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| **Aberrant nasal epithelial responses to *rhinovirus* in paediatric acute wheeze** |
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| **Introduction/Aim:** *Rhinovirus* C (RV-C) followed by RV-A are the most common viruses associated with paediatric hospital presentations for acute wheeze/asthma (AWA). RV-C is associated with increased severity and shorter time to recurrence. We hypothesised that nasal epithelial cells (NECs) from AWA children have impaired responses to RVs, and that would be worse in response to RV-C.**Methods:** NECs from AWA children (n=14; 12 males; mean age 7.7±2.8 (SD) years) and non-wheezing controls (NWC; n=13; 8 males; 7.7±1.12 years) were fully differentiated and inoculated with clinically derived RV-C15 or RV-A16, at a clinically relevant titre, 1x105 copies/ml (100μl). Host-responses were assessed over 72hr: viral load and receptor gene-expression qPCR; barrier integrity permeability assay and qPCR; and anti-viral RANTES ELISA. Viral load was presented as Log2-transformed copies/ml, and other data as Log2(fold-change) to non-infected cultures.**Results:** AWA vs NWC:Viral load peaked at 24hr, was higher in NWC at 72hr with RV-C (72hr AWA 11.21±3.16 vs NWC 14.76±2.21 p<0.05) and was similar with RV-A. Receptor gene-expression, and barrier integrity were similar. RANTES was dampened in AWA in response to RV-C (48hr AWA 0.83±2.28 vs NWC 3.85±2.31 p<0.01; 72hr AWA 1.15±1.70 vs NWC 2.83±2.28 p<0.05) and heightened to RV-A (24hr AWA 2.63±2.35 vs NWC 1.13±0.76 p<0.01; 48hr AWA 4.39±2.51 vs NWC 2.91±1.21 p<0.05; 72hr AWA 4.65±2.90 vs NWC 2.71±1.37 p<0.01). RV-C vs RV-A: RANTES release in AWA was delayed with RV-C infection (24hr RV-C -1.19±1.04 vs RV-A 2.63±2.35 p<0.001).**Conclusion:** Children with AWA may have an anti-viral response that is less efficacious to RV-C and exaggerated to RV-A. This response may be species-specific, suggesting why RV-C causes more severe exacerbations. RANTES may play a key role in acute wheezing in childhood. **Grant Support:**Research Training StipendStan & Jean Perron Research Excellence AwardWACRFNHMRC**Key Words:** Asthma, Childhood, Rhinovirus, Acute Wheeze, Epithelium. |