National Jewish Health
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Bacteria Implicated in Steroid-Resistance Among Asthmatics

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DENVER — A series of experiments by researchers at National Jewish Health have implicated the remains of bacterial cell walls in the development of resistance to corticosteroids, the main controller medication for asthma. Steroid-resistance is a major management problem in asthma and accounts for a disproportionate amount of healthcare costs.

The source of the bacterial remains, known as endotoxin, is unclear. However, recent research at National Jewish Health indicates that asthma patients can have bacterial infections, which could produce significant amounts of endotoxin. Dogs are another suspected source of the endotoxin. The researchers, led by National Jewish Health Professor of Pediatrics Donald Leung, MD, PhD, published their findings in *The Journal of Allergy and Clinical Immunology*.

"Steroid-resistance disables the most effective medication for the control of asthma," said Elena Goleva, PhD, Assistant Professor of Pediatrics at National Jewish Health and lead author of the paper. "Our findings clearly point to endotoxin as a contributor to this difficult-to-manage condition. They have launched us to a promising new avenue of research we hope can improve patients' response to steroids, leading to better control of their disease."

The research team reported three distinct findings supporting a role for endotoxin in the development of steroid-resistance. First, they evaluated gene expression in cells taken from the lungs of 10 steroid-resistant asthma patients and eight patients with steroid-sensitive asthma. These experiments indicated that a distinct set of genes, which are associated with the recognition of endotoxin, and with an immune response to bacterial products were expressed at higher levels in steroid-resistant asthma patients.

Second, steroid-resistant asthma patients had on average over five times more endotoxin in their lung fluid than did steroid-sensitive patients.

Third, the researchers tested how prolonged exposure to endotoxin altered the response of white-blood cells to steroids. Immune-system cells taken from six non-asthmatic people showed a significantly reduced response to steroids after they had been incubated for 24 hours with the steroid dexamethasone.

"Taken together, these findings provide strong evidence for the role of endotoxin in steroid-resistance," said Dr. Leung. "Our challenge now is to determine the source of the endotoxin, confirm its role in steroid-resistance, and find ways to reduce endotoxin exposure or counter its negative effects."

Co-author Richard Martin, MD, Chair of Medicine at National Jewish Health, has previously published findings indicating that many chronic asthma patients have low-level bacterial infections that may make their asthma worse. He is currently leading a $7.5 million study of the effects of the bacteria *mycoplasma* on asthma. Such bacteria could be the source of endotoxin.

Other researchers also recently reported that presence of dogs, but not cats, increases the amount of endotoxin in the home. Following up on this, Dr. Leung and his colleagues found that 66 percent of 18 patients with steroid-resistant asthma lived with at least one dog, compared to 38 percent of patients with steroid-sensitive asthma.

Media Contacts

Our team is available to arrange interviews, discuss events and story ideas.

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