Predisposition to helminth infection in man

I FIND it difficult to accept the basic assumptions made by Anderson and May[1] in their model of herd immunity, at least as it applies to schistosome infection. They initially assume that certain individuals are predisposed to heavy infections. In field studies of individuals with treated Schistosoma mansoni infections[3], this was not the case. The supposition is supported by studies of hookworm infections[4]. Even if predisposition to heavy schistosome infection were shown to exist, it would be premature to attribute this to lack of immunity or to assume that such individuals cannot be successfully vaccinated.

Anderson and May also assume that immunity to schistosome infection is correlated with the intensity of infection and cite the more rapid decline in faecal egg counts in a heavily infected population examined by Siongok et al[5] compared with more lightly infected persons examined by Abdel-Wahab et al.[6]. My objections here are that the difference in faecal egg counts between these populations was not great (464 eggs per g of faeces in 5–9-yr-old males in the study by Abdel-Wahab et al.[6] and 650 eggs per g in the groups examined by Siongok et al.[5]) and the report of Ongom and Bradley[7] is not cited. In this last study the decline in egg excretion was gradual although 5–9-yr-old boys excreted an average of 793 eggs per g faeces. In the very lightly infected populations in Puerto Rico and St Lucia (geometric means of 20–30 eggs per g faeces in 5–9-yr-olds), egg excretion was maintained at relatively stable levels for many years[8,9]. Resistance of mice to reinfection is clearly related to infection intensity[10], but a large part of this resistance is nonspecific[11] and is related to infection intensities that generally are not relevant for humans[12].

The experimental study by Crombie and Anderson[13] also presents problems and does not provide convincing evidence for the death of significant numbers of S. mansoni worms in mice. Although dead worms are visible in the livers of mice for months after treatment[14], I rarely encounter them in the livers of untreated mice. Certainly, the more heavily infected mice die sooner than the less heavily infected ones, a point considered by the authors but dismissed, without presentation of data, as a cause of decreasing intensity of infection with time. The mouse model is an inherently difficult one in which to pursue this point, as nearly all chronically infected mice develop large portal-systemic collateral veins with resultant shunting of some worms into the pulmonary circulation (my unpublished data), where their survival is probably

limited. Such collaterals also develop in patients with severe disease, but such patients form a small part of the population and would not be important epidemiologically.

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1. Anderson, R. M. & May, R. M. Nature 315, 493–496 (1985).
2. Mahmoud, A. A. F., Siongok, T. A., Ouma, J., Houser, H. B. & Warren, K. S. Lancet i, 849–851 (1983).
3. Sturrock, R. F. et al. Trans. R. Soc. trop. Med. Hyg. 77, 363–371 (1983).
4. Shad, G. A. & Anderson, R. M. Science 228, 1537–1540 (1985).
5. Siongok, T. K. A. et al. Am. J. trop. Med. Hyg. 25, 273–284 (1976).
6. Abdel-Wahab, M. F. et al. Am. J. trop. Med. Hyg. 29, 868–874 (1980).
7. Ongom, V. L. & Bradley, D. J. Trans. R. Soc. trop. Med. hyg. 66, 835–851 (1972).
8. Hiatt, R. A., Cline, B. L., Ruiz-Tiben, E., Knight, W. B. & Berrios-Duran, L. A. Am. J. trop. Med. Hyg. 29, 1228–1240 (1980).
9. Barnish, G., Jordan, P., Bartholomew, R. K. & Grist, E. Trans. R. Soc. trop. Med. Hyg. 76, 602–609 (1982).
10. Dean, D. A. Expl. Parasit. 55, 1–104 (1983).
11. Dean, D. A., Minard, P., Murrell, K. D. & Vannier, W. E. Am. J. trop. Med. Hyg. 27, 957–965 (1978).
12. Cheever, A. W. Trans. R. Soc. trop. Med. Hyg. 63, 781–795 (1969).
14. Cheever, A. W., DeWitt, W. B. & Warren, K. S. Am. J. trop. Med. Hyg. 14, 239–253 (1965).

ANDERSON ET AL. REPLY—The assumption of predisposition to heavy (or light) infection is not central to the framework of our model[1] of herd immunity to helminth infection (see equations (1) and (2) of ref. 1). It is simply an optional extension which can be used to investigate the potential influence of heterogeneity in either exposure to infection (that is, behavioural factors) or the host's ability to restrict parasite establishment and survival (that is, immunological factors which may be under genetic control) on the transmission and control of helminths in human communities. Such heterogeneity is a central feature of the epidemiology of helminths, as indicated by the high degrees of aggregation observed in parasite distributions within human populations[2]. However, the interesting issue raised by Cheever centres on the question of whether or not predisposition is an important component of the epidemiology of schistosome parasites. We believe it is. The two studies cited by Cheever do not address the statistical question of whether there is a positive association (in large samples of people, stratified according to age and sex) between faecal egg counts in individual patients before treatment and after an interval of reinfection following chemotherapy[3,4]. The first such analysis of this question[7] for Schistosoma mansoni infection in a rural community in Kenya[5,6], reveals a highly significant posi-

tive association (12-month period of reinfection in 8–15-yr-old children, Kendall's $\tau = 0.347$, $n = 117$, $P < 0.0001$; ref. 7) between pretreatment egg counts (in eggs per g, e.p.g.) and counts following an interval of reinfection after chemotherapeutic treatment[7]. Whether this observed pattern is a consequence of differences in contact with infection, or in immunological competence of the host, is unclear at present. Work in progress (the same field study[5,6]) on individual patterns of contact with water and faecal egg output should improve our understanding of this issue. More broadly, recent field studies record evidence for predisposition to heavy infection with Ascaris[8,9], hookworm[10] and Trichuris[11].

We disagree with Cheever's interpretation of the relevant data on the question of a positive association between the force of transmission and the degree of convexity of age-intensity of infection profiles (Fig. 1b in ref. 1). In the 5–9-yr-old age classes in the two studies we cited[12,13], the intensity of infection (mean e.p.g. per person sampled, including boys and girls) was 690 eggs per g faeces in the high transmission area and 144 eggs per g in the low transmission area. Furthermore, in the study of Ongom and Bradley[14] (within a high transmission area of Uganda), the average intensity of infection (boys and girls) fell from a maximum of 1,128 eggs per g of faeces in the 5–9-yr-old class to a minimum of 404 eggs per g of faeces in the 40–49-yr-old class; again, a marked convex pattern was associated with a high net force of transmission. The studies in Puerto Rico and St. Lucia[15,16], cited by Cheever, further support our argument, as in these areas of low transmission intensity, mean faecal egg counts remain relatively stable over a wide range of age classes. More generally, a recent statistical study, using a range of epidemiology surveys for S. mansoni and Schistosoma haematobium, of the relationship between the maximum average intensity of infection (commonly in the child/teenage age groups) and the rate of decline in average intensity from child to adult groups reveals a highly significant positive correlation (J.A.C., unpublished).

With respect to our experimental studies[17], juvenile and dead adult worms were recovered from mice throughout the long periods of repeated exposure to infection; this suggests that populations of adult parasites in individual mice are subject to continual recruitment and mortality. We discounted parasite-induced host mortality as the major cause of the convex profiles of change in mean parasite burden with duration of exposure (= mouse age) (Fig. 1a in ref. 17) as at all sampling points in the trickle studies, the distribution of worm numbers per mouse