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Title: Pulmonary effects of perfluorocarbon emulsion therapy on Streptococcus pneumoniae infection in sickle cell mice

Mrs. Nawal 641 Helmi nh118@le.ac.uk, Prof. Peter 642 Andrew pwa@le.ac.uk and Dr. Hitesh 643 Pandya hp28@le.ac.uk MD. 1 Department of Infection, Immunity and Inflammation, University of Leicester, United Kingdom, LE1 9HN.

Body: Perfluorocarbon emulsions (PFCEs) are a potential alternative therapy to blood transfusion in severe sickle cell lung disease. However, there are few data on the effects of PFCEs in sickle cell disease. In this study, we investigated the effects of intravenous therapy with PFCE on transgenic sickle cell and control mice infected with Streptococcus pneumoniae or vehicle. Methods: Mice were injected intravenously with single dose of saline or PFCE (3ml/Kg) +/- S. pneumoniae strain (D39) and harvested at 72 hours or on showing signs of 2+ lethargy. A second group of mice were injected with PFCE daily for 1 week. Histological analysis of lungs was performed using H&E sections and light microscopy. In addition, white blood cell analysis was performed using flow cytometry. Results: S. pneumoniae-infected mice treated with PFCE died earlier than those treated with vehicle and were less able to clear S. pneumoniae from the bloodstream. In the absence of infection, mice treated with a single dose of PFCE showed mild inflammatory changes in the lung. However, mice treated with PFCE for 1 week did not show any histological abnormalities. The inflammatory response in healthy mice injected with PFCE was significantly higher compared to sickle cell mice. Conclusions: Single-dose PFCE therapy causes lung injury mice whereas chronic PFCE therapy does not. In addition, the inflammatory response to PFCE therapy is different in healthy and sickle cell mice. Further studies are required to determine mechanisms of inflammatory responses in sickle cell mice and whether supplemental oxygen therapy improves outcomes in mice infected with S. pneumoniae and treated with PFCE.