Mifepristone Deaths Raise Unanswered Questions

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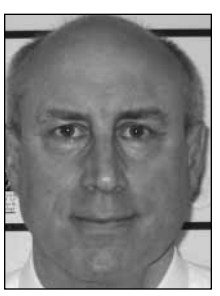
CHARLESTON, S.C. — Recent deaths due to sepsis following medical abortion may be the result of an interaction between factors specific to mifepristone—one of the drugs used in the abortions—and *Clostridium sordellii,* the cause of infection in at least three of the five patients who died, James A. McGregor, M.D., said at the annual meeting of the Infectious Diseases Society for Obstetrics and Gynecology.

Five deaths linked with the use of mifepristone (Mifeprex) for medical abortion have been reported and prompted revisions to the product's package insert. The Food and Drug Administration and the drug's maker, Danco Laboratories LLC, announced the most recent change in July. The insert will now advise physicians to tell patients to seek care if they develop diarrhea, nausea, or vomiting with or without abdominal pain after using the drug.

The first of the five deaths that prompted the warnings occurred in Canada in 2001 during a clinical trial of mifepristone. That case and two others that occurred in California since 2003 were associated with *C. sordellii* infection. The cause of infection in the two other deaths, which also occurred in California, has not been identified, but all five patients died after using oral mifepristone followed by vaginal misoprostol, rather than the FDA-approved regimen, which consists of oral mifepristone followed by oral misoprostol.

In a poster presented at the meeting, Dr. McGregor of the University of Southern California, Los Angeles, described case findings in the two California patients with confirmed *C. sordellii* infection and toxic shock–like syndrome.



Both were previously healthy, young (aged 18 and 22), primiparous women treated with the modified mifepristone/misoprostol medical abortion protocol, including 200-mg mifepristone orally followed by 800-mcg misoprostol inserted vaginally the next day. They reported to emergency departments within 6 days complaining of abdominal pain, nausea, and light-headedness or faintness. Both were afebrile, tachycardic, tachypneic, and hypotensive.

Laboratory findings demonstrated hemoconcentration and dramatic leukocytosis, and both patients suffered refractory shock and cardiopulmonary arrest.

"Mifepristone has multiple pharmacologic properties that may interfere with innate immune responses to infection, toxin exposures, and inflammatory stimuli," he said in an interview.

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DR. MCGREGOR

The drug is long-lasting, and it blocks steroid stress responses and the inflammation-dampening effects of cortisol, he explained. *C. sordellii,* which is present in the vagina in 5% of all women and in up to 29% of women after pregnancy loss, can be toxigenic, he added.

Based on the findings from the cases he presented, he proposes that the following five factors comprise a case definition of *C. sordellii*–associated toxic shock–like syndrome after pregnancy termination:

► Previously well woman with early pregnancy.

► Onset of nonspecific complaints of flu-like illness, such as abdominal/pelvic pain, faintness, and/or light-headedness, within 2 weeks of pregnancy termination.

► Physical findings of hypotension, tachycardia, tachypnea, and fever or hypothermia.

► Laboratory findings of elevated hematocrit and hemoglobin levels, dramatic leukocytosis left shift with increased band forms greater than 10%, and positive culture or nucleic acid–based microbial testing for *C. sordellii*.

► Exclusion of other toxic shock syndromes or other toxic shock–like syndromes, including sepsis syndrome caused by other bacteria, viruses, fungi, or parasites.

Research on host-environment susceptibility factors might further elucidate the mechanisms of this syndrome and contribute to primary prevention, he added.

He speculated that infection recognized early might be treated successfully with combined approaches including appropriate antibiotics, a protein C inhibitor (a new treatment for shock), high-dose steroids, and surgical removal of infected tissues.

Danco has noted that more than 460,000 prescriptions for mifepristone have been written since its approval in 2000, making the fatal sepsis rate about 1 in 100,000. ■