**EMBARGOED FOR RELEASE: 11 A.M. (ET) TUESDAY, MAY 5, 2015**

Media Advisory: To contact Dale N. Gerding, M.D., call Stasia Thompson at 708-216-5155 or email thoms@lumc.edu.

**Oral Administration of Non-Aggressive Strain of *C difficile* Reduces Risk of Recurrence of *C difficile* Infection**

Among patients with *Clostridium difficile* infection (CDI) who recovered following standard treatment with the antibiotics metronidazole or vancomycin, oral administration of spores of a strain of *C difficile* that does not produce toxins colonized the gastrointestinal tract and significantly reduced CDI recurrence, according to a study in the May 5 issue of *JAMA.*

*C difficile* is the cause of one of the most common and deadly health care–associated infections, linked to 29,000 U.S. deaths each year. Rates of CDI remain at unprecedented high levels in U.S. hospitals. Clinical infection also has a recurrence rate of 25 percent to 30 percent among affected patients. Not all strains of *C difficile* produce toxins. Nontoxigenic *C difficile* strains that lack the genes for toxin production are also found in the hospital environment and can colonize hospitalized patients, although patients are usually asymptomatic. Gastrointestinal colonization by these nontoxigenic *C difficile* strains (in both humans and hamsters) has shown promising results as a potential way to prevent CDI, according to background information in the article.

Dale N. Gerding, M.D., of the Edward Hines Jr. VA Hospital, Hines, Il., and Loyola University Chicago, Maywood, Il., and colleagues randomly assigned 173 adult patients who were diagnosed as having CDI (first episode or first recurrence) to receive 1 of 4 treatments: oral liquid formulation of nontoxigenic *C difficile* strain M3 (VP20621; NTCD-M3), 104 spores/d for 7 days (n = 43), 107 spores/d for 7 days (n = 44), 107 spores/d for 14 days (n = 42), or placebo for 14 days (n = 44). Prior to enrollment, these patients had all successfully completed treatment with metronidazole, oral vancomycin, or both at 44 study centers in the United States, Canada, and Europe.

Among 168 patients who started treatment, 157 completed treatment. *Clostridium difficile* infection recurrence was 30 percent among patients receiving placebo compared with 11 percent among all patients receiving NTCD-M3. The lowest recurrence was in 5 percent of patients receiving 107 spores/d for 7 days. Fecal colonization with NTCD-M3 occurred in 69 percent of NTCD-M3 patients: 71 percent with 107 spores/d and 63 percent with 104 spores/d. Colonization with NTCD correlated with reduced recurrence of CDI: recurrence occurred in 2 percent patients who were colonized vs 31 percent of patients who received NTCD-M3 but were not colonized.

One or more treatment-emergent adverse events were reported in 78 percent of patients receiving NTCD-M3 and 86 percent of patients receiving placebo. Diarrhea and abdominal pain were reported in 46 percent and 17 percent of patients receiving NTCD-M3 and 60 percent and 33 percent of placebo patients, respectively. Serious treatment-emergent adverse events were reported in 7 percent of patients receiving placebo and 3 percent of all patients who received NTCD-M3. Headache was reported in 10 percent of patients receiving NTCD-M3 and 2 percent of placebo patients.

The researchers write that the mechanism by which NTCD prevents recurrent CDI is not known; however, there may be an association with the presence of NTCD in the stool (colonization) with reduced infection from toxigenic *C difficile* and in animal models with prevention of CDI when challenged with toxigenic strains. “The most likely hypothesized mechanism of action of NTCD-M3 is that it occupies the same metabolic or adherence niche in the gastrointestinal tract as does toxigenic *C difficile* and, once established, is able to outcompete resident or newly ingested toxigenic strains.”

The authors note that the sample size of the study was small, so many of the findings should be confirmed in larger studies.

(doi:10.1001/jama.2015.3725; Available pre-embargo to the media at <http://broadcast.jamanetwork.com/>)

**Editor’s Note**: This study was sponsored by ViroPharma Incorporated, which is now part of the Shire group of companies. Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, etc.

# # #