

The impact of detection of respiratory viruses on at-risk patient populations

Alicia Brooke Mitchell

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Respiratory viruses are ubiquitous and are known to cause acute disease in otherwise healthy individuals and may be associated with severe morbidity and mortality in those with underlying chronic diseases. However, respiratory viruses do not always result in disease. The frequency and implications of asymptomatic carriage within at-risk patient populations remain poorly understood.

This thesis explores the development of a novel methodology for detection of respiratory viruses utilising exhaled breath captured in electret filter, using PCR-based detection. Evaluation of this methodology in different clinical cohorts was carried out, specifically exploring rates of asymptomatic detection in patients with bronchiectasis during stable phases and in patients intubated in the ICU, looking within the filter contained in the ventilator circuit. Finally, demonstration of the dynamics of the human respiratory virome in a cohort of patients undergoing lung transplantation, utilising the previously confirmed methodologies, completed this body of work.

The exhaled breath methodology was tested in the two clinical cohorts described above and demonstrated detection of both upper and lower respiratory tract viruses. Results correlated well with traditional

sampling methods. The major finding from these studies was the high rate of detection of respiratory viruses in the absence of symptoms and signs suggestive of acute respiratory infection.

Examination of the prospective lung transplant cohort also confirmed a significant rate of asymptomatic viral carriage and provided new insights into the dynamics of the respiratory virome. This project provides evidence that viruses are transplanted within the donor lung and remain detectable for many months after transplantation. There was no evidence, however, that detection of virus correlated with concurrent acute cellular rejection.

Taken together, these studies have allowed development of a novel clinical viral sampling methodology which may have important clinical and diagnostic ramifications. Ultimately, they have enhanced our understanding of asymptomatic viral infection. As well, the role of community-acquired respiratory viruses as transient members of the human respiratory virome has now been revealed for the first time.

Dr Alicia Mitchell
School of Biomedical Sciences
University of Technology, Sydney
Broadway NSW 2007

