

NON-TOXIGENIC *CLOSTRIDIUM DIFFICILE* (CD) PROTECTS HAMSTERS AGAINST HISTORIC AND EPIDEMIC TOXIGENIC “BI” STRAINS

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Epidemic CD [restriction endonuclease analysis (REA) group BI] has been associated with multiple hospital outbreaks and increased severity of CD-associated disease (CDAD). Non-toxigenic CD prevents CDAD in hamsters challenged with toxigenic CD strains. We tested the efficacy of two non-toxigenic types (REA types M3 & T7) in preventing disease in hamsters challenged with one of two toxigenic BI types (REA types BI6 & BI1), both previously shown to be 100% fatal in this model.

Group 1 consisted of 20 assay hamsters and 2 control hamsters challenged with epidemic type BI6. Clindamycin was given orally (30 mg/kg) to all 22 hamsters on Day 0 to render them susceptible to CD infection. Two groups of 10 hamsters were orally inoculated on Day 2 with 10⁶ spores of T7 or M3. Control hamsters did not receive M3 or T7. All hamsters were challenged on Day 5 with an oral dose of 100 spores of epidemic toxigenic strain BI6. Group 2 consisted of 20 assay hamsters and 2 control hamsters treated identically to those in Group 1, but challenged on Day 5 with 100 spores of historic type BI1. Colonization was confirmed by stool culture, and CD strains identified by REA typing.

In Group 1, the 2 BI6 control hamsters died on Days 7-8. Nine of the 10 M3-treated hamsters colonized with M3 and remained well until study end (Day 36). One M3-inoculated hamster failed to colonize with M3 and died on Day 7. All 10 T7-inoculated hamsters colonized with T7, and 5 remained well until study end. The other 5 became co-colonized with BI6, and died between Days 7 and 20. In Group 2, the 2 BI1 control hamsters died on Day 7. All 10 M3-inoculated hamsters and all 10 T7-inoculated hamsters colonized with M3 or T7 and remained well until study end (Day 36).

M3 prevented fatal CDAD in 9/10 hamsters challenged with BI6 (P<.0003) and 10/10 challenged with BI1 (P<.00005). T7 prevented fatal disease in 5/10 hamsters challenged with BI6 (P<.02), and 10/10 challenged with BI1 (P<.00005). Colonization with non-toxigenic CD (especially type M3) is highly effective in preventing CDAD in hamsters caused by REA group BI strains, and provides a novel approach with high potential to prevent CDAD caused by the new epidemic CD strains in humans.