Title: Abnormalities in lung clearance index in CF infants diagnosed by newborn screening

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Body: Newborn screening (NBS) in CF offers the potential to prevent lung damage before the onset of clinical symptoms. The lung clearance index (LCI), measured by multiple breath washout has shown promise as a marker of early lung disease in patients with CF. Therefore we aimed to determine whether LCI could be used to distinguish between subjects with CF and healthy subjects in the first 2 years of life. Healthy infants (3 months – 2 years) completed MBW testing as part of the infant pulmonary function protocol of the Canadian Healthy Infant Longitudinal Development Study (CHILD Study). Infants (3 months – 2 years) with diagnosed CF attending the Respiratory Medicine Clinic at the Hospital for Sick Children were invited to complete MBW testing. MBW was measured 51 healthy infants and 18 infants with CF diagnosed by NBS. Despite NBS, infants born with CF were smaller (Height-for-age z-score (-1.19 (-0.58; -1.81) and lighter (mean difference weight-for-age z-score (-0.40 (-0.98; 0.19) compared with healthy controls. The LCI was on average 0.4 units higher in CF (mean LCI 7.32 (SD 0.91)) compared to healthy controls (6.92 (SD 0.61)). Adjusting for the relationship between LCI and height in the first 2 years of life, LCI was 0.67 (95%CI -1.34; -0.01) z-scores higher in CF compared to healthy infants, although overlap was considerable (Figure). Therefore, despite newborn screening early abnormalities in LCI are present in CF patients LCI underscoring the need for new treatment approaches to address early lung disease. Supported by CIHR and the Lynn and Arnold Irwin Foundation.