Hygiene Hypothesis in Action

Mechanism demonstrated for key immune theory

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Researchers have long suspected that the global spike in allergic and autoimmune diseases is linked to a decline in exposure to germs in childhood, especially in urban settings. But until now, no one has been able to directly demonstrate a biologic support or a mechanistic basis for the theory, known as the hygiene hypothesis.

In a **paper** published online March 22 in the journal *Science,* researchers at Brigham and Women's Hospital and Harvard Medical School provide new evidence supporting the hygiene hypothesis, as well as a potential mechanism.

The researchers compared the immune systems of mice lacking bacteria or any other microbes with those of mice living in a normal environment with

microbes. They found that germ-free mice had exaggerated inflammation of the lungs and colon resembling asthma and colitis, respectively. The cause was hyperactivity of a unique class of T cells previously linked to these disorders in both mice and humans.

Importantly, the researchers found that exposing the germ-free mice to microbes during their first weeks of life, but not when exposed later in adult life, led to a normalized immune system and prevention of diseases. Moreover, the protection provided by early-life exposure to microbes was long-lasting, as predicted by the hygiene hypothesis.

“These studies show the critical importance of proper immune conditioning by microbes during the earliest periods of life,” said **Richard Blumberg**, HMS professor of medicine and chief for the BWH **Division of Gastroenterology, Hepatology and Endoscopy**. “Also, now knowing a potential mechanism will allow scientists to potentially identify the microbial factors important in determining protection from allergic and autoimmune diseases later in life.” Blumberg and **Dennis Kasper** of the Channing Laboratory at Brigham and Women’s were senior authors on the paper.

— R. Alan Leo

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