

Study documents failure rate of antibiotic treatment for gonorrhea

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In an examination of the effectiveness of cefixime, the only oral cephalosporin antimicrobial recommended for treatment of *Neisseria gonorrhoeae* (gonorrhea) infections, researchers found a clinical treatment failure rate of nearly 7 percent for patients treated at a clinic in Toronto, according to a preliminary study published in the January 9 issue of *JAMA*.

"Because of *Neisseria gonorrhoeae* resistance to all prior first-line antimicrobial agents, cephalosporin [antibiotic] therapy with adjuvant [azithromycin](#) or [doxycycline](#) is recommended for treatment of gonorrhea," according to background information in the article. [Cefixime](#) is the only oral cephalosporin recommended for gonorrhea treatment. "An increase in the minimum inhibitory concentration [MIC; lowest concentration of an antimicrobial agent that will prevent the growth of an organism] of *N. gonorrhoeae* to cefixime, and to a lesser extent, an intramuscularly administered cephalosporin, ceftriaxone, has been identified in cultured isolates worldwide. The [World Health Organization](#) has sounded alarms for the threat of untreatable gonorrhea."

Vanessa G. Allen, M.D., M.P.H., of [Public Health Ontario](#), Toronto, Canada, and colleagues conducted a study to determine whether *N. gonorrhoeae* strains with reduced susceptibilities to cefixime are associated with clinical failures. The study group consisted of *N. gonorrhoeae* culture-positive individuals identified between May 2010 and April 2011 and treated at a sexual health clinic in Toronto with cefixime as recommended by [Public Health Agency of Canada](#) guidelines. The primary outcome measure for the study was cefixime treatment failure, defined as the repeat isolation of *N. gonorrhoeae* at the test-of-cure visit identical to the pretreatment isolate by molecular typing and explicit denial of re-exposure.

There were 291 *N. gonorrhoeae* culture-positive individuals identified. Of 133 who returned for test

of cure, 13 were culture positive; 9 patients were determined to have experienced cefixime treatment failure, with an overall rate of clinical [treatment failure](#) of 6.77 percent. The rate of clinical failure associated with a cefixime MIC of 0.12 µg/mL or greater was 25 percent compared with 1.90 percent of infections with cefixime MICs less than 0.12 µg/mL.

"This study presents the first series of clinical failures of gonorrhea associated with the use of cefixime in North America, identified by the concurrent strategies of routine test-of-cure and culture-based testing for *N. gonorrhoeae*," the authors write.

"In light of the increases in cefixime MICs among isolates of *N. gonorrhoeae* across North America, this study offers preliminary clinical data to support the recent CDC recommendations that cefixime is no longer optimal first-line therapy for the successful treatment of gonorrhea. As elevated MICs to ceftriaxone are also emerging, albeit at 1 to 2 MIC dilutions less than the cefixime MIC, proactive strategies for the identification of clinical failures of *N. gonorrhoeae* to this last commercially available agent are required."

In an accompanying editorial, Robert D. Kirkcaldy, M.D., M.P.H., of the Division of STD Prevention, Centers for Disease Control and Prevention, Atlanta, and colleagues write that the findings of this study, of documented cephalosporin treatment failures in North America, although expected, "its arrival is deeply troubling; clinicians now face the emergence of cephalosporin-resistant *N. gonorrhoeae* without any well-studied, effective backup [treatment](#) options."

"New antibiotics for treating gonococcal infections are needed. A clinical trial sponsored by the National Institute of Allergy and Infectious Diseases examining novel combinations of existing drugs just completed enrollment, and a small study of a new

oral agent is ongoing. But the antibiotic pipeline is running dry: continued investment in antibiotic development is critical. Meanwhile, the gonococcus has continued to develop the capability to defeat each new antibiotic used. The threat of drug-resistant gonorrhea is increasing and has reached North America. Clinicians, drug developers, and public health professionals must act now."

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