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Measles epidemic in the urban community of Niamey: transmission patterns, vaccine efficacy and immunization strategies, Niger, 1990 to 1991

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From October 1, 1990, until April 28, 1991, 13 578 cases of measles were reported in the urban community of Niamey, Niger. Vaccine coverages (one dose of Schwarz vaccine given after 9 months) in urban community of Niamey were, respectively, 63% at the age of 12 months and 73% at 24 months before the epidemic. Incidence rates were the highest among children ages 6 to 8 months and 9 to 11 months and 22% of the cases were less than 1 year old. Vaccine efficacy estimates ranged from 86 to 94% according to age groups and the method used (screening method, case control study, retrospective cohort study). The risk of transmission of illness increased with the intensity of contact with a case. Contact with a health facility 7 to 22 days before onset of rash was not a risk factor. Seasonal migrants in Niamey were more likely to develop measles. Recommendations included implementation of an early two dose schedule of measles immunization during the outbreak, vaccination offered at each contact with a health facility, radio and television advertising for measles immunization and distribution of vitamin A to all measles cases.

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BACKGROUND

Despite the progress achieved by the Expanded Programme on Immunization (EPI) of the World Health Organization, measles is still a major public health problem in many parts of the developing world.[1,2] High case fatality ratios (CFR) are frequently observed,[3,4] and urban areas are associated with higher incidence rates and CFR than those observed in rural areas.[5,6] High age-specific attack rates have been observed in infants less than 1 year of age,[3,7,8] and recent recommendations from the Global Advisory Group of the EPI focus on the administration of measles vaccine at 6 months to high risk population (children hospitalized, those affected by disasters, in outbreak or refugee camps).[9,10]

This report describes the epidemiologic characteristics, the risk factors for illness and the recommendations developed during a measles outbreak that occurred in the urban community of Niamey (UCN), Niger, between October, 1990, and May, 1991.

INTRODUCTION

Niger is an African sahelian country of 7.9 million population. The country is divided into 8 districts and according to a census performed in 1988, 15.2% of the population live in urban areas, of whom 445 715 are in the UCN.[11] Until 1987 immunization was performed at fixed sites and by mobile teams. The EPI was started in late 1987 and the measles immunization strategy is based on the Schwarz vaccine administered at 9 months of age during routine immunization theoretically offered at each contact with a health center (dispensaries and mother and child health clinics) as well as by mobile teams operating in remote areas of Niger. With the use of World Health Organization methodology,[12,13] a nationwide cluster sampling survey performed in December, 1990, showed an overall measles vaccine coverage of 33% among 12- to 23-month-old children with coverages ranging from 22 to 73% according to districts. In the UCN, coverage was 73% (National Division of Expanded Programme on Immunization, Niamey, unpublished data).

Data describing monthly occurrence of measles cases as reported by health facilities from 1975 were available at the ministry of health. During the past 15 years cases of measles have occurred annually in Niamey, and in 1985 an outbreak accounted for more than 15 000 cases (Fig. 1).

In addition to the above surveillance system, for early warning purposes a weekly report of infectious diseases such as measles was started in 1985 through the weekly official telegram information system which provides the number of cases reported by each of the 8 districts of Niger without breakdown by age and no count of deaths. In October, 1990, a rise in the number of measles cases reported through that system was noticed in the UCN, and in January, 1991, an outbreak investigation was requested by the National Division of the EPI. The objectives of the study were to measure the magnitude of the epidemic, to identify high risk groups in the population, to estimate vaccine efficacy by age groups and to search for risk factors for transmission and severity of illness.

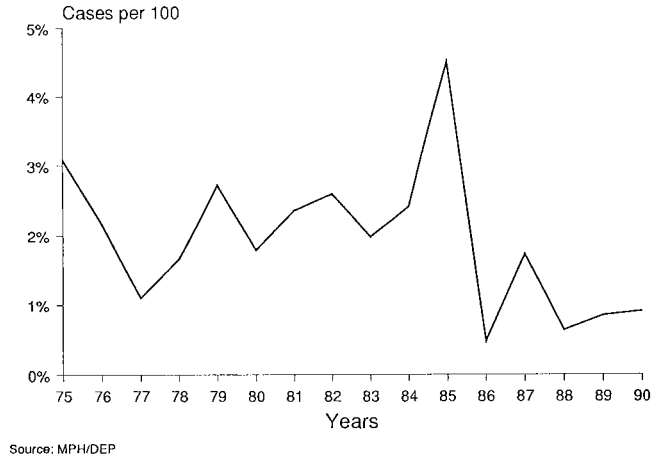


FIG. 1. Measles annual incidence rates among total population of the Urban Community of Niamey, Niger, 1975 to 1990.

METHODS

Descriptive epidemiology. With the use of national annual surveillance reports available since 1975, incidence rates per year were estimated for the UCN. A review of the information collected since October 1, 1990, in the clinic log books of the 29 health facilities of UCN was performed by an epidemiologist. From October 1, 1990, to January 31, 1991, a case of measles was identified as a person diagnosed with measles as written on the clinic log book by the consulting physician or nurse. From February 1, 1991, a case definition was implemented and a case was defined as any person presenting with a generalized rash lasting $\geqq$ 3 days and a temperature $\geqq$ 38.3°C (if measured, otherwise fever as mentioned by the health personnel) and one of cough, coryza or conjunctivitis.[14] Information collected from the log books included date of onset of measles, treatment, age, sex and vaccination status. Incidence rates by age group were calculated and expressed as the number of cases per 1000 person months. The population distribution by month of age was estimated from the 1988 census data extrapolated using a 4.6% annual growth rate in Niamey. The number of persons belonging to one age group were multiplied by the duration of the outbreak in months to obtain a person time denominator.

Because population of a single area of the UCN could consult in other areas and because addresses were not recorded, health facility location could not be used as a basis for calculating attack rates by place.

Vaccine efficacy. Vaccine efficacy was assessed using three methods.

Method 1. The screening method took into account the proportion of cases vaccinated (PCV) obtained from a review of the log books from the 29 health clinics of Niamey between October 1, 1990, and April 28, 1991, and the proportion of the population vaccinated (PPV) among children ages 9 to 11 months and 12 to 23 months obtained from the vaccine coverage survey performed in December 1990 in UCN. Vaccine efficacy (VE) was calculated as VE = (PPV − PCV)/[PPV (1 − PCV)].[15] Confidence Limits of VE were calculated using the upper and lower 95% confidence limits of the vaccine coverage estimate based on the EPI formula.[12] Vaccine status among cases was collected from consultation log books and corresponded to information obtained from mothers' interview with or without checking the vaccination card. If vaccination status was not mentioned on the log books, cases were excluded from analysis.

Method 2. A retrospective cohort study was performed on February 28, 1991, in one area of the UCN with a high incidence of measles (quartier Boukoki, population 40 000). Four subareas were defined and from the center of each subarea a direction was selected at random. From these starting points 165 households were selected by going from one household to the closest one. Information regarding, age, sex, vaccination and disease status was collected among all children less than 60 months old. Measles status was assessed through a mothers' interview using a standard case definition.[14] Children with past history of measles before October 1, 1990, and children without vaccination cards were excluded from the analysis of VE.

Incidence density rates of measles were compared among children vaccinated and not vaccinated, within each of the following age groups: 9 to 11 months, 12 to 23 months and 24 to 59 months. The amount of days contributed by each child into the cohort of unvaccinated or vaccinated children was computed for each age group. A child was considered to be immunized if vaccinated before February 15, at least 14 days before rash onset (among cases), if vaccinated after 9 months (272 days) and if vaccination was documented on the vaccination card. Children vaccinated before 9 months of age or less than 14 days before rash onset were not considered to have contributed to the cohort of vaccinated children.[15] Vaccinated children started to contribute to the cohort of vaccinated children at Day 14 after vaccination. The date of rash onset minus 14 days (incubation) was the basis for identification of the age group the case belonged to.

Incidence density rates of measles were calculated for the period October 1, 1990, to February 28, 1991, among vaccinated (IRV) and unvaccinated children (IRNV). Vaccine efficacy was measured as VE = (IRNV − IRV)/IRNV[15] and 95% confidence limits were calculated with the use of Taylor series confidence limits.[16]

Method 3. A matched pair case-control study was carried out among children ages 6 to 59 months and served for estimation of VE as well as risk factors for transmission and severity of illness. A total sample of 250 pairs of cases and controls was planned to meet required sample size for both studies (For VE, type one error = 5%, expected OR = 0.25, beta error = 10% and expected vaccine coverage = 60% among controls within each age group: 9 to 11, 12 to 23 and 24 to 59 months).

New cases of measles were consecutively enrolled within a 12-day period at the consultation of six health centers in the UCN.

For each case one control matched for age and sex was randomly selected from the children attending the same health facility the same week for a different illness. Based on the number of measles cases and number of consultations performed the previous day, a sampling interval was calculated and controls were selected by systematic sampling from a random start. Matching was done within 1 month below the age of 6 months and otherwise within the following age intervals (6 to 8, 9 to 11, 12 to 17, 18 to 23, 24 to 35 and 36 to 59 months). Children with a past history of measles (obtained from mothers' interview) before October 1, 1990, were not eligible for the control group.

For each case and control vaccine status was obtained from the health card only. A vaccination was considered as valid if performed after 9 months (272 days) and more than 14 days before the day of rash onset among the matched cases. Children vaccinated before 9 months of age or less than 14 days before rash onset were excluded from analysis.[15] If mothers or attendants did not have the vaccination card during the consultation at the health centers, they were taken home by car and vaccine status was documented. When the vaccination card was lost, children were excluded.

The VE was estimated from the matched pair OR as VE = 1 − OR, and 95% confidence limits were calculated using the methods of Greenland and Robins.[17]

Risk factors for illness. The case-control study was also used to assess risk factors for measles including nosocomial transmission. Information regarding contact with a health facility (dispensary, mother and child health care clinic, hospital) during the period 7 to 22 days before rash onset was collected from mothers interviewed. In order to ensure comparability of opportunity of exposure to the virus among cases and controls, the analysis was restricted to pairs including only index cases. Place of contact with a case (household, compound, or outside the compound), type of housing, family size and time since arrival in Niamey

were also documented. Matched pair OR and 95% confidence limits (CL) were calculated.[17] In order to assess confounding and interaction between different risk factors, a conditional multivariate analysis was performed[18] using an Egret® software package (Statistics and Epidemiology Research Corporation).

CFR. Hospital CFR was obtained from a review of the log books at Niamey hospital, the only site for hospital admission in the UCN.

The overall case-fatality ratio in the general population of cases was estimated from the sample of cases included in the case-control study who were visited at home 15 days after rash onset. Because of time constraints, 15 days instead of 30 were chosen for assessing the outcome after rash onset.

Evaluation of the immunization strategy recommended, 1 year after the outbreak. An early two dose schedule for measles immunization (one dose of standard Schwarz vaccine at 6 months and a second dose at 9 months) was implemented during the outbreak. One year after the epidemic (June, 1992), a cluster sampling survey (30 clusters of 30 children ages 12 to 23 months) was selected in the UCN to assess measles vaccine coverage. Vaccine status was documented on card.

RESULTS

Incidence rates. Annual incidence rates documented since 1975 showed that measles cases were observed every year in the UCN, and a major epidemic was notified in 1985 (Fig. 1). From October 1, 1990, until April 28, 1991, the review of the log books of health facilities identified 13 578 cases of measles in the UCN. The peak of the epidemic was observed during the first week of January, 1991, with more than 900 cases reported. The overall reported incidence density rate (IR) was 4.45 cases/1000 person months. The highest age-specific IR were observed among children ages 6 to 8 months and among children ages 9 to 11 months (Table 1).

Cases detected by the weekly official telegram information system in the UCN did not differ by more than 3% from the number of cases retrospectively identified by reviewing the dispensary log books (Fig. 2).

Case-fatality ratio. *Hospital-based.* Among the 13 578 reported cases 1413 (10.4%) were admitted to Niamey National Hospital, the only site where cases can be hospitalized in Niamey. Information on death was available for 1210 of them (85.6%) of whom 34,4% died ($n = 416$).

Population-based case-fatality ratio. The overall CFR was estimated from 242 of the 258 cases included in the case-control study (16 cases lost to follow-up). Sixteen deaths occurred giving a CFR within 15 days of rash onset of 6.6% (95% CL 3.4 to 9.8). Unfortunately no control patient was followed up to 15 days in order to provide a reference group for mortality.

Vaccine efficacy. *Screening method.* Using the vaccine coverage figures of 73% for children 12–23 months and 63% for children 9–11 months, VE efficacies estimated by the screening method were, respectively, 89.6% and 86.5% (Table 2).

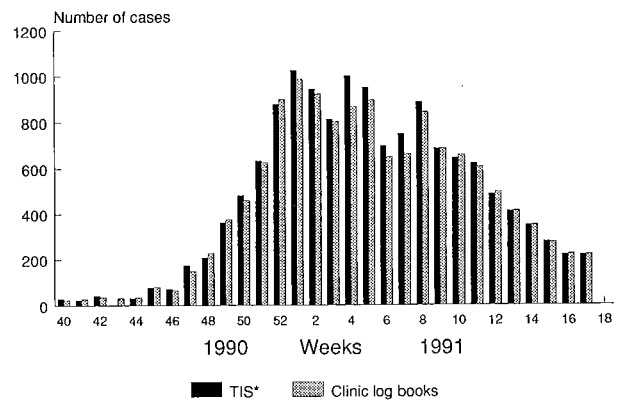
Retrospective cohort. The retrospective cohort study was performed in 165 households (725 children 9 to 59 months) of the Boukoki area. Unvaccinated children ages 9 to 59 months were 8.4 times more likely to develop measles than vaccinated children (VE = 89.3%). VE did not vary among different age groups (Table 2). VEs by age at vaccination were, respectively, 25.9% for the group vaccinated between 9 and 12 months, 94.4% for 12 to 23 months and 88.4% for 24 to 59 months.

Case-control study. Two hundred fifty-eight pairs were enrolled. VE estimates were slightly higher than those obtained by the screening and retrospective cohort methods although the differences were not significant. Exclusion of children vaccinated after the onset of the outbreak[10] made no difference to the VE estimate and VE did not vary according to the child's age at interview (Table 2).

TABLE 1. Measles; reported incidence rates (IR) by age group, Urban Community of Niamey, Niger, October, 1990, to April, 1991

Age	Person Time*	Cases	IR/1000†
0–5 months	68 628	455	6.63
6–8 months	34 314	1368	39.87
9–11 months	34 314	1199	34.94
12–59 months	454 440	6824	15.02
5–14 years	870 835	2269	2.61
≧15 years	1 586 711	1080	0.68
Unknown		383	
Total	3 049 242	13 578	4.45

* Estimated from the 1988 census figures. The number of children belonging to an age group at time T were multiplied by the duration of the outbreak (7 months).
† Incidence density rate = cases/1000 person month.



Source: MPH-DEP/clinic log books
* Telegram Information System

FIG. 2. Number of measles cases notified weekly by the "telegram information system" and number of cases collected from the review of clinic log books, urban community of Niamey, 1990.

TABLE 2. Measles vaccine efficacy (Schwarz vaccine) by age, estimated from 3 different methods, Niamey, Niger, 1991

Screening Method

Age (months)	PPV (%)	Reported cases	PCV	VE (%)	95% CL
9–11	63	1199	198/1057*	86.5	79.6–91.5
12–23	73	2220	433/1967†	89.6	83.4–94.2

Retrospective Cohort Study

Age	Vaccinated	Person time	Cases	IR	VE (%)	95% CL
9–11	Yes	1219	2	1.64	25.9	0.0–83.9
	No	4069	9	2.21		
12–23	Yes	14 830	4	2.7	94.4	84.1–98.0
	No	6448	31	48.08		
24–59	Yes	25 231	9	3.6	88.4	76.0–94.4
	No	12 705	39	30.7		
9–59	Yes	41 280	15	3.63	89.32	81.45–93.85
	No	23 222	79	34.02		

Matched Pair Case-Control Study

Age	No. of pairs	Discordant pairs		OR	VE (%)	95% CL
		CV	CNV			
9–11	30	1	9	0.11	89	12–99
12–23	59	2	31	0.06	94	73–98
24–59	74	4	43	0.09	91	74–97
9–59	153	7	83	0.08	92	82–96

* Based on information obtained from 1057 of 1199 cases (88.2%).
† Based on information obtained from 1967 of 2220 cases (88.6%).
Person time, person month contributed by each individual in the study; CV, number of discordant pairs where the case is vaccinated; CNV, number of discordant pairs where the case is not vaccinated.

TABLE 3. Measles cases and controls matched on age, sex and health facility; distribution of pairs according to potential risk factors, Niamey, Niger, 1991

Potential Risk Factors	No. of Pairs	No. of Discordant Pairs		OR	95% CL
		CE	CNE		
Health centers*	258	36	33	1.09	0.68–1.75
<6 months in Niamey†	258	46	22	2.09	1.21–3.48
Type of housing‡	256	46	18	2.56	1.48–4.41
Family size§	258	65	54	1.20	0.84–1.73

* Attended a health center at least once during the period 7 to 22 days before rash onset.
† Living in Niamey for less than 6 months *vs.* more than 5 months.
‡ Huts *vs.* concrete.
§ >5 *vs.* <6.
CE, Discordant pairs where the case is exposed; CNE, discordant pairs where the case is not exposed.

Risk factor for illness. Cases of measles were more likely than controls to live in huts compared to concrete houses. Cases of measles were also more likely to have been living in UCN for less than 6 months than controls. Cases were not more likely than controls: (1) to have had contact with a health facility within the period 7 to 22 days before onset of rash; or (2) to belong to a large family (>5) (Table 3). A conditional logistic regression model was used to assess confounding. Vaccine status, contact with a health facility, family size, time since arrival in the UCN and location of contact with a case were variables forced into the model. Vaccine status and location of contact with a case were independent risk factors for illness (Table 4). In particular children exposed to a case in the family were more likely to develop measles than children exposed to a case in the compound, who were themselves more likely to develop measles than those children exposed to a case outside the compound. Analysis was done with index cases only and the findings did not change (data not shown).

TABLE 4. Measles risk factors for illness among children ages 9 to 59 months: cases and controls matched for age, sex and health center; multiple logistic regression, conditional maximum likelihood estimation

Exposure	Coefficient	OR	95% CL	Reference Category
Vaccination	−2.861	0.06	0.02–0.18	Unvaccinated
<6 months in Niamey	0.085	1.09	0.49–2.44	≧6 months
Huts	0.133	1.14	0.50–2.63	Concrete
Health center	0.347	1.42	0.69–2.91	No visit
No. of consultations within the past 6 months*				
1	0.147	1.16	0.40–3.38	No consultation
2	−0.035	0.97	0.33–2.84	No consultation
3	−0.023	0.80	0.25–2.55	No consultation
4	−0.037	0.69	0.27–1.78	No consultation
Contact with measles				
Outside†	0.949	2.59	0.74–9.03	No contact
Compound†	2.634	13.94	3.17–61.3	No contact
Family	2.916	18.47	3.59–95.1	No contact

* Children who visited health centers in Niamey at least 1 time, 2 times, 3 times, 4 times and more, compared with no visit, in the previous 6 months (according to parents).
† Children who had a contact in the family, in the compound or outside the compound, compared with children with no contact during the period 7 to 22 days before rash onset.

DISCUSSION

Urban outbreak. Our first objective was to measure the magnitude of the outbreak and to identify high risk groups. This urban outbreak of measles is the largest experienced in Niger within the past 5 years. High incidence rates were observed below 12 months, the highest being between 6 and 8 months. This type of information is frequently used to emphasize the need for having available a vaccine with a higher efficacy at 6 months than currently available. However, if high vaccine coverage had been reached in older children, the children below 9 months of age would have also been less likely to develop measles. This stresses the need to achieve high vaccine coverage in Niger.

Vaccine coverage of 63% between 9 and 11 months and 73% between 12 and 23 months is not sufficient to prevent occurrence of epidemics and interrupt transmission durably.[19, 20] In Niamey the EPI was recently started (1987) and no information was available on the vaccine coverage above 23 months. Accu-

mulation of susceptible children since the last major outbreak in Niamey in 1985 (>15 000 cases) has led to an overall 14 517 cases from October 1, 1990, to December 31, 1991. The epidemic has extended to other districts and 87 922 cases have been reported nationwide from January 1, 1991, until December 31, 1991.

In Niamey the weekly official telegram information system has proved to be an excellent tool for early warning of epidemic. Information forwarded through this channel to the ministry of health properly reflected information collected from the dispensary registries.

Vaccine efficacy. The second objective of the study was to measure vaccine efficacy by age group. VE below the age of 60 months ranged from 86 to 94% according to the age and to the method used. This was slightly above the expected range suggesting that low vaccine efficacy was not the cause of the outbreak. In the cohort study the VE of 25.9% in the age group 9 to 11 months was most likely related to the small number of cases in this age category. In the same age group the case-control study and the screening method provided higher point estimates with narrower 95% confidence intervals.

Case and vaccine status ascertainment bias as well as cases or controls selection bias may have occurred in each of the three methods used.[21] Since VE estimates were high, only potential biases that may have led to an overestimation of the VE are important. In the case-control study controls selected at the health center consultation may have been more likely to be frequent users of health facilities and to attend vaccination sessions than the general population. The proportion of controls vaccinated may have been overestimated compared with the general population therefore leading to an overestimate of VE. Use of health care during the past 6 months (excluding the month before onset) was compared between cases and controls. Controls were more frequent users of health facilities than cases of measles. However, taking into account frequency of consultation during the 6 previous months (conditional logistic regression model), VE was still high (VE = 94%, 95% CL 82 to 98).

Controls selected in the case-control study never had measles in the past (before or during the present outbreak). A better selection procedure should have allowed the selection in the control group of measles cases with date of onset posterior to the date of onset of the matched case (because these persons were appropriate controls at the time of onset of the matched case even if they became cases later on). Avoiding such persons in the control group may have increased the proportion of immunized controls, therefore leading to an overestimate of the VE.

The high incidence rate under 5 years of age in this population may limit the use of the odds ratio to estimate the relative risk in this situation leading to an overestimation of VE compared to the result of the cohort study.

Taking into account these limitations, the VE estimates were good and results suggested a good technique of vaccine administration and an adequate cold chain.

In this study three methods were used to estimate vaccine efficacy. Among them we believe that the method comparing incidence density rates among vaccinated and unvaccinated children was preferable mainly because it is the only method correctly measuring the rate and the probability of illness. Secondly the logistical burden to undertake the census required for this method was lower than the logistical constraints of the case-control study. In addition the difficulties of choosing controls was therefore avoided. Lastly the cohort study allowed easy stratification of data by age during the analysis.

In the study of risk factors for illness, only vaccine status and location of contact with a measles case appeared to play a major role in the outcome after controlling for confounding. Particularly results do not suggest that exposure to a health facility within the period 7 to 22 days before onset was a risk factor for illness[7] (even after controlling for frequency of contact with a health facility during the previous 6 months). The case-control study was carried out late in the outbreak. At this time intrafamilial transmission may have been more prevalent than nosocomial transmission. However, this lack of association persisted when the analysis was restricted to pairs including only index cases. Cases were more likely to be recently arrived (seasonal migrants) in UCN. This has stressed the need to emphasize immunization for this particular population subgroup.

Recommendations to control the outbreak included: to immunize children at 6 months of age during the outbreak period with a second dose at 9 months; to make vaccines available, vaccination card checked and immunization offered at every contact with a health facility; to accelerate the vaccination program performed by the mobile teams; to distribute vitamin A to all measles cases; to finance and carry out television and radio advertising regarding the need for measles immunization; to implement adequate handling of all cases with antibiotics, eye ointment and vitamin A.

Control measures, however, did not include a mass immunization campaign. Recommendations from the 1989 Global Advisory Group meeting in Tokyo do not advise mobilizing enormous amount of human and financial resources to control measles outbreaks. However, in a country like Niger where the EPI was recently started, high incidence rates can be expected and the usefulness of mass campaign may need to be thought of carefully. This outbreak has resulted in 85 048 cases nationwide (National Information Sys-

tem, unpublished data) and if we accept a CFR of 10%, has probably led to 8500 deaths. In this respect it should be noted that the CFR (6.6%) of the current survey sample of 242 cases was observed at Day 15 after rash onset among children who had all received vitamin A (100 000 IU for children 6 to 12 months old and 200 000 IU for children older than 1 year).

If vaccination coverage of 90% above 9 months of age had been achieved before the outbreak, using the proportion of children aged more than 9 months in our study (86.6%), and assuming a vaccine efficacy of 85%, 56 343 cases would have been prevented nationwide in 1991.

The introduction of vaccination at 6 months with a second dose at 9 months during the outbreak has not led to a high vaccine coverage before 9 months. Among the 900 children included in the 1992 survey, 570 belonged to the 6- to 8-month age group during the outbreak and had therefore been eligible for immunization at that age in 1991. One hundred seventy-six of the eligible children (30.9%) received a first dose of Schwarz vaccine before 9 months of age. The return rate for the second dose was 57.4% before 12 months and 67.0% before 24 months. One year after the epidemic and the implementation of the control measure, the overall vaccine coverage among children ages 12 to 23 months was 61.4%. Among children ages 12 to 23 months, 50.2% were vaccinated before 12 months of age.

In comparison the 1990 vaccine coverage among 12- to 23-month-old children in Niamey, before the implementation of the early two dose schedule, showed that 63% of the children were immunized at 12 months of age and that 73% of the children ages 12 to 23 months were immunized.

Similarly among Mozambican refugees in Malawi, immunizations were administered on a single dose schedule (one dose of Schwarz at 9 months) or an early two dose schedule (one dose between 6 and 9 months and a second dose after 9 months) according to the site of settlement of the refugees. Data comparison showed that,, respectively, 68.0% of children exposed to an one dose schedule and 60.6% of those exposed to an early two dose schedule were immunized at 12 months of age. Overall 83.7% (one dose schedule) and 82.5% (two dose schedule) were immunized between 12 and 24 months of age (P Malfait and A Moren, unpublished data).

CONCLUSION

Very high vaccine coverage must be achieved and sustained to avoid such large outbreaks. The high incidence rates observed in the age groups 6 to 8 months and 9 to 11 months emphasize the need for: high vaccine coverage in urban areas; reliable extended surveillance and monitoring of disease and vaccine efficacy; aggressive and early control measures during outbreaks; and once high vaccine coverage is achieved, implementation of the early two dose schedule. Since the identification of the decreased survival associated with the use of high titer measles vaccines, the expectation for routine use of a highly efficient measles vaccine at 6 months of age has become very unrealistic in the future.[22, 23]

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Nephropathia epidemica (hemorrhagic fever with renal syndrome) in children: clinical characteristics

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The clinical characteristics of serologically verified nephropathia epidemica, the Scandinavian form of hemorrhagic fever with renal syndrome, were studied in Swedish children who were <15 years of age. In 1990 to 1992, 14 cases were prospectively followed. A retrospective survey during 1984 to 1990 disclosed another 18 cases. Among the 32 cases (20 boys, 12 girls, 3 to 15 years of age; median age, 11 years), the most common symptoms were fever (100%), headache (100%), abdominal pain (93%), vomiting (91%) and back pain (76%). Laboratory findings included elevated serum creatinine concentration (19 of 28) and thrombocytopenia (7 of 22). Urinalysis showed proteinuria (31 of 31 patients) and hematuria (24 of 30). Six children had mild hemorrhagic manifestations (epistaxis, metrorrhagia, and petechiae). No severe complications occurred. The clinical symptoms of children with nephropathia epidemica seem to be similar to those found among adult nephropathia epidemica cases.

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INTRODUCTION

Hemorrhagic fever with renal syndrome (HFRS) is a group of zoonoses caused by viruses with a worldwide distribution belonging to the hantavirus genus in the Bunyaviridae family.[1] At least five serotypes of hantaviruses are now identified: Hantaan- and Seoulviruses in Asia; Puumala virus in Central and Northern Europe; Belgrade/Dobrava virus in the Balkan countries; and Prospect Hill in the United States.[2–4] In the Americas there is increasing evidence for hantavirus infections both in rodents and in man.[5–7] Prospect Hill virus is the only hantavirus that has thus far not been associated with human infection. A recent outbreak of severe illness with several fatal cases in the southwestern United States may been associated with a previously unknown hantavirus.[8]

In many parts of Asia, especially in China and Korea, HFRS is a significant disease with hundreds of thousands of persons infected each year and a case-fatality rate of 5 to 15%.[9] The need for prophylaxis is obvious and recently vaccines against HFRS have been developed.[10–12]

The type of HFRS that is endemic in Scandinavia and Central Europe, i.e. nephropathia epidemica (NE), is caused by Puumala virus and the bank vole (*Clethrionomys glareolus*) is its main animal reservoir. NE is a less severe form of HFRS, although hemorrhagic complications as well as fatal cases have been described.[13–15]

The clinical features of NE in adult patients include high fever, abdominal and/or back pain, headache,