

11. Bancalari E, Claure N. Definitions and diagnostic criteria for bronchopulmonary dysplasia. *Semin Perinatol* 2006;30:164-70.
12. Inder TE, Volpe JJ. Mechanisms of perinatal brain injury. *Semin Neonatol* 2000;5:3-16.
13. Engbers AGJ, Flint RB, Voller S, de Klerk JCA, Reiss IKM, Andriessen P, et al. Enantiomer specific pharmacokinetics of ibuprofen in preterm neonates with patent ductus arteriosus. *Br J Clin Pharmacol* 2020;86:2028-39.
14. Mitra S, Florez ID, Tamayo ME, Mbuagbaw L, Vanniyasingam T, Veroniki AA, et al. Association of placebo, indomethacin, ibuprofen, and acetaminophen with closure of hemodynamically significant patent ductus arteriosus in preterm infants: a systematic review and meta-analysis. *JAMA* 2018;319:1221-38.
15. Ohlsson A, Shah SS. Ibuprofen for the prevention of patent ductus arteriosus in preterm and/or low birth weight infants. *Cochrane Database Syst Rev* 2020;1:CD004213.
16. El-Khuffash A, Levy PT, Gorenflo M, Frantz ID 3rd. The definition of a hemodynamically significant ductus arteriosus. *Pediatr Res* 2019;85:740-1.
17. Evans N. Preterm patent ductus arteriosus: a continuing conundrum for the neonatologist? *Semin Fetal Neonatal Med* 2015;20:272-7.
18. McNamara PJ, Sehgal A. Towards rational management of the patent ductus arteriosus: the need for disease staging. *Arch Dis Child Fetal Neonatal Ed* 2007;92:F424-7.
19. Sehgal A, McNamara PJ. Coronary artery perfusion and myocardial performance after patent ductus arteriosus ligation. *J Thorac Cardiovasc Surg* 2012;143:1271-8.
20. Kluckow M, Lemmers P. Hemodynamic assessment of the patent ductus arteriosus: beyond ultrasound. *Semin Fetal Neonatal Med* 2018;23:239-44.

50 Years Ago in *THE JOURNAL OF PEDIATRICS*

Oral rehydration solution in children with cholera: proof of an important concept for child health

Nalin DR, Cash RA. Oral or nasogastric maintenance therapy in pediatric cholera patients. *J Pediatr* 1971;78:355-8.

After pioneering trials in adults,¹ Nalin and Cash reported on the use of oral rehydration solutions (ORS) in children with cholera. These children, from what is now Dhaka, Bangladesh, were dehydrated and losing water and electrolytes at a ferocious rate (~9 mL/kg/hour). After a 6-hour stabilization period with intravenous (IV) fluids, the children were then switched to oral or nasogastric ORS, titrated in amounts to match losses through diarrhea or vomitus. Eight of 12 children required no further IV fluids, and positive water-electrolyte balance was observed in all.

This understated but revolutionary proof of concept trial showed that "...pediatric cholera patients absorb the solution of glucose and electrolytes from their intestinal tracts in sufficient quantity to maintain positive fluid and electrolyte balance." The report led to the application of ORS in much more prevalent diarrheal diseases, including those caused by other bacteria and viruses. Many trials have shown ORS to be equivalent if not superior to IV fluids, including studies of children in the US.²

What are the other lessons 50 years on? ORS may be an important adjunct therapy for Ebola virus and Coronavirus disease 2019 infections,³ and ORS use in the setting of IV shortage is not limited to resource-poor countries.⁴ The development of oral rehydration therapy stands as a role model for science, highlighting the critical importance of support for research, field work, innovation, and global collaboration.⁵

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References

1. Nalin DR, Cash RA, Islam R, Molla M, Phillips RA. Oral maintenance therapy for cholera in adults. *Lancet* 1968;2:370-3.
2. Spandorfer PR, Alessandrini EA, Joffe MD, Localio R, Shaw KN. Oral versus intravenous rehydration of moderately dehydrated children: a randomized, controlled trial. *Pediatrics* 2005;115:295-301.
3. D'Amico F, Baumgart DC, Danese S, Peyrin-Biroulet L. Diarrhea during COVID-19 infection: pathogenesis, epidemiology, prevention, and management. *Clin Gastroenterol Hepatol* 2020;18:1663-72.
4. Patino A, Marsh R, Nilles E, Baugh C, Rouhani S, Kayden S. Facing the shortage of IV fluids—a hospital-based oral rehydration strategy. *N Engl J Med* 2018;378:1475-7.
5. Nalin DR, Cash RA. 50 years of oral rehydration therapy: the solution is still simple. *Lancet* 2018;392:536-8.