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Title: Small airways function in children with mild asthma and normal FEV_1

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Body: Background Small airways disease is a hallmark in adults with persistent asthma but little is known in children with mild asthma and normal spirometry. Objective To assess ventilation heterogeneity, a marker of small airways function, using an easy single-breath washout (SBW) technique in school-aged children with mild asthma and normal FEV_1 and healthy age-matched controls. Methods Primary outcome was the double-tracer gas phase III slope (S_{DTG}), an index of ventilation heterogeneity in acinar airways derived from the tidal double-tracer gas SBW test. SBW testing is done during normal tidal breathing. Double-tracer gas constitutes 26.3% helium and 5% sulfur hexafluoride. Triplicate SBW and spirometry tests were performed in all children (n = 66) at baseline and after bronchodilation in asthmatic children (n = 31). Results Acinar (S_{DTG}) ventilation heterogeneity was significantly increased in asthma compared to controls. S_{DTG} was abnormal (≤-2 z-scores) in 11/31 asthmatic children, FEF_{25-75} in 3/31 and FEV_1 in 0/31. After bronchodilaton S_{DTG}, FEF_{25-75} and FEV_1 significantly changed: Average (95% CI) change given as percentage from baseline was 36 (15-56)%, 17 (9-25)% and 6 (3-9)%, respectively. Conclusion Abnormal acinar ventilation heterogeneity in one third of children suggests that small airways disease may be present despite rare and mild asthma symptoms and normal spirometry. The easy tidal SBW technique has potential as a clinical and research outcome in children with asthma.