

#### PUBLICATIONS OF THE NEWTON INSTITUTE

Models for Infectious Human Diseases: Their Structure and Relation to Data



#### Publications of the Newton Institute

Edited by J. Wright

Deputy Director, Isaac Newton Institute for Mathematical Sciences

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# MODELS FOR INFECTIOUS HUMAN DISEASES

Their Structure and Relation to Data

edited by

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## Introduction

## Valerie Isham and Graham Medley

#### The epidemiology of infectious human diseases

Understanding and controlling the spread of infections is of vital importance to society, and in the past century the epidemiology of human disease has become a subject in its own right. Theory and applicable techniques have been developed to study both the evolution of disease within individual people and the transmission of infections through populations. Mathematics has an important role to play in these studies, which raise challenging problems ranging from broad theoretical issues to specific practical ones, and in recent years there have been significant advances in developing and analysing mathematical models of disease progression. For example, in human diseases in particular, the problems of modelling population heterogeneity are especially important.

Over the last decade there has been a great deal of work concerned with HIV and AIDS. This has been concentrated mainly in two areas: the statistical estimation of various parameters associated with HIV infection (for example, the probability of vertical transmission; the description of the incubation period from infection to clinical disease; the estimation from reported AIDS cases of the number of people infected), and the description of transmission of HIV within and between populations (for example, the characterisation of networks of risk behaviour; the impact of different control strategies). To an extent, the growth of studies in this area has become divorced from the study of other infections, and therefore one of the primary purposes of this volume is to bring together work on modelling a wide range of human diseases so as to encourage cross-fertilisation between AIDS related research and research of the epidemiology of other infections.

A second purpose is to encourage more constructive interaction between the different areas within the epidemiology of human disease, especially between those concerned with transmissible disease and non-transmissible disease. The epidemiology of non-transmissible disease is a well-developed subject and has helped define the risk of developing disease from exposure to environmental and other hazards. The spectrum of disease caused by HIV infection tends to have a long incubation period, such that the population patterns of AIDS are not directly related to those of HIV infection. Consequently, there should be some sharing of techniques and ideas between these two areas. In the same vein, there is now much interest in the description of the genetic evolution of HIV within individuals that should be related to the study of within host variation of other infections, such as malaria.



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The development of mathematical theories of disease, especially transmissible disease, has largely occurred without the direct involvement of areas that rely on the application of the theory: community medicine and public health. A third purpose of the volume is to encourage theoretical and empirical researchers to confront each other, and to reveal areas where more positive collaboration is desirable, if not essential.

Finally, the epidemics of HIV and AIDS have highlighted the need for more rigorous use of quantitative techniques for the prediction of future trends and their health-care implications. This area has been short of theoretical study, and a fourth aim of the volume is to encourage researchers to consider the use to which predictive models may be put.

An ideal opportunity for leading research workers to collaborate in identifying and addressing current issues relating to the role of mathematical modelling in the epidemiology of human disease, has been provided by the Isaac Newton Institute for Mathematical Sciences (University of Cambridge), through its sponsorship of a six-month research programme entitled *Epidemic Models: Their Structure and Relation to Data*. This programme, which ran from January-June 1993, brought together scientists with a great variety of mathematical expertise (including applied probability, deterministic modelling and data analysis) and with close involvement in applied fields across the spectrum of social, medical and biological sciences. Its specific aim was to foster interdisciplinary cooperation in tackling problems relating to a wide range of human, animal and plant diseases. A priority was to encourage interaction between the development of theoretical results, the use of relevant expert knowledge from applied fields and the analysis of data.

During the *Epidemic Models* programme, three major workshops were held to promote this interdisciplinary interaction: the first dealt with general issues across the whole field, while the second and third were concerned with more specific topics, respectively the spread and persistence of animal and plant diseases, and of infectious human diseases. The papers in this volume were presented at the third of these, a week-long workshop focusing on human diseases, while two related volumes, Mollison (1995) and Dobson and Grenfell (1995), publish papers from the two earlier workshops. A general review of the area of mathematical models of epidemics with substantial discussion is also provided by the proceedings of a Discussion Meeting of the Royal Statistical Society (see Mollison, Isham and Grenfell, 1994).

#### The format of this volume

Following the aims described above, five themes were chosen. These were

• Transmissible diseases with long development times and vaccination strategies.



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- Dynamics of immunity (the development of disease within individuals).
- Population heterogeneity (mixing).
- Consequences of treatment interventions.
- Prediction.

Within each theme there are between two and four main papers, invited specifically to contrast different aspects of the topic. Broadly, these aspects have been chosen to contrast work that is (a) theoretical/mathematical, (b) data-based, with regard to a specific disease, and (c) related to policy or control implications. These papers are followed by invited discussion and then by short papers on the same general theme, contributed at the workshop, together with further discussion.

The policy of inviting people to discuss the same topic from different view points is perhaps the most innovative aspect of this volume. At the workshop, this policy was a great success although there were often contrasts in communication and understanding between people from different disciplines supposedly studying the same natural phenomenon. In particular, the gulf that exists between the statistical science (stochastic) and mathematical modelling (deterministic) approaches to the transmission of infectious diseases was exposed. It is rare for these two areas to be equally represented at meetings such as this, and perhaps it will turn out that the most important results of this workshop will have been the informal discussions that took place between sessions, and the contacts, links and new collaborations that have been generated between these two areas. This aspect of the workshop cannot be documented here but we hope that it will surface in the future development of our subject.

In this volume, within each theme can be found the corresponding invited and contributed papers, a written version of the invited discussion together with an edited summary of some of the more important points made in the contributed discussion from the floor of the meeting, and the authors' responses to all the discussion. Where written versions were supplied for the contributed discussion, this is indicated by the symbol (\*\*) by the discussant's name. Where no such symbol appears, the contribution has been written by the editors according to their understanding of what was said. We apologise to the discussants for any resulting misrepresentation of their questions or views.

Inevitably, individual contributed papers did not always fall neatly within one of our chosen themes but sometimes addressed issues related to two or more of them. The allocation of papers to themes has therefore resulted in a certain degree of overlap between the topics. Also, since many of the contributed papers describe work in progress, the level of detail and completeness of these



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varies considerably. However, the inclusion of all these papers adds to the picture of the wide range of diseases and approaches that come under the epidemic modelling umbrella. Where possible, especially in the case of very recent work, references have been added to indicate where further details may be found.

Following this Introduction, a list is given of all the registered participants at the Infectious Human Diseases Workshop, together with their permanent affiliations at the time of the meeting (some being temporarily affiliated to the Isaac Newton Institute). These affiliations will not be repeated on the individual papers, where only those of non-participating collaborators will be given.

We are grateful to all those whose active participation and enthusiasm contributed to the success of the Workshop, and especially to all the invited speakers, for all their efforts in giving stimulating, thought-provoking and timely verbal accounts of recent work and in providing excellent and carefully-prepared written accounts. All the participants will want to join us in thanking the Institute's Director, Sir Michael Atiyah, and then Deputy Director, Professor Peter Goddard, for the facilities and hospitality provided to us by the Isaac Newton Institute and, through them, all the staff of the Institute for their unfailingly cheerful and willing help in the face of the many demands made on them connected with the Workshop.

Finally, and most importantly, we wish to record our gratitude to the Wellcome Trust for the financial support that they provided for this Workshop. This help was invaluable in enabling us to contribute towards travelling and subsistence expenses, thereby allowing as wide as possible a participation in the meeting.

Valerie Isham and Graham Medley

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