Infections caused by *Clostridium perfringens* and *Paeniclostridium sordellii* after unsafe abortion

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After the legalisation of abortion in the USA in 1973, the risk of infectious morbidity and mortality from this procedure notably decreased. With increasingly restrictive legislation targeting access to safe abortion services, reviewing infectious complications of unsafe pregnancy termination is crucial, particularly the diagnosis and management of life-threatening clostridial (and related anaerobic bacterial) infections that can complicate unsafe abortion. This Review deals with two especially devastating infections that are well-documented causes of septic abortion: the anaerobic, spore-forming pathogens *Clostridium perfringens* and *Paeniclostridium sordellii*. We seek to familiarise the reader with these bacteria, the clinical syndromes they can cause (with a focus on toxic shock syndrome), and provide a review of diagnosis and treatment options.

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Introduction

Unsafe abortion is defined by WHO as a procedure of pregnancy termination, either by people lacking the necessary skills, or in an environment that does not conform to minimal medical standards, or both.[1] Infections are a potential complication of unsafe abortion, but given the access to safe abortion in much of the world, practitioners might not be familiar with this spectrum of consequences. In this Review, we discuss the characteristics of such infections and review appropriate management, which involves urgent surgical assessment and antimicrobial therapy.

Following the legalisation of abortion in the USA in 1973, the risk of infectious morbidity and mortality from this procedure decreased dramatically in the country;[2] the number of deaths associated with abortion decreased by 50% in the first 5 years.[3] The case fatality rate (CFR) per 100 000 legal abortions fell by nearly 80% between the initial period of 1973–77 (CFR 2·09) and the period of 2013–17 (CFR 0·44).[3] These marked declines had predictable effects on the training experiences of generations of health-care practitioners. As Eschenbach wrote, "Before 1973, septic abortions were an integral part of obstetric and gynecologic residency training and of practicing physician's knowledge as to the need to immediately remove the infected placenta. For example, the number of hospital admissions for septic abortion was 105 women to Boston City Hospital in 1955–1956 and was 87 women to a Pittsburgh hospital in 1965–1967. However, most physicians who have been trained in the 40 years since Roe *vs* Wade never cared for a patient with a septic abortion or were provided detailed training on its treatment."[4]

Data indicate a direct correlation between laws that increasingly restrict abortion access and the incidence of unsafe abortions (and abortion-associated mortality).[5] With increasingly restrictive legislation targeting access to safe abortion services, reviewing infectious complications of unsafe practices in pregnancy termination is crucial, with a particular emphasis on diagnosis and management, along with an overview of life-threatening clostridial (and related anaerobic bacterial) infections that can complicate unsafe abortion.

Methods of unsafe abortion

Safe abortions are done using standard aseptic surgical techniques; with the advent of medical (non-surgical) abortion, these methods have evolved even further. The practices used to carry out unsafe abortion vary widely[6,7] and often reflect availability of and access to perceived abortifacients (chemical abortion), tools (direct injury to the vagina, cervix, or fetus), or blunt external trauma. As such, the range of risks to the recipient is broad. Chemical abortion can include ingesting material believed to induce fetal injury or death (eg, turpentine or

Key messages

- With increasingly restrictive legislation targeting access to safe abortion services, infectious complications of unsafe pregnancy termination might increase in frequency.
- Septic abortion refers to any abortion, whether induced or a miscarriage, that is complicated by uterine infection, including endometritis. The incidence of septic abortion is higher when abortions are unsafely attempted.
- Clinicians should recognise symptoms of severe septic abortions because diagnosis and therapy must be made quickly to avert severe morbidity or death. These rapidly progressive, life-threatening intrauterine infections complicating abortion are caused by the anaerobic, gram-positive bacteria *Clostridium perfringens (C perfringens)* and *Paeniclostridium sordellii (P sordellii)*.
- *C perfringens* and *P sordellii* are well-known causes of septic abortion, particularly in the setting of unsafe abortion, and usually present with lower abdominal or pelvic pain; refractory hypotension; exaggerated leucocytosis; and evidence of tissue oedema, gas, and necrosis in the uterus and effusions in the chest, abdomen, and pelvis.
- Treatment of these infections, which are complicated by the production of potent bacterial toxins, includes emergent surgical source control, broad-spectrum antimicrobial therapy, and supportive care.

bleach). Any of these methods can induce morbidity or mortality. Finally, the performance of unauthorised dilation and curettage can occur in unsanitary or contaminated environments, creating a profound risk for introduction of potential pathogens—both from the external environment and from the cervicovaginal microbiota—into the reproductive tract.[5] These unsafe procedures can result in dead tissue from the placenta or fetus being left behind in the body, proving a nidus for bacteria to proliferate, isolating themselves from a blood network supplying immune cells (or antibiotics), and subsequently causing serious infection.

Complications after unsafe abortion

More than 73 million pregnancies are estimated to end in abortion worldwide each year[8] and of these, an estimated 25 million abortions are classified as unsafe.[9] Unsafe abortion is a major cause of maternal morbidity and mortality. Nearly 7 million women receive treatment for complications from unsafe abortion procedures annually in low-income and middle-income settings,[10] with an estimated 23 000–68 000 deaths.[6,9] Medical complications associated with unsafe abortion include haemorrhage; sepsis; peritonitis; reproductive tract infections; and trauma to the cervix, vagina, uterus, and abdominal organs.[11] Among patients with serious complications from abortion, severe infection is second only to haemorrhage as the most common complication.[12]

Infections can complicate abortion regardless of the technique, but severe infections are more likely to occur following physical trauma. The term "septic abortion" refers to any abortion, whether a miscarriage or induced, that is complicated by uterine infection, including endometritis. Infection can complicate safe abortion but is uncommon. In relatively high-income countries where abortion is legal, the rate of fatal sepsis following medically induced pregnancy termination is very low (<1 per 100 000 cases),[13,14] with an overall incidence of infection in this population of less than 0·5%.[13,14] In people undergoing legal, surgical abortion procedures (eg, dilation and curettage) in high-income countries, the rate of infection requiring intravenous antibiotics is less than 0·4%.[13,14] Worldwide, the rate of infection after surgical abortion has been estimated to be in the range of 0·1–4·7%.[13] Notably, antibiotic prophylaxis is recommended in the setting of surgical abortion, also reducing the risk of infectious complications.[15]

Infectious complications are more common when abortions are unsafe. Infections might not be diagnosed or treated in a timely manner, reflecting social determinants of health such as poor access to health-care facilities, or reluctance on the part of the abortion recipient to seek care or disclose either the pregnancy or the abortion.[16] As noted by Haddad and Nour, "With unsafe abortion, the additional risks of maternal morbidity and mortality depend on what method of abortion is used, as well as on women's readiness to seek post-abortion care, the quality of the facility they reach, and the qualifications (and tolerance) of the health provider."[5] WHO has estimated that 20–30% of unsafe abortions result in reproductive tract infections.[6] Studies from global settings estimate that the incidence of sepsis after unsafe abortion is in the range of 3–15% in primary and secondary health facilities, but might exceed 50% in tertiary health-care centres, which might be more likely to care for patients who are critically ill.[4]

Previous, culture-based studies of septic abortion revealed that these infections can be monomicrobial or polymicrobial, and often include anaerobic or microaerophilic pathogens, but are not usually complicated by severe shock.[17–19] However, here we address two particularly severe infections that are well-documented causes of septic abortion complicated by toxic shock and a high mortality: the anaerobic, spore-forming pathogens *Clostridium perfringens (C perfringens)*[12] and *Paeniclostridium sordellii (P sordellii)*.[20] Other relatively common causes of severe sepsis or toxic shock after unsafe abortion include infections caused by the aerobic pathogens *Streptococcus pyogenes*, *Escherichia coli*, and *Staphylococcus aureus*.[4] In this Review, we discuss *C perfringens* and *P sordellii*, the clinical syndromes they can cause (with a focus on toxic shock syndrome), and review diagnostic strategies and treatment. This Review aims to help equip clinicians to better identify such infections quickly and take steps to improve outcomes. Unfortunately, even with early recognition and management, these infections are associated with severe morbidity and high mortality.

Clostridium and *Paeniclostridium* infections after abortion

Two specific bacterial genera from the family *Peptostreptococcaceae* (*Clostridium* cluster XI) have repeatedly been reported to cause severe and often life-threatening infections following the termination of pregnancy: *C perfringens* (formerly *Bacillus welchii* or *C welchii*[21]) and *P sordellii* (formerly *C sordellii*). Although other clostridia (and other anaerobes, particularly the *Bacteroides* species[17,18]) can be identified in post-abortion infections, *C perfringens* and *P sordellii* are most described in the context of life-threatening, severe disease, and will therefore serve as the focus of this Review.

C perfringens and *P sordellii* are spore-forming, anaerobic, gram-positive bacilli that primarily cause toxin-associated diseases in humans. These related bacteria are environmentally stable in their spore form and the spores can remain dormant for hundreds (and perhaps thousands) of years, despite harsh conditions.[22] The spores are ubiquitous and are likely ingested inadvertently from the environment, where they transiently (or more stably) colonise the human gastrointestinal tract. A recent multicentre study identified *C perfringens* in rectal swabs of nearly one in ten women and *P sordellii* in nearly one in 30 women of reproductive

age.[23] When the spores gain access to nutrient-rich, oxygen-poor environments they can germinate into replicating, vegetative bacteria that release toxins and cause disease (including gangrene and necrotising skin and soft tissue infections), often accompanied by malodorous gas production and sometimes complicated by toxic shock.

Pathogenesis of post-abortion infections

The current model of reproductive tract infections caused by *C perfringens* and *P sordellii* posits that these bacteria move from the gastrointestinal tract, as either spores or vegetative bacteria, into the genital tract (via the perineum), where they are introduced into anatomic niches hospitable for infection. Examples of such niches include tissue injured by trauma or surgical instruments, non-viable decidual tissue, retained products of conception (placental or fetal tissues), or clotted blood. Infection can quickly spread into, and through, underlying endometrial and myometrial tissue, sometimes resulting in bacteraemia.[4] When physical trauma is coupled with poor hygiene, circumstances favour infection.[24] Many unsafe methods of abortion cause tissue damage, resulting in macroscopic or microscopic areas of relatively hypoxic (or anaerobic), non-viable tissue or clotting. Proliferation within areas of devitalised or hypoxic tissue also limits penetration of immune cells and systemic antibiotics to the site of infection. Once *C perfringens* and *P sordellii* replicate and express toxins, such infections can progress rapidly from asymptomatic to locally symptomatic, systemically symptomatic, and death. In the context of lack of access to safe abortion, any delay in the removal of dead tissue can allow proliferation of these bacteria in an anaerobic tissue environment.[4] Rapid proliferation results in the quick accumulation of toxins, which cause haemodynamic collapse.[25,26] When haemodynamic collapse occurs, treatment is unlikely to prevent death.

Notably, infections characterised by either *C perfringens* or *P sordellii* can be polymicrobial.[27] The extent to which other microorganisms, including aerobes, contribute to the overall clinical picture of these infections is not entirely clear, but synergy among diverse pathogens in the setting of necrotising soft tissue infections is believed to be important in accelerating their clinical course and worsening disease severity.[28]

C perfringens

C perfringens was discovered in 1891 by Welch.[29] This anaerobe is associated with many different types of infections, primarily food-borne, toxin-dependent gastroenteritis (food poisoning)[30] and gas-forming myonecrosis or gangrene.[31] *C perfringens* has been suggested to be responsible for up to 80–90% of traumatic gas gangrene in humans.[31,32] *C perfringens* has long been implicated in post-abortion infections,[33,34] particularly those accompanied by gas gangrene or toxic shock syndrome. *C perfringens* and related clostridia have been implicated in less than 5% of episodes of septic abortion in relatively small case series.[17,24] Although other clostridia (and *P sordellii*) have also been identified in the context of abortion-related sepsis, such as *C septicum,*[35] they are not nearly as common as *C perfringens*.

C perfringens is classified into seven types according to the production of six major typing toxins, namely alpha (CPA), beta, epsilon, iota, enterotoxin, and necrotic enteritis B-like toxin.[36] The toxin most closely associated with the ability of *C perfringens* to cause gas gangrene or myonecrosis and toxic shock is the α-toxin, CPA,[36] a multifunctional zinc metalloenzyme comprising of phospholipase C and sphingomyelinase activities. This α-toxin is implicated in haemolysis, myonecrosis, leucocytosis, platelet aggregation, vasoconstriction, and inhibition of neutrophil differentiation.[36] Another toxin, referred to as theta toxin or perfringolysin O, is a pore-forming cytotoxin that might also play a role in muscle necrosis, working synergistically with CPA, by causing tissue destruction and preventing bacterial lysis by host immune cells.[36]

P sordellii

P sordellii was first isolated in 1922 by the Argentinean microbiologist Alfredo Sordelli.[20] It has also been denoted as *Bacillus sordellii*, *C sordellii*, and *C oedematoides*.[3,4] The name was most recently changed to *P sordellii* in 2016.[37] This anaerobe can cause similar abortion-related infectious complications to *C perfringens*; however, it is less frequently implicated as a cause of infection following unsafe or illegal abortion than is *C perfringens*.[20] The reasons for this are not entirely clear, but might reflect the fact that *P sordellii* is less frequently observed in the gastrointestinal and genitourinary tract of reproductive-age women than is *C perfringens*.[38]

Over the past two decades, *P sordellii* and, to a lesser extent, *C perfringens* have been identified as extremely rare causes of post-abortion toxic shock syndrome following medical abortion with oral mifepristone combined with vaginally applied misoprostol.[39,40] Although the causal mechanism is not definitively known, data in animal models suggest that topical misoprostol suppresses the local immune response through a variety of mechanisms, including a reduction in TNF-α production and phagocytosis of *P sordellii* by macrophages.[40] Notably, reports of these infections declined once buccal administration of misoprostol was recommended instead of vaginal administration in the USA,[41,42] but if this change caused the apparent reduction in cases remains unclear. Vaginal misoprostol is still used commonly worldwide, and is recommended by WHO as part of medical abortion regimens.[15] There is currently no evidence of a causal relationship between the safe and legal use of these medications as currently recommended and an increased risk of infection or death.[14]

Panel: Signs and symptoms of abortion-associated *Clostridium perfringens* and *Paeniclostridium sordellii* infections

Vital sign abnormalities

- Fever—might not be present, particularly when toxic shock is occurring[4,27,39,47]
- Tachycardia—can be disproportionately high relative to the degree of fever[34,47]
- Tachypnea—with or without dyspnoea[4]
- Hypotension—can be severe and treatment-refractory[34,47]

Symptoms

- Chills[21,27,47]
- Lower abdominal pain[21,27,47]
- Vomiting[21,27,34,47]
- Diarrhoea[21,27,34,47]
- Dizziness[39]
- Weakness[39]
- Uterine bleeding[49]
- Foul cervicovaginal discharge[21,49]

Physical signs

- Jaundice—associated with *C perfringens*[21,34,47]
- Peripheral cyanosis[47]
- Cold, clammy extremities[47]
- Low urine output or acute renal injury[4,21,47]
- Mental alertness preserved until late in the disease[32,34,47]
- Metastatic gas gangrene— particularly of the muscles of the thigh. People might also have perineal vesicles or bullous lesions and on legs or trunk.[34,47,50]

Laboratory abnormalities

- Severe anaemia—when haemolysis or bleeding have occurred (haemolysis is more common with *C perfringens*)[20,21,47]
- Haemoconcentration—particularly common with *P sordellii* toxic shock[20]
- Exaggerated leucocytosis or leukemoid reaction[21,27]

Radiographic abnormalities

- Chest imaging (radiograph, computed tomography)—pleural effusions[48]
- Abdominal, pelvic imaging (computed tomography, MRI)—peritoneal effusions, soft tissue gas, signs of tissue oedema or necrosis[48]

Similar to *C perfingens*, the pathophysiology of *P sordellii*-related toxic shock syndrome is characterised by the production of cytotoxins.[43] *P sordellii* can make two large cytotoxins, haemorrhagic and lethal, with the lethal cytotoxin being more strongly implicated in causing toxic shock syndrome *in vivo*.[44,45] This toxin-mediated shock is highly fatal. Survival following *P sordellii* toxic shock has not, to our knowledge, been reported in the case of septic abortion, although at least one postpartum case of *P sordellii* toxic shock syndrome did not result in death.[46]

Clinical presentation of *C perfringens* and *P sordellii* infections

With restriction to safe abortion likely to increase in the USA, clinicians should be alert to the possibility that a person who has illicitly terminated a pregnancy might be reluctant to share such information for fear of repercussion. Although this Review focuses on recognition and management of severe infections, clinicians evaluating such patients should be aware of their local (state) laws and should have access to resources that can provide appropriate support and counselling to their patients.

Notably, the clinical pictures of *C perfringens* and *P sordellii* infections are similar, whether they arise from induced abortion or miscarriage. *C perfringens* infection following abortion has a characteristic clinical presentation.[47] After an abortion, the appearance of fever, violent shaking chills, body aches, and lower abdominal pain, often associated with vomiting and occasionally diarrhoea, herald the onset, which can develop very rapidly within 1–3 days, particularly when physical instruments or foreign bodies are used.[21,47] A "dark, putrid, foul-smelling" cervicovaginal discharge is not uncommon.[21] When toxic shock is evident on presentation, fever is usually absent.[20,39] Notably, the absence of fever is a hallmark of severe *P sordellii* infection.[48] Following medical abortion, cases of clostridial infection generally present within a week,[39] often with uterine bleeding or foul cervicovaginal discharge that can contain blood clots.[12,49] Common signs and symptoms of these types of infections are presented in the panel. A rash is usually absent, but jaundice can occur with haemolysis, a feature of some *C perfringens* infections. Patients with sepsis following abortion or miscarriage should have a pelvic examination, investigating any trauma to and pus or foul-smelling fluid emanating from the cervix.[4] Clinicians should search for any visible tissue remaining in the cervix. Notably, the uterus might only be mildly tender,[49] even in cases of severe infection.[4]

C perfringens and *P sordellii* are also associated with a treatment-refractory toxic shock syndrome. This "*Clostridium*-associated toxic shock" has been defined as an acute fatal illness including at least one finding from each of these clusters: (1) leukemoid reaction (peripheral white blood cell count of more than 50 000 cells per μL[51]), haemoconcentration, or hypotension; (2) focal gastrointestinal or gynaecological symptoms; and (3) pleural, pericardial, or peritoneal effusions.[48,52] Although the pathogenesis is complex, for *C perfringens*, it appears that both CPA and perfringolysin O play important roles in generating the refractory shock associated with infection.[53]

Diagnosis

Sepsis in pregnancy, including in the setting of partial or complete abortion, requires evaluation for several

potential causes, including pyelonephritis, appendicitis, pneumonia, chorioamnionitis, endometritis, pancreatitis, septic pelvic thrombophlebitis, cellulitis, myositis, and necrotising soft tissue infections.[54] The initial diagnosis of *C perfringens* or *P sordellii* must be suspected on clinical grounds, with prompt initiation of broad-spectrum antibiotics, including the use of agents active against these pathogens. Treatment is discussed in the next section of the Review.

The results of physical examination are important (panel). Vital signs can be markedly abnormal in *C perfringens* and *P sordellii* pelvic infections and fever might or might not be present. Tachycardia, tachypnea, and hypotension are frequently observed. Patients might appear jaundiced, pale, or cyanotic. Mental acuity might be intact despite clear signs of severe infection. Examination should seek evidence of uterine infection, or infection of the surrounding skin and soft tissues. This assessment for a reproductive tract infection requires evaluation for trauma to the perineum, vagina, or cervix; the presence of cervicovaginal discharge or bleeding or passing clots; cervical or uterine tenderness, or both; soft tissue crepitus; the presence of bullae; local oedema; and tenderness out of proportion to physical examination findings. Areas of skin changes should be marked to track progression, which can be rapid. Finding crepitus on physical examination (or gas on radiographic imaging) should suggest the presence of these pathogens. However, because these infections are often confined to the uterus, there might not be any cutaneous signs of infection (until late in the progression of infection). Shock that is out of proportion to physical examination, or shock that is highly refractory to treatment with volume resuscitation or vasopressive agents should also signal the possibility of severe clostridial infection.

Laboratory studies should include routine peripheral blood counts, screening for common electrolytes (eg, bicarbonate, calcium, chloride, magnesium, potassium, and sodium), and assessment of renal and hepatic function with addition of a creatine kinase (to evaluate for myositis). Serum lactate and blood coagulation studies can also be helpful in evaluating for sepsis and haematological complications. Blood cultures (including anaerobic cultures) should be obtained as soon as possible, because bacteraemia is not uncommon in the setting of septic abortion,[17,18] although these are usually negative in cases of post-abortion *C perfringens* or *P sordellii* infection.[48,55] Urine analysis and culture can help evaluate for pyelonephritis, which can mimic septic abortion and is the leading cause of septic shock in pregnancy.[54] Clinicians should consider obtaining an anaerobic culture, if available, of endocervical secretions to aid in diagnosis of these infections.[56] Prognostic scoring systems applied in the setting of necrotising soft tissue infections, such as the Laboratory Risk Indicator for Necrotizing Fasciitis,[57] have not been formally evaluated for use in gynaecological infections caused by *C perfringens* or *P sordellii*.

Complete blood counts can reveal significant anaemia as a reflection of haemorrhage or severe intravascular haemolysis, a complication of *C perfringens* CPA toxin.[53,58] However, in cases of *P sordellii* toxic shock, the massive third spacing from lethal cytotoxin-dependent cardiovascular collapse can result in haemoconcentration.[20] A leukemoid reaction suggests the presence of these bacteria.

Blood cultures should be obtained, because bacteraemia can be observed with severe abortion-associated infections, including *C perfringens*, and in at least one report nearly a third of patients had bacteraemia.[27]

Radiographic imaging such as computed tomography or plain radiographs can reveal foreign bodies and evidence of oedema, necrosis, or gas in soft tissues. Pleural, pericardial, or peritoneal effusions are common.[48] An MRI can also help diagnose myositis and fasciitis. However, patients might not be stable enough to undergo advanced imaging, so portable, bedside tests might be required. Furthermore, ultrasound can reveal foreign bodies and gas in the soft tissues.

The most rapid diagnostic clue might be Gram stain of affected tissue or discharge or drainage from the vagina, cervix, or other affected areas, examining for gram-positive rods consistent with *C perfringens* and *P sordellii*, or gram-positive cocci suggestive of *S aureus* or *S pyogenes*.[39] Both aerobic and anaerobic cultures should be obtained from tissue, discharge, or blood samples. Tissue can be subjected to immunohistochemistry or targeted PCR assays, but these tests take time and might not be available at most health-care facilities.[39] Unfortunately, commercially available rapid diagnostic tests remain unavailable.

Treatment

Treatment of these infections is urgent, and the first principle of management is source control, with debridement or evacuation of any products of conception (placental, membranous, or fetal tissues) and any foreign body that might have been introduced as part of an attempt at abortion. Prompt surgical consultation is important so that debridement of infected, necrotic, hypoxic, or dusky-appearing tissue, a strategy also used in the management of other necrotising soft tissue infections, can be performed.[59] Frequent re-evaluation is necessary to ensure the adequacy of initial debridement and absence of further tissue necrosis, particularly if shock or sepsis do not respond to surgical source control, and might dictate the need for additional surgical debridement.[59]

The empiric antimicrobial treatment of post-abortion sepsis should be broad to cover the myriad of aforementioned causes.[54] Empiric antibiotic regimens might include the combination of ampicillin, gentamicin, and metronidazole,[19] or single, broad-spectrum agents

such as carbapenems, or beta-lactam or beta-lactamase inhibitor drugs (eg, piperacillin–tazobactam).[4] If toxic shock syndrome is suspected, it is important to remember that some aerobic bacteria can cause this syndrome in the setting of pregnancy or abortion, particularly *S aureus* (including methicillin-resistant isolates) and *S pyogenes*.[39]

To our knowledge, no randomised controlled trials are available to inform on best approaches to managing severe *C perfringens* and *P sordellii* infections of the reproductive system. Recommended treatment includes usual supportive measures (including best practices for managing septic shock), antibiotic therapy, and aggressive and timely source control through surgical debridement to remove infected or necrotic tissue (including the uterus).[39] These infections can progress rapidly and despite modern therapy, the mortality from such infections approaches 70–90%.[20,46,56] As noted by Gorbach regarding *C perfringens* myonecrosis, "This is a disease that begins where other diseases end, with death."[32] A combination of supportive care, source control, and antibiotics remain mainstays of treatment.

Empiric antibiotic therapy targeting clostridia species, *P sordellii,* and other organisms known to cause toxic shock should be immediately initiated.[39] These bacteria remain susceptible to many antibiotics including the beta-lactams (penicillin, ampicillin, or combination beta lactam–beta lactamase inhibitors, such as ampicillin–sulbactam or piperacillin–tazobactam), clindamycin, tetracycline, metronidazole, vancomycin, carbapenems, and oxazolidinones.[39] They are resistant to aminoglycosides and sulfonamides. Given the broad differential diagnosis of septic abortion, starting with medications like piperacillin–tazobactam or carbapenems combined with coverage for methicillin-resistant *S aureus* (eg, linezolid, daptomycin, or vancomycin) is reasonable. If the specific use of antibiotics such as linezolid or clindamycin, applied in cases of *S pyogenes*-associated necrotising soft tissue infections to limit bacterial toxin production,[60] is beneficial in these cases typically dominated by anaerobes remains unclear. However, because a rapid diagnosis is challenging and the clinical features overlap with *S pyogenes* infection, we recommend that either clindamycin or linezolid is part of an initial, empiric regimen, especially when toxic shock is evident or suspected (eg, piperacillin–tazobactam plus linezolid).

Intravenous immunoglobulin is recommended in the setting of *S pyogenes* infection with toxic shock syndrome.[61] If intravenous immunoglobulin would benefit patients with toxic shock caused by *C perfringens* or *P sordellii* infection remains unclear, but this has been used in previous cases involving toxigenic clostridia[46,62] and, until *S pyogenes* can be excluded, we recommend its use. A more selective targeting of toxins using antitoxin-specific antibodies (polyclonal or monoclonal) has long been entertained, even with some anecdotal success (reviewed in[20,63]), but remains experimental. For example, antibodies directed against lethal cytotoxins have been shown to improve outcomes in mouse models of *P sordellii* infection.[44] Finally, there is not a proven role for hyperbaric oxygen in these infections, but it might help with postoperative wound healing once a patient is stable enough to receive treatment.[64]

Search strategy and selection criteria

Reference material for this Review was identified through searching the PubMed and Google Scholar search engines for papers published in English between from inception until Aug 22, 2022, on July 6, 2022, and Aug 22, 2022, including the search terms "abortion", "septic abortion", "unsafe abortion", "*Clostridium sordellii*", "*Paeniclostridium sordellii*", "*Clostridium perfringens*", "*Clostridium welchii*", and "toxic shock syndrome". References were also identified within the bibliographies of sources identified via the aforementioned search strategy.

Conclusions

The anaerobic pathogens *C perfringens* and *P sordellii* are uncommon causes of serious, life-threatening infections after abortion and the risk for these bacteria is higher following unsafe or illegal abortion than with legal, safe procedures. A high index of suspicion is needed to identify these infections and initiate potentially life-saving care. Time is of the essence in these diseases of intoxication and tissue destruction. A multidisciplinary approach including experts in critical care, obstetrics and gynecology, surgery, radiology, and infectious diseases should be mobilised rapidly when septic abortion is suspected. Access to safe, legal abortion has been proven to reduce the incidence of septic abortion and remains a major preventive tool in the fight against these devastating infections.

Contributors

DMA and JMM were both involved in conceptualisation and writing of both the original draft and reviewing and editing. Both authors accept responsibility for the decision to submit for publication.

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