was 1.60 (95% confidence interval [CI], 1.02–2.51), $P = .04$.
2. Of those subjects who received a PPI and vancomycin alone, the relapse rate was 28.0% (7/25), compared to 10.3% (8/78) in those who received vancomycin alone and no PPI. The unadjusted OR was 3.40 (95% CI, 1.09–10.63), $P = .05$.
3. Of those who received any treatment (metronidazole or vancomycin or both) and a PPI, the relapse rate was 33.8% (68/201), compared to 21.7% (123/568) for those who did not receive a PPI. The unadjusted OR was 1.85 (95% CI, 1.30–2.64), $P < .01$.
4. Of those patients who received both metronidazole and vancomycin as well as a PPI, the relapse rate was 42.9% (21/49), compared to 26.2% (37/141) for those who received both agents but not a PPI. The unadjusted OR was 2.11 (95% CI, 1.07–4.16), $P = .03$.

Our data suggest that PPI use is associated with a significantly increased risk of relapse, in unadjusted analyses, for both those who were treated with metronidazole and those who were treated with vancomycin. However, this analysis has several limitations. Our conclusions are based on unadjusted numbers, so unaccounted-for confounders may affect the results. Nevertheless, in our logistic regression model PPI use remained an independent predictor of relapse when adjusted for other factors, including age, metronidazole treatment, antibiotic exposure, and length of stay. In addition, the number of patients in our study who received vancomycin alone was small. In the subgroup of patients who received both metronidazole and vancomycin, there was an extremely high relapse rate in those who were given a PPI versus those who were not. It is possible that those patients had treatment failure with metronidazole; however, our data collection technique did not allow for that level of granularity.

In summary, our retrospective cohort study suggests that the use of a PPI is a predictor of readmission independent of choice of treatment. However, our study was not designed to address whether the concurrent use of PPI and metronidazole might lead to primary treatment failures. Dr Daniell presents an interesting insight that certainly deserves more study.

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Identification of *Clostridium difficile* Ribotype 027 for the First Time in Mainland China

To the Editor—Although several studies have shown that the incidence of infection with *Clostridium difficile* is increasing in Asia as a consequence of widespread use of broad-spectrum antibiotics,[1] very little is known about the epidemiology of *C. difficile*–associated diarrhea in developing countries. The hypertoxigenic epidemic strain of *C. difficile*, named ribotype 027, has also rarely been detected in Asia, especially in China.[2,3]

In a retrospective study, we performed epidemiologic screening of patients with *C. difficile* infection (CDI) and investigated the characteristics and epidemiology of *C. difficile*–associated diarrhea in a large teaching hospital in South China. Fresh stool samples were collected from patients with suspected CDI over a 2-year period (December 2009–May 2012). Of the 3,660 stool samples, 572 (15.6%) were positive for *C. difficile* toxin by direct polymerase chain reaction (PCR).[4,5] Logistic regression analysis showed that previous antibiotic use ($P = .04$) and CDI experience ($P < .01$) were significant risk factors for toxin-positive diarrhea. *C. difficile* ribotype 027 was not found, although 7 cases of specimens detected binary toxin successfully.

We also studied the relationship between CDI and inflammatory bowel disease. Stool specimens from 406 patients with inflammatory bowel disease, including 241 patients with Crohn's disease and 165 with ulcerative colitis, were collected from January 2010 to April 2013 in Nanfang Hospital. Thirty-four patients with Crohn's disease and 34 patients with ulcerative colitis were positive for *C. difficile*, with positive rates of 14.1% and 20.6%, respectively. Three stool samples were

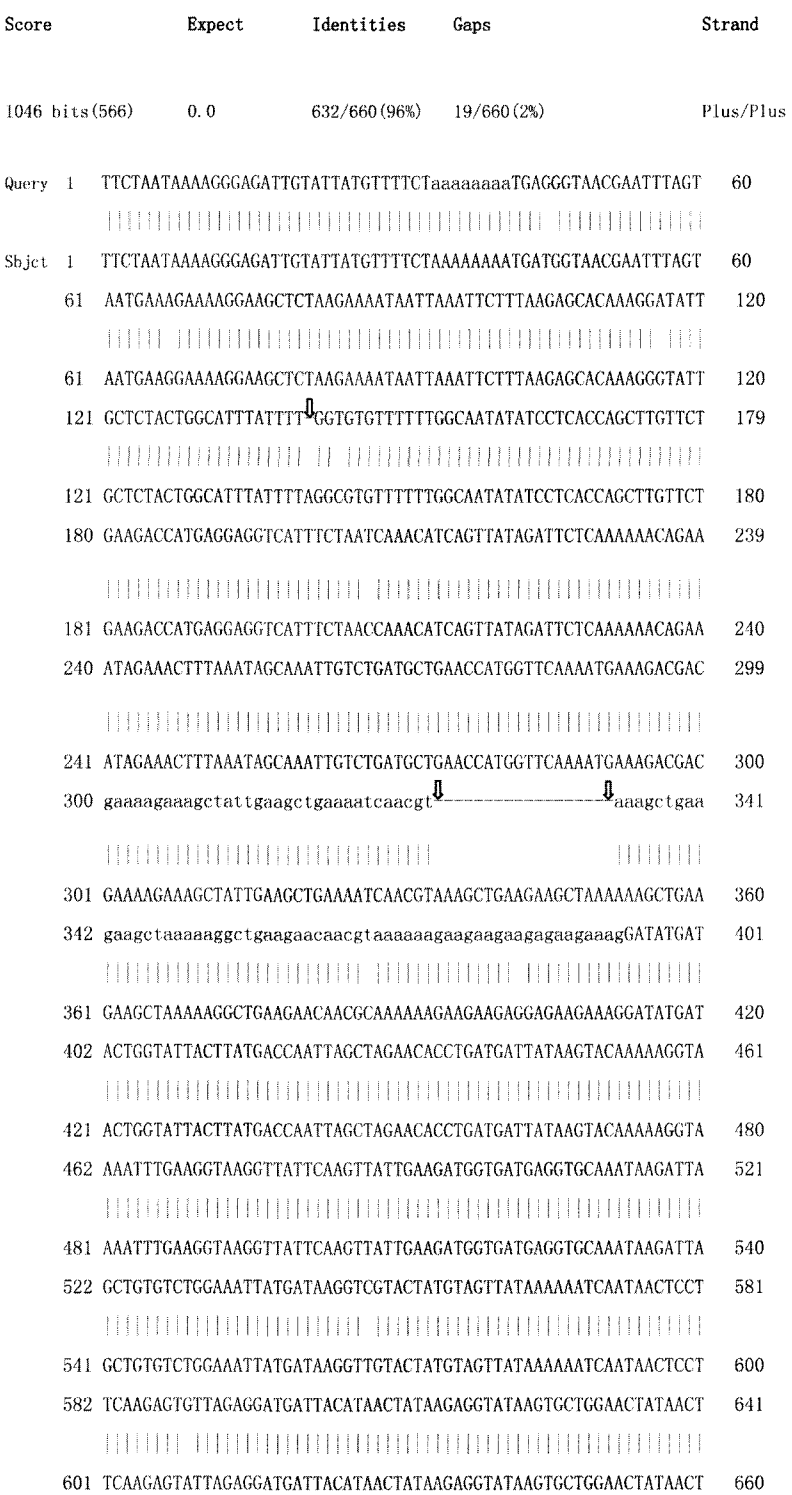

FIGURE 1. Query, *tcdC* gene of the isolated strain from a patient with Crohn's disease that contains both the 18–base pair deletion and a single-nucleotide deletion compared with the *tcdC* gene of API10463; sbjct (subject), *tdcC* gene of the reference strain (API10463).

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found to contain binary toxin genes, one of which ultimately proved to contain ribotype 027. This represents the first report of the presence of ribotype 027 in Mainland China and may indicate the onset of ribotype 027 CDI spreading in China.

The total of 10 *C. difficile* strains that tested positive for the binary toxin genes were isolated and further analyzed if they were ribotype 027. Only 1 strain isolated from the patient with Crohn's disease was characterized as ribotype 027 by PCR ribotyping.[6-8] Sequence analysis of *tcdC* showed a single base pair (bp) deletion and a well-documented 18-bp deletion; the rest of the sequence was identical to the sequence results for the reference strain (API10463; Figure 1).[6,9,10] The results were confirmed by Gene Xpert (Cepheid, GX-XVI), which detects the toxin B gene (*tcdB*), the binary toxin gene (*cdt*), and the *tcdC* gene deletion at nt 117.

Characteristics of the patient with *C. difficile* ribotype 027 were analyzed. On October 29, 2012, a 44-year-old female patient with chronic abdominal pain and recurrent diarrhea (6 or more bowel movements per day) lasting for 3 years was admitted to Nanfang Hospital. She and her family members had never been abroad before. Medical history included hospitalizations in a local hospital because of enterophthisis and antitubercular therapy (isoniazid, rifampin, streptomycin), but her condition did not improve. In 2011, she was admitted to Nanfang Hospital and received a diagnosis of Crohn's disease. The patient was treated with long-term mesalazine and dexamethasone and later 3 infusions of infleximab therapy. During her October 2012 admission, she developed a relapse of diarrhea and tested positive for *C. difficile* ribotype 027. She recovered after 2 weeks of oral vancomycin treatment. No relapse of CDI was reported over the next 5 months. During these months, she was readmitted 4 times for treatment of Crohn's disease and each time tested for CDI. However, *C. difficile* was isolated from her bowel movements again on July 8, 2013. Toxigenic culture and PCR ribotyping demonstrated that the bacterial pathogen causing the diarrhea was *C. difficile* ribotype 027. Genomics and restriction endonuclease analysis showed that both infections were caused by the same ribotype 027 strain.

C. difficile is the cause of many cases of antibiotic- or immunosuppressant-associated diarrhea worldwide. Given the epidemic potential and the severity of the disease, especially among the elderly population, surveillance of *C. difficile* must be introduced along with enhanced prevention and treatment strategies.

Antituberculosis agents are rarely associated with CDI. Among these agents, only rifampin is thought to be a cause of CDI, because of its antibiotic effect on a wide range of bacteria, whereas isoniazid and ethambutol have little or no activity against anaerobes. The patient underwent a period of rifampicin treatment, which supports the premise that antituberculosis treatment may be a risk factor for CDI. The patient was also treated with 3 infusions of infleximab, which demonstrates the importance of identifying risk factors—such as previous hospitalization, antibiotic therapy, and immunosuppression—in the development of *C. difficile*–associated diarrhea.

C. difficile may be an important emerging pathogen in Asia, because it has a strong impact on healthcare systems and costs. CDI can prolong hospital stay and strain hospital systems struggling with high occupancy rates. The aging demographic trend in China may worsen CDI rates, given the increased risk of this disease in elderly patients. The recent detection of *C. difficile* PCR ribotype 027 in multiple Asian countries calls for continued vigilance in clinical and laboratory surveillance, enhanced infection control, and active antimicrobial stewardship so as to address this emerging threat. CDI caused by the hypervirulent strain 027 had never been officially reported in Mainland China before this report. We strongly advise microbiological laboratories to cultivate toxin A– and toxin B–positive stool samples and to apply typing methods to the isolates to obtain more insight into the *C. difficile* types circulating throughout Asia. In summary, the epidemic *C. difficile* 027 strain is now present in China, and enhanced screening for this ribotype in other regions of the country is urgently needed.

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Increase in Chlorhexidine Minimal Inhibitory Concentration of *Acinetobacter baumannii* Clinical Isolates after Implementation of Advanced Source Control

To the Editor—Advanced source control is a strategy to decrease the burden of skin colonization and/or oral cavity carriage of multidrug-resistant pathogens.[1,2] One example of this approach is the use of chlorhexidine bathing with or without oral care to potentially reduce patients' risk of infection associated with healthcare worker hand contamination during healthcare encounters.[1,3,4] To date, the associations of chlorhexidine use and the emergence of chlorhexidine-resistant gram-negative bacteria remain limited.[5-7] We report the associations of combined chlorhexidine baths and oral care associated with the emergence of chlorhexidine with increased in the minimum inhibitory concentration (MIC) of *Acinetobacter baumannii* isolates at a Thai hospital.

Thammasat University Hospital is a 650-bed university hospital located in central Thailand. Hospital units implemented an advanced source control strategy on May 1, 2011, in response to the increased incidence of extensively drug-resistant (XDR) *A. baumannii*, defined as isolates resistant to all available systemic antibiotics except polymyxin B or tigecycline.[8] Fifty consecutive clinical XDR *A. baumannii* isolates obtained during the prechlorhexidine period (October 1, 2010–April 30, 2011) were compared for the MIC 50/90 to 50 consecutive XDR *A. baumannii* isolates during the postchlorhexidine period (May 1, 2011–April 30, 2012). Bacterial isolates were tested by the standard microbroth dilution method recommended by the Clinical Laboratory Standards Institute.[9] Briefly, 100 μL of an overnight bacterial suspension, adjusted to 10^6 colony forming units/mL + 100 μL of the chlorhexidine dilution (1–128 μg/mL), were mixed in a 96-well plate and incubated at 35°C. The MIC was defined as the lowest concentration that inhibited visible growth after 24 hours. Data collection included specimen source, hospital unit, chlorhexidine consumption (liter/unit/month), chlorhexidine MICs 50/90 for *A. baumannii*, and incidence of XDR *A. baumannii*. Pearson correlation was used to correlate the monthly consumption of chlorhexidine, the change in chlorhexidine MIC, and the prevalence of XDR *A. baumannii*.

In a comparison of the *A. baumannii* MIC 50/90 during the pre- and postchlorhexidine advanced source control periods, the most common specimens were sputum (70/100; 70%) and blood cultures (11/100; 11%). Most clinical specimens were submitted from intensive care units (70/100; 70%) and medical units (15/100; 15%). There was an overall increase in chlorhexidine consumption and *A. baumannii* chlorhexidine MIC 50/90 among all hospital units and all infection sites after implementing advanced source control (Table 1). Although there was a correlation between chlorhexidine consumption and *A. baumannii* chlorhexidine MIC ($r = 0.69$, $P = .01$), the incidence of XDR *A. baumannii* did not increase across hospital units or specimen sources (Table1).

The mechanism of chlorhexidine resistance in *A. baumannii* is purportedly associated with bacterial efflux pumps.[10] In this study, although the magnitude of chlorhexidine exposure resulting in the increase in *A. baumannii* chlorhexidine MICs 50/90 during the 12-month advanced source control period, it did not achieve the threshold for the emergence of chlorhexidine-resistant XDR *A. baumannii* detection, yet our data suggest that ongoing active surveillance for chlorhexidine-resistant *A. baumannii* as well as its MIC 50/90 is needed to evaluate the emergence of chlorhexidine-resistant *A. baumannii*.

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