BOOK REVIEW

THE BIOMATHEMATICS OF MALARIA. THE BIOMATHEMATICS OF DISEASES NO. 1, Norman T. J. Bailey, Charles Griffin and Co., London, 1982. No of pages: xii + 210. Price: £16.50, $88.00.

According to estimates quoted in this book, approximately 350 million people live in areas where no efforts have ever been made to control endemic malaria. World-wide, approximately 150 million people have malaria. In Africa, among children under five years old, every year roughly a million die of malaria. The number of reported malaria cases doubled over the five years ending in 1978.

These crude and not very reliable figures justify humanitarian concern about malaria. Probably no other single disease threatens the health of more people. In addition to its direct effects on mortality and morbidity, malaria indirectly affects economic, demographic and military planning. Hence malarial epidemiology interests many people besides scientists.

This is the first book devoted to the *mathematical* epidemiology of malaria. To my knowledge, the bibliography covers completely the relevant published work, and much unpublished work, done prior to 1982. The book is written unpretentiously and, for readers trained in the appropriate mathematics or prepared to take it on faith, simply. It gives a clear sense of the limitations of what has been accomplished and the potential of what could be achieved.

The book is addressed to two different audiences: 'biomathematicians who may have opportunities for serious work in this field' and 'those who may be involved in collaborating with biomathematicians and in using the practical techniques developed' for the surveillance and control or eradication of malaria. I believe the book's successes and limitations in reaching these two audiences are different, and will review them separately.

Any student or scholar who contemplates doing research on the mathematical epidemiology of malaria will need to know everything in this book, and more. Understanding the technical parts of the book requires mastery of generating functions and elementary partial differential equations at the level of Bailey's fine text, *The Elements of Stochastic Processes with Applications to the Natural Sciences* (1964).

The heart of the book, roughly the middle half of it, consists of three chapters (6, 7 and 8) which review the general theory of host-vector diseases, the elementary population dynamics of malaria, and recent advances in the population dynamics of malaria.

The general theory of host-vector diseases is developed in chapter 6 on the basis of assumptions with very little specific relevance to malaria. Bailey defends this development: 'The gradual accumulation of knowledge into a body of general theory helps to avoid much duplication of research through existence theorems, threshold theorems, standard solutions to typical equations, knowledge of the number and type of steady states, occurrence or non-occurrence of oscillatory behavior, etc.' (p. 59). But he candidly notes 'the slightly unsatisfactory situation in which contradictory assumptions are made in more general theory according to convenience' (p. 86).

The level of abstraction in chapter 6 is indicated by the remarkable insight, due to Ronald Ross in 1911 according to Bailey, that there is an analogy between malaria and heterosexually transmitted venereal diseases because infection must pass back and forth between two distinct populations. Malaria and venereal diseases have few other biological properties in common.

The elementary population dynamics of malaria are described in chapter 7 by a few ordinary differential equations in which one variable is typically the fraction of the human population infected with malaria and another variable is the fraction of the mosquito population infected with malaria. It is usually found that these equations have two stationary solutions. In one, malaria is absent; in the other, malaria is endemic.

A sufficient condition for the absence of malaria to be stable is that a certain combination of parameters, known as the basic reproduction rate of malaria, be below a certain critical level. A result of this form is called a threshold theorem. Bailey observes that 'all the different forms of mathematical analysis [concur] that reduction of the mosquito population alone below a certain critical level would be sufficient to eliminate malaria, i.e. without the need to attempt a complete eradication of the mosquito' (p. 101).

However, the mathematical models that yield threshold theorems are generally based on assumptions that are contradicted by data. For example, these models typically ignore age structure in the human population and immunological differences associated with age, genetic variation and evolution in the human, mosquito and parasite populations, and environmental changes within a year and from year to year. Although malaria has been eradicated from temperate North America and Europe, major and sustained efforts at eradication in tropical areas have failed, notwithstanding the availability of the elementary models reviewed in this chapter. Near the end of the chapter, Bailey records the correct observation of Dietz in 1970 that, if certain assumptions are relaxed, pushing the basic reproduction rate below some critical value 'might be neither sufficient nor necessary to achieve eradication within a specified period of time' (p. 115). The elementary models of malarial population dynamics seem to be of little practical use as guides to the eradication or control of malaria. Even as pedagogical vehicles, these models are more likely to mislead by oversimplification than they are to edify.

Recent advances in the population dynamics of malaria, described in chapter 8, are the work chiefly of Dietz, Molineaux and Thomas (DMT). They helped plan and analysed the results of a unique field study of malarial epidemiology, parasitology, immunology and control conducted from 1971 to 1976 in Kano, Nigeria, jointly by the World Health Organization (WHO) and the Government of Nigeria. The book by L. Molineaux and G. Gramiccia, *The Garki Project: Research on the Epidemiology and Control of Malaria in the Sudan Savanna of West Africa* (WHO, Geneva, 1980) reports, in my opinion, both the best field study and the best epidemiological modelling of malaria that have ever been done.

In outline, DMT developed a compartmental model for the transitions of the human population among various states of infection. Importantly, DMT distinguished the transition rates of people who were 'immune' from those of people who were not 'immune'. The more my colleagues and I have struggled to develop alternative models to explain the data at DMT's disposal, the more admiring we have become for their achievement.

Nevertheless, the success of DMT's model should not be overstated. Bailey (pp. 32, 128) restates unwittingly their published claim that their model predicts certain prevalence data successfully, as judged by lack of significance of a chi-squared test of goodness of fit. In fact, DMT were aware, and Jerry Nedelman independently recently discovered by reanalysis of the data, that the published chi-squared statistic was computed incorrectly. The correct value is much larger than that quoted, large enough to reject the goodness of fit of the model's predictions. In spite of the tremendous progress that DMT's model represents, there is room for much further progress.

Bailey's chapter on recent advances in the population dynamics of malaria also gives useful reviews of the models of Dutertre and Nasell, deriving some of the latter's results more simply.

These three core chapters for researchers are followed by brief accounts of statistical estimation problems, control theory and sensitivity theory. The chapter on estimation problems is laudable for bringing to attention the innovative estimation techniques, based on martingales, introduced into epidemiology by Niels Becker, and for emphasizing, by repeated examples, that standard errors or confidence intervals should accompany every point estimate of a parameter.

I have two reservations about this chapter. First, the techniques illustrated or mentioned for estimating the variability of an estimated parameter are classical ones. Epidemiologists could benefit from knowing about and using the resampling techniques described, for example, by Bradley Efron, *The Jackknife, The Bootstrap and Other Resampling Plans* (SIAM, 1982).

Secondly, I do not find in this chapter or anywhere else in the book a review of how statistics about malaria are currently gathered or of how useful statistics about malaria ought to be gathered. When Bailey's book discusses data, it takes them largely as given. I believe that gathering better data in better ways will contribute materially to progress in the biomathematics of malaria. How to do this merits discussion.

Let me summarize now the strengths and weaknesses of the book, as I see them, for researchers in the biomathematics of malaria. The strengths are that this book provides in one place the biological background necessary to understand mathematical models of malarial dynamics and a complete review of those models, and that it modestly sets the epidemiology of malaria in the context of larger concerns for economic development and human welfare.

The principal weakness in addition to those mentioned earlier is the book's lack of contact with current progress in biological understanding of malaria. The Trager–Jensen technique (1976) for the *in vitro* cultivation of the malarial parasite has already yielded important new information about the stages of the malarial life cycle within the human host and promises much more, but is not mentioned here. Though there are scattered references to the need for modelling the spread of insecticide and drug resistance, recent studies of the genetics of the malarial parasite and mathematical models for the coevolution of host and parasite are omitted. The beautiful (because simple) mathematical analysis of the selective advantage of abnormal haemoglobins in the presence of falciparum malaria in northern Nigeria, described by Molineaux and Gramiccia, does not appear.

The core chapters of this book proceed from the most general theory to the most particular model of DMT. This ordering is natural to a mathematically trained writer and congenial to mathematically trained readers, who are accustomed to proceed from theorems to corollaries. In the perspective of a policy-making user of mathematical models, to which I now turn, the reverse ordering might be more useful and persuasive.

To prepare the policy maker for the current limitations of mathematical models in aiding control efforts in the tropics, I would suggest first reminding him or her of the very long prior evolutionary history of malarial infections in vertebrates, going far back into reptilian history at least. Malarial infections are not a new problem. There is no reason to expect that they will be easy to eliminate.

Then, before launching into any model, I would warn him (or her, for the last time) that a certain amount of formal mathematics will be involved, and that he should feel comfortable skipping the equations and reading the words if the equations are opaque.

I would initiate the account of models with the achievements of DMT. Even though DMT do not succeed fully in describing the real world, they do demonstrate a knowledge of it. I would pursue the questions of statistical estimation, control theory and sensitivity theory as concretely as possible in the context of the model of DMT. Hoping by then to have convinced the policy maker that the mathematical modelling of malaria is a difficult but not a frivolous exercise, I would introduce the elementary models of Ross and Macdonald and finally the general theory of host-vector diseases.

With this background, the policy maker would be able to attach concrete meaning to Bailey's wise general remarks about the scope and role of biomathematics, the theory and practice of modelling, and the prospects for systems analysis in public health.

For a policy maker, in sum, I believe a different order of presentation is appropriate. Even with the present ordering, policy makers could at least be told that another path through the book might be better for them.

I can still recall the excitement I felt when I went to the university bookstore as an entering student and came across Bailey's then recent book on *The Mathematical Theory of Epidemics* (1957), as well as my disappointment that the seemingly outrageous price prevented me from buying it. Fortunately, the second edition was much more comprehensive and, to me, less overpriced. I feel much the same excitement about Bailey's present book on malaria and continuing gratitude for his pioneering expositions, as well as renewed disappointment at the U.S. price of this book. I look forward to the second edition of this book. May it record much progress, and may it be cheaper.

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