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SHORT REPORT: ASSESSING FIELD VACCINE EFFICACY FOR MEASLES IN FAMINE-AFFECTED RURAL ETHIOPIA

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Abstract. Measles is a major cause of mortality in complex emergencies. Both high vaccination coverage and vaccine efficacy are required to prevent major epidemics of measles in such situations. Evaluation of field vaccine efficacy is a critical but underutilized component of program monitoring in emergencies, and is particularly important in rural areas where the integrity of the cold chain is difficult to guarantee. In July 2000, we evaluated the field vaccine efficacy for measles vaccination by comparing the incidence of cases in vaccinated and unvaccinated groups during a two-stage cluster survey of 563 children in Ethiopia. Approximately 30% of the measles cases occurred in vaccinated children. Estimated field vaccine efficacy for measles was 66.9% in children 9–36 months old. The finding of a field vaccine efficacy for measles less than 80% warrants formal assessment of measles vaccine efficacy, particularly in famine emergencies where measles is associated with a high case fatality rate.

Measles is a major cause of mortality in complex emergencies, particularly in isolated rural areas of developing countries where natural immunity may be low and coverage of a routine Expanded Program on Immunization (EPI) may be inadequate. Case-fatality rates for measles of 10–33% have been reported during such situations. Children less than two years of age and malnourished children are at increased risk for mortality during such measles outbreaks.[1,2] Vaccination coverage greater than 95% with an effective vaccine is required to prevent measles outbreaks during complex emergencies.[3] In addition, measles vaccine efficacy, which is approximately 85% among children 9–12 months old and 95% among those 12 months to 5 years old, needs to be maximized to prevent outbreaks.[4] Evaluation of field vaccine efficacy is one method that can be used to rapidly assess the quality of vaccine and gauge the need for more formal evaluation.

In 2000, severe famine caused high mortality in the Gode district of Ethiopia.[5] Cases of measles were first reported in the district in early 2000, and a partial campaign targeting children 9–59 months old was conducted in February 2000. However, measles cases continued to be reported in the district, and a proportion of these cases occurred among vaccinated children. In July 2000, we collected data on measles vaccination status and measles disease occurring during the previous two weeks among 563 children 9–48 months of age at the time of vaccination. Because vaccination cards had not been distributed previously, the vaccination status of children was determined by maternal recall. Mothers were asked about any immunization received by the child. There was no functioning routine EPI, and the February campaign was the only immunization campaign in recent years. Cases were ascertained by interviewing the mother regarding morbidity during the previous two weeks. The standard World Health Organization case definition for measles was used.[6] Field vaccine efficacy was evaluated using the methods described by Orenstein and others for outbreak investigations in large populations, which included cluster sampling.[4] We calculated age-specific attack rates and vaccine efficacies using the following three formulas:

$$\text{Attack rate in unvaccinated (ARU)} = \frac{\text{No. cases in unvaccinated population}}{\text{Unvaccinated population}}$$

$$\text{Attack rate in vaccinated (ARV)} = \frac{\text{No. cases in vaccinated population}}{\text{vaccinated population}}$$

$$\text{Vaccine efficacy (VE)} = \frac{\text{ARU} - \text{ARV}}{\text{ARU}} \times 100$$

Of the 563 children 9–48 months of age surveyed, 342 (60.7%) were reported as having been vaccinated against measles. The estimated coverage decreased with decreasing age and was only 56.9% among children 9–24 months of age. During the previous two weeks, 33 cases of measles were reported, with 10 (30%) of the cases occurring in vaccinated children. Attack rates in the unvaccinated and vaccinated populations were highest in children 9–24 months of age (Table 1). This age group also had the lowest field vaccine efficacy.

Measles field vaccine efficacy in rural populations with low natural immunity should be assessed in children 9–36 months of age for a more accurate estimate of vaccine efficacy.[2] Children in this age group may have been vaccinated, but in rural isolated communities they are likely to have had limited exposure to natural disease. Inclusion of older children, who are more likely to have been exposed to measles infection, may render inaccurate the denominator of the attack rate in the unvaccinated population[2] and may result in an underestimation of the field vaccine efficacy. Although there is no information on prior disease outside of the two-week time period used in the survey, the lack of difference in results for field vaccine efficacy between different age groups in our study suggests that the bias discussed above was not significant and that the rural population may have had little exposure to wild measles virus before the outbreak. There may have been other factors present that could have influenced the estimation of vaccine field efficacy, such as human immunodeficiency virus (HIV). Children who are positive for this virus may

TABLE 1
Estimated age-specific measles attack rates and field vaccine efficacies in the Gode district of Ethiopia, 2000*

	9–24 months old (n = 160)	9–36 months old (n = 349)	9–48 months old (n = 563)
Unvaccinated children	69	149	221
Cases in unvaccinated children	9	18	23
Attack rate in unvaccinated children	13.0% (4.9–21.1)	12.1% (6.76–17.4)	10.4% (6.3–14.5)
Vaccinated children	91	200	342
Cases in vaccinated children	4	8	10
Attack rate in vaccinated children	4.4% (0.10–8.7)	4.0% (1.2–6.8)	2.9% (2.0–3.8)
Vaccine efficacy	66.3% (23.1–90.5)	66.9% (40.1–93.7)	71.9% (55.1–88.7)

* Values in parentheses are 95% confidence intervals.

not have seroconverted following immunization; therefore, vaccine efficacy could have been underestimated. However, cases may have been missed if HIV-positive children did not develop the classic measles rash, as has been demonstrated in measles cases among HIV-positive children.[7]

We have attempted to minimize other potential biases. The risk for exposure in different age groups is comparable because the overall attack rate was greater than 5% in all age groups.[4] Although we determined vaccination status by maternal recall and not vaccination records, we believe that it was a good estimator of coverage. Previous studies have demonstrated maternal recall of vaccination status to be fairly accurate, with 85% of mothers able to accurately recall the vaccination status of their children.[8] In addition, there had been no functioning EPI for several years in the Gode district, with the sole immunization campaign being the measles campaign in February 2000.

Despite low coverage in the Gode district and an ongoing measles epidemic starting in December 1999, a measles vaccination campaign with sufficient coverage and an efficacious vaccine were not implemented until August 2000. Public health recommendations for complex emergencies have been assembled into a set of minimum standards and guidelines for humanitarian intervention.[9] Programs based upon these recommendations are systematically applied in refugee camps during the initial emergency phase. These recommendations, such as mass measles vaccination campaigns, the provision of adequate water and sanitation facilities and sufficient food aid, should be used in other acute emergencies, and not just limited to refugee situations. Measles vaccination, concurrent with vitamin A distribution, is a life-saving intervention that needs to be implemented immediately in all types of complex emergencies. Vaccination coverage particularly in camps or where epidemiology suggests cases are occurring in older children, should exceed 90% and extend to children 12–15 years of age because children will be susceptible in areas where there has been no functioning immunization program and little exposure to disease.

Under ideal circumstances, measles vaccine has 85% efficacy when administered to children at nine months of age.[4] The cold chain is particularly vulnerable in hot, rural areas in developing countries, where infrastructure is poor and monitoring may be inadequate. A vaccine efficacy of less than 80% necessitates further investigation of vaccine management and administration.[4] Among children 9–36 months of age in our survey, the estimated vaccine coverage was 57.3% and the estimated field vaccine efficacy was 66.9%. Consequently, the measles epidemic in the Gode district continued through August 2000, contributing to approximately 971 deaths in the district. In famine emergencies, measles field vaccine efficacy can be assessed using simple methods that compare attack rates in vaccinated versus unvaccinated children during a cluster survey. This evaluation may be the first indication of problems with the cold chain or vaccine administration and lead to a formal survey of vaccine efficacy.

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