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**Title:** Environmental tobacco smoke exposure increases respiratory viral infection susceptibility in children with acute asthma

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**Body:** Background: Respiratory viral infection (RVI), particularly by human rhinovirus (HRV), is the most common cause of asthma exacerbations in children requiring hospitalization. Environmental tobacco smoke (ETS) exposure is a risk factor for asthma exacerbation. Thus, we hypothesized that ETS exposure may play a role in asthma exacerbation by increasing susceptibility to RVI. Aim: To determine if ETS exposure in asthmatic children results in increased susceptibility to viral infection, specifically to HRV. Method: Children with acute asthma (n= 460, 60.6% male, age 0-16 years), presenting to Emergency Department were studied. ETS exposure was determined by questionnaire, which was validated by measuring urinary cotinine and creatinine levels in a subset of children. RVI to 6 common respiratory pathogens was determined by immunofluorescence (IF) using virus specific monoclonal antibodies, cell culture isolation and indirect IF, the Respiratory MultiCode-Plx Assay or by PCR. Results: Among 377 children in whom ETS exposure was available, 133 were exposed and 240 were not. Of these children, testing for viruses was done in 96 and 180, respectively. A virus was detected in 95.8% of those exposed to ETS and tested for viruses versus 86.1% of those not exposed and tested. In total, 88.4% of children had a RVI and of these 83.7% were HRV positive. ETS exposure was associated with RVI in these children (OR=3.78, 95%CI 1.28-11.13, p=0.016), as was with HRV-infection (OR=1.89, 95%CI 1.07-3.34, p=0.028). Conclusion: ETS exposure increases an asthmatic child's susceptibility to RVI, particularly HRV infection and this is likely to predispose to acute asthma exacerbations.