Infections Due to Non-O1 *Vibrio cholerae* in Southern Taiwan: Predominance in Cirrhotic Patients

Wen-Chien Ko, Yin-Ching Chuang, Guang-Chang Huang, and Shiu-Yuan Hsu

From the Department of Internal Medicine, National Cheng Kung University Hospital, and the Department of Medicine, National Cheng Kung University Medical College, Tainan; and the Southern Branch Laboratory, National Institute of Preventive Medicine, Department of Health, Kaohsiung, Taiwan

Although Taiwan is not an area where cholera is endemic, from October 1988 to October 1997 30 episodes of non–O1, non–O139 *Vibrio cholerae* infection were noted at the National Cheng Kung University Hospital in Taiwan. Infections generally occurred in hot seasons, and two episodes were concomitant with *Vibrio vulnificus* infection. Three major clinical presentations were found: bacteremia with concurrent spontaneous bacterial peritonitis or invasive soft-tissue infections that occurred solely in cirrhotic patients; self-limited acute febrile gastroenteritis that occurred in patients with no underlying medical disease; and necrotizing fasciitis or cellulitis that often resulted from a wound on extremities. Other manifestations included fatal pneumonitis in a drowned man and acute pyosalpinx. The differential diagnosis of invasive infections in cirrhotic patients should include infections due to non-O1 *V. cholerae* or *V. vulnificus*, and a third-generation cephalosporin and a tetracycline analogue or a fluoroquinolone alone is recommended for treatment of severe vibrio infections.

Currently, there are at least 139 serogroups of *Vibrio cholerae* [1]. *V. cholerae* O1 has been well known to be the etiologic agent of cholera, an epidemic or pandemic diarrheal disease. Only the cholera toxin–producing bacteria, including classical and El Tor biotypes of serogroup O1 or O139, have the potential to cause cholera, and they rarely cause extraintestinal infection. Strains of *V. cholerae* not agglutinating with O1 antiserum are referred to as non-O1 or nonagglutinating *V. cholerae*. They are morphologically and biochemically indistinguishable from serogroup O1 [2]. Isolates of *V. cholerae* have been recognized to be heterogeneous for pathogenicity for humans. As is typical for serotype O1, non-O1 *V. cholerae* may cause sporadic cases and occasional outbreaks of diarrheal diseases [2], but non-O1 *V. cholerae* can lead to invasive extraintestinal diseases, often occurring in immunocompromised persons [3, 4].

Suggestive clinical clues for *V. cholerae* infections include travel, seawater or freshwater exposure, or ingestion of raw seafood [5]. Because Taiwan is a subtropical island, a natural environment suitable for the growth of *V. cholerae*, and an area where chronic hepatitis B virus infection is hyperendemic, there are many people with postnecrotic cirrhosis who are susceptible to invasive infections due to *V. cholerae*. To elucidate the clinical presentations of and the morbidity and mortality caused by non–O1 *V. cholerae* infections in Taiwan, a retrospective case survey in a university hospital was conducted.

Materials and Methods

To identify cases of vibrio infections at the National Cheng Kung University Hospital (NCKUH), Tainan, Taiwan, we reviewed the records of the microbiological laboratory from October 1989 to October 1997. The medical records of patients with non–O1 *V. cholerae* infections were screened. Clinical data including demographic characteristics, underlying diseases, results of laboratory studies, treatment course, and clinical outcome were collected. Because of the retrospective nature of this study, culture of seafood or environmental water was not performed.

In Vitro Antibiotic Susceptibility Testing

Twenty-six isolates of *V. cholerae* were available for in vitro antibiotic susceptibility testing by means of the Kirby-Bauer method with use of Mueller-Hinton agar. Drugs tested included the following (μg per disk): gentamicin (10), amikacin (30), ampicillin (10), piperacillin (100), ampicillin/sulbactam (10/10), ticarcillin/clavulanate (75/10), piperacillin/tazobactam (100/10), cephalexin (30), cefuroxime (30), cefixime (5), ceftriaxone (30), cefotaxime (30), ceftazidime (30), imipenem (10), norfloxacin (10), ofloxacin (5), ciprofloxacin (5), tetracycline (30), minocycline (30), chloramphenicol (30), and trimethoprim-sulfamethoxazole (1.25/23.75). The guidelines of the performance procedures and the breakpoint diameters for interpretation of the National Committee for Clinical Laboratory Standards were used [6].

Identification of Species

The identification of *V. cholerae* was as follows. Curved gram-negative bacteria with positive oxidase reaction, β-hemo-
lysis on a blood agar plate, growth of yellow colonies on thiosulfate citrate bile salts sucrose agar, susceptibility to 10 μg and 150 μg of vibriostatic agent O-129 (Rosco, Tåstrup, Denmark), tolerability to 1% salt solution, and intolerability to 10% salt solution were identified as *V. cholerae*. Typical biochemistry profiles for *V. cholerae* included positive nitrate reduction, indole production, catalase production, citrate utilization, Voges-Proskauer test, ornithine decarboxylase production, and lysine decarboxylase production and negative arginine dihydrolase production and urea hydrolysis [7, 8]; these characteristics were noted by the API 20E System (bioMérieux Vitek, Hazelwood, MO) or by traditional biochemistry reactions in test tubes. Serotyping was determined with use of O1 antisera (Difco Laboratories, Detroit) and O139 antisera (Denka Seiken, Tokyo). Serotyping of all strains with use of O139 antisera was performed at the Southern Branch Laboratory, National Institute of Preventive Medicine, Department of Health, Kaohsiung, Taiwan, a reference laboratory for cholera toxin--producing *V. cholerae*.

**Definitions of Terminology**

Leukocytosis was defined as a total leukocyte count of >12,000/mm³, and thrombocytopenia was defined as a platelet count of <100,000/mm³. Early mortality was defined as death within 96 hours after visiting the hospital, and late mortality was defined as death occurring after at least 96 hours of hospitalization and before discharge from the hospital. The degree of decomposition of hepatic cirrhosis was assessed by the scoring system proposed by Pugh et al. [9] that is based on serum albumin and bilirubin levels, prolongation of prothrombin time, amount of ascites, and degree of hepatic encephalopathy.

**Results**

During an 8-year period at NCKUH, 30 *V. cholerae* isolates from 30 different patients were identified. All isolates were non-O1, non-O139 serotypes; these identifications were confirmed by the reference laboratory. Infections due to these isolates generally occurred in hot-weather months, especially from May to September (figure 1). In vitro antibiotic susceptibility testing by the disk diffusion method showed that non-O1 *V. cholerae* was susceptible to many drugs, including combinations of a β-lactam agent and a β-lactamase inhibitor, broad-spectrum β-lactam agents, aminoglycosides, and fluoroquinolones (table 1). According to the sites of infection, cases due to these agents were categorized into three groups: bacteremia, gastrointestinal infections, and other infections.

**Bacteremia**

One-half of the 30 isolates were recovered from blood; therefore, bacteremia was the most common presentation of *V. cholerae* infection (table 2). Of the 15 patients with bacteremia, 14 were male. The mean age of the patients with bacteremia was 56 years (range, 38 to 79 years). Without exception, all 15 patients had hepatic cirrhosis, and 13 had decompenated hepatic function (those with scores ≥10 were classified as Pugh class C). Coexisting underlying diseases included gallbladder stones (4 cases), hepatoma (4), diabetes mellitus (1), and congestive heart failure (2). Two patients had polymicrobial bacteremia: one had concomitant *Vibrio vulnificus* bacteremia, and one had *Escherichia coli* bacteremia. Only two patients had contact with raw seafood before the infectious episode.

All infections were community-acquired. Initial clinical presentations included fever (14 cases), chills (11), abdominal pain (9), and diarrhea (9). Hypotension was noted in 10 patients. The leukocyte count at the onset of bacteremia ranged from 4,000 to 24,100/mm³, and leukocytosis (leukocyte count, 12,700 to 24,100/mm³; mean, 19,525/mm³) was noted only in four patients. The concurrent platelet count ranged from 20,000 to 222,000/mm³, and thrombocytopenia (platelet count, 20,000 to 76,000/mm³; mean, 55,750/mm³) was found in 12 patients.

**Acute Gastrointestinal Infections**

There were eight cases of acute gastroenteritis (table 3). No gender predominance was found (four males and four females). The mean age of the patients was 37.8 years (range, 22 to 51 years), which was younger than that for patients with bacteremia. None of the patients had chronic underlying illnesses. Copathogens were discovered in fecal specimens from two patients: *Vibrio parahaemolyticus* and *Plesiomonas shigelloides*, respectively. The prehospital courses were short (range, <24 to 72 hours). These eight patients presented with watery diarrhea (8 cases), fever (temperature, 38.2–39.2°C; 6), abdominal cramps (6), nausea or vomiting (6), and chills (4). One patient initially had watery diarrhea without fever and later had self-limited bloody stools.

Leukocytosis (leukocyte count, 12,800 to 26,400/mm³; mean, 19,042/mm³) was noted in seven cases; in contrast, platelet counts (188,000 to 329,000/mm³; mean, 230,625/mm³) were normal in all cases. Hospital courses in all cases were short (1–2 days) and no sequelae occurred, regardless of whether the patient was treated with antibiotics.
Nonbacteremic, Nonintestinal Infections

Seven strains were isolated from specimens other than blood or feces (table 4). Three strains were isolated from surgical specimens from the extremities of patients with necrotizing fasciitis. These three patients had certain underlying diseases: chronic hepatic disease (two cases) and congestive heart failure (one case). In the latter case (case 1 in table 4), small bullae and a purpuric, necrotic skin lesion were found (figure 2, left panel). One additional strain was isolated from a traumatic wound specimen from a diabetic patient with cellulitis.

All four patients with soft-tissue infections had prior minor trauma that provided a portal of entry for bacteria. Two of these patients had contact with clam and fish 1 and 2 days, respectively, before their admissions. Another patient’s right arm was stuck by an unknown plant 5 days prior to the infection. Antibiotic therapy, a cephalosporin with or without a tetracycline analogue, and surgical fasciectomy, in cases of necrotizing fasciitis, cured all four of these patients.

One strain, accompanied by *V. vulnificus*, was isolated from a sputum sample from a patient who had drowned in a contaminated pond and subsequently died of bilateral aspiration pneumonia, acute respiratory distress syndrome, and septic shock. Another strain was recovered from the salpinx uterina of a woman who presented with fever, abdominal pain in the right lower quadrant, and leukocytosis. Purulent salpingitis was the final diagnosis. The patient denied consumption of raw seafood before this illness and had been swimming only once at a beach 6 months before. The clinical significance of the last isolate and other enteric bacteria, incidentally discovered in a normal appendix (case 7 in table 4), was uncertain.

**Table 1.** Results of in vitro antibiotic susceptibility testing (disk diffusion method) for 26 clinical isolates of non-O1, non-O139 *Vibrio cholerae* recovered from patients in southern Taiwan.

<table>
<thead>
<tr>
<th>Drug</th>
<th>No. (%) of susceptible isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin</td>
<td>25 (96)</td>
</tr>
<tr>
<td>Amikacin</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>22 (85)</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>25 (96)</td>
</tr>
<tr>
<td>Ampicillin/sulbactam</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Ticarcillin/clavulanate</td>
<td>24 (92)</td>
</tr>
<tr>
<td>Piperacillin/tazobactam</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Cephalothin</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>25 (96)</td>
</tr>
<tr>
<td>Cefixime</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Ceftriazone</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Imipenem</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Ciprofloxac*</td>
<td>25 (100)</td>
</tr>
<tr>
<td>Tetracycline*</td>
<td>22 (88)</td>
</tr>
<tr>
<td>Minocycline</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>23 (88)</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>23 (88)</td>
</tr>
</tbody>
</table>

* Only 25 isolates were tested.

Discussion

In Taiwan, a subtropical island where the prevalence of chronic infection due to endemic hepatitis B virus is high, many individuals have hepatic cirrhosis and are susceptible to non–O1 *V. cholerae* infection [10, 11] or *V. vulnificus* infection [12]. In such an area where both organisms are endemic, non-O1 *V. cholerae* appears to behave clinically and biologically like *V. vulnificus* in many ways, as shown in table 5. Both organisms cause invasive soft-tissue infections and bacteremia associated with high rates of mortality. They are susceptible to many antibiotics and preferably grow in warm temperatures. Infections caused by either pathogen occur more commonly during hot seasons.

Risk factors for these vibrio infections are similar (i.e., exposure to seawater and ingestion of raw seafood). Patients with
non–O1 \textit{V. cholerae} septicemia associated with soft-tissue infection have often been described as having localized cellulitis with small bullous lesions [13–15]. We found that dermatologic presentations of patients with necrotizing soft-tissue infections caused by \textit{V. cholerae} and \textit{V. vulnificus} were similar [16], except that hemorrhagic bullae caused by \textit{V. cholerae} seemed fewer and smaller.

Host susceptibility is important not only for bacteremia caused by non-O1 \textit{V. cholerae} but also for that caused by other \textit{Vibrio} species [17]. Non–O1 \textit{V. cholerae} bacteremia has often been described in individuals with certain underlying disorders, such as cirrhosis, hematologic malignancies [3], or other immunosuppressed conditions [18–20]. The predominance of cirrhotic patients in our series probably reflects a high prevalence of postnecrotic cirrhosis in the community. In addition to primary bacteremia, secondary bacteremia with invasive soft-tissue infections and SBP were typical patterns. The relevant explanations for the mechanism of invasive vibrio infections frequently occurring in patients with cirrhosis remain obscure; there are many hypotheses, such as decreased serum bactericidal activity, impaired filtration function in the cirrhotic liver, or increased serum iron levels [21], but the precise role of each

### Table 2. Clinical characteristics of 15 patients with non–O1, non–O139 \textit{Vibrio cholerae} bacteremia in southern Taiwan.

<table>
<thead>
<tr>
<th>Patient no., age (y)/sex</th>
<th>Concurrent pathogen in blood</th>
<th>Underlying disease(s) (Pugh score)*</th>
<th>Infection(s) other than bacteremia</th>
<th>Antibiotic therapy, duration (d)</th>
<th>Outcome</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 62/M Blood</td>
<td>\textit{Vibrio vulnificus}</td>
<td>Cirrhosis (11)</td>
<td>Cefotaxime, 2</td>
<td>Died of sepsis</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>2, 55/M Blood</td>
<td>Blood</td>
<td>Cirrhosis (13)</td>
<td>Cefotaxime, 2; Cephalothin, 6; and chloramphenicol, 4</td>
<td>Survived</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3, 43/M Blood</td>
<td>Blood</td>
<td>Cirrhosis (14)</td>
<td>Cefotaxime and amikacin, 3</td>
<td>Died of sepsis</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>4, 59/M Blood</td>
<td>Blood</td>
<td>Cirrhosis (5), hepatoma</td>
<td>Cefalothin, 6; then amoxicillin/ clavulanate, 8</td>
<td>Survived</td>
<td>Associated with esophageal varices bleeding</td>
<td></td>
</tr>
<tr>
<td>5, 38/M Blood</td>
<td>Blood</td>
<td>Cirrhosis (8)</td>
<td>Cefuroxime, 7; and netilmicin, 5</td>
<td>Survived</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6, 66/M Blood</td>
<td>Blood</td>
<td>Cirrhosis (11), gallbladder stone, congestive heart failure</td>
<td>Amoxicillin/ clavulanate, 3 Cefotaxime, 17; and minocycline, 12</td>
<td>Survived</td>
<td></td>
<td>Fasciotomy</td>
</tr>
<tr>
<td>7, 52/M Blood</td>
<td>Blood</td>
<td>Cirrhosis (12)</td>
<td>SBP</td>
<td>Survived</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8, 48/M Blood</td>
<td>Blood</td>
<td>Cirrhosis (11)</td>
<td>Necrotizing fasciitis</td>
<td>Survived</td>
<td></td>
<td>Fasciotomy</td>
</tr>
<tr>
<td>9, 60/M Blood, ascites</td>
<td>Blood</td>
<td>Cirrhosis (11), gallbladder stone, hepatic</td>
<td>Cefotaxime, 2; Ceftriazone, 2</td>
<td>Died of sepsis</td>
<td>and hepatic rupture</td>
<td></td>
</tr>
<tr>
<td>10, 69/M Blood, ascites</td>
<td>Blood</td>
<td>Cirrhosis (12), gallbladder stone, hepatic</td>
<td>SBP, cellulitis SBP</td>
<td>Survived</td>
<td>Associated with esophageal varices bleeding</td>
<td></td>
</tr>
<tr>
<td>11, 50/M Blood</td>
<td>Blood</td>
<td>Escherichia coli</td>
<td>Cirrhosis (12), hepoma</td>
<td>Cefazolin, 10 Cefradine and netilmicin, 10; then ceftriazone, 16; and netilmicin, 7</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>12, 54/M Blood</td>
<td>Blood</td>
<td>Cirrhosis (10), gallbladder stone, hepatic</td>
<td>Cefazolin, 10 Cefradine and netilmicin, 10; then ceftriazone, 16; and netilmicin, 7</td>
<td>Survived</td>
<td></td>
<td>Associated with esophageal varices bleeding</td>
</tr>
<tr>
<td>13, 61/M Blood</td>
<td>Blood</td>
<td>Cirrhosis (12), gallbladder stone</td>
<td>Ceftriazone, 10</td>
<td>Died of hepatic failure and sepsis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14, 79/F Blood, wound specimen</td>
<td>Blood</td>
<td>Cirrhosis (11), congestive heart failure</td>
<td>Ceftriazone, 12</td>
<td>Died of hepatic failure</td>
<td>Fasciotomy</td>
<td></td>
</tr>
<tr>
<td>15, 44/M Blood</td>
<td>Blood</td>
<td>Cirrhosis (10), diabetes mellitus</td>
<td>Norfloxacin, 3; then ofloxacin, 14</td>
<td>Survived</td>
<td>No hospitalization</td>
<td></td>
</tr>
</tbody>
</table>

**NOTE.** SBP = spontaneous bacterial peritonitis.

* Pugh score defined in [9].
water or seafood before the onset of *V. cholerae* infection. However, because of the retrospective nature of this study, the proportion of patients with a history of travel, exposure to contaminated water, or ingestion of undercooked seafood was probably underestimated. Both the occurrence of extraintestinal infections and the exposure histories suggest that non–O1 *V. cholerae* can be acquired from the environment.

Because of the lack of a controlled clinical comparison, the optimal therapeutic regimen for invasive non–O1 *V. cholerae* infections remains unsettled. Clinical experiences with the treatment of other vibrio infections may serve as a model. The fact that ampicillin (despite in vitro susceptibility) has been dropped as an agent of therapy for cholera [3] and the fact that resistance of non–O1 strains to ampicillin has been increasingly reported [22] make this agent no longer indicated as therapy for non–O1 *V. cholerae* infections. Tetracycline has been suggested as the drug of choice for treatment of vibrio infections [2]; however, there was increasing resistance to tetracycline in our non–O1 *V. cholerae* isolates, and minocycline was more active than tetracycline.

Recently, our research group demonstrated that a combination regimen (cefotaxime plus minocycline) showed a synergistic antibacterial effect in vitro [23] and in mice experimentally infected by *V. vulnificus* [24], another dangerous halophilic organism for cirrhotic patients. Our clinical experience with the treatment of *V. vulnificus* infection also favored such a regimen. In this series, three patients with necrotizing fasciitis (case 8 in table 2 and cases 2 and 4 in table 4) who were treated with cefotaxime and minocycline or doxycycline and fasciotomy survived. Although there is no prospective clinical data to verify the clinical efficacy of this particular combination, it seems reasonable to administer combination therapy

### Figure 2.
*Left panel:* A 75-year-old woman with necrotizing fasciitis caused by non–O1 *Vibrio cholerae* on whom a purpuric, necrotic lesion over the right forearm was noted 2 days after she had handled fish. *Right panel:* A cirrhotic patient with non–O1 *V. cholerae* bacteremia who presented with swelling, tenderness, and erythema over the left lower leg had subcutaneous abscess formation around the ankle.

### Table 3.
Clinical characteristics of eight patients with acute gastroenteritis caused by non-O1, non-O139 *Vibrio cholerae* in southern Taiwan.

<table>
<thead>
<tr>
<th>Patient no., age (y)/sex</th>
<th>Copathogen in stool</th>
<th>Presentation(s) other than diarrhea</th>
<th>Prehospital course (d)</th>
<th>Initial leukocyte count (×10³/mm³)</th>
<th>Antibiotic therapy, duration (d)</th>
<th>Hospital course (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 42/F</td>
<td></td>
<td>Fever, abdominal pain</td>
<td>2</td>
<td>13,000</td>
<td>Ciprofloxacin, 3</td>
<td>2</td>
</tr>
<tr>
<td>2, 27/F</td>
<td></td>
<td>Fever, chills, abdominal pain, nausea or vomiting</td>
<td>1</td>
<td>8,500</td>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>3, 34/M</td>
<td></td>
<td>Fever, abdominal pain, nausea or vomiting</td>
<td>2</td>
<td>26,100</td>
<td>Ampicillin, 1</td>
<td>1</td>
</tr>
<tr>
<td>4, 34/M</td>
<td></td>
<td>Fever, chills, nausea or vomiting</td>
<td>1</td>
<td>16,300</td>
<td>Cephradine, 2</td>
<td>2</td>
</tr>
<tr>
<td>5, 51/F</td>
<td><em>Plesiomonas shigelloides</em></td>
<td>Chills, abdominal pain, nausea or vomiting, headache</td>
<td>2</td>
<td>12,800</td>
<td>Cefhalothin and gentamicin, 1</td>
<td>1</td>
</tr>
<tr>
<td>6, 22/M</td>
<td></td>
<td>Fever, chills, abdominal pain, nausea or vomiting</td>
<td>1</td>
<td>18,500</td>
<td>Amoxicillin and TMP-SMZ, 3</td>
<td>1</td>
</tr>
<tr>
<td>7, 48/F</td>
<td><em>Vibrio parahaemolyticus</em></td>
<td>Fever, abdominal pain, nausea or vomiting</td>
<td>1</td>
<td>26,400</td>
<td>Cephalexin, 3</td>
<td>1</td>
</tr>
<tr>
<td>8, 44/M</td>
<td></td>
<td>Bloody stools</td>
<td>3</td>
<td>20,200</td>
<td>Ciprofloxacin, 3</td>
<td>1</td>
</tr>
</tbody>
</table>

NOTE. TMP-SMZ = trimethoprim-sulfamethoxazole.
for severe non–O1 *V. cholerae* infections. Newer quinolones were extremely active against serotypes O1 and O139 and non–O1 *V. cholerae* for which the MIC<sub>90</sub> was 0.5 μg/mL [22], and these agents will theoretically be another good choice for treatment of invasive non–O1 *V. cholerae* infections.

Acute gastroenteritis is well recognized as the most common manifestation of non–O1 *V. cholerae* infection and can occur sporadically or as an outbreak. Usually, it is a self-limited diarrheal illness of short duration, but the median duration of illness has been reported to be up to 6.4 days [25]. Patients with

### Table 4. Clinical characteristics of seven patients with infections other than bacteremia or gastroenteritis that were caused by non-O1, non-O139 *Vibrio cholerae* in southern Taiwan.

<table>
<thead>
<tr>
<th>Infection type:</th>
<th>Positive culture</th>
<th>Copathogen(s)</th>
<th>Clinical diagnosis</th>
<th>Specific exposure</th>
<th>Underlying disease(s)</th>
<th>Clinical presentation(s)</th>
<th>Antibiotic therapy, duration (d)</th>
<th>Surgery</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft tissue</td>
<td>Debrided tissue</td>
<td>Coagulase-</td>
<td>Necrotizing</td>
<td>惦惦街j</td>
<td>Congestive heart</td>
<td>Fever, right hand swelling, hypotension</td>
<td>Cefotaxime, 14</td>
<td>Fasciotomy and skin grafting</td>
<td>Survived</td>
</tr>
<tr>
<td>1, 75/F</td>
<td>specimen</td>
<td>negative</td>
<td>fasciitis on right hand</td>
<td>惦惦街j</td>
<td>failure</td>
<td>Fever, right hand swelling, hypotension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2, 72/F</td>
<td>Debrided tissue</td>
<td>None</td>
<td>Necrotizing</td>
<td>惦惦街j</td>
<td>Cirrhotis,</td>
<td>Fever, chills, left arm swelling, hypotension</td>
<td>Cefotaxime, 18, 7</td>
<td>Fasciotomy and skin grafting</td>
<td>Survived</td>
</tr>
<tr>
<td>specimen</td>
<td></td>
<td>none</td>
<td>fasciitis on left hand and forearm</td>
<td>惦惦街j</td>
<td>gallbladder stone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3, 52/M</td>
<td>Wound specimen</td>
<td>None</td>
<td>Cellulitis on left lower leg</td>
<td>惦惦街j</td>
<td>Diabetes mellitis</td>
<td>Fever, chills, right hand swelling</td>
<td>Cefotaxime, 12, and doxycycline, 8</td>
<td>Fasciotomy and primary sutureting</td>
<td>Survived</td>
</tr>
<tr>
<td>4, 77/F</td>
<td>Pus</td>
<td>Coagulase-</td>
<td>Necrotizing</td>
<td>惦惦街j</td>
<td>Chronic viral hepatitis</td>
<td>Fever, chills, right hand swelling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>specimen</td>
<td>negative</td>
<td>negative</td>
<td>fasciitis on right hand and forearm</td>
<td>惦惦街j</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Sputum</td>
<td><em>Vibrio vulnificus</em></td>
<td>Bilateral aspiration pneumonia and acute respiratory distress syndrome</td>
<td>惦惦街j</td>
<td>None</td>
<td>Dyspnea, altered mentality, hypotension</td>
<td>Cefoxitin and tobramycin, 1</td>
<td>None</td>
<td>Died within 24 h</td>
</tr>
<tr>
<td>5, 58/M</td>
<td></td>
<td></td>
<td>Drowned in a dirty pond</td>
<td>惦惦街j</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6, 47/F</td>
<td>Salpinx uterina</td>
<td>None</td>
<td>Purulent salpingitis</td>
<td>惦惦街j</td>
<td>None</td>
<td>Fever, abdominal pain</td>
<td>Cefoxitin and netilmicin, 7</td>
<td>Salpingectomy</td>
<td>Survived</td>
</tr>
<tr>
<td>7, 15/M</td>
<td>Appendix</td>
<td><em>Escherichia coli, Enterococcus, Proteus mirabilis</em></td>
<td>Uncertain</td>
<td>惦惦街j</td>
<td>Abdominal pain</td>
<td>Clindamycin and fosfomycin, 2</td>
<td>Appendectomy</td>
<td>Survived</td>
<td></td>
</tr>
</tbody>
</table>

### Table 5. Similar clinical characteristics of non–O1, non–O139 *Vibrio cholerae* and *Vibrio vulnificus* infections.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non–O1, non–O139 <em>V. cholerae</em> infection</th>
<th><em>V. vulnificus</em> infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seasonal variation</td>
<td>Warm-weather months</td>
<td>Warm-weather months</td>
</tr>
<tr>
<td>Risk factor</td>
<td>Ingestion of raw seafood and exposure to seawater</td>
<td>Ingestion of raw seafood and exposure to seawater</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal infection</td>
<td>Occasional</td>
<td>Rare</td>
</tr>
<tr>
<td>Epidemic diarrhea</td>
<td>Rare</td>
<td>Not reported</td>
</tr>
<tr>
<td>Cholera</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extraintestinal infection</td>
<td>Skin or by mouth</td>
<td>Skin or by mouth</td>
</tr>
<tr>
<td>Portal of entry</td>
<td>Immunocompromised, particularly cirrhotic persons</td>
<td>Immunocompromised, particularly cirrhotic persons</td>
</tr>
<tr>
<td>Susceptible hosts</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>Nearly one-half</td>
<td>More than one-half</td>
</tr>
<tr>
<td>Cellulitis or necrotizing fasciitis</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td>Cutaneous bullae</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td>Spontaneous bacterial peritonitis</td>
<td>Occasional in cirrhotic patients</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
acute gastroenteritis have abdominal cramps, fever, nausea, and vomiting [4], as did our patients, and nearly 25% of patients in one series [23] surprisingly had bloody stools. In our series, the severity of acute gastroenteritis, for which patients visited our emergency department, is very likely to be overrepresented. It is not surprising to find that a patient with acute non–O1 *V. cholerae* gastroenteritis simply has diarrhea and abdominal discomfort. The mainstay of treatment for non–O1 *V. cholerae* gastroenteritis in most cases depends on fluid and electrolyte replacement. Antimicrobial agents may be helpful in severe cases of gastroenteritis [2].

The fact that *V. cholerae* isolates from sputum are often seen in cases of near drowning [26], as in one of our cases, had equivocal significance. It is hard to distinguish simple contamination from a true pathogen of aspiration pneumonia, unless there is concomitant bacteremia caused by the same organism. As for the woman with typical presentations of purulent salpingitis, only *V. cholerae* was isolated from the surgically removed uterine tube; therefore, it was considered to be the etiologic agent of pyosalpinx (which to our knowledge has never been reported in the English-language literature). However, the portal of entry of *V. cholerae* in this patient is unknown. Except for a history of swimming at a beach 6 months before her illness, she denied any contact with raw seafood or seawater.

Similar to *V. vulnificus*, non–O1, non–O139 *V. cholerae* is a virulent pathogen in susceptible hosts (especially those with hepatic cirrhosis) and often causes bacteremia and invasive soft-tissue infections. Treatment of such potentially lethal infections with cefotaxime and a tetracycline analogue or one of the fluoroquinolones may be better than traditional monotherapy with bacteriostatic tetracycline. Prevention is the best treatment. Therefore, particularly for cirrhotic patients, it is wise to avoid any contact with contaminated seawater or freshwater or consumption of raw or undercooked seafood.

References