Emerging Respiratory Infections: Influenza, MERS-CoV and extensively drug-resistant Tuberculosis

Concerns over avian influenza viruses have heightened as the number of human H7N9 cases continues to rise and new subtypes such as H10N8 are found to infect and cause severe disease in humans. In the New England Journal of Medicine, Li and colleagues describe the results of field investigations from the first 139 confirmed H7N9 cases, reporting that most cases had recent exposure to poultry and were epidemiologically unrelated although limited human-to-human transmission could not be ruled out in four families.[1] In the Lancet, Yu et al report that closure of live poultry markets (LPM) in the spring of 2013 reduced the mean daily number of infections by an estimated 97% to 99% and recommend that LPM closures should be immediately implemented in affected areas in future outbreaks to minimise the risk of human infection.[2] However in a related comment piece, Fournie and Pfeiffer remind us that the apparent effect of LPM closures on incidence may have been driven by strong consumer reactions to the threat of infection irrespective of LPM closures and argue that closures alone could potentially promote informal marketing of poultry which may enable spread of the virus and make targeted surveillance and risk management more difficult.[3]

The importance of the animal/human interface has also been illustrated through the emergence of Middle East respiratory syndrome coronavirus (MERS-CoV). Reporting in Emerging Infection Diseases, Meyer and colleagues found antibodies against MERS-CoV were common in samples taken from dromedary camels in 2003, well before the first human cases were identified.[4] In the New England Journal of Medicine, Azhar et al report identical full genome sequences from MERS-CoV isolates taken from a patient who died of MERS-CoV and his symptomatically infected dromedary camel.[5] This provided strong evidence that MERS-CoV could be transmitted from camels to humans and establishes camels as a potentially important source of infection although other species such as bats may also be involved.

Fortunately, unlike the 2009 influenza pandemic strain (H1N1pdm09), neither MERS-CoV nor influenza A H7N9 (or any other influenza subtypes recently found to infect humans) have evolved the ability to spread efficiently between humans. National influenza pandemic preparedness plans involved widespread stockpiling of antivirals and the 2009 pandemic provided an opportunity to study their effectiveness. New research on the effectiveness of neuraminidase inhibitors in reducing mortality among hospitalized A(H1N1)pmd09 patients has been encouraging.[6] Whilst the effectiveness of antivirals on reducing mortality would ideally be derived from randomised controlled trials, a recent meta-analysis of trial data was only able to collect data on 5 reported deaths, only one of which was from a respiratory cause.[7] The comparative rarity of such events underscores the need for high quality observational research to inform policy and practice. Muthuri, Venkatsan and colleagues collected individual-level data from around the world on patients hospitalized with influenza A H1N1pdm09.[6] After adjusting for treatment propensity and potential confounders the results of their meta-analysis indicate that compared to no treatment, neuraminidase inhibitor treatment at any time during illness was associated with a reduction in mortality risk (adjusted odds ratio [OR] 0.81). This association was strongest in adults (OR 0.75) but weaker and not significant in children. The timing of treatment was also

important as early treatment (within 2 days of illness onset) was associated with a reduction in mortality (OR 0.48) compared to later treatment. Questions remain about the most effective and cost effective means of ensuring those most likely to benefit are treated early.

In contrast to acute respiratory infections which have the potential to emerge and spread rapidly, the inexorable emergence of drug resistant, multi-drug resistant (MDR) and now extensively drug-resistant (XDR) tuberculosis has played out over decades. In Nature Genetics, using whole genome sequencing of 1,000 prospectively collected TB isolates from patients in Russia, Casali and colleagues provide evidence against the theory that acquiring drug resistance typically comes with a fitness cost and reduced transmissibility.[8] Their findings illustrate the critical need to strengthen tuberculosis control to prevent the emergence and spread of MDR and XDR tuberculosis. Further evidence from South Africa shows the long infectious periods and alarmingly high levels of mortality among XDR patients: at 60 months of follow-up 73% of XDR patients had died and a further 10% had failed treatment.[9] There has been a long-standing need to develop new drugs and treatment regimens for tuberculosis and this research underscores this urgent need.

Emerging respiratory infections highlight the complex interplay between: the organisms; the environment; animal and human host biology; behavior and challenges in clinical management. Interdisciplinary approaches are needed to address these multi-faceted issues and to ensure that research findings help inform prevention, management and control strategies.

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