



Current trends and newer concepts on diagnosis, management and prevention of respiratory tract infections

Alimuddin Zumla

Respiratory tract infections cause millions of deaths each year worldwide. They are among the top six causes of death in low-income, middle-income and high-income countries [1–3] and impose a huge economic burden on the health services of all countries. Respiratory tract infections can present in adults and children in a variety of community based and hospital settings and display a contextual variety of clinical presentations from the minimally symptomatic to the rapidly fulminant. This volume of current opinions written by global experts consists of 16 comprehensive articles, which review the current literature and provide up to date information on the epidemiology, diagnosis, management and prevention of a range of pulmonary infectious diseases. Advances in technology and newer concepts for development of rapid diagnostic tests and biomarkers for respiratory tract infections are also reviewed.

Mass gatherings are events such as religious festivals, music concerts, or sports events that attract large numbers of people that far exceed the capacity of routine health and public safety measures. Managing such events requires providing for all eventualities from infectious disease outbreaks to security against bioterror attacks. The scale and increasing frequency of these large international events pose substantial risks to the spread of infectious diseases, particularly the potential for rapid transmission of bacterial and viral respiratory infections amidst substantial crowding and population density. Three major mass gatherings events that took place in 2012, the UEFA European Football Championship known as ‘Euro 2012’ (8 June to 1 July 2012), The London Olympics (27 July to 12 August 2012), and the annual 2012 Hajj pilgrimage (24–29 October 2012), each attracted several million people from all over the globe. These events focused attention of the UK Health Protection Agency, Ministry of Health of the Kingdom of Saudi Arabia and the WHO, who together with interested academics formally established the specialty of mass-gatherings medicine [4]. Memish and co-workers

(pp. 192–197) review the literature on respiratory tract infections at the Hajj where an estimated 4 million pilgrims visit Mecca and Madinah for at least 2 weeks, living in close proximity to each other. A large majority of them develop a range of upper and lower bacterial and viral respiratory tract infections. Pneumonia is a major cause of critical illness during Hajj and pilgrims require hospitalization with high associated mortality [5]. The authors emphasize the basic practice of hand hygiene, face masks, and contact avoidance, together with pretravel vaccination to decrease the risk of acquiring respiratory tract pathogens.

Recent advances are aimed at improving outcomes and reducing the burden of diseases due to community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), and ventilator-associated pneumonia (VAP). The review on CAP by Muhammad Irfan *et al.* (pp. 198–208) reminds us of the increasing recognition of the role of coinfections in CAP and strategies that include approval of pneumococcal conjugate vaccines for at risk adults will also be relevant to those attending mass gatherings. The increasing global life expectancy is likely to increase the elderly population, therefore further research directed at CAP prevention in this vulnerable population group in view of changing demography and increased attendance at mass gatherings is becoming important. Diego Viasus

Division of Infection and Immunity, Center for Clinical Microbiology, Royal Free Hospital, University College London, London, UK

Correspondence to Alimuddin Zumla, GCDS, FRCP (Lond), FRCP (Edin), FRCPath(UK), PhD(Lond), FSB, MFMLM, Professor of Infectious Diseases and International Health, Division of Infection and Immunity, Center for Clinical Microbiology, Royal Free Hospital, University College London, 2nd Floor, Rowland Hill Street, London NW3 2PF, UK. Tel: +44 07901 638375; e-mail: a.zumla@ucl.ac.uk

Curr Opin Pulm Med 2013, 19:189–191

DOI:10.1097/MCP.0b013e32835f8265

This is an open access article distributed under the Creative Commons Attribution License 4.0, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

et al. (pp. 209–215) review recent literature on antibiotic resistance of respiratory pathogens, and the advances in antibiotic therapy for CAP. Resistance to the antibiotics commonly used in CAP is frequently being documented over the years. Several new antibiotics have been developed for treating mild to moderate CAP, with promising results. However, data regarding their efficacy and safety in patients with severe CAP are lacking. Antione Andreumont *et al.* (pp. 216–228) highlight the recent evidence on clinical epidemiology, trends in bacterial resistances, diagnostic tools, and therapeutic options in HAP, with a special focus on VAP.

Matthew Bates *et al.* (pp. 229–237) review the literature on autopsy studies from Africa and show that lower respiratory tract infections are often the most prevalent infectious disease causes of death in Africa and are often associated with HIV coinfection. Pulmonary infections are particularly common in the immunosuppressed host. Santino Capocci and Marc Lipman (pp. 238–243) review the literature on the epidemiology, diagnosis, treatment and prevention of HIV-related pulmonary infections other than mycobacterial disease. They illustrate that with widespread antiretroviral medication usage, the pattern of HIV-associated pulmonary disease is changing. Although opportunistic infections such as *Pneumocystis jirovecii* pneumonia still occur in people not receiving antiretroviral therapy, HIV-related infections are similar to those present in the general population. Gauri Godbole and Vanya Gant (pp. 244–250) review emerging threats, newer modalities of diagnostic tests, and emerging treatment options in patients with HAP. They inform us that pulmonary infection remains the most frequent infectious complication in the immunocompromised host and these complex infections are often mixed, have atypical presentations and can be due to multidrug resistant organisms.

Oana Ciofu *et al.* (pp. 251–258) discuss respiratory bacterial infections in cystic fibrosis patients in whom chronic upper and lower respiratory tract infections remain the single most prominent cause of the increased morbidity and mortality. Continuous microbiological surveillance is very important in keeping the patients stable. The field of fungal respiratory tract infections continues to evolve and develop with many recent key advances. Gemma Hayes and David Denning (pp. 259–265) highlight key recent advances in fungal respiratory infections, encompassing developments in epidemiology, diagnostics, and management; focusing on *Aspergillus* spp., *Pneumocystis jirovecii*, and *Cryptococcus* spp. as key pathogens. Their review reminds us that challenges remain in almost all areas, with further work

needed to identify the true burden of *Aspergillus* spp. disease and address the increasing problem of azole resistance.

Tuberculosis (TB) remains a major global public health problem and although the global incidence rate has slowly declined to an estimated 1.4 million cases in 2011 [6], an alarming 630 000 of multidrug-resistant TB (MDR-TB) cases exist globally. The highest risk of MDR-TB among TB patients is in countries of Eastern Europe, India, and South Africa. Alarmingly, extensively drug-resistant TB has now been reported from 84 countries, and the rising tide of drug-resistant TB now poses major challenges for global TB control. Four articles cover TB in this journal. Emanuele Pontali *et al.* (pp. 266–272) discuss recent evidence on epidemiology, diagnosis, and treatment of MDR-TB that has peaked in eastern European countries such as Belarus, where a record 35.5% MDR-TB among new cases have been reported from Minsk. Andrew Nunn *et al.* (pp. 273–279) inform us in their review that there is an urgent need to develop better regimens, to shorten treatment and to effectively manage both drug-sensitive and drug-resistant disease. They describe the promising new TB drug development portfolio and encouraging data on a number of TB drugs that are about to enter phase II or phase III trials. Steve Lawn (pp. 280–288) reviews a growing body of literature regarding the use of the Xpert MTB/RIF assay for diagnosis of pulmonary TB in a range of clinical settings, including among inpatients, those with HIV coinfection and in children with culture-positive disease, illustrating that there is continued momentum regarding developments in new TB diagnostics. Next generation fully automated molecular assays that use isothermal amplification may in the future be more readily implemented at the point of care. Despite advances in TB diagnostics no new TB biomarker has yet been identified [7]. Tapan Mukerjee *et al.* (pp. 289–297) review advances in nanotechnology for diagnosis and treatment of TB. They cover the prospect of using nanotechnology for the detection of mycobacterial strains and nanotechnology-based drug delivery system for effective eradication of mycobacterial infections.

Current standard diagnostic tests for acute and chronic bacterial and viral infections are laborious and time consuming. Currently, all ill patients presenting with any form of respiratory tract infections (CAP, HAP, VAP, or respiratory tract infections in the immunosuppressed) are treated empirically without an accurate diagnosis of the causative microorganism and their antibiotic sensitivity patterns. Correctly identifying the exact microorganism causing respiratory tract infections and treating with appropriate antibiotics they are susceptible to is essential, as morbidity and mortality rates are

high. Respiratory tract infections remain difficult to diagnose accurately as a broad range of pathogens and opportunistic microorganism are involved in their cause. Kate Reddington *et al.* (pp. 298–304) review literature on recently available commercial multiparametric molecular diagnostics tests for the detection of respiratory tract infections. They emphasize that reliability of the molecular drug resistance markers chosen, the need for the quantitative detection of some organisms, and throughput are also important considerations for new technology developers. As point of care diagnostic tools become available so will an array of biomarkers of disease activity, monitoring treatment efficacy and cure. Mervyn Singer (pp. 305–309) reviews the growing literature on biomarkers of sepsis and suggests that new biomarkers will facilitate early and accurate diagnosis, faster recognition of impending organ dysfunction, optimal selection, and titration of appropriate therapies, and more reliable prognostication of risk and outcome. Travis Henry and Kristopher Cummings (pp. 310–317) summarize imaging findings of common parasitic infections of the lung in the context of the life cycle and pathophysiology of each parasite.

With recent exciting advances in technology, the future promises a wide array of rapid point-of-care diagnostics and biomarker tools on the horizon that may become available within the next decade and could revolutionize the management of respiratory tract infections, reducing mortality and morbidity worldwide.

Acknowledgements

Professor Zumla acknowledges support from European Union FW7; the European and Developing Countries Clinical Trials Partnership (EDCTP grants REMOX, PANACEA and TB-NEAT); the UK Medical Research Council (MRC); UBS Optimus Foundation, Switzerland; University College London Hospitals Comprehensive Biomedical Research Centre (UCLH-CBRC); and the UCLH National Health Service (NHS) Foundation Trust.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Lozano R, Naghavi M, Foreman K, *et al.* Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2013; 380:2095–2128.
2. Lim SS, Vos T, Flaxman AD, *et al.* A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2013; 380:2224–2260.
3. Murray CJ, Vos T, Lozano R, *et al.* Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2013; 380:2197–2223.
4. Al Rabeeah A, Memish ZA, Zumla A, *et al.* Mass gatherings medicine and global health security. *Lancet* 2012; 380:3–4.
5. Mandourah Y, Al-Radi A, Ocheltree AH, *et al.* Clinical and temporal patterns of severe pneumonia causing critical illness during Hajj. *BMC Infect Dis* 2012; 12:117.
6. WHO. Global tuberculosis report 2012 [Internet]. Geneva: World Health Organization; 2012. Available from: http://www.who.int/tb/publications/global_report/en/index.html. [Accessed 16 January 2013]
7. McNerney R, Maeurer M, Abubakar I, *et al.* Tuberculosis diagnostics and biomarkers: needs, challenges, recent advances, and opportunities. *J Infect Dis* 2012; 205 (Suppl 2):S147–S158.