SUNDAY

574 *Coronavirus NL63* Illnesses in Infancy are a Risk Factor for Asthma at Age Six

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RATIONALE: In infancy, rhinovirus illnesses and severe RSV bronchiolitis indicate increased risk for recurrent wheezing and asthma, but there is less information about other viruses. We evaluated the frequency and severity of metapneumovirus (HMPV) and coronavirus (HCV) infections in a high-risk group of infants.

METHODS: Nasal lavage samples were obtained in the first year of life during scheduled study visits and symptomatic respiratory illnesses as part of the Childhood Origins of Asthma Project (COAST). Samples (n = 567) were analyzed by Respiratory Multicode Assay (RMA) for HMPV, HCV-229E, HCV-OC43, HCV-NL63 and HCV-SARS.

RESULTS: HMPV was isolated in 10.7% of samples during illnesses (n = 291), and also occurred with other respiratory viruses (4.8%). 47.8% of HMPV illnesses included wheezing. HCV were isolated in 19.2% of the samples during illnesses and included HCV-OC43 (10.0%) and HCV-NL63 (9.6%). In addition, HCV was commonly detected together with other respiratory viruses (6.5%). Of all HCV illnesses (n = 42), 33.3% included wheezing; however, HCV-NL63 had a significantly higher wheezing rate compared to HCV-OC43 (37.5% vs. 4.5%, p = 0.028). Children who had at least one HCV-NL63 illness during infancy were significantly more likely to have asthma at age 6 compared to those without HCV-NL63 illnesses (52.2% vs. 25.0%, p = 0.007). Having either HCV-OC43 or HMPV was not a risk factor for asthma at age 6.

CONCLUSIONS: Improvements in viral diagnostics has allowed for identification of viruses that are difficult to culture. In infancy, HCV-NL63, HCV-OC43 and HMPV were significant causes of wheezing illnesses, however, only HCV-NL63 was significantly associated with asthma development at age six.

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575 Seasonal Distribution Of Respiratory Viruses In Pediatric Asthma In Trinidad West Indies

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RATIONALE: The seasonal distribution of respiratory viruses associated with pediatric asthma is well documented in temperate climates, but has not received similar attention in the tropics.

METHODS: Nasal specimens were collected during the dry (n = 38, January to May) and rainy (n = 112, June to December) seasons from asthmatic children, 2-16 years, who (a) presented to A&E (n = 70) for nebulization or (b) were clinically stable (n = 80) during the previous 3 months. A novel, high-throughput Respiratory MultiCode PCR assay (UW-Madison & EraGen Biosciences, Madison, WI) was used to detect respiratory viruses.

RESULTS: Viral prevalence was similar ($\chi2 = 0.026$, p = 0.872) in both the dry (n = 10, 26.3%) and rainy (n = 28, 25.0%) seasons. Coronavirus OC43 or NL63 (n = 2, 5.3%) and human metapneumovirus (n = 1, 2.6%) were detected only in the dry season, whereas RSV B (n = 6, 5.4%), enterovirus (n = 3, 2.7%) and influenza A (n = 2, 1.8%) were exclusive to the rainy season. Parainfluenza virus (PIV 2, Dry, n = 1, 2.6%; PIV1, Rainy, n = 1, 0.9%) and rhinovirus (Dry, n = 6, 15.8%; Rainy, n = 19, 17.0%) were detected throughout the year. All specimens were negative for RSV A, influenza B, coronavirus 229E & SARS, PIV 3 and adenovirus. Prevalence of rhinovirus was not significantly ($\chi2 = 0.028$, p = 0.867) associated with any particular season, but it was the most prevalent virus in both seasons. Rhinovirus demonstrated a significantly higher ($\chi2 = 7.736$, p = 0.005) prevalence in children who needed to be nebulized (n = 18, 25.7%) compared with stable (n = 7, 8.8%) asthmatics.

CONCLUSIONS: Rhinovirus is the major viral trigger for pediatric asthma in Trinidad and is not associated with seasonality in this tropical climate.

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576 Analysis of Airway Immune System Responses to Rhinovirus Infection in Children and Resultant Tendency to Wheeze

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RATIONALE: We hypothesize that children identified as wheezers will present with increased levels of inflammatory cytokines and decreased levels of anti-viral cytokines in nasal lavage samples during symptomatic RV infection compared to non-wheezers during symptomatic RV infection.

METHODS: To test this hypothesis, children enrolled in the Childhood Origins of ASThma (COAST) project provided nasal lavage samples during symptomatic respiratory infections and at scheduled well visits at ages 5 and 6 years. Children with a history of wheezing were sampled when well, during an uncomplicated cold and during a wheezing illness. Children with no history of wheezing were sampled when well and ruing an uncomplicated cold. Innate cytokine profiles were assayed using a Beadlyte® Human Multi-Cytokine Flex Kit, and detection of the cytokines were evaluated using the Luminex 100™ IS for the following cytokines: IL-6, IL-10, IL-12 (p40), IFN-γ, IFN-α, and TNF-α. Interleukin-8 levels were evaluated by ELISA.

RESULTS: Interleukin-6, IL-10, IFN-γ, and IL-8 were present in measurable concentrations. Concentrations of IL-6 were significantly higher during symptomatic RV infection than when well (14.6 vs. 9.91, p<0.001). The % detectability of IL-10 and IFN- γ were significantly higher during symptomatic RV infection than when well (23.9 vs. 5.0, p=0.045; 54.3 vs. 0, p=0.022 respectively). Concentrations of IFN-γ tended to be higher in non-wheezers than in wheezers during symptomatic RV infection (13.9 vs. 8.1, p=0.077).

CONCLUSIONS: During symptomatic RV illness, non-wheezers presented with higher levels of IFN-γ than wheezers, suggesting the possibility that wheezers may have a depressed anti-viral response, which may not be as effective at fighting viral infections.

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577 Myosin Light Chain Kinase (MYLK) Variants that Confer Increased Risk of Sepsis and Acute Lung Injury are Associated with Asthma and Associated Phenotypes

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RATIONALE: Asthma is a heritable trait characterized by lower airway smooth muscle contraction and inflammation. Myosin light chain kinase is a multifunctional protein involved in regulation of bronchial contractility and other activities relevant to asthma. Previously we identified *MYLK* variants/haplotypes that confer risk for sepsis and acute lung injury (ALI).