Airway inflammation and airway hyperresponsiveness (AHR) are fundamental features of asthma. Migration of inflammatory cells from the circulation into the airways is mediated in part by adhesion molecules such as intercellular adhesion molecule (ICAM)-1, which are expressed on vascular endothelial cells, and the β2 integrin CD11b/CD18, which is expressed on neutrophils. Increasing evidence suggests that ICAM-1 and CD11b/CD18 also have signaling capabilities, suggesting that they might modulate airway reactivity independently of their adhesion properties.

In previous studies from this laboratory, we have demonstrated that antibodies to ICAM-1 and CD11b significantly reduced endotoxin-induced airway inflammation but did not affect AHR. To further define the separate contributions of ICAM-1 and CD11b to endotoxin-induced inflammation and AHR, we exposed ICAM-1-deficient mice, CD18-deficient mice, and background strain control (ie, wild-type) mice to an aerosol of endotoxin for 4 h. Endotoxin-exposed, CD18-deficient mice showed no changes in AHR or neutrophil inflammation in the lung compared to endotoxin-exposed, wild-type mice. However, while endotoxin-exposed ICAM-1-deficient mice did not develop airway hyperreactivity, they mounted a normal inflammatory response to this toxin. The phenotypic differences that we observed in the ICAM-1-deficient mice and the mice previously treated with ICAM-1 antibodies suggest that the IV administered ICAM-1 antibodies specifically prevent neutrophils from infiltrating the lung after endotoxin exposure but that reduced neutrophilic inflammation by itself has no effect on lipopolysaccharide endotoxin-induced AHR. Moreover, it appears that ICAM-1 is not required to facilitate the movement of neutrophils or polymorphonuclear leukocytes from the vascular space to the airspace, however, disruption of ICAM-1 prevents that development of lipopolysaccharide-induced AHR.

In aggregate, our results suggest that ICAM-1 plays a pivotal role in the development of AHR and airway inflammation that are induced by endotoxin. Additionally, our results indicate that distinct mechanisms are responsible for the development of endotoxin-induced AHR and endotoxin-induced airway inflammation.

**Reference**


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**Intercellular Adhesion Molecule-1 Plays a Pivotal Role in Endotoxin-Induced Airway Disease**

**David M. Brass, PhD; Jordan D. Snav, MD, PhD; and David A. Schwartz, MD, MPH, FCCP**

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**Abbreviations:** AHR = airway hyperresponsiveness; ICAM = intercellular adhesion molecule

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