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Title: Cytokine and chemokine release in response to Pseudomonas aeruginosa (PA), by bronchial epithelium of the native airway and transplanted lung of paediatric cystic fibrosis (CF) lung transplant recipients

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Body: Introduction Infection and inflammation are implicated in the pathophysiology of Bronchiolitis Obliterans Syndrome (BOS), the major cause of mortality following lung transplantation. It is unclear if the cytokine and chemokine release by Cystic Fibrosis (CF) airway epithelium in response to pathogens differs from that of the transplanted lung. Aims We hypothesised that there is no difference in the cytokine and chemokine release in response to Pseudomonas aeruginosa (PA), by the epithelium of the native CF airway and the transplanted lung. Methods 5 children who had lung transplantations for CF (Great Ormond Street Hospital for Children, London, UK), were studied. Bronchoscopic brushings from above and below the airway anastomosis were cultured to differentiated ciliated epithelium in an air-liquid interface (ALI). The epithelium was exposed to late exponential cultures of PA (10^6 CFU per ml). The culture supernatants were harvested at baseline and 5 hours post PA exposure. The cytokines and chemokines in the culture supernatants were measured using a multiplex ELISA based protein array (SECTOR Imager 6000, MSD). Results There were no differences in baseline levels of cytokines and chemokines. 5 hours after exposure to PA, the release of chemokines - CCL2, CCL5, CCL13, CXCL8 and the cytokines - IL1β, IL13 and TNFα, by the native CF epithelium was significantly higher ($p<0.01$) compared to that from the transplanted lung. Conclusion The differential cytokine and chemokine release in response to pathogens may be contributory to the exaggerated inflammatory response of the CF epithelium.