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Title: LSC 2013 abstract - Perinatal antibiotic treatment affects murine microbiota, immune responses, and pathology in models of allergic asthma and hypersensitivity pneumonitis

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Body: Rates of allergic airway disease are steadily rising in developed countries, arguing for an environmental etiology. Epidemiological studies have pointed to a role for the infant gut microbiota in immune system development that could alter allergic disease susceptibility. To investigate whether changes in gut microbiota impact disease severity in murine models of asthma and hypersensitivity pneumonitis (HP), we administered clinical doses of antibiotics to mice during different periods in their development. Allergic asthma is characterized by Th2-type inflammation, whereas HP is described as a Th1/Th17-polarized disease. Consistent with their opposing immune etiologies, these two diseases were exacerbated after different antibiotic exposures. Mice receiving perinatal vancomycin developed more severe asthma relative to control animals, as demonstrated by increased airway inflammation (Th2-type), antigen-specific serum IgE and lung pathology. Our data suggest that increased asthma severity is mediated by a mechanism involving elevated IgE levels and reduced regulatory T cell populations. This effect was not observed in mice given streptomycin, nor when either antibiotic was administered to adult mice. Conversely, the severity of HP was unaffected by vancomycin, but increased after streptomycin treatment; this was demonstrated by increased airway inflammation (Th1/Th17-type), IFNγ and IL-17 cytokine expression and lung pathology. These results present an interesting dichotomy, where contrasting shifts in gut flora appear to have opposite consequences depending on the immunological nature of the disease.