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Title: The role of neutrophils in viral clearance during respiratory syncytial virus (RSV) disease

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Body: Background: Neutrophils are the most numerous cell in the airway during RSV bronchiolitis. We have found neutrophils in bronchoalveolar lavage (BAL) from infants with RSV disease contain RSV proteins. I hypothesise that neutrophils may play a vital role in viral clearance in the airway. Methods: Highly purified neutrophils from whole blood of healthy adult donors were incubated with A2 strain RSV in the presence of GM-CSF, used as a neutrophil pro-survival factor. Samples were taken at 2, 4, 6 and 20 hours for quantitative PCR of RSV N gene and FACS analysis of RSV F, G and N protein. Results: Interaction of RSV and neutrophils was shown in vitro, with neutrophils being RSV F, G and N protein positive by FACS analysis. Quantitative PCR revealed a 1000-2000 fold increase in RSV N gene expression compared to the L32 housekeeping gene, maximal between 2-4 hours with some inter-donor variability. This expression reduced in all experiments by 20 hours, suggesting that RSV phagocytosis was occurring followed by degradation. I have gone on to show that the uptake is autologous serum dependant, with a strong dose response. Uptake is 5-fold higher when comparing 0.1% serum with 10% serum (p<0.05). Conclusion: Phagocytosis of complement-opsonized bacteria, assisted by antibodies, is a well-documented role for the neutrophil. Here we have shown a similar process may be involved in viral clearance as part of the immune response to viral invasion. Experiments are on-going investigating whether a relative complement or antibody insufficiency may contribute to the susceptibility of infants to severe RSV disease.