896 Wheeze, Recurrent Wheeze, Nd Rhinovirus and Respiratory Syncytial Virus Infections during the First 5 Years of Life; Observations from a Birth Cohort in Rural Ecuador

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RATIONALE: There are limited data from the rural tropics on the association between respiratory viral infections and wheezing in early childhood. We investigated the association between wheeze and rhinovirus (RV) and respiratory syncytial virus (RSV) infections during the first 6 years of life in a rural birth cohort in Ecuador.

METHODS: We did passive surveillance for influenza-like illnesses and wheeze in a birth cohort of 2,404 children in a rural tropical Ecuador from birth to 6 years. Nasopharyngeal swabs were collected from symptomatic children and routinely from asymptomatic children and analysed for the presence of RSV and RV RNA by real-time PCR.

RESULTS: We analysed 400 swabs from a sample of 50 asymptomatic children, 48 children with influenza-like illness and no wheeze (ILI/noW), and 214 children presenting with 302 episodes of wheeze. Wheeze was more strongly associated with RV infection (adj. OR 6.2, 95% CI 2.3-16.8, P<0.001) than ILI/noW alone (adj. OR 2.7, 95% CI 0.9-8.4, P=0.091) compared to controls. Children with wheeze and ILI/noW had a higher risk of RSV infection compared to controls (ILI, age-adjusted OR 8.5, 95% CI 1.0-72.8, P=0.05; RV, adj. OR 6.3, 95% CI 0.8-47.7, P=0.076).

CONCLUSIONS: Our data indicate that RV infection in our population is a risk factor for wheezing illness in under 7s while RSV infection is related more to ILI irrespective of wheeze. Partial sequencing in future analyses will define rhinovirus subtypes to determine if RV sub-types are more strongly associated with wheeze and the later development of asthma.

897 Diesel Exhaust Particles Exacerbate Allergic Rhinitis in Mice By Disrupting the Nasal Epithelial Barrier

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RATIONALE: A traffic-related air pollutant, diesel exhaust particles (DEP), is considered an environmental factor that adversely affects allergic diseases. However, the direct effect of DEP on allergic rhinitis (AR) and the underlying molecular mechanisms are poorly understood.

METHODS: Mice were sensitized by intraperitoneal injection of ragweed pollen, followed by nasal challenge with ragweed pollen in the presence or absence of DEP. The frequency of sneezing was evaluated immediately after each nasal challenge. Immunological parameters and nasal histology were examined 24 hours after the final challenge.

RESULTS: Mice challenged with ragweed pollen plus DEP showed increased frequency of sneezing compared with mice challenged with pollen alone, while Th2-type immune responses against the allergen were comparably induced in both groups. Interestingly, intranasal DEP pretreatment before ragweed pollen challenge increased ragweed-pollen-induced sneezing to levels comparable with the co-administration group. *In vitro* examination revealed that DEP reduced the expression of a tight junction (TJ) protein, zonula occludens-1, and increased paracellular permeability of cultured nasal epithelial cells. Additionally, intranasal administration of DEP, but not ragweed pollen, disrupted nasal mucosal TJs *in vivo*.

CONCLUSIONS: Our results demonstrate that DEP disrupts TJs, leading to an increased permeability of nasal epithelial cells. This may result in the promotion of allergen delivery into subepithelial tissues contributing to the exacerbation of antigen-specific IgE bearing mast-cell-mediated immediate allergic responses.

898 Inhalational Exposure to House Dust Conditions Pulmonary Conventional Dendritic Cells to Induce T Helper 2 Responses Against Innocuous Antigens

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RATIONALE: House dust, which contains a complex mixture of allergens and microbial products, can promote allergic sensitization to innocuous antigens. Our objective was to identify the pulmonary dendritic cell (DC) subsets responsible for inducing T helper 2 (Th2) responses following airway exposure to house dust extract (HDE).

METHODS: The airways of C57BL/6 mice were exposed to ovalbumin (OVA) alone or in combination with either HDE or the viral mimetic poly(I:C). After 16 hours, pulmonary DC subsets were isolated by flow activated cell sorting and cultured with naïve OVA-specific CD4(+) T cells. T helper differentiation was determined by measurement of IL-4, IL-13 and IFN-gamma.

RESULTS: Airway exposure to HDE resulted in the accumulation and activation of conventional (c) DCs and monocyte-derived (mo) DCs. However, only cDCs induced Th2 differentiation following HDE exposure. HDE specifically conditioned lung DCs to stimulate Th2 responses, as cDCs exposed to poly(I:C) failed to induce Th2 differentiation. HDE and poly(I:C)-exposed cDCs expressed comparable costimulatory molecules and stimulated equivalent T cell proliferation, indicating that Th2 induction was not the consequence of suboptimal DC maturation by HDE. HDE exposure suppressed IL-12p40 expression in lung cDCs, suggesting a possible mechanism for Th2 induction.

CONCLUSIONS: HDE conditions pulmonary cDCs to preferentially induce Th2 responses against innocuous inhaled antigens. Transcriptional analysis of HDE-conditioned cDCs may reveal previously unknown factors involved with Th2 differentiation, and thus identify novel therapeutic targets for allergic asthma.