

Large Outbreak of Measles in a Community with High Vaccination Coverage: Implications for the Vaccination Schedule

Angela Domínguez,^{1,2,6} Nuria Torner,^{2,6} Irene Barrabeig,² Ariadna Rovira,² Cristina Rius,^{3,6} Joan Cayla,^{3,6} Elsa Plasencia,² Sofia Minguell,² M. Rosa Sala,² Ana Martínez,² Josep Costa,⁴ Mar Mosquera,^{5,6} Carmen Cabezas,² and the Working Group for the Study of the Measles Outbreak in Catalonia^a

¹Department of Public Health, University of Barcelona, ²Department of Health, Generalitat of Catalonia, ³Public Health Agency of Barcelona, and ⁴Microbiology Department, Hospital Clínic of Barcelona, Barcelona, ⁵National Microbiology Centre, Carlos III Health Institute, Madrid, and ⁶CIBER Epidemiología y Salud Pública (CIBERESP), Spain

Background. Attempts to eliminate measles from a country or region may be disrupted by an imported case that affects indigenous persons. The objective of this study was to analyze epidemiological and clinical characteristics of a measles outbreak in Catalonia, Spain, in 2006.

Methods. Data on cases of measles reported to the Department of Health, Generalitat of Catalonia, during the period 28 August 2006 through 8 July 2007 were collected. Suspected cases were confirmed by determination of measles-specific immunoglobulin M antibodies and/or detection of virus genome. Incidences were calculated using the estimated population of Catalonia for 2006, and 95% confidence intervals were determined assuming a Poisson distribution. The association between proportions was determined using the χ^2 test and Fisher's exact test. The level of statistical significance was set at $\alpha = .05$.

Results. A total of 381 cases were confirmed, for an incidence of 6.6 cases per 100,000 persons. A total of 89.5% of cases occurred in nonvaccinated persons, mainly those aged ≤ 15 months (incidence, 278.2 cases per 100,000 persons; mean age of patients, 12 months). Indigenous subjects accounted for 89.8% of cases, and laboratory confirmation of results was obtained for 87.1%. Measles genotype D4 was identified in all sequenced samples.

Conclusions. The age distribution of cases of measles among children aged <15 months suggests that the first dose of vaccine should be routinely administered at the age of 12 months.

Measles is a highly contagious disease caused by a morbillivirus that results in substantial morbidity and mortality worldwide [1] and has a case-fatality rate of ~ 1 death per 1000 persons [2]; in developing countries, the case-fatality rate may reach almost 100 cases per 1000 persons [3]. In 2005, it was estimated that there were >20 million cases of measles and $>300,000$ associated deaths worldwide, the majority of which were in Southeast Asia and in Africa; measles control is difficult

in this setting, where there is also a high prevalence of HIV infection [4, 5].

The virus is highly transmissible, and 90%–95% of the population must be immune to interrupt transmission [6, 7]. Therefore, the rate of vaccination coverage (with 2 doses of vaccine) must be maintained at $>90\%$ [8].

Given the characteristics of the disease, the lack of an animal reservoir, and the availability of valid diagnostic tests and of a safe, effective vaccine, experts considered measles to be potentially eradicable [9]. The European Region of the World Health Organization (WHO) designed a strategic plan to eliminate indigenous measles in the region by 2007, but in 2003, after analyzing the evolution of the disease and the difficulties in implementing national plans, the objective of elimination of endemic measles was postponed to 2010 [8]. The success in controlling the disease varies be-

Received 19 May 2008; accepted 15 July 2008; electronically published 29 September 2008.

^a Members of the working group are shown at the end of the text.

Reprints or correspondence: Dr. Angela Domínguez, Dept. of Public Health, University of Barcelona, Casanova 143, 08036 Barcelona, Spain (angela.dominguez@ub.edu).

Clinical Infectious Diseases 2008;47:1143–9

© 2008 by the Infectious Diseases Society of America. All rights reserved.

1058-4838/2008/4709-0004\$15.00

DOI: 10.1086/592258

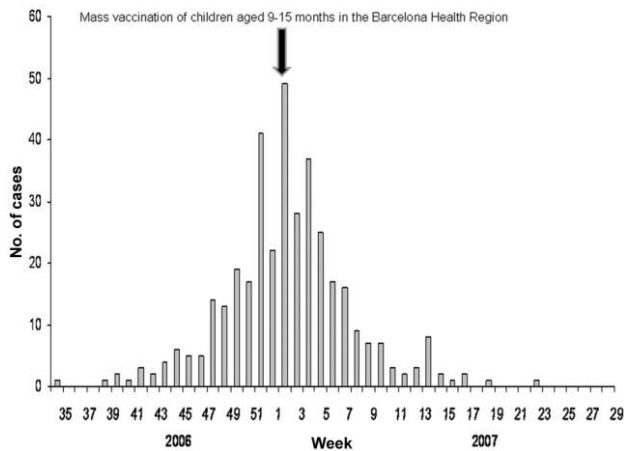


Figure 1. Distribution of confirmed cases of measles, by date of rash onset, August 2006–June 2007.

tween countries, and although most national vaccination schedules already include administration of 2 doses of vaccine, coverage rates are still suboptimal [10]. Large outbreaks of measles in Europe have occurred, with >1000 cases and some deaths in The Netherlands in 1999 [11] and in Germany [12], in Ukraine [13], and among Romanian gypsies [14] in 2006.

In accordance with the recommendations of the European Region of the WHO, Spain launched a measles elimination program in 2001, and in 2004, the circulation of indigenous measles was interrupted [15]. However, until worldwide eradication is achieved, elimination of measles from a country or region is potentially reversible, because the virus can be reintroduced and cause epidemics that can substantially affect the indigenous population [16, 17].

Catalonia, a region in northeastern Spain with ~7 million inhabitants, >14% of whom are immigrants [18], began requiring the administration of 1 dose of the measles, mumps, and rubella (MMR) vaccine at the age of 12 months in the routine vaccination schedule in 1980. In 1987, the timing of the administration of the first dose shifted to 15 months of age, and in 1988, a second dose of MMR vaccine was added to the schedule at 11 years of age, to replace the rubella vaccine administered to girls [19]. To ensure that the proportion of vaccinated children aged <10 years was >95% and to achieve elimination of the disease by the year 2000, children aged 4 years began to receive the second dose of vaccine starting in 1998 [20].

During the period 2000–2005, the incidence of measles in Catalonia was very low, and outbreaks were either related to imported cases or affected families that had not received any dose of the vaccine for philosophical reasons. No transmission chains involved the indigenous population [21]. On 11 October 2006 (week 41), a case of measles in a girl (age, 14 months) born in Catalonia was reported to the Department of Health

of Catalonia (Barcelona). Three related cases were detected among immigrants of Bosnian origin, 1 of whom had been in Italy during the incubation period. All of the patients resided in the Barcelona region. Given the successive transmission chains that were detected among children who had still not received the first dose of vaccine, in January 2007, mass vaccination of children aged 9–15 months in the Barcelona region was initiated. Mass vaccination was subsequently extended to the Tarragona region when cases appeared there. The objective of the present study was to analyze the epidemiological and clinical characteristics of the measles outbreak that began in Catalonia at the end of 2006.

MATERIALS AND METHODS

Data were collected from the register of clinically suspected cases of measles reported to the epidemiological surveillance units of the Department of Health of the Generalitat of Catalonia (Barcelona). The study period was from 28 August 2006 (the date of the onset of rash in the index case) to 8 July 2007 (2 maximum incubation periods [21 days] after the onset of rash in the last confirmed case on 7 June).

A suspected or clinically compatible case was defined as a case of measles that met the clinical case definition (maculopapular rash, fever [temperature, >38°C], and cough, conjunctivitis, and/or coryza). Laboratory-confirmed cases were defined as suspected cases in which a virological diagnosis was confirmed by presence of IgM and/or detection of measles virus genome in a urine specimen. Epidemiologically confirmed cases were defined as suspected cases that had been epidemiologically linked to a confirmed case. Cases in persons who had undergone recent vaccination (i.e., vaccination \leq 45 days prior to the onset of rash) were considered to be confirmed cases on the basis of genotype D4–positive results of PCR of urine specimens or by epidemiological link to a confirmed case, if the urine specimen yielded negative PCR results or was not available.

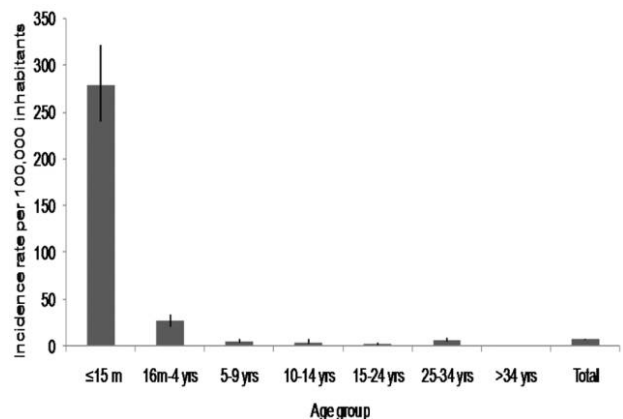


Figure 2. Incidence of confirmed cases of measles, by age group, Barcelona and Tarragona health regions of Spain. m, Months; yrs, years.

Table 1. Distribution of confirmed cases of measles, according to age group and vaccination status.

Age group	No. of cases		Vaccination status					
			0 doses		1 dose		2 doses	
	Indigenous population	Immigrant population	Indigenous population	Immigrant population	Indigenous population	Immigrant population	Indigenous population	Immigrant population
≤15 months	179 ^a	11 ^a	176	11	3	0	0	0
16 months–4 years	59	7	33	7	26	0	0	0
5–9 years	11	2	10	2	0	0	1	0
10–14 years	9	1	5	1	0	0	4	0
15–24 years	8	2	8	2	0	0	0	0
25–34 years	57	11	52	9	5	2	0	0
>34 years	19	5	19	5	0	0	0	0
Total	342	39	303	37	34	2	5	0

^a $P = .007$.

Discarded cases were defined as cases with no epidemiological link to a confirmed case and negative laboratory test results (i.e., negative serologic test results or negative results of both serologic tests and PCR) or as cases that did not meet the clinical definition [22].

To avoid false-negative results, we used the following sample collection criteria: blood samples were obtained ≤72 h after the onset of rash [23], and urine samples were collected within the first week after the onset of rash [24]. Measles-specific antibodies were determined in the microbiology laboratory of the Hospital Clinic of Barcelona with use of an EIA (Measles ELISA; Vircell). Urine samples were frozen at -40°C until shipment to the National Microbiology Center of the Carlos III Health Institute (Madrid) for testing by multiple-nested PCR, which was designed to detect measles, rubella, and parvovirus B19 viruses simultaneously. If the PCR yielded positive results for measles virus, confirmation was obtained with a second aliquot from the sample using a measles-specific nested PCR [25, 26].

Vaccination status was determined either by checking vaccination cards and medical records or by determining serum IgG levels. If the vaccination status could not be verified, the person was considered to be unvaccinated.

The indigenous population was defined as all persons born in Catalonia, including those who were born to immigrant parents. To study possible contacts, people exposed to a suspected case during the infectious period (4 days before and 4 days after the appearance of rash) were studied, and susceptible persons were treated in accordance with established procedures [19].

The incidence of measles was calculated using the estimated 2006 population of Catalonia in the affected regions. The 95% CIs were calculated assuming a Poisson distribution. The χ^2 test and Fisher's exact test were used to determine whether the differences between proportions were statistically significant. The level of statistical significance was established at $\alpha = .05$.

RESULTS

During the study period, 538 suspected cases of measles were reported in Catalonia. Three hundred eighty-one of the cases were confirmed, and 157 were eliminated; 6 of the cases eliminated from further study involved vaccine reactions. The highest incidence of cases occurred between the last week of December 2006 and the first week of February 2007, when a total of 203 confirmed cases occurred; the greatest number of cases ($n = 49$) occurred during the second week of January 2007. Figure 1 shows the time distribution of confirmed cases.

The global incidence of the 2 affected regions, the Barcelona

Table 2. PCR results for laboratory-confirmed and discarded cases of measles, according to date of collection of the urine sample.

Case, time of sample collection ^a	PCR result			Percentage of PCR results	
	Positive	Negative	Total	Positive	Negative
Confirmed cases					
0 days	54	6	60	90.0	...
1–3 days	94	12	106	88.7	...
4–6 days	35	7	42	83.3	...
7–10 days	7	3	10	70.0	...
≥10 days	4	3	7	57.1	...
Total	194	31	225	86.2	...
Discarded cases					
0 days	...	16	16	...	100.0
1–3 days	...	47	47	...	100.0
4–6 days	...	25	25	...	100.0
7–10 days	...	14	14	...	100.0
≥10 days	...	1	1	...	100.0
Total	...	103	103	...	100.0

NOTE. Data are no. of cases, unless otherwise indicated.

^a Times are no. of days after onset of rash.

Table 3. Distribution of confirmed cases, according to age group, hospitalization, vaccination status, and complications.

Age group	No. of patients		Vaccination status					
	Hospitalized patients	Nonhospitalized patients	0 doses		1 dose		2 doses	
			Hospitalized patients	Nonhospitalized patients	Hospitalized patients	Nonhospitalized patients	Hospitalized patients	Nonhospitalized patients
15 months ^b	25 (13.2)	165	25	162	...	3
16 months–4 years ^d	5 (7.6)	61	4	35	1	26
5–9 years	4 (30.8)	9	3	9	1	...
10–14 years	0 (0)	10	...	6	4
15–24 years	3 (30.0)	7	3	7
25–34 years ^e	19 (27.9)	49	17	44	2	5
>34 years	4 (16.7)	20	4	20
Total	60 (15.7)	321	56	283	3	34	1	4

NOTE. Data are no. (%) of patients.

^a Respiratory complications included pneumonia and bronchitis.

^b Three nonhospitalized patients presented with otitis and diarrhea, and 1 patient presented with bronchitis and diarrhea.

^c Thrombocytopenia.

^d Four nonhospitalized patients presented with diarrhea and otitis.

^e One nonhospitalized and 3 hospitalized patients presented with diarrhea and otitis, 1 nonhospitalized patient presented with diarrhea and hepatitis, 1 hospitalized patient presented with diarrhea and pneumonia, and 1 hospitalized patient presented with diarrhea, otitis, and pneumonia.

^f Appendicitis.

^g Tonsillitis.

^h Oral candidiasis.

and Tarragona health regions (population, 5,684,454 inhabitants), was 6.5 per 100,000 inhabitants (95% CI, 5.9–7.2 per 100,000 inhabitants) The incidence, according to age group, ranged from 0.74 cases per 100,000 persons (95% CI, 0.5–1.1 cases per 100,000 persons) among persons aged >34 years to 278.2 cases per 100,000 persons (95% CI, 239.5–321.3 cases per 100,000 persons) among children aged ≤15 months (figure 2). Of the 381 cases, 355 (93.2%) occurred in the Barcelona health region (incidence, 6.9 cases per 100,000 inhabitants; 95% CI, 6.2–7.6 cases per 100,000 inhabitants), and 19 cases (5.0%) occurred in the Tarragona health region (incidence, 3.5 cases per 100,000 inhabitants; 95% CI, 1.95–5.4 cases per 100,000 inhabitants). Six cases occurred among residents of other health regions who had attended hospitals in the Barcelona health region, where they were contacts of cases; there were no resulting transmission chains of infection in their respective regions.

Of the 381 confirmed cases, 342 (89.8%) occurred among indigenous subjects. A total of 340 (89.2%) of 381 cases occurred among nonvaccinated subjects, 187 (55.2%) of whom were mainly aged ≤15 months; 36 individuals (9.4%) had received 1 dose of MMR vaccine, and 5 (1.3%) had received 2 doses. The titers of measles-specific IgG antibodies were determined and/or urine PCR was performed for the 5 patients with confirmed (IgM-positive) cases who had received 2 doses of vaccine. In 2 cases, positive urine PCR results indicated infection; in the other cases, urine specimens were not available, and the analysis of IgG antibodies yielded inconclusive findings. Therefore, these cases were classified as confirmed cases, because they fulfilled clinical criteria and were set within the context of the outbreak.

A total of 51.5% of the cases occurred in men, and 48.5% occurred in women. No statistically significant differences were observed in the proportion of cases among vaccinated men (21 of 193 cases; 18 men had received 1 dose of vaccine, and 3 had received 2 doses) and of cases among vaccinated women (18 of 185 cases; 16 women had received 1 dose, and 2 had received 2 doses; $P = .5$).

The mean age of the 381 patients with confirmed cases was 15 months (range, 1 month to 50 years). The distribution, by age group, is shown in table 1. Of the patients aged ≤15 months, 52.2% were indigenous children, and 28% were immigrants ($P = .007$).

Of the adults, 11 were health care workers (age range, 19–37 years), none of whom had been vaccinated, with the exception of 1 person who received 1 dose of MMR vaccine. Three hundred forty-two (89.8%) of the 381 cases occurred in the indigenous population, and 39 (10.2%) occurred among immigrants, 2 of whom (age, >25 years) had received 1 dose of MMR vaccine.

Laboratory confirmation was obtained in 330 cases (86.6%). One hundred forty (42.4%) of the 330 cases were confirmed by determination of measles-specific IgM antibodies, 65 (19.7%) were confirmed by PCR detection of measles virus genome in urine specimens, and 129 (39.1%) were confirmed by both techniques. A total of 328 urine samples were analyzed (accounting for 61.0% of 538 suspected cases), of which 194 (59.1%) yielded positive PCR results and 134 yielded negative results (table 2). Of these results, 118 corresponded to the D4 genotype. No other genotype was detected in the samples an-

Table 3.

		Complications							
		Respiratory ^a		Otitis		Hepatitis		Others	
Hospitalized patients	Nonhospitalized patients	Hospitalized patients	Nonhospitalized patients	Hospitalized patients	Nonhospitalized patients	Hospitalized patients	Nonhospitalized patients	Hospitalized patients	Nonhospitalized patients
2	20	3	6	2	10	...	1	...	1 ^c
1	10	1	4
1	1
...
1	...	1
10	6	3	...	2	4	2	...	2 ^{f,g}	...
...	4	1	1	...	1	2 ^{e,h}	...
15	41	9	6	4	19	2	2	4	1

alyzed, and only 3 differed in 1 or 2 nucleotides, with respect to the main sequence of the 456 nucleotides sequenced.

Of the 51 remaining cases, 41 (80.4%) were confirmed by epidemiological link, and 10 (19.6%) were classified as clinically compatible because samples were unavailable or there was evidence of direct contact with a confirmed case.

Sixty patients (15.7%) required hospitalization. Complications occurred in 91 cases (23.9%), of which 35 required hospitalization; 25 were ambulatory cases. The most common complications were diarrhea and/or vomiting (56 cases [14.7%]), otitis (20 cases [5.2%]), and pneumonia (8 cases [2.1%]). No significant differences in the type of complication were observed between patients aged <15 years and older patients. The highest frequency of hospitalization (30.8%) was observed for patients aged 15–24 years, and a significant difference was observed in the hospitalization rate between patients aged <15 years (12.2%) and those aged ≥15 years (26.2%) ($P = .001$). Complications were significantly more common among unvaccinated patients (87 [25.7%] of 339 unvaccinated persons) than among patients who had received ≥1 dose of vaccine (4 [10%] of 40 patients; $P < .04$) (table 3). There were no deaths. The source of infection was identified in 181 cases (family environment, 56 cases; day-care or preschool centers, 68 cases; health care centers, 37 cases; and the neighborhood, 20 cases).

DISCUSSION

This outbreak of measles was the largest in Catalonia in the 20 years since the introduction of routine vaccination. The first cases were clearly imported but gave rise to various transmission chains in the indigenous population, changing the situation of measles elimination that had existed in Catalonia since 2000. In Catalonia, the great majority of immigrants come from underdeveloped countries with poor vaccination coverage. Although immigrants are offered the same health care services as the indigenous population, the rate of MMR vaccination coverage is only 93.3% among immigrants, compared with 98.9%

for the indigenous population [27]. This, together with the existence of susceptible individuals in some population groups and the enormous mobility of European residents, many of whom are immigrants, may explain why there are enough susceptible subjects to ensure the succession of various transmission chains [28]. Theoretically, the rejection of vaccination for philosophical reasons may also have contributed to this outbreak, but in our experience, outbreaks associated with this reason are self-limiting [29], and this particular outbreak would not have occurred without the previously mentioned circumstances.

This outbreak shows that high national and regional vaccination coverage rates do not, in themselves, guarantee maintenance of elimination. Parker et al. [30] reported an outbreak of 43 cases in Indiana in 2005; the rate of vaccination coverage among the schoolchildren was 98%. Ehresmann et al. [31] described a similar phenomenon. In The Netherlands, where the national rate of coverage is 96%, an outbreak in 1999 caused almost 3000 cases among people who rejected vaccination for religious reasons [11]. In Spain, Castell et al. [32] reported an outbreak that affecting >300 people in 1995; the rate of vaccine coverage was 95%. More recently, an outbreak of almost 200 cases occurred in Andalusia, Spain, where the vaccination coverage rate was >95% [16].

The proportion of cases requiring hospitalization (15.8%) is situated between the 8.8% rate reported in the Indiana outbreak [30] and the 51% rate reported in the Ukraine outbreak [13]. Other studies have also reported differing figures [11, 32, 33]. Hospitalization of patients with measles probably has more to do with how cases are managed than with their severity; therefore, this may not be a good parameter for evaluating the magnitude and severity of an outbreak. In addition, there is a risk of nosocomial cases occurring both among patients visiting the hospital for other reasons and among health workers; this could increase disease transmission [16, 30, 34, 35].

Although the rate of hospitalization was moderate in the outbreak we describe, exposure in a health care center affected

37 persons (10%). In addition to supporting the recommendation of vaccination of health care workers, this event suggests that hospitalization should be reserved for serious cases, and home care should be encouraged during outbreaks. Pneumonia, a classic complication of measles, occurred in 2.1% of patients—a percentage similar to or even greater than that reported in studies from Germany [12] but lower than rates reported in other studies [16, 30, 34] and evidently very different from the figure of 26.5% reported by Van den Hof et al. [36] from The Netherlands. The methodologies used to record complications during outbreaks are probably not homogenous and should accord international guidelines [22], because this information is important in evaluating the magnitude of the problem.

The distribution of cases by age clearly shows that children who were younger than the age of administration of the first dose of vaccine (15 months) were the most affected, accounting for 50% of the cases. The incidence rate of 278.2 cases per 100,000 persons was greater than the incidence reported in an outbreak in Ireland (158 cases per 100,000 persons) [37]. In the outbreak in Andalusia, this age group accounted for 25% of cases, with an incidence rate of 552 cases per 100,000 persons [38]. The fact that only 11 cases were reported among immigrant children aged ≤ 15 months may be because these children are more likely to stay at home than to attend a day care center.

Only 25.6% of the cases occurred in adults. In a recent outbreak of 18 cases in Scandinavia, adults accounted for 72% of cases [39], and in an outbreak of 59 cases in Madrid, adults accounted for almost 60% of cases. However, in large outbreaks, the proportion of cases among adults is normally much lower than that among children [16]. As Orenstein et al. [40] suggest, it is difficult to believe that adult patients can sustain a transmission chain in the general population. Likewise, several authors suggest that, if there are high coverage rates among schoolchildren, it is difficult for the outbreak to propagate in the community, even if there are susceptible adults [30, 31]. Therefore, we consider high rates of coverage with 2 vaccine doses for children to be essential, and the rates should be distributed homogeneously, avoiding pools of susceptible children. The important role played by children aged ≤ 15 months in the outbreak suggests that measles antibodies transferred passively by the mother were not sufficient to combat the circulation of the virus in as-yet-unvaccinated children. For this reason, in accordance with expert opinion [10, 41], we suggest lowering the age at which the first dose of MMR vaccine is administered to 12 months.

In this outbreak, 87% of cases were laboratory confirmed, similar to the 96% rate for the outbreak in Andalusia [38, 42] and the 88% rate for the outbreak in Madrid [15] but much higher than the proportion found in other countries. In the

United States, Parker et al. [30] found that 41% of cases were confirmed, and Ehresmann et al. [31] reported that 64% of cases were confirmed. The proportion of laboratory-confirmed cases was 32% in a study from Italy [43], 33% in a study from Germany [12], 20% in a study from Ireland [37], and 18% in a study from The Netherlands [36].

Although laboratory confirmation is not essential to confirm a case during an outbreak, it does reflect an improvement of disease surveillance that involves not only the laboratory and epidemiological surveillance units, but also attending physicians, and should thus be encouraged. In addition, if a large number of clinical samples are available for molecular epidemiological study, it can be determined whether all cases occurred as part of the same outbreak.

Finally, timely reporting of cases to avoid delays in investigating and managing the outbreak is essential. In this outbreak, the index case was not detected until 6 weeks after the onset of symptoms (29 August 2006), and this, together with the interval between reporting of the first cases and the initiation of mass vaccination of all children aged 9–15 months in the region (second week of January 2007), contributed to a greater spread of the outbreak. Logically, the sooner mass vaccination is initiated, the sooner circulation of the virus can be interrupted. However, the problem lies in evaluating the capacity of diffusion during the initial phases of the outbreak. Therefore, we suggest that, in communities where the wild virus has not immunized women of childbearing age, as in Catalonia, the first dose of the vaccine should be administered routinely at 12 months of age. In addition, if there is evidence that transmission is occurring in children who are younger than this age, mass vaccination of children aged < 12 months should be performed as soon as possible, although these children should still receive the first routine vaccine dose when they reach 12 months of age.

MEMBERS OF THE WORKING GROUP FOR THE STUDY OF THE MEASLES OUTBREAK IN CATALONIA

P. Godoy and J. Batalla (Department of Health, Generalitat of Catalonia, Barcelona; and CIBER Epidemiología y Salud Pública [CIBERESP], Spain); J. Alvarez, R. Urbano, C. Arias, J. Torres, N. Camps, L. Urbitzondo, J. M. Jansà, and A. Plasencia (Department of Health, Generalitat of Catalonia); J. Guix (Public Health Agency of Barcelona); A. Guarga and X. Sintés (Barcelona Health Region); E. Zabaleta and G. Jodar (Catalan Institute of Health, Barcelona); M. V. Martínez and I. Peña-Rey (National Epidemiology Center, Madrid, and CIBERESP); T. Castellanos (National Epidemiology Center); and J. E. Echevarría and F. de Ory (National Microbiology Center, Madrid, and CIBERESP).

Acknowledgments

We are grateful for the collaboration and support received from the following persons and institutions during the investigation and management of the outbreak: N. Rabella (Microbiology Services of Hospital de la Santa Creu i Sant Pau, Barcelona, Spain); T. Juncosa, J. J. Garcia, and L. Rozas (Hospital Saint Joan de Déu, Espluges de Llobregat, Spain); M. Campins (Preventive Medicine Service of the Hospital Universitari Vall d'Hebron, Barcelona); O. Urraca (Hospital de Nens de Barcelona); and all health professionals from the departments of Pediatrics, Emergency, Microbiology, Preventive Medicine, Primary Health Care, and Vaccination of the Barcelona and Tarragona health regions.

Financial support. Department of Health of the Generalitat of Catalonia, Spain.

Potential conflicts of interest. All authors: no conflicts.

References

- Cherry JD. Measles virus. In: Feigin RD, Cherry JD, Demoler GJ, Kaplan SL, eds. Textbook of pediatric infectious diseases. Philadelphia: Saunders, 2004:2283–312.
- Gindler J, Tinker S, Markowitz L, Atkinson W, Dales L, Papania MJ. Acute measles mortality in the United States, 1987–2002. *J Infect Dis* 2004; 189(Suppl 1):S69–77.
- Nandy R, Handzel T, Zaneidou M, et al. Case-fatality rate during a measles outbreak in eastern Niger in 2003. *Clin Infect Dis* 2006; 42:322–8.
- Wolfson LJ, Strebel PM, Gacic-Dobo M, Hoekstra EJ, McFarland JW, Hersh BS. Has the 2005 measles mortality reduction goal been achieved? A natural history modelling study. *Lancet* 2007; 369:191–200.
- Helfand RF, Moss WJ, Harpaz R, Scott S, Cutts F. Evaluating the impact of the HIV pandemic on measles control and elimination. *Bull World Health Organ* 2005; 83:329–37.
- Muller CP, Kremer JR, Best JM, Dourado I, Triki H, Reef S. Reducing global disease burden of measles and rubella: report of the WHO Steering Committee on research related to measles and rubella vaccines and vaccination, 2005. *Vaccine* 2007; 25:1–9.
- Asaria P, MacMahon E. Measles in the United Kingdom: can we eradicate it by 2010? *BMJ* 2006; 333:890–5.
- World Health Organization. Progress in reducing global measles deaths: 1999–2004. *Wkly Epidemiol Rec* 2006; 81:90–4.
- Dowdle WR. The principles of disease elimination and eradication. *Bull World Health Organ* 1998; 76(Suppl 2):22–5.
- Spika JS. Measles elimination 2010 target: the need to meet the specific risk group. *Euro Surveill* 2006; 11:202.
- Centers for Disease Control and Prevention. Measles outbreak—Netherlands, April 1999–January 2000. *MMWR Morb Mortal Wkly Rep* 2000; 49:299–303.
- van Treeck U. Measles outbreak in Germany: over 1000 cases now reported in Nordrhein Westfalen. *Euro Surveill* 2006; 11:E060511.
- Spika JS, Aidyralieva C, Mukharskaya L, et al. Measles outbreak in The Ukraine, 2005–2006. *Euro Surveill* 2006; 11:E060309.
- Loewenberg S. The health of Europe's most marginalised populations. *Lancet* 2006; 368:2115.
- Peña-Rey I, Castellanos T, Suárez B, Alcalde E, Martínez de Aragón MV. Evaluación del plan nacional de eliminación del sarampión en España: año 2005. *Boletín Epidemiológico Semanal (BES)* 2006; 14:121–7.
- García-Comas L. Measles outbreak in the region of Madrid, Spain, 2006. *Euro Surveill* 2006; 11:E060330.
- Perucha M, Ramalle-Gomara E, Lezaun ME, et al. A measles outbreak in children under 15 months of age in La Rioja, Spain, 2005–2006. *Euro Surveill* 2006; 11:267–70.
- Institut d'Estadística de Catalunya. Anuari Estadístic de Catalunya. 1 September 2007. Available at: <http://www.idescat.net/es/>. Accessed 15 December 2007.
- Departament de Sanitat i seguretat Social. Guia per a l'eliminació del xarampió a Catalunya. Barcelona: Generalitat de Catalunya, 1998.
- Dominguez A, Vidal J, Plans P, et al. Measles immunity and vaccination policy in Catalonia. *Vaccine* 1999; 17:530–4.
- Departament de Salut. El xarampió a Catalunya: malaltia importada i desplaçament cap a l'edat adulta. *Butlletí Epidemiològic de Catalunya (BEC)* 2005; 26:81–5.
- Surveillance guidelines for measles and congenital rubella infection in the WHO European Region. 2003. Available: <http://www.euro.who.int/document/>. Accessed 15 December 2007.
- Helfand RF, Heath JL, Anderson LJ, Maes EF, Guris D, Bellini WJ. Diagnosis of measles with an IgM capture EIA: the optimal timing of specimen collection after rash onset. *J Infect Dis* 1997; 175:195–9.
- Centers for Disease Control and Prevention. Manual for the surveillance of vaccine-preventable diseases. 2006. Available at: <http://www.cdc.gov/vaccines/Pubs/surv-manual/>. Accessed 9 July 2008.
- Mosquera MM, Ory F, Echevarria JE. Measles virus genotype circulation in Spain after implementation of the national measles elimination plan 2001–2003. *J Med Virol* 2005; 75:137–46.
- Mosquera MM, de Ory F, Moreno M, Echevarria JE. Simultaneous detection of measles virus, rubella virus, and parvovirus B19 by using multiplex PCR. *J Clin Microbiol* 2002; 40:111–6.
- Borras E, Dominguez A, Batalla J, et al. Vaccination coverage in indigenous and immigrant children under 3 years of age in Catalonia (Spain). *Vaccine* 2007; 25:3240–3.
- Hersh BS, Markowitz LE, Maes EF, et al. The geographic distribution of measles in the United States, 1980 through 1989. *JAMA* 1992; 267:1936–41.
- Barrabeig I, Rovira A, Torner N, Dominguez A. Brote familiar de sarampión en un municipio de la comarca de la Anoia (Barcelona). *Vacunas* 2004; 5:10–5.
- Parker AA, Staggs W, Dayan GH, et al. Implications of a 2005 measles outbreak in Indiana for sustained elimination of measles in the United States. *N Engl J Med* 2006; 355:447–55.
- Ehresmann KR, Crouch N, Henry PM, et al. An outbreak of measles among unvaccinated young adults and measles seroprevalence study: implications for measles outbreak control in adult populations. *J Infect Dis* 2004; 189(Suppl 1):S104–7.
- Castell J, Fernando PE, Rullan JV, Nieto-Sandoval A. Intervention in a measles outbreak. *Enferm Infecc Microbiol Clin* 1996; 14:426–32.
- van den Hoff S, Meffre CM, Conyn-van Spaendonck MA, Woonink F, de Melker HE, van Binnendijk RS. Measles outbreak in a community with very low vaccine coverage, the Netherlands. *Emerg Infect Dis* 2001; 7(3 Suppl):593–7.
- Boncompagni G, Incandela L, Bechini A, et al. Measles outbreak in Grosseto, central Italy, 2006. *Euro Surveill* 2006; 11:E060803.
- Filia A, Brenna A, Pana A, Cavallaro GM, Massari M, Ciofi degli Atti ML. Health burden and economic impact of measles-related hospitalizations in Italy in 2002–2003. *BMC Public Health* 2007; 7:169.
- van den Hoff S, Conyn-van Spaendonck MA, van Steenberghe JE. Measles epidemic in the Netherlands, 1999–2000. *J Infect Dis* 2002; 186:1483–6.
- Gee S, Carton M, Cotter S. Measles increase in Ireland, 2004. *Euro Surveill* 2004; 8. Available at: <http://www.eurosurveillance.org/ew/2004/040923.asp#3>. Accessed 18 July 2008.
- García F. Actuación ante un brote de sarampión: la experiencia de Almería en el año 2003. In: Campins M, Moragas F, eds. *Vacunas*. Barcelona: Proas Science, 2004:189–201.
- Muscat M, Christiansen AH, Persson K, et al. Measles outbreak in the Oresund region of Denmark and Sweden. *Euro Surveill* 2006; 11(3):E060330.
- Orenstein WA, Strebel PM, Papania M, Sutter RW, Bellini WJ, Cochi SL. Measles eradication: is it in our future? *Am J Public Health* 2000; 90:1521–5.
- Pabst HF, Boothe PM, Carson MM. A comparison of alternate immunization regimes for measles in vaccinated populations. *Vaccine* 1999; 17:182–92.
- Mosquera MM, de OF, Gallardo V, et al. Evaluation of diagnostic markers for measles virus infection in the context of an outbreak in Spain. *J Clin Microbiol* 2005; 43:5117–21.
- Filia A, Curtale F, Kreidl P, et al. Cluster of measles cases in the Roma/Sinti population, Italy, June–September 2006. *Euro Surveill* 2006; 11:E061012.