Rotavirus vaccine — time to act

Graeme L Barnes and Ruth F Bishop

Rotavirus vaccines are finally available, and introducing them into the routine vaccination schedule will have a significant impact on the health of children

After a dramatic false start, oral rotavirus vaccines are now available to prevent severe, dehydrating diarrhoea in small children. Rotavirus infection in children can be as severe as cholera in adults, but affects a group who cannot complain. Since its discovery in Australia in 1973, rotavirus has become accepted as the single most common cause of severe diarrhoea in children worldwide. It still kills over 500 000 young children each year. In Australia, it is estimated that 10 000 children require hospitalisation annually[1,2] (more than 4000 actually coded for proven rotavirus[3]), and as Schultz reports in this issue of the Journal (*page 354*), the impact on Indigenous children is especially severe.[4] Oral rehydration has greatly reduced mortality, but the World Health Organization recognises the potential of rotavirus vaccines to further reduce under-5-year mortality rates, Goal 4 of the Millenium Development Goals.[5]

It is exciting to have two efficacious oral rotavirus vaccines, ROTARIX (GlaxoSmithKline [GSK], Boronia, VIC) and RotaTeq (Merck/CSL, Parkville, VIC) licensed this year in Australia. Each has been extensively tested in placebo-controlled trials of more than 60 000 participants. Both vaccines prevented severe disease, and reduced the need for hospitalisation by 85%–94%. There was a reassuring lack of intussusception, a rare (one in 10 000–32 000) event associated with RotaShield, the first licensed rotavirus vaccine, which led to its withdrawal from the United States market in 1999, just 12 months after its introduction.[6] Re-analysis of the data suggested that the intussusception risk emerged in infants receiving the first vaccine dose after 3 months of age.[7] Thus both GSK and Merck/CSL state that the first dose should be administered before that time.

Several issues remain to be resolved with these two new vaccines. Efficacy has not been established in developing countries. Availability will depend on distribution (including the need for a cold chain), the ability to piggyback rotavirus vaccines with other routine vaccinations, and manufacturing capacity. The greatest uncertainty is the cost of the vaccine. Current prices exceed $200 per course in the private market. While tier pricing and subsidisation by international agencies for poorer countries is being considered, it is not clear whether these mechanisms will sustain programs in most parts of the world. Hence, other candidate vaccines linked to developing country manufacture are under early development in China, India, Indonesia and elsewhere.

Who should get rotavirus vaccine in Australia? Ideally all children under 3 months of age, as all will eventually be exposed

to rotavirus, and one in 25 will be admitted to hospital for rotavirus gastroenteritis during the first 5 years of life. Morbidity across our country is high. Apart from the 10 000 annual hospital admissions, there are 22 000 visits to emergency departments and 115 000 visits to general practitioners.[2] Nosocomial infection rates are as high as 14% in children's hospital wards and may be higher in childcare centres.[8,9] Schultz's report indicates that Indigenous children have 2–4 times the disease burden of non-Indigenous children.[4] Gastroenteritis in Indigenous children comes with comorbidities and a significantly increased average length of hospital stay. Add to that the large costs of air transport of patients for hospital admission in northern and western Australia and the disruption to remote families, and the case for rotavirus vaccination of Indigenous infants becomes compelling. The Northern Territory Health Department recognised the importance of rotavirus infection by making it a notifiable disease, and Queensland recently followed suit. Breaking news is that from October 2006, the NT Government will include rotavirus vaccine in the routine vaccination schedule for NT children.[10]

The only real issue is cost. A 1999 cost–benefit analysis suggested that break-even vaccine cost was $78 per course,[11] somewhat less than current prices. However, the community should be prepared to pay something to prevent this wretched disease.

For maximum benefit, the first dose should be given before 3 months of age. Infants under 6 months of age accounted for 24% and 9% of rotavirus gastroenteritis cases in studies in the NT and Melbourne, respectively.[4,12] In Africa, many infants are infected in the first 2 weeks of life.[13] There is enthusiasm for giving the first dose of vaccine within the first month of life, but neither licensed vaccine has been tested at this age.

Roll-out of a universal program in Australia has a few caveats. The inevitable concern about intussusception, in spite of the reassuring clinical trial results, probably means that catch-up campaigns, where the first dose is given after 3 months of age, will not happen. Evidence of the spectrum of protection afforded by both vaccines against the full range of human rotavirus serotypes is still lacking. There is a need to continue national strain surveillance to ensure that the current vaccines are appropriately protective against the range of serotypes in Australia, and to monitor the effect of vaccine pressure on the evolution of strains.

After three decades, there is real excitement at suddenly having such an effective tool to prevent a common, miserable disease affecting infants and children. Rotavirus vaccination is not only justified on the basis of disease burden, but will be welcomed by all who care for sick children. It will not be hard to measure real improvement for Indigenous children in the NT, given the baseline data presented elsewhere in this issue of the Journal.[4] While other candidate vaccines are in development, there is no excuse for waiting any longer for a national program. The improvement in child health will be obvious.

Competing interests

Both authors have participated in educational programs sponsored by GlaxoSmithKline and Merck/CSL. The authors are developing another candidate rotavirus vaccine in collaboration with Q-Gen, Brisbane, and BioFarma PT, Indonesia. Intellectual property rights will be held by WHO, Geneva.

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References

1 Carlin JB, Chondros P, Masendycz P, et al. Rotavirus infection and rates of hospitalisation for acute gastroenteritis in young children in Australia, 1993–1996. *Med J Aust* 1998; 169: 252-256.
2 Galati JC, Harsley S, Richmond P, Carlin JB. The burden of rotavirus-related illness among young children on the Australian health care system. *Aust N Z J Public Health* 2006. In press.
3 Newall A, MacIntyre R, Wang H, et al. Burden of severe rotavirus disease in Australia. *J Paediatr Child Health* 2006. In press.
4 Schultz R. Rotavirus gastroenteritis in the Northern Territory, 1995–2004. *Med J Aust* 2006; 185: 354-356.
5 Conclusions and recommendations from the Strategic Advisory Group of Experts to the Department of Immunization, Vaccines and Biologicals. Rotavirus vaccines. *WHO Wkly Epidemiol Rec* 2006; 81: 8. http://www.who.int/vaccines/news/reh_01.pdf (accessed Sep 2006).
6 Centres for Disease Control and Prevention. Withdrawal of rotavirus vaccine recommendation. *MMWR Morb Mortal Wkly Rep* 1999; 48: 1007.
7 Simonsen L, Viboud C, Elixhauser A, et al. More on RotaShield and intussusception: the role of age at the time of vaccination. *J Infect Dis* 2005; 192 (Suppl 1): S36-S43.
8 Ringenbergs ML, Davidson GP, Spence J, Morris S. Prospective study of nosocomial rotavirus infection in a paediatric hospital. *Aust Paediatr J* 1989; 25: 156-160.
9 Ferson MJ, Stringfellow S, McPhie K, et al. Longitudinal study of rotavirus infection in child-care centres. *J Paediatr Child Health* 1997; 33: 157-160.
10 Toyne P, Minister for Health. Territory to fund rotavirus vaccine. Northern Territory Government media release, 23 August 2006. http://www.health.nt.gov.au/docs/minister_06aug23_rotavirus.pdf (accessed Sep 2006).
11 Carlin JB, Jackson T, Lane L, et al. Cost effectiveness of rotavirus vaccination in Australia. *Aust N Z J Public Health* 1999; 23: 611-616.
12 Barnes GL, Uren E, Stevens KB, Bishop RF. Etiology of acute gastroenteritis in hospitalized children in Melbourne, Australia, from April 1980 to March 1993. *J Clin Microbiol* 1998; 36: 133-138.
13 Cunliffe NA, Kilgore PE, Bresee JS, et al. Epidemiology of rotavirus diarrhea in Africa: a review to assess the need for rotavirus immunization. *Bull World Health Org* 1998; 76: 525-537. ❑