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Vibrio alginolyticus infections in the USA, 1988–2012

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SUMMARY

Vibrio alginolyticus causes soft tissue and bloodstream infection; little systematically collected clinical and epidemiological information is available. In the USA, *V. alginolyticus* infections are reported to the Cholera and Other *Vibrio* Illness Surveillance system. Using data from 1988 to 2012, we categorised infections using specimen source and exposure history, analysed case characteristics, and calculated incidence rates using US Census Bureau data. Most (96%) of the 1331 *V. alginolyticus* infections were from coastal states. Infections of the skin and ear were most frequent (87%); ear infections occurred more commonly in children, lower extremity infections more commonly in older adults. Most (86%) infections involved water activity. Reported incidence of infections increased 12-fold over the study period, although the extent of diagnostic or surveillance bias is unclear. Prevention efforts should target waterborne transmission in coastal areas and provider education to promote more rapid diagnosis and prevent complications.

Key words: skin and soft tissue infection, ear infection, *Vibrio alginolyticus*, surveillance.

BACKGROUND

Vibrio alginolyticus, a halophilic bacterium found in marine and estuarine environments, causes severe soft tissue infections, sepsis, and other extraintestinal infections. People come into contact with the bacteria through water exposure or through eating contaminated seafood [1–6]. *V. alginolyticus* is one of roughly a dozen *Vibrio* species that cause human illness and can cause significant morbidity and mortality [7, 39]. *Vibrio* infections have been reported to the Cholera and Other *Vibrio* Illness Surveillance (COVIS) system in the USA since 1988. Surveillance started in the Gulf Coast states and has expanded over time, and *Vibrio* infection became nationally notifiable in 2007. An analysis of both COVIS data and data from the 10-state Foodborne Diseases Active Surveillance Network (FoodNet) from 1996 to 2010 showed a dramatic increase in the incidence of *V. alginolyticus* infection in both systems [1]. For many years, *V. alginolyticus* was the third most common *Vibrio* species reported in human illness, but since 2007, during a period of increasing overall vibriosis rates, it has been the second most common, despite substantial increases in other species [8]. However, little systematically collected clinical and epidemiological information is available regarding *V. alginolyticus* infection.

Although most vibriosis caused by other species is foodborne, *V. alginolyticus* is predominantly transmitted by water [1, 6], which is reflected by geographic clustering in coastal regions [6] and multiple case

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reports of otitis externa and traumatic wound infections involving seawater exposure [9–19, 36]. Significant morbidity, including multiple surgeries, prolonged antibiotic treatment, amputations, and other complications [9–11, 13, 14, 20] can occur. Clinical suspicion is important as special media are needed to isolate *Vibrio* organisms, which may delay diagnosis and appropriate treatment.

We have reviewed surveillance data on *V. alginolyticus* infections in the USA to describe the epidemiology and clinical presentation, and to provide the basis for recommendations for improving prevention.

METHODS

Surveillance and reporting of culture-confirmed vibriosis in the USA, through COVIS (http://www.cdc.gov/nationalsurveillance/cholera_vibrio_surveillance.html), was established in 1988 in the Gulf Coast states of Alabama, Florida, Louisiana, and Texas. Reporting expanded outside of the Gulf Coast in the mid-1990s, and vibriosis became nationally notifiable in 2007 [1]. COVIS collects information on isolates, demographics, pre-existing conditions, clinical features of infection, including presence of a wound, treatments and outcomes, as well as information on travel, seafood, and seawater exposures in the 7 days before illness onset.

For *V. alginolyticus* infections reported to COVIS from 1988 through 2012, we reviewed state and geographical region, patient demographics (age, sex, race), clinical information, and patient exposure(s) (seawater or sea life contact and seafood consumption) in the 7 days before illness onset. Clinical information included source of the isolate (blood, wound, stool, other), patients' pre-existing conditions (specifically liver disease, alcohol use, and immunodeficiency), features of the illness, treatment, and outcome.

Infection site was categorised as (1) blood; (2) gastrointestinal (GI); (3) skin, soft tissue, and other non-sterile sites (hereafter called 'skin-related sites'); and (4) unknown using standard COVIS methods (http://www.cdc.gov/ncezid/dfwed/pdfs/covis-annual-report-2013-508c.pdf; report appendix). The skin-related sites were divided into ear, lower extremity, and other (including head, trunk, upper extremity, and less-common sites) based on the source(s) of the isolate(s). Ear infections were classified as otitis media only if the isolate was specifically described as from a middle or inner ear source (e.g. inner ear fluid, inner ear aspirate); other isolates from the ear were classified as otitis externa. Ear infections were included in the skin-related sites category because very few middle ear infections were reported. We determined the likely transmission route (foodborne, non-foodborne, unknown) from the reported infection site(s) and exposure(s) (single *vs.* multiple exposures and type(s) of exposure, such as seafood consumption or recreational water activity) using COVIS's standard method, as above, without distinction between confirmed and probable routes of transmission.

We conducted analyses nationally, for each state individually, and also for four US regions: the Gulf Coast, Atlantic, Pacific, and Non-Coastal states.[1] We calculated descriptive statistics and determined mechanisms of transmission using data from 1988 to 2012. We calculated incidence rates using previously described methods by dividing the annual number of laboratory-confirmed infections by US Census Bureau population estimates for the surveillance area [1]. To account for the expansion of the surveillance system over time, states were included in the surveillance area from the first year they reported a case [1]. We limited incidence rate calculations to 1996–2012, when reporting had expanded beyond the Gulf Coast states, and focused on 2007–2012 for incidence rate and clinical comparisons, when vibriosis was nationally notifiable. Analysis was conducted using SAS version 9.3 (SAS Institute, Cary, North Carolina).

RESULTS

Epidemiologic observations

A total of 1331 *V. alginolyticus* infections were reported during 1988–2012. Of these, 1272 (96% of all reported cases with an average of 75 cases/year) were reported from 1996 to 2012, after reporting expanded beyond the Gulf Coast, and 825 (62% of all reported cases with an average of 138 cases/year) from 2007 to 2012, after reporting became nationally notifiable. The incidence rate of reported infections increased 12-fold, from 0·005 infections per 100 000 population in 1996 to 0·064 in 2012 nationally (Figure 1) during the period of expanding surveillance. During 2007–2012, when surveillance was

1 Gulf Coast (Alabama, Florida, Louisiana, Mississippi, and Texas), Atlantic (Connecticut, Delaware, Georgia, Massachusetts, Maryland, Maine, North Carolina, New Hampshire, New Jersey, New York, Rhode Island, South Carolina, and Virginia), Pacific (California, Hawaii, Oregon, Washington, and Alaska), Non-Coastal states including the District of Columbia.

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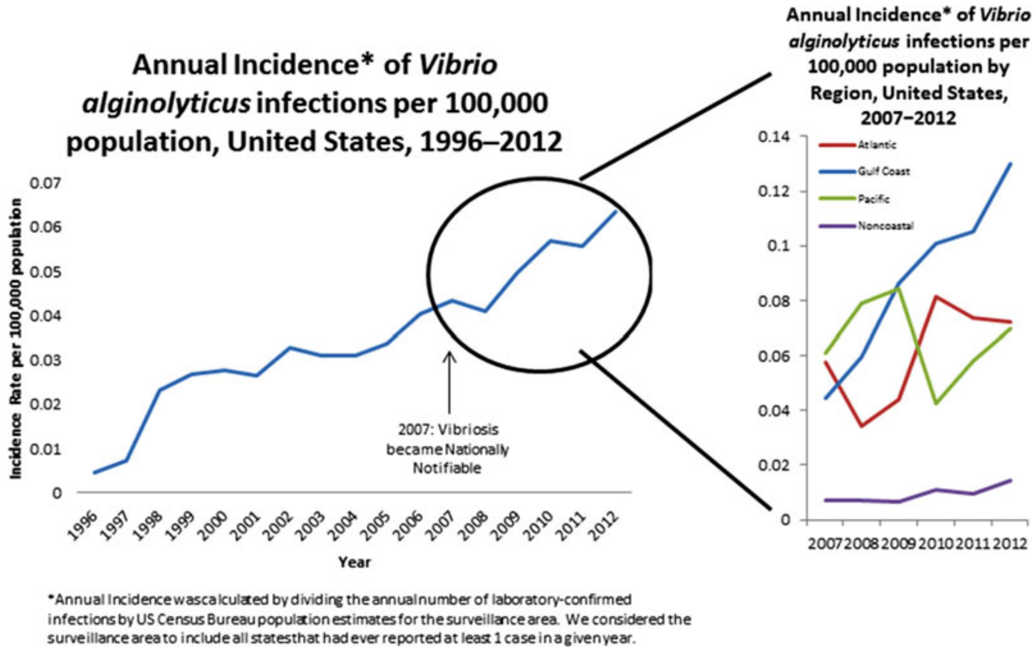

Fig. 1. Annual incidence of *Vibrio alginolyticus* infections per 100 000 population nationally (1996–2012) and by region (2007–2012), USA.

stable, most of the increase in reported incidence occurred in the Gulf Coast region, where reported incidence increased from 0·04 per 100 000 population in 2007 to 0·13 in 2012.

The Gulf Coast reported 528 (40%) infections, the Atlantic 393 (30%), and the Pacific 351 (26%). The number varied substantially by state within the Gulf Coast and Pacific regions, whereas much less variability was observed within the Atlantic region (Supplementary Table S1). Non-Coastal states reported 59 cases (4%), mostly (33, 56%) in patients who reported out-of-state travel; the destination was the Atlantic or Gulf Coast regions for all 23 patients with information reported. Infections peaked during the summers, with the largest number of cases reported during July. The median age of patients was 33 years (0–92 years). Most (913, 70%) were male (Table 1), with at least 60% males in all groups. Information on race was reported for 1140 (86%) patients; the most commonly reported races were white (842/1140, 74%) and black or African American (61/1140, 5%). Information on ethnicity was reported for 592 (44%) patients; because the data were so incomplete, we did not conduct further analysis.

Clinical observations

Most (1162; 87%) infections were in skin-related sites, with an increasing percentage over time. Focusing on 1996–2012, when numbers were large enough for proportions to be relatively stable, the percentage of infections that were in skin-related sites increased from <80% in the mid-1990s to >90% in the 2000s. Infections of skin-related sites were responsible for most of the increase in incidence, increasing 10-fold from 0·0048 infections per 100 000 population in 1996 to 0·047 in 2012. The lower extremity (455, 34% of all infections) and ear (437, 33% of all infections) were the most common skin-related infection sites. Both blood and GI infections were rare and increased minimally, each with 0·0017 infections per 100 000 population reported in 2012. Ear infections were usually described as draining otitis externa (422/437 ear infections with information, 97%); otitis media was uncommon (15, 3%). The next most common other skin-related sites, reported in 270 patients, were upper extremity, head, and trunk. GI infections occurred in 5% (62), blood infections in 4% (56), and the site was not reported in 4% (51). In younger age groups, especially children <10 years of age, most skin-related infections were of the ear, whereas in older age groups, especially those ⩾50 years of age, most were of the lower extremity (Figure 2). During 2007–2012, lower extremity infections were more common in the Gulf Coast (207/433, 48%) than in the Pacific (125, 29%) and Atlantic Coasts (101, 23%).

Most patients (794/1040 with information reported, 76%) did not report any pre-existing conditions.

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Table 1. *Characteristics of Vibrio alginolyticus infections, USA, 1988–2012*

Demographic and clinical information	Number	%
Patient demographics		
Gender	*n* = 1307	
Male	913	70
Female	392	30
Age (years)	*n* = 1276	
<1–9	213	17
10–19	250	20
20–29	135	10
30–39	149	12
40–49	156	12
50–59	130	10
>60	243	19
Clinical findings		
Infection site	*n* = 1331	
Gastrointestinal	62	5
Blood	56	4
Skin related	1162	87
Lower extremity	455	34
Ear*	437	33
Other	270	20
Unknown	51	4
Outcomes	Number/total respondents	
Hospitalisation	235/1202	20
Death	12/1170	1
Treatment with antibiotics	1047/1156	91
Complications and invasive treatment of non-foodborne infections	*n* = 60	
Debridement	20	33
Skin graft	7	12
Other surgery or wound care	13	22
Amputation	8	13
Hearing loss	2	3

* Infections of the ear were predominantly otitis externa (422/437 (97%)).

Another 204 (15%) reported one or more comorbidities. Heart disease and diabetes were the most commonly reported comorbidities (among those with information reported, 107/894 (10%) and 107/895 (10%), respectively). Alcohol use (47, 5%), liver disease (28, 3%), and immunodeficiency (28, 3%) were each relatively uncommon overall. However, in patients with blood infection, 42% (16/38) reported diabetes, 36% (20/56) heart disease, 11% (6/56) alcoholism, and 5% (3/56) liver disease. Comorbid conditions were uncommon in patients with ear infections (no single condition was reported by >2%) and lower extremity infections. Diabetes was reported in 15% (58/386) of patients with lower extremity infections, and heart disease in 11% (49/455). Overall, cellulitis (396/1022, 39%) and fever (198/1006, 20%) were the most commonly reported clinical findings at presentation. Fever was infrequently reported by patients with ear infections (<15%) (Table 2). Diarrhoea was very common in patients with GI infections (84%), as was cellulitis in patients with blood (49%) and lower extremity (66%) infections. Patients with GI infection reported a median of 10 stools per day (range 3 to >24); 28% (12/43) reported bloody stools. Hospitalisation was reported by 20% of patients, and 1% (12) died. Information on cause of death was available for seven and included drowning (2), cardiac causes (6, specified as heart failure in 3), and intracerebral haemorrhage (1). *V. alginolyticus* was isolated from the blood in 8 (66%) of the 12 patients who died. Most patients were treated with antibiotics (1047/1156, 91%), but the details of antibiotic therapy were rarely reported. Most patients with blood infections were hospitalised (43/51, 84%), whereas about a quarter of patients with GI infection (14/58, 24%), lower extremity infection (104/419, 25%), and other skin-related infections (61/237, 26%) were hospitalised. Hospitalisation was uncommon in patients with ear infections (5/388, 1%). Any type of invasive treatment or complication was reported in 18% of patients with blood infections and 11% of those with lower extremity infections. These complications and invasive treatments were described in 60 of the non-foodborne infections, including debridement (33%), amputation (13%), skin grafting (12%), and hearing loss (3%) (Table 1). Debridement, skin grafts, and amputation were most commonly reported by patients with lower extremity infections, although some type of surgery or wound care were also reported by patients with ear or other skin-related site infections. None of the patients with GI disease reported complications or invasive treatment (Table 2).

Circumstances of exposure

A likely transmission route could be assigned for all but 89 (6%) reported infections, with non-foodborne transmission accounting for 86% (1141/1331) and foodborne transmission for 8% (101). Of patients with non-foodborne infections, 83% (829/998) reported exposure to a body of water, usually salt water (706/802, 88%). The most commonly reported water-related activities among these patients were

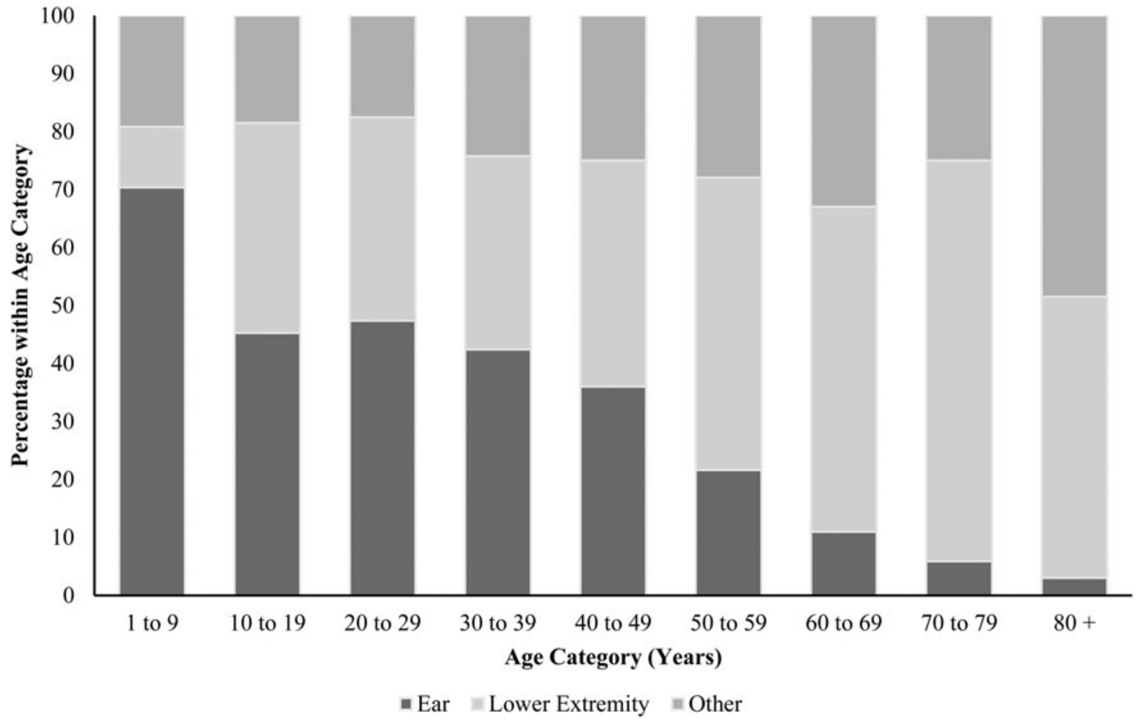

Fig. 2. Percentage of *Vibrio alginolyticus* infections by age category for skin-related sites, USA, 1988–2012.

swimming, diving, or wading (595/758, 78%), followed by walking on the beach, shore, or falling on rocks or shells (370/661, 56%), and boating, skiing, or surfing (197/641, 31%). Activities such as cleaning seafood, being bitten by sea life, or performing construction or repairs were uncommon. Wound exposure was reported by 71% (521/745) of patients with non-foodborne transmission, with 50% of wounds sustained during the water activity (258), 44% reported as pre-existing (229), and the remainder unknown. A variety of pre-existing wounds were described, including chronic ulcerations of the feet and lower extremities, recently sustained cuts, scrapes, or bug bites, as well as history of ear-related wounds described in more detail below. Exposures did not differ substantially by geographical region or by gender.

The types of water activity reported were similar for patients with lower extremity and ear infections. However, patients with a lower extremity infection were more likely to have reported wound exposure (of wounds either sustained during activity or pre-existing) during water activity (294/329 (89%)) than patients with ear infections (68/198 (34%)). Fifty-eight patients with ear infections gave a description of a wound or other breach of the tympanic membrane (either sustained during activity or pre-existing), with 19 reporting tympanic membrane rupture and 14 reporting pre-existing tympanostomy tubes. Patients whose illness was categorised as foodborne reported eating a variety of seafood, most commonly fish, shrimp, crab, and clams. The majority of patients with a GI infection were categorised with foodborne transmission (55/62 (89%)). Seven patients with GI infection whose illnesses were not categorised as foodborne all had stool isolates and reported water exposure but did not report seafood consumption. *V. alginolyticus* was isolated from the stool in 61 patients with GI infection and from the gallbladder in one. We do not have information on whether additional pathogens were identified in stool specimens from these patients.

DISCUSSION

Our analysis of 25 years of US National Surveillance Data shows that 95% of *V. alginolyticus* infections were non-foodborne, primarily waterborne. This transmission pattern contrasts with other *Vibrio* species [7, 8, 25], which are transmitted primarily by food, and it leads to several characteristic epidemiologic findings. First, more than 95% of *V. alginolyticus* infections were reported from coastal states. Second, skin-related infection sites, mainly of the lower extremities and external ear, account for a large

Table 2. *Clinical findings and complications and invasive treatment by infection site, Vibrio alginolyticus infections, USA, 1988–2012*

	GI* (n = 62) n/N (%)	Blood (n = 56) n/N (%)	Skin-related infection sites		
			LE† (n = 455) n/N (%)	Ear (n = 437) n/N (%)	Other (n = 270) n/N (%)
Selected clinical findings					
Fever	17/55 (31)	28/46 (61)	74/366 (20)	43/335 (13)	32/185 (17)
Nausea	24/53 (45)	11/41 (27)	20/362 (6)	14/338 (4)	16/189 (8)
Vomit	20/54 (37)	12/42 (29)	15/360 (4)	5/341 (1)	9/186 (5)
Diarrhoea	47/56 (84)	7/42 (17)	15/361 (4)	12/336 (4)	10/185 (5)
Cellulitis	0/47 (0)	21/43 (49)	254/386 (66)	19/334 (6)	96/191 (50)
Bullae	0/45 (0)	3/33 (9)	46/325 (14)	6/324 (2)	18/160 (11)
Shock	0/46 (0)	8/41 (20)	2/340 (1)	1/322 (<1)	2/170 (1)
Complications and invasive treatment‡					
Any sequela	0/38 (0)	7/39 (18)	41/370 (11)	8/357 (2)	11/189 (6)

* Gastrointestinal (GI).
† Lower extremity (LE).
‡ Complications and invasive treatment were: debridement (19), skin graft (9), other surgery or wound care (15), amputation (8), and hearing loss (2).

majority of *V. alginolyticus* infections, likely because transmission occurs primarily through direct contact with water. Third, ear infections predominated in children, whereas lower extremity infections predominated in older adults. Routine beach activities, such as swimming, diving, or wading; walking on a beach or shore; or boating, skiing, or surfing were most commonly reported; some patients reported falling on rocks or shells, but for the most part, the exposures were not traumatic. We hypothesise that the predominance of males overall and of ear infections in younger age groups and lower extremity infections in older adults reflect exposure-related factors. These findings indicate that effective prevention could be targeted to the coasts and to beachgoers and persons whose work involves salt water activities, although it would ideally not be limited to these groups, since disease is not limited to these groups. Our data also suggest that incidence has increased markedly, although improved awareness of and surveillance for infections may explain some part of the increase.

A closer look at skin-related infection sites reveals some interesting but unexplained observations. For instance, we observed that ear infections were relatively evenly distributed across all coastal regions, while lower extremity infections were more common in the Gulf Coast. We wondered whether Gulf Coast catastrophes – Hurricane Katrina in 2005 and the Deepwater Horizon oil spill in 2010 – might have been associated with higher risk of lower extremity infections, but temporal analyses did not support this idea (data not shown). Also, a higher proportion of infections were of the blood in the Atlantic and Gulf Coast regions than in the Pacific region. Differences in exposure do not appear to explain these observations, as exposures for patients with non-foodborne infections did not differ substantially by region. There is data suggesting that other *Vibrio* species, such as *vulnificus* and *parahaemolyticus* are present in higher concentrations in both water and shellfish, and for a longer part of the year, in the Gulf Coast compared with other US coastal regions [26, 27]. This supports the possibility that patients are exposed to higher concentrations of *V. alginolyticus* in Gulf Coast waters. It is also possible that mild infections are less likely to be diagnosed in areas with lower incidence.

Our review sheds light on clinical aspects of *V. alginolyticus* infection. As in other studies, our review shows that *V. alginolyticus* was rarely isolated from stool [1, 6, 19]. Stool isolation does not in itself elucidate whether *V. alginolyticus* was a cause of diarrhoea or was present incidentally. Stool culture is unlikely to be performed in patients who do not have diarrhoea. Therefore, although the patients categorised as having GI infection in our review usually had both diarrhoea and seafood exposure, without a control group, it is unclear whether *V. alginolyticus* is associated with GI symptoms. Our data indicate that most patients with *V. alginolyticus* infection were generally healthy before their infection and confirm that liver disease, alcohol use, and immunodeficiency are seen less commonly with *V. alginolyticus* infections than in *V. vulnificus* infection [6]. However, in our data, patients in whom *V. alginolyticus* was isolated from the blood were more likely to report diabetes mellitus, heart disease, or alcoholism than patients with infection at other sites. Too, the proportion of patients in our review with these conditions is greater than the proportion in corresponding age groups in the general population [21, 22, 24]. These comorbid conditions may increase the risk of invasive infection after an initial skin or soft tissue infection, although none of the patients in our reports had isolates from more than one site.

Not surprisingly, clinical features of *V. alginolyticus* infection reflect the site of infection, with cellulitis usually reported in lower extremity infections, sometimes with bullae, and fever usually reported in blood infections, sometimes with shock. Overall, fever was relatively uncommon. None of the clinical features on the COVIS report form were common in ear infections, likely because the form has no ear-specific items. Although our data did not frequently describe ear infections specific to the middle ear, numerous patients reported injury to the tympanic membrane or pre-existing tympanostomy tubes, leading us to believe our data underestimates the amount of otitis media present. The mortality rate in our review was low, but as supported by previous case reports [9, 11, 13, 19, 20], morbidity was substantial, including complications requiring debridement, skin grafting, and in some cases even amputation. Almost all patients were treated with antibiotics, but the data do not allow us to assess timeliness of diagnosis and appropriateness of antimicrobial therapy overall or in patients with more severe infections or outcomes. Antimicrobial susceptibility testing conducted by the National Antimicrobial Resistance Monitoring System (NARMS) show that *V. alginolyticus* isolates are almost always resistant to ampicillin and susceptible to other agents [28].

Although changes in reporting related to vibriosis becoming nationally notifiable make interpretation of possible increasing infections in other regions more challenging, the large increase we observed in the Gulf Coast is unlikely to be attributable entirely to surveillance artefact or increased clinical suspicion because COVIS surveillance has been active in this region for more than two decades. The laboratory methods used for detection of *Vibrio* species did not change significantly during the study period. Some authors have proposed that warming of surface water temperatures and an increase in water salinity could lead to increased exposure to this organism [29–32]. In Europe, vibriosis outbreaks have been associated with heatwaves [33, 34]. Data from the National Oceanic and Atmospheric Administration indicate that surface water temperatures have increased along the US coasts as well as in many coastal regions worldwide [23].

Our results indicate roles for both primary prevention of infection and secondary prevention of bad outcomes. Avoiding all exposure to natural bodies of marine or estuarine water when a wound is present would likely greatly reduce risk but may be unrealistic for many. Wearing a waterproof dressing and washing wounds immediately after water exposure may provide some protection [35, 37, 38]. Seeking care early if a wound is worsening is important. The data give little insight into the types of pre-existing wounds that pose the greatest risk for *V. alginolyticus* infection. Guidance is still needed regarding prevention of external otitis and the best method of preventing wound exposure, but parents and paediatricians should be aware of *V. alginolyticus* as a potential cause of both otitis externa and otitis media, especially in coastal areas and among patients with water exposure or ear trauma. Physicians may want to consider the depth or extent of pre-existing wounds and the risk of severe outcomes in particular patients when giving advice regarding water activity. Education of healthcare providers, especially those working in coastal areas, on the presentation of and risk factors for *V. alginolyticus* infection might help with timely diagnosis and treatment. Several case reports describe repeated hospitalisations for severe but unrecognised *V. alginolyticus* infection resulting in the need for surgical management [9–13]. Thus, consideration of *Vibrio* in a patient with salt water exposure and lower extremity or ear infections is important, so that appropriate treatment can be initiated, and diagnostic testing can be requested. For example, alerting the laboratory that *V. alginolyticus* is an organism of interest should prompt the laboratory to plate the specimen on buffered charcoal yeast extract agar plates in addition to the standard media, in order to increase the likelihood that *Vibrio* will be isolated, if present. At the same time, continued collaboration between federal, state, and local health and environmental agencies to monitor *V. alginolyticus* infections in humans and in the environment, as well as continue to investigate the exposures identified as increasing risk of infection, is important to monitor whether the increases we have documented continue.

SUPPLEMENTARY MATERIAL

The supplementary material for this article can be found at https://doi.org/10.1017/S0950268817000140

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DECLARATION OF INTEREST

None.

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