Rotavirus in the Northern Territory before and after vaccination




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Globally, rotavirus vaccines have been found to have reduced effectiveness in resource-poor and high disease burden settings. Prior to vaccination, the burden of rotavirus gastroenteritis was substantially higher among Indigenous children in the Northern Territory (NT) than among other Australian children, giving rise to concern about the likely impact of vaccination in this population. Post-licensure studies in the NT indicate that vaccination protects infants against hospitalisation in this setting, but vaccine effectiveness (VE) among older children and against heterotypic serotypes needs to be more clearly determined.

The Northern Territory (NT) commenced routine vaccination with the human rotavirus vaccine (HRV, Rotarix™, GlaxoSmithKline) for all infants in October 2006, several months before rotavirus vaccination was funded for all Australian children. At that time the safety and efficacy of both licensed vaccines had been demonstrated in Europe and in the Americas[1,2], but neither vaccine had been trialled in Asia or in sub-Saharan Africa – resource-poor settings where previous rotavirus vaccine candidates had failed[3]. Field trials have since established that although current rotavirus vaccines provide protection in these settings, efficacy is lower than in high-income settings[4-6].

The setting

Aboriginal and Torres Strait Islander Australians comprise almost one-third of the NT population and account for around 40% of births[7]. The majority of the Indigenous population live in remote or very remote locations[8] and living conditions in remote communities are poor[9]. Households are typically crowded and facilities for washing and for storing food and preparing meals are, more often than not, inadequate[10]. Rates of ear, skin and respiratory infection are high among NT Indigenous children[11-17] and the infant mortality rate remains threefold greater than the national average[18].

Pattern of diarrhoeal disease

Admissions coded for enteric infection among NT Indigenous infants occur at a rate 10-fold higher than among non-Indigenous infants[12]. Children admitted for gastroenteritis frequently have comorbidities[19,20] and disease is often complicated by dehydration, acidosis and electrolyte disturbances. Underlying environmental enteropathy, which has been documented in a large proportion of hospitalised children, may partly account for the frequency of complications[20]. Nonetheless, deaths of Indigenous children directly attributable to diarrhoeal disease are now rare[21], and this likely reflects better outpatient management of dehydration, prompt aeromedical retrieval and improved inpatient care.

In studies prior to vaccine introduction, rotavirus was detectable in about 25% of hospitalisations for diarrhoea[22,23]. This is lower than the proportion of hospitalisations attributed to rotavirus elsewhere in Australia (~50%)[22] and is likely due to a high contribution from other enteric pathogens, especially enterovirulent strains of *Escherichia coli* (EVEC)[23,24]. The average length of stay for rotavirus gastroenteritis in the NT declined from nine days in the mid-1990s[22] to five days more recently[25], but this is still considerably longer than the average two-day hospitalisation for children elsewhere in Australia[25].

Rotavirus transmission

In the NT, a biennial pattern of winter/dry season rotavirus

epidemics lasting two to four months was noted in the 1990s[26]. In the decade before vaccine introduction, widespread epidemics occurred on average at least once per year. Epidemics occur more frequently in the cooler months, although they have also occurred in the warmer summer/wet season months. There has been no consistent pattern for the direction of spread of rotavirus strains either into or within the NT, with spread from both the arid south to the tropical north and vice versa observed at different times[27].

Rotavirus epidemics place a substantial strain on health services[26,28] and can spread to affect communities separated by hundreds of kilometres within days[26]. During one epidemic in Central Australia, the surge in hospitalisations was so great that the administration of Alice Springs Hospital resorted to flying in nursing staff from Darwin[26]. High attack rates also place enormous demands on remote clinics and the requirement for aeromedical evacuation, especially for very young children[28]. In addition to significant economic costs, this results in social dislocation and disruption for remote families.

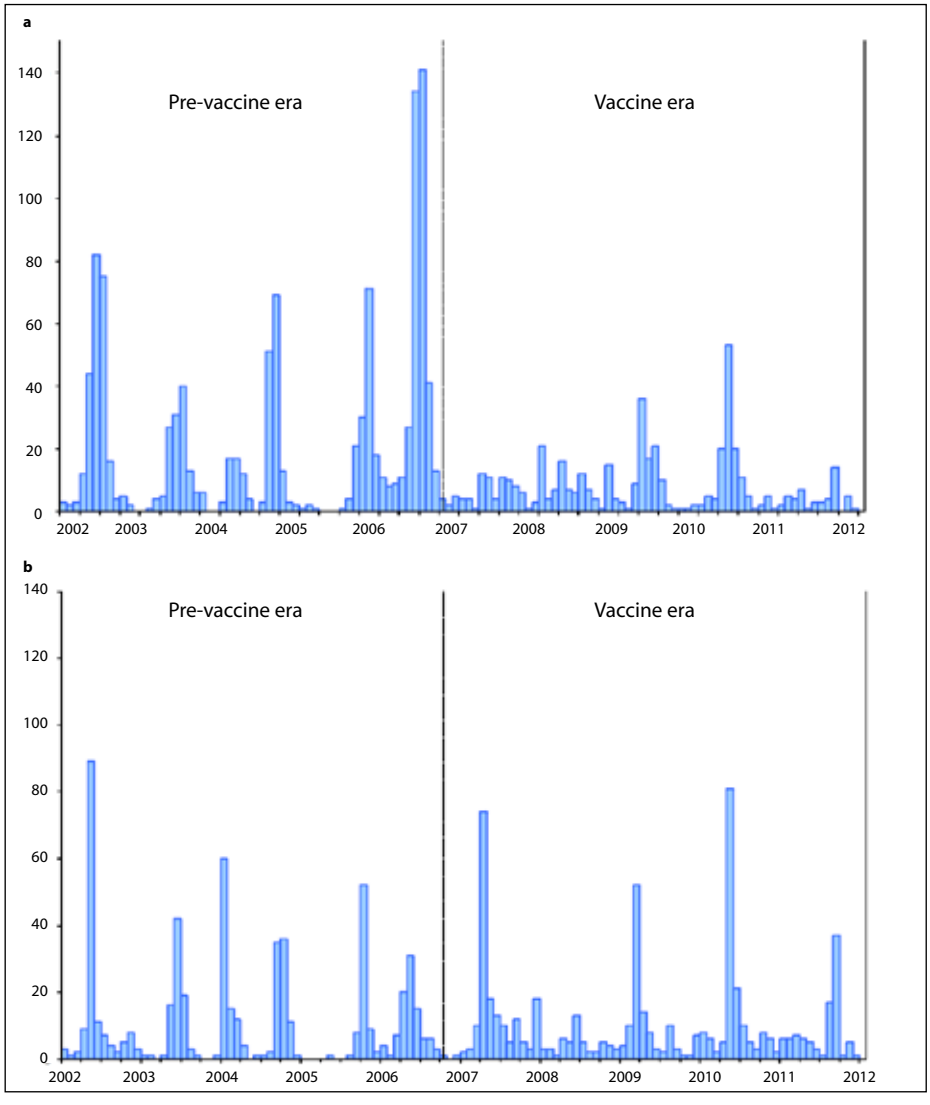

Figure 1. Monthly rotavirus notifications for children aged 0 to 35 months, for (a) the 'Top End' and (b) Central Australia of the Northern Territory, 2002 to mid-2010.

The impact of vaccination

Compared to the marked decline in rotavirus hospitalisations and laboratory confirmations documented elsewhere in Australia since implementing routine vaccination[29,30], the decline in notifications in the NT has been less dramatic, particularly in Central Australia (Figure 1). The overall rate of rotavirus notifications among children aged <3 years declined by 42% between the five years before vaccine introduction, 2002–2006, and the five years after, 2007–2011 (from 3.1 to 1.8 per 100 child years respectively). In Central Australia, where the vast majority of notifications occur among Indigenous children, no decline in the notification rate was observed over this period (4.3 versus 4.3 per 100 child years for 2002–2006 and 2007–2011 respectively). This mirrors a lesser decline in hospitalisations among Indigenous compared to other children observed across Australia[31]. In 2010, two-dose vaccine coverage (by 25 weeks) in the NT was 83% for non-Indigenous and 74% for Indigenous infants. Rotavirus remains the single most important cause of hospitalisation for gastroenteritis in the NT, although a greater proportion of hospitalisations are accounted for by other enteric pathogens and mixed infections occur frequently[32].

Estimates of vaccine effectiveness

Post-licensure assessments of vaccine effectiveness (VE) in the NT have provided disparate estimates. In 2007, several months after vaccine introduction, a widespread G9P[8] rotavirus epidemic occurred in Central Australia[33]. Most hospitalisations occurred among children who were too old to have been eligible for vaccination. Among vaccine-eligible infants (all of whom were <12 months old), VE against hospitalisation for rotavirus-confirmed gastroenteritis was estimated to be 85% (95% CI: 23 to 97%)[33].

Between May 2008 and September 2010, a prospective case-control study (the TROVE Study) was undertaken in the NT using active hospital-based surveillance of gastroenteritis admissions up to age 36 months. An interim analysis was conducted following a rotavirus epidemic in Central Australia in mid-2009[34]. Most rotavirus-confirmed cases were typed as G2P[4], a genotype which is completely heterotypic to the G1P[8] HRV strain. Overall VE against rotavirus hospitalisation was 19% (95% CI: -105 to 68%). *Post hoc* analysis suggested that VE might have been higher among infants <12 months than among older children[34].

In mid-2010, a further G1P[8] strain epidemic occurred in Central Australia with a smaller number of hospitalisations also in the Top End. Final analysis of the TROVE Study, including data from the 2010 epidemic, should shed further light on some of the factors which impact on vaccine performance in the NT. Of particular interest are the influence on VE of infecting serotype, waning immunity and intestinal co-infection with non-rotavirus pathogens.

Conclusion

Like high-burden settings internationally, preliminary evidence indicates that rotavirus vaccination might be relatively less protective against severe disease in the NT than elsewhere in Australia. However, the much higher baseline risk of hospitalisation in this setting suggests that the absolute benefit of vaccination may nonetheless be greater. Future research should concentrate on identifying modifiable factors which predispose to vaccine failure and consider strategies to optimise immunogenicity. In the meantime, the best prospect to further reduce the disease burden include efforts to optimise vaccine coverage and to address deficiencies in housing.

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