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Title: LSC 2013 abstract - Differential susceptibility of fetal and adult lung to respiratory syncytial virus infection and modulation by cytokine environment

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Body: Early life exposure to respiratory viral infections has been associated with the development of chronic respiratory disease. We hypothesised that in early life, cytokine priming of the lung has potential long term effects on the pulmonary immune response, affecting anti-viral responses and contributing to susceptibility to asthma later in life. We investigated the differential effects of inflammatory cytokine priming on the immune response to RSV infection throughout different ages of life and in different tissue compartments from the respiratory tract. Lung tissue was harvested from human embryos and lung surgical specimens from young and adult subjects. Tissue, bronchial epithelial cells and also A549 cells were pre-treated for 24 h with cytokines that mimic Th1 environment (IFNy, 10ng/ml), Th2 (IL-4 and/or IL-13, 10ng/ml) and bacterial infection (LPS, 1µg/ml) before being infected with RSV A at MOI=1 for 48 h. In the initial experiments cytokines were also added to the cells after the RSV infection. RSV replication was greater in the embryonic tissue compared to adult. Incubation with LPS increased viral infection in tissues and lowered it in A549, IFNy always reduced RSV replication and Th2 cytokines had variable effects but reduced viral infection in A549. The effects of the cytokine milieu persisted even after pre-treatment alone, suggesting the impact of epithelial priming may be longstanding. These early data suggest that the cytokine environment can impact on subsequent responses to viral infection with differential effects possibly under epigenetic influence.