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Foot Infection by *Clostridium sordellii*: Case Report and Review of 15 Cases in France

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We report a case of foot infection by *Clostridium sordellii* and review 15 human infections registered at a Reference Center in France during the period 1998 to 2011. All strains were found nontoxigenic, lacking the lethal toxin gene coding for TcsL. Like *Clostridium septicum*, several *C. sordellii* infections were associated with intestinal neoplasms.

CASE REPORT

A 78-year-old patient living alone under bad cognitive and hygienic conditions in a rural village of South of France was hospitalized for 4 days in August 2008 for confusion, major asthenia, and fever (38.2°C). Dehydration was marked, and diabetes mellitus and dyslipemia were discovered that necessitated insulin therapy. A burn on the foot (caused by exposure to boiling water) was colonized with a methicillin-resistant *Staphylococcus aureus* strain that necessitated only local treatment. Previous history was unremarkable, with treated arterial hypertension, episodes of painful constipation in 2005, acute epigastralgy 2 years before in 2006 with ultrasound echographic and nuclear magnetic resonance imaging (MRI), as well as endoscopic gastroscopy and *Helicobacter pylori* investigation all negative. Fifteen days later, the patient was admitted to the emergency ward with confusion, vertigo, fever (39°C), and abdominal pain beginning at the right hypocondrium and later at the epigastrium. There was neither shock (arterial tension of 17/7.2), nor were there pulmonary, urologic, clinical, or biological signs. Computed tomography scan examination revealed neither angiocholitis nor appendicitis. At the time of admission, there were 18,300 leukocytes/mm^3, including 16,300 polymorphonuclear leukocytes (PMNs). The C-reactive protein level was slightly elevated (42 mg/liter, increasing 2 days later to 160 mg/liter). Coagulation was normal (prothrombin index, partial prothrombin time [PTT], and fibrinogen). Biochemistry was unremarkable (ionogram, glycemia, troponin, and pancreatic, muscular, and hepatic enzymes). Only renal clearance was slightly disturbed (60 ml/min/1.73 m^2, as estimated by the Modification of Diet in Renal Disease [MDRD] Study equation), although in the same range as before, and more remarkably, the bilirubin level was elevated (24 μmol/liter; normal, 2 to 22 μmol/liter): all bilirubin was constituted of free indirect bilirubin, meaning hemolysis. Bilirubinemia was normal (14 μmol/liter) at the preceding hospitalization 3 weeks before. The patient had hemoconcentration (hemoglobin, 153 g/liter [usually 12 to 13 g/liter before and at late controls]; total proteins, 80 g/liter [usually around 65 g/liter]). Blood cultures were rapidly drawn, but the malleolar lesion, still present and now painful, was not sampled, and antibiotherapy started less than 3 h after admission, with metronidazole given at 500 mg three times a day (t.i.d.) and ceftriaxone given at 1 g/day. A Gram-positive spore-forming (subterminal or terminal spores) rod-shaped bacterium was evidenced within 11 h from anaerobic blood cultures (BacT/Alert FN; bioMérieux, Durham, NC). Colonies on Columbia sheep blood agar (bioMérieux, Marcy l'Etoile, France) plates were nonhemolytic and grayish with an irregular margin. Strain was kept frozen in 15% glycerolyzed brain heart infusion (BHI) broth at −75°C after only two subcultures and shipped at that time to the reference laboratory.

Identification based on reference methods (1), as well as using commercial kits (rapid ID 32A; BioMérieux, Marcy L'Etoile, France), or analysis of metabolic end products (volatile and nonvolatile fatty acids) by gas-liquid chromatography (2) gave typical urease- and indole-positive *Clostridium sordellii*. Virulence factor (neuraminidase or sialidase) and toxin (lethal toxin [TcsL]) genes were determined by PCR according to the method described by Popoff (3). The isolate was found negative for the TcsL gene and positive for the neuraminidase gene. To further characterize the *C. sordellii* isolate, termed CS166.08, whole-genome sequencing was performed as previously described (4), as well as for the reference *C. sordellii* strains IP82 and VPI 9048 (5, 6). While this study was in progress, VPI 9048 sequences were made available in GenBank, and the gene sequence of TcsH was described (7–9). The DNA sequences of the 16S rRNA genes were 99% identical in CS166.08 and the type strain of the species, further supporting that this isolate belongs to the species *C. sordellii* (Table 1). CS166.08 also retains conserved *C. sordellii* phospholipase C and neuraminidase gene sequences (Table 1). Phospholipase C activity was not detected on egg yolk agar after a 4-day incubation period in an anaerobic atmosphere with strains VPI 9048 and CS166.08. Compared to a phospholipase C-positive strain, such as strain IP82, which has a run of 6 G bases at positions 66 to 71 in its nucleotide sequence (KM657127) that leads to a predicted native protein of 399 residues, strains VPI 9048 (KM657126) and CS166.08

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TABLE 1 Analysis of virulence factor genes and genes coding for proteins involved in DNA mobility in the genomes of *C. sordellii* VPI 9048, IP82, and CS166.08[a]

Gene product, gene no.[b] (GenBank accession no.)	% nucleotide identity (GenBank accession no.)[c]		
	VPI 9048	IP82	CS166.08
16S rRNA (AB075771)[d]	98.8 (KM657123)	99.0 (KM657124)	99.0 (KM657125)
Phospholipase C, H476_3275	100.0 (KM657126)	98.9 (KM657127)	97.8 (KM657128)
Sialidase, H476_2657	100.0 (KM657129)	99.5 (KM657130)	97.6 (KM657131)
TcsL, H476_0269	100.0 (KF726110)	97.9 (KF726114)	−
TcsH, H476_0271, 7,794 bp[e]	99.2 (KF726111 [7,857 bp])	95.1 (KF726115; pseudogene [1,186 bp])	−
TcsH (KC814176 [7,857 bp])[e]	100.0 (KF726111 [7,857 bp])	95.2 (KF726115 [1,186 bp])	−
TcsR sigma factor, H476_0272	100.0 (KF726113)	96.2 (KF726117)	−
TcsE holin, H476_0270	100.0 (KF726112)	99.8 (KF726116)	−
Recombinase RecA-like family, H476_0278	100.0	96.2	86.3
Plasmid replication protein, H476_0274	100.0	98.8	−
Replication protein Rep_3 superfamily, H477_0270	99.0	99.6	−
Type IV secretion system conjugative DNA protein, HA476_0297	100.0	97.9	−
Type IV secretion system coupling DNA, H476_0302	100.0	96.5	−
Type IV secretion system VirD4 component, H477_0297	98.7	100.0	−
Type IV secretion system VirD4 component, H477_0298	97.2	99.8	−
RecA recombinase, H477_0275	96.2	100.0	−
Transposase, H476_0286	100.0	−	−
Transposase, H476_0321	100.0	−	−
TraB family protein, H476_0319	100.0	−	−

[a] Whole-genome sequencing of the three strains was performed as previously described (4). DNA homology between target genes from GenBank, including sequences from VPI 9048 (NZ_AQGJ00000000.1) and ATCC 9714 (NZ_APWR00000000.1), and the whole-genome sequences obtained in this study was investigated by BLAST. The results are expressed as percentages of nucleotide identity.

[b] H476_xxxx genes are from VPI 9048 genome contigs (NZ_AQGJ00000000.1), and H477_xxxx genes are from ATCC 9714^T genome contigs (NZ_APWR00000000.1).

[c] −, the gene is lacking.

[d] Sequence from strain ATCC 9714^T.

[e] Gene H476_0271 lacks 63 nucleotides compared to the sequences of accession no. KC814176 or KF726111 (7,857 bp [positions 7098 to 7161]).

(KM657128) have runs of 5 G bases and 7 G bases, respectively, that lead to reading frame shifts and subsequent truncated proteins. Strain CS166.08 lacks the toxin genes coding for TcsL and TcsH, as well as the genes associated with the *C. sordellii* toxin gene locus, including TcsR and TcsE (7). Evidence for genes encoding proteins involved in DNA mobilization, such as type IV secretion system conjugative DNA transfer and coupling DNA-binding domain proteins, plasmid replication protein, transposases, and DNA transfer protein from the TraB family (Table 1), has been found in the *C. sordellii* toxin gene locus (7). All of these DNA mobilization genes are missing in CS166.08 (Table 1). IP82 produces only TcsL not TcsH type IV secretion system transfer genes, but it lacks transposase genes. This strongly suggests that *C. sordellii* toxin genes are localized in a mobile element, possibly a plasmid, and that nontoxigenic strains derive from toxigenic strains by loss of such a mobile DNA element. The case report associated with CS166.08 could result from a nontoxigenic strain, or CS166.08 is a nontoxic derivative after subculture of an initial toxic strain by loss of the plasmid or mobile element carrying toxin genes. A nontoxigenic *C. sordellii* strain has been reported to be associated with a polymicrobial cholangitis (10). However, the severity of the case presented in this study rather suggests the involvement of a toxigenic strain. In our hands, *C. sordellii* isolates often lacked the TcsL gene, although TcsL was evidenced in clinical samples, such as intestinal contents from animals who died of enterotoxemia. This observation suggests that the toxin-negative isolates probably derived from toxigenic strains. The toxin genes might have gone lost in the course of subculturing. From 1998 to January 2011, 16 *C. sordellii* isolates of human origin were sent to the National Reference Center (NRC) (Table 2). The strains showed the standard properties of *C. sordellii*. However all strains (16/16) were found PCR negative for the TcsL gene, probably supporting the instability of the toxin gene. In contrast, the neuraminidase gene was detected in all of the tested strains (10/10). The mean age of the patients was 61.1 years (minimum, 38 years; maximum, 85 years). The male/female sex ratio of patients was 1.0. Sample origins were known for 15 out of 16 cases: 7 from blood culture, 2 from skin, and 1 each from synovial fragment, stool culture, intra-abdominal sample, ascitic fluid, peritoneal fluid, and finger necrosis (Table 2). Most *C. sordellii* strains isolated from infected wounds were associated with myonecrosis or cellulitis. One *C. sordellii* strain was isolated from stool in a context of pseudomembranous colitis, and 5 strains were obtained from blood cultures of patients with underlying neoplasms (2 intestinal neoplasms, 1 hepatic neoplasm, 1 pulmonary neoplasm, and 1 endometrium neoplasm).

Clostridium sordellii, is a Gram-positive, spore-forming bacterium and an obligatory anaerobe. This bacterium is an environmental rod found in soil and occasionally in animal and human intestine. It is one of the *Clostridium* species responsible for myonecrosis and gangrene in humans and animals. Up to 4% of cases of *Clostridium* myonecrosis were reported to be caused by *C. sordellii* (11). Cases of *Clostridium* gangrene are now infrequent in humans, but *C. sordellii* is responsible for sporadic cases of gas gangrene subsequent to trauma or surgery, and it is a more com-

TABLE 2 Cases of *C. sordellii* infections reported to the NRC from 1998 to 2011[a]

Yr	Age (yr)/sex	Presenting illness or condition	Sample origin
2011	83/F	Hepatic adenocarcinoma (originated from the gallbladder)	Blood culture
2010	73/F	Perforated acute appendicitis	Peritoneal fluid
2010	50/F	Lawn mower accident: D2 D3 amputation followed by an important necrosis	Finger necrosis
2009	62/M	Ascites	Ascitic fluid
2008	38/M	Polytraumatism (motorbike fall): cellulitis, myonecrosis	Blood culture (2/6 positive)
2008	78/M	Superinfected foot wound	Blood culture[b]
2007	Unknown/F	Colonic surgery	Unknown
2006	65/M	Intestinal obstruction (underlying disease, cancer)	Blood culture (1/4 positive)
2004	85/F	Pseudomembranous colitis	Stool culture
2004	55/F	Necrotizing fasciitis	Blood culture (3/6 positive): mixed culture with a group G *Streptococcus* strain
2002	68/M	Pulmonary neoplasm with metastasis	Blood culture
2000	45/M	Intestinal neoplasm	Intra-abdominal sample
2000	65/F	Endometrium neoplasm: peritoneum carcinosis	Blood culture
1999	>21/M	Finger wound after a cut (pork butcher)	Skin
1999	Unknown/M	Skin ulcer	Skin
1998	66/F	Bone infection	Synovial fragment

[a] All of the *C. sordellii* strains were PCR negative for the TcsL gene and PCR positive for the neuraminidase gene where tested (11/11). No toxicity was evidenced in the culture supernatant from all strains by the mouse bioassay.
[b] This case is more completely described above.

mon cause of myonecrosis in injection drug users (12–14). Infection by this bacterium is characterized by a marked local edema and variable production of gas, followed by extensive tissue necrosis and total absence of leukocyte infiltration and tissue inflammatory response, severe hypotension, shock, and absence of hemolysis, (14). Sporadic cases of *C. sordellii* infections are commonly encountered in women after a postpartum wound, endometritis, or postabortion disease. Although rare, these cases are all dramatic. A fulminant toxic shock syndrome (irreversible hypotension, apyrexia, hemoconcentration with hyperproteinemia, leukocytosis, and high hematocrit) accompanies the local infection of uterus or perineum. Pleural effusions and serosanguineous ascites have been reported in almost all of the cases (15–23). In the recent period, several cases of fatal toxic shock syndrome due to *C. sordellii* were reported following medical abortion (15, 24–33). From a series of 45 cases of *C. sordellii* infections, 8 (18%) were associated with normal childbirth, 5 (11%) with medical abortion, 2 (0.4%) with spontaneous abortion, 10 (22%) with drug injection, and 19 (43%) occurred after trauma or surgery. The issue was fatal in 31 of 45 patients (68%) within 2 to 6 days after the initial infection (34). In addition, *C. sordellii* is responsible for bacteremia and arthritis, resulting in a high rate of mortality (35, 36). A few cases of *C. sordellii* pericarditis and pleuropneumonia have been reported, which probably result from aspiration of oropharyngeal flora associated with pulmonary embolism and valvular heart disease (37, 38). *C. sordellii* bacteremia without myonecrosis of skeletal muscle are rare but often fatal (mortality of >50%). The portal of entry is presumed to be mainly the gastrointestinal tract, and trauma to the anus through manual self evacuation is a possible cause. A few cases were consecutive to a transcutaneous biopsy, such as liver biopsy or transrectal prostatic biopsy. These infections can be found in all ages. Underlying malignancy and being immunocompromised are aggravating risk factors (11, 35, 39, 40). More rarely, *C. sordellii* infections can occur as small pseudo-outbreaks (41).

In contrast, *C. sordellii* diseases are more common in animals. *C. sordellii* induces large outbreaks of enterotoxemia in animals, mainly in sheep and lambs (42–47), sporadic cases of necrotic and hemorrhagic enteritis in cattle (42, 43), and equine myopathy (48). *C. sordellii* toxic infections in sheep and lambs most often result in sudden death, in which no characteristic postmortem abnormalities are observed. However, some animals show a marked edema and emphysema of the abomasum wall. Moreover, *C. sordellii* is associated with sudden death in periparturient sheep (49). The most relevant feature of *C. sordellii* pathologies in humans and animals, whatever the initial site of infection, consists of a rapid and fatal toxic shock syndrome, indicating a major role of toxin(s) in the onset of the disease. However, the cause of the death has not been yet deciphered.

C. sordellii lethal toxin (TcsL) is the major virulence factor. TcsL disrupts the actin cytoskeleton through inactivation of Rho- and Ras-GTPases, such as Rac, Ras, Rap, and Ral, by glucosylation at the conserved Thr35/37 (50). This leads to a disorganization of the intercellular junctions, mainly basolateral junctions by redistribution of the whole E-cadherin–catenin complex from the cell membrane to the cytosol, and to an increase in epithelial and endothelial barrier permeability (51–53). Thereby, TcsL is a potent edematogenous toxin. Locally, TcsL induces a degeneration of skeletal neuromuscular tissues (54), and when injected intravenously into mice, TcsL causes an increase in lung endothelial vascular permeability that results in massive extravasation of blood fluid in the thoracic cage, profound dehydration, hypoxia, and finally cardiorespiratory failure (55). In addition, TcsL represses glucocorticoid receptor transactivation, thus impairing the anti-inflammatory response, and this effect is amplified in the presence of the glucocorticoid antagonist RU486 (56). This could explain, at least partially, the association of TcsL-dependent toxic shock with RU486. It is noteworthy that the gene encoding TcsL is unstable, and most of the strains lose their toxin gene after isolation from clinical specimen, compromising their identification.

Clostridium septicum is well known to be associated with malignancy (57, 58). In addition to its involvement in gangrene, *C.*

sordellii could be an occasional agent of superinfection of certain neoplasms. Although *C. sordellii* toxi-infections are rare in humans, they are always severe and dramatic. For this reason, an attentive survey of these infections is required.

Nucleotide sequence accession numbers. The nucleotide gene sequences obtained from whole-genome sequencing of the strains VPI 9048, AIP82, and CS166.08 done in this study have been deposited in the GenBank database under the following accession numbers: 16S rRNA, KM657123 to KM657125; phospholipase C, KM657126 to KM657128; and sialidase (neuraminidase), KM657129 to KM657131, respectively.

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REFERENCES

1. **Jousimies-Somer HR, Summanen P, Citron DM, Baron EJ, Wexler HM, Finegold SM.** 2002. Anaerobic bacteriology manual, 6th ed. Star Publishing Company, Belmont, CA.
2. **Carlier JP.** 2002. The metabolic end-products—a rapid identification tool for common anaerobic bacteria isolated in clinical microbiology. Recent Res Dev Microbiol **6:**157–175.
3. **Popoff MR.** 2002. Detection of toxigenic clostridia. PCR detection of microbial pathogens. Methods Mol Biol **216:**137–152. http://dx.doi.org/10.1385/1-59259-344-5:137.
4. **Bouvet P, Ruimy R, Bouchier C, Faucher N, Mazuet C, Popoff MR.** 2014. An atypical *Clostridium* strain related to the *Clostridium botulinum* group III strain isolated from a human blood culture. J Clin Microbiol **52:**339–343. http://dx.doi.org/10.1128/JCM.00390-13.
5. **Martinez RD, Wilkins TD.** 1992. Comparison of *Clostridium sordellii* toxins HT and LT with toxins A and B of *C. difficile*. J Med Microbiol **36:**30–36. http://dx.doi.org/10.1099/00222615-36-1-30.
6. **Popoff MR.** 1987. Purification and characterization of *Clostridium sordellii* lethal toxin and cross-reactivity with *Clostridium difficile* cytotoxin. Infect Immun **55:**35–43.
7. **Sirigi Reddy AR, Girinathan BP, Zapotocny R, Govind R.** 2013. Identification and characterization of *Clostridium sordellii* toxin gene regulator. J Bacteriol **195:**4246–4254. http://dx.doi.org/10.1128/JB.00711-13.
8. **Thiele TL, Stuber TP, Hauer PJ.** 2013. Detection of *Clostridium sordellii* strains expressing hemorrhagic toxin (TcsH) and implications for diagnostics and regulation of veterinary vaccines. Vaccine **31:**5082–5087. http://dx.doi.org/10.1016/j.vaccine.2013.08.065.
9. **Genth H, Pauillac S, Schelle I, Bouvet P, Bouchier C, Varela-Chavez C, Just I, Popoff MR.** 2014. Haemorrhagic toxin and lethal toxin from *Clostridium sordellii* strain vpi9048: molecular characterization and comparative analysis of substrate specificity of the large clostridial glucosylating toxins. Cell Microbiol **16:**1706–1721. http://dx.doi.org/10.1111/cmi.12321.
10. **Walk ST, Jain R, Trivedi I, Grossman S, Newton DW, Thelen T, Hao Y, Songer JG, Carter GP, Lyras D, Young VB, Aronoff DM.** 2011. Nontoxigenic *Clostridium sordellii*: clinical and microbiological features of a case of cholangitis-associated bacteremia. Anaerobe **17:**252–256. http://dx.doi.org/10.1016/j.anaerobe.2011.06.009.
11. **Cunniffe JG.** 1996. *Clostridium sordellii* bacteraemia. J Infect **33:**127–129. http://dx.doi.org/10.1016/S0163-4453(96)93100-X.
12. **Kimura AC, Higa JI, Levin RM, Simpson G, Vargas Y, Vugia DJ.** 2004. Outbreak of necrotizing fasciitis due to *Clostridium sordellii* among black-tar heroin users. Clin Infect Dis **38:**e87–e91. http://dx.doi.org/10.1086/383471.
13. **Smith C, Goslin B.** 2013. *Clostridium sordellii* surgical site infection after breast mass excision: case report. Surg Infect (Larchmt) **14:**160–162. http://dx.doi.org/10.1089/sur.2011.060.
14. **Tsokos M, Schalinski S, Paulsen F, Sperhake JP, Puschel K, Sobottka I.** 2008. Pathology of fatal traumatic and nontraumatic clostridial gas gangrene: a histopathological, immunohistochemical, and ultrastructural study of six autopsy cases. Int J Legal Med **122:**35–41. http://dx.doi.org/10.1007/s00414-007-0163-9.
15. **Agrawal P, Garg R.** 2012. Fulminant leukemoid reaction due to postpartum *Clostridium sordellii* infection. J Glob Infect Dis **4:**209–211. http://dx.doi.org/10.4103/0974-777X.103899.
16. **Anonymous.** 2005. *Clostridium sordellii* toxic shock syndrome after medical abortion with mifepristone and intravaginal misoprostol—United States and Canada, 2001-2005. MMWR Morb Mortal Wkly Rep **54:**724. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5429a3.htm.
17. **Bitti A, Mastrantonio P, Spigaglia P, Urru G, Spano AI, Moretti G, Cherchi GB.** 1997. A fatal postpartum *Clostridium sordellii* associated toxic shock syndrome. J Clin Pathol **50:**259–260. http://dx.doi.org/10.1136/jcp.50.3.259.
18. **Ho CS, Bhatnagar J, Cohen AL, Hacker JK, Zane SB, Reagan S, Fischer M, Shieh WJ, Guarner J, Ahmad S, Zaki SR, McDonald LC.** 2009. Undiagnosed cases of fatal *Clostridium*-associated toxic shock in Californian women of childbearing age. Am J Obstet Gynecol **201:**459.e1–459e7. http://dx.doi.org/10.1016/j.ajog.2009.05.023.
19. **McGregor JA, Soper DE, Lovell G, Todd JK.** 1989. Maternal deaths associated with *Clostridium sordellii* infection. Am J Obstet Gynecol **161:**987–995. http://dx.doi.org/10.1016/0002-9378(89)90768-0.
20. **Rorbye C, Petersen IS, Nilas L.** 2000. Postpartum *Clostridium sordellii* infection associated with fatal toxic shock syndrome. Acta Obstet Gynecol Scand **79:**1134–1135. http://dx.doi.org/10.1034/j.1600-0412.2000.0790121134.x.
21. **Sinave C, Le Templier G, Blouin D, Leveille F, Deland E.** 2002. Toxic shock syndrome due to *Clostridium sordellii:* a dramatic postpartum and postabortion disease. Clin Infect Dis **35:**1441–1443. http://dx.doi.org/10.1086/344464.
22. **Soper DE.** 1986. Clostridial myonecrosis arising from an episiotomy. Obstet Gynecol **68:**26S–28S.
23. **Zane S, Guarner J.** 2011. Gynecologic clostridial toxic shock in women of reproductive age. Curr Infect Dis Rep **13:**561–570. http://dx.doi.org/10.1007/s11908-011-0207-7.
24. **Cohen AL, Bhatnagar J, Reagan S, Zane SB, D'Angeli MA, Fischer M, Killgore G, Kwan-Gett TS, Blossom DB, Shieh WJ, Guarner J, Jernigan J, Duchin JS, Zaki SR, McDonald LC.** 2007. Toxic shock associated with *Clostridium sordellii* and *Clostridium perfringens* after medical and spontaneous abortion. Obstet Gynecol **110:**1027–1033. http://dx.doi.org/10.1097/01.AOG.0000287291.19230.ba.
25. **Couzin J.** 2006. Infectious disease. RU-486-linked deaths open debate about risky bacteria. Science **312:**986. http://dx.doi.org/10.1126/science.312.5776.986.
26. **Fischer M, Bhatnagar J, Guarner J, Reagan S, Hacker JK, Van Meter SH, Poukens V, Whiteman DB, Iton A, Cheung M, Dassey DE, Shieh WJ, Zaki SR.** 2005. Fatal toxic shock syndrome associated with *Clostridium sordellii* after medical abortion. N Engl J Med **353:**2352–2360. http://dx.doi.org/10.1056/NEJMoa051620.
27. **Greene MF.** 2005. Fatal infections associated with mifepristone-induced abortion. N Engl J Med **353:**2317–2318. http://dx.doi.org/10.1056/NEJMp058260.
28. **Meites E, Zane S, Gould C.** 2010. Fatal *Clostridium sordellii* infections after medical abortions. N Engl J Med **363:**1382–1383. http://dx.doi.org/10.1056/NEJMc1001014.
29. **Miech RP.** 2005. Pathophysiology of mifepristone-induced septic shock due to *Clostridium sordellii*. Ann Pharmacother **39:**1483–1488. http://dx.doi.org/10.1345/aph.1G189.
30. **Murray S, Wooltorton E.** 2005. Septic shock after medical abortions with mifepristone (Mifeprex, RU 486) and misoprostol. CMAJ **173:**485. http://dx.doi.org/10.1503/cmaj.050980.
31. **Soper DE.** 2007. Abortion and clostridial toxic shock syndrome. Obstet Gynecol **110:**970–971. http://dx.doi.org/10.1097/01.AOG.0000288224.47104.7b.
32. **Wiebe E, Guilbert E, Jacot F, Shannon C, Winikoff B.** 2004. A fatal case of *Clostridium sordellii* septic shock syndrome associated with medical abortion. Obstet Gynecol **104:**1142–1144. http://dx.doi.org/10.1097/01.AOG.0000142738.68439.9e.
33. **Winikoff B.** 2006. *Clostridium sordellii* infection in medical abortion. Clin Infect Dis **43:**1447–1448. http://dx.doi.org/10.1086/508895.
34. **Aldape MJ, Bryant AE, Stevens DL.** 2006. *Clostridium sordellii* infection: epidemiology, clinical findings, and current perspectives on diagnosis and treatment. Clin Infect Dis **43:**1436–1446. http://dx.doi.org/10.1086/508866.

35. **Abdulla A, Yee L.** 2000. The clinical spectrum of *Clostridium sordellii* bacteraemia: two case reports and a review of the literature. J Clin Pathol **53:**709–712. http://dx.doi.org/10.1136/jcp.53.9.709.
36. **Gredlein CM, Silverman ML, Downey MS.** 2000. Polymicrobial septic arthritis due to *Clostridium* species: case report and review. Clin Infect Dis **30:**590–594. http://dx.doi.org/10.1086/313686.
37. **Buchman AL, Ponsillo M, Nagami PH.** 1991. Empyema caused by *Clostridium sordellii*, a rare form of pleuropulmonary disease. J Infect **22:**171–174. http://dx.doi.org/10.1016/0163-4453(91)91613-3.
38. **Chaudhry R, Verma N, Bahadur T, Chaudhary P, Sharma P, Sharma N.** 2011. *Clostridium sordellii* as a cause of constrictive pericarditis with pyopericardium and tamponade. J Clin Microbiol **49:**3700–3702. http://dx.doi.org/10.1128/JCM.00933-11.
39. **Matten J, Buechner V, Schwarz R.** 2009. A rare case of *Clostridium sordellii* bacteremia in an immunocompromised patient. Infection **37:**368–369. http://dx.doi.org/10.1007/s15010-008-8192-y.
40. **Spera RV, Jr, Kaplan MH, Allen SL.** 1992. *Clostridium sordellii* bacteremia: case report and review. Clin Infect Dis **15:**950–954. http://dx.doi.org/10.1093/clind/15.6.950.
41. **Aronoff DM, Thelen T, Walk ST, Petersen K, Jackson J, Grossman S, Rudrik J, Newton DW, Chenoweth CE.** 2010. Pseudo-outbreak of *Clostridium sordellii* infection following probable cross-contamination in a hospital clinical microbiology laboratory. Infect Control Hosp Epidemiol **31:**640–642. http://dx.doi.org/10.1086/652774.
42. **Al-Mashat RR, Taylor DJ.** 1983. Bacteria in enteric lesions of cattle. Vet Rec **112:**5–10. http://dx.doi.org/10.1136/vr.112.1.5.
43. **Al-Mashat RR, Taylor DJ.** 1983. *Clostridium sordellii* in enteritis in an adult sheep. Vet Rec **112:**19. http://dx.doi.org/10.1136/vr.112.1.19.
44. **Lewis CJ, Naylor R.** 1996. Sudden death in lambs associated with *Clostridium sordellii* infection. Vet Rec **138:**262.
45. **Lewis CJ, Naylor RD.** 1998. Sudden death in sheep associated with *Clostridium sordellii*. Vet Rec **142:**417–421. http://dx.doi.org/10.1136/vr.142.16.417.
46. **Popoff MR.** 1984. Bacteriological examination in enterotoxaemia of sheep and lamb. Vet Rec **114:**324. http://dx.doi.org/10.1136/vr.114.13.324.
47. **Richards SM, Hunt BW.** 1982. *Clostridium sordellii* in lambs. Vet Rec **111:**22.
48. **Unger-Torroledo L, Straub R, Lehmann AD, Graber F, Stahl C, Frey J, Gerber V, Hoppeler H, Baum O.** 2010. Lethal toxin of *Clostridium sordellii* is associated with fatal equine atypical myopathy. Vet Microbiol **144:**487–492. http://dx.doi.org/10.1016/j.vetmic.2010.01.024.
49. **Clark S.** 2003. Sudden death in periparturient sheep associated with *Clostridium sordellii*. Vet Rec **153:**340.
50. **Popoff MR, Bouvet P.** 2009. Clostridial toxins. Future Microbiol **4:**1021–1064. http://dx.doi.org/10.2217/fmb.09.72.
51. **Aronoff DM.** 2013. *Clostridium novyi*, *sordellii*, and *tetani*: mechanisms of disease. Anaerobe **24:**98–101. http://dx.doi.org/10.1016/j.anaerobe.2013.08.009.
52. **Boehm C, Gibert M, Geny B, Popoff MR, Rodriguez P.** 2006. Modification of epithelial cell barrier permeability and intercellular junctions by *Clostridium sordellii* lethal toxins. Cell Microbiol **8:**1070–1085. http://dx.doi.org/10.1111/j.1462-5822.2006.00687.x.
53. **Popoff MR, Geny B.** 2009. Multifaceted role of Rho, Rac, Cdc42 and Ras in intercellular junctions, lessons from toxins. Biochim Biophys Acta **1788:**797–812. http://dx.doi.org/10.1016/j.bbamem.2009.01.011.
54. **Barbier J, Popoff MR, Molgo J.** 2004. Degeneration and regeneration of murine skeletal neuromuscular junctions after intramuscular injection with a sublethal dose of *Clostridium sordellii* lethal toxin. Infect Immun **72:**3120–3128. http://dx.doi.org/10.1128/IAI.72.6.3120-3128.2004.
55. **Geny B, Khun H, Fitting C, Zarantonelli L, Mazuet C, Cayet N, Szatanik M, Prevost MC, Cavaillon JM, Huerre M, Popoff MR.** 2007. *Clostridium sordellii* lethal toxin kills mice by inducing a major increase in lung vascular permeability. Am J Pathol **170:**1003–1017. http://dx.doi.org/10.2353/ajpath.2007.060583.
56. **Tait AS, Dalton M, Geny B, D'Agnillo F, Popoff MR, Sternberg EM.** 2007. The large clostridial toxins from *Clostridium sordellii* and *C. difficile* repress glucocorticoid receptor activity. Infect Immun **75:**3935–3940. http://dx.doi.org/10.1128/IAI.00291-07.
57. **El-Masry S.** 2005. Spontaneous gas gangrene associated with occult carcinoma of the colon: a case report and review of literature. Int Surg **90:**245–247.
58. **Mirza NN, McCloud JM, Cheetham MJ.** 2009. *Clostridium septicum* sepsis and colorectal cancer—a reminder. World J Surg Oncol **7:**73. http://dx.doi.org/10.1186/1477-7819-7-73.