8 Lent, H. and Wygodzinsky, P. (1979) *Bull. Am. Mus. Nat. Hist.* 163, 123–520
9 D'Alessandro, A. (1976) in *Biology of the Kinetoplastida* (Vol. 1) (Lumsden, W.H.R. and Evans, D.A., eds), pp 327–403, Academic Press
10 Schaub, G.A. and Breger, B. (1988) *Med. Vet. Entomol.* 2, 309–318
11 Miles, M.A. (1978) in *Biology of the Kinetoplastidia (Vol. 2)* (Lumsden, W.H.R. and Evans, D.A., eds), pp 117–196, Academic Press
12 Zeledon, R. (1976) in *New Approaches in American Trypanosomiasis Research* Sci. Publ. No. 318, Pan American Health Organization
13 Garcia, E.S. *et al.* (1984) *Mem. Inst. Oswaldo Cruz* 79, 33–37
14 Garcia, E.S. and Dvorak, J.A. (1982) *Am. J. Trop. Med. Hyg.* 31, 259–262
15 Alvarenga, N.J. and Leite, M.A.B. (1982) *Trans. R. Soc. Trop. Med. Hyg.* 76, 708–710
16 Alvarenga, N.J. and Brener, Z. (1978) *Acta Trop.* 35, 315–317
17 Garcia, E.S. and Gilliam, F.C. (1980) *J. Parasitol.* 66, 1052–1053
18 Hecker, H., Schwarzenbach, M. and Rudin, W. (1990) *Parasitol. Res.* 76, 311–318
19 Azambuja, P., Guimarães, J.A. and Garcia, E.S. (1983) *J. Insect Physiol.* 29, 833–837
20 Azambuja, P. *et al.* (1989) *Braz. J. Med. Biol. Res.* 22, 597–599
21 Azambuja, P., Mello, C.B. and Garcia, E.S. (1989) in *Host-regulated Developmental Mechanisms in Vector Arthropods* (Borovsky, D. and Spielman, A., eds), pp 270–276, University of Florida Press
22 Garcia, E.S. *et al.* (1989) *Z. Naturforsch.* 44c, 317–322
23 Stiles, J.K. *et al.* (1990) *Parasitology* 101, 369–376
24 Pereira, M.E.A., Andrade, A.F. and Ribeiro, J.M.C. (1981) *Science* 211, 597–600
25 Welburn, S.C., Maudlin, I. and Ellis, D.S. (1989) *Med. Vet. Entomol.* 3, 77–82
26 Maudlin, I. and Welburn, S.C. (1989) *Trop. Med. Parasitol.* 39, 56–58
27 Molyneux, D.H., Wallbanks, K.R. and Ingram, G.A. (1987) in *Host–Parasite Cellular and Molecular Interactions in Protozoal Infections* (Chang, K.P. and Snary, D., eds), pp 387–396, Springer-Verlag
28 Zeledon, R., Bolanos, R. and Rojas, M. (1984) *Acta Trop.* 41, 39–43
29 Boker, C.A. and Schaub, G.A. (1984) *Z. Parasitenkd.* 70, 459–469
30 Bonaldo, M. *et al.* (1988) *J. Cell Biol.* 106, 1349–1358
31 Goldenberg, S. (1990) in *Parasites: Molecular Biology, Drug and Vaccine Design* (Azabian, N. and Cerami, A., eds), pp 1–6, Wiley-Liss
32 Rembold, H. (1989) *Econ. Med. Plant Res.* 3, 57–72
33 Garcia, E.S. *et al.* (1990) *J. Insect Physiol.* 36, 679–682
34 Garcia, E.S., Gonzalez, M.S. and Rembold, H. (1989) in *Host-regulated Developmental Mechanisms in Vector Arthropods* (Borovsky, D. and Spielman, A., eds), pp 263–269, University of Florida Press

Morbidity, Due to Schistosomiasis mansoni, and its Control in Subsaharan Africa

B. Gryseels and A.M. Polderman

The measuring and monitoring of morbidity are essential components of schistosomiasis control programmes. Bruno Gryseels and Anton Polderman assess the objectives, difficulties and importance of morbidity control of schistosomiasis mansoni in subsaharan Africa.

The concept of 'morbidity control' of schistosomiasis through population-based chemotherapy, made possible by the development of new drugs and screening techniques, is now widely advocated and applied in many endemic countries[1–3]. This new strategy yields impressive results in the short term, appealing to health officials, funding agencies and epidemiologists alike. However, considerable problems must be faced in the longer term. In areas where control is most needed, transmission is generally intense; the initial success of chemotherapy is often followed by rapid reinfection unless treatment is repeated at regular intervals for a still undetermined period. Indeed, the impact of chemotherapy on transmission appears to be limited, as shown by experiences with targeted[4,5], selective[6,7] and indiscriminate[8] mass treatment, even if combined with (focal) mollusciciding[9,10].

Population-based chemotherapy is also a costly and demanding strategy. Single-dose schistosomicides such as praziquantel are expensive and the costs of screening and drug delivery are even higher. Per capita costs of operational control programmes are typically from one to several dollars, which is often more than the total health expenditure[11]. External support is thus required but is generally limited over time; the long-term continuity, essential to cope with reinfection, can often not be assured with national means. The apparent success of control projects that are set on achieving quick results but not on consolidating sustainable structures and measures may completely vanish in the few years after the foreign assistance comes to an end. It is now recognized that integration of schistosomiasis control into existing health structures is essential in maintenance phases[12]. However, most primary health care systems in Africa face a multitude of old and new problems, while manpower, expertise and resources are scarce.

The implementation of population-based chemotherapy should thus be clearly justified by the demonstration of important specific morbidity and of its reduction by the intended intervention.

Bruno Gryseels and Anton M. Polderman are at the Laboratory of Parasitology and Institute for Tropical Medicine, Faculty of Medicine, University of Leiden, PB 9605, 2300 RC Leiden, The Netherlands.

Objectives of morbidity control

For schistosomiasis mansoni, the most important pathology to be prevented is decompensated portal hypertension (DPH) due to periportal liver fibrosis. Its clinical consequences, in particular oesophageal varices, may be fatal, but develop insidiously and can remain asymptomatic until irreversible damage has occurred. This is indeed a strong argument for community-based, 'preventive' chemotherapy, although recent sonographic studies indicate that even advanced liver fibrosis may be more reversible after treatment than previously thought[13,14]. In classic foci such as Egypt and Brazil, DPH due to schistosomiasis is or was so frequent that the need for control was in no doubt; in the past decades, chemotherapy has been applied on a wide scale in these countries. Remarkably, in Brazil, serious hepatosplenic disease seems to disappear also in areas not submitted to control[15].

In subsaharan Africa, there are undoubtedly areas where schistosomiasis mansoni is also a serious public health problem. The most notable and best-described example is the West Nile region in Uganda, where community-based and clinical surveys, as well as hospital records, have demonstrated high morbidity and mortality attributable to advanced schistosomiasis[16–18]. However, a review of the literature shows that the occurrence of DPH due to schistosomiasis has been convincingly demonstrated in only a few other areas in subsaharan Africa[11]. Over the past years, we have performed morbidity surveys in three subsaharan foci of various intensities. In all three, clinical portal hypertension could scarcely be demonstrated. The most striking case is Maniema (Eastern Zaire), undoubtedly one of the most intense foci in the world. Although dysenteric syndromes and massive hepatosplenomegaly are highly frequent, haematemesis or other signs of DPH are virtually unknown[19]. In the more moderate foci of the Rusizi Plain and Lake Cohoha (both in Burundi), increased frequencies of (mostly mild) organomegaly can be related to the presence of infection, both at the individual and at the community level, but in nearly 7000 subjects examined no suspected cases of DPH have been detected[20,21]. Cases of periportal liver fibrosis due to schistosomiasis have been histologically documented in Maniema[22] as well as in Burundi (T. Niyongabo, MD thesis, University of Burundi, 1983) but few if any cases ever seem to reach the decompensated, full-blown clinical stage. The Maniema example (and others) illustrates that intense infections alone are insufficient to cause severe pathology. Other possible contributing factors have been reviewed by Chen and Mott[23], but for the most part the varying morbidity patterns of schistosomiasis mansoni remain unexplained.

It can be argued that subclinical liver fibrosis, without symptomatic DPH, is in itself serious enough to justify 'preventive treatment'. However, in contrast with cirrhosis, the hepatocellular function in liver fibrosis remains preserved in principle. As long as no DPH develops, we have so far no objective evidence that liver fibrosis leads to other forms of functional morbidity. Adequate methods for the visualization of liver fibrosis had been lacking until the recent application of field sonography[24,25]. Studies with this technique are still scarce, particularly in subsaharan Africa. Systematic autopsy studies are also notoriously lacking. We have no idea about either the frequency or the public health impact of asymptomatic liver fibrosis.

Increased frequencies of liver enlargement have been shown in (heavily) infected groups in most endemic areas[11,21] and are generally considered to be an indication of schistosomiasis morbidity[2]. However, neither in autopsy studies[26] nor in ultrasound studies[27] could hepatomegaly be found to be related to the presence of periportal fibrosis or to any other functional pathology. Splenomegaly can be a direct consequence and indicator of portal hypertension, as demonstrated in field and clinical studies in Uganda and in Kenya[16,17,28]. In most subsaharan areas, splenomegaly is nevertheless predominantly related to malaria, though schistosomiasis may be a contributing[20] and, in some intense foci, even the main etiological factor[19]. In our and other studies, schistosomiasis-related organomegaly was observed mainly in children and declined or even disappeared in adults. It is thus probably due to a reversible inflammatory reaction rather than to chronic fibrosis[22].

It can thus be questioned whether increased rates of liver and spleen enlargement are reliable indicators for severe morbidity and whether they can justify control measures when the occurrence of DPH cannot be documented. In the near future, ultrasound studies may throw more light on the frequency of (subclinical) liver fibrosis in endemic areas. However, the occurrence of sonographically demonstrable liver fibrosis would not automatically prove a significant public health impact in terms of functional morbidity.

The intestinal morbidity due to *Schistosoma mansoni* infection is generally less emphasized than hepatomegaly and splenomegaly in the concept of morbidity control. In most field studies, an important association of diarrhoea and particularly dysenteric syndromes with the presence/intensity of infection has nevertheless been shown at the individual as well as at the community level (for reviews see Refs 11,23). However, schistosomiasis is only one component of the important and complex problem of diarrhoea in subsaharan Africa. Furthermore, diarrhoea due to schistosomiasis can be relatively simply detected, diagnosed and treated. Control of intestinal morbidity can thus be achieved by improving the curative health care for schistosomiasis (and other causes of diarrhoea for that matter). This would appear a more cost-efficient and sustainable measure than large-scale preventive treatment.

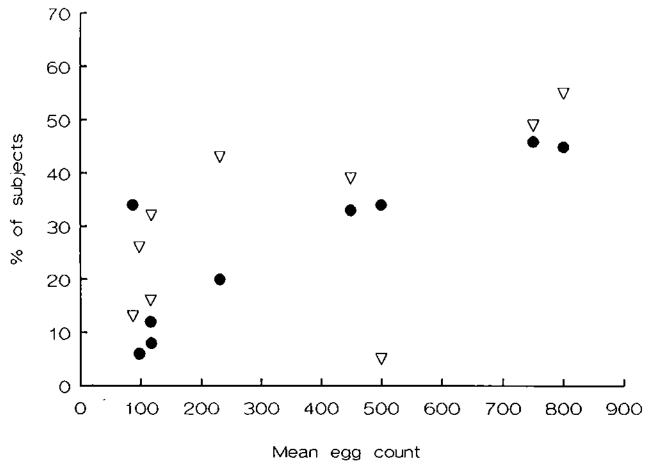

Fig 1. Relationship between mean egg count and frequency of hepatomegaly (closed circles). and diarrhoea (open triangles) in subjects infected with Schistosoma mansoni *in various subsaharan foci.*

The impact of schistosomiasis on the physiological and economic capacity has been the subject of many studies (for reviews see Refs 11,29) and forwarded as an economic rationale for control. The measured effects, if present, are either marginal or dubious. It is difficult to identify valid control populations as the distribution of schistosomiasis is often linked to geographic, socioeconomic and ethnic factors. Indicators for the specific impact of schistosomiasis, as one factor among the many infections and deficiencies that affect health in most endemic communities, cannot readily be defined. In Maniema, probably one of the most ideal situations for a comparative study is found, with either very high or very low prevalences and intensities of infection in communities that are otherwise highly comparable. Nevertheless, ergometric studies with different methods could not show measurable differences of physiological capacity between (heavily) infected and uninfected subjects or communities[19,30]. Even in this intense focus, an economic rationale for control could thus not be provided.

Egg count as a measure of morbidity

The relationship between morbidity and faecal egg count in schistosomiasis mansoni is an important notion in morbidity control. The assumption that people with intense infections are most at risk of disease and that this risk can be estimated with faecal egg counts has led to proposals for a strategy of 'targeted mass therapy' (Refs 31,32), in which only people with high egg counts are treated. However, such discriminative strategies are seldom used, if only because they are not easily accepted by authorities, populations and health workers alike. Moreover, the budgetary advantages are limited because, in operational programmes, the costs of screening and delivery far outweigh those of drugs.

'Selective mass treatment', in which the entire population or specific groups (such as school children) are screened and all positive subjects receive treatment, is the most widely applied strategy. In urinary schistosomiasis, reagent strips for haematuria provide a sensitive, rapid and easy screening method for infection and morbidity, applicable also in primary health care approaches[33]. In schistosomiasis mansoni, stool examination is still the only reliable screening method; even though the widely applied Kato technique provides many advantages, it remains time consuming, demanding in equipment and trained personnel and relatively insensitive. In Burundi, up to 40% of the infections found on repeated examination were not detected in a routine screening with a single Kato slide[34].

It is moreover questionable whether any selection procedure based on egg count is really justified. Although a high egg count may predispose an individual to the development of (future) severe pathology, the correlation of egg count with actual disease at the moment of diagnosis is much less evident than is generally accepted. The autopsy study of Cheever[26], on which the relationship is supposed to be based, has shown that Symmers' fibrosis was found mostly in people with high *worm*

Table 1. Relationship between hepatomegaly in children and the presence and intensity of infection with *Schistosoma mansoni* in various subsaharan foci

Country	Presence	Intensity	Reference
Ethiopia	No	No	37
Sudan	No	No	38
Kenya (Kisumu)	No	Inverse	39
Burundi	Yes	No	20
Uganda	Yes	>100 epg[a] 53% and 76%[b]	16
Zaire	Yes	>200 epg[a] 33% and 60%[b]	19
Kenya (Machakos)	Yes	>400 epg[a] 25% and 48%[b]	35
Botswana	No	>1600 epg[a] 5% and 17%[b]	40

[a] Cut-off point, in eggs per gram, above which hepatomegaly rates are significantly increased.
[b] Frequency of hepatomegaly under and above the cut-off point.

Table 2. Intra- and intercommunity analyses of schistosomiasis morbidity patterns in three African foci

		% Frequency of symptoms							
			Study population[a]			Egg output group[b]			
Symptom	Focus	Control population	All	Sm+	Sm−	I	II	III	IV
Diarrhoea	Maniema[c]	3	53	–	–	33	60	59	60
	Rusizi[d]	19	28	32	27	29	45	28	11
	Cohoha[e]	19	36	43	32	31	28	61	56
Abdominal pain	Maniema	25	63	–	–	45	64	69	75
	Rusizi	79	73	80	61	83	85	69	80
	Cohoha	83	86	88	84	92	83	87	88
Fatigue	Maniema	19	33	–	–	24	43	33	41
	Rusizi	1	3	3	3	2	3	0	0
	Cohoha	0.5	6	9	4	7	4	10	20
Hepatomegaly	Maniema	9	45	–	–	25	30	42	62
	Rusizi	17	31	35	26	33	37	35	35
	Cohoha	9	30	45	21	31	41	58	60
Splenomegaly	Maniema	5	29	–	–	22	25	33	35
	Rusizi	27	33	40	25	38	42	39	50
	Cohoha	7	18	26	13	12	26	26	52

[a] Sm+, Sm−: subjects with or without eggs of *S. mansoni* in faeces.
[b] Maniema: I: 1–100 II: 101–600 III: 601–2000 IV: >2000 eggs per gram (epg).
Rusizi, Cohoha: I: 1–100 II: 101–350 III: 351–1000 IV: >1000 epg.
[c] Maniema (Zaire): Endemic (n=547, prevalence 96%) versus nonendemic village (n=363) in forest tin-mining area; malaria holoendemic.
[d] Rusizi plain (Burundi): Irrigated (n=712, prevalence 53%) versus nonirrigated areas (n=785) in rice and cotton culture; malaria mesoendemic.
[e] Cohoha (Burundi): Endemic (n=552, prevalence 38%) versus nonendemic (n=365) in peninsulas on high plateau lake; malaria hypoendemic.

loads. However, the relationship between worm load and faecal egg count was rather variable and actually absent in cases with Symmers' fibrosis. No further correlation between worm load or faecal egg count and other pathology was shown. In one series of 27 cases with sonographically proven Symmers' fibrosis in the Sudan, Homeida and colleagues[24] found that 26 were negative upon stool examination.

A series of population-based morbidity studies are also considered as supportive of a more or less direct relation between egg load and disease. In Fig. 1, the relationship is plotted between mean egg count and the frequency of hepatomegaly and diarrhoea, observed in various community-based morbidity studies in subsaharan Africa[16,19–21,35–39]. It is seen that, although a standard cut-off point cannot readily be defined, morbidity is indeed related to egg counts *at the community level*. However, this does not imply that the relationship between egg load and pathology is present also *at the individual level*, on which a selective approach in population-based chemotherapy could be based. It has also been stated that 'a high proportion of children with *S. mansoni* egg counts over 100 eggs per gram (epg) of faeces have enlarged livers and spleens' (Ref. 1). Data from subsaharan foci are summarized in Table 1. Apart from the questionable relevance of organomegaly as an indicator for morbidity, as discussed above, no relationship of hepatomegaly to egg count or even the presence of infection could be shown in at least some of the studies. In others, the intensity levels above which liver enlargement increased looks more like an exponential series than a uniform cut-off point of 100 epg. Furthermore, it is clear that hepatomegaly rates are still considerably increased also in lower egg count groups.

In our morbidity studies we have compared morbidity patterns not only between egg output groups within the endemic community but also with (almost) unaffected control populations. Some essential results are summarized in Table 2. In each focus, the frequencies of hepatomegaly, splenomegaly and diarrhoea were higher in infected than in noninfected subjects, with some variations with age. The correlation with the intensity of infection was limited, particularly in adults and in foci with relatively low egg counts. However, in all areas and for all symptoms the differences of morbidity rate between endemic and control populations were more important than between egg count groups within the affected community. Indeed, morbidity rates were generally higher in the lowest or even negative egg count groups of the endemic community than in the control populations.

This observation can be explained by several hypotheses. Due to the limited sensitivity and day-to-day variability of routine egg counts, the determination of the infection status of an individual based on a stool examination can be imprecise. There may also be a considerable time lag between the presence of (heavy) infection and the development of serious disease[27]. Whatever the explanation, there is the implication that quantitative and even qualitative egg counts are not an ideal basis for selecting individuals for treatment in community-based chemotherapy.

From an operational point of view, large-scale microscopic screening requires considerable equipment, logistics, trained personnel and management, and can generally not be integrated into primary health care activities. Moreover, if we accept that population-based chemotherapy is justified only in areas with serious morbidity, where prevalences are generally high, then the relevance of selective strategies is even more questionable; screening results (partly erroneously) in the exclusion of only a small proportion of the community. Indiscriminate mass treatment is then probably the most appropriate and cost-efficient strategy, though it is clear that its application requires a well-designed, inbuilt monitoring system on which follow-up strategies can be based. The latter should clearly include durable transmission control measures, for which new research efforts should urgently be initiated.

Conclusions

Chemotherapy for the control of schistosomiasis should be selective at the community level rather than at the individual level. The main problem is then how to identify target populations of intervention. Simple, specific indicators are not available for schistosomiasis mansoni. However, significant frequencies of haematemesis, ascites or dysenteric syndromes can be made apparent from community interviews, health records and local clinical experience, and can further be documented in relatively simple surveys. It is questionable whether more moderate morbidity patterns justify the high cost of community-based chemotherapy. If the occurrence of DPH or severe dysenteric syndromes is not apparent from clinical practice and health records, then either they are of little importance or the health services are not able to appreciate such important pathology. In both cases, the available resources are better spent on the improvement of basic health care than on schistosomiasis control.

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References

1 World Health Organization (1983) *White paper WHO/SCHISTO/83.68*
2 World Health Organization (1985) *WHO Technical Report Series* No. 728
3 Liese, B. (1986) *Parasitology Today* 2, 339–345
4 Polderman, A.M. and Manshande, J.P. (1981) *Lancet* i, 27–28
5 Polderman, A.M. and De Caluwé, P. (1989) *Trop. Med. Parasitol.* 40, 177–180
6 Wilkins, H.A. (1989) *Parasitology Today* 5, 83–88
7 Gryseels, B. and Nkulikyinka, L. (1989) *Trans. R. Soc. Trop. Med. Hyg.* 82, 219–228
8 Brinkmann, U.K. *et al.* (1988) *Trop. Med. Parasitol.* 39, 167–174
9 Polderman, A.M. (1984) *Soc. Sci. Med.* 19, 1073–1080
10 Werler, C. (1989) *Trop. Med. Parasitol.* 40, 234–236
11 Gryseels, B. (1989) *Trop. Med. Parasitol.* 40, 134–142
12 Korte, R. and Mott, K.E. (1989) *Trop. Med. Parasitol.* 40, 130–133
13 Qurashi, M. *et al.* (1991) *Am. J. Trop. Med. Hyg.* 44, 444–451
14 Homeida, M.A. *et al.* (1988) *Lancet* ii, 437–440
15 Kloetzel, K. and Schuster, N.H. (1987) *Trans. R. Soc. Trop. Med. Hyg.* 81, 365–370
16 Ongom, V.L. and Bradley, D.J. (1972) *Trans. R. Soc. Trop. Med. Hyg.* 66, 835–851
17 Ongom, V.L. *et al.* (1972) *Trans. R. Soc. Trop. Med. Hyg.* 66, 852–863
18 Williams, E.H., Hayes, R.J. and Smith, P.G. (1986) *J. Trop. Med. Hyg.* 89, 193–211
19 Gryseels, B. and Polderman, A.M. (1987) *Trans. R. Soc. Trop. Med. Hyg.* 81, 202–209
20 Gryseels, B. (1988) *Trans. R. Soc. Trop. Med. Hyg.* 83, 582–587
21 Gryseels, B. and Nkulikyinka, L. (1990) *Trans. R. Soc. Trop. Med. Hyg.* 83, 542–547
22 Gigase, P.L.J. (1982) *Acta Leiden.* 49, 41–53
23 Chen, M.G. and Mott, K.E. (1988) *Trop. Dis. Bull.* 85, R1-R56
24 Homeida, M. *et al.* (1988) *Am. J. Trop. Med. Hyg.* 38, 86–91
25 Doehring-Schwerdtfeger, E. *et al.* (1990) *Am. J. Trop. Med. Hyg.* 41, 63–69
26 Cheever, A.W. (1968) *Am. J. Trop. Med. Hyg.* 17, 38–64
27 Homeida, M. *et al.* (1988) *Am. J. Trop. Med. Hyg.* 39, 196–201
28 de Cock, K.M. *et al.* (1982) *Am. J. Trop. Med. Hyg.* 31, 579–588
29 Tanner, M. (1989) *Trop. Med. Parasitol.* 40, 143–148
30 Van Ee, J.H. and Polderman, A.M. (1984) *Trop. Geog. Med.* 36, 259–266
31 Kloetzel, K. (1967) *Tran. R. Soc. Trop. Med. Hyg.* 61, 609–610
32 Warren, K.S. and Mahmoud, A.A.F. (1976) *Trans. Am. Assoc. Physicians* 89, 195–202
33 Savioli, L. and Mott, K.E. (1989) *Parasitology Today* 5, 333–337
34 Gryseels, B., Nkulikyinka, L. and Engels, D. *Am. J. Trop. Med. Hyg.* (in press)
35 Arap Siongok, T.K. *et al.* (1976) *Am. J. Trop. Med. Hyg.* 25, 273–284
36 Gryseels, B. (1984) *Ann. Soc. Bel. Med. Trop.* 64, 249–266
37 Hiatt, R.A. and Mehari, G-M. (1977) *Am. J. Trop. Med. Hyg.* 26, 473–481
38 Omer, A.H.S. *et al.* (1976) *J. Trop. Med. Hyg.* 79, 151–157
39 Smith, D.H., Warren, K.S. and Mahmoud, A.A.F. (1979) *Am. J. Trop. Med. Hyg.* 28, 220–229
40 Friis, H. and Byskov, J. (1987) *Trop. Geogr. Med.* 39, 251–255

Thank You

This is the last issue of *Parasitology Today* with which I have been involved and Caroline Ash is now back at the helm. With all my other commitments, it would have been impossible for me to have edited *Parasitology Today* had it not been for the co-operation and unstinting help I received from authors, referees and the numerous parasitologists I have consulted over the past four months. The strength of any journal lies in its unseen army of contributors and behind *Parasitology Today* there is a force to be reckoned with. I cannot thank you all personally so I am taking this opportunity to do so here.
Thank you everyone.

Frank Cox