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Title: Nitric oxide biosynthesis by primary ciliary dyskinesia respiratory epithelial cells is similar to non-PCD patients

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Body: Introduction The mechanism for the extremely low levels of nasal nitric oxide (NO) seen in patients with primary ciliary dyskinesia (PCD) has not been elucidated. A hypothesis has been that the respiratory epithelial cells in these patients do not biosynthesise normal levels of NO. NO is rapidly metabolised to nitrite, which is considered to be a surrogate marker of NO. Aims To compare the total nitrite concentrations of differentiated ciliated respiratory epithelial cells from PCD and non-PCD patients at baseline and following stimulation. Methods Airway epithelium from PCD and non-PCD patients was obtained by nasal brushing and cultured at air liquid interface (ALI) until differentiated and ciliated. PBS was incubated for 30 minutes on the apical surface of the ALI cultures and total nitrite detected by kit assay (Enzo Life Sciences). Basolateral incubation with 10 mg/ml IL-1β/IFNγ/TNFα for 18 hours stimulated NO biosynthesis via nitric oxide synthase (NOS) activity. Results Total nitrite concentration in differentiated PCD (n=5) and non-PCD (n=7) cultured epithelium was similar both at baseline, 16.1±1.1 mmol/l and 17.8±3.2 mmol/l respectively (mean±SD, p=0.14) and after stimulation; PCD (n=4) 32.0±12.7 mmol/l and non-PCD (n=4) 33.2±11.0 mmol/l respectively (p=0.46). Conclusion NO biosynthesis in differentiated ciliated airway epithelium from PCD patients is similar to non-PCD patients at baseline and following NOS stimulation. As nasal NO is increasingly used for screening of PCD, further work assessing the upper airway's role in the low levels of nasal NO seen is warranted. Data collection continues.