The epidemiology of influenza and its control

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Abstract

In this chapter we highlight how recent advances in influenza epidemiology can inform existing strategies for disease control. As a field, influenza epidemiology has benefited greatly from analysis of large data sets regarding hospitalization, mortality, and outpatient visits. These data have allowed comparison of the impact of influenza in various climates and the evaluation of the direct and indirect benefits of vaccination, the latter through the vaccination of “transmitter populations” such as school children, to achieve herd immunity. Moreover, the resolution of influenza epidemiology has undergone a leap to the molecular level due to the integration of new antigenic and viral genomic data with classical epidemiological indicators. Finally, the new data have led to an infusion of quantitative studies from the fields of evolutionary and molecular biology, population genetics and mathematics.

The progress can be seen in many forms. The emerging field of molecular influenza epidemiology is providing deeper insight into global patterns of viral emergence, the important role of reassortment in generating genetic novelty, and global diffusion of virus variants – including the mysterious but crucial role of the Tropics, especially Southeast Asia, as a source of new variants. Deeper stratification of contemporary and historic epidemiological data is providing a more detailed picture of the effect of age and other host characteristics on outcomes, as well as better estimates of the transmissibility of pandemic and seasonal influenza viruses. Re-examination of observational studies of vaccine effectiveness in seniors is leading to reconsideration of seasonal and pandemic vaccine priorities, while mathematical modelers have developed tools to explore optimal strategies for mitigating a future pandemic. The field of influenza epidemiology has rapidly progressed in the past decade and become truly multidisciplinary. Progress could be sustained in the next decade by even closer ties with virology, evolutionary biology, immunology, and genetics.

Introduction

Influenza viruses evolve continuously, challenging mammalian and avian hosts with new variants and causing complex epidemic patterns with regard
to age, place and time. Human influenza viruses cause disease through a variety of direct and indirect pathological effects. The direct effects include destruction of infected cells, damage to respiratory epithelium, and immunological responses that cause general malaise and pneumonia. Indirect consequences of infection include secondary bacterial infection pathogens as a result of tissue damage and exacerbation of underlying co-morbid conditions such as cardiovascular disease, renal disease, diabetes or chronic pulmonary disease [1, 2]. Morbidity and mortality associated with influenza is frequently cited as that which falls within broad disease categories, such as pneumonia and influenza (P&I), respiratory illness, or all-cause (AC) mortality. In the latter case, influenza infection is usually not laboratory confirmed but its health impact can be determined through statistical inference, based on seasonal coincidence of virus circulation and disease outcomes [3–5].

Given the difficulty of directly measuring influenza morbidity and mortality, time-series models have been developed to elucidate patterns of disease within various age groups and populations [5–13]. Such models allow for quantification of disease burden by season and severity of circulating strains [9]. Historical archived data have also elucidated the links between influenza transmission across geographic regions and population movements [14], and allowed comparison of the impact and transmissibility of past pandemics and epidemics in multiple countries [15–24]. Similar models applied to prospective syndromic surveillance data have allowed the study of the epidemiological signature of recurring and reemerging strains of influenza on populations [25]. Mathematical modeling and statistical analyses of influenza activity in tropical countries have rekindled interest in the old mystery of the seasonal drivers of influenza, and offered new insights into the circulation patterns of this virus at the global and regional scales [26–28] (Fig. 1).

The field of influenza epidemiology has recently undergone a quantum leap in resolution due to the increased availability of antigenic and viral genomic data and the integration of these data with classical epidemiological indicators [29–33]. The emerging field of molecular influenza epidemiology (also known as “phylodynamics” [29]) has already provided a much clearer picture of the complex dynamics of global influenza virus circulation and reassortment patterns. The growing number of available influenza genome sequences from specimens collected around the world has started to create a more coherent picture of the global epidemiology of influenza, in particular the interplay between virus evolution, population immunity and impact.

Throughout this chapter, our intention is to highlight how influenza epidemiology can help refine existing strategies for influenza control, especially vaccination. We begin by examining the spatial and temporal spread of seasonal influenza, and we discuss how old and new analytical tools are reshaping quantitative thinking in influenza epidemiology and control. We