the last 25 years.[1] Nevertheless, at least 1.8 million preventable deaths occur each year in young children with gastroenteritis in developing communities where ORT is not available.[1]

Despite proven efficacy, ORT is under-utilised in developing and developed communities.[34,35] Possible reasons for this include the pressure to prescribe medications; the perception that ORT is not a 'drug' and iv fluids are superior; and that ORT does not stop diarrhoea. Above all, is lack of understanding of the physiology underpinning diarrhoea and the rational for ORT. In the USA, direct health costs resulting from failure to use ORT are over $1 billion per year.[35] The challenge is to persuade carers and clinicians of the benefits and safety of ORT and ensure this remarkable therapy is available to all children.

References

1 Fontaine O, Garner P, Bhan MK. Oral rehydration therapy: the simple solution for saving lives. *BMJ* 2007;334:14.
2 World Health Organization, United Nations Children's Fund. *Oral rehydration salts. Planning, establishment and operation of production facilities.* WHO, UNICEF 1985;85:1–136.
3 Walker-Smith JA, Elliott E, Heuschkel R, Phillips A. Paediatric gastroenterology 1966–2000. *Clin Med* 2008;8:292–5.
4 Cunha-Ferriera RCM, Cash RA. History and development of ORT. *Clin Therap* 1990;12(Suppl A):2–13.
5 Darrow DC. The retention of electrolyte during recovery from severe dehydration due to diarrhoea. *J Pediatr* 1946;28:515–40.
6 Harrison HE. The treatment of diarrhoea in infancy. *Pediatr Clin N America* 1954;1:335–48.
7 Chaterjee HN. Control of vomiting in cholera and oral replacement of fluid. *Lancet* 1953;2:1063.
8 Phillips RA. Water and electrolyte losses in cholera. *Fed Proc (Baltimore)* 1964;23:705–9.
9 Hirschhorn N, Kinzie JL, Sachar DB *et al.* Decrease in net stool output in cholera during intestinal perfusion with glucose containing solutions. *N Eng J Med* 1968;279:176–81.
10 Pierce NF, Sack RB, Mitra RC *et al.* Replacement of water and electrolyte losses in cholera by an oral glucose electrolyte solution. *Ann Intern Med* 1969; 70:1173–81.
11 Mahalanabis D, Choudhuri AB, Bagchi NG *et al.* Oral fluid therapy of cholera among Bangladesh refugees. *Johns Hopkins Med J* 1973;132: 197–205.
12 Rao MC. Oral rehydration therapy: new explanations for an old remedy. *Annu Rev Physiol* 2004;66:385–417.
13 Farthing MJG. Oral rehydration: an evolving solution. *J Pediatr Gastroenterol Nutr* 2002;34:S64–S67.
14 Schedl HP, Clifton JA. Solute and water absortion by human small intestine. *Nature* 1963;199:1264–7.
15 Schultz SG, Zalusky R. Ion transport in isolated rate ileum. II. The interaction between active sodium and active sugar transport. *J Gen Physiol* 1964;47:1043–59.
16 Sladen GE, Dawson AM. Interrelationships between the absorptions of glucose, sodium and water by the normal human jejunum. *Clin Sci* 1969;36:119–32.
17 Water with sugar and salt. *Lancet.* 1978;2:300–1.
18 Wright EM, Hirayama BA, Loo DDF *et al.* Structure and function of the Na+/glucose cotransporter. *Acta Physiol Scand Suppl* 1998;643: 257–64.
19 Elliott EJ, Watson AJ, Walker-Smith JA, Farthing MJG. Effect of bicarbonate on efficacy of oral rehydration therapy: studies in an experimental model of secretory diarrhoea. *Gut* 1988;28:1052–7.
20 Elliott EJ, Armitstead JA, Farthing MJG, Walker-Smith JA. Bicarbonate in oral rehydration solutions: a double-blind controlled trial in gastroenteritis. *Aliment Pharmacol Therap* 1988;2:253–62.
21 Hunt JB, Elliott EJ, Farthing MJG. Efficacy of a standard United Kingdom oral rehydration solution (ORS) and a hypotonic ORS assessed by human intestinal perfusion. *Aliment Pharmacol Ther* 1989;3:565–71.
22 Elliott EJ, Hunt JB, Cameron D, Walker-Smith JA, Farthing MJG. Clinical experience of an hypotonic oral rehydration solution for treatment of paediatric gastroenteritis in the United Kingdom. *Clin Therap* 1990;12:(Suppl A):86–94.
23 Elliott EJ, Watson AJM, Walker-Smith JA, Farthing MJG. Search for the ideal oral rehydration solution: studies in a model of secretory diarrhoea. *Gut* 1991;32:1314–24.
24 Hunt JB, Elliott EJ, Farthing MJG. Comparison of rat and human intestinal perfusion models for assessing efficacy of oral rehydration solutions. *Aliment Pharmacol Ther* 1991;5:49–59.
25 Hunt JB, Elliott EJ, Fairclough PD, Clark ML, Farthing MJG. Water and solute absorption from hypotonic glucose-electrolyte solutions in human jejunum. *Gut* 1992;33:479–83.
26 Hunt JB, Thillainayagam AV, Carnaby S *et al.* Absorption of a hypotonic oral rehydration solution in a human model of cholera. *Gut* 1994;35:211–4.
27 Hartling L, Bellemare S, Wiebe N *et al.* Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children. *Cochrane Database Syst Rev* 2006;3:CD004390.
28 World Health Organization, United Nations Children's Fund. *Joint statement – oral rehydration salts (ORS) – a new reduced osmolarity formulation.* Accessed September 2006. www.who.int/medicines/publications/pharmacopoeia/OralRehySalts.pdf
29 Hahn S, Kim Y, Garner P. Reduced osmolarity oral rehydration solution for treating dehydration due to diarrhea in children: systematic review. *BMJ* 2001;323:81–5.
30 Murphy C, Hahn S, Volmink J. Reduced osmolarity oral rehydration solution for treating cholera. *Cochrane Database Syst Rev* 2006;3.
31 Fontaine O, Gore S, Pierce NF. Rice-based oral rehydration solution for treating diarrhoea. *Cochrane Database Syst Rev* 2004;1.
32 Allen SJ, Okoko B, Martinez E, Gregorio G, Dans LF. Probiotics for treating infectious diarrhoea. *Cochrane Database Syst Rev* 2006;3.
33 Greenhough WB. The human, societal, and scientific legacy of cholera. *J Clin Invest* 2004;113:334–9.
34 Vashintha VM. Letters. Doctors in India still seem not to be convinced. *BMJ* 2001;323:1068.
35 Kelly DG, Nadeau J. Oral rehydration solution: a 'low-tech' oft neglected therapy. *Pract Gastroenterol* 2004;51–62.

Inflammatory bowel disease in children

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The incidence of inflammatory bowel disease (IBD), particularly Crohn's disease (CD), in children appears to be increasing. About 20% of patients with IBD present before the age of 19, and thus a significant burden of this illness falls on adolescents and young adults.

Paediatricians and adult gastroenterologists must be increasingly aware of the management priorities of these young people with potentially disabling chronic intestinal disease. Children with such complex chronic disorders should have easy access to a multidisciplinary team that includes paediatric dietitan,

psychologist, IBD nurse specialist and paediatric gastroenterologist. Diagnosis to standard criteria is important.[1] Optimal care involves close liaison with local service providers, experienced adult colorectal surgeons, radiologists and adult gastroenterologists. The latter are fundamental in striving for a seamless transition of care from adolescence into young adulthood.

Despite the huge advances in the understanding of disease pathogenesis and the development of new classes of intervention, the long-term, side-effect-free maintenance of disease remission remains a distant aim. Dramatic improvements in achieving a remission from active disease followed the introduction of sulphasalazine and corticosteroids in the 1950s and 1960s. In addition, over the last 30 years, a steroid-free, nutritional option for inducing disease remission has been repeatedly demonstrated in children with CD.[2] It has become clear that the use of exclusive, whole protein liquid diets (exclusive enteral nutrition) is at least as effective as corticosteroid therapy in achieving a remission in children with CD. Aside from some newer derivatives/formulations of sulphasalzine and topically released corticosteroids, there has been little other change in agents able to induce remission in mild to moderate IBD.

Since its introduction in the 1950s, azathioprine has gradually become the cornerstone of maintenance therapy in both moderate to severe CD and ulcerative colitis in adults and children.[3] Almost 2 in 3 children with CD are likely to receive this drug at some time. There is now, however, also some evidence that methotrexate has a role in maintaining remission in adults with severe CD.[4]

Remarkable changes in IBD management have occurred in the last decade. With the arrival of potent new classes of biological therapies has come a need to review established treatment philosophies. The classic new biological therapy during this time has been infliximab, a chimeric anti-TNFα monoclonal antibody. This has proven effective both in inducing and maintaining disease remission in children and adults with severe, active CD.[5,6]

Although large studies were initially completed only in adult patients, clinical trials have been, and are continuing to be done in children. One of the drivers for these studies has been the potential use of growth-sparing maintenance therapies during the pubertal growth spurt.[7] In addition, quality of life has become central in the management of adolescent sufferers.

Inevitably the arrival of infliximab has been followed by the development of biological therapies directed at almost all parts of the inflammatory cascade that results in mucosal destruction. The term 'mucosal healing' has become more widely accepted as marker of treatment success and also as a measure of maintenance agent efficacy.

There have also been attempts to understand whether aggressive intervention very early in the disease process might modify its natural history. The data needed to confirm whether the risks of a 'top-down' approach warrant its widespread use over the conventional 'step-up' approach are still outstanding. Although there is tantalising anecdotal evidence suggesting the early use of biological agents may ameliorate the course of the disease, larger, longer-term studies are essential before adopting this radical new philosophy.[8] Clinicians are still unable to confidently predict those patients whose clinical course might warrant early, more aggressive intervention (perhaps even with surgery). Until such a time, we have a responsibility to spare those patients, who can be successfully managed conventionally, the early exposure to potent agents with limited long-term safety data.

Potential risks of malignancy are almost impossible to quantify in small populations of young patients. Paediatricians must therefore be all the more informed about the potential benefits of novel agents over their well-tried and tested conventional predecessors. Intervention with potent immunological agents such as infliximab should be just as appropriate in children as it is in adults if their only alternative is a very poor quality of life and/or permanently disfiguring surgery. In my own practice infliximab is still reserved only for children meeting the recommended National Institute for Health and Clinical Excellence criteria for patients over 17 years of age, ie those with severe disease not amenable to surgical treatment or other conventional therapies such as azathioprine.

Complementary and alternative therapies are used by adult and child IBD sufferers alike, and physicians must continue to be aware of this while a cure remains elusive. Although there are some potentially promising interventions, much of the evidence remains poor and largely anecdotal.

Children being diagnosed with IBD today have a huge range of treatment options at their disposal. The challenge for all involved in the care of these young people is to carefully assess these options, explain their relative merits, and then tailor them to each individual's specific needs.

References

1 Inflammatory bowel disease in children and adolescents: recommendations for diagnosis – the Porto criteria. *J Pediatr Gastroenterol Nutr* 2005;41:1–7.

2 Heuschkel RB, Menache CC, Megerian JT, Baird AE. Enteral nutrition and corticosteroids in the treatment of acute Crohn's disease in children. *J Pediatr Gastroenterol Nutr* 2000;31:8–15.

3 Markowitz J, Grancher K, Kohn N, Lesser M, Daum F. A multicenter trial of 6-mercaptopurine and prednisone in children with newly diagnosed Crohn's disease. *Gastroenterology* 2000;119:895–902.

4 Feagan BG, Fedorak RN, Irvine EJ *et al.* A comparison of methotrexate with placebo for the maintenance of remission in Crohn's disease. *N Engl J Med* 2000;342:1627–32.

5 Stephens MC, Shepanski MA, Mamula P *et al.* Safety and steroid-sparing experience using infliximab for Crohn's disease at a pediatric inflammatory bowel disease center. *Am J Gastroenterol* 2003;98:104–11.

6 Rutgeerts P, D'Haens G, Targan S *et al.* Efficacy and safety of retreatment with anti-tumor necrosis factor antibody (infliximab) to maintain remission in Crohn's disease. *Gastroenterology* 1999;117:761–9.

7 Jaspers GJ, Verkade HJ, Escher JC *et al.* Azathioprine maintains first remission in newly diagnosed pediatric Crohn's disease. *Inflamm Bowel Dis* 2006;12:831–6.

8 de Ridder L, Benninga MA, Taminiau JA, Hommes DW. Infliximab as first-line therapy in severe pediatric Crohn disease. *J Pediatr Gastroenterol Nutr* 2006;43:388–90.