Zinc and Cholera

To The Editor—The study by Berni Canani et al. [1] of zinc’s inhibitory effect on cholera toxin (CT)—induced ion secretion in human enterocytes is of interest, but it was not clear from their article whether the authors ever tested the efficacy of zinc given after CT had altered ion transport in their Ussing chamber model. Many substances can block the effects of CT when given before or simultaneously with the toxin [2–4], but most have not proven effective when given after the CT-induced flux changes have become established. If zinc proves ineffective when given after CT-induced changes have already been established, it should not be recommended as therapy for patients with cholera. Studies of zinc salts given in such a sequence are indicated.

However, another possibility suggests itself, should zinc prove to have clinical efficacy when given before CT—that of mass prophylactic use of dietary zinc supplements in endemic cholera-affected areas, particularly before or at the onset of outbreaks, which typically are seasonal. The efficacy of zinc prophylaxis would require confirmation that a safe and tolerable dose of an absorbable zinc salt results in the desired effect in a clinical setting, such as human volunteer studies, which have been performed to test cholera vaccines [5].

With regard to inclusion of zinc in oral rehydration solutions (ORSs), this would require clinical demonstration of noninterference by zinc with ORS absorption, since zinc has been reported to interfere with salt and water absorption [6], and, although zinc enhances glucose absorption, it does so without increasing water and sodium absorption [7]. The effects of zinc on other ORS substrates have not been reported.

David R. Nalin
West Chester, Pennsylvania

References

Potential conflicts of interest: none reported.
Reprints or correspondence: Dr. David R. Nalin, West Chester, PA 19382 (nalin david@hotmail.com).
The Journal of Infectious Diseases 2005;192:1672 © 2005 by the Infectious Diseases Society of America. All rights reserved. 0022-1899/2005/19209-0023$15.00

Reply to Nalin

To the Editor—Our experimental approach aimed to test the effects of the direct zinc-enterocyte interaction on trans-epithelial ion transport, under basal or cholera-stimulated conditions. We used a well-established in vitro experimental model and observed increased ion absorption under basal conditions and a substantial reduction of cholera toxin (CT)–induced secretion. In this experimental model, we tested zinc before CT-induced ion secre-

tion [1]. Nalin [2] suggests that zinc may not prevent secretion once it has already been triggered by CT. However, intestinal ion secretion is a dynamic process in vivo, in which CT is continuously produced, binding new available enterocyte receptors in association with rapid intestinal epithelium turnover and spreading of pathogens throughout the entire gastrointestinal tract [3]. Administration of zinc to a patient with cholera might not, perhaps, inhibit ion secretion induced by CT already injected into the enterocyte, but it would certainly be effective in the subsequent phase of newly produced toxin-binding receptors.

The idea of prophylactic administration of zinc to children in developing countries is based on the protective effects of zinc against intestinal and extraintestinal infections. Its efficacy and safety have been described in several articles [4–8]. Our data add to those on the efficacy of zinc by showing a novel mechanism of action against diarrhea. As reported in these studies, dosages of 10–40 mg/day are safe and well tolerated, without any significant adverse events [4–8]. Our results support the importance of zinc dosage. In human enterocyte monolayers mounted in an Ussing chamber, we observed an increase in short-circuit current in response to excess zinc load, indicating that additional ion secretion may be induced by administration of high zinc concentrations and providing direct proof of the danger of administration of excessive amounts of this element [2]. Our data confirm previous observations reporting that high zinc concentrations (1.8–3.6 mmol/L) are able to induce ion secretion [9]. However, these concentrations are logarithmically different from those investigated in our study (10–35 μmol/L), which were
able to induce a net proabsorptive effect at the intestinal level. Interestingly, in an in vivo animal model of diarrhea, zinc was unable to interfere with oral rehydration solution (ORS) efficacy in reducing dehydration [10]. Finally, in a recent clinical study, it was reported that ORS supplemented with zinc was effective in reducing the severity of acute diarrhea without reducing ORS intake [11].

We believe that zinc should be considered as an addition to the composition of the new universal ORS [12]. This addition would not only enhance ORS efficacy but also increase its use, by introducing an active component capable of reducing water loss, rather than relying on components that only replace fluid loss, as with the standard ORS. This could be an even more important aspect of adding zinc to ORS than its direct ion proabsorptive/antisecretory effects, given that ORS is still now largely underused throughout the world.

Potential conflicts of interest: none reported.

Reprints or correspondence: Dr. Roberto Berni Canani, Dept. of Pediatrics, University “Federico II,” Naples, Italy (berni@unina.it).

The Journal of Infectious Diseases 2005;192:1672–3 © 2005 by the Infectious Diseases Society of America. All rights reserved. 0022-1899/2005/19209-0024$15.00

References

HIV and Leprosy in the Eastern United States

To the Editor—The management of patients with coexisting HIV and Mycobacterium tuberculosis infections is complicated by multiple issues, including the timing of the initiation of highly active antiretroviral therapy (HAART), potential complex drug interactions and additive adverse effects, and the possibility of developing an immune reconstitution inflammatory syndrome (IRIS) that may be severe. According to the current recommendations from the Department of Health and Human Services (DHHS), HAART (which is usually indicated for patients with a CD4+ cell count of <200 cells/mm3 or a history of an AIDS-defining illness) should be withheld from HIV-positive patients with concomitant tuberculosis—with the possible exception of patients with a CD4+ cell count of <50 cells/mm3—until 4–8 weeks after initiation of the multidrug regimen for tuberculosis [1]. The recent retrospective study by Dheda et al. has suggested that HAART reduces the risk of death and new AIDS-defining illnesses in HIV-positive patients requiring treatment for tuberculosis and that delaying HAART in patients with a CD4+ cell count of <100 cells/mm3 may increase the risk of death or developing an opportunistic infection [2]. Perhaps the DHHS recommendations for the initiation of HAART in patients with HIV and M. tuberculosis coinfections should also apply to patients with HIV and coinfection with another mycobacterium, such as M. leprae. In the past, M. leprae infection was thought to put a patient at no additional risk for the development of leprosy, and coinfection has not been reported to alter the clinical manifestations or course of leprosy [3–5]. However, a number of recent reports from Brazil, Europe, and the Caribbean have identified leprosy as an acute presentation caused by the development of IRIS after the initiation of HAART [6–9]. We now report the first case, to our knowledge, of coinfection with HIV-1 and M. leprae in the eastern United States.

A previously healthy 22-year-old Sudanese refugee presented to the dermatologist at Wake Forest University Baptist Medical Center with saddle nose deformity, madarosis, and diffuse infiltration of his ears and cheeks. The patient also exhibited generalized xerosis and pruritis as well as multiple annular, poorly demarcated, infiltrated, hypopigmented plaques on his trunk and upper arms and several soft, dermal nodules on his arms. He had evidence of glove and stocking peripheral sensory neuropathy and no motor neuropathy. A positive Fite-stain biopsy of 1 skin lesion was diagnostic of lepromatous leprosy. Polymerase chain reaction of DNA extracted from the skin biopsy amplified M. leprae heat-shock protein 65, and the results of the subsequent restriction frag-