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Single dose of antibiotic leaves mice highly vulnerable to intestinal infection

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Yet another study adds to the growing evidence that antibiotics can disrupt the balance of the intestinal flora, with negative effects on health. A team of researchers from the Memorial Sloan Kettering Cancer Center, New York City, has shown in mouse models that a single dose of the commonly used antibiotic, clindamycin, wiped out nearly 90 percent of bacterial taxa, leaving the mice unusually susceptible to infection by Clostridium difficile, a bacterial pathogen that is innocuous for most health people but that can cause severe diarrhea in individuals following antibiotic treatment. Their research appears in the January issue of the journal *Infection and Immunity*.

Clindamycin was already known to be "highly associated with the development of Clostridium difficile infections" in humans and mice, says corresponding author Eric G. Pamer. In earlier work, Trevor Lawley had shown that clindamycin administration results in chronic shedding of C. difficile spores by infected mice. The researchers, who included Pamer's colleagues Charlie Buffie and Joao Xavier, hypothesized that "clindamycin-mediated destruction of the complex but stable networks of interacting and interdependent bacterial species [in the intestine] would result in marked instability of the microbiota," that would leave the mice vulnerable to infection, says Pamer, adding that "Our long-term goal is to determine which intestinal bacteria provide resistance to Clostridium difficile infection."

Following the single dose of clindamycin, the investigators "found that mice became highly susceptible to infection and developed severe

weight loss, and had a mortality rate of roughly 40 percent," says Pamer. "Surviving mice continued to be infected with C. difficile for 28 days and had persistent bowel inflammation."

Next the team investigated clindamycin's impact on the intestinal microbioata, by isolating the contents of the small intestine and the cecum, and using the "454 deep DNA sequencing platform" to identify species. "To our surprise, roughly 87 percent of the bacterial species that were present prior to antibiotic treatment were undetectable following clindamycin administration, a loss of diversity that persisted for the 28 day duration of this study," says Pamer. During this time, the bacterial species composition fluctuated wildly.

The study demonstrates how the application of deep sequencing platforms to analyze complex microbial populations, such as those that inhabit the human gut can lead to understanding, and perhaps predicting susceptibility to infection by highly antibiotic resistant bacteria, such as C. difficile or vancomycin resistant Enterococcus, says Pamer.

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More information: C.G. Buffie, et al., 2011. Profound alterations of intestinal microbiota following a single dose of clindamycin results in sustained susceptibility to Clostridium difficile-induced colitis. *Infect. Immun.* 80:62-73.

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