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Heightened immunity to colds makes asthma flare-ups worse, research shows

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People often talk about "boosting" their immunity to prevent and fight colds. Nutritional supplements, cold remedies and fortified foods claim to stave off colds by augmenting the immune system.

A new University of Michigan study shows this strategy might actually be flawed. The results may hold important implications for individuals with asthma, who often experience life-threatening flare-ups due to infections with cold viruses.

The study, using a novel mouse model, shows that, in the airways, the immune response to the common cold is actually maladaptive. Mice that were engineered to have a reduced innate immune response to the common cold actually showed less - not more - airway inflammation and bronchoconstriction (airway spasm) following infection.

The results of this study appeared online ahead of print in the journal *PLoS Pathogens*, currently available online. Marc B. Hershenson, M.D., professor of pediatrics and communicable diseases and director of the division of pediatric pulmonology, is the study's senior author.

"You often hear that people want to boost their immunity to prevent and fight colds," says Hershenson. "However, boosting the immune response could increase inflammation. Up to now there have been no convincing data supporting the theory that the immune response might be deleterious. In our study, we offer the first direct evidence that limiting the immune response reduces the manifestations of rhinovirus

infection."

"In our model, cold-induced asthma flare-ups were caused by the body's immune response to the virus, not the virus itself. Chemicals produced by the immune system inflame cells and tissues, causing asthma symptoms such as cough and wheeze," Hershenson explained.

Hershenson and his group hypothesized that limiting the immune response to viral infection would actually reduce their symptoms. Using a rhinovirus 1B, a cold virus strain that replicates in mouse lungs, they infected mice deficient in MDA5 and TLR3 - two receptors that trigger the protective defenses of the immune system against viruses and other pathogens.

MDA5-deficient mice showed a delayed defensive response to the infection, leading to a small increase in the level of virus in the lungs. Nevertheless, these mice showed less airway inflammation and bronchoconstriction following infection compared to wild-type mice. TLR3-deficient mice also showed diminished airway responses.

In addition, MDA5- and TLR3-null mice that were made asthmatic by exposure to allergen showed decreased airway inflammatory and contractile responses in response to rhinovirus infection compared to normal mice. These results suggest that, in the context of rhinovirus infection, reducing the mouse's innate immune system led to reduced inflammatory signaling pathways and reduced airways inflammation and hyper-responsiveness.

"This study shows that, once you have a cold, elements of the immune response actually make the symptoms worse," Hershenson adds. "A better strategy might be to modulate the immune response in asthma patients with colds."

More information: Wang Q, Miller DJ, Bowman ER, Nagarkar DR, Schneider D, et al. (2011) MDA5 and TLR3 Initiate Pro-Inflammatory Signaling Pathways Leading to Rhinovirus-Induced Airways Inflammation and Hyperresponsiveness. *PLoS Pathog* 7(5): e1002070. doi:10.1371/journal.ppat.1002070