



Infection and Medication Abortion

When medication abortion was introduced in the U.S., some assumed that there was little likelihood of infection, since there was no instrumentation of the cervix or uterus. In fact, the rate of infection with medication abortion is very low. In a review of the literature, Shannon et al.¹ found that <1% of patients undergoing medication abortion developed infection, less than the rate of infection reported with surgical abortion. Furthermore, the majority of infections are uncomplicated and are treated as outpatients. During one quarter in 2003, Planned Parenthood affiliates providing mifepristone were surveyed about numbers of patients treated for infection as outpatients. The results showed that 2 patients in 1,000 were treated for infection as outpatients. Some of these patients did not meet clear diagnostic criteria, but were treated for presumptive endometritis based on clinician judgment.

However, despite the fact that infection is rare, we now know that serious infection, although uncommon, can occur and rarely can even be fatal. Of the four infection-related deaths that have occurred in the United States since introduction of mifepristone, two are attributed to the organism *Clostridium sordellii* (*C. sordellii*). The Centers for Disease Control (CDC) is performing laboratory testing to determine the causative organism in the remaining two U.S. deaths. In addition, a death during Canadian clinical trials is attributed to *C. sordellii* sepsis.

This article reviews serious infections with typical and atypical presentations after a medication abortion. The article is organized according to four key topics: **(1) Signs and symptoms of typical post-abortion infection;** **(2) Recommended work-up if infection is suspected;** **(3) Atypical rare infection;** and **(4) More about *C. Sordellii* and sepsis.**

1. Signs and symptoms of typical post-abortion infection

The continuum of endometritis, endomyometritis and sepsis typically presents with pelvic pain and fever. (Endometritis is inflammation of the endometrium; endomyometritis is inflammation of the endometrium and the myometrium – the muscular tissue of the uterus; sepsis is bacterial infection that has become systemic and entered the blood system.)

“A typical presentation is increasing pelvic pain several days after the abortion. Sometimes vaginal bleeding is increased, and normal or increased bleeding obscures purulent discharge. On examination, the uterus is tender and may be slightly enlarged. The adnexa should be evaluated for tenderness or masses. ...

“Women with endometritis should be treated immediately. Women with mild endometritis, without adnexal tenderness or high fever, can be treated as outpatients. ... An acceptable approach is to use the regimens for outpatient treatment for pelvic inflammatory disease. ...

“Postabortal infection may progress rapidly from endometritis to endomyometritis, salpingitis and diffuse pelvic inflammatory disease. ... Women who have adnexal peritonitis, high fever (e.g., over 38.5°C) or significant leukocytosis [high WBC] should be hospitalized for treatment with parenteral [IV] antibiotics.”²

When PID is treated in the outpatient setting, choose one of the regimens recommended in the CDC STD Treatment Guidelines with 14 days of anaerobic coverage.

2. Recommended work-up if infection is suspected

If chlamydia and gonorrhea screening laboratory tests were not performed initially, those tests should be done. An assessment needs to be done to determine whether the patient is a candidate for treatment as an outpatient, or whether she should be referred for inpatient treatment (IV antibiotics).

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The patient should have a thorough examination, which includes:

- History that focuses on differentiating typical versus atypical infection
- Vital signs, including temperature, blood pressure, pulse, and hematocrit or hemoglobin
- WBC count with differential
- Abdominal palpation and auscultation of bowel sounds
- Speculum examination
- Bimanual examination for assessment of uterine tenderness and adnexal tenderness and presence/absence of adnexal masses
- Gonorrhea and chlamydia laboratory testing, if not performed previously

If typical endometritis is diagnosed and outpatient treatment is initiated, it is important to ascertain whether the patient is responding to the medications and her condition is improving. Many clinicians call the patient in 24 hours to touch base. The patient should be re-examined in 48-72 hours to be sure that her symptoms are abating. If the patient is not improving, or if her condition is worsening, she should be referred for inpatient treatment. A summary of her care should be either sent with her to the ER, or the ER attending should be called to be sure hospital staff knows that she has already been treated with the outpatient PID regimen and has not improved.

Patients with the following conditions should not be treated in the outpatient setting, but should be managed in the hospital setting:

- Patient is clinically unresponsive to oral antimicrobial therapy.
- Patient is unable to follow or tolerate outpatient oral regimen.
- Patient has severe illness, (either acute or chronic), nausea and vomiting and a high fever (greater than 102.2°F).
- Patient has tubo-ovarian abscess.
- Patient has an allergy to antibiotics which precludes the use of the CDC-listed PID outpatient treatment regimens.
- Patient has recurrent PID, defined as more than two episodes in the past 12 months.
- Atypical rare infection – see below.

3. Atypical rare infection

Five women in North America (four in the United States) have died from sepsis after undergoing medication abortion. According to Danco Laboratories, LLC, *Clostridium sordellii* was identified in three of the five North American fatalities. The causative organism in the other two deaths has not been identified.

C. sordellii is a spore-forming bacteria found in soil and in the intestinal tracts of 0.05 to 0.5% of the population. The opinion of infectious disease consultants is that infection caused by *C. sordellii* after medication abortion was due to an unknown environmental exposure or fecal contamination.

If *C. sordellii* causes a pelvic infection, the early presentation is different from that of typical endometritis. The patient is usually afebrile with multiple vague abdominal and GI complaints, which may include abdominal pain, bloating, nausea, and vomiting. Early symptoms mimic viral infections. If patients experience abdominal pain or flu-like symptoms more than 24

hours after taking misoprostol, the clinician must evaluate for atypical pelvic infection.

An article³ reviewing case reports of postpartum endometritis caused by *C. sordellii* presents the following clinical findings:

- sudden onset with influenza-type symptoms in previously healthy women
- progressive refractory hypotension
- local and spreading tissue edema
- absence of fever

Laboratory findings include:

- marked leukocytosis (very high WBC)
- elevated hematocrit or hemoglobin (hemoconcentration)

In order to make a diagnosis, the work-up previously listed in section 2 should be done. Heightened suspicion for atypical endometritis is based upon signs and symptoms with careful attention to:

- Vital signs, including BP, pulse, temperature
- Hemoglobin or hematocrit
- WBC with differential

Signs of atypical sepsis

- abdominal pain/ bloating/ distention 24 hours or later following misoprostol
- patient feels ill disproportionate to clinical signs
- may report weakness, fatigue, malaise, nausea, vomiting
- elevated WBC with left shift
- high hemoglobin or hematocrit
- low BP
- rapid pulse
- may be afebrile

If the WBC is elevated with a marked left shift or the hemoglobin/ hematocrit is higher than expected, or the patient is tachycardic or hypotensive, with or without fever *AND* she has flu-like symptoms *OR* abdominal pain or bloating, suspect atypical endometritis. *The next part of the work-up for atypical endometritis should take place in the hospital.*

Because hospital (emergency department) personnel may be unfamiliar with medication abortion complications and atypical presentation of infection following medication abortion, contact must be made with the ER physician. If possible, the on-call OB/GYN and infectious disease physicians covering the emergency department should also be contacted to alert hospital physicians of the following:

- the expanded FDA label, advising rare presentations of atypical sepsis
- the hallmarks of atypical sepsis
- the aspects of the patient's evaluation indicating that she may be experiencing atypical infection

Once you have alerted the hospital physicians of the above, tactfully inform them of the following recommendations and reminders:

- Clostridial organisms are anaerobic gram positive rods.
- Consideration should be given to culturing the cervix, endometrium, and blood for aerobic and anaerobic organisms.
- A gram stain (from cervix or endometrial sample) should be performed immediately, since preliminary aerobic culture results will take at least 24 hours and preliminary anaerobic results may take longer.
- Endometrial cultures (e.g., aspiration with Pipelle) are apt to be a truer reflection of the existence of invasive pathogens and, if carefully taken, are less likely than cervical cultures to contain contaminants.

If the gram stain shows gram positive rods in a patient who is developing symptoms of atypical infection, the working diagnosis of *C. sordellii* should be made and the following treatment should be initiated:

- IV broad spectrum antibiotics with anaerobic coverage
- Cardiovascular supportive care
- Frequent monitoring
- If products of conception remain, uterine aspiration should occur, once the first dose of antibiotics has been infused and the woman is hemodynamically stable.

5. More about *C. sordellii* and sepsis

The medical literature indicates that a very small proportion of the general population of women have vaginal colonization of *C. sordellii*. The bacteria may also be present in women's intestinal and rectal areas and cause no symptoms whatsoever, not producing any toxins. This is called "colonization" and is not considered to be a health problem. Very few of those women develop actual infection, which may occur during menstruation, miscarriage, abortion or childbirth. There are only about 20 obstetrical/gynecologic reports of *C. sordellii* in the medical literature. Although there have been non-gynecologic superficial infections with *C. sordellii*, such as ear infection and postoperative wound infection in which the patient survived, in all of the documented reports of deep-tissue infection (such as endometritis), the outcome was fatal.

Once *C. Sordellii* actively infects tissue, the bacteria release toxins. The toxins cause necrosis (tissue death), edema and hemorrhagic fluid accumulation in the target organ (uterus).³ The toxins also lead to changes within the blood vessels which cause them to leak fluid into surrounding tissue. Because fluid is leaking from the blood vessels, hypovolemia results. Hypovolemia and the shock state lead to adult respiratory distress syndrome (ARDS).⁴ This cascade of events is known as septic shock. The patient experiencing septic shock will exhibit the following signs and symptoms:

- tissue swelling
- low blood pressure
- high hematocrit or hemoglobin (fluid component of the blood moves out of the blood vessels into surrounding tissue, therefore leaving the remaining red blood cells in a more highly concentrated solution)

Septic shock, whether caused by *C. sordellii* or other organisms, is difficult or impossible to treat once it is established.

Multiple vital organs affected by the toxins are unable to function properly. Antibiotics may kill the bacteria itself, but aren't effective against the toxins that already have been released and that will lead to cardiopulmonary collapse.

More is unknown than is known about this organism. For instance, it is possible that some women with very early *C. sordellii* infection may have been treated empirically with broad spectrum aerobic and anaerobic antibiotics and survived, yet because anaerobic cultures were never done, the diagnosis was not made.

Is there a test for *C. sordellii*?

Testing for *C. sordellii* requires an anaerobic culture. Once the specimen is taken, it must be quickly placed in an anaerobic environment. In other words, this culture usually would be done in a hospital setting; there is no practical anaerobic culture that could be done in an outpatient setting.

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Information about WBC with left shift:

The WBC (white blood cell) count is a test to measure the amount of white cells, also called leukocytes, in the blood. The main function of WBCs is to fight infection, defend the body against invasion by foreign organisms, and to produce antibodies. When an infectious process starts, the body produces WBCs to combat the infection. This is why the WBC count serves as a useful guide to the severity of the disease process.

There are different types of white blood cells. Some are formed in response to allergies, some in response to viruses, others in response to parasites and some in response to bacteria. Each type of WBC performs a specific function. The categorization of the WBCs is called the differential (differential white blood cell count). The types of WBCs traditionally are listed in a certain order with neutrophils appearing first. Neutrophils (polymorphonuclear segmented neutrophils, also called "polys" or "segs") are the most numerous and important type of white blood cell that are the primary defense against bacterial invasion. In their immature stage of development, they are referred to as "band" cells, appearing on the left (earlier stages) of the developmental timeline for maturing neutrophil cells. An abnormally high percentage of bands and immature neutrophils, known as a "left shift" from the normal developmental stage percentages, combined with a high overall WBC, indicates a serious developing bacterial infection. The body mobilizes to fight the infection by gearing up production of neutrophils, churning out new ones that are seen by laboratory counters as a relatively high percentage of immature forms, compared to the usual distribution of various maturational cell stages.

Patients with viral infections will not usually have an elevated WBC. If the WBC is elevated, the differential will be shifted to the right. With a bacterial infection, the WBC will often be high, with a left shift.

Antibiotics and medication abortion

The FDA stated that at this time, there was not sufficient information to recommend the use of prophylactic antibiotics. The FDA stated that reports of fatal sepsis in women undergoing medical abortion is very rare (approximately 1 in 100,000). Prophylactic antibiotic use carries its own risk of serious adverse events such as severe or fatal allergic reactions. Also, prophylactic use of antibiotics can stimulate the growth of “superbugs,” bacteria resistant to everyday antibiotics. Finally, the FDA stated that it was not known which antibiotic and regimen (what dose and for how long) will be effective in cases such as the ones that have occurred.

Overview of sepsis

Sepsis is a problem that is generating considerable attention in healthcare worldwide. Septicemia is the 10th leading cause of death in the United States, according to the CDC. The International Sepsis Forum (ISF) estimates that 750,000 people in North America develop sepsis each year, with similar estimates for Europe. Researchers estimate that 215,000 Americans die every year from sepsis. Over the past 22 years, the incidence of sepsis has grown by an average of 8.7 percent a year in the United States, according to researchers at Emory University School of Medicine and the CDC. A coalition of associations such as the American Association of Critical-Care Nurses, American College of Emergency Physicians, American Thoracic Society, International Sepsis Forum and others have worked together to create guidelines for early recognition and appropriate management of severe sepsis and septic shock.

¹Shannon C, Brothers LP, Phillip NM, Winikoff B. (2004) Infection after medical abortion: a review of the literature. *Contraception*, 70, 183-190.

²Stubblefield PG, Borgatta L. Complications of Induced Abortion. In: Pearlman MD, Tintinalli JE, Dyne PL. *Obstetric & Gynecologic Emergencies: Diagnosis and Management*. New York: McGraw-Hill; 2004.

³Rørbye C, Petersen IS, Nilas L. Postpartum *Clostridium sordellii* infection associated with fatal toxic shock syndrome. *Acta Obstetrica et Gynecologica Scandinavica*, 2000;79:1134-5.

⁴Abdulla A, Lee L. The clinical spectrum of *Clostridium sordellii* bacteraemia: two case reports and a review of the literature. *Journal of Clinical Pathology*, 2000;51:709-12.

⁵Townsend CM. *Sabiston Textbook of Surgery*. 17th ed. Philadelphia, PA: WB Saunders; 2004.

Planned Parenthood Centers Have Provided Mifepristone Abortion to **168,856 Women**

81 centers don't provide surgical abortion but offer medication abortion as part of women's health care

In the U.S., 168,856 women have received mifepristone abortion at Planned Parenthood centers from 1/1/01 to 6/30/05.

- In the first half of 2005 alone, 31,008 women received medication abortion
- in the 2nd quarter 2005, 26% of first-trimester abortions at Planned Parenthood centers were medication abortions
- 29% of Planned Parenthood centers nationwide now provide abortion

Planned Parenthood knows the needs of its communities. There are many women in this country that live long distances from the metropolitan centers where abortions are offered. Prior to availability of medication abortion, access to abortion was difficult or impossible. By expanding medication to 81 sites that formerly offered no abortion services, Planned Parenthood has made access to early abortion a reality for many women who don't have the resources to travel to metropolitan areas for a surgical procedure. Because of the expansion of medication abortion, women are now able to access early abortion at clinics in remote mountainous areas, desert communities, and inner cities where abortion previously was not available. In addition to geographic access, women who prefer anonymity or who live in very conservative areas report that receiving care in the context of a family planning service feels more private. Expanded availability and use of mifepristone abortion has demonstrated its effectiveness, safety, and acceptability to U.S. women.

Comparison of # of sites providing abortion prior to mifepristone approval and in mid-2005

