CONCLUSIONS. The results of this study showed that early colonization of the gut microflora with different species of bacteria affects B-cell activation and maturation. *E. coli* and bifidobacteria colonization may lead to more B-cell activation and maturation, whereas *S. aureus* colonization may lead to lower counts of circulating memory B cells.

REVIEWER COMMENTS. This study was the first to demonstrate that gut bacterial colonization may affect B-cell activation and maturation in humans. The study showed that early colonization of the gut with *S. aureus*, which is increasingly common with improved sanitary conditions in the Western world, is associated with lower counts of circulating memory B cells in infants, whereas early colonization with *E. coli* and bifidobacteria is associated with B-cell activation and maturation. The study team suggests that *S. aureus* colonization may reflect low diversity of gut microbiota and *E. coli* and bifidobacteria colonization may reflect greater diversity of gut microbiota. Whether either the gut microbiome or lower levels of B-cell activation and maturation in early life are risk factors for developing allergic disease is unknown, but evidence linking either to allergic disease would support the conduct of prevention studies aimed at increasing the diversity of the gut microbiome.


Sharon K. Ahluwalia, MD
Elizabeth C. Matsui, MD, MHS
Baltimore, MD

Peripheral Education of the Immune System by Colonic Commensal Microbiota

PURPOSE OF THE STUDY. To determine if the gut microbiota is important for the development of regulatory T cells (T<sub>REG</sub>), which help maintain tolerance by regulating inflammatory responses in the intestine.

STUDY POPULATION. Studies were performed in mice.

METHODS. The authors evaluated T-cell receptor (TCR) diversity and specificity of T<sub>REG</sub> and effector T cells isolated from the gut and peripheral lymphoid tissues. The authors then performed T-cell transfer studies to determine if lymphocytes specific for the gut microbiota had pathogenic potential in mice genetically predisposed for spontaneous colitis.

RESULTS. The authors discovered that the TCR repertoire for colonic T<sub>REG</sub> was distinct from that for other effector T cells in the gut and T<sub>REG</sub> isolated from other lymphoid tissues. A significant proportion of colonic T<sub>REG</sub> were specific for antigens derived from gut bacteria. Unlike conventional T<sub>REG</sub>, which are derived in the thymus, colonic T<sub>REG</sub> primarily developed from naive T cells in peripheral tissue. The TCR repertoire of colonic T<sub>REG</sub> was shaped by the animal’s own unique microbiome, as T<sub>REG</sub> from one mouse did not recognize colonic bacteria from another mouse unless they were first co-housed. Finally, the authors demonstrated that in mice genetically predisposed for spontaneous colitis, naive T cells could develop into pathogenic effector T cells rather than T<sub>REG</sub>.

CONCLUSIONS. In normal mice, T cells that recognize commensal bacteria preferentially differentiate into T<sub>REG</sub> in the colon, thereby promoting tolerance to the gut microbiota and preventing the development of detrimental inflammatory disease.

REVIEWER COMMENTS. The gut microbiome has gained significant attention recently for its putative importance in human health and disease. In experimental animals, it has long been known that homeostasis critically depends on proper bidirectional communications between the microflora and the immune system. However, little is known about the specific mechanism or mechanisms by which an animal tolerates these trillions of microbes. The studies by Lathrop et al add direct evidence that each animal develops its own repertoire of peripherally induced T<sub>REG</sub> that are critically involved in promoting tolerance to foreign antigens in its gut. These findings also infer that alteration of the gut microbiota as seen with indiscriminate antibiotic use could disrupt the development of T<sub>REG</sub>, thereby predisposing individuals to developing immunopathology, such as inflammatory bowel disease or food allergies.


Timothy P. Moran, MD, PhD
Brian P. Vickery, MD
Durham, NC

Reduced Diversity of the Intestinal Microbiota During Infancy Is Associated With Increased Risk of Allergic Disease at School Age

PURPOSE OF THE STUDY. To investigate the potential association between the diversity of neonatal intestinal microbiota and the development of atopic disorders in childhood.

STUDY POPULATION. Four hundred eleven infants born in Copenhagen to mothers with a history of asthma were enrolled from the years 1998 to 2001.

METHODS. Infants had an initial visit at 1 month of age and were subsequently seen for a scheduled visit every 6 months until the age of 6 years. Atopic disease was assessed through examination by doctors at the clinical research unit with support from symptom diaries kept by
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Pediatrics 2012;130;S47
DOI: 10.1542/peds.2012-2183ZZZ

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