

Advances in
PARASITOLOGY

Edited by

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VOLUME 24

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PREFACE

We hope that this volume will provide, as we hope previous volumes have done, an interesting mixture of stimulating and up-to-date reviews in the broad field of parasitology. Now that so much emphasis is being placed on the "molecular" aspects of the subject—with very fruitful results in many areas—we feel it is important not to forget that parasitology is, essentially, an ecological subject concerned fundamentally with inter-specific relationships. The reviews in this volume by R. M. Anderson and R. M. May, L. E. A. Symons, and H. Hoogstraal particularly remind us of this, as indeed does that by J. J. Petersen—while also emphasizing a practical and economically important aspect of the subject. Dr. Petersen's review, covering the Mermithidae, will be complemented by a second instalment by R. Bedding in a subsequent volume, dealing with the Tylenchida and Rhabditida. M.-C. Durette-Desset's review is in the classical tradition of evolutionary morphology and taxonomy—fundamental building blocks in the structure of parasitology, the importance of which should not be forgotten. It also provides fascinating reasoned speculations on the coevolution of parasites and hosts. We intend that any apparent bias against protozoology in this volume will be corrected in the next two, though the protozoa are of course, included within the two general reviews in the current volume and Dr. Hoogstraal's contribution also relates very closely to protozoology.

1985

J. R. BAKER
R. MULLER

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Helminth Infections of Humans: Mathematical Models, Population Dynamics, and Control

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I. INTRODUCTION

The methods employed in the epidemiological study of helminth infections within human communities have changed surprisingly little over the

past 60 years. The pioneering work of various American and European epidemiologists in the early 1920s, on hookworm and other intestinal nematodes, compares very favorably in quality with much of the recently published work (e.g., Stoll, 1923; Cort, 1922; Payne, 1924; Augustine, 1923a,b, 1926; Chandler, 1925; Sawyer, 1925; Hill, 1926; Docherty, 1926; Kendrick, 1934). The methods they employed, the large samples of people they examined, and the conclusions they arrived at remain as relevant today as when their work was first published.

In one sense this is a tribute to the early research. In another sense, however, it is perhaps an indication of a lack of progress in this field of epidemiological study. Many factors may help explain this observation, not least of which are the numerous practical difficulties inherent in the field study of endoparasites of man, where ethical considerations prohibit certain forms of experimental work and where indirect methods must be employed to record changes in parasite prevalence and intensity within human communities. The hope that advances in our understanding of immunological responses to helminth invasion would yield reliable diagnostic methods, of a quantitative character, has as yet to be realized. This is to a large extent a consequence of the complexity of the surface antigenic structure of macroparasites and the difficulties encountered in the identification of stage-specific surface or excretory antigens which do not cross-react serologically with those of other parasite species. Modern biochemical methods employing monoclonal antibody techniques may resolve these difficulties. Encouragingly, some progress has already been made in this direction; for example, reliable diagnostic methods should soon be available for detecting the presence or absence of filarial infections in man (Maizels *et al.*, 1983). It could be argued, however, that past concern with the relevance of immunological processes in helminth transmission have to some extent distracted attention from the basics of good epidemiological study such as quantitative measures of levels of infection, good sampling design, innovative experimental approaches in field study, and analysis of the significance of human or vector behavior.

To an ecologist it may appear surprising that the advances made over the past 50 years in our understanding of the population dynamics of animal and plant species have not had a greater impact on epidemiological research. This may be a consequence of the tendency for medical attention to be focused on the course of parasitic infection (and the associated pathology) within an individual person as opposed to the community as a whole. Indeed this trend is equally apparent in research on the control of helminth parasites. There exists a marked discrepancy between our knowledge of how to treat an individual and how to control the infection within a community.

A community approach clearly depends on a thorough and detailed understanding of the population dynamics of human parasites. This important but neglected area of epidemiological study is one in which mathematical methods can play a significant role. The rationale and philosophy behind the application of mathematics to medical or biological research have been expounded by many people in recent years (e.g., Fisher, 1930; Bartlett, 1960; Maynard-Smith, 1968; May, 1974; Bailey, 1975). We therefore do not wish to repeat these arguments but simply point out a few of particular relevance to helminth epidemiology.

There has been a tendency among tropical public health workers to reject the insights produced by mathematical models on the grounds that too many simplifying assumptions are made despite known biological complexity. This is sometimes true and needs to be rectified, but there is an important counterargument. It is often necessary, and indeed helpful, carefully to eliminate simple hypotheses as explanations of observed phenomena before moving onto more complex postulates. The failure to do so will leave the lingering doubt that although the biological phenomena under study is complex by nature, a few simple processes may dominate the generation of observed patterns. Simple mathematical models in which the biological assumptions are clearly and precisely defined can be of great help in removing or confirming these doubts. Indeed, as illustrated in this article, simple sets of assumptions can lead to complicated patterns of dynamic behavior and it is as well to be aware of this when interpreting observed patterns. Helminth life cycles are often complex, involving more than one host species and many distinct parasite development stages. In such circumstances, the most refined intuition, perhaps built up from many years of field experience, may often fail correctly to interpret the factors responsible for dynamic changes in parasite abundance and distribution. In the face of biological complexity the rigour of mathematical description can aid in interpretation and, equally importantly, point to the factors or processes which must be measured or quantified in order to understand observed events. In the sense defined above, mathematical or theoretical work serves as (1) a means of eliminating hypotheses as explanations of observed trends; (2) an aid to the interpretation of multidimensional processes; and (3) a guide to field measurement and experimentation. In these roles mathematical methods are primarily of value in the elucidation of qualitative as opposed to quantitative concepts or principles.

In a quantitative sense, if enough is known about the biology and epidemiology of a particular parasite, models can also be employed as predictive tools. This role is of particular importance in the design of policies and methods for parasite control or eradication within human communi-

ties. The success of this type of approach, however, is critically dependent on a detailed and thorough knowledge of the population biology of the parasite and its host (or hosts).

This article considers the role of mathematical models in investigations of the population or transmission dynamics of human helminths. Throughout, mathematical details are kept to a minimum and we concentrate on the biological assumptions employed in model construction, the insights that emerge from model analysis, the comparison of predictions with observed trends, and the estimation of parameter values from epidemiological data. The article is organized as follows. We first give a brief account of observed epidemiological patterns, concentrating on age-prevalence and age-intensity trends. The next section gives a brief historical review of the development of mathematical models of helminth infections. The following three sections discuss mathematical models for schistosome flukes, for intestinal nematodes, and for the filarial infections. Section VIII attempts to condense the essential features of the models for specific infections in order to provide a general framework for the description of helminth transmission dynamics. The general framework is employed in Section IX to consider the design of control policies for helminth infections in human communities. The final section focuses on future developments.

II. EPIDEMIOLOGICAL PATTERNS

Much of the mathematical literature on the dynamics of infectious diseases is open to the criticism that insufficient attention is given to the comparison of predictions with observation and to the estimation of the model's parameters from epidemiological data. Before proceeding to discuss various types of models for the dynamics of helminth infections, we therefore provide a very brief overview of the available kinds of data. Our aim is simply to point out a few general patterns and trends arising from a comparative study of epidemiological surveys of helminth infections in human populations.

The majority of published data records changes in the prevalence and average intensity of infection over a series of age classes within the human community. Invariably such data is collected at one point in time, or over a short time interval, and may therefore be described as horizontal in nature. More rarely, longitudinal studies are performed where changes through time are recorded. Note, however, that if parasite population abundance within the human community has remained relatively stable over long periods of time (as is often the case in rural communities in developing countries) changes with human age are equivalent to changes

through time. We refer to the graphical representation of changes in prevalence and intensity with human age as age-prevalence or age-intensity curves. Their form in a given community clearly reflects the magnitude of parasite transmission. The average intensity of helminth infection is invariably measured by indirect means, such as faecal egg counts. These indirect measures are often a poor reflection of worm load, being subject to much variation due to sampling error and other factors. These problems are discussed more fully in Section VIII. For the time being we assume that indirect measures are simply a crude reflection of worm abundance.

We focus on the major helminths of man: the schistosome flukes, the intestinal nematodes (hookworms, *Ascaris*, *Trichuris*), and the filarial nematodes. Four general points emerge from a review of epidemiological survey data. (In this review we have concentrated on studies employing sample sizes greater than 500 people.)

1. A most remarkable feature is the comparative stability of helminth populations within human communities in the face of perturbations induced either by climatic factors or by human intervention. This is in part a consequence of the human hosts' inability to acquire strong immunity to reinfection, so that helminth infections are persistent in character with hosts being continually reinfected. A marked contrast exists between human helminths and human viral or bacterial infections: the latter invariably exhibit considerable fluctuations in prevalence through time. Some examples of helminth population stability are displayed in Fig. 1. These represent three different facets of the issue: the rate of return of helminth abundance to the precontrol level following intervention by chemotherapy, changes in age-prevalence curves over a 13-year period in one community, and changes in the overall prevalence of infection over a 7-year period.

This observed stability suggests that regulatory constraints on parasite population growth—induced by density-dependent checks on parasite survival, establishment, and fecundity—play an important role in the transmission dynamics of helminths within human communities. Such mechanisms may arise as a consequence of host responses to infection or as a result of resource limitation within the habitat of the parasite.

2. The major helminth parasites of man do not reproduce within the human host to directly increase adult worm population size but produce transmission stages which either pass to the exterior via the faeces or urine or leave the host via ingestion by a biting arthropod vector. As such, adult parasite population growth within an individual person is simply controlled by immigration and death processes. In the simplest case in which the immigration and death rates are constant and unaffected by factors such as host age or parasite density, the average burden of adult parasites

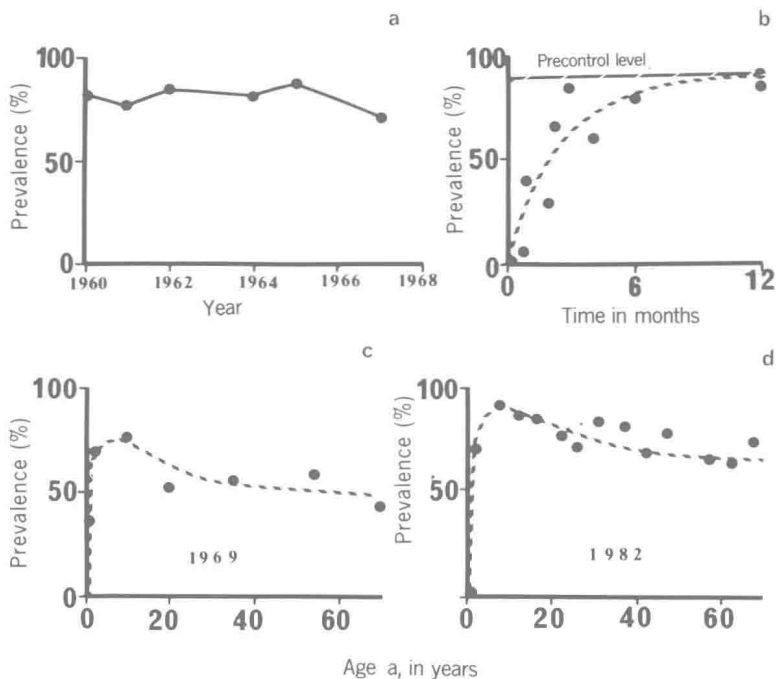


FIG. 1. Examples of long- and short-term changes in helminth abundance. (a) Changes in the overall prevalence of *Schistosoma haematobium* within a community in Iran over a 7-year period (data from Rosenfield *et al.*, 1977). (b) The rate of return of the prevalence of infection of *Ascaris lumbricoides* to its precontrol level following chemotherapy within a rural community in Iran (data from Croll *et al.*, 1982). (c) and (d) Age-prevalence data for *A. lumbricoides* infection in a rural community in Burma obtained from surveys carried out in 1969 (c) and 1982 (d) (data from Hliang *et al.*, 1983).

will grow monotonically as the human host ages to reach a plateau. The level of this plateau is simply determined by the rate of immigration per unit time multiplied by the average life expectancy of the adult worm. Thus, in the absence of any complications induced, for example, by host responses to infection, we might expect age-prevalence and age-intensity curves to reflect the basic qualitative properties of an immigration-death process as outlined above. This is partially the case as illustrated in Figs. 2-6. In general, prevalence increases initially as the human host ages to approach a maximum value. Thereafter a variety of trends are apparent, depending on the species of parasite, the geographical location, and the behaviour and habits of the human community. In certain instances, particularly noticeable among the patterns recorded for the intestinal nematodes (Figs. 2-4), the prevalence increases monotonically with age to a plateau in a manner entirely consistent with a simple immigration-death process. In other instances, as illustrated by the patterns re-

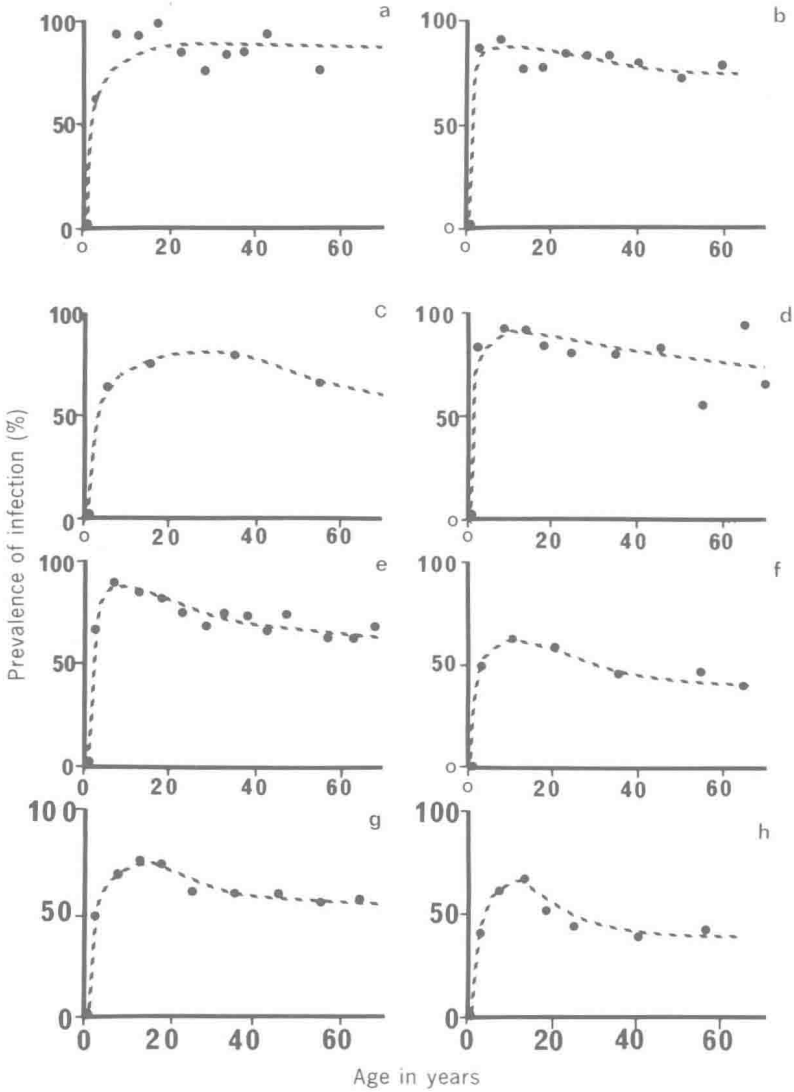


FIG. 2. Age-prevalence curves for *Ascaris lumbricoides*. (a) Iran (data from Croll *et al.*, 1982). (b) Philippines (Palo, inland districts) (Pesigan *et al.*, 1958). (c) Java (Cross *et al.*, 1970). (d) Philippines (Cabera *et al.*, 1975). (e) Burma (Hliang *et al.*, 1983). (f) Latin America (Botero, 1975). (g) Sri Lanka (Fernando and Balasuriya, 1976). (h) Bangladesh (Hossain *et al.*, 1981).

corded for the schistosome flukes and filarial worms (Figs. 5 and 6), prevalence declines after the attainment of a maximum value as people move into the older age classes. These trends may reflect any combination of a variety of processes including age-dependent contact with infec-

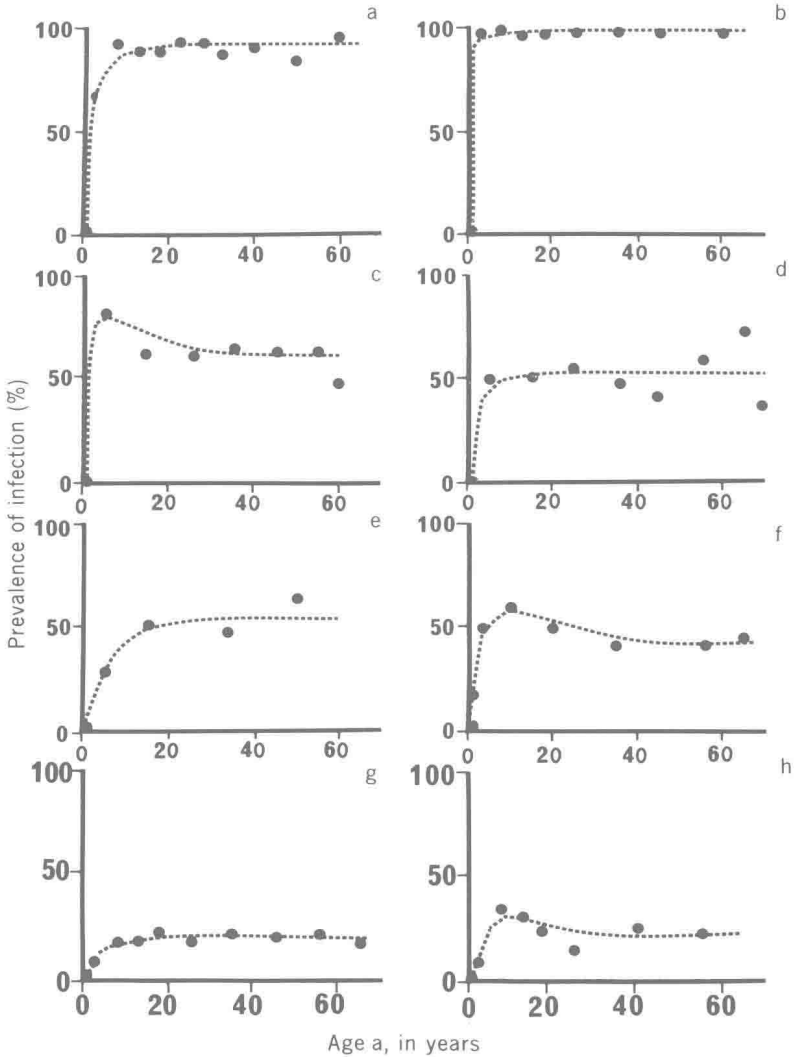


FIG. 3. Age-prevalence curves for *Trichuris trichiura*. (a) Philippines (Palo, coastal regions) (Pesigan *et al.*, 1958). (b) Philippines (Lewert *et al.*, 1979). (c) Singapore (Schacher and Danaraj, 1960). (d) Malaysia (Khan and Anuar, 1977). (e) Philippines (Cross *et al.*, 1970). (f) Latin America (Botero, 1975). (g) Sri Lanka (Fernando and Balasuriya, 1976). (h) Bangladesh (Hossain *et al.*, 1981).

tive stages, host responses whose severities increase with age as a consequence of repeated exposure to infection (acting on either parasite establishment or survival or both), age-dependent human mortality dependent on experience of parasitic infection, and age-related changes in