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Inflammation Enhances Intestinal Infection

A healthy intestinal tract is a wondrous ecosystem. In humans, more than 500 different kinds of bacteria reside there, helping to keep us fit and functioning.

But when pathogenic microbes or chemicals inflame the intestine, the balance of microbial power shifts. According to a new study from the laboratory of Howard Hughes Medical Institute (HHMI) international research scholar B. Brett Finlay, inflammation creates an environment that helps invading bacteria thrive.

In the August 15, 2007 issue of the journal *Cell Host and Microbe*, Finlay and his colleagues at the University of British Columbia report that host-mediated inflammation, which occurs in response to an infectious agent, chemical trigger, or genetic predisposition, markedly alters the microbial community in the intestines.

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> **- B. Brett Finlay**

"There is no doubt that changes and shifts in the numbers (of bacteria) and host inflammation play a key role and can facilitate infection by making a more favorable environment" for invading pathogens, said Finlay.

The group's findings in mice help portray how bacterial populations in the intestine ebb and flow. The research revealed that surprisingly, inflammation, a defensive reaction by the body that causes pain and swelling, can actually work to the advantage of pathogens.

A healthy bacterial ecosystem in the intestine is essential for well-being. Bacteria that live there help promote tissue growth, enhance the development of the intestine, jump start the acquisition of nutrients, bolster the immune system, and defend against pathogens. Resident bacteria help keep pathogens

at bay, for example, by out-competing them for space, nutrients, and the cell receptors bacteria depend on.

But despite their importance, there are many unanswered questions about how intestinal microbiota, which colonize every human almost instantly after birth, interact and function under healthy and unhealthy circumstances. One key question, said Finlay, is what happens to the normal biota when you experience diarrhea or other intestinal disease?

"No one has really looked at what happens to the normal biota during infections," Finlay explained.

To answer the question, Finlay and his team turned to mouse models of human diseases, including *E. coli* diarrhea and *Campylobacter jejuni*, a bacterium that is a leading cause of bacterial diarrhea but does not cause inflammation in mice. By sampling stools and labeling the bacteria found there, Finlay's group obtained a broad profile of the major groups of bacteria that inhabit the colon and how those populations change when confronted with disease.

The most important finding, Finlay said, was that in both sets of mice, there was a significant reduction in the total number of bacteria, while the numbers of proteobacteria and enteric bacteria - two major groups of bacteria that include many pathogens -- increased.

And when inflammation occurs, it seems to alter the intestinal environment in ways that make it easier for pathogens to settle in and do their dirty work.

"Once we got going, we realized inflammation was playing a role," Finlay explained. "If you trigger inflammation, you get profound shifts in the numbers and distribution" of the major groups of bacteria that inhabit the intestine.

To be sure that inflammation was responsible for the changes they had observed, Finlay's team induced inflammation in other ways - both chemically and through the use of mice genetically disposed to inflammation. Inflammation on its own, Finlay said, was enough to perturb the composition of the microflora community in the intestine in a similar manner.

That finding, he said, may have implications for better understanding non-infectious inflammatory bowel disease such as ulcerative colitis and Crohn's disease.

However, no matter what causes intestinal inflammation and subsequent swings in the gut's bacterial populations, the microbial community there has the ability to reset itself to pre-disease conditions, Finlay's team observed. In infected mice, once the immune system had cleared the infection, the composition of microbiota populations returned to the number and

distribution seen in uninfected animals.

Overall, the new study provides a snapshot of how the richly populated intestinal ecosystem changes when challenged by disease. "It gives us a completely consistent and reproducible picture of what's going on," Finlay said.