Journal of Infection (2015) xx, 1–10

ELSEVIER

BIA British Infection Association

www.elsevierhealth.com/journals/jinf

REVIEW

Point-of-care testing for respiratory viruses in adults: The current landscape and future potential

Nathan J. Brendish [a], Hannah F. Schiff [b], Tristan W. Clark [c,*]

[a] *NIHR Wellcome Trust Clinical Research Facility, University Hospital Southampton NHS Foundation Trust, Southampton, UK*
[b] *Department of Respiratory Medicine, Hampshire Hospitals NHS Foundation Trust, Basingstoke, UK*
[c] *Department of Clinical and Experimental Sciences and Respiratory Biomedical Research Unit, University of Southampton, UK*

Accepted 17 July 2015
Available online ■ ■ ■

KEYWORDS
Point-of-care testing;
Respiratory viruses;
Influenza;
Adults;
Acute respiratory illness;
Antimicrobial resistance

Summary Respiratory viruses are responsible for a large proportion of acute respiratory illness in adults as well as children, and are associated with a huge socio-economic burden worldwide. Development of accurate point-of-care tests (POCT) for respiratory viruses has been listed as a priority by the World Health Organisation and replacing the current paradigm of empirical antimicrobial use with directed use is a listed goal of the movement for reduction in antimicrobial resistance. POCTs for respiratory viruses have previously been limited by the poor sensitivity of antigen detection based tests and by a limited range of detectable viruses. Highly accurate molecular platforms are now able to test for a comprehensive range of viruses, can be operated by non-laboratory staff and can generate a result in approximately 1 h, making them potentially deployable as POCTs. The potential clinical benefits of POC testing for respiratory viruses in adults include a reduction in unnecessary antibiotic use, improved antiviral prescribing for influenza and rationalisation of isolation facilities. We review here the burden of disease, the currently available molecular platforms with potential for POCT use and the existing evidence for clinical and economic benefits of testing for respiratory viruses in adults.

* Corresponding author. LF101, Faculty of Medicine, University of Southampton, Southampton General Hospital, Mailpoint 801, South Academic Unit, Tremona Road, Southampton, SO16 6YD, UK. Tel.: +44 (0) 2381208209; fax: +44 (0) 2381205023.
E-mail address: t.w.clark@soton.ac.uk (T.W. Clark).

http://dx.doi.org/10.1016/j.jinf.2015.07.008

Please cite this article in press as: Brendish NJ, et al., Point-of-care testing for respiratory viruses in adults: The current landscape and future potential, J Infect (2015), http://dx.doi.org/10.1016/j.jinf.2015.07.008

Introduction

Acute respiratory tract infections are responsible for an estimated 4.25 million deaths each year and are the third most common cause of death worldwide.[1] Although bacteria have previously been considered to be the principal aetiological agents of severe respiratory infection, the global importance of respiratory viruses in all age groups has been increasingly recognised in recent years.[2–4] Diagnostic technology for respiratory virus detection has evolved rapidly over the last two decades from viral culture and immunofluorescence to the current standard of molecular detection by polymerase chain reaction (PCR). This review focuses on the currently available molecular diagnostic platforms for respiratory virus detection with potential for use as point-of-care tests (POCT) and explores the current landscape for POCT in adults.

Respiratory viruses: clinical and economic burden of disease

Improvements in the sensitivity of diagnostic testing for respiratory viruses with the widespread use of nucleic amplification techniques such as PCR have helped to accurately define the burden of viral disease over the past two decades. In children respiratory viruses have been detected by molecular diagnostic techniques in 43–67% of cases of community acquired pneumonia (CAP),[5] over 90% of infants with bronchiolitis,[6] and approximately 85% of asthma exacerbations.[7] In adults approximately 20–40% of CAP cases,[8–12] 50–70% of asthma exacerbations[13] and 30–50% of chronic obstructive pulmonary disease exacerbations[14] are associated with respiratory virus detection. In hospitalised adults with acute respiratory illness, viruses are the most commonly detectable pathogen (being detected in around 50%) with bacterial detection being much less frequent, although antibiotic use is almost universal.[4] Furthermore, preceding viral infection is thought to be a key predisposing event to secondary bacterial infections in the lung and other sites in the respiratory tract.[15–17] Respiratory viruses including influenza have also been implicated in precipitating non-respiratory illnesses such as myocardial infarction, venous thromboembolism, stroke and loss of diabetic control.[18–22]

Infections with respiratory viruses are frequent events in all age groups and result in an enormous burden on health systems as well as the economic costs in direct medical expenses and indirect productivity losses. Direct medical expenses include outpatient clinic visits, emergency department visits, hospitalisations and treatment costs, including over-the-counter medication and drug prescriptions. Indirect productivity losses include missed workdays for adult patients and caregivers. In Europe direct costs attributed to pneumonia are estimated at approximately €10.1 billion annually and indirect costs of lost work days at €3.6 billion.[23]

Based on the 2003 population size, seasonal influenza epidemics resulted in an average of 610,660 life-years lost, 3.1 million hospital days and 31.4 million outpatient visits in the USA.[24] Direct medical costs averaged US$10.4 billion annually, and projected lost earnings due to illness and loss of life amounted to US$16.3 billion annually. The total economic burden of annual influenza epidemics using projected statistical life values amounted to US$87.1 billion.[25] The common cold also causes a significant economic burden with a US-based study estimating that non-influenza, viral respiratory tract illnesses (mostly common colds) cost around US$40 billion in 2001.[26]

Influenza

The influenza virus causes seasonal epidemics leading to excess hospitalisations and death mainly in the elderly and in patients with co-morbidity.[27,28] It causes severe illness in up to 5 million people and around half a million deaths per year worldwide.[29] Annual seasonal influenza vaccine is recommended in at risk groups[30] however vaccine uptake is sub-optimal[31,32] and high quality evidence for significant protection in the elderly is lacking.[33,34] The rate of hospitalisation in adults with influenza has been estimated at 5 to 20 per 100,000 overall[35,36] and may be as high as 1200 per 100,000 in those over 85 years old.[37] In adults hospitalised with laboratory confirmed influenza, 10–30% are admitted to critical care units and 3–15% die in hospital,[38,39] with outcomes being predicted by co-morbidity.[40] As noted above, in addition to acute respiratory presentations, influenza may precipitate decompensated cardiovascular disease, myocardial infarction, collapse or diabetic emergencies[20–22,41] and so many hospitalised cases of influenza are likely to remain undiagnosed. A recent Canadian study estimated that only around 1 in 14 emergency department visits due to influenza virus infection were correctly attributed to influenza.[42] It is likely, therefore, that the burden of influenza and its economic impact have been under-estimated.

Respiratory syncytial virus

RSV is the principle cause of bronchiolitis in infants but is now increasingly recognised as a major cause of severe respiratory illness in adults, with some studies suggesting a disease burden similar to that of influenza.[43,44] RSV affects all age groups and a study of hospitalised children and adults that calculated disability adjusted life years (DALYs) concluded that influenza and RSV were consistently the greatest causes of disease across all age groups.[45] Adults at high risk of severe RSV disease include the frail elderly, those with chronic cardio-respiratory disease and the immunocompromised. The mortality rate of RSV infection in adults and the elderly is similar to that of influenza (7–8%) but may reach 30–70% in the heavily immunocompromised[46] contrasting with the negligible RSV-related mortality in infected children.

Rhinovirus

Picornaviruses are responsible for the majority of common colds and adults typically suffer two to four symptomatic episodes per year.[47] They are also responsible for the majority of exacerbations of asthma in adults and a significant proportion of exacerbations of COPD.[13,14,48] Common colds cause an estimated 20 million lost workdays per year in the

Please cite this article in press as: Brendish NJ, et al., Point-of-care testing for respiratory viruses in adults: The current landscape and future potential, J Infect (2015), http://dx.doi.org/10.1016/j.jinf.2015.07.008