Evidence Suggests that Changes in the Bacteria and Fungi in the Gastrointestinal Tract can Intensify the Immune System's Reaction to Common Allergens. By News-Medical.Net

If you want to avoid allergies or asthma, scientists at the University of Michigan Medical School suggest you start paying more attention to what's in your gut. In the January 2005 issue of Infection & Immunity, U-M researchers report new evidence suggesting that changes in the normal mixture of microflora – bacteria and fungi in the gastrointestinal tract – can intensify the immune system's reaction to common allergens, like pollen or animal dander, in the lung and increase the risk of developing chronic allergies or asthma.

"Our research indicates that microflora lining the walls of the gastrointestinal tract are a major underlying factor responsible for the immune system's ability to ignore inhaled allergens," says Gary Huffnagle, Ph.D., an associate professor of internal medicine and of microbiology and immunology in the U-M Medical School. "Change the microflora in the gut and you upset the immune system's balance between tolerance and sensitization."

To test their hypothesis, Huffnagle and Mairi C. Noverr, Ph.D., a U-M post-doctoral fellow, have developed the first mouse model designed to mimic how humans develop allergies following antibiotic therapy. In a just-published study in the current issue of Infection & Immunity, they report results of new experiments linking changes in GI tract microflora to an overzealous allergic response in the lung.

Instead of sensitizing them to an allergen in advance, Noverr gave normal Balb/C laboratory mice a five-day course of antibiotics, which killed their gut bacteria, followed by a single oral introduction of the yeast Candida albicans. Increased growth of C. albicans in the gut is a common side-effect of antibiotics.

After stopping the antibiotics, Noverr inserted ovalbumin – a commonly used experimental allergen derived from egg whites – via the nasal cavities of all the mice in the study. Then, she examined the mice for the presence of an allergic response in the airways and compared results between mice that received antibiotics and those that did not.

"The antibiotic-treated mice showed increased airway hypersensitivity to ovalbumin compared to mice that didn't receive antibiotics," Noverr says. "These results confirm our previous experiments, in which we used a genetically different strain of laboratory mice [C57BL/6] and a different type of allergen – mold spores, instead of ovalbumin." Results of Huffnagle and Noverr's previous work were published in the August, 2004 issue of Infection & Immunity. It was the first study linking changes in GI tract microflora to an allergic response in the lung.

"In our new study, we found that differences in host genetics and the type of allergen used didn't matter. The immune responses were literally identical," Huffnagle says. "It confirms our earlier findings that gut microflora are the key to maintaining a balanced immune response, that changing the composition of microflora in the gut predisposes animals to allergic airway disease, and that allergic sensitization can occur outside the lungs."

Noverr and Huffnagle suspect that changes in gut microflora caused by widespread use of antibiotics and a modern high-fat, high-sugar, low-fiber diet could be responsible for a major increase, over the last 40 years, in cases of chronic asthma and allergies in Western industrialized countries.

"The recent increase in allergies and asthma has been attributed to what's called the 'hygiene hypothesis,' the idea that children in Western countries are not exposed to enough infections early in life to prevent the immune system from reacting to harmless antigens," Noverr explains. "We're coming at it from a different angle. Our emphasis is on what's going on in the GI tract."

The link between lung and gut may not seem obvious at first. But Huffnagle points out that every time we swallow, particles of dust, pollen and spores – trapped by mucus-producing cells and tiny hairs lining the respiratory tract – are washed into the stomach where they come in direct contact with immune cells in the GI tract

"Think of the body as a big tube with everything from nose to rear end exposed to allergens from the outside world," Huffnagle says. "The immune system's normal response to all this stuff we constantly inhale is to actively ignore it – a reaction we call tolerance. The key to tolerance is an immune cell called a regulatory T cell."

Discovered just a few years ago, regulatory T cells are under intense research scrutiny, because of their ability to moderate or cool down the immune response.

"If lungs are repeatedly exposed to an allergen, regulatory T cells learn to recognize the allergen as not dangerous and something that can be safely ignored," Huffnagle says. "Most researchers think that tolerance develops in the lungs, but we believe it actually occurs in the gut. When immune cells in the GI tract come in contact with swallowed allergens, that interaction triggers the development of regulatory T cells, which then migrate to the lungs."

Everyone has a personal microbial fingerprint – a unique mix of bacteria and fungi living in the stomach and intestines – which develops in the first years of life. As long as the balance of gut microflora remains stable, tolerance continues. But anything that alters this intestinal balance – taking antibiotics, switching from breast milk to formula, eating a high-sugar, low-fat diet – interferes with the system and can lead to problems. "One short course of antibiotics is not going to give everyone allergies," Huffnagle says "But if you are taking antibiotics while your diet consists of white bread and fried food, you are not going to maintain the healthy microflora balance you need to maintain tolerance. If you inhale mold spores or pollen during this period, our studies indicate you are much more likely to become sensitized to them."

In future research, Huffnagle hopes to learn whether changing only the diet of his experimental mice will alter gut microflora and change the immune response to allergens in the same way as antibiotics. Noverr plans to focus on identifying the microbial compounds that activate the immune response and learning how bacterial dietary supplements called probiotics can affect this microbial balance in a positive way.

"We are not advocating that people stop using antibiotics when they are medically necessary," Huffnagle cautions. "But we are advocating that people understand the importance of eating a healthy diet, with lots of fruits and vegetables, after taking antibiotics to help restore the normal mix of GI microflora as quickly as possible."

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