Research pinpoints how early-life antibiotics turn immunity into allergy

August 20 2024

Credit: Pixabay/CC0 Public Domain

Researchers at the University of British Columbia have shown for the first time how and why the depletion of microbes in a newborn's gut by antibiotics can lead to lifelong respiratory allergies.

In a study published today in the *Journal of Allergy and Clinical Immunology*, a research team from the school of biomedical engineering (SBME) has identified a specific cascade of events that lead to allergies and asthma. In doing so, they have opened many new avenues for exploring potential preventions and treatments.

"Our research finally shows how the gut bacteria and antibiotics shape a newborn's immune system to make them more prone to allergies," said senior author Dr. Kelly McNagny (he/him), professor in the SBME and the department of medical genetics.

"When you see something like this, it really changes the way you think about chronic disease. This is a well-sculpted pathway that can have lasting consequences on susceptibility to chronic disease as an adult."

Allergies are a result of the immune system reacting too strongly to harmless substances like pollen or pet dander, and a leading cause for emergency room visits in kids. Normally, the immune system protects us from harmful invaders like bacteria, viruses and parasites. In the case of allergies, it mistakes something harmless for a threat—in this case, parasites—and triggers a response that causes symptoms like sneezing, itching or swelling.

The stage for our immune system's development is set very early in life. Research over the past two decades has pointed toward microbes in the infant gut playing a key role. Babies often receive antibiotics shortly after birth to combat infections, and these can reduce certain bacteria. Some of those bacteria produce a compound called butyrate, which is key to halting the processes uncovered in this research.

Dr. McNagny's lab had previously shown that infants with fewer butyrate-producing bacteria become particularly susceptible to allergies. They had also shown that this could be mitigated or even reversed by

providing butyrate as a supplement in early life.

Now, by studying the process in mice, they have discovered how this works.

Mice with depleted gut bacteria who received no butyrate supplement developed twice as many of a certain type of immune cell called ILC2s. These cells, discovered less than 15 years ago, have quickly become prime suspects in allergy development.

The researchers showed that ILC2s produce molecules that 'flip a switch' on white blood cells to make them produce an abundance of certain kinds of antibodies. These antibodies then coat cells as a defense against foreign invaders, giving the allergic person an immune system that is ready to attack at the slightest provocation.

Every cell, molecule and antibody described along this cascade increases dramatically in number without butyrate to dampen them.

Butyrate must be given during a narrow window after birth—a few months for humans, a few weeks for mice—in order to prevent the proliferation of ILC2s and all that follows. If that opportunity is missed and ILC2s multiply, then the remaining steps are assured and remain with somebody for life.

Now that researchers know what those other steps are, they have many more potential targets for halting the cascade, even after the supplementation window has closed.

"We can now detect when a patient is on the verge of developing lifelong allergies, simply by the increase in ILC2s," said Ahmed Kabil (he/him), the study's first author and a Ph.D. candidate in the SBME. "And we can potentially target those cell types instead of relying on supplementation

with butyrate, which only works early in life."

As Dr. McNagny and study co-lead Dr. Michael Hughes point out, treating people's allergies with antihistamines and inhalers relieves the symptoms but does not cure the disease. To achieve more lasting progress, researchers must target the cells and mechanisms that build this hypersensitive immune system. Until now, there hadn't been a selective way to do that.

With this new understanding, patients can look forward to more effective, long-term solutions that address the root of the problem, paving the way for a future where allergies are managed more effectively, or perhaps avoided altogether.

More information: Ahmed Kabil et al, Microbial intestinal dysbiosis drives long-term allergic susceptibility by sculpting an ILC2-B1 cell–innate IgE axis., *Journal of Allergy and Clinical Immunology* (2024). DOI: 10.1016/j.jaci.2024.07.023

Provided by University of British Columbia