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Diagnosis of respiratory viral infections in cystic fibrosis by PCR using sputum samples

To the Editors:

Recent epidemics of virulent respiratory viruses, such as H1N1 influenza and severe acute respiratory syndrome coronavirus (SARS-CoV), have highlighted the clinical importance of methods for the rapid and accurate detection of respiratory virus infection [1, 2]. A diagnosis of a respiratory viral infection may have implications for infection control measures and treatment of patients [3]. Molecular-based techniques offer a more rapid and sensitive method for diagnosis of respiratory viral infection than viral culture or serology [4]. PCR-based methods can be applied to nasal and/or throat swab samples for the rapid detection of common respiratory viruses [5]. As the majority of adults with cystic fibrosis (CF) produce sputum during infective exacerbations, we investigated whether sputum is a suitable medium for the diagnosis of respiratory viral infections in patients with CF using a PCR method, by comparing results of PCR tests from paired sputum and nasal swab samples collected from patients with symptoms of a viral respiratory illness.

We prospectively collected paired nasal swab and sputum samples from adult patients with CF who presented with symptoms of a respiratory viral illness during the period December 2008 to June 2009. Flocked nasal swab samples were transported to the laboratory in viral transport medium (Microtest™ M4RT®; Remel, Lenexa, KS, USA).

The samples were investigated using an in-house PCR method to detect common respiratory viruses (rhinovirus, influenza A, influenza B, parainfluenza types 1–3, adenovirus, respiratory syncytial virus (RSV) and metapneumovirus).

Permission for the study was granted by the local medical ethics committee. All patients gave verbal informed consent for participation in the study.

Group results were compared by a McNemar test using the SPSS statistical package, version 15 (SPSS Inc., Chicago, IL, USA).

Paired samples were analysed from 53 patients. 25 (47.2%) patients had positive results with 26 viruses detected: 13 rhinovirus, three influenza A, three influenza B, three parainfluenza type 3, two adenovirus, one RSV and one metapneumovirus. Of the 25 positive results, all (100%) sputum samples were positive, whilst 17 (68%) nasal swab samples were positive ($p=0.008$). One patient had both positive nasal and sputum samples for rhinovirus, but the sputum sample was also positive for adenovirus.

The importance of rapid, specific and sensitive tests for respiratory viral infections has been highlighted by recent epidemics of virulent respiratory viruses, such as H1N1 pandemic influenza [1] and SARS-CoV [2]. This study has shown that sputum, which is a readily available sample, is a suitable specimen for analysis by PCR for the rapid diagnosis of common respiratory viral infections. A previous study also reported success in detection of virus infection using a PCR technique with sputum samples for patients with CF, but did not compare yield with traditional nasal samples [6]. In our clinical practice, the sensitivity of PCR is greater using sputum than nasal swab samples.

Tissue culture and serology were previously used as the standard tools for screening for viral infections, but have

disadvantages compared with modern molecular methods, including a lower sensitivity and greater delay before the result is available [7, 8]. The prompt and accurate detection of a respiratory virus infection in patients with underlying lung disease is important for a number of reasons. Anti-viral medications are sometimes indicated for patients with a suspected or confirmed respiratory viral infection, particularly RSV or influenza [9]. Some respiratory viral infections are associated with increased morbidity and mortality in patients with chronic lung disease [10]. Confirmation of a respiratory viral infection may therefore prompt early institution of close monitoring and supportive measures, or commencement of pre-emptive antibiotic therapy to prevent clinical deterioration from an accompanying bacterial exacerbation, particularly for those patients with known chronic bacterial infection. In addition, infection control measures may require prompt diagnosis of a respiratory viral infection [3]. For example, since this study ended, a case of pandemic H1N1 influenza was positive by sputum PCR but negative by nasal swab PCR. In some cases, the identification of a respiratory virus by PCR was not confirmed from a nasal swab specimen but was confirmed from an accompanying sputum sample. As many adults with CF and other chronic lung diseases produce sputum during infective exacerbations, this may be an easily available and acceptable specimen to obtain from patients for screening for viral infection, with greater sensitivity than nasal swab samples.

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Exacerbations of idiopathic pulmonary fibrosis treated with corticosteroids and cyclophosphamide pulses

To the Editors:

Acute exacerbations (AEs) are now recognised as a frequent and severe complication of idiopathic pulmonary fibrosis (IPF). In a large series, 1- and 3-yr incidences were 14.2% and 20.7%, respectively [1]. New diagnostic criteria were published in 2007 [2]. The pathogenesis of these episodes remains unknown, although invasive procedures have been described as possible triggers. Prognosis is poor, with a short-term mortality rate of 45–85%. There is no consensus regarding treatment, as no published study has compared the efficiency of different treatment regimens, and treatment often differs between patients within a given study [1–4]. Since 2005, exacerbations of IPF identified in our referral centre (Centre Hospitalier Régional de Lille, Lille, France) have been treated with pulses of methylprednisolone followed by pulses of cyclophosphamide [5]. The main goal of the present retrospective study was to evaluate the mortality of exacerbations of IPF treated with this regimen.

Following admission for aggravation of dyspnoea, a series of tests were run to determine diagnosis and functional impairment. When an exacerbation of IPF was diagnosed, patients were treated with a methylprednisolone pulse (1,000 mg) at days 1–3