Community studies of influenza: new knowledge, new questions

From the 1940s to the early 1980s, a series of prospective, community-based studies provided seminal insights into the epidemiology of common respiratory infections. These observational studies consistently showed that influenza is a common cause of respiratory illness in the community, and the findings have been widely used to inform influenza control policies, such as influenza immunisation. In The Lancet Respiratory Medicine, the report of the Flu Watch study by Andrew Hayward and colleagues continues in this productive scientific tradition but brings it up to date through the use of molecular diagnostic techniques.

Hayward and colleagues recruited and prospectively studied five successive cohorts of households across England over six periods of influenza transmission between 2006 and 2011. Participants aged 5 years and older provided paired preseason and postseason blood samples for influenza serology and all participating households were contacted weekly to identify any cases of cough, cold, sore throat, or “flu-like illness”. Any participant reporting such an illness was asked to submit a nasal swab on day 2 of the illness for influenza virus detection by RT-PCR. A particular strength of the Flu Watch study was the analysis of health-care consulting behaviours through linkage with the participant’s primary health-care records. The study was therefore able to estimate the incidence of influenza infection, the proportion of influenza infections that were symptomatic, and the proportion of symptomatic infections that resulted in consultation with a primary-care practitioner.

The findings reaffirm earlier reports that there are high rates of serological evidence of influenza infection without corresponding disease. Hayward and colleagues report that roughly 20% of the community shows serological evidence of influenza infection each season, but that most infections (about 75%) are asymptomatic or at least so mild that they are not identified through weekly active surveillance for respiratory illness. Even among individuals with a respiratory illness and PCR-confirmed influenza infection, classical definitions of influenza-like illness have low sensitivity and only 17% of individuals consult a medical practitioner. This low sensitivity shows that surveillance of medically attended illnesses provides a partial and biased picture, and is vulnerable to changes in consulting, testing, or reporting practices. As such, it is clear that reliable estimates of the infection and clinical attack rates during the early stages of an influenza epidemic requires the collection of standardised data across the whole range of disease severity, from the community, primary care, and secondary care.

In view of the undoubtedly high rates of subclinical influenza infection, an important unanswered question is the extent to which mild and asymptomatic influenza infections contribute to transmission. Case-ascertained household transmission studies have shown substantial heterogeneity in the amount and duration of viral shedding and, if the area under the curve of viral shedding is believed to correlate with transmissibility, suggest that 80% of transmission is attributable to 20% of clinically symptomatic cases. However, these estimates are not adjusted for differing contact patterns of sick and well individuals. What is more, serologically defined infection rates are underestimates, because the widely used four-fold or greater rise in haemagglutination inhibiting (HI) antibody titre between paired serum samples is an overly stringent criterion for defining infection in epidemiological studies and a proportion of infected individuals do not produce an appreciable HI antibody response. A large number of well individuals mixing widely in the community might, even if only mildly infectious, make a substantial contribution to onward transmission. This might have important implications for the effectiveness of case isolation and social distancing measures in reducing overall transmission rates.

In a global context, the Flu Watch findings are a valuable addition to the data accumulating from contemporary longitudinal community-based influenza studies in other countries. Although there is substantial consistency in serologically defined infection rates per season between settings with very different climates and socioeconomic conditions, the headline figures might obscure important heterogeneities in the timing and intensity of transmission that may affect the
feasibility and impact of interventions. For example, in tropical regions the timing of influenza epidemics is less predictable compared with temperate regions, which is problematic for vaccine strain selection and the scheduling of immunisation programmes. In regions where several influenza epidemics can occur in a single year, the annual (rather than seasonal) rate of infection might be higher than in regions that experience only one influenza season per year. This might affect the development and maintenance of immunological protection against clinically apparent disease and the strength of immunological selection pressures acting upon the viruses. A direct comparison of data from different cohorts would be an invaluable next step towards a comprehensive understanding of the global epidemiology of influenza.

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Statins for non-cystic fibrosis bronchiectasis

Non-cystic fibrosis bronchiectasis is a disorder associated with permanent dilatation of proximal cartilage-containing bronchi; the prevalence of this disorder is increasing worldwide. The pathogenesis of bronchiectasis has been described as a vicious circle of events with three main components: airway damage, infection, and ongoing inflammation. The airway inflammatory response is associated with accumulation of various cells (e.g., neutrophils, lymphocytes, and macrophages) and proinflammatory mediators. Neutrophilic inflammation can be present even without overt infection, suggesting some dysregulation of the innate immune response. Treatment of bronchiectasis is directed at addressing the three components of the disease process, and recent research has focused on the potential benefit of various anti-inflammatory therapeutic approaches.

Long-term, low-dose macrolide treatment has been the most promising anti-inflammatory strategy, and use of these agents in selected patients with bronchiectasis is recommended. Alternative anti-inflammatory treatments include oral and inhaled corticosteroids, oral and inhaled non-steroidal anti-inflammatory drugs, agents targeting specific mediators (such as the interleukins), and various other novel compounds, but with scant evidence of efficacy and a paucity of data. Recent findings suggest that statins could be useful in patients with bronchiectasis because of their noted anti-inflammatory and immunomodulatory effects, and at least two clinical studies of atorvastatin are ongoing. Statins have several modulatory effects on neutrophils, including decreasing production of reactive oxygen species and reduction of neutrophil migration. Furthermore, in people with bronchiectasis, clearance of apoptotic cells in the airway is defective, which contributes to ongoing airway inflammation. Statins augment the clearance of apoptotic cells (efferocytosis) both in vivo and in vitro.

In The Lancet Respiratory Medicine, Pallavi Mandal and colleagues present the results of a randomised controlled trial of atorvastatin in patients with stable bronchiectasis. Patients had clinically significant bronchiectasis, confirmed on chest CT, with cough and sputum production in the stable state and two or more chest infections in the preceding year. Adults (aged 18–79 years) received either atorvastatin 80 mg daily (n=30) or placebo (n=30) over a 6-month period. The primary outcome...