Cholera Strengthened By Trip Through Gut

Pathogenic squatters. In this mouse small intestine, Vibrio cholerae bacteria (inset) have latched onto cells lining the gut.

Poor sanitation promotes the spread of cholera, but that’s not the only way humans foster the deadly diarrheal disease. Microbiologists have discovered that the human gut seems to prime the bacteria responsible. Before Vibrio cholerae exit the body in watery stools, something about the intestinal environment causes them to rev up the activity of certain genes. These genes, in turn, seem to prepare them for ever more effective colonization of their next victims, possibly fueling epidemics, says Andrew Camilli, a microbiologist at Tufts University School of Medicine in Boston.

“The hypothesis that passage through the host enhances infectivity is quite provocative,” comments Matthew Waldor, a microbiologist at Tufts—New England Medical Center in Boston. Adds Vic DiRita, a microbiologist at the University of Michigan, Ann Arbor: “It’s really amazing. It may explain the rapid and explosive nature of these epidemics.”

A thwarted experiment put Camilli and his colleagues on the trail of this so-called hyperinfectivity. He and others had long wondered why cholera epidemics become rampant as quickly as they do. Camilli thought the microbes residing in the human gut might develop defenses against the gut’s acid environment. As a result, more of the excreted, acid-tolerant bacteria would survive in subsequent hosts. But when the researchers went to Dhaka, Bangladesh, to get fresh Vibrio to test this idea, technical difficulties foiled the experiment.

Instead, graduate students Susan Butler and D. Scott Merrell, who is now at Stanford University School of Medicine, made a peculiar observation. While in Bangladesh, they injected mice with a mixture of bacteria grown in the lab and isolated from human stools. The stool-derived bacteria greatly outcompeted the lab-derived bacteria, the researchers found, calculating that the former were up to 700 times more infectious than the latter.

This increased infectivity lasted at least 5 hours in bacteria living in pond water—long enough for someone to drink the infected water, says Camilli. However, the hyperinfectivity disappeared when the microbes were grown more than 18 hours in the lab, the team reports in the 6 June issue of *Nature*.

To understand what made excreted Vibrio different from their laboratory counterparts, Camilli and Stanford microbiologist Gary Schoolnik looked for changes in gene expression. They exposed a microarray made with pieces of *Vibrio*’s genes to Vibrio RNA isolated from fresh stools or lab strains. Some 3120 of the 3357 genes studied were equally active. But in the stool-derived sample, 44 genes were more active and 193 were less active.

When the researchers looked at the most logical suspects for increased infectivity, the University of Michigan, Ann Arbor: “It’s really amazing. It may explain the rapid and explosive nature of these epidemics.”