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THE ROYAL SOCIETY

Preface

Epidemiology is a very interdisciplinary subject, which uses concepts and techniques from a wide diversity of scientific and medical fields. The diversity includes, for example, statistics, mathematics, molecular biology, immunology, ecology, demography and clinical medicine. Much of the methodology of epidemiological study has a firm statistical template, largely due to its evolution in the study of non-infectious disease problems. Infectious diseases present special problems for epidemiologists, due to the very dynamic relationship of the interaction of the pathogen population with the individual patient and with the community or population of patients. Inside the host, the interaction is complex due to the evolving contest between pathogen population growth and the various humoral and cellular arms of the immune system. Within populations it is the subtleties of the transmission process, and its relationship with the densities of infectious, susceptible and immune hosts, that often creates complex temporal changes in the incidence of infection and disease.

Over the past two decades, research on the epidemiology of infectious disease agents has broadened to encompass new techniques and fresh concepts. Of particular importance has been the introduction of molecular methods in epidemiological study, which has provided many exciting opportunities for the study of pathogen evolution within human communities. Our understanding of various groups of viruses, bacteria and protozoa, is changing due to the growing volume of molecular epidemiological studies that chart phylogenetic relationships and genetic diversity. For example, genetic exchange between individual organisms in pathogen populations seems to be much more common than once thought. This has important implications in a variety of areas, including the evolution of resistance to chemotherapeutic agents. The measurement of genetic diversity within pathogen populations often reveals strain structure, which can be of great significance to both transmission and pathogenesis. The generation of antigenic diversity via mutation or recombination enables pathogens to persist in host populations that have a high degree of herd immunity to the ancestors of the new variants. Understanding the pattern of this diversity, and the forces that shape its evolution, is of obvious importance to the development of vaccines for the important antigenically diverse pathogens such as HIV-1, the malarial parasites and the pneumococcal bacteria.

Other emerging fields of great importance include linkage studies of genetic diversity in human populations, and infection plus associated disease. Increasingly, population genetic research is revealing that small deletions or substitutions in specific genes can have a marked impact on host susceptibility to infection plus the likelihood of subsequent disease. The most striking example of the significance of such research has been in the study of the pathogenesis of HIV-1. Common allelic variants in the human CCR5 and CCR2 chemokine receptor genes are associated with slower progression to AIDS after infection. The opportunities for a greatly enhanced understanding of the prevailing patterns of infection and disease in defined communities will expand rapidly as the number of whole genome sequences of both pathogens and hosts increases over the coming decade.

Statistics has long been an integral part of epidemiological study. The role of mathematical methods in the description and analysis of infection and disease processes, however, has been slower to gain wide acceptance in the biological and medical literatures. Encouragingly, in recent years progress has been made in promoting a more analytical approach to dissecting observed epidemiological patterns along methodological lines widely used in physics and engineering. Simple mathematical models and associated analyses have been very successful in capturing key patterns in diverse problems in infection and immunity. These include long-term oscillations in the incidences of certain viral and bacterial infections, the rapid decay in HIV-1 viral loads following anti-retroviral therapy, and the association between infection and disease for infections with long incubation periods such as the transmissible spongiform encephalopathies (TSEs) induced by abnormal prion aetiological agents.

Statistical methods will of course continue to play a vital role in epidemiological study, particularly in the conventional fields of clinical trial design, survival analysis, meta-analysis and the study of associations. They will also be vital in developing areas such as risk analysis, and the use of patient databases as indicators of both public health and intervention success or failure.

Scientific advances present an ever-increasing range of options for the treatment of the major causes of morbidity and mortality. The spiralling costs of meeting the growing public expectations, triggered in part by these advances, are increasingly encouraging a culture in which cost-effectiveness of treatment is under critical scrutiny. This is equally true in the commercially managed health-care systems in the United States as it is in the United Kingdom's government-funded National Health Service. Current approaches to the cost–benefit analysis of infectious disease prevention and treatment are rather crude and typically

underestimate benefits. The approaches adopted for chronic non-infectious disease problems are not appropriate for infections where the benefit includes both direct and indirect components. Vaccination is a good example. Those vaccinated obviously gain a direct benefit. Concomitantly, by accepting immunization, they also create an indirect benefit by reducing the number or density of people who can transmit the infection to those still susceptible in the community. This important area of health economics will undoubtedly benefit from advances in the epidemiological study of the transmission dynamics of infectious diseases, since the latter provide a quantitative template with which to estimate the indirect benefit.

These various strands in recent research on the epidemiology of infectious diseases are captured in the series of papers published in this special volume of series B of the *Philosophical Transactions of the Royal Society of London*. They show clearly how a diversity of new scientific approaches is being bought to bear on a wide range of epidemiological problems in infection and immunity. These approaches are greatly improving our understanding both of observed pattern and of how best to intervene to control infection and associated disease.

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