Editorials

More Great News for Readers

OUR FUTURE DEPENDS upon our young people. As we teach them, we learn from them; as we guide them, they refresh us. They follow us; they lead us.

In the interest of teaching and learning and leadership, the journal plans to publish periodic sections written by medical students, intended to be read by all. Co-editors Valentina Chen and Robert Cutler, MD, have found deep wells of interest among medical schools and are ready to tap these wells. Ms Chen is a third-year student at the Stanford University School of Medicine. Her undergraduate years were spent at the Johns Hopkins University and Peabody Institute, where she earned a Bachelor of Arts degree in Biophysics and an advanced degree in piano, respectively. She was editor-in-chief of an undergraduate literary magazine. Dr Cutler is Professor of Neurology and Neurological Sciences and Senior Associate Dean for Faculty Affairs at the Stanford University School of Medicine. He attended Harvard College, Tufts University School of Medicine and trained at the University of Chicago where he served on the faculty before moving to Stanford. The following editorial outlines the new section's content and procedures. We welcome your participation as authors, reviewers, and, best of all, readers.

LINDA HAWES CLEVER, MD

Medical Student Section

THE WESTERN JOURNAL OF MEDICINE is pleased to announce the introduction of a new Medical Student Section beginning in 1992. The student section will contain materials written exclusively by medical students. Emphasis will be placed on articles of interest and relevance to practicing physicians. Clinical reviews and results of student research, as well as articles on health care, medical education, and international health are some examples. The section will also contain nonscientific works such as poetry, graphics, photography, editorials, student public service projects, and personal reflections on life in medical school.

The Medical Student Section will appear in the journal on a quarterly basis beginning in January 1992. Manuscripts submitted for publication will be reviewed initially by the editors of the student section, Valentina N. Chen, Stanford University medical student III, and Robert W. P. Cutler, MD, Senior Associate Dean for Faculty Affairs, Stanford University, and then peer-reviewed by experts in the related field.

Submissions currently are being accepted. All manuscripts (and further inquiries) should be sent to Valentina N. Chen, THE WESTERN JOURNAL OF MEDICINE, 221 Main Street, San Francisco, CA 94105. When preparing material for the Medical Student Section, please refer to the Instructions for Authors included in each issue of the journal.

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A Lethal Leviathan—*Vibrio vulnificus*

ONE OF THE MAJOR HAZARDS resulting from the consumption of such gastronomic delights as raw shellfish is the potential exposure to a myriad of bacterial, viral, or parasitic pathogens or to toxins secreted by dinoflagellates.[1] Although illnesses caused by Norwalk and hepatitis A viruses are by far the most frequent infections associated with raw shellfish ingestion, these virally induced syndromes are usually self-limiting and do not pose serious long-term side effects or result in secondary sequelae as a consequence of their primary infections. In contrast, however, and as highlighted in the review article by Koenig and co-workers in this issue,[2] *Vibrio vulnificus* infections can be devastating and life-threatening if prompt medical recognition and intervention are not forthcoming.

Vibrio vulnificus is a halophilic organism existing in a number of marine habitats (water, sediment, shellfish) from Maine to the state of Washington; it is rarely, if ever, recovered from freshwater samples. Environmental studies of this bacterium indicate that high concentrations are normally associated with warmer coastal waters such as those found in the Gulf of Mexico and along the lower Atlantic seaboard from the Carolinas to Florida. Not well known is the fact that many environmental vibrios, some of which are currently unnamed, are phenotypically similar to *V vulnificus* and cannot invariably be separated using simple biochemical procedures. This fact complicates the analysis of the environmental frequency, distribution, and concentration of this bacterium.

Originally described in a seminal study performed by the Centers for Disease Control in 1976,[3] *V vulnificus* is one of only a handful of the more than 30 known *Vibrio* species that are pathogenic for humans. Fortunately, *V vulnificus* possesses unique phenotypic properties (lactose fermentation *o*-nitrophenyl-β-D-galactopyranoside–positive) that aid in its immediate recognition and separation from other clinically important but less pathogenic members. Retrospective analyses of biochemical data on *Vibrio parahaemolyticus* organisms recovered from cases of fulminant invasive infection before the recognition of this species indicate that many of these septic episodes were not due to *V parahaemolyticus* but rather to *V vulnificus*.

In the original studies by the Centers for Disease Control and as outlined in the current review article, the hallmark of this organism is invasive disease. This attribute has been repeatedly emphasized by the coining of such phrases as "monster from the deep," "Neptune's revenge," and "gastronomic hazard" associated with various reports on the invasive nature of this bacterium.[4] Since its original designation as a species in 1979, *V vulnificus* has emerged as one of the three leading species (along with *Vibrio cholerae* and *V parahaemolyticus*) involved in human disease and, with *V cholerae* non-01, accounts for 95% of all septicemic infections reported to the Centers for Disease Control involving vibrios.[4] In almost all cases of *V vulnificus* septicemia, dissemination has arisen through antecedent attachment and colonization of the gastrointestinal tract after the consumption of raw shellfish, particularly oysters. Persons most prone to the development of such systemic infections include those with hepatic disease (cirrhosis, hepatitis, chronic alcoholism), cancer, or hyperferremia (hemochromatosis, thalassemia). Surprisingly, only a few instances of *V vulnificus* bacteremia have been documented in patients with the acquired immunodeficiency syndrome (AIDS) or AIDS-related complex. An additionally intriguing observation is

the failure of most studies on *V vulnificus* bacteremia to document gastroenteritis in as many as 50% of the patients studied immediately preceding their septic episode. This suggests that either many *V vulnificus* strains produce minimal gastrointestinal symptoms or that they multiply to such a minor extent in the bowel before invasion and dissemination through the mucosa that overt infection does not occur. Regardless, few studies have reported the isolation of *V vulnificus* from feces in patients with bacteremia.

Wound infections caused by *V vulnificus* most often occur in persons who have introduced the bacterium into traumatized external sites during commercial (fishing, crabbing, shucking oysters) or recreational (boating, wading) use of marine facilities. For those without underlying disease, infections are not life-threatening, do not disseminate, and respond to appropriate treatment including antimicrobial therapy and debridement. In rare instances, apparently healthy persons have had fulminant wound infections develop that have led to septicemia and a fatal outcome. For persons with underlying illnesses, the prognosis is much poorer because wound infections in them often rapidly progress to bacteremia with a high mortality rate.

The third syndrome described in the article by Koenig and associates, gastroenteritis, is controversial at best. To date, only two articles have been published that describe a tenuous association between the recovery of *V vulnificus* from stool specimens and gastrointestinal symptoms. In the larger of these two investigations, five of the seven persons with diarrhea and cultures positive for *V vulnificus* simultaneously harbored other recognized or reputed enteropathogens (including *Shigella* species) in their stools.[5] Furthermore, there is anecdotal information in the literature to suggest that *V vulnificus* can be asymptomatically carried in the gut, and there is little in vitro evidence of an enteropathogenic mechanism, although enterotoxin production in rabbit ileal loops has been described.

Probably the most frustrating aspect of this bacterium is the current lack of correlation between its in vitro and in vivo pathogenicity. The in vivo passage of *V vulnificus* in mice enhances pathogenicity, as does the administration of strains to iron-overloaded mice; a direct correlation in patients with hyperferremia or hepatic dysfunction has not been demonstrated, however. In addition to those virulence characteristics described in the article of Koenig and colleagues, *V vulnificus* has been reported to produce other cell-associated or extracellular factors such as pili, hemolysins, a mucinase, chondroitinase, and hyaluronidase; none of these has been directly linked to clinical infections. Unfortunately, the most recent genetic studies on the *V vulnificus* cytolysin, once thought to be a critical factor in virulence, now indicate that it plays a much reduced role in pathogenicity.[6] Probably the most attractive candidate at present is the acidic mucopolysaccharide capsule of *V vulnificus*.[4] Present in virulent strains, spontaneous mutants lacking this factor are nonpathogenic in mice, and acapsular isogenic mutants constructed in vitro through transposon mutagenesis show decreased resistance to the bactericidal activity of normal serum and are less virulent in the mouse model.[7] A direct correlation with in vivo pathogenicity is lacking, however, and most pathogenic strains (encapsulated; opaque colony) undergo phase variation in vitro to a nonpathogenic form (acapsular; translucent colony). What occurs in vivo during the infection process is presently unknown.

Over the past 15 years, our knowledge of the microbiology, environmental distribution, clinical syndromes, and susceptible patient populations associated with *V vulnificus* has significantly increased. On the down side is the fact that little progress has been made in the areas of environment-to-human transmission of this microbe, on the pathophysiology of infection, and on the important variables that regulate the virulence and pathogenic potential of this invasive bacterium. Currently there is a dearth of information on what concentrations of *V vulnificus* in raw seafood are required to elicit clinical disease (infectious dose). Also troublesome is the fact that, like *V parahaemolyticus*, strains of *V vulnificus* recovered from raw shellfish do not match the biotype of patient isolates even when the environmental strain is recovered from the same lot of seafood as that consumed by the affected person. How differences observed in the virulence potential of *V vulnificus* strains in vitro translate to the in vivo situation and transmissibility from environmental sources (infectivity) is also unknown. It is hoped that research in these areas over the next five years will answer some of these questions.

Overall, *V vulnificus* does not pose a serious health risk to the general population, but, for certain highly susceptible persons (liver disease, hyperferremia), efforts should be directed toward the education of these persons to avoid eating raw shellfish, in particular raw oysters, irrespective of current culinary trends. In septic persons with a food, recreational, or travel history documenting possible exposure to the marine environment or its by-products, *V vulnificus* infection should always be considered in the differential diagnosis because of the rapid progression of such infections to lethal results. In addition, one recent alarming note is a report of *V vulnificus* septicemia in persons with no known exposure to seafoods or the ocean.[8] Because of this, it is imperative that Gram's stains of blood cultures displaying curved bacilli with or without pleomorphic forms (coccal, bulbous) be reported as suspicious for the presence of *Vibrio*. Once colonies are identified and in view of the limited number of *Vibrio* species associated with sepsis (*V cholerae* non-01, *V vulnificus*), rapid tests (oxidase, indole, and *o*-nitrophenyl-β-D-galactopyranoside–positivity) can lead to a presumptive diagnosis of *V vulnificus* bacteremia, and appropriate medical staff can then be alerted. With concerted educational, diagnostic, and research efforts geared toward the prevention and treatment of systemic *V vulnificus* infections, the deadly punch of this "sea monster" can be diminished in the near future.

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