function, slow the rate of respiratory decline, and decrease the need for intravenous treatment. In combination with oral ciprofloxacin, nebulised colistin can eradicate early *P. aeruginosa* infection. Aerosolised antibiotic treatment appears safe in short term trials but long term safety data are not available and patients should be monitored routinely.

It is with interest and anticipation that studies with the Halolite nebuliser (Medic-Aid Ltd, Bognor Regis, West Sussex, UK) are awaited. Timing of antibiotic delivery to the first part of the inspiratory cycle should improve drug deposition and efficacy,⁸ reduce waste, and possibly improve compliance. Patient adherence to nebulised antibiotics delivered with standard equipment is likely to be only about 60%.²⁷⁻²⁸ We still do not know the minimum effective dose for nebulisation. Individual practices vary between 80 mg and 300 mg bid for aminoglycosides. Colistin is empirically prescribed at doses between 0.5 MU and 2 MU according to the child's weight. The Halolite, if fulfilling its promise, will necessitate revision of dosage schedules.

Nebulised antibiotic treatments in CF have progressed from a good idea derived from clinical experience to a more scientific approach to drug dosage and delivery. Only the preservative free tobramycin has been studied in an adequately powered trial, but many others document significant clinical and microbiological response to less expensive drug formulations—that is, the standard preparations for intravenous use delivered as an aerosol; to evaluate TOBI fully we need a direct comparison between them.

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Is prolonged rotavirus infection a common cause of protracted diarrhoea?

Before Ruth Bishop's identification in Melbourne of human rotavirus in 1973, paediatricians could offer only platitudes by way of explanation when confronted with young children with acute diarrhoea. Since then it has become clear that rotavirus is the most common cause of gastroenteritis in children under 2 years of age living in either developed or developing countries.¹ Its pathogenic mechanisms have been largely elucidated, mainly by studying an analogous infection in piglets caused by transmissible gastroenteritis agent.²⁻³ Rotavirus probably causes diarrhoea by increasing the turnover of enterocytes along the villus axis, leading to the population of blunted villi by immature cells that are incapable of normal absorption, and are more crypt-like and secretory in nature.⁴⁻⁶ Rota-

virus can also reduce sucrase-isomaltase expression in human enterocytes by blocking sucrase-isomaltase transport to the apical membrane without apparent cell destruction. Reduction in activity is correlated to rotavirus induced alterations in the enterocyte cytoskeleton.⁷ There is also a single unconfirmed report of elaboration of a secretagogue by rotavirus: purified NSP4 (non-structural glycoprotein of rotavirus) potentiates chloride secretion by a calcium dependent signalling pathway.⁸

In some children a clinical episode indistinguishable from acute gastroenteritis is followed by protracted diarrhoea, so called post-gastroenteritis syndrome. This is more likely to occur in developing countries, where pre-existing malnutrition and enteropathies may lead to

protracted diarrhoea in 8–20% of children initially presenting with acute gastroenteritis.⁹ In developed countries this happens in up to 5% of cases, and its causes are far from clear.¹⁰ Secondary lactose intolerance may occur, and many children exhibit an intolerance to cows' milk protein and often several other proteins.^{10–11} Management is pragmatic, and comprises mainly nutritional support. Most children in developed countries survive, but in developing countries mortality is still high.¹²

A recent report from the Melbourne group now suggests that persistent rotavirus infection may play a greater role in post-gastroenteritis syndrome and protracted diarrhoea than previously thought.¹³ Until now, rotavirus excretion was generally thought to stop within 10 days of the onset of symptoms in most children, and within 20 days of onset in all.^{14–15} Enzyme immunoassay (EIA) is the technique commonly used for detection of rotavirus in stool, but reverse transcriptase–polymerase chain reaction (RT–PCR) is up to 25 times more sensitive than EIA in detecting rotavirus in serially diluted faecal suspensions. It has both higher sensitivity and specificity.^{16–17} Using an RT–PCR technique, Bishop's group studied the duration of rotavirus excretion in 37 children admitted to hospital with acute rotavirus infection.¹³ Excretion ceased within 10 days in 17 children and within 20 days in 26 of the 37 children. However, extended excretion between 25–57 days was seen in 11 children. Only one child seemed to have been re-infected with rotavirus. In contrast, rotavirus excretion estimated by EIA ranged from 4–29 days, and only 12 children had detectable excretion between 10 and 29 days. Extended excretion of rotavirus was significantly linked with intermittent antirotavirus IgA coproantibody boosts. Most of these boosts were associated with rotavirus excretion. Eight of the 11 children with extended rotavirus excretion between 25 and 57 days developed mild diarrhoea and vomiting associated with excretion or coproantibody boosts during the 100 days' surveillance.

It is clear that prolonged rotavirus excretion is not only a feature of immunodeficiency¹⁸ but is also seen in about one third of immunocompetent young children. Intermittent mild diarrhoea seen in significantly increased numbers of children excreting rotavirus for one to two months could explain some cases of post-gastroenteritis syndrome. Moreover, children excreting rotavirus for prolonged periods could become reservoirs of human rotavirus and contribute to its survival between epidemics. As new diagnostic procedures indicate that rotavirus infection may be the

cause of protracted diarrhoea in some children, who may have otherwise undetected infection, an effective rotavirus vaccine becomes even more important.

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