Effectiveness of Measles Vaccination After Household Exposure During a Measles Outbreak

A Household Contact Study in Coburg, Bavaria

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Background: A measles outbreak was recently observed in Coburg, Bavaria, in a population with vaccination rates of 76.5% in 5- to 6-year-old children in the years preceding the outbreak. Only a small proportion of children had received 2 vaccinations against measles. Vaccine effectiveness is estimated in a household contact study and also by a screening method.

Methods: A household contact study was conducted in families with at least 1 measles case by standardized computer-assisted telephone interviews to assess secondary attack rate and to estimate vaccine effectiveness. Vaccine effectiveness was also estimated with Farrington's screening method with information from school entry examinations and from questionnaires of confirmed measles cases in the Coburg outbreak.

Results: Thirty-eight children were primary cases. Of their contacts, 20 children were included in the study as secondary cases (1 vaccinated), and 23 children were contacts who did not develop measles (12 vaccinated once and 4 vaccinated twice), resulting in a vaccine effectiveness of 90% (95% confidence interval, 35–97%) for one vaccine dose. The proportion of the population vaccinated reached 81.5% during the outbreak and the proportion of the cases vaccinated was 10.9%, resulting in a vaccine effectiveness estimated using the screening method of 97.2% (95% confidence interval, 95.7–98.3%).

Conclusions: With the use of 2 approaches to estimate the effectiveness of measles vaccination, a consistently high vaccine effectiveness of 90% or above was shown during a measles outbreak in Western Europe.

Key Words: measles, vaccine, effectiveness, outbreak

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With the elimination of measles imminent in many countries, there will be few opportunities to assess the effectiveness of measles vaccines. This, however, is still an issue because the effectiveness of 1 injection of measles vaccine is high, but not complete.[1] The German Standing Committee on Vaccination (Ständige Impfkommission) recommends the first measles vaccination at the age of 11–14 months and a second vaccination at the age of 15–23 months.[2] The average vaccination rate for at least 1 dose of measles vaccine in 5- to 6-year-old children in Germany was 91.3% in 2000–2002.[3] In Coburg, a measles outbreak with 1191 reported cases was recently observed in a population with vaccination rates of 76.5% in this age group in the years preceding the outbreak and only a small proportion of children vaccinated twice.[4] This gave us the opportunity to estimate the measles vaccine effectiveness (VE) in a household contact study ($VE_{household}$) and using the screening method ($VE_{screening}$).[5]

MATERIALS AND METHODS

Household Contact Study. According to the German "infectious diseases protection law," all cases of measles must be reported to the local public health authorities. During the measles outbreak in Coburg between November 2001 and June 2002, local health authorities sent a questionnaire to the reporting families to confirm measles by means of clinical symptoms and to evaluate vaccination status. Additionally families were asked to participate in a household contact study. The families' names, addresses and telephone numbers were sent to the principle investigator (S.A.) if the families gave written informed consent. These families were given further details on the household contact study and were asked to provide certificates of vaccination for every family member. Standardized computer-assisted telephone interviews were conducted by trained interviewers. Household members were interviewed regarding the onset and duration of measles symptoms, history of measles, exposure to other measles cases in public institutions, existence of other diseases, medications, breast-feeding, vaccination status and date of vaccination.

Case Definition. For this outbreak setting, the case definition for measles required a generalized maculopapular rash with fever >38.4°C for >3 days and at least one of the following signs: cough; coryza; Koplik spots; or conjunctivitis. A primary case was the first household member who acquired measles. Coprimary cases were defined as measles patients who developed a fever within 4 days after the onset of a rash in the primary case. Secondary cases were confirmed measles

patients who developed a fever within 5–25 days after the onset of a rash in the primary case. Contacts were all household members who had contact with measles cases in the household during their infectious period.

Inclusion Criteria. Household members were included in the study if they met the following inclusion criteria: contact with measles cases in their infectious period; younger than 19 years of age at the time of the onset of disease; and no immunosuppression. Only secondary cases and contacts without a history of measles were included in the final analysis of vaccine effectiveness.

Data Analysis. To reduce bias caused by different exposure of vaccinees and nonvaccinees to measles secondary attack rates were determined in families in a household contact study. In this setting, the exposure is generally uniform.[6] The data of the household contact study were used to estimate $VE_{household}$ as follows: $VE_{household} = (ARU - ARV)/ARU*100$, where ARU is the attack rate in unvaccinated persons and ARV is the attack rate in vaccinated persons, respectively.[6]

$VE_{screening}$ was estimated by the screening method with the formula $VE_{screening} = 1 - PCV/(1 - PCV) * (1 - PPV)/PPV$.[5]

Information about the proportion vaccinated (PCV) was taken from the questionnaires of confirmed measles patients 5 years or older. We selected these age groups under the assumption that vaccination status was constant in older age groups. The proportion of the population vaccinated (PPV) was estimated from school entry examinations in Coburg between September 2001 and June 2002 in 5- to 6-year-old children. Confidence intervals were calculated by the exact method of Katz. Statistical analyses were performed with SAS Software version 8.

RESULTS

Household Contact Study. During the Coburg outbreak, 1191 cases of measles were reported. We requested the families of 762 measles cases to send written consent to be contacted by the principal investigator, and 86 parents agreed to participate in a telephone interview. Four of the families could not be reached by telephone, and 27 had fewer than 2 children living in the household, leaving 55 families with a total of 124 children for the household contact study. All of these families participated. In these 55 families, 38 children (69%) fulfilled the criteria of the clinical case definition for measles and were defined as primary cases. In most of the 17 excluded cases, the reason for exclusion was that the duration of the rash was <4 days.

Forty-seven children were household members and had contact with the primary cases during their infectious period. Twenty-three of them were contacts but did not acquire measles. Two of the contacts were vaccinated during the incubation period, 1 with the first vaccination and 1 with the second. These children were counted according to their former vaccination status.[6] Of the 24 potential secondary cases, 4 children were excluded because they did not meet the case definition, leaving 20 children to be counted as secondary cases. Six secondary cases were younger than 2 years of

TABLE 1. Vaccination Status of Participants

Vaccine Status	Measles	No Measles	Total	Attack Rate(%)
None	19 (95)*	7 (30)	26 (60)	73
1 dose†	1 (5)	12 (52)	13 (30)	8
2 doses	0 (0)	4 (17)	4 (9)	0
Total	20 (100)	23 (100)	43 (100)	

*Numbers in parentheses, percent.
†$VE_{household}$ (for 1 dose only) = 90% (95% CI 35–97%).

age, of whom 3 were younger than 1 year. There were no coprimary cases.

Of the 43 exposed children included in the final analysis, 25 were female and 18 were male. Median age was 5 years 3 months in measles cases and 6 years 6 months in contacts without measles. None of the included children had a history of measles. Vaccinated participants had been immunized between 1984 and April 2002. Vaccination status of the participants is shown in Table 1. ARV (1 vaccination) was 8%, whereas ARU was 73%, resulting in a $VE_{household}$ for 1 vaccination of 90% [95% confidence interval (95% CI), 35–97%]. $VE_{household}$ for 1 or more vaccinations was 92% (95% CI 48% to 98%). No child with >1 vaccination contracted measles; therefore $VE_{household}$ for 2 immunizations was not calculated.

Screening Method. In school entry examinations in Coburg during 2001 and 2002, 1437 children 5–6 years of age were examined. Of those, 1368 presented certificates of vaccination (95.2%), and 81.5% of these 1368 children had been vaccinated at least once (PPV). In the Coburg measles outbreak, 229 persons had confirmed measles and were 5 years or older. Twenty-five of them had been vaccinated, so that PCV was 10.9% resulting in a $VE_{screening}$ of 97.2% (95% CI 95.7–98.3).

DISCUSSION

The measles outbreak in Coburg offered the rare opportunity in an industrialized country in Western Europe to estimate the effectiveness of one measles vaccine injection during an outbreak situation in a household contact study and to compare these findings to vaccine effectiveness estimates by a population-based screening method. Vaccine effectiveness is often questioned by antivaccination lobbyists, citing that measles is observed among vaccinated persons, especially in outbreak settings. Both estimates calculated here showed a high vaccine effectiveness with corresponding VE estimates of 90% or greater. We believe that this study is the first household contact study on effectiveness of measles vaccination during an outbreak in Europe.

To test the validity of our estimates, sensitivity analyses were performed. Originally we confined our analyses to cases according to a strict clinical case definition. In an outbreak situation, however, it might be justified to be less strict, because most presumed measles cases observed in the outbreak are likely to be cases. Excluding the duration of rash from the case definition for measles resulted in 45 instead of 38 primary cases, with 25 instead of 20 secondary cases (24

not vaccinated) and 28 instead of 23 contacts without measles (10 not vaccinated, 13 vaccinated once, 5 vaccinated twice). However, these changes did not alter the $VE_{household}$ of 90%. Counting the 2 children vaccinated during the incubation period as vaccinated (assigned to their former vaccination status in accordance with the recommendations given by Orenstein et al[6] in the base case calculations) did not change the $VE_{household}$ estimates (data not shown).

In a sensitivity analysis for the VE estimation using the screening method, we also applied the PPV of the years preceding the outbreak (76.5% in the years 1998 and 1999 to 2000 and 2001) to estimate $VE_{screening}$. The estimate for the $VE_{screening}$ was 96.3% which does not differ substantially from the estimate based on the post outbreak vaccination coverage data (97.2%).

Our data are in line with the results of other published household contact studies from Australia, Palau and Korea, which estimated a VE between 86 and 92%.[7–9] In comparison with our study, those studies had smaller numbers of vaccinated participants. In addition, only Guris et al[8] stratified by number of vaccinations, whereas no information about the number of vaccinations was given in the other studies.

There are limitations of our study. Only 86 families of 1191 cases (some of them were siblings) agreed to participate in the study. For reasons of data protection requirements in Germany, we could not recontact families who answered the questionnaire but did not send back the written informed consent for the household contact study. It is possible that there was an overrepresentation of vaccination critics who denied their children vaccinations in the nonparticipant group, whereas participants of the household contact study may have been more likely to have their children vaccinated. This would likely result in underestimation of vaccine effectiveness. The confidence interval around $VE_{household}$ was wide because only one child with vaccination acquired measles.

We used a clinical case definition without serologic confirmation. However, Hutchins et al[10] were able to show that the positive predictive value of a clinical case definition in a situation with a high incidence is 74%. In the Coburg outbreak, cumulative incidence was 882 cases/100,000 inhabitants.[4]

Our data confirm the effectiveness of either 1 or 2 doses of measles vaccine in an outbreak situation.

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