IN BRIEF

Antibiotic-Induced Disruption of Intestinal Microbiota Leads to Increased Mortality From a Respiratory Viral Infection

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Allergy and Immunology, *Microbiome*

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Recent study indicates that antibiotic use disrupts gastrointestinal microbial communities and can indirectly influence host immune response, even in distant tissues.

"The indiscriminate and overuse of antibiotics may have further reaching consequences than just evolution of antibacterial-resistant superbugs," says physician-scientist Mitchell Grayson, MD, lead author of a new study published in *Frontiers in Immunology*.

Dr. Grayson, who is chief of the Division of Allergy and Immunology at Nationwide Children's Hospital and professor of Pediatrics at The Ohio State University, and colleagues at the Medical College of Wisconsin explored the impact of the

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21%, 6 Votes
ROBOTICS AND ARTIFICIAL INTELLIGENCE:
25%, 7 Votes

gastrointestinal microbiota on the pulmonary antiviral immune response.

The mouse parainfulenza virus type I, Sendai virus (SeV), is in the same family as respiratory syncytial virus (RSV) and human parainfluenza viruses. Wild-type mice infected with the virus typically clear the infection 10 to 12 days after inoculation, and fewer than 5 percent of these mice die from the infection. In the study, mice that ingested water containing the non-absorbable antibiotic streptomycin had a reduction of 85 percent in microbial diversity in the intestine, and as expected, there was no effect on lung microbial diversity.

However, when these mice were infected with SeV, mortality increased to 83 percent and was associated with a dysregulated immune response. Importantly, this increased mortality was seen in mice given two weeks of antibiotic treatment before the SeV infection, but not with one week of treatment or therapy during the viral infection, suggesting that it takes time for the altered intestinal microbiota to influence the lung immune response.

Two parallel mechanisms appeared to be influencing mortality in streptomycin-treated, SeV-infected mice, according to the publication. First, the team demonstrated that overproduction of interferon γ (IFNγ) in the lung increased the mortality of infected mice. In accordance with this, neutralizing IFNγ completely prevented mortality. Because IFNγ-producing cell numbers were not increased, the researchers hypothesized that the per-cell IFNγ production may have increased. The authors were able to determine that the most likely source of the increased IFNγ was a Lin-CD4+ cell, possibly an innate lymphoid cell.

Second, the dysregulated immune response was also characterized by a decrease in the number of regulatory T cells in both the lung and intestine.

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Indeed, adoptive transfer of regulatory T cells to the lung also prevented increased mortality.

“It has been shown that some microbial products like butyrate correlate with regulatory T cell numbers. The question that we have,” says Dr. Grayson, “is could this effect be due to changes in these kinds of short chain fatty acids – which we know are necessary for normal T cell development and maintenance.”

Though any connection between IFNγ overproduction and regulatory T cells remains unclear, this study supports the idea that antibiotic use disrupts gastrointestinal microbial communities and can indirectly influence host immune response, even in distant tissues.

“The microbiome is far more involved in many diseases. More than we have given it credit for, currently more than we understand,” says Dr. Grayson. “From a physician’s perspective, we still tend to treat the microbiome as a static community, whereas from the experimental side, we’re saying it is changing all the time and its state at any point can impact all kinds of diseases.”

The authors point out that humans with the least diverse microbiota, infants and the elderly, are also the same populations that tend to have the highest viral mortality rates, including to RSV.

Reference:

Grayson MH, Camarda LE, Hussain S-RA, Zemple SJ, Hayward M, Lam V, Hunder DA, Santoro JL, Rohlfing M, Cheung DS, Salzman NH. Intestinal microbiota disruption reduces regulatory T cells and increases respiratory viral infection mortality through increased IFNγ production. *Frontiers in Immunology.* 10 July 2018;9:1587.

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