

# Final report for CRC for Asthma 2006

## Heterogeneity in Asthma

### *Background and Summary*

The heterogeneity project conducted by Ms Sue Downie, was supported by funding from the CRC of Asthma and has been a very successful project. The basis of the project is the measurement of heterogeneity (or unevenness) of ventilation in the lungs. This was measured by the multiple breath nitrogen washout test (MBNW) and was set up through collaborations with Dr Sylvia Verbanck of Vrije University in Belgium, who is one of the pioneers of the test. The MBNW is a test of small airway function because the basis of lung ventilation resides predominantly in the small airways in asthma. With this test, Ms Sue Downie conducted a prospective clinical study to examine the significance of this test of small airway function in asthma, in the context of understanding the underlying basis of asthma and in the context of routine management. This study was complex on many fronts; the interaction with 3M who supplied the drugs (QVAR and Respocort), the design of hardware and software by the Biomedical Group, training to conduct the test and perform the complex analyses and conducting a prospective treatment study that required complex tests to be performed regularly over the duration of the 3 month treatment period. Data collection was completed by the end of June 2005 and the data analysis was completed 2 months later.

We found that information derived from the MBNW test is indeed highly significant in asthma. We found that having patchy ventilation across the lungs (ventilation heterogeneity) is strongly predictive of having airway hyperresponsiveness (a fundamental physiologic abnormality in asthma) which changes slowly with treatment. Importantly, the predictive value was independent to and stronger than airway inflammation, also known to predict airway hyperresponsiveness. We found that the improvement in small airway function was similar between the two drugs (QVAR was potentially better on theoretical considerations) and that the improvement was slow and incomplete. We could conclude generally that 1) our results have significantly progressed the understanding of the underlying basis of asthmatic airway function, 2) that small airway function is important in asthma since it reflects the severity of one of the most important abnormalities of asthmatic airways, 3) the abnormality detected by this test is slow to improve and remains normal in the majority of patients, hence reinforcing the need for long-term treatment and 4) this test is potentially very useful for monitoring treatment responses, both to existing drugs and to novel treatments, especially since it is a non-invasive measurement albeit conducted in a lung function laboratory. There are currently 3 manuscripts in either revision or being drafted.

## **Publications**

### **Papers Published**

1. King GG, Salome CM. Multi-modality measurements of small airways disease. *European Respiratory Journal* 2006; 27: 250-2.
2. King GG, Downie SR, Verbanck S, Thorpe CW, Berend N, Salome CM, et al. Effects of Methacholine on Small Airway Function Measured by Forced Oscillation Technique and Multiple Breath Nitrogen Washout in Normal Subjects. *Respiratory Physiology and Neurobiology* 2005; 148: 165-177.

### **Papers submitted**

1. Downie S, Salome C, Verbanck S, Thompson B, Berend N, King G. Ventilation heterogeneity is a major determinant of airway hyper-responsiveness in asthma. *Journal of Allergy and Clinical Immunology* 2006

### **Papers being drafted**

1. Downie S, Salome C, Verbanck S, Thompson B, Berend N, Thorpe, CW, King G. The Relationship Between Ventilation Heterogeneity and Forced Oscillatory Conductance in Asthmatic Adults Before and After Methacholine Challenge.
2. Downie S, Salome C, Verbanck S, Thompson B, Berend N, King G. The effects of treatment with QVAR versus Respicort on small airway function in asthma.