５．各種文献資料

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244	2	Food and Drug Administration. 1985. Action Levels For Poisonous Or Deleterious Substances In Human Food And Animal Feed. U.S. Department of Health and Human Services, Public Health Service, Washington, D.C. 13 pages.	197	
244	3	Food and Drug Administration. 2001. Fish and Fisheries Products Hazards & Controls Guidance, Third Edition. U.S. Department of Health and Human Services, Public Health Service, Office of Seafood, 5100 Paint Branch Parkway, College Park, Maryland 20740-3835. 326 pages.	198	
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422	・	同上	同上	

＊1、情報収集した過程で入手した文献。

＊2、該当文献が入手できなかったことから、該当文献が参照している下記の文献を添付。

Offshore Suspension Relaying To Reduce Levels of Vibrio vulnificus in Oysters(Crassostrea virginica)

Section IV. Guidance Documents
Chapter II. Growing Areas

Guide Contents

.04 Action Levels, Tolerances And Guidance levels for Poisonous or Deleterious Substances in Seafood

Because shellfish are filter feeders, they can readily accumulate substances from the water column. The types of poisonous or deleterious substances that have been recovered from shellfish include heavy metals, pesticides, petroleum products, polychlorinated biphenyls, and naturally occurring marine biotoxins. The source of these contaminants may be industrial, agricultural, mining, spillage, sewage, dredging operations, sludge dumps, and naturally occurring toxigenic marine organisms.

The FDA has established action levels, tolerances and guidance levels for poisonous or deleterious substances to control the levels of contaminants in human food including seafood (FDA Federal Register, 1977; FDA, 1985). Action levels are established and revised according to criteria specified in the ***Code of Federal Regulations*** (21 CFR 109 and 509), and are revoked when a regulation establishing a tolerance for the same substance and use becomes effective. Action levels and tolerance represent limits at or above which FDA will take legal action to remove adulterated products, including shellfish, from the market. Action levels and tolerances, are established based on the unavoidability of the poisonous or deleterious substance and do not represent permissible levels of contamination where it is avoidable. Guidance levels are used to assess the public health impact of the specified contaminant.

Table 1 lists action levels, tolerances and guidance levels established by the FDA for poisonous or deleterious substances in seafood including shellfish. Notices are published in the ***Federal Register*** as new action levels are established or as existing action levels are revised or revoked. Should any of these notices affect Table 1, FDA will issue an interpretation advising NSSP participants of this revision or addition.

Table 1
Action Levels, Tolerances and Guidance Levels for Poisonous or Deleterious Substances in Seafood

Class of Substance	Substance	Level	Food Commodity[a]	Reference
Deleterious Substance	Aldrin/Dieldrin[c]	0.3 ppm	All Fish	CPG sec 575.100[b]
	Chlordane	0.3 ppm	All Fish	CPG sec

				575.100[b]
	Chlordecone[d]	0.3 ppm	All Fish	CPG sec 575.100[b]
		0.4 ppm	Crabmeat	CPG sec 575.100[b]
	DDT, DDE, TDE[e]	5.0 ppm	All Fish	CPG sec 575.100[b]
	Diquat[g]	0.1 ppm	All Fish	40 CFR 180.226
	Glyphosate[g]	0.25 ppm	Fin Fish	40 CFR 180.364
		3.0 ppm	Shellfish	40 CFR 180.364
Toxic Elements	Arsenic	76 ppm	Crustacea	FDA Guidance Document
		86 ppm	Molluscan Shellfish	FDA Guidance Document
	Cadmium	3 ppm	Crustacea	FDA Guidance Document
		4 ppm	Molluscan Shellfish	FDA Guidance Document
	Chromium	12 ppm	Crustacea	FDA Guidance Document
		13 ppm	Molluscan Shellfish	FDA Guidance Document
	Lead	1.5 ppm	Crustacea	FDA Guidance Document
		1.7 ppm	Molluscan Shellfish	FDA Guidance Document
	Nickel	70 ppm	Crustacea	FDA Guidance Document
		80 ppm	Molluscan Shellfish	FDA Guidance Document
	Methyl Mercury	1.0 ppm	All Fish	CPG sec 540.600
	Heptachlor / Heptachlor Epoxide[f]	0.3 ppm	All Fish	CPG sec 575.100
	Mirex	0.1 ppm	All Fish	CPG sec 575.100
	Polychlorinated Biphenyls (PCBs)[g]	2.0 ppm	All Fish	21 CFR 109.30
	2,4-D[g]	1.0 ppm	All Fish	40 CFR 180.142

Natural Toxins	Paralytic Shellfish Poison (PSP)	80 μg/100g	All Fish	CPG sec 540.250
	Neurotoxic Shellfish Poison (NSP)[e]	20 MU	Clams, mussels, Oysters, fresh frozen or canned	NSSP MO
	Amnesic Shellfish Poison (ASP)	20 ppm	All Fish (except in the viscera of Dungeness crab where 30 ppm is permitted	Compliance Program 7303.842

Note: the term "fish" refers to fresh or saltwater fin fish, crustaceans, other forms of aquatic animal life other than birds or mammals and all mollusks as defined in *21 CFR 123.3(d)*.

Footnotes for Table 1

a) Unless otherwise specified, the action levels, tolerances and other values listed apply to both the raw and processed food commodity. Procedures for sample collection and analyses are specified in Sections 420 and 450 of the ***FDA Investigations Operation Manual***; ***FDA Pesticide Analytical Manual*** **(PAM)** Volume I or II; ***AOAC Official Methods of Analysis***; ***APHA Recommended Procedures for the Examination of Sea Water and Shellfish***, Fourth Edition, 1970; or, peer reviewed literature for domoic acid (ASP) methodologies.

b) References designated as CPG represent the FDA Compliance Policy Guides and all associated numbers as they appear in appropriate sections of FDA's Compliance Policy Guides Manual.

c) The action level for aldrin and dieldrin are for residues of the pesticides individually or in combination. However, in adding amounts of aldrin and dieldrin do not count aldrin or dieldrin found at the level below 0.1 ppm for fish.

d) Previously listed as Kepone, the tradename for chlordecone.

e) The action level for DDT, TDE, and DDE are for residues of the pesticides individually or in combination. However, in adding amounts of DDT, TDE, and DDE do not count any of the three found below 0.2 ppm for fish.

f) The action level for heptachlor and heptachlor epoxide are for the pesticides individually or in combination. However, do not count heptachlor or heptachlor epoxide found below 0.1 ppm.

g) The levels published in 21 CFR and 40 CFR represent tolerances rather than guidance levels or action levels.

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LIST OF FDA ACTION LEVELS

SUBSTANCE	COMMODITY	ACTION LEVEL	REFERENCE[1]
Mirex	Fish	0.1 ppm	Memo, 5-7-76 from Edwin L. Johnson EPA
Monitor	Produces (except those for which tolerances are established)	0.1 ppm	Memo 3-21-73 from John R. Wessel. Memo 3-19-73 from Douglas D. Campt, EPA
Paralytic Shellfish Toxin	Clams, Mussels, Oysters, fresh, frozen, canned	80 micrograms/ 100 grams meat	7408.04
Phosvel	Peppers	0.1 ppm	Memo, 2-25-74 from Sam D. Fine Assoc. Commissioner for Compliance
	Green Beans	0.1 ppm	
Polybrominated Biphenyls (PBB's)	Milk & Dairy Products (fat basis)	0.3 ppm	"A Review of Congressman Wm. M. Brodhead's Petition to Reduce FDA's Action Levels for Polybromominated Biphenyls (PBB) In Food", July 27, 1977
	Meat (fat basis)	0.3 ppm	
	Eggs	0.05 ppm	
	Animal Feed	0.05 ppm	

(continued)

device will be used at or near room temperature;

OR

- Comparing the temperature reading on the device with the reading on a known accurate reference device (e.g., a thermometer traceable to National Institute of Standards and Technology (NIST) standards) under conditions that are similar to how it will be used (e.g., steam temperature, water temperature, product internal temperature) within the temperature range at which it will be used;

AND

- Once in service, check the temperature-indicating device or temperature-recording device daily before the beginning of operations. Less frequent accuracy checks may be appropriate if they are recommended by the instrument manufacturer and the history of use of the instrument in your facility has shown that the instrument consistently remains accurate for a longer period of time. In addition to checking that the device is accurate by one of the methods described above, this process should include a visual examination of the sensor and any attached wires for damage or kinks. The device should be checked to ensure that it is operational and, where applicable, has sufficient ink and paper;

AND

- Calibrate the temperature-indicating device or temperature-recording device against a known accurate reference device (e.g., a NIST-traceable thermometer) at least once a year or more frequently if recommended by the device manufacturer. Optimal calibration frequency is dependent upon the type, condition, past performance, and conditions of use of the device. Consistent temperature variations away from the actual value (drift) found during checks and/or calibration may show a need for more frequent calibration or the need to replace the device (perhaps with a more durable device). Devices subjected to high temperatures for extended periods of time may require more frequent calibration. Calibration should be performed at a minimum of two temperatures that bracket the temperature range at which it is used;

AND

- Calibrate other instruments as necessary to ensure their accuracy;

AND

- Review monitoring, corrective action, and verification records within 1 week of preparation to ensure they are complete and any critical limit deviations that occurred were appropriately addressed.

Marine Noncholera *Vibrio* Infections in Florida

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ABSTRACT: In the past decade, there has been a dramatic increase in the number of reported cases of clinical illness from noncholera (marine) vibrio infections, leading to a greater recognition of this potentially lethal disease. The wide spectrum of pathogenicity of this organism is reflected in the six cases in this report, varying from simple gastroenteritis to focal necrotizing cellulitis to fatal septicemia. We have reviewed the fundamental clinical differences between *Vibrio vulnificus* and other noncholera vibrio infections. Physicians treating patients with a history of exposure to coastal waters and/or seafood should be aware of the clinical features and the potential for significant morbidity and mortality of associated *Vibrio vulnificus* infections.

MARINE *Vibrio* organisms, which appear to be ubiquitous in virtually all coastal waters, may represent an important but often unrecognized source of clinical infection. Historically, *Vibrio cholera* (0-group 1) has been of primary interest to clinicians because of the diarrheal and septic manifestations of cholera infection. The noncholera vibrios, previously dismissed as "nonagglutinable vibrios" because of their failure to agglutinate in *Vibrio cholerae* antiserum, were not recognized as significant pathogens until relatively recently (Table 1).[1-4]

Marine vibrios are classified into four recognized pathogenic species: *Vibrio cholerae, V parahaemolyticus, V alginolyticus,* and *V vulnificus* (Table 1).[5,6] *Vibrio parahaemolyticus* was reported in 1950 as the etiologic agent in the outbreak of epidemic Japanese seafood poisonings manifested by gastroenteritis.[7] In 1964, it became apparent that a "variant" form of *Vibrio parahaemolyticus* with the unique characteristic of fermenting lactose was capable of causing significant extraintestinal infections.[5] Known only as a lactose-positive halophilic vibrio until it was later named *Vibrio vulnificus,* the organism has been implicated in fatal septicemias and focal soft tissue infections in persons with marine exposure through contact with seawater or ingestion of raw and/or partially cooked shellfish. Review of records from both the Centers for Disease Control (CDC) and the Florida State Health Department has revealed six cases since 1976 of documented *Vibrio vulnificus* infections in Florida. With an increased awareness of the clinical syndromes and techniques of culture and identification, it is likely that clinical disease caused by this marine organism will be more frequently diagnosed.

Following are brief descriptions of the six reported cases.

CASE REPORTS

Case 1. A 57-year-old white man was admitted to Tampa General Hospital on Oct 4, 1981, with the sudden onset of chills, fever to 106 F (41.1 C), nausea, vomiting, and generalized myalgias. He had previously been well, and he denied diarrhea or abdominal pain. An episode of ascites three months earlier and a history of alcohol ingestion suggested probable alcoholic liver disease, though confirmatory hepatic biopsy had been declined by the patient.

The patient related having eaten raw oysters, obtained from the Apalachicola Bay region, 24 hours before the onset of the febrile episode. Physical examination revealed no focus of infection. Specimens of blood and urine were obtained for culture. Treatment with cefoxitin and tobramycin led to rapid defervescence within 24 hours, but on the second hospital day there was soft tissue swelling of the left ankle, with ecchymotic dermal changes. Aspirates for Gram stain and culture of the leg lesion were negative. Initial blood cultures grew a gram-negative, lactose-positive *Vibrio*, confirmed as *Vibriovulnificus*. The patient completed a ten-day course of antibiotic therapy and had no adverse sequelae to the infection.

Case 2. A 62-year-old white man visiting Fort Lauderdale, Florida, consumed approximately two dozen raw oysters on Dec 27, 1979. The man was reportedly in good health except for "borderline diabetes" and had no history of hepatic dysfunction. In less than 24 hours after eating the oysters, he reported to a local emergency room with nausea and generalized myalgias. After antiemetic medication, he was released from the emergency room, but returned on

TABLE 1. Classification of Vibrio Organisms

Vibrio cholerae
Group O 1
Nongroup O 1
Noncholera vibrios
V parahaemolyticus
V alginolyticus
V vulnificus
Group F *Vibrio* (EF6)
V metschnikovii (enteric group 6)

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Supported in part by Florida Sea Grant No. 125 720073/257*V73.

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Dec 29 with a hemorrhagic rash on the lower extremities. In the subsequent 30 hours of hospitalization, his condition deteriorated and he died of septic shock and disseminated intravascular coagulation. Four blood cultures grew halophilic lactose-positive *Vibrio* organisms, as did a biopsy of the hemorrhagic skin lesion.

Review of the case by the Florida State and County Health Departments revealed the oysters to have originated from Apalachicola Bay, Florida. Bacteriologic analysis of oysters from the restaurant where the patient had eaten failed to reveal any *Vibrio* organisms, but it was not clear whether the cultured oysters were from the same shipment as the ones ingested by the patient.

Case 3. A 39-year-old commercial fisherman had noticed a small cut on his left calf before diving in Gulf waters off Dauphin Island, Alabama, on June 17, 1979. Two days later, he had marked swelling, reddening, and pain in the left ankle, extending to the groin. On admission to Sacred Heart Hospital in Pensacola, Florida, his temperature was 103 F (39.4 C), and there was extensive cellulitis of the left leg. Cultures taken from a blistered area on the left ankle revealed lactose-positive halophilic *Vibrio*. After treatment with erythromycin and cefamandole, the patient's symptoms resolved.

Case 4. A 69-year-old white man employed as a commercial shrimper received small cuts on the hand while fishing in waters off Dauphin Island, Alabama. One day later he noticed swelling and reddening of the dorsoradial aspect of his hand, concomitant with the onset of chills. On the following day, he reported to a Pensacola emergency room, where the diagnosis of probable insect bite was entertained. When the redness, pain, and swelling progressed, he returned to the emergency room, and extensive blistering was noted over the skin. Cultures were taken and treatment for cellulitis was instituted with cefazolin. Four days after the initial injury, with failure to respond to outpatient management, the patient was admitted for parenteral antibiotics and surgical debridement of necrotic tissue on the affected hand. Treatment with tetracycline combined with extensive surgical debridement resulted in adequate healing.

Case 5. A 4 lb 14 oz baby girl was born one month prematurely at Port St. Joseph, Florida, in September 1976. Three hours after birth she developed bloody diarrhea, with 12 stools in 24 hours. After stool cultures and institution of aqueous penicillin therapy, the infant was transferred to a hospital in Pensacola, where colistin was started as well as continued intensive care. After three days of treatment, the diarrhea resolved and no further problems were noted. Stool cultures revealed *Vibrio vulnificus*, confirmed by the Florida State Health Department.

Parental history showed the mother had been an oyster shucker, though she had terminated her employment during the second trimester of pregnancy. The father was a shrimp and oyster fisherman in the Apalachicola Bay and the family took weekly trips to the Bay. Consumption of seafood by this family was seasonal, though the mother denied oyster ingestion during the 12 weeks before the baby's birth. She had had a mild flu-like illness with nausea, vomiting, and fatigue for the 72 hours before delivery, but no definite maternal infection was identified.

Case 6. A 75-year-old fisherman from Steinhatchee, Florida, was admitted on Sept 24, 1981, because of an insect bite on the dorsum of the right hand 36 hours earlier. Examination revealed a pinpoint site of injury compatible with an insect bite. Pain continued, and by afternoon the hand was swollen and tender. The patient was seen 24 hours after the injury with a massively swollen right hand, the dorsum covered with small blebs and vesicles. The patient was febrile and in a toxic condition.

After cultures of the site were obtained, the patient was given cefoxitin sodium (Mefoxin) intravenously, dexamethasone into the site of injury, and tetanus toxoid intramuscularly. He became afebrile on the fourth hospital day, though residual swelling and necrosis of the skin of the dorsum of the right hand were apparent. Initial cultures revealed a gram-negative rod sensitive to cefoxitin, chloramphenicol, ampicillin, tetracycline, cephalosporin, and gentamicin. The patient was discharged on Sept 30 with continued cephalosporin therapy and eventual resolution of the infection.

DISCUSSION

In 1964, the CDC recognized a halophilic marine *Vibrio* with a predilection for extraintestinal sites of infection which appeared similar but not identical to *Vibrio parahaemolyticus* and *Vibrio alginolyticus*. Because the bacterium was thought to be a variant of *V parahaemolyticus* with the unique ability to ferment lactose, cases may have initially been incorrectly identified as *V parahaemolyticus* infection.[8,9]

By July 1979, 41 reports of disease due to the lactose-positive *Vibrio* had accumulated, with evidence of a clinical course and pathogenicity distinctly different from those of the other marine *Vibrio* infections.[1]

Epidemiologic studies have confirmed the widespread occurrence of these marine organisms in the United States coastal waters, as well as worldwide.[10-14] It appears that *Vibrio* infections are seasonal, generally occurring during the summer months, and correlated with marine recreational or occupational exposure and with ingestion of raw or inadequately cooked seafoods. The seasonal incidence of clinical infection may also be influenced by the fluctuations of organism concentration in seawater as it approaches the optimal growth temperature of 35 to 37 C.[15] It has been estimated that the generation time for *V parahaemolyticus* is less than ten minutes and that ingestion of ten organisms will lead to an organism population of 1 million in three to four hours.[16]

Of all the pathogenic noncholera *Vibrio* species, *V parahaemolyticus* has been responsible for the greatest number of cases. A 1950 Japanese epidemic of gastroenteritis was traced to contaminated *shirasu* (sardines), resulting in 272 cases of gastroenteritis with 20 fatalities.[7] Subsequent estimates attribute *V parahaemolyticus* as the etiologic agent in 47% of cases of diarrhea from food poisoning occurring in Japan during the summer months.[5] The major clinical manifestation of *V parahaemolyticus* infection appears to be self-limited gastroenteritis,[10] with only rare cases of septicemia or focal infection in sharp contrast to infection with *V vulnificus* (Table 2).

Vibrio alginolyticus is manifested by otitis or localized soft tissue infection of low morbidity which is often self-limited[17,18] (Table 2). One isolated death in a debilitated patient has been reported.[19]

In contrast to the other marine *Vibrio* infections, *Vibrio vulnificus* may cause septicemia or focal necrotizing cellulitus, and only rarely gastroenteritis,[20,21] though diarrhea is an associated manifestation in an estimated 17% of septicemic patients. The septicemia may mimic a flu-like syndrome with chills, nausea, vomiting, and fever as high as 106 F (41.1 C), as in our Case 1. The onset generally begins within 24 hours after seafood ingestion or exposure to marine waters, as in Cases 1, 2, and 3. Each of the patients with septicemia proven by blood cultures subsequently had secondary cutaneous lesions on the previously normal skin of a lower extremity. In Cases 2 and 3, *V vulnificus*

TABLE 2. Features of *Vibrio* sp Infections Occurring in the United States

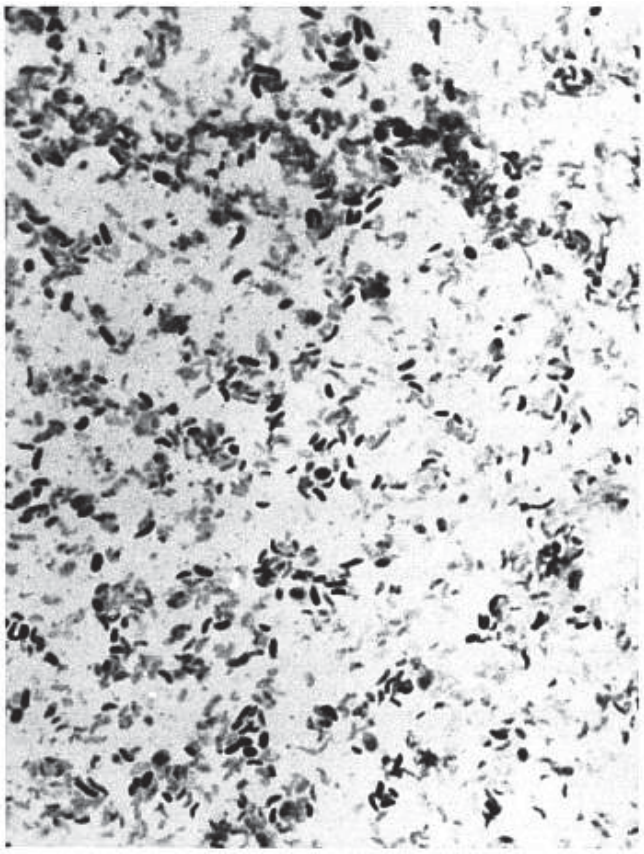
Vibrio *species*	*Reservoirs*	*Disease*	*Mode of Transmission*	*Risk Factors*
V cholera (group O 1)	Man, seafood, seawater	Gastroenteritis Septicemia	Food, water Food, water	Unknown Hepatic disease
V cholera (nongroup O 1)	Seawater, seafood, animals, man	Gastroenteritis Septicemia Tissue infection	Seafood, seawater Seafood Seawater	Unknown Hepatic disease Wounds
V parahaemolyticus	Seawater, seafood	Gastroenteritis Tissue infection	Seafood Seawater	Unknown Wounds
V vulnificus	Seawater, seafood	Tissue infection Septicemia	Seawater Seafood	Wounds Hepatic disease
V alginolyticus	Seawater	Ear and tissue infections	Seawater	Wounds
Group F (EF6) *Vibrio*	Unknown	Gastroenteritis (?)	Unknown	Unknown
V metschnikovii (enteric group 16)	Unknown	Gastroenteritis (?)	Unknown	Unknown

was cultured from the ecchymotic skin site. An estimated 75% of patients with septicemia have evidence of underlying hepatic disease, and there is an overall mortality of 40% in this subset of patients.[1]

A second clinical presentation is that of a localized, often necrotizing cellulitis, as in Cases 3, 4, and 6. The soft tissue infections may cause extensive necrosis and vasculitis, at times requiring surgical debridement or occasionally amputation of the affected limb.[22] An estimated 30% of persons with such wound infections have an underlying disease process such as diabetes mellitus, alcoholism, or congestive heart failure.[5] The lesion begins generally in the lower extremity, with erythema progressing to vesiculation and bullae that eventually ulcerate.[11,20,21] The skin lesions are seen primarily in patients with breaks in the skin, or as secondary lesions of normal skin in patients with septicemia. Cases 4 and 6 suggest that the focus of the initial skin lesion may have been an insect bite. Although both of these individuals were exposed through their occupations to marine waters, the question of insect vector transmission could be entertained but is not currently substantiated.

Treatment of the marine vibrio infection depends on the identification of the specific species. Lactose-positive *Vibrio vulnificus* is uniformly susceptible to penicillin, while *Vibrio parahaemolyticus* and *V alginolyticus* differ in having β-lactamase activity, producing resistance to penicillin, carbenicillin, and ampicillin.[23] Observations with the penicillin resistance and the occurrence in some cases of multiple drug resistance by both *V parahaemolyticus* and *V alginolyticus* emphasize the importance of drug susceptibility studies. Tetracycline appears to be the antibiotic of choice in *V alginolyticus* and *V parahaemolyticus* infection, as well as being adequate coverage in *V vulnificus* infection. In 33 specimens of *V vulnificus*, all were sensitive to penicillin, ampicillin, carbenicillin, cephalothin, chloramphenicol, gentamicin, tetracycline, nitrofurantoin, and sulfasoxazole.[24]

In laboratory identification, the *V vulnificus* species has until recently been classified merely as "noncholera vibrios." The halophilic vibrios are characterized by a unique ability to grow in high concentrations of salt as a consequence of adaptation to a marine environment. As motile gram-negative rods (Figure), sometimes indistinguishable from enteric bacteria, they may be misidentified as coliforms. Although selective media may be necessary for the isolation of *Vibrio* cultured from stool specimens, the extraintestinal cultures of blood and skin sites generally have sufficient saline (0.5%) to sustain *Vibrio* growth. An



High-power microscopic view of *Vibrio vulnificus* organism with evidence of curvilinear gram-negative rods.

increased yield on culture may be obtained by use of thiosulfate citrate bile salts sucrose (TCBS) agar. The two distinctive reactions of lactose fermentation and production of B-D-galactosidase, as well as lower saline tolerance, allows differentiation from the other *Vibrio* species.[24]

Poole and Oliver[25] provided the first experimental data on the pathogenicity and mortality of *Vibrio vulnificus* in animals. They were able to demonstrate that the organism was lethal to mice when 10^6 organisms were injected either intraperitoneally, subcutaneously, or intravenously. The disease manifestations in the mice paralleled those in humans in that subcutaneous injection led to severe local infection with edema and eventual tissue necrosis, and intraperitoneal injection led to bacterial invasion with subsequent septicemia, and death. The primary mechanism of death was loss of vascular integrity, with significant volume depletion, hypotension, and eventual vascular collapse. A further parallel between this experimental work and observations in humans is that ingestion of *V vulnificus* was not lethal, but that *V vulnificus* is substantially more virulent than *V parahaemolyticus* when injected subcutaneously. The mortality in mice from subcutaneous injection of *V vulnificus* was 100% as compared to no mortality when *V parahaemolyticus* was injected.

Host response appears to play a role in the pathogenicity of *V vulnificus*, as suggested by increased morbidity and mortality in patients with liver disease.[1-3] Additional information comes from a study of Carruthers and Kabat,[26] who noted that some strains of *V vulnificus* were not susceptible to bacterial action of normal serum by the complement pathway. Other strains activated the classic pathway well but the alternate pathway much less efficiently. This may have significance in that previous work has shown the cirrhotic host to have a suboptimal response to the activation of the classic complement pathway.[27] Therefore, if these patients must depend on the alternate pathway, and *V vulnificus* is a poor activator of this pathway, then the infection may be more virulent in this situation.

More recently, *V vulnificus* has been found to produce a heat labile, antigenic extracellular toxin.[28,29] Confirmation and further elucidation of the mechanism of this toxin is required before its place in the pathogenesis of human disease is established, but it appears to possess the qualities one would expect in light of the tissue manifestations of the disease (vascular permeability, cytolytic effects, etc).

In summary, noncholera marine *Vibrio* organisms appear to be a normal part of the marine environment throughout the world. An increased recognition of the potential disease from these species has led to cases showing a spectrum from simple, self-limited gastroenteritis to severe necrotizing cellulitis to fatal septicemia. *Vibrio vulnificus* has unique microbiologic characteristics with the ability to grow in high concentrations of salt and to ferment lactose in culture media. Antibiotic susceptibility testing shows *Vibrio vulnificus* to be sensitive to the majority of antibiotics (penicillin, tetracycline, chloramphenicol, gentamicin, sulfasoxazole, and nitrofurantoin), while other noncholera vibrios may frequently exhibit multiple drug resistance. The case reports herein underscore the necessity to consider these organisms in patients with recreational or occupational exposure to marine waters or a history of ingestion of raw or poorly cooked seafoods.

Acknowledgments. We thank the numerous H.R.S. health workers who participated in the initial epidemiologic investigations. In addition, we would like to thank Ms. Betty Page, Tampa, Fla; Dr. J. Dyal, Perry, Fla; Dr. Thomas Hoyt and Dr. E. Westmark, Pensacola, Fla; and Dr. M. Szczeshey, Ft. Lauderdale, Fla.

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after thorough irrigation with scolecidal solution; when this is done, the cavity should be left filled with normal saline to allow progressive resorption and dead-space collapse so as to prevent dead-space infection and subsequent cholangitis.[9] In about one third of cases, there has been local recurrence of echincoccosis in the peritoneal cavity or in other viscera. Other complications include those associated with surgical procedures in general and bacterial infection of the intracystic dead space with subsequent ascending cholangitis. Mebendazole in a dose of 40 mg/kg/day has been advocated in other countries for inoperable cases and for "prophylactic" chemotherapy whenever there is a possibility of recently ruptured cyst.[10] Its efficacy, however, is questionable.

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