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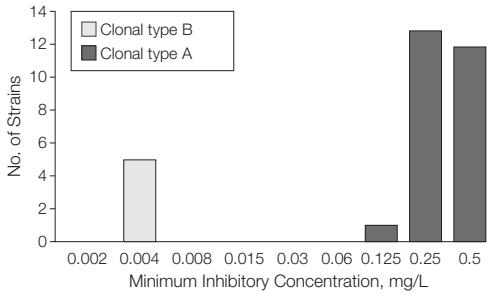
RESEARCH LETTER

Susceptibility to Fluoroquinolones of *Vibrio cholerae* O1 Isolated From Diarrheal Patients in Zimbabwe

To the Editor: Cholera is endemic in many countries in Asia, Latin America, and Africa. Sub-Saharan African countries, particularly Angola, Congo, Mozambique, and Zimbabwe, have been strongly affected by cholera in recent years, with a large epidemic occurring in Zimbabwe in 2008. From August 2008 until February 2009, 70 640 patients were reported with cholera in Zimbabwe, of whom 3467 died.[1] On request from the World Health Organization, a team from the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDRB), went to Zimbabwe to assess the cholera situation and provide assistance to control the outbreak. Preliminary data on the antibiotic resistance of *Vibrio cholerae* O1 strains that were isolated from the patients in Zimbabwe are reported.

Methods. Stool and rectal swab specimens were collected from randomly selected patients at 4 cholera treatment centers in Zimbabwe, including Beatrice Road Infectious Diseases Hospital and Budiriro in Harare province, Chinhoyi in Mashonaland West, and Binga in Matebeleland North provinces. *V cholerae* O1 was isolated and identified following standard procedures.[2] The presence of virulence-associated genes (including genes encoding cholera toxin) and the major colonization factor (toxin coregulated pilus) were tested by specific polymerase chain reaction assays.[2] The strains were also subjected to ribotyping to assess clonal relationship.[3] The minimum inhibitory concentrations (MICs) of ciprofloxacin, tetracycline, and azithromycin were determined using Etest (AB bioMérieux, Solna, Sweden) following standard procedures. The measured MICs were rounded to the nearest higher 2-fold dilution. The strains were also tested for sensitivity using the disk diffusion method. Protocols were approved by the Ministry of Health and Child Welfare and the World Health Organization, Harare, Zimbabwe, and patients provided oral consent for participation.

Figure. Ciprofloxacin Susceptibility of 31 *Vibrio cholerae* O1 Isolates From Zimbabwe



The measured minimum inhibitory concentrations were rounded to the nearest higher 2-fold dilution.

Results. A total of 64 stool and rectal swab samples were collected from January 16 to January 27, 2009. *V cholerae* O1 was isolated in 38 samples (59%). All isolates belonged to the El Tor biotype; 31 and 7 isolates belonged to Ogawa and Inaba serotypes, respectively. Of the 38 isolates, 31 strains were available for further testing. Two distinct ribotype patterns (A and B) were observed among the isolates.

All strains were susceptible to azithromycin and tetracycline, with MIC_{90} (MIC required to inhibit the growth of 90% of organisms) of 0.125 mg/L and 0.5 mg/L, respectively. The MIC_{90} of ciprofloxacin was 0.5 mg/L, with a distinction between the ciprofloxacin susceptibility of ribotype A and ribotype B. The ciprofloxacin MIC of ribotype A ranged from 0.125 to 0.5 mg/L. The ciprofloxacin MIC of type B was 0.004 mg/L (FIGURE). Thus, the ciprofloxacin MICs of clonal type A were 30 to 125 times higher than those of clonal type B and within 1 to 3 two-fold dilutions of the susceptibility breakpoint of 1 mg/L. The strains of clone B were susceptible to nalidixic acid by disk diffusion, but clone A strains were resistant. All strains were resistant to furazolidone and trimethoprim-sulfamethoxazole.

Comment. To our knowledge, this is the first description of an outbreak of cholera with reduced susceptibility against fluoroquinolones on the African continent. Nalidixic acid resistance has been reported in Ghana and Mozambique, but no quantitative susceptibility tests or MICs were performed and no resistance to fluoroquinolones was detected.[4]

Ciprofloxacin resistance may be associated with progressive multiple mutations in the *gyrA* gene[5]; nalidixic acid resistance may therefore have facilitated the emergence of resistance to the fluoroquinolones. Reduced susceptibility of *V cholerae* against ciprofloxacin (MIC, 0.25 mg/L) has been reported previously in patients hospitalized in Bangladesh and was associated with therapy failure in these patients.[6] The reported reduced susceptibility is therefore reason for concern.

Antimicrobial susceptibility is often not determined in cholera, and qualitative antimicrobial susceptibility tests (eg,

disk diffusion) may fail to detect strains with reduced susceptibility. Longitudinal surveillance of antimicrobial susceptibility of *V cholerae* O1 using quantitative (MIC) methods is therefore recommended for early detection of emergence of resistance.

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Study concept and design: Midzi, Cravioto, Endtz.
Acquisition of data: Midzi, Charimari.
Analysis and interpretation of data: Islam, Cravioto.
Drafting of the manuscript: Midzi, Charimari.
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CORRECTIONS

Incorrect Funding Source: In the Original Contribution entitled "Comparison of Liquid-Based Cytology With Conventional Cytology for Detection of Cervical Cancer Precursors: A Randomized Controlled Trial" published in the October 28, 2009, issue of *JAMA* (2009;302[16]:1757-1764), a funding institution was incorrectly identified in the "Funding/Support" section on page 1764. The last sentence of the section that read "Dr Arbyn also received funding from the Foundation Against Cancer" should have read "Dr Arbyn also received funding from the Belgian Foundation Against Cancer."

Incomplete Sentence: In the Original Contribution entitled "Cardiometabolic Risk of Second-Generation Antipsychotic Medications During First-Time Use in Children and Adolescents" published in the October 28, 2009, issue of *JAMA* (2009;302[16]:1765-1773), data were left out of a sentence in the abstract on page 1765. The sentence in the Design, Setting, and Patients section that read "There were 205 patients who completed the study (61.7%)" should have read "Of these patients, 272 had at least 1 postbaseline assessment (80.5%), and 205 patients completed the study (60.7%)." This article was corrected online for error in data on October 27, prior to publication of the correction in print.

Table Column Heading Error: In the Original Contribution entitled "Attitudes, Training Experiences, and Professional Expectations of US General Surgery Residents: A National Survey," published in the September 23/30, 2009, issue of *JAMA* (2009;302[12]:1301-1308), the column headings for "Men" and "Women" in Table 3 on page 1306 were inverted.

Missing Byline Information: In the Original Contribution entitled "Effects of Exercise Training on Health Status in Patients With Chronic Heart Failure: HF-ACTION Randomized Controlled Trial," published in the April 8, 2009, issue of *JAMA* (2009;301[14]:1451-1459), an error occurred in the byline on page 1451. The byline should have included "for the HF-ACTION Investigators" as the last line. Also on page 1451, the following footnote should have appeared: "**A list of the HF-ACTION Investigators** is published on page 1449."