Ventilation Heterogeneity and Airway Closure
- The Physiologic Basis of Airways Disease?

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Asthma is characterised by airway inflammation and structural remodelling of the airways and these pathologies contribute to airways obstruction. Airway hyperresponsiveness (AHR), the ability of airways to narrow too easily and too much in response to provoking stimuli, is part of the definition of asthma and is associated with impaired development of lung function in childhood and severe AHR is a risk factor for severe and life-threatening asthma attacks. Airway inflammation is regarded as the underlying cause of AHR but the mechanisms are unclear, particularly since AHR is associated with both eosinophilic, neutrophilic and pauci-granulocytic asthma and is also seen in COPD. Modelling studies have shown that airway heterogeneity can markedly increase airway resistance. Therefore ventilation heterogeneity, reflecting even small airway to airway variations in airway inflammation or remodelling may be an important physiological determinant of AHR. We have recently shown that ventilation heterogeneity in the conducting airways is a strong determinant of AHR both before and after inhaled corticosteroid treatment suggesting that airway remodelling should be an important therapeutic target for intervention in asthma.

Airway closure, which could be regarded as the end of the spectrum of ventilation heterogeneity, has also been associated with the risk of severe asthma exacerbations and with a requirement for oral corticosteroid treatment. Imaging studies have shown that the number of non-ventilated lung regions correlates with asthma severity as measured by clinical symptoms and spirometry. We have recently conducted studies in asthmatics and non-asthmatics to look at the propensity for airways of a given size to close during induced bronchoconstriction. These studies, using a closing index derived from spirometry and the forced oscillation technique, failed to show a correlation between premature airway closure and AHR. These findings do not rule out that the magnitude or distribution of airway closure may be clinically important in asthma but rather that premature airway closure is not a pathophysiological determinant of AHR.