Cholera and Other Types of Vibriosis: A Story of Human Pandemics and Oysters on the Half Shell

J. Glenn Morris, Jr.

Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, and Baltimore Veterans Affairs Medical Center, Baltimore, Maryland

Vibrios are ubiquitous in the aquatic environment and are commonly present in or on shellfish and other seafood. A small subset of strains/species are able to cause human disease, including the cholera toxin–producing strains of Vibrio cholerae that are responsible for epidemic/pandemic cholera; thermostable direct hemolysin–producing strains of Vibrio parahaemolyticus; and Vibrio vulnificus, which can cause fulminant sepsis. Cholera outbreaks can be initiated by transmission of “epidemic” V. cholerae strains from their environmental reservoir to humans through seafood or other environmentally related food or water sources. “Nonepidemic” strains of V. cholerae and strains of other Vibrio species, including V. parahaemolyticus and V. vulnificus, are generally acquired by eating seafood (particularly raw oysters/oysters on the half shell). Although the primary clinical manifestation of infection with these strains is gastroenteritis, they can also cause wound infections and (particularly for V. vulnificus) septicemia in persons who have liver disease or are immunocompromised.

Vibrio species are free-living bacteria found in aquatic environments throughout the world. They tend to be more common in warmer waters (temperatures >17°C–20°C) [1, 2]; depending on the species, they tolerate a range of salinities. In one study in the Chesapeake Bay, Vibrio vulnificus was present in water at counts of ∼10⁴ organisms/mL, Vibrio cholerae–Vibrio mimicus at counts of 10⁴ organisms/mL, and Vibrio cincinnatiensis at counts of 10² organisms/mL [2]. As would be anticipated, given their abundance in water, Vibrio species are also commonly isolated in samples from fish and shellfish, and, after concentration by filter-feeding shellfish such as oysters, may be present at concentrations that are 100-fold higher than those in the surrounding water [1]. During warm summer months, virtually 100% of oysters will carry V. vulnificus and/or Vibrio parahaemolyticus [1, 3, 4]; densities in US Gulf Coast oysters often exceed 10⁴ organisms/g of oyster meat. Although vibrios do not appear to affect oysters, some species may be pathogenic to marine life: for example, Vibrio damsela causes lesions in damsel and other fish, and Vibrio shiloi is an important cause of coral bleaching.

Vibrio species that are associated with human illness are listed in table 1, together with Centers for Disease Control and Prevention (CDC) data on the number of reported cases and deaths in the United States in 1999. “Epidemic” strains of V. cholerae carrying a suite of specific virulence genes cause the disease cholera, and other, “nonepidemic” strains are associated with gastroenteritis, wound infections, and septicemia in susceptible hosts [5–8]. V. parahaemolyticus is a common cause of gastroenteritis and the leading cause of foodborne illness in Japan [9]; it, too, can cause wound infections and septicemia in susceptible hosts. V. vulnificus is the leading cause of death in the United States associated with seafood consumption, which is the result of its ability to cause severe wound infections and sepsis in patients who are immunocompromised or have underlying liver disease [10]. Although other Vibrio species have been linked with gastroenteritis or wound infections, the number of cases is relatively small, and, in some instances, it...
Table 1. *Vibrio* species implicated as causes of human disease and number of deaths associated with infection with these species.

<table>
<thead>
<tr>
<th><em>Vibrio</em> species</th>
<th>Clinical presentation</th>
<th>No. of cases (no. of deaths)⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gastroenteritis</td>
<td>Wound or ear infection</td>
</tr>
<tr>
<td><em>V. cholerae</em></td>
<td>++ (+) —</td>
<td>5 (0)⁴</td>
</tr>
<tr>
<td>Epidemic (O1, O139)</td>
<td>++ + (+)</td>
<td>45 (0)</td>
</tr>
<tr>
<td>Nonepidemic</td>
<td>++ + —</td>
<td>10 (0)</td>
</tr>
<tr>
<td><em>V. mimicus</em></td>
<td>++ + (+)</td>
<td>116 (1)</td>
</tr>
<tr>
<td><em>V. parahaemolyticus</em></td>
<td>++ + (+)</td>
<td>19 (0)</td>
</tr>
<tr>
<td><em>V. fluvialis</em></td>
<td>++ + (+)</td>
<td>1 (0)</td>
</tr>
<tr>
<td><em>V. furnissii</em></td>
<td>++ (+) —</td>
<td>13 (0)</td>
</tr>
<tr>
<td><em>V. hollisae</em></td>
<td>++ + (+)</td>
<td>83 (31)⁵</td>
</tr>
<tr>
<td><em>V. vulnificus</em></td>
<td>+ ++ ++</td>
<td>28 (0)</td>
</tr>
<tr>
<td><em>V. alginolyticus</em></td>
<td>— + + —</td>
<td>2 (0)</td>
</tr>
<tr>
<td><em>V. damselae</em></td>
<td>— + + —</td>
<td>0 (0)</td>
</tr>
<tr>
<td><em>V. cincinnatiensis</em></td>
<td>— — —</td>
<td>0 (0)</td>
</tr>
<tr>
<td><em>V. carchariae</em></td>
<td>(+) —</td>
<td>1 (0)</td>
</tr>
<tr>
<td><em>V. metschnikovii</em></td>
<td>(+) —</td>
<td></td>
</tr>
</tbody>
</table>

**NOTE.** ++, Most common clinical presentation; +, neither rare nor most common clinical presentation; (+), rare clinical presentation.

a Data reflect *Vibrio* infections reported to the Centers for Disease Control and Prevention during 1999. Data are from the 24 states that reported cases; for many of these states, reporting of *Vibrio* infections is not routine, and consequently nos. may not reflect the true no. of cases. Data were kindly provided by R. Tauxe, US Centers for Disease Control and Prevention, Atlanta.

b Data include 4 cases associated with foreign travel.

c The 31 reported deaths are from a group of 75 cases for which data on death were available.

is unclear whether isolation of the organism represented asymptomatic colonization or infection. Given the ubiquitousness of the genus in the environment, asymptomatic colonization does occur. Perhaps one of the earliest known indicators of this was the identification of *Vibrio metschnikovii* DNA in the colonic contents of the >5000-year-old “Tyrolean Iceman” found frozen in an alpine glacier [11].

**CHOLERA AND EPIDEMIC *V. CHOLEREA***

Cholera is characterized by the rapid onset of profuse, watery diarrhea, which, if untreated, can lead to dehydration, circulatory collapse, and death. Seven cholera pandemics have been recorded since 1817. The seventh pandemic (caused by *V. cholerae* strains in O group 1, biotype El Tor) originated in the Celebes in Indonesia in 1961 and spread through trade, tourism, and pilgrimage routes to Asia, Europe, Africa, and the South Pacific. In January 1991, explosive outbreaks of the seventh pandemic strain occurred in cities along the Peruvian coast, with further epidemic spread through South and Central America. In 2001, 184,311 cholera cases and 2728 cholera-related deaths were reported to the World Health Organization from 58 countries [12]; the actual number of cases and deaths likely is much greater than this total, because there is significant underreporting of cholera in many countries, and there are countries known to have had cholera outbreaks in 2001 that reported no cases. In contrast to the early 1990s (figure 1), when cases were concentrated in the Americas, the majority of reported cases in 2001 were from Africa and occurred in association with recent epidemics in southern and western Africa [12].

**Microbiology and pathogenesis.** *V. cholerae* is traditionally classified by O group (with >150 O types currently recognized in the widely used Sakazaki grouping system) and by biotype (classical and El Tor) and serotype (Ogawa, Inaba, and, rarely, Hikojima) [13]. Until recently, *V. cholerae* strains belonging to serogroup O1 were believed to be the sole etiologic agents of cholera. However, since late 1992, *V. cholerae* serogroup O139 has emerged as a second etiologic agent of cholera in the Indian subcontinent and neighboring countries [14, 15], and there are suggestions that strains in other *V. cholerae* serogroups can cause cholera-like disease [16–18].

The signs and symptoms of cholera are caused by cholera toxin (CT), a protein enterotoxin that elicits profuse diarrhea. CT activates cyclic adenosine monophosphate, leading to increased Cl⁻ secretion and decreased NaCl-coupled absorption. Glucose, potassium, and bicarbonate absorption, however, remain intact, as does glucose-linked enhancement of sodium and water absorption. Thus, although plain salt water is non-
absorbable during cholera and aggravates the diarrhea, the addition of glucose renders the solution absorbable, providing a physiologic basis for oral rehydration [13, 19].

Genes for cholera toxin are carried by the CTX phage and can be transferred between \( V. \) cholerae strains [20]. Virulence also has been linked with the presence of the \( Vibrio \) pathogenicity island (VPI) [21], which carries key genes involved in intestinal colonization. However, both the CTX phage and VPI can be found in strains that lack epidemic potential [17], which suggests that there are other, as yet unidentified factors underlying the ability of a \( V. \) cholerae strain to spread in epidemic fashion. In this context, there has been some very interesting recent work suggesting that, in the human intestine, epidemic \( V. \) cholerae strains shift to a hyperinfectious form that is passed in the “rice water” stools characteristic of cholera, with at least short-term persistence of this form in the environment [22].

**Epidemiology.** After passage of a pandemic wave through a geographic region, cholera generally settles into an endemic pattern of seasonal outbreaks separated by periods of quiescence. In South America, for example, cases are concentrated in the summer months of January and February. Studies that we have conducted in Peru show that the seasonal cholera epidemics are often heralded 2 months before they occur by increases of \( V. \) cholerae in the environment (triggered, in turn, by seasonal increases in water temperature) [23], with apparent subsequent “spillover” of the bacterium into human populations. As humans become infected, \( V. \) cholerae present in their feces contaminate food and water sources and further increase environmental \( V. \) cholerae levels, resulting in amplification of the organism and initiation of the epidemic cycle. The occurrence and intensity of epidemics also has been linked with global climatic events; epidemic intensity has peaked along the west coast of South America and in Bangladesh in association with the occurrence of the El Niño southern oscillation [24, 25].

In the United States, we have a small environmental focus of potentially epidemic \( V. \) cholerae along the Gulf Coast, inhabited by what appears to be a single clone that has persisted for >30 years. Cholera cases caused by this strain have generally been linked to consumption of undercooked crab or raw oysters harvested from the Gulf Coast [26, 27]. Between 1995 and 2000, there were 6 cholera cases in the United States that were linked with this focus and an additional 8 cases that were associated with imported seafood [28]. However, with rare exceptions, the sporadic seafood-associated cholera cases that have occurred in the US population have not spread beyond the seafood-associated index case, presumably because of the higher levels of sanitation present in this country. Other foods implicated in US cases in recent years include commercial frozen fresh coconut milk (imported from Thailand) [29] and cut cantaloupe (probably contaminated by an asymptomatic, infected food handler) [28]. Cooked rice appears to be a particularly effective vehicle for transmission of cholera, and rice has been implicated in a number of outbreaks, in settings as diverse as African funerals [30], a US oil rig platform [31], and a luxury cruise ship in Thailand (the latter outbreak was caused by an O139 strain) [32].
For unknown reasons, persons with blood group O are significantly more likely to have severe cholera [33]. Factors that predispose to hypochlorhydria (e.g., malnutrition, gastrectomy, and acid-reducing medications), by decreasing the gastric acid barrier to infection, also increase susceptibility to illness. The atrophic gastritis and hypochlorhydria associated with chronic *Helicobacter pylori* infection has also been associated with an increased risk of severe cholera [34].

**Clinical presentations, diagnosis, and management.** Despite the dread inspired by the term “cholera,” the majority of persons infected with epidemic *V. cholerae* strains do not have severe illness: 75% of persons infected with strains of the classical biotype have inapparent or mild disease, and 93% of persons infected with biotype El Tor strains (which are responsible for the most recent pandemic) have illnesses that are inapparent or mild [35]. The incubation period for cholera ranges from 12 h to 5 days. In the most severe cases (cholera gravis), rates of diarrhea rapidly increase during the first 24 h of illness, peaking at rates of up to 1 L/h. Diarrheal stools have a pale gray “rice water” appearance. In the absence of appropriate rehydration, this degree of purging can lead to circulatory collapse and death within a matter of hours. Dehydration is reflected in a higher plasma protein concentration, hematocrit, serum creatinine level, urea nitrogen level, and plasma specific gravity. Stool bicarbonate losses and lactic acidosis associated with dehydration can result in severe acidosis, manifested by decreases in blood pH and plasma bicarbonate and an increase in the serum anion gap [36]. Despite profound potassium loss, uncorrected acidosis may be associated with a normal or high serum potassium level. Plasma sodium and chloride concentrations remain in the normal range. Among properly treated patients, deaths are rare (in 2001, the case-fatality rate for all of South America was <0.25% [12]).

The clinical diagnosis of cholera is based on rapid onset of diarrhea and vomiting with dehydration and the presence of profuse “rice water” stool in an appropriate epidemiologic setting. Laboratory diagnosis is based on isolation of the organism from stool. This generally requires use of a selective medium (such as thiosulfate–citrate–bile salt–sucrose (TCBS) agar; for specimens sent to clinical microbiology laboratories in the United States, it is generally necessary to specifically request use of this medium (which is also required for isolation of other *Vibrio* species) for samples from suspected cholera cases. The diagnosis also can be made by serologic testing.

Treatment of cholera is based on replacement of fluids lost through diarrhea by oral or, in severe cases, intravenous rehydration [19, 37]. Antibiotics, such as tetracycline (table 2), can shorten the duration of diarrhea and reduce the period of carriage. However, antibiotic therapy should always be regarded as ancillary to vigorous rehydration. It also should be recognized that many epidemic strains are resistant to recommended antibiotics. In general, resistance has been most common among isolates from Asia [28], but tetracycline resistance has been seen in the recent cholera outbreaks in Mozambique, South Africa, and Madagascar [38, 39]. These observations underscore the need for antimicrobial susceptibility testing of all *V. cholerae* isolates, particularly those that may have been acquired outside of the United States.

**Prevention.** Outside of the context of endemic or seasonal epidemic cholera, the risk of acquiring the disease is low and can be further reduced by maintenance of good sanitation and provision of safe potable water. However, as long as there are environmental foci of epidemic strains (such as the one seen along the US Gulf Coast), it is not possible to totally eliminate the risk of *V. cholerae* infection. Cooking of seafood and shellfish reduces but does not eliminate the risk: in studies conducted by the CDC, epidemic *V. cholerae* could still be isolated from infected crabs that had been boiled for 8 or steamed for 25 min, cooking times that resulted in crabs that were red in appearance, with meat that was firm and appeared to be well cooked [26]. Although a great deal of recent work has been done on development of cholera vaccines, including development of oral attenuated vaccines, no cholera vaccine is currently commercially available in the United States [40].

**NONEPIDEMIC *V. CHOLERAE***

Strains of *V. cholerae* that do not carry the virulence factors necessary to cause epidemic cholera have been implicated as causes of diarrheal disease, wound infections, and, in susceptible hosts, septicemia [5–8, 41, 42]. Epidemiologic studies and studies involving volunteers have linked the occurrence of diarrheal illness to production of a heat-stable enterotoxin (NAG-
ST) similar to that produced by enterotoxigenic *Escherichia coli* [43, 44]; diarrheal illness has also been linked to production of CT or a CT-like toxin and to the ability of a strain to colonize the intestine [41, 42]. In contrast to *V. cholerae* O1, which is not encapsulated (and which, with 1 or 2 possible exceptions, does not cause sepsis), >90% of nonepidemic *V. cholerae* produce a polysaccharide capsule; heavily encapsulated strains are significantly more likely to be isolated in samples from patients with septicemia than are strains with minimal or no encapsulation. As is true for other vibrios, nonepidemic strains of *V. cholerae* are part of the normal, free-living bacterial flora in estuarine areas throughout the world. In areas such as the US Gulf Coast, these strains are several orders of magnitude more common than are epidemic *V. cholerae* strains in the environment. Isolation is not associated with the presence of fecal coliforms, which is the marker currently used by state and national regulatory agencies in the United States to regulate shellfish harvesting waters. Although illness due to nonepidemic *V. cholerae* has been linked at a global level to contaminated water and a variety of foods, particularly seafood [41, 42], oysters appear to be the primary vehicle of infection in the United States [45].

The most common manifestation of nonepidemic *V. cholerae* infection is diarrhea. The incubation period, judging by outbreak reports and volunteer studies, is short (<24 h). Abdominal cramps may be prominent; bloody diarrhea is occasionally reported [45]. Illness is usually mild and self-limited, although a diarrheal stool volume of 5.3 L was seen in a volunteer who received 10⁶ cfu of one nonepidemic strain [43]. Nonepidemic *V. cholerae* strains have also been isolated from persons with septicemia. The case-fatality rate in a recent case series from Taiwan was 47% [7]; in older US literature, the rate exceeds 60% [46]. Illness appears to be confined to persons with cirrhosis or other liver disease or who are immunocompromised [7, 46]. The route of entry of the organism in these cases is not well defined, although foods containing the organism would be a likely source.

As with epidemic *V. cholerae*, treatment of diarrhea is dependent on adequate rehydration. Septicemia requires aggressive antibiotic therapy and supportive care. Although no controlled studies are available, a combination of minocycline (100 mg q12h po) and cefotaxime (2.0 g q8h iv) [47] or use of a “newer” fluoroquinolone [48] has been recommended for treatment of sepsis caused by *V. vulnificus* and would appear to be reasonable in management of sepsis caused by *V. cholerae*.

**V. PARAHAEMOLYTICUS**

In the fall of 1950, there was an outbreak of food poisoning in Osaka, Japan. Of 272 patients with acute gastroenteritis, 20 died. These deaths led to an intensive investigation of the outbreak and, ultimately, to the identification of an etiological agent that was named *“V. paraahaemolyticus”*. *V. paraahaemolyticus* is halophilic, or salt loving, and requires NaCl for growth. Isolates from ill persons have traditionally been differentiated from (presumed nonpathogenic) isolates from environmental sources on the basis of hemolytic activity seen when these isolates are grown on special medium (Wagatsuma agar); this is termed the “Kanagawa reaction,” named for the Japanese prefecture where the original study was done. Hemolytic activity in Kanagawa-positive strains of *V. paraahaemolyticus* has been linked with production of thermostable direct hemolysin (Vp-TDH) [49]. TDH-related hemolysins have also been identified that appear to have phenotypic activity similar to that of Vp-TDH and share sequence homology with Vp-TDH [50].

Although *V. paraahaemolyticus* has always been recognized as an important enteropathogen, there has been a striking increase in the incidence of *V. paraahaemolyticus* infections since the mid-1990s. This increase has been noted in multiple countries, including Japan [51] and the United States [52], and appears to be associated with the appearance of a new clonal group with pandemic potential, which includes isolates in serotypes O3:K6, O4:K68, and O1:K untypeable [53]. It has been suggested that rising water temperatures in shellfish-growing areas have served as a cofactor in the increasing incidence of cases of *V. paraahaemolyticus* infection in the United States [52, 54]. Further work is needed to assess the relative impact of water temperature and of the appearance of O3:K6 and related strains. Before 1980, *V. paraahaemolyticus* outbreaks in the United States were associated with seafood but not specifically with consumption of raw oysters; in contrast, in the 1990s, raw oysters were the vehicle of transmission in 11 (69%) of the 16 *V. paraahaemolyticus* outbreaks reported to the CDC [52].

*V. paraahaemolyticus* infection most commonly causes gastroenteritis. In a summary of clinical data from 202 patients with *V. paraahaemolyticus* gastroenteritis that were reported to the CDC between 1973 and 1998 [52], manifestations included diarrhea (98%), abdominal cramps (89%), vomiting (55%), and fever (52%); 29% of patients reported bloody diarrhea. In foodborne outbreaks, the median incubation period was 17 h (range, 4–90 h), and the median reported duration of illness was 2.4 days (range, 8 h to 12 days). A frank dysentery-like syndrome has been reported in association with *V. paraahaemolyticus* in India and Bangladesh [55]. Although this syndrome is not as common in the United States, there is 1 report of a US patient with blood and leukocytes in stool specimens and superficial colonic ulcerations noted on sigmoidoscopy [56]. *V. paraahaemolyticus* also is a cause of infection in wounds with contact with seawater [5, 8] and has been linked with occasional cases of primary septicemia (i.e., septicemia without an obvious focus of infection). As is true for other *Vibrio* species, serious wound infections and sepsis occur
most commonly in persons with underlying liver disease, alcoholism, or (particularly for wound infections) diabetes [52]. In the 1973–1998 CDC case series [52], the case-fatality rate among persons with *V. parahaemolyticus* septicemia was 29%.

Blood agar and other nonselective media support the growth of *V. parahaemolyticus*, but isolation from feces generally requires the use of a selective medium, such as TCBS. As is true for other diarrheal diseases, the key to management of *V. parahaemolyticus* gastroenteritis is provision of adequate rehydration. Although there are no data on antimicrobial efficacy, patients with persistent diarrhea (duration >5 days) may benefit from treatment with tetracycline or a quinolone. In the absence of data, it would appear reasonable to use the treatment protocols recommended for *V. vulnificus* infection (outlined below) for severe *V. parahaemolyticus* wound infections or septicemia.

**V. vulnificus**

*V. vulnificus*, which was first identified in 1979 simply as a halophilic, lactose-positive marine vibrio [10], causes severe wound infections, septicemia, and gastroenteritis [10, 57–60]. The majority of clinical and environmental *V. vulnificus* isolates reported to date are of biotype 1. Strains of biotype 2 (now known as “serovar E”) cause sepsis in eels but do not affect humans; biotype 3 strains have been described in association with wound infections related to handling of live fish (tilapia) from fish farms in Israel [61]. As has been reported for non-O1 *V. cholerae*, *V. vulnificus* strains produce a polysaccharide capsule that has been strongly linked to virulence [62]. Typing systems based on the capsule have not been developed, in part because of the great diversity seen in capsular types: in one study of 120 strains, 96 different capsular types (“carbotypes”) were identified [63]. *V. vulnificus* is very sensitive to the degree of binding of iron by transferrin in the host and to serum ferritin concentration [64, 65]. The organism grows rapidly in serum with transferrin that is >70% saturated with iron, with growth restricted at lower saturation percentages (in healthy adults, transferrin is ~30% saturated). This may explain the increase in the risk of disease in persons with hemochromatosis or who are alcoholic and malnourished and therefore have low concentrations of transferrin and correspondingly high saturation of transferrin [64]. Estrogen has been found to play a protective role in mouse models of *V. vulnificus* sepsis [66], which is interesting in light of the fact that the majority of human cases occur in men.

Like other vibrios, *V. vulnificus* occurs naturally in estuarine or marine environments. The highest numbers (in water and oysters) are found in areas with intermediate salinities (5–25 parts per thousand) and warmer temperatures (optimally, >20°C) [1, 3, 4]. *V. vulnificus* is the most common cause of serious vibrio infections in the United States (table 1); the incidence reported in community-based studies in coastal regions is ~0.5 cases/100,000 population/year [10, 57, 60]. Bacteremia without an obvious focus of infection (primary septicemia) occurs in persons who are alcoholic or who have chronic underlying illnesses, such as liver disease, cirrhosis, or hemochromatosis (table 3) [10, 57–60]. In one study, an increased risk of infection was associated with consumption of as little as 30 mL (1 oz) of alcohol per day [60]. Infection is generally acquired through consumption of oysters containing the organism. Wound infections occur after exposure to estuarine water. Typical exposures include wounds acquired while opening an oyster or in a boating accident. Wounds may become infected in healthy hosts. However, the most severe manifestations are seen in persons with underlying defects in host defense mechanisms.

Based on the number of cases reported to the Florida Health Department between 1981 and 1992, the annual rate of illness from *V. vulnificus* infection for adults with self-reported liver disease in Florida who ate raw oysters was 7.2 cases/100,000 adults, 80 times the rate among adults without known liver disease who ate raw oysters (0.09 cases/100,000 adults) [67]. Given the frequency of isolation of *V. vulnificus* from oysters, the incidence of disease is still much smaller than might be expected, even when the need for an appropriate host is taken into account [67]. This may reflect the need for a high infectious dose or possible differences among strains of *V. vulnificus* in their ability to cause illness. In support of the latter hypothesis, there are suggestions that certain ribotypes, carbotypes, or 16S rRNA sequence polymorphisms [68] are more common among clinical strains than among strains from the environment.

Patients with primary septicemia present with fever and hypotension (table 3); one-third have shock at initial presentation or become hypotensive within 12 h of hospitalization [57]. Distinctive bullous skin lesions have been reported in 50%–90% of patients [57, 58]. Thrombocytopenia is common, and there is often evidence of disseminated intravascular coagulation. More than 50% of patients with primary septicemia die; the mortality rate exceeds 90% for those who are hypotensive within 12 h of initial presentation [57]. Wound infections range from mild, self-limited lesions to rapidly progressive cellulitis and myositis. Patients who survive severe *V. vulnificus* infections often have some degree of residual disability. This does not appear to be related to the actual infection, which clears readily with antibiotic therapy, but rather to the consequences of multiple organ system failure and the prolonged hospitalization associated with occurrence of a shock syndrome [42].

A presumptive clinical diagnosis of *V. vulnificus* sepsis can be made on the basis of (1) the occurrence of shock or hypotension, or other signs suggesting sepsis (for wound infections, evidence of rapidly progressive cellulitis or myositis); (2) a history of cirrhosis, chronic alcoholism, immunosuppression,
or hemochromatosis; (3) a history of recent consumption of raw oysters or exposure of wounds to estuarine water; and (4) the presence of characteristic bullous skin lesions [42]. A definitive diagnosis requires isolation of *V. vulnificus* from samples of blood, from wounds or skin lesions (if present), or of stool. Blood agar and other nonselective media, including media used in commercial blood culture systems, are adequate for isolation from blood and wound samples; TCBS agar is necessary for isolation from stool.

The early administration of antimicrobial agents is critical to successful treatment. Case-fatality rates increase significantly with increasing time between onset of symptoms and initiation of therapy [57]. There is a suggestion, from a large series of cases in Florida, that antimicrobial therapy combinations that included tetracycline were more efficacious [57]. Recent in vitro and animal studies from Taiwan have led to recommendations that patients be treated with minocycline (100 mg q12h po) and cefotaxime (2.0 g q8h iv) [47] or a “newer” fluoroquinolone [48].

**SUMMARY**

As long as oysters and other shellfish are harvested from warm waters and eaten raw or with minimal cooking, there is risk of infection with *Vibrio* species. In the developing world, sporadic seafood-associated infections with epidemic *V. cholerae* may
serve as a trigger for cholera epidemics. In the United States, despite the presence of an environmental focus of epidemic V. cholerae, there is less risk of epidemic disease because, presumably, of the extant level of sanitation. However, the risk of sporadic vibrio infection remains. The risk is greatest for persons who are immuno compromised, have cirrhosis (or a history of heavy ingestion of alcohol), or have conditions predisposing them to increased saturation of transferrin with iron. Persons in these risk groups should avoid eating raw oysters (including oysters on the half shell), particularly during the summer and early fall, when water temperatures may exceed 20°C, and should try to minimize exposure of wounds to warmer estuarine or marine waters.

References

40. Centers for Disease Control and Prevention. Update on cholera vaccine.
54. Daniels NA, Ray B, Easton A, et al. Emergence of a new *Vibrio para-

55. Hughes JM, Boyce JM, Aleem ARMA, Wells JG, Rahman ASMM, Cur-
lin GT. *Vibrio parahaemolyticus* enterocolitis in Bangladesh: report of an

56. Bolen JL, Zamiaska SA, Greenough WB III. Clinical features in enteritis

Syndromes of *Vibrio vulnificus* infections: clinical and epidemiological

58. Park SD, Shon HS, Joh NJ. *Vibrio vulnificus* septicemia in Korea: clinical
and epidemiologic findings in seventy patients. J Am Acad Dermatol
1991;24:397–403.

59. Shapiro RL, Alkekruse S, Hutzwagner L, et al. The role of Gulf Coast
oysters harvested in warmer months in *Vibrio vulnificus* infections in

60. Johnston JM, Becker SF, McFarland LM. *Vibrio vulnificus*: man and

and microbiological features of *Vibrio vulnificus* biogroup 3 causing
outbreaks of wound infection and bacteremia in Israel. Lancet 1999;

62. Wright AC, Simpson LM, Oliver JD, Morris Jr. Phenotypic evalu-
ation of acapsular transposon mutants of *Vibrio vulnificus*. Infect

63. Bush CA, Patel P, Gunawardena S, et al. Classification of *Vibrio vul-
ificus* strains by the carbohydrate composition of their capsular poly-

64. Brennt EC, Wright AC, Dutta SK, Morris Jr. Growth of *Vibrio vulni-
ficus* in serum from alcoholics: association with high transferrin

blood from patients with chronic liver diseases: association with phago-
cytosis by neutrophils and serum ferritin levels. J Infect Dis 1999;
179:275–8.

66. Merkel SM, Alexander S, Zufall E, Oliver JD, Huet-Hudson YM. Es-
ternal role for estrogen in protection against *Vibrio vulnificus*–induced

67. Centers for Disease Control and Prevention. *Vibrio vulnificus* infections

68. Nilsson WB, Paranype RH, DePaola A, Strom MS. Sequence poly-
morphism of the 16S rRNA gene of *Vibrio vulnificus* is a possible