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Title: Airway wall responses to tidal breathing and deep inspiration

Mr. Thomas K 13453 Ansell anselt01@student.uwa.edu.au [1], Dr. Peter B. 13454 Noble pnoble@meddent.uwa.edu.au [2], Prof. Howard W. 13455 Mitchell mitchell@cyllene.uwa.edu.au [1] and Dr. Peter 15922 McFawn pkm@cyllene.uwa.edu.au [1]. [1] School of Anatomy, Physiology and Human Biology, University of Western Australia, Perth, WA, Australia, 6009 and [2] Centre for Neonatal Research and Education, University of Western Australia, Perth, WA, Australia, 6009 .

Body: Introduction Mechanical stretch attenuates airway smooth muscle (ASM) force production, which may explain the reversal of bronchoconstriction (i.e. bronchodilation) following a deep inspiration (DI) in vivo. We measured the effect of simulated DI on both narrowing and ASM force in isolated bronchi. Methods Bronchial segments were dissected from pig lungs and maintained in organ bath chambers. Airway narrowing (% volume) to acetylcholine (ACh, 10^{-7}M - $3x10^{-3}$M) was measured under static transmural pressure (P_{tm}) conditions and during fixed P_{tm} oscillations simulating tidal breathing ($\Delta 5cmH_2O$) with intermittent DI ($\Delta 25cmH_2O$). In a separate group of experiments, the above protocols were repeated using fixed volume oscillations to simulate tidal and DI breathing whilst measuring the increase in P_{tm} produced by ASM contraction. Under each condition, airway wall stiffness was measured from the change in P_{tm} and volume during tidal oscillations. Results Under static conditions, maximal response to ACh was 92.3±4.3% narrowing (n=6) and 73.5±9.2cmH_2O P_{tm} (n=4). DI to $\Delta 25cmH_2O$ reversed ~60% narrowing at low doses of ACh but had no affect at moderate or high doses, whereas fixed volume DI attenuated ASM force to 12.7±5.6cmH_2O (t-test, $p<0.01$) even at high doses. At maximal contraction to ACh, stiffness increased ~10 fold in both groups of which DI had no affect under fixed P_{tm} conditions but reversed 60.9±4.4% ($p<0.001$) under fixed volume oscillation conditions. Conclusions The mechanical loading conditions present during tidal breathing and DI influence the airway response to mechanical stretch. Inhibition of bronchoconstriction to mechanical stretch is minimal during fixed Ptm oscillations particularly at high levels of ASM activation.