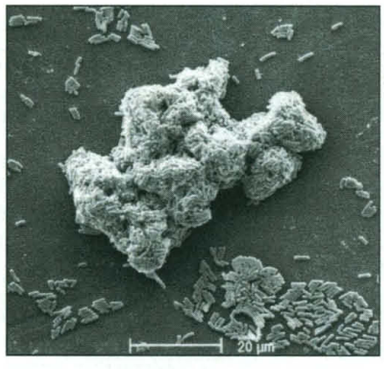
MICROBIOLOGY

A Tangled Tale of *E. coli* Virulence

Most people would do anything to avoid a bout of diarrhea. But along with 59 other brave souls at Stanford University, I lined up last year to drink a microbial cocktail the very thought of which seems guaranteed to turn the bowels to water. Sequestered in the clinical research center for 3 days, we anxiously awaited the first signs of the bacterial onslaught and clutched at our last remaining vestiges of dignity as nurses and scientists monitored the outcome. Our sacrifice for science—for which we were paid $300—was not in vain: It turns out that our diarrheal responses revealed a subtle feature of the mechanism that helps explain the virulence of enteropathogenic *Escherichia coli* (EPEC), a common cause of diarrhea in children in developing countries.



BIEBER *ET AL.*

Togetherness. Mutant bacteria stick tightly together—perhaps too tightly.

On page 2114, Stanford microbiologist Gary Schoolnik and his colleagues confirm expectations that hairlike appendages on the surface of EPEC known as bundle-forming pili (BFP) are critical to the full virulence of these bacteria. The pili bundle together into ropelike filaments that interweave among bacteria, binding them into large aggregates. But the tests also suggest that another key to EPEC's virulence is the ability of the pili to disentangle themselves so the bacteria can go on to infect new intestinal cells. "The results are very surprising," says microbiologist Michael Donnenberg of the University of Maryland, Baltimore.

Schoolnik and members of his team have been studying EPEC's pili since they discovered them in 1991 (*Science*, 1 November 1991, p. 710). A strong hint that pili are important for virulence came when they and others mutated some of the 14 genes known to control pili formation and produced strains of bacteria lacking these appendages: The organisms couldn't attach to epithelial cells in the test tube or form bacterial aggregates. As the group now reports, the bugs proved relatively benign when fed to human volunteers. However, another mutant strain—dubbed the *bfpF* mutant—has produced more unexpected results.

At first glance the *bfpF* mutant seemed to be an overachiever. Schoolnik and Donnenberg independently showed that these bacteria aggregate into clusters and stick to epithelial cells in greater numbers than the wild-type EPEC. They also seemed to produce more pili and adhere more closely to human cells than their wild-type cousins. But when the Stanford group used time-lapse photomicrography to take a look at their behavior, they found a subtle difference: Wild-type bacteria form aggregates that disperse over time, but the *bfpF* mutants remained clumped together in a mass.

"We had a bet in the lab at that point," says Schoolnik. "Some bet that it [the F mutant] would have increased virulence, some bet that it would have no virulence." So they recruited more volunteers and returned to the clinical research center. The results were significant. Only four of 13 volunteers developed diarrhea, succumbing to doses of 2×10^{10} or 1×10^{11} mutant bacteria, compared to 11 of 13 in another set of volunteers who received doses of wild-type EPEC ranging from 5×10^{8} to 2×10^{10}. The EPEC mutant "does almost everything better in vitro, yet causes so much less disease when given to volunteers," says Donnenberg.

Schoolnik's team concludes that the *bfpF* mutant can infect and colonize the human gastrointestinal tract but fails to disperse, which severely reduces its power to cause diarrhea. "It all links in together very nicely and very logically," says Alan Phillips, a pediatric gastroenterologist from London's Royal Free Hospital. "If you can't aggregate and disaggregate, then you're not going to colonize very effectively."

Microbiologist James Kaper of the University of Maryland, Baltimore, agrees that the study provides "conclusive evidence that BFP are required for full virulence of this organism." But he is not yet convinced that the human tests prove that aggregate dispersal is critical for virulence. "The dispersal phase is a reasonable hypothesis," he says, but the mutant bacteria may colonize different sites in the intestine, or other unknown factors may contribute to reduced virulence.

Donnenberg agrees that human tests can't answer all the questions. "We consider the human model the gold standard, but there are big limitations," he says. "The volunteer is a big black box. We put bugs in one end and measure diarrhea out the other end, and what happens inside we really have no clue."

–Kristin Weidenbach

Kristin Weidenbach is a science writer in Boston. She received the highest dose of the bfpF *strain.*

ECOLOGY

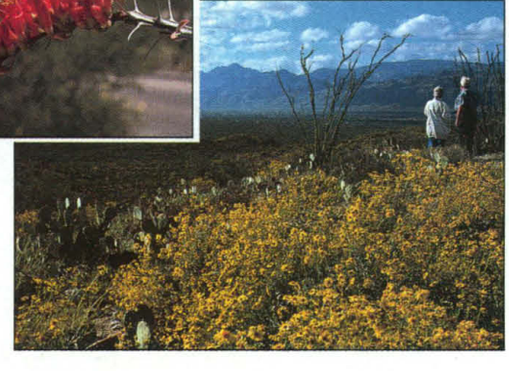
El Niño Drives Spectacular Flower Show

TUCSON, ARIZONA—The serrated Tucson Mountains that rise above their namesake city are usually hospitable only to cacti and other hardy desert life-forms. This spring, however, the Tucsons' volcanic soil—along with much of the rest of the Southwestern desert—erupted in wildflowers, from golden poppies to velvet-red ocotillo and the sunflower blooms of brittlebush. Experts have proclaimed the display one of the desert's most dazzling blooms of the century.

The rainbow-hued outburst came courtesy of El Niño, the Pacific Ocean warm-up blamed for the rainstorms last winter that drenched much of the Southwest and triggered fluky weather elsewhere in the Americas. Although the capricious climate was a bane to many a mud-encrusted homeowner, it has been a boon to scientists hoping to learn more about how wildflowers survive in harsh climates—and why not every flower blooms in every rainy year.

Good wildflower blooms hit the Southwest about once a decade, says botanist Mark Dimmitt of the Arizona-Sonora Desert Museum near Tucson. But the last banner year, he says—when "all you have to do is go out in the desert and see flowers everywhere"—was 1979. Nineteen relatively flower-poor years followed, until last winter's El Niño, combined with a late-September hurricane that swept inland from the Baja Peninsula.

Throughout the winter and early spring, El Niño–driven storms dumped two to four



Wonderland. Ocotillo *(inset)* and brittlebush helped fuel El Niño's floral fireworks.

PHOTOS: R. A. LOVETT