Stimulated breathing movements in isolated bronchi: the impact on airway narrowing

P.K. McFawn,[1] R.L. Jones,[3] A. Cairncross,[1] H.W. Mitchell,[1] A.L. James[3] and P.B. Noble,[1,2] [1]School of Biomedical, Biomolecular and Chemical Sciences, The University of Western Australia, Crawley, WA 6009, Australia, [2]School of Women's and Infants' Health, The University of Western Australia, Crawley, WA 6009, Australia and [3]Department of Pulmonary Physiology, Sir Charles Gairdner Hospital, Nedlands, WA 6009, Australia.

Background: Deep inspiration (DI) produces a pronounced bronchodilator response in healthy humans but this response is impaired in obstructive lung diseases including both asthma and chronic obstructive pulmonary disease (COPD). How stretch of bronchi causes bronchodilation is still unclear although oscillatory stretch of isolated airway smooth muscle (ASM) reduces force production, suggesting that DI *in vivo* may directly inhibit ASM contraction. Loss of the response in disease could be due to a fundamental change in the ASM or a change in the loads applied to the muscle. For example reduced airway compliance in disease could impair the response to DI by limiting the stretch of smooth muscle, while loss of parenchymal attachments in COPD may prevent the loads from lung inflation being transmitted to the airway.

Aim: Using bronchi from human lung cancer patients measure the effect of DI *in vitro* to determine if the failure of DI to produce bronchodilation is an intrinsic property of diseased bronchi or changes with airway stiffness. Secondly to use isolated animal tissue to show that hyperinflation will impair the DI bronchodilation response.

Methods: Bronchi were obtained following lung resection from cancer patients who had normal spirometry (n=8) or fixed airflow obstruction (n=7, FEV1<80% predicted and FEV1/FVC<0.7). Airway narrowing to acetylcholine was measured under static conditions or during "tidal" oscillations with intermittent "DI", simulated by varying transmural pressure using a motorized syringe pump. Airway narrowing was determined from the % decrease in lumen volume. To investigate the effect of DI amplitude on the bronchodilation response airways were contracted to carbachol (CCh 3×10^{-6}M) during tidal breathing (from 5 to 10cm H_2O *i.e.* Δ5cm H_2O, 0.25Hz) and DI of three different amplitudes (Δ10, 25 or 55cm H_2O) applied following contraction.

Results: Under static conditions maximum airway narrowing was similar in airways from non-obstructive and obstructive subjects and was 30±3% and 42±10% respectively. In tidally oscillated airways narrowing was substantially reduced by DI (P<0.001) to a similar extent in both groups. After DI airway narrowing fell to 13±3% and 18±5% in airways from obstructive and non-obstructive subjects respectively. All DI amplitudes used produced an initial bronchodilation which reconstricted. Increasing the DI transmural pressure caused a greater change in luminal volume during DI and a greater bronchodilation following the DI (P<0.05). Contraction to CCh cause approximately a 20% fall in specific compliance (P<0.05) which was reversed by DI (P<0.05). For each DI amplitude the change in lumen volume during the DI was strongly correlated to the specific compliance of the bronchi before DI (r>0.87,P<0.01).

Conclusions: Isolated human bronchi show a bronchodilation response to DI that is proportional to the expansion of the airway caused by the DI. The amount of stretch produced by a DI depends on airway wall compliance suggesting that increased airway stiffness in disease could suppress the DI response by limiting the stretch of bronchi during lung inflation. In subjects with fixed airflow obstruction, a reduced response to DI may not be universally related to an abnormality of the airway wall.