Neutrophil activation in infants hospitalized with severe respiratory viral infection

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Background: The immune response to viral respiratory tract infections (vRTI) includes recruitment of circulating neutrophils to the lungs. Recruitment requires cellular activation, which can be measured by CD11b surface expression. Little is known about cell surface expression of CD11b in vRTI. We aim to describe CD11b expression on the circulating neutrophils of infants hospitalized with vRTI. **Methods:** Hospitalized infants < 2 years of age with a documented vRTI attributed to a single virus and healthy infant controls were included in the study. After obtaining informed consent, whole blood was collected into a syringe coated with EDTA. Neutrophil CD11b expression was determined using flow cytometry, gating on CD16+ granulocytes following exposure to increasing concentrations of CXCL1 (0-100 nM), a potent inducer of CD11b surface expression. A sample of infants with vRTI were seen in follow-up at 2, 6 and 10 weeks post-discharge. Whole blood was obtained at each visit for neutrophil CD11b expression analysis. **Results:** 12 infants with vRTI were included with a mean age of 75 days (range 11 - 420 days), 4 (33%) were males. 7 healthy infants were included with a mean age of 73 days (range 16 – 129 days), 2 (29%) were males. Infants were diagnosed with human metapneumovirus (HMPV, 2 (17%)), respiratory syncytial virus (RSV, 8 (67%)), and coronavirus (CoV, 2 (17%)). Neutrophils from infected infants exhibited a mean fold increase of 1.1 (range 1-1.3) with increasing concentration gradient of CXCL1 stimulant, compared to healthy infant controls which exhibited a mean fold increase of 3.5 (range 1.3 – 5.7). 5 infants (2 RSV, 2 HMPV, 1 CoV) were seen in follow up. Neutrophils in infants with vRTI showed recovery of CD11b expression after CXCL1 stimulation between 2 and 10 weeks after discharge. **Conclusion**: Circulating neutrophils obtained from vRT-infected infants resist CXCL-1 associated increases in CD11b surface expression suggesting that even prior to recruitment to the airways, circulating neutrophils are already highly activated.

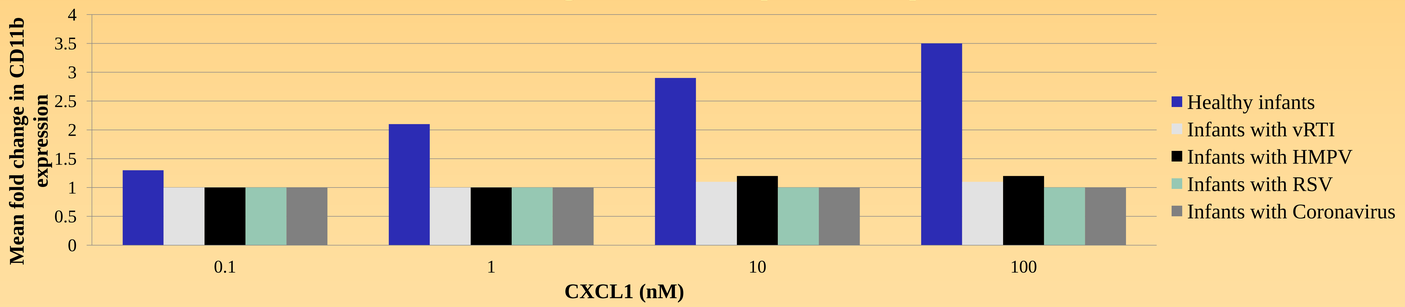
Introduction

- Neutrophils are recruited to the lungs during a viral respiratory tract infection (vRTI) as part of the immune response.
- The objective of this study was to measure and compare the neutrophil CD11b surface expression (a marker of cellular activation) in healthy infants and those who are hospitalized with a vRTI.

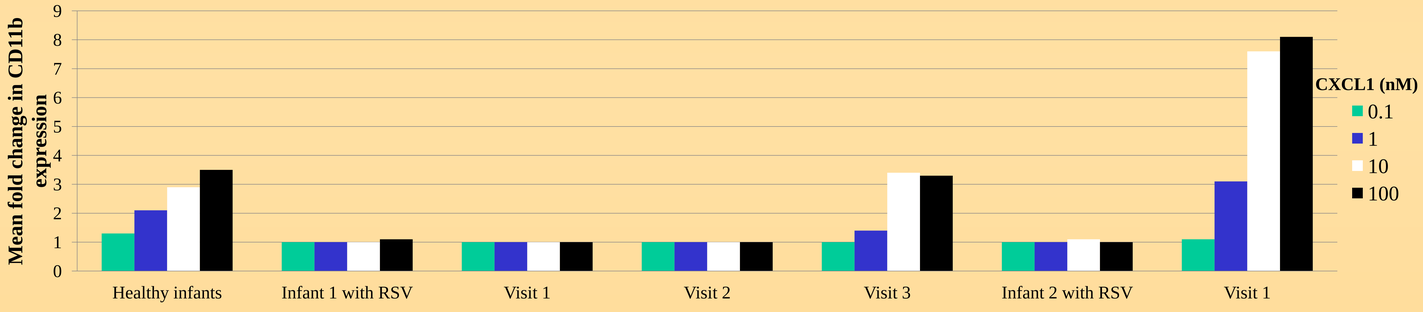
Methods

- Hospitalized children < 2 years of age with a documented vRTI due to a single virus and healthy controls were included.
- Blood was drawn and cell surface expression of CD11b was measured using flow cytometry.
- Neutrophils were exposed to increasing concentration of CXCL1 (CD11b inducer) and CD11b surface measured subsequently with gating of CD16-positive granulocytes.
- A small subset of children were followed up post hospital discharge. Visits 1, 2 and 3 were at 2, 6 and 10 weeks post discharge respectively.

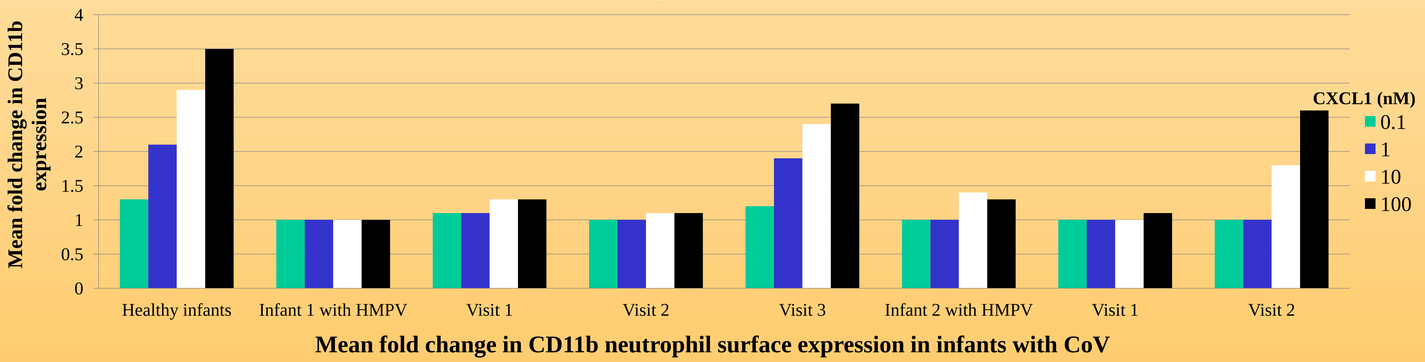
Mean fold change in CD11b neutrophil surface expression



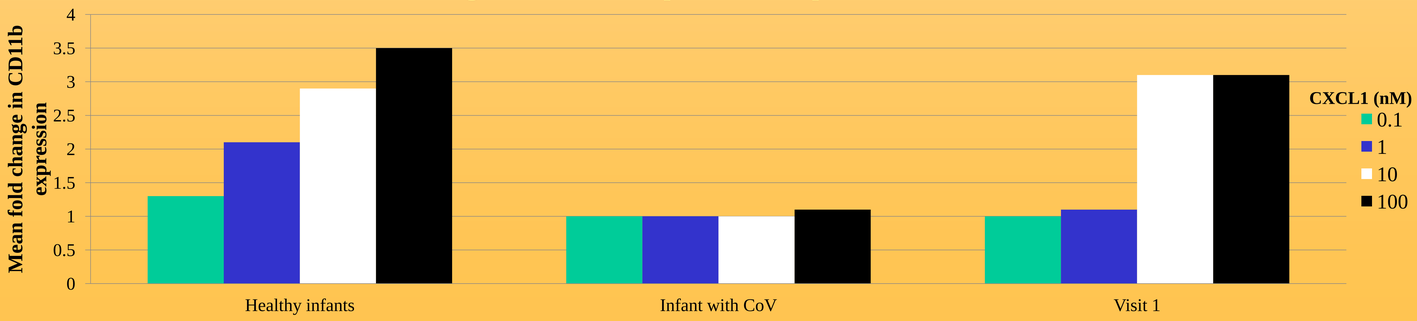
Mean fold change in CD11b neutrophil surface expression in infants with RSV



Mean fold change in CD11b neutrophil surface expression in infants with HMPV



Mean fold change in CD11b neutrophil surface expression in infants with CoV



Results

- 12 infants with vRTI were included (mean age: 75 days): human metapneumovirus (HMPV): 2 infants, respiratory syncitial virus (RSV): 8 infants and coronavirus virus (CoV): 2 infants.
- 7 healthy infants were included for comparison (mean age: 73 days).
- Mean fold increase of CD11b expression was 1.1 (range 1-1.3) in infants with vRTI. Healthy infants had a mean fold increase of 3.5 (range 1.3-5.7).
- 5 infants with vRTI (2 RSV, 2 HMPV, 1 CoV) were followed up post discharge. Neutrophil CD11b expression showed recovery at 2 and 10 weeks post discharge.

Conclusion

- Circulating neutrophils obtained from vRT-infected infants resist CXCL-1 associated increases in CD11b surface expression suggesting that even prior to recruitment to the airways, circulating neutrophils are already highly activated.

References

1. McNamara, P.S. & Smyth, R.L. (2002). The pathogenesis of respiratory syncytial virus disease in childhood. *British Medical Bulletin* 61:13-28.
2. Geerdink, R.J., Pillay, J., Meyaard, L., & Bont, L. (2015). Neutrophils in respiratory syncytial virus infection: A target for asthma prevention. *Journal of Allergy & Clinical Immunology* 136(4): 838-47.

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