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 (sevoﬂurane) as well as injections of contrast media, which have shown to have immunomodulatory effects and to signiﬁcantly decrease inducible TNF-α after Lipopolysaccharide stimulation [9].

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

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