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In their comprehensive review of *Clostridium difficile*-associated diarrhea (CDAD), Susan Poutanen and Andrew Simor[1] refer to the use of anion-binding resins (colestipol or cholestyramine). It is important to highlight the timing of administration of these agents in relation to other oral therapeutic agents (metronidazole or vancomycin). In addition to binding the toxin and spores of *C. difficile*, the binding agents may also bind orally administered therapeutic agents to various degrees, thereby negating their effect. Ideally, resin binders should be given either an hour before or 4 to 6 hours after administration of the oral antibiotics[2] to avoid this problem. However, in clinical practice, especially in hospitals, I have found that the binders and other agents are often given simultaneously; many of the patients have recurrent disease, are described as being resistant to metronidazole (an otherwise rare situation) and are subsequently given oral vancomycin, which is more costly. I believe that this is a common cause of iatrogenic resistance to oral metronidazole.

There are no studies of this phenomenon (i.e., no evidence in this era of evidenced-based and "evidence-made"[3] medicine), but on the basis of a theoretical understanding of the pathophysiology of CDAD, I often administer 10 to 14 days of oral metronidazole followed by 5 to 7 days of oral cholestyramine (to bind the remaining spores in the gut) and have observed a very low rate of recurrence. It is time to prospectively evaluate this simple strategy of sequential therapy in the management of CDAD in a randomized trial.

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[The authors respond to Dr. Parmar:]

We agree with Malvinder Parmar that the role of anion-binding resins in the treatment of CDAD needs to be studied further. Anion-binding resins, such as cholestyramine and colestipol, have been shown to bind *C. difficile* toxins[1] and have consequently been proposed as potentially useful in the treatment of CDAD, as we mentioned in our review.[2] Parmar also suggests that anion-binding resins may also bind *C. difficile* spores, but to the best of our knowledge, this phenomenon has not been described in published reports. Small numbers of mostly anecdotal reports of success and failure with the use of anion-binding resins in the treatment of CDAD have been published (summarized by Ariano and associates[3]), but no large randomized controlled trials have been completed to definitively determine the role of resins. Anion-binding resins have been shown to bind vancomycin[1,4] and theoretically may bind other antibiotics such as metronidazole, although we are not aware of any published data specifically describing this. Given the possibility of antibiotic binding by resins, some authors have suggested not using anion-binding resins in the treatment of CDAD,[5] whereas others recommend using them only if administered at different times from metronidazole or vancomycin.[6] As Parmar suggests, more study is needed to address the optimal indication and timing of anion-binding resins in the treatment of CDAD.

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Cobalamin deficiency in elderly patients

Emmanuel Andrès and colleagues,[1] in their comprehensive review of diagnosis and treatment of vitamin B_{12} (cobalamin) deficiency, fail to consider 2 elements relevant to the Canadian experience.

First, because Canada's flour supply is fortified with folic acid,[2] plasma homocysteine level (determined primarily by folate status) is much less effective in the diagnostic work-up of suspected cobalamin deficiency.[3] In a large population-based study, we established the