjects examined. *Oesophagostomum* infections appeared to be clustered but a clear explanation for such aggregation of infections remains unknown. At the individual level, an association between hookworm and *Oesophagostomum* infections exists: persons infected with hookworm had a five-fold higher risk of being infected with *O. bifurcum*. Adult females were comparatively more infected than their male counterparts. In terms of family size, level of hygiene or the presence of animals in the compounds, no association could be demonstrated. Representatives of the Bimoba-tribe appeared to be significantly more infected than those of the other tribes. This association, however, was found to be a geographical phenomenon: the Bimoba are mostly living in villages with the highest infection rates.

Chapter 3 shows that ultrasonically-visible nodular pathology which reflects morbidity due to *Oesophagostomum* infections was high in the area. Out of 928 persons who underwent both parasitological and ultrasound investigations, 44% had third-stage *O. bifurcum* larvae present in their stools while in 34% ultrasonically visible nodules were detected along the colon wall. Lesions were mostly found in the ascending and transverse colon. Significant correlations existed between the intensity of infection in terms of larvae found in stool cultures and the presence of nodules. This was true both at the village and at the individual level. Individuals who developed multi-nodular pathology also had higher larval counts than those with uni-nodular pathology. These observations suggest that the presence of nodular pathology and probably the risk of severe disease are directly related to the intensity of infection.

In **chapter 4**, we present a qualitative description of the nodular lesions detected by ultrasound. Of 1470 patients who underwent abdominal ultrasound examination within two years, a total of 637 anechogenic nodular lesions with posterior wall acoustic enhancement were detected. Most lesions were solitary in nature and only a few occurred in clusters and appeared as complex lesions. Complex lesions appeared either in chain along the colon wall (arranged circularly or longitudinally) or as a grape-like cluster constituting a tumour. The lesions were mostly detected in the colon wall and frequently the adjacent colon wall appeared hyperechogenic and showed signs of pericystic oedema. In only 3 patients, lesions could be detected in the anterior abdominal wall. Identification of anechogenic lesions with posterior wall acoustic enhancement and increased hyperechogenic adjacent bowel wall suggests that the histotropic stage of *O. bifurcum* infection causes cystic lesions associated with intense inflammation thus confirming previous histological findings.

Chapter 5 describes the results of the impact of albendazole treatment on *Oesophagostomum* and hookworm infections. The effect of treatment of a cohort of 146 persons treated with a single, 400-mg dose of albendazole was evaluated three weeks later. The ‘cure rate’ was 79.0% and the ‘egg-reduction rate’ was 73.5% among subjects who had a positive Kato before treatment. When treatment impact was evaluated by the coproculture method, a ‘cure rate’ of 98.0% was obtained for *O. bifurcum* but 51.3% for hookworm. . ‘The ‘larval reduction rate’ among those still positive for hookworm after treatment was 79.8%. For *Oesophagostomum* the larval reduction rate could not be reliably calculated as only one person remained positive. The ‘egg-/larva-reduction rates’ among those heavily infected with hookworm prior to treatment were >90%, irrespective of whether results from Kato smears or the coprocultures were used for data analysis. These results confirm that a single dose of albendazole is very likely to cure an *O. bifurcum* infection and to reduce greatly the intensity but not the prevalence of hookworm infections.

In **Chapter 6**, the impact of repeated mass treatment is described using two single, 400-mg doses of albendazole (6 months apart) at the population level. The prevalences of infection had decreased from 53.0% to 5.4% for *O. bifurcum* and from 86.9% to 36.9% for hookworm after twelve months. Twenty-four months after the baseline survey and following a total of four rounds of treatment,

prevalences were further reduced to 0.8% and 23.4% for *O. bifurcum* and hookworm respectively. Mass treatment also resulted in a significant decrease in the geometric mean larval counts of *O. bifurcum* from 3.0 to 0.1 and of hookworm from 47.2 to 1.8 over the same period. Treatment coverage ranged from 70% to 79%. In the adjacent control area where no mass treatment took place, *Oesophagostomum* –prevalence and -intensity increased from 18.5% to 37.0% and from 0.4 to 1.4 respectively; for hookworm, both prevalence (from 86.1% to 91.3%) and intensity (from 54.8 to 74.3) greatly increased.

The study confirms that the prospect of eliminating human oesophagostomiasis from the intervention area, while simultaneously achieving an important reduction of hookworm prevalence by repeated albendazole mass treatment, could be achievable.

In **chapter 7**, the impact of albendazole-based mass treatment to control morbidity is assessed and compared with the situation in a control area where no mass treatment was carried out. Following two rounds of mass treatment in one year the morbidity marker, ultrasound-detectable nodules, declined from 38.2 to 6.2%. There was also a shift from multinodular pathology, often seen in heavy infections, to uni-nodular lesions. In the control villages where no treatment took place, the rate of nodular pathology did not significantly change (from 21.5% to 19.0%) but a higher proportion of the subjects developed multinodular pathology compared with that found at baseline. This study therefore concluded that repeated albendazole treatments equally reduce *O. bifurcum*-induced morbidity to a significant level.

In **Chapter 8** extended observations are summarized of a collaborative study with the LFEP in Ghana. It was shown that *Oesophagostomum* prevalence continued to go down even though mass treatments were stopped. Hookworm infections, on the other hand, started to increase again. It is suggested that the reservoir of remaining *Oesophagostomum* infections, after a number of mass treatments, was too small to serve as an appropriate reservoir for renewed transmission.

The impact of two yearly LFEP-based albendazole treatments was evaluated in a number of sentinel villages where a first *Oesophagostomum* survey was carried out 9 years ago. The results show that operational large scale population-based

albendazole treatment can reduce *Oesophagostomum* prevalence in a similar way as in the research setting extensively described in this thesis.

The prominent general conclusions

From an operational point of view it can be concluded from the study that:

1. The ultrasound-visible pathology is correlated with the intensity of infection in terms of the numbers of larvae cultured.
2. The short-term efficacy of albendazole on *Oesophagostomum* infection is very good and significantly better than it is for hookworm infections.
3. The prevalence of infection as well as the frequency of seeing ultrasound-visible lesions caused by *Oesophagostomum* infection rapidly decreased after treatment.
4. The prevalence of *Oesophagostomum* infection remains low and transmission seems to have stopped in the intervention area. The results suggest that effective control and possibly elimination of human infection in the area are achievable goals.
5. For hookworm infection, the prevalence and intensity of infection are greatly reduced but transmission is not interrupted. Prevalence and intensity rise again when yearly treatments are stopped.

It is too early to draw final conclusions on the elimination of human oesophagostomiasis in the endemic area. Careful monitoring of the *Oesophagostomum* situation during the next few years will be necessary to consolidate the successes achieved so far and to ascertain whether or not the elimination of the parasite will be possible.

The integration of the activities to control human oesophagostomiasis and lymphatic filariasis is shown highly profitable. Intense and continued collaboration is needed to avoid gaps: to avoid left over foci of *Oesophagostomum* transmission in places where albendazole control of filariasis is considered unnecessary. Such foci exist in Togo.