

CORRESPONDENCE



Fluid Solutions in Dengue Shock Syndrome

TO THE EDITOR: Wills et al. (Sept. 1 issue)¹ recently described a study of three fluid solutions, including 6 percent dextran 70, for resuscitation of children with the dengue shock syndrome. The authors observed a high rate of allergic-type reactions (fever without cardiorespiratory compromise) to dextran 70, suggesting that hydroxyethyl starch may be a preferable treatment.

Although such reactions are not true allergic events, they raise the issue of safety with dextran solutions. Severe dextran-induced anaphylactoid reactions have been well recognized since the 1970s. Fortunately, dextran 1 (Promit) usually prevents such reactions. When it is administered immediately before dextran 40 or 70, dextran 1 acts as a hapten inhibitor that binds dextran-specific antibodies and blocks larger molecules of dextran 40 or 70 from forming immune complexes. Hapten inhibition with dextran 1 has been found to reduce the incidence of severe dextran-induced anaphylactoid reactions from 1 in 2000 to 1 in 70,000.^{2,3}

The Food and Drug Administration's Blood Products Advisory Committee recently recommended adding information about the prophylactic benefit of dextran 1 to the package insert for dextran products to increase awareness among providers.⁴

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2. Promit professional. Stockholm: Meda Pharmaceuticals, September 2000 (package insert).
3. Hedin H, Ljungstrom K-G. Prevention of dextran anaphylaxis: ten years experience with hapten. *Int Arch Allergy Immunol* 1997;113:358-9.
4. Food and Drug Administration, Blood Products Advisory Committee. 83rd Meeting, July 21, 2005 (transcript). (Accessed November 15, 2005, at <http://www.fda.gov/cber/advisory/bp/bpmain.htm>.)

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TO THE EDITOR: The article by Wills et al. is timely since the city of Delhi, India, is currently witnessing a seasonal rise in the number of dengue cases. However, a few points in the article need closer scrutiny. Previous studies on the subject have shown that colloids do not offer any advantage over crystalloids but only increase treatment costs.^{1,2} To clarify the effect of fluids in moderately severe shock, it is unnecessary to consider group 2 in the study by Wills et al., in which no subjects received crystalloids. Subjects in group 2 are reported to have had severe shock, yet the mean diastolic blood pressure in these children was higher than that of the children with moderate illness. Because anyone who administers the fluids, changes the bottle of fluid, or looks at the fluid in an intravenous line would immediately recognize the nature of the fluid from its color and turbidity, it

is unclear how blinding was maintained in the study. The low mortality in the trial illustrates a selection bias against the inclusion of sicker patients, thereby making the question of the choice of intravenous fluids superfluous.

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2. Dung NM, Day NP, Tam DT, et al. Fluid replacement in dengue shock syndrome: a randomized, double-blind comparison of four intravenous-fluid regimens. *Clin Infect Dis* 1999;29:787-94.

THE AUTHORS REPLY: Zinderman et al. correctly state that hapten inhibition reduces the incidence of allergic reaction to dextran solutions. Such reactions are rare in children, and Promit is not used here during management of the dengue shock syndrome. The reactions we observed were not against dextran molecules but were probably caused by the presence of a residual pyrogen from the manufacturing process.

Goel and Thabab refer to previous work on fluid resuscitation from our unit, as a result of which the present study was designed. These early studies did not provide definitive results, and in fact, the second study suggested possible benefits from colloid use. Their letter also highlights an important issue regarding the changes in blood pressure that occur as the dengue shock syndrome worsens. With increasing cardiovascular compromise, the diastolic pressure rises toward the systolic and the pulse pressure narrows. Finally, there is decompensation, and both pressures disappear abruptly. The higher diastolic pressure in group 2 is thus a marker of the increased severity in this group.

Great care was taken to ensure blinding. Three bottles of the assigned fluid were supplied for each patient and were sealed inside identical opaque containers with only the (identical) injection port visible, into which the staff could insert a cloudy plastic infusion set without breaking the seal. An independent research assistant removed all containers from the ward, still sealed, within 24 hours after the enrollment of patients. Close inspection of infusion sets did reveal minor differences, but since each patient had only a single line, we think it is unlikely that busy staff had time for the investigation required to compromise blinding.

All patients who presented with the dengue shock syndrome but were not enrolled in the study for various reasons (as discussed in our article) were treated in the same way as the 512 patients in the formal study, apart from the initial blinded resuscitation. For all the patients who were not enrolled in the study, there were identical observations and outcome evaluations recorded in similar study files, and all patients in this group recovered fully. The only death among all 641 children admitted with the dengue shock syndrome during the trial period occurred in a study patient. Meticulous clinical management combined with appropriate use of intravenous fluids can greatly reduce mortality from the dengue shock syndrome.

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Dengue in Travelers

TO THE EDITOR: Wilder-Smith and Schwartz (Sept. 1 issue)¹ mention that serotypes of dengue virus are distinguishable by the plaque-reduction neutralization test.² But they neglect to include this test in Table 2 of the article, which lists laboratory tests for the diagnosis of dengue. The concept that the plaque-reduction neutralization test is more spe-

cific than other serologic assays for the diagnosis of dengue and other flavivirus infections³ is confirmed by recent experience at the Wadsworth Center, operated by the New York State Department of Health. Since 1999, with the introduction of West Nile virus into the United States, the plaque-reduction neutralization test has been particu-