Colloids and Crystalloids to Treat Dengue Fever in Children

QUESTION
Should children with dengue fever be treated with intravenous colloids compared to crystalloids?

CONTEXT	Dengue Fever
Dengue fever is a mosquito-borne disease that affects between 50 and 100 million people a year worldwide, especially in the Americas, South East Asia, the Western Pacific, Africa, and the Eastern Mediterranean. Dengue fever is manifested by fever with a maculopapular rash in children, and by a mild febrile illness and the classic debilitating disease (e.g. the “breakbone fever”) in adults. Dengue fever ranges from undifferentiated febrile illness to dengue hemorrhagic fever and, in the most severe cases, dengue shock. In areas with poor health care facilities, dengue fever and dengue hemorrhagic fever can be fatal in up to 5% of the cases. Intravenous fluids to expand plasma volume seem to be an effective treatment for dengue hemorrhagic fever. Among children, these include colloids such as dextran 70, hydroxyethyl starch, and gelafundin, as well as crystalloids such as sodium chloride and Ringer’s lactate solution. The optimal regime to rapidly correct hypovolemia without fluid overload, however, remains unclear.	

INTERVENTION	Colloids and crystalloids
Recurrence of dengue shock: There was no difference between colloid and crystalloid treatment regarding recurrence of dengue shock. *Moderate quality evidence.*	
Need for additional intravenous treatment: There was no difference between colloid and crystalloid treatment regarding need for additional intravenous treatment. *Moderate quality evidence.*	
Total volume of intravenous fluids used: There was no difference between colloid and crystalloid treatment regarding intravenous fluids used. *Low quality evidence.*	
Incidence of adverse side effects: Colloid treatment was associated with a higher incidence of side effects than crystalloid treatment. *Low quality evidence.*	

Summary of the Evidence	
Benefits	A Clinical Evidence review (date of search: June 2008) was found [1]. It identified 13 randomized controlled trials (RCT) that evaluated the effects of supportive treatments for dengue hemorrhagic fever and dengue shock in children. Of these, three focused on colloid and crystalloid treatment. This review found no significant differences between colloid and crystalloid treatment regarding recurrence of dengue shock: One RCT [2] reported a median of one episode in each comparison group (P=0.46), and an additional RCT [3] reported 24/90 (27%) episodes with colloids compared to 20/81 (25%) episodes with crystalloids (RR 1.02, 95%CI 0.56 to 1.85). This RCT also reported no differences regarding the total volume of fluids infused until full recovery from shock (P=0.95). There were no significant differences regarding need for further infusion of fluids. One RCT [2] found no difference between further need of colloids (p=0.70) or crystalloids (p=0.16). The other RCT [3] found that 17/56 (30%) of children with sodium chloride, 20/55 (36%) of children with Ringer's lactate, 17/55 (31%) of children with dextran 70, and 15/56 (267%) of children with gelafundin needed additional fluids (p=0.75). A later RCT [4] found no difference between Ringer's lactate and colloid solutions with respect to need of further treatment with colloids (RR 1.08, 95%CI 0.78 to 1.47, p=0.65).
Risks	One RCT [2] found no adverse events attributable to the compared treatments, although it may have been underpowered to detect them. Other RCT [3] reported fever, chills, recurrence of dengue shock, severe epitaxis, and other side effects associated to the use of colloids, as well as need for diuretic treatment associated with both colloid and crystalloid treatment. Finally, and additional RCT [4] found a higher incidence of allergic reactions associated with the use of colloids.
Applicability	Colloids and crystalloids seem equally effective treatments for dengue fever, dengue hemorrhagic fever, and dengue shock. However, crystalloids seem to be a safer option than colloid treatment. There is no information available on the use of colloids or crystalloids in adults with dengue fever. However, findings in children can be applied in adults.
Commentaries	Two of the considered RCT [2], [3] were likely underpowered to detect differences between groups consistently. The Clinical Evidence review found that there is no difference between colloid and crystalloid treatment regarding fluid overload if the same volumes are used [1].

Costs	According to two systematic reviews, colloid treatment is substantially more expensive than crystalloid treatment [5], [6].

1. Alejandria M. Dengue Haemorragic Fever or Dengue Shock Syndrome in Children. Clin Evid (Online). 2009;2009. pii: 0917.
2. Dung NM, Day NPJ, Tam DTH, et al. Fluid replacement in dengue shock syndrome: a randomized, double-blind comparison of four intravenous-fluid regimens. Clinical Infectious Diseases 1999;29:787–794
3. Ngo NT, Cao XT, Kneen R, et al. Acute management of dengue shock syndrome: a randomized double-blind comparison of 4 intravenous fluid regimens in the first hour. Clinical Infectious Diseases 2001;32:204–213
4. Wills BA, Nguyen MD, Ha TL, et al. Comparison of three fluid solutions for resuscitation in dengue shock syndrome. New England Journal of Medicine 2005;353:877-889
5. Choi PT, Yip G, Quinonez LG, Cook DJ. Crystalloids vs. colloids in fluid resuscitation: a systematic review. Critical Care Medicine 1999; 27(1): 200-210
6. Bisonni R, Holtgrave D, Lawler F, Marley D. Colloids versus crystalloids in fluid resuscitation: an analysis of randomized controlled trials. Journal of Family Practice 1991; 32 (4): 387-390

TABLE	GRADE Evaluation of Clinical Outcomes								
Number of Studies (N)	**Outcome**	**Comparison**	**Type of Evidence**	**Quality**	**Consistency**	**Direct Evidence**	**Size of Effect**	**GRADE**	**Comments**
2 (272)	Recurrence of dengue shock	Colloids vs. crystalloids	4	0	0	-1	0	Moderate	Delayed measure of outcome
1 (222)	Need for additional intravenous treatment	Colloids vs. crystalloids	4	0	0	-1	0	Moderate	Delayed measure of outcome
3 (655)	Volume of intravenous fluid used	Colloids vs. crystalloids	4	-1	0	-1	0	Low	Delayed measure of outcome, poor methodological quality
3 (784)	Side effects	Colloids vs. crystalloids	4	-1	0	-1	0	Low	Delayed measure of outcome, poor methodological quality
Type of evidence: 4 = RCT; 2 = Observational studies; 1 = Non-analytic studies / Expert opinion									