American Journal of Epidemiology
Vol. 149, No. 4
Printed in U.S.A.

Waning of Vaccine-induced Immunity: Is It a Problem in Africa?

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While we appreciate the comments of Strebel et al. (1), we believe that they misinterpreted our paper (2) on the role of schools in measles transmission by concluding that we thought the outbreak "was due primarily to waning of vaccine-induced immunity among school-age children" (1, p. 302). As Strebel et al. pointed out, the main reason for the outbreak was low coverage in the older age group (5–14 years) in conjunction with a marked reduction in the incidence of measles over the past 10 years. Because of the high measles vaccine coverage in younger age groups (see table 1), many children in Niakhar have come through the first 5 years of life without being infected with measles virus. However, we believe that waning of vaccine-induced immunity has played a role. Although this was not the main point of the present paper (2), it has been emphasized by us in a number of other papers (3, 4). Since this issue has implications for vaccination policy, we will address this point.

Strebel et al. (1) believe that there is no indication of waning immunity in our paper and that there is a downward bias in vaccine efficacy due to faulty methodology. In support of this view, they claim that waning immunity should lead to lower vaccine efficacy among older children. Vaccine efficacy was 76 percent in children aged 10–14 years as compared with 81 percent in children aged <5 years (2). However, this argument misses the point stressed in our paper; the children's ages at vaccination with standard vaccine were totally different in these age groups, the median age being 295 days for those aged <5 years and 1,017 days for those aged 10–14 years. As table 1 shows, when data were adjusted for age and intensity of exposure, the secondary attack rates were significantly lower among children vaccinated after 365 days of age than among those vaccinated before 12 months of age with standard-titer Schwarz measles vaccine (rate ratio = 0.40, 95 percent confidence interval (CI) 0.16–0.99). For children vaccinated with standard-titer measles vaccine before 12 months of age (table 1), the attack rate after exposure at home was significantly increased among children aged 5–14 years (rate ratio = 2.85, 95 percent CI 1.41–5.73) in comparison with those aged <5 years. With advancing age, more of the vaccinated children are likely to have had either unreported or subclinical measles infection (3) resulting in persistent natural immunity, with consequent declining secondary attack rates among older children. The increased secondary attack rate observed among older children in the present study is therefore consistent with waning vaccine-induced immunity, which is likely to be most marked among children vaccinated early in life. The imputed methodological problems of the study (1) would have no effect on the comparison of attack rates in different age groups. Whether waning immunity will translate into declining vaccine efficacy with age depends on whether misclassification of vaccination status and measles history is the same in all age groups. In the present study, vaccine efficacy for children vaccinated before 12 months of age declined from 82 percent (95 percent CI 66–90) for children aged <5 years to 46 percent (95 percent CI 7–68) for children aged 5–14 years.

Other observations support the existence of waning immunity. Among children who received a well-controlled standard-titer Schwarz measles vaccine at

Received for publication and accepted for publication September 21, 1998.

Abbreviation: CI, confidence interval.

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TABLE 1. Secondary attack rates in a measles epidemic, by intensity of exposure, vaccination status, and age at vaccination, among children who received standard titer Schwarz measles vaccine, Niakhar, Senegal, 1994–1995*

Age group (years)	Vaccination status and age (days) at vaccination	Secondary attack rate (%)			
		In compound	In household	In hut	Total
0–4	Vaccinated				
	<366	6/85 (7)	2/38 (5)	6/76 (8)	14/199 (7)
	>365	0/4 (0)	0/4 (0)	1/3 (33)	1/11 (9)
	Unvaccinated	5/21 (24)	6/14 (43)	9/18 (50)	20/53 (38)
5–9	Vaccinated				
	<366	6/25 (24)	2/13 (15)	4/25 (16)	12/63 (19)
	>365	1/24 (4)	0/5 (0)	2/19 (11)	3/48 (6)
	Unvaccinated	7/27 (26)	1/5 (20)	8/12 (67)	16/44 (36)
10–14	Vaccinated				
	<366	0/1 (0)	0/0 (0)	1/1 (100)	1/2 (50)
	>365	1/15 (7)	0/6 (0)	2/20 (10)	3/41 (7)
	Unvaccinated	7/32 (22)	2/4 (50)	9/17 (53)	18/53 (34)
All	Vaccinated				
	<366	12/111 (11)	4/51 (8)	11/102 (11)	27/264 (10)
	>365	2/43 (5)	0/15 (0)	5/42 (12)	7/100 (7)
	Unvaccinated	19/80 (24)	9/23 (39)	26/47 (55)	54/150 (36)

* Includes children aged 5 months to 14 years who had no history of measles.

10 months of age in a vaccine trial, as many as 19 percent had antibody levels below the protective level 5–7 years after initial vaccination (3). Vaccine efficacy has declined from 100 percent in 1987–1990 (5) during the initial phase of the trial to 66 percent in the present study (2) without any change in epidemiologic methods. The phenomenon of declining vaccine efficacy may have become more pronounced in recent years because there has been less exposure to measles infection; we have found that exposure to natural measles is important in maintaining protective antibody levels among vaccinated children (4).

We readily agree that the major priority in measles control is provision of the first dose of vaccine to unvaccinated children. However, if there is indeed waning immunity, we may have to study the cost-effectiveness of different multidose regimens. Moreover, there is no a priori reason why a multidose regimen should distract from delivery of the first dose of vaccine; in our experience, a multidose program increases children's likelihood of getting the first dose (6).

Those attempting to implement measles control strategies in Africa may be faced with a real dilemma: keep the age of vaccination low, with consequent waning immunity, or improve vaccine efficacy by raising the age of measles vaccination, at the cost of having more measles-related deaths at younger ages. This dilemma is likely to be further aggravated by declining measles antibody levels among infants born to immunized mothers, which may force us to lower the age of measles vaccination even further. Now is the time to seriously examine the phenomenon of waning vaccine-induced immunity, for measles as well as for other vaccine-preventable diseases, in order to improve the impact of the Expanded Programme on Immunization in developing countries.

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