Reply to Plötz et al

To the Editor—We read with interest the letter by Plötz et al regarding the role of ventilation in the innate immune dysfunction evidenced in patients with severe respiratory syncytial virus (RSV) lower respiratory tract infection (LRTI) [1]. Understanding the role of innate immune dysfunction in the development of severe RSV-LRTI is an important issue that needs to be further explored. Disease severity in children with RSV LRTI is the result of a complex interaction between both viral factors and the host immune response [2]. A growing body of evidence in vitro but more important in children with RSV LRTI (both ventilated and nonventilated) has shown that children with severe disease display inadequate innate, and possibly adaptive, immune responses and suggests that the host immune response to RSV is impaired in the most severe forms of the disease [3–6]. In the past years there has been a shift in the management of infants with severe RSV LRTI, and the use of noninvasive ventilatory support is being widely used in most centers [7]. In our study, we included infants receiving support by invasive ventilation (mechanical; n = 4 infants) and noninvasive ventilation (continuous positive airway pressure, bilevel positive airway pressure, and SiPAP is a mode of positive airway pressure (a brand); n = 15 infants). Overall, intensive care unit infants showed a significantly impaired production of blood tumor necrosis factor α (TNF-α) after Lipopolysaccharide stimulation at 24 hours of admission compared with infants with moderate disease admitted to the pediatric ward, even after excluding from the analyses the 4 patients that received mechanical ventilation (P = .04). In addition, 74% of infants admitted to the ward required supplemental oxygen by nasal cannula, and those that required oxygen and thus had a more severe disease also showed significantly decreased inducible TNF-α concentrations in the blood compared with infants that did not require supplemental oxygen (P = .03), suggesting that factors other than positive pressure ventilation may contribute to the severity of the disease.

In the study conducted by Plötz et al, children (n = 12; median age, 3.5 months) without preexisting lung pathology briefly exposed to mechanical ventilation showed decreased systemic production of TNF-α, interleukin 6 and interferon γ [8]. In that study, all infants had a medical history of congenital heart disease, which may by itself be associated with impaired immune responses and poses an increased risk for more severe lung disease. Patients were assayed after undergoing a cardiac catheterization for diagnostic purposes and received anesthetics (sevorflurane) as well as injections of contrast media, which have shown to have immunomodulatory effects and to significantly decrease the response to endotoxin [9,10]. Given the interactions between all these factors and the lack of a control group, it is hard to conclude that the intubation and short time of mechanical ventilation was the main causative agent of the decrease in functional capacity of peripheral leukocytes observed.

In our study, we attempted to limit the influence of confounders by only including previously healthy infants (median age, 2.6 months) with no preexisting medical conditions or exposure to previous immunomodulatory therapies, including systemic steroids. Nevertheless, it remains unclear whether children who develop severe RSV disease are born with an already impaired immune response and RSV just uncovers their abnormal immune system or whether RSV infection is the main contributor to that relative state of “immune insufficiency.” Further studies analyzing sequential samples and controlling for potential contributors to immunomodulation are needed to help elucidate the mechanisms responsible for innate immune suppression observed in critically ill RSV-infected children.

Notes

Financial support. This work was supported in part by intramural grants to A. M. and by the Clinical And Translational Research Program (grant 270810) sponsored by the Research Institute at Nationwide Children’s Hospital to C. M.

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Cesar Mella, Mark W. Hall, Octavio Ramilo, and Asuncion Mejias

Center for Vaccines and Immunity, The Research Institute at Nationwide Children’s Hospital, The Ohio State University College of Medicine, Columbus

References


Downloaded from https://academic.oup.com/jid/article-abstract/208/11/1924/854011 by guest on 15 December 2018


Received 17 June 2013; accepted 18 June 2013; electronically published 16 September 2013.

Correspondence: Asuncion Mejias, MD, PhD, Center for Vaccines and Immunity, The Research Institute at Nationwide Children’s Hospital, The Ohio State University College of Medicine, 700 Children’s Dr, WA 4022, Columbus, OH 43205 (asuncion.mejias@nationwidechildrens.org).

The Journal of Infectious Diseases 2013;208:1924–5
© The Author 2013. Published by Oxford University Press on behalf of the Infectious Diseases Society of America. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com.
DOI: 10.1093/infdis/jit514