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Letters

Letters commenting on recent articles as well as letters reporting cases, outbreaks, or original research are welcome. Letters commenting on articles should contain no more than 300 words and 5 references; they are more likely to be published if submitted within 4 weeks of the original article's publication. Letters reporting cases, outbreaks, or original research should contain no more than 800 words and 10 references. They may have one Figure or Table and should not be divided into sections. All letters should contain material not previously published and include a word count.

Rotavirus P[4]G2 in a Vaccinated Population, Brazil

To the Editor: Gurgel et al. provide an early examination of postmarketing surveillance data from Brazil, one of the first countries to implement routine childhood immunization with Rotarix vaccine (1). In a community with reported vaccination coverage of 50%, the P[4]G2 strain was detected in all 21 rotavirus-positive stool samples identified during November 2006-February 2007. Although monitoring effectiveness of Rotarix against P[4]G2 strains is of interest (2), the small sample size, short duration of surveillance, and lack of a comparison group preclude firm assessment of an association between P[4]G2 predominance and vaccination.

Because Rotarix was introduced in Brazil in March 2006, most children >12 months old (66 [51%] of 129) in the study were ineligible for vaccination. Genotype P[4]G2 was the only strain identified even in older children, which suggests either a change in disease ecology from vaccination or the random circulation of P[4]G2 strains in the community. Ongoing hospital-based surveillance during 2006 in 3 regional countries that had not introduced rotavirus vaccine (El Salvador, Guatemala, and Honduras) showed that P[4]G2 was the predominant circulating strain (prevalence 68%-81%). Thus, as previously documented (3,4), the predominance of P[4]G2 strains after Rotarix introduction in Brazil could represent a natural shift unrelated to vaccination.

Evaluation of vaccine effectiveness against specific strains will allow full assessment of the public health impact of vaccination. Although the data are sparse in the study from Gurgel et al., a comparison of the odds of vaccination among rotavirus-positive (cases) versus rotavirus-negative (controls) children shows 80% vac-

cine effectiveness against P[4]G2 strains among infants <1 year of age, in accordance with recently published data from a controlled trial (5). To further elucidate vaccine impact, we are providing support for vaccine effectiveness studies in Nicaragua and El Salvador and conducting strain monitoring before and after licensure throughout Latin America.

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To the Editor: Gurgel et al. described the predominance of P[4]G2 rotaviruses in a vaccinated population in Aracaju, northeastern Brazil (1). However, several limitations need to be addressed to avoid misinterpretation of data that could lead to loss of confidence in the vaccine in Brazil and other countries.

Brazil was one of the first countries in Latin America to introduce a live, oral, attenuated human rotavirus vaccine into a public-sector health program. Nevertheless, vaccine coverage levels vary considerably across regions (~40% to >80%) and are ~50% in some parts of northern and northeastern Brazil. Therefore, drawing conclusions about the vaccine's protection and prevailing rotavirus genotypes in a setting where coverage is still low seems premature.

Two findings require special consideration. First, although the number of patients is small, children <1 year of age showed a reduced risk for severe rotavirus diarrhea among vaccinated (7%) patients compared with nonvaccinated (26%) patients: $p < 0.05$; odds ratio (OR) 0.20; exact 95% confidence interval (CI) 0.029-1.24. Second, surveillance was conducted for only 4 months, which did not allow for demonstration of a true representative pattern of strain distribution over time. The sequential changing predominance of rotavirus serotypes occurring over time has been well documented for many years (2).

The authors stated that the "vaccine does not afford complete protection against infection" (1). For those not paying close attention to data analysis, this statement could be misinterpreted to mean that the vaccine may not protect against P[4]G2. To the contrary, even with a small sample size and low vaccine coverage, additional analyses of the original data show that the live, oral, attenuated human rotavirus vaccine can protect against the 100% predominance of P[4]G2.

In a large phase III trial conducted in Latin America and Finland, a nonsignificant but protective trend was observed against severe disease associated with P[4]G2 (3). Furthermore, in a subsequent meta-analysis, protection against P[4]G2 rotavirus gastroenteritis of any severity was 81% (95% CI 31-96) and protection against severe rotavirus gastroenteritis was 71% (95% CI 20-91) (4).

To reinforce the hypothesis that predominance of P[4]G2 strains in Aracaju is unrelated to vaccine use, it is worth mentioning that P[4]G2 rotaviruses appear to display an ~10-year cyclic pattern of occurrence in Brazil (5). Although the data presented in the original article may cause misinterpretation about vaccine protection, the article highlights the need for well-designed postmarketing studies to assess both vaccine impact and strain surveillance, in compliance with recent World Health Organization recommendations (6).

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In Response: We acknowledge the comments by Patel et al. (1) and by Linhares and Velázquez (2) about our article that documented the presence of a single rotavirus genotype (P[4]G2) in Aracaju, northeastern Brazil, after the introduction of a human, monovalent rotavirus vaccine (3). Both letters emphasize that the predominance of P[4]G2 may be caused by a natural genotype variation unrelated to vaccination. We agree that our observation could be explained by natural variation of circulating rotavirus genotypes in the region, but an alternative possibility is that the introduction of the G1P[8] rotavirus vaccine into the childhood immunization schedule created conditions in which P[4]G2 strains had a selective advantage over strains with which the vaccine shares G type, P type, or both.

According to a systematic review of rotavirus genotypes reported in the 25 years preceding introduction of the vaccine in Brazil, the prevalence of P[4]G2 strains varied from 19% (1986-1995) to 12% (1996-2000) to 1% thereafter, thus not reaching the detection rate we observed in Aracaju (R.Q. Gurgel et al., unpub data). Furthermore, in the ensuing 8-month period, no genotype other than P[4]G2 had been detected in Aracaju, suggesting that our initial findings were not spurious (R.Q. Gurgel et al., unpub data). In addition, in a separate study we conducted in Recife, a city 500 km north of Aracaju, we observed a significant increase in the proportion of G2 strains

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detected from 47% (21/45) during the 3-month period immediately after vaccine introduction (March 2006-May 2006) to 100% (11/11) during the same 3-month period 1 year after the vaccine introduction (March 2007-May 2007) (4). We believe that our findings are consistent with results of field trials that indicated that the vaccine provided relatively less protection against P[4]G2 strains than against other rotavirus strain types (5).

The beneficial impact of rotavirus vaccination in northeastern Brazil is reflected in the reduction of the detection rate of rotavirus among severe diarrhea cases in our study in Recife, which fell from 27% (45/166 cases) to 5.0% (11/221 cases) in the postvaccine 3-month reporting periods, respectively (4). Our data from Aracaju are indicative of heterotypic protection, although this is not statistically significant (1), against P[4]G2 strains. Further postlicensure studies in Brazil are required to document continuing

effectiveness of the national vaccination program as well as to closely monitor the circulating rotavirus strain types (6).

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Erratum: Vol. 14, No. 4

In the article "Reassortant Avian Influenza Virus (H5N1) in Poultry, Nigeria, 2007" by I. Monne et al., the author affiliations contain errors. Isabella Monne, Tony M. Fausan, Alice Fusaro, Paola De Benedictis, Giovanna Cattoli, and Ilaria Capua are affiliated with Istituto Zooprofilattico Sperimentale delle Venezie, Legnaro, Padova, Italy.

We regret any confusion this error may have caused.

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