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REVIEW

Epidemiology, pathogenetic mechanism, clinical characteristics, and treatment of *Vibrio vulnificus* infection: a case report and literature review

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Abstract

Vibrio vulnificus is a Gram-negative bacterium that belongs to the Vibrionaceae family. It represents a deadly opportunistic human pathogen which grows in water with the proper temperature and salinity, and is mostly acquired from seafood eating or direct contact. In susceptible individuals, a traumatic infection could be fatal, causing severe wound infection and even septic shock, and may require amputation. Global warming plays an important role in the geographical area expanding of Vibrio disease. The pathogenesis of *Vibrio vulnificus*–associated sepsis is very complex, including iron intake, cell injury, and adhesion-related protein and virulence regulation. *Vibrio vulnificus* infection mainly manifests clinical subtypes such as primary sepsis, traumatic infection, and gastroenteritis, with rapid symptom progression and signs of multiple organ dysfunction syndrome (MODS). It is important to assess these pathogenetic mechanisms in order to select more appropriate measures to prevent and treat *Vibrio vulnificus* infections, including antibiotic usage and surgical intervention. In this work, we report a typical case of successful treatment of necrotizing fasciitis caused by *Vibrio vulnificus*, and review the epidemiology, pathogenetic mechanism, clinical characteristics, and treatment of *Vibrio vulnificus* infection.

Keywords *Vibrio vulnificus* · Sepsis · Epidemiology · Pathogenesis · Clinical characteristics · Treatment

Introduction

Vibrio vulnificus is a Gram-negative, halophilic, alkaliphilic marine bacterial pathogen commonly living on plankton and shellfish, especially oysters, which grow in water at temperature between 15 and 27 °C and salinity from 0.7 to 1.6% of the harbor, river, and sea junctions as well as inland salt lakes. The bacterium was reported firstly to cause calf gangrene and endotoxin shock in 1970 [1, 2], and termed *V. vulnificus* whose opportunistic pathogenesis of infection was reported over the world in 1979 [2, 3]. Humans can be infected after eating seafood contaminated with *V. vulnificus* or direct contact in a wound. *V. vulnificus*–associated sepsis is a fatal disease with the mortality rate over 50%, which is more severe in patients with chronic liver disease. It is highly prevalent in some coastal cities in the USA, Japan, and Taiwan.

In this report, we shared a successful diagnosis and treatment case of sepsis shock caused by *V. vulnificus* infection in our hospital in Shanghai, a coastal city of eastern China, and summarized the related epidemiological characteristics, pathogenetic mechanisms, clinical manifestations, and treatment methods.

Case report

A 72-year-old woman with no significant medical history was admitted to the intensive care unit (ICU) with a diagnosis of severe sepsis shock caused by an accidental sting from a river shrimp on the dorsum of the right foot 2 days before. After the sting, the patient rapidly developed vomiting, unconsciousness, incontinence, with ecchymoses and blisters around the wound on the right lower extremity. The ecchymoses

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expanded rapidly, and the blisters enlarged and ruptured within 12 h. The patient's condition deteriorated rapidly, and developed sepsis shock the next day and was immediately admitted to the ICU. Physical examination revealed that the right lower limb was severely inflamed with ecchymosis and several blisters (Fig. 1a). The patient underwent debridement immediately after admission (Fig. 1b). The wound effusion was cultured, and *V. vulnificus* was detected within 48 h.

Treatment measures, including anti-infection with meropenem and levofloxacin, fluid resuscitation, vasoactive agents, active debridement and dressing change, and continuous renal replacement therapy (CRRT) were applied, and vital signs were gradually improved on day 7. On the same day, magnetic resonance imaging (MRI) was performed and showed extensive swelling in the soft tissue of the right lower limb (Fig. 2a). After a series of treatments, the wound showed no improvement but instead progressed to necrotizing fasciitis (Fig. 1c, d). Computed tomographic angiography (CTA) scan on day 19 revealed stenosis and occlusion of the right posterior tibial and peroneal arteries (Fig. 2b). Finally, right below-knee amputation was carried out on day 20 after admission, and the patient achieved recovery and was discharged from the ICU on day 26.

Epidemiology

V. vulnificus sepsis overtly has regional and seasonal characteristics, and is sporadic every year. More than 95% of lethal *V. vulnificus* infections occur in subtropical regions, especially in the western hemisphere and the Atlantic Ocean, including Europe, America, Singapore, Thailand, and Japan. In China, it is mainly prevalent in Taiwan and Hong Kong, and the southeast coastal cities of the mainland [4–6].

The elevated incidence of *V. vulnificus* infection is not limited to the abovementioned countries. Indeed, the geographical area of Vibrio-associated disease is expanding, most likely due to rising ocean temperatures [7, 8]. Some studies have also identified a relationship between Vibrio and salinity [9, 10] while others do not [11, 12], and the relationship between salinity and temperature may be complex [13]. High prevalence of *V. vulnificus* was found to be associated with a salinity level of 5 to 20‰, with the maximum environmental salinity tolerance of approximately 33–36‰ [14, 15].

The infection rate is higher in males than females (86.1% and 13.9%, respectively), because of higher proportion of exposure to seawater and seafood, as well as an elevated incidence of liver disease due to the higher proportion of drinking in men than women.

Studies found that global warming may have affected marine ecology as well as disease emergence in Israel [16–18], which may reflect the direction and path of disease transmission via the warm currents of the global world. Multiple studies have suggested that the environmental temperature is critical for the pathogenic effects of *V. vulnificus* [19–26]. For example, bacterial richness and virulence are closely related to water temperature. The density of *V. vulnificus* increases slowly at low temperature, but rapidly at normal temperature (18 to 26 °C), and stop increasing at high temperatures [20].

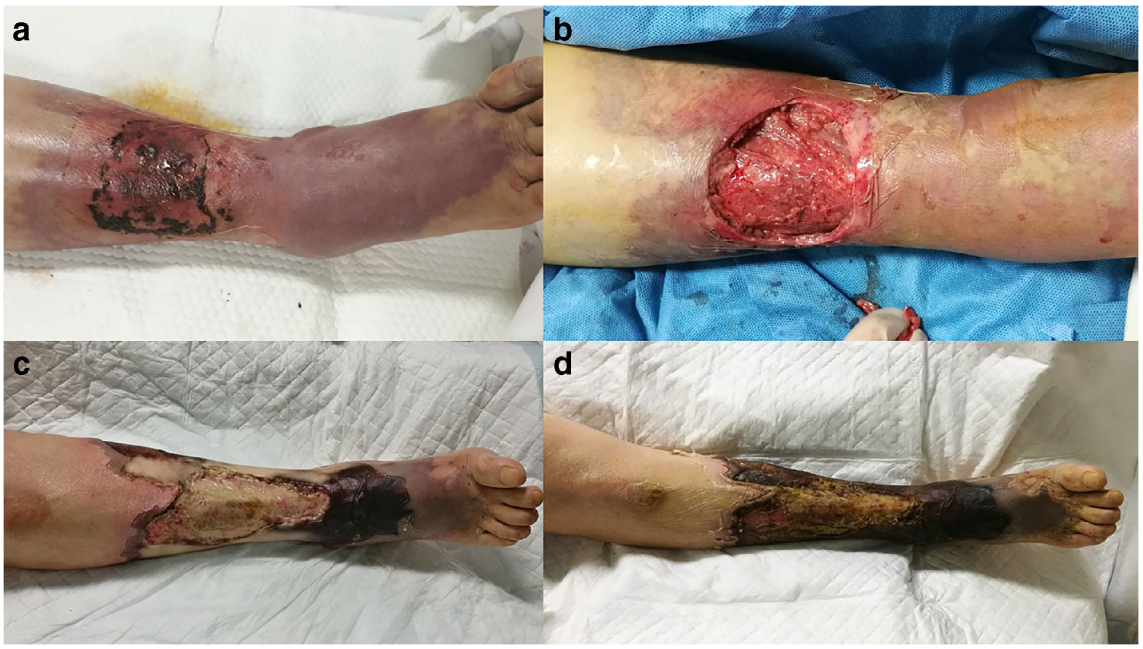

Fig. 1 Progress of the right lower limb necrotizing fasciitis. **a** Admission day: leg wound showed inflammation, swelling, and several blisters. **b** Admission day: leg wound showed redness after debridement on admission day. **c** Day 7 after admission: skin of right lower limb appeared black and soft tissue began to show necrosis. **d** Day 15 after admission: skin of right lower limb showed progressive soft tissue necrosis

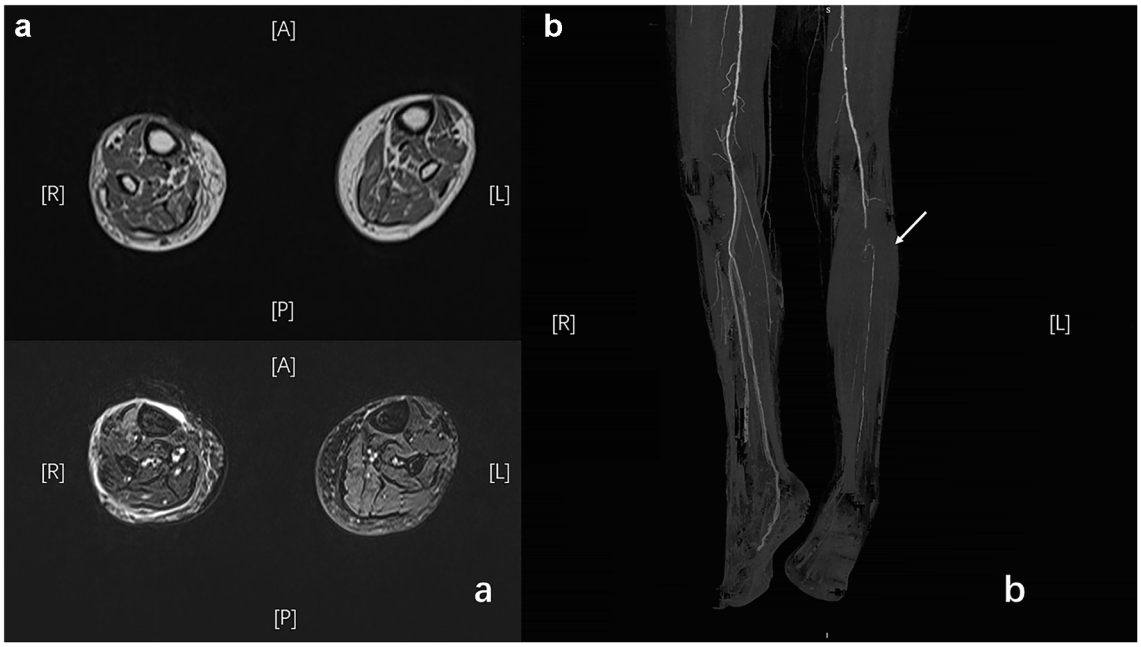

Fig. 2 Results of MRI and CT scan. **a** MRI results showed extensive swelling in soft tissue of right lower limb. **b** CT scan showed stenosis and occlusion of right posterior tibial artery and peroneal artery (white arrow)

Cooling shellfish, immediately storing them between 0 and 4° and rationally using antibiotics could reduce the amounts of pathogenic *V. vulnificus* and critical events.

V. vulnificus infection has an obvious peak in summer, and most cases occur from April to November. According to previous reports, seasonal *V. vulnificus* infection has slightly shorter durations in Japan (from June to November) and the USA (from May to October) [27, 28]. Farmed fish and shellfish are usually harvested from April to early November with the sea coast temperature above 20 °C, the ideal temperature for *V. vulnificus* growth, and the tropical warm water lasts longer than that of temperate and subtropical countries or regions. It is not surprising that in warm or harvest months, wound contact with seawater, dealing with seafood, or consumption of raw seafood may lead to increased amounts of *V. vulnificus* infection. Although the annual average temperature of Taiwan is above 15 °C, the *V. vulnificus* infection rate is low during the period from December to February because of reduced fishing activities associated with the powerful northeaster waves usually that arrive in Taiwan in winter [4].

Pathogenetic mechanism

The pathogenesis of *V. vulnificus* sepsis is very complex, and the following factors may be associated.

CadC, cadB, and cadA activation can enhance *V. vulnificus* tolerance to gastric acid. Meanwhile, capsular polysaccharide (CPS) confers bacterial resistance to phagocytosis, which is related to *V. vulnificus* survival in vivo.

Excessive serum iron amounts can significantly increase the half-lethal rate and pathogen load of *V. vulnificus*. Multiple animal experiments and clinical findings show that elevated serum iron increases *V. vulnificus* infection through various ways of which the specific mechanisms remain unclear. Iron concentration affects *V. vulnificus*, which through the main ferric uptake regulator (FUR) directly or indirectly inhibits the transcription of the major regulator of quorum-sensing gene, SmcR, and affects the entire iron uptake process to escape the expression of innate immune-related genes. PAJUELO et al. [29] firstly reported FUR inhibition of bacterial metabolic regulators and transmembrane DNA ligation regulatory proteins in Vibrio [30]. It was confirmed that high serum iron levels are prominent features in many *V. vulnificus* infection patients [31].

Cell injury is another factor in the pathogenesis of *V. vulnificus*. Virulence factors of *V. vulnificus*, including cytolysin, repeats-in-toxin A1 (RtxAl), and extracellular protease (ECPase), can directly cause cell injury [32–34]. A study found that *V. vulnificus* enters the body and activates the MD2-TRL4-NF- κB pathway, inducing an inflammatory and anti-inflammatory reaction imbalance, which plays an important role in its pathogenesis.

Outer membrane protein U (OmpU) that binds to fibronectin as a major component of the mammalian extracellular matrix represents a secretory protein of *V. vulnificus* outer membrane and is involved in bacterial adhesion. In addition to the OmpU protein, *V. vulnificus* also has immunogenic lipoprotein A (I1pA), which acts as an adhesin and immunogen to activate intracellular TLR1/TLR2, MyD88, MAPKs, NF-κB, and AP-1 pathways by inducing Toll-like receptor 1/2 in human

monocytes (THP-1), triggering an inflammatory cascade that releases a large amount of inflammation factors [34].

The cAMP-cAMP receptor protein (CRP) system regulates bacterial virulence factors, including cytolysin, metalloproteinase, and iron uptake systems. Another virulence regulator, AphB, has a wide range of functions which include acid neutralization, motility, adhesion, and pathogenicity. Recent studies have found that AphB also induces intestinal epithelial cells to produce cytokine-8 (interleukin-8, IL-8) [35]. Moreover, hemolysin considered a potential common virulence regulator of bacteria is a major regulator of *V. vulnificus* toxicity, regulating the repeats-in-toxin A1 (rtxA1), vvhA, and vvpE genes [36].

Clinical characteristics

The trend of *V. vulnificus* infection increases with climate warming and marine activities, as well as the presence of high-risk factors such as alcohol, liver disease, systemic diseases, and diabetes [29]. *V. vulnificus* infection mainly manifests the following clinical subtypes, including primary sepsis, traumatic infection, gastroenteritis, and basic diseases.

The pathogen enters the bloodstream through the gastrointestinal tract by eating raw shellfish such as oysters or directly through open wounds, and then induces sepsis. The main disease manifestations include acute fever, chills, shock, skin, and muscle damage. Individuals infected through gastrointestinal tract show symptoms of acute gastroenteritis including diarrhea, nausea, vomiting, abdominal pain, and dyspnea. Typical skin and muscle lesions include local or flaky erythema and ecchymosis, blood blisters with exudation, necrosis and cellulitis, necrotizing fasciitis, and muscle inflammation. After contacting with seawater or infected marine animals, skin and muscle damage rapidly develop into necrosis and lead to severe sepsis, which might result in a life-threatening condition [37, 38]. The calf lesions could progressively worsen within a few hours and quickly spread to the thigh. A definite contact history, rapidly deteriorating systemic state, and local typical bloody bullous lesions are diagnosed as important clues to detect sepsis caused by *V. vulnificus* infection. Hypotension or shock, rapid progression of symptoms, and multiple organ dysfunction syndrome (MODS) occur within 24–48 h in most patients, with a mortality rate exceeding 50% [39].

V. vulnificus infection more commonly occurs in fishery-processing personnel during the period from April to November [40, 41]. A history of basic diseases, such as long-term alcoholism and chronic liver disease, would increase the risk of *V. vulnificus* infection [42]. Previous studies have shown that individuals with impaired immune system or chronic liver diseases, such as cirrhosis, are eight times more likely to develop the disease in comparison with healthy people. Another striking observation is that *V. vulnificus* infection is highly associated with age, and only one death case < 25 years old of the 70 cases was reported, compared with a mortality rate of 49% in 40–60-year-old patients [43].

Treatment

After exact pathogenic diagnosis, appropriate and timely treatment is extremely important. Early susceptibility testing suggested that *V. vulnificus* is sensitive to various antibiotics. The US Centers for Disease Control (CDC) recommended third-generation cephalosporins combined with tetracyclines as the recommended treatment for V. vulnificus infection. Nevertheless, increasing evidence indicates that *V. vulnificus* has different degrees of resistance to various antibiotics worldwide and diverse sea areas in recent years [44, 45]. Antibiotic treatment of *V. vulnificus*–infected patients should be customized in different countries. For example, doxycycline is recommended as the first-line treatment in Italy [46]. Meanwhile, ceftazidime is recommended as the first-line treatment in the USA and India [47]. In some researches, quinolones are considered superior to tetracyclines, and cephalosporin combined with quinolones is more effective [48, 49].

Early debridement and necessary amputation play a vital role in improving prognosis of *V. vulnificus*–infected patients. Early surgical intervention can improve prognosis, and experienced surgeons should assess whether emergency surgery is needed to treat the infection as soon as possible [50]. In patients with severe hemodynamic instability, low platelet count and severe coagulation disorders, emergency incision, and drainage should be preferred [51]. The skin of the infected limb is incised to bluntly separate the subcutaneous tissue, and fascia is exposed until the sarcolemma under local anesthesia or venous analgesia. The method of incision is determined according to the coagulation function, skin tension, and extent of lesion. After the operation, a gauze soaked with iodophor and sulfamethazine solution is externally applied to facilitate the change of dressing and timely evaluation of the wound. The affected limb should be amputated to save life if muscle necrosis is too severe to mend.

It is necessary to admit the patient to the intensive care unit (ICU) as soon as possible to continue further intensive monitoring and comprehensive treatment. Early continuous renal replacement therapy (CRRT) is helpful in patients with MODS by eliminating endotoxin and inflammatory mediators. Non-invasive or invasive mechanical ventilation should be adopted for patients with acute lung injury or acute respiratory distress syndrome (ARDS).

Prevention

Clinical awareness is critical for the prevention of *V. vulnificus* infection, especially in patients with low immune function. Individuals may be infected by eating marine products contaminated with the bacteria or directly contacting the bacteria

with open wounds. Fifty percent of the patients die from MODS within 48 h of onset [52]. Since *V. vulnificus* infection is highly lethal, its prevention is extremely important. It is advised that high-risk individuals should avoid eating raw seafood in the summer season, keeping the damaged skin or open wounds away from seawater. In case of recent exposure to seawater or seafood, patients with lower limb infection, fever, hypotension, and other symptoms should seek early diagnosis and treatment of *V. vulnificus* infection, as it is a critical factor in improving prognosis.

Conclusion

V. vulnificus is a deadly and opportunistic human pathogen which usually infects humans through eating seafood or direct contact with open wounds. *V. vulnificus* infection could rapidly progress to sepsis shock and even death. Early culture and diagnosis, rational use of antibiotics, timely debridement, and even amputation can save the patient's life. For patients with low immune function, clinical awareness of prevention is especially important.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent Written informed consent was obtained from the patient, and the patient's identity has been kept confidential and cannot be revealed from the whole article.

References

1. Roland FP (1970) Leg gangrene and endotoxin shock due to vibrio parahaemolyticus–an infection acquired in New England coastal waters. N Engl J Med 282(23):1306. https://doi.org/10.1056/nejm197006042822306
2. Yun NR, Kim DM, Lee J, Han MA (2015) pH level as a marker for predicting death among patients with Vibrio vulnificus infection, South Korea, 2000-2011. Emerg Infect Dis 21(2):259–264. https://doi.org/10.3201/eid2102.131249
3. Williams TC, Froelich BA, Phippen B, Fowler P, Noble RT, Oliver JD (2017) Different abundance and correlational patterns exist between total and presumed pathogenic Vibrio vulnificus and V. parahaemolyticus in shellfish and waters along the North Carolina coast. FEMS Microbiol Ecol 93(6). https://doi.org/10.1093/femsec/fix071
4. Huang KC, Weng HH, Yang TY, Chang TS, Huang TW, Lee MS (2016) Distribution of fatal Vibrio vulnificus necrotizing skin and soft-tissue infections: a systematic review and meta-analysis. Medicine 95(5):e2627. https://doi.org/10.1097/md.0000000000002627
5. Oishi H, Ura Y, Mitsumizo S, Nakashima M (2006) A collective review of Vibrio vulnificus infection in Japan. Kansenshogaku Zasshi 80(6):680–689
6. Hsueh PR, Lin CY, Tang HJ, Lee HC, Liu JW, Liu YC, Chuang YC (2004) Vibrio vulnificus in Taiwan. Emerg Infect Dis 10(8):1363–1368. https://doi.org/10.3201/eid1008.040047
7. Baker-Austin C, Trinanes JA, Taylor NGH, Hartnell R, Siitonen A, Martinez-Urtaza J (2012) Emerging Vibrio risk at high latitudes in response to ocean warming. Nat Clim Chang 3(1):73–77. https://doi.org/10.1038/nclimate1628
8. Levy S (2015) Warming trend: how climate shapes Vibrio ecology. Environ Health Perspect 123(4):A82–A89. https://doi.org/10.1289/ehp.123-A82
9. Johnson CN, Flowers AR, Noriea NF 3rd, Zimmerman AM, Bowers JC, DePaola A, Grimes DJ (2010) Relationships between environmental factors and pathogenic Vibrios in the northern Gulf of Mexico. Appl Environ Microbiol 76(21):7076–7084. https://doi.org/10.1128/aem.00697-10
10. Igbinosa EO, Obi CL, Okoh AI (2011) Seasonal abundance and distribution of Vibrio species in the treated effluent of wastewater treatment facilities in suburban and urban communities of Eastern Cape Province, South Africa. J Microbiol (Seoul, Korea) 49(2):224–232. https://doi.org/10.1007/s12275-011-0227-x
11. Singleton FL, Attwell R, Jangi S, Colwell RR (1982) Effects of temperature and salinity on Vibrio cholerae growth. Appl Environ Microbiol 44(5):1047–1058
12. Sobrinho Pde S, Destro MT, Franco BD, Landgraf M (2014) A quantitative risk assessment model for Vibrio parahaemolyticus in raw oysters in Sao Paulo State, Brazil. Int J Food Microbiol 180:69–77. https://doi.org/10.1016/j.ijfoodmicro.2014.04.008
13. Johnson CN, Bowers JC, Griffitt KJ, Molina V, Clostio RW, Pei S, Laws E, Paranjpye RN, Strom MS, Chen A, Hasan NA, Huq A, Noriea NF 3rd, Grimes DJ, Colwell RR (2012) Ecology of Vibrio parahaemolyticus and Vibrio vulnificus in the coastal and estuarine waters of Louisiana, Maryland, Mississippi, and Washington (United States). Appl Environ Microbiol 78(20):7249–7257. https://doi.org/10.1128/aem.01296-12
14. Macian MC, Arias CR, Aznar R, Garay E, Pujalte MJ (2000) Identification of Vibrio spp. (other than V. vulnificus) recovered on CPC agar from marine natural samples. Int Microbiol 3(1):51–53
15. Froelich BA, Williams TC, Noble RT, Oliver JD (2012) Apparent loss of Vibrio vulnificus from North Carolina oysters coincides with a drought-induced increase in salinity. Appl Environ Microbiol 78(11):3885–3889. https://doi.org/10.1128/aem.07855-11
16. Paz S, Bisharat N, Paz E, Kidar O, Cohen D (2007) Climate change and the emergence of Vibrio vulnificus disease in Israel. Environ Res 103(3):390–396. https://doi.org/10.1016/j.envres.2006.07.002
17. Bisharat N, Agmon V, Finkelstein R, Raz R, Ben-Dror G, Lerner L, Soboh S, Colodner R, Cameron DN, Wykstra DL, Swerdlow DL, Farmer JJ 3rd (1999) Clinical, epidemiological, and microbiological features of Vibrio vulnificus biogroup 3 causing outbreaks of wound infection and bacteraemia in Israel. Israel Vibrio Study Group Lancet (London, England) 354(9188):1421–1424
18. Bisharat N, Raz R (1996) Vibrio infection in Israel due to changes in fish marketing. Lancet (London, England) 348(9041):1585–1586. https://doi.org/10.1016/s0140-6736(05)66199-5
19. Kim DM, Jung SI, Jang HC, Lee CS, Lee SH, Yun NR, Neupane GP, Park KH (2011) Vibrio vulnificus DNA load and mortality. J Clin Microbiol 49(1):413–415. https://doi.org/10.1128/jcm.01913-09
20. Motes ML, DePaola A, Cook DW, Veazey JE, Hunsucker JC, Garthright WE, Blodgett RJ, Chirtel SJ (1998) Influence of water temperature and salinity on Vibrio vulnificus in Northern Gulf and Atlantic Coast oysters (Crassostrea virginica). Appl Environ Microbiol 64(4):1459–1465

21. Watanabe H, Miyoshi S, Kawase T, Tomochika K, Shinoda S (2004) High growing ability of Vibrio vulnificus biotype 1 is essential for production of a toxic metalloprotease causing systemic diseases in humans. Microb Pathog 36(3):117–123
22. Kaspar CW, Tamplin ML (1993) Effects of temperature and salinity on the survival of Vibrio vulnificus in seawater and shellfish. Appl Environ Microbiol 59(8):2425–2429
23. Miyoshi N, Shimizu C, Miyoshi S, Shinoda S (1987) Purification and characterization of Vibrio vulnificus protease. Microbiol Immunol 31(1):13–25
24. Shinoda S, Miyoshi S (2011) Proteases produced by vibrios. Biocontrol Sci 16(1):1–11
25. Natividad-Bonifacio I, Fernandez FJ, Quinones-Ramirez EI, Curiel-Quesada E, Vazquez-Salinas C (2013) Presence of virulence markers in environmental Vibrio vulnificus strains. J Appl Microbiol 114(5):1539–1546. https://doi.org/10.1111/jam.12149
26. Elgaml A, Higaki K, Miyoshi S (2014) Effects of temperature, growth phase and luxO-disruption on regulation systems of toxin production in Vibrio vulnificus strain L-180, a human clinical isolate. World J Microbiol Biotechnol 30(2):681–691. https://doi.org/10.1007/s11274-013-1501-3
27. Shapiro RL, Altekruse S, Hutwagner L, Bishop R, Hammond R, Wilson S, Ray B, Thompson S, Tauxe RV, Griffin PM (1998) The role of Gulf Coast oysters harvested in warmer months in Vibrio vulnificus infections in the United States, 1988-1996. Vibrio Working Group. J Infect Dis 178(3):752–759
28. Inoue Y, Ono T, Matsui T, Miyasaka J, Kinoshita Y, Ihn H (2008) Epidemiological survey of Vibrio vulnificus infection in Japan between 1999 and 2003. J Dermatol 35(3):129–139. https://doi.org/10.1111/j.1346-8138.2008.00432.x
29. Pajuelo D, Hernandez-Cabanyero C, Sanjuan E, Lee CT, Silva-Hernandez FX, Hor LI, MacKenzie S, Amaro C (2016) Iron and Fur in the life cycle of the zoonotic pathogen Vibrio vulnificus. Environ Microbiol 18(11):4005–4022. https://doi.org/10.1111/1462-2920.13424
30. Stefanova D, Raychev A, Arezes J, Ruchala P, Gabayan V, Skurnik M, Dillon BJ, Horwitz MA, Ganz T, Bulut Y, Nemeth E (2017) Endogenous hepcidin and its agonist mediate resistance to selected infections by clearing non-transferrin-bound iron. Blood 130(3):245–257. https://doi.org/10.1182/blood-2017-03-772715
31. Thiaville PC, Bourdage KL, Wright AC, Farrell-Evans M, Garvan CW, Gulig PA (2011) Genotype is correlated with but does not predict virulence of Vibrio vulnificus biotype 1 in subcutaneously inoculated, iron dextran-treated mice. Infect Immun 79(3):1194–1207. https://doi.org/10.1128/iai.01031-10
32. Lee SJ, Jung YH, Oh SY, Song EJ, Choi SH, Han HJ (2015) Vibrio vulnificus VvhA induces NF-kappaB-dependent mitochondrial cell death via lipid raft-mediated ROS production in intestinal epithelial cells. Cell Death Dis 6:1655. https://doi.org/10.1038/cddis.2015.19
33. Song EJ, Lee SJ, Lim HS, Kim JS, Jang KK, Choi SH, Han HJ (2016) Vibrio vulnificus VvhA induces autophagy-related cell death through the lipid raft-dependent c-Src/NOX signaling pathway. Sci Rep 6:27080. https://doi.org/10.1038/srep27080
34. Lee NY, Lee HY, Lee KH, Han SH, Park SJ (2011) Vibrio vulnificus IlpA induces MAPK-mediated cytokine production via TLR1/2 activation in THP-1 cells, a human monocytic cell line. Mol Immunol 49(1–2):143–154. https://doi.org/10.1016/j.molimm.2011.08.001
35. Kim WB, Lee BC, Choi SH (2012) Vibrio vulnificus AphB is involved in interleukin-8 production via an NF-kappaB-dependent pathway in human intestinal epithelial cells. Biochem Biophys Res Commun 417(4):1265–1270. https://doi.org/10.1016/j.bbrc.2011.12.122
36. Liu M, Crosa JH (2012) The regulator HlyU, the repeat-in-toxin gene rtxA1, and their roles in the pathogenesis of Vibrio vulnificus infections. MicrobiologyOpen 1(4):502–513. https://doi.org/10.1002/mbo3.48
37. Baker-Austin C, Oliver JD (2016) Rapidly developing and fatal Vibrio vulnificus wound infection. IDCases 6:13. https://doi.org/10.1016/j.idcr.2016.07.014
38. Arici E, Evald A, Holmgaard DB, Quist L, Poulsen SD, Worm SW (2017) Amputation of an arm due to infection with Vibrio vulnificus after beach holiday. Ugeskr Laeger 179(48)
39. Horseman MA, Surani S (2011) A comprehensive review of Vibrio vulnificus: an important cause of severe sepsis and skin and soft-tissue infection. Int J Infect Dis 15(3):e157–e166. https://doi.org/10.1016/j.ijid.2010.11.003
40. Majere RA, Cortina S (2017) Necrotizing wound infection from a tilapia fish injury. CMAJ 189(14):E539–e541. https://doi.org/10.1503/cmaj.160663
41. Hendren N, Sukumar S, Glazer CS (2017) Vibrio vulnificus septic shofck due to a contaminated tattoo. BMJ Case Rep 2017. https://doi.org/10.1136/bcr-2017-22019
42. Jones MK, Oliver JD (2009) Vibrio vulnificus: disease and pathogenesis. Infect Immun 77(5):1723–1733. https://doi.org/10.1128/iai.01046-08
43. Baker-Austin C, Oliver JD (2018) Vibrio vulnificus: new insights into a deadly opportunistic pathogen. Environ Microbiol 20(2):423–430. https://doi.org/10.1111/1462-2920.13955
44. Elmahdi S, DaSilva LV, Parveen S (2016) Antibiotic resistance of Vibrio parahaemolyticus and Vibrio vulnificus in various countries: a review. Food Microbiol 57:128–134. https://doi.org/10.1016/j.fm.2016.02.008
45. Serratore P, Zavatta E, Fiocchi E, Serafini E, Serraino A, Giacometti F, Bignami G (2017) Preliminary study on the antimicrobial susceptibility pattern related to the genotype of Vibrio vulnificus strains isolated in the north-western Adriatic Sea coastal area. Ital J Food Saf 6(4):6843. https://doi.org/10.4081/ijfs.2017.6843
46. Zanetti S, Spanu T, Deriu A, Romano L, Sechi LA, Fadda G (2001) In vitro susceptibility of Vibrio spp. isolated from the environment. Int J Antimicrob Agents 17(5):407–409
47. Shaw KS, Rosenberg Goldstein RE, He X, Jacobs JM, Crump BC, Sapkota AR (2014) Antimicrobial susceptibility of Vibrio vulnificus and Vibrio parahaemolyticus recovered from recreational and commercial areas of Chesapeake Bay and Maryland Coastal Bays. PLoS One 9(2):e89616. https://doi.org/10.1371/journal.pone.0089616
48. Trinh SA, Gavin HE, Satchell KJF (2017) Efficacy of ceftriaxone, cefepime, doxycycline, ciprofloxacin, and combination therapy for Vibrio vulnificus foodborne septicemia. Antimicrob Agents Chemother 61(12):e01106–17. https://doi.org/10.1128/aac.01106-17
49. Tang HJ, Chang MC, Ko WC, Huang KY, Lee CL, Chuang YC (2002) In vitro and in vivo activities of newer fluoroquinolones against Vibrio vulnificus. Antimicrob Agents Chemother 46(11):3580–3584
50. Stevens DL, Bryant AE (2017) Necrotizing soft-tissue infections. N Engl J Med 377(23):2253–2265. https://doi.org/10.1056/NEJMra1600673
51. Hong GL, Lu CJ, Lu ZQ, Li MF, Qiu QM, Liang H, Wu B (2012) Surgical treatment of 19 cases with vibrio necrotising fasciitis. Burns 38(2):290–295. https://doi.org/10.1016/j.burns.2011.04.013
52. Osaka K, Komatsuzaki M, Takahashi H, Sakano S, Okabe N (2004) Vibrio vulnificus septicaemia in Japan: an estimated number of infections and physicians' knowledge of the syndrome. Epidemiol Infect 132(5):993–996