Household-acquisition of measles and illness severity in an urban community in the United States*

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SUMMARY

Studies from developing countries suggest that persons with household-acquired (HA) measles are at greater risk of severe illness than persons with community-acquired (CA) infection. Reported measles cases occurring among Milwaukee residents from May 1989 to June 1990 were used to assess whether household-acquisition was a risk factor for severe measles in the United States. A case was classified as HA if onset of rash occurred 7–18 days after onset of rash in another case in the same household. Hospitalization rates were similar for 128 patients with HA measles (27%) and for 1004 patients with CA measles (26%). Multiple logistic regression was used to evaluate the association between hospitalization and household-acquisition after controlling for socioeconomic status, measles vaccination history, age, race, and date of onset of rash. Patients with HA measles were no more likely to be hospitalized than patients with CA measles (odds ratio 0.9, 95% confidence interval 0.6, 1.5). HA measles cases were not more severe than CA measles cases during this urban outbreak in the United States.

INTRODUCTION

Identification of factors associated with increased measles severity could stimulate delivery of preventive services to persons at greatest risk. Factors previously associated with severe measles include poor nutrition, suboptimal clinical care, and young age at time of infection [1–4]. Greater intensity of exposure has also been suggested as a risk factor for severe measles, based on studies conducted in developing countries which demonstrated that cases acquired within households are more severe than cases acquired outside [5–10]. Moreover,

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analyses of historical data from measles outbreaks in England during the late nineteenth century and in Denmark during the early twentieth century have shown a similar pattern [11, 12]. Measles outbreaks occurring in the City of Milwaukee during 1989 and 1990 provided an opportunity to assess the relationship between household transmission and measles severity in an urban United States population in the late twentieth century.

METHODS

Study population

In Wisconsin, all suspected or confirmed cases of measles are notifiable to the respective local public health agency and the Division of Health (DOH) within 24 h of the time measles is suspected. For the purpose of this study, a case of measles was defined as an illness characterized by a generalized maculopapular rash for ≥ 3 days, a temperature ≥ 38.3 °C, and at least one of the following: cough, coryza, or conjunctivitis [13]. The surveillance case records of persons with measles reported to the Wisconsin Division of Health were reviewed. Data in the records were collected by public health professionals from city or state health departments during routine interviews with family members or health-care providers of reported case-patients using a standardized measles case surveillance form. Measles-related hospitalization was used to identify case-patients with severe illness. History of measles vaccination required either written documentation of the date that measles vaccine was administered or telephone confirmation from the health care provider who administered the vaccine. A person was classified as vaccinated against measles only if vaccine was administered ≥ 15 days prior to onset of rash. Fatal cases were further investigated by hospital record review. A death was classified as measles-related if it occurred secondary to a known complication of measles within 30 days of rash onset. Of 1196 Milwaukee city residents who experienced rash onset from 1 May 1989 to 30 June 1990, the records of 1146 included complete home address and date of rash onset and were included in the review.

Case classification

Case-patients were grouped into households by home address. Cases were then classified as either household-acquired or community-acquired. A case was classified as household-acquired if rash onset occurred 7–18 days after rash onset in a previous household case. A case was classified as community-acquired if it occurred in a household with only one reported measles case or if rash onset occurred 0–3 days or ≥ 21 days after rash onset in a previous household case. For 14 case-patients with rash onset 4–6 days or 19–20 days after rash onset in a previous household case, the most likely setting of measles exposure could not be determined, and they were excluded from the analysis. (Fig. 1) Thus, 1132 case-patients were included in the analysis. Using the home address listed in the case record, each household was assigned to one of 218 census tracts within the city. Census tract-specific median annual household income (MAHI) from the US Special Census of 1985 was available for 215 census tracts allowing estimation of case-patient socioeconomic status (SES) for 1102 (97%) case-patients [14].

Fig. 1. Interval from rash onset in the initial household case-patient until rash onset in other case-patients in 163 households with multiple reported cases of measles, Milwaukee, 1989-90. ▨, Household-acquired; ■, not included in analysis; ▩, community-acquired.

Data analysis

Epiinfo version 5.01a (Centers for Disease Control, Atlanta, GA) was used for univariate analysis. Tests for statistical significance were performed using the Mantel-Haenszel chi-square test or chi-square for linear trend. Taylor series confidence intervals were calculated for relative risks. Mult-LR (Ludwig Cancer Institute, São Paulo, Brazil) was used to perform multiple logistic regression by the unconditional maximum likelihood method [15]. Continuous variables (census tract MAHI, age, and date of rash onset) were categorized and analysed using a logistic regression model for convenient estimation of adjusted odds ratios and 95% confidence intervals.

RESULTS

Description of study population

Of 1132 case-patients with records which included a complete home address, 128 (11%) had onset of rash 7-21 days after rash onset in another household member and were classified as having household-acquired measles. The remaining 1004 cases were classified as community-acquired, including 754 cases occurring as a single case in the household, 163 cases occurring as the initial case within a household where multiple cases occurred, and 87 cases in patients with rash onsets 0-3 days or ≥ 21 days after rash onset in a previous household case (Fig. 1).

The 1132 cases occurred during two distinct outbreaks [16]. An outbreak of 31 cases during May and June 1989 primarily involved previously vaccinated students at one high school; a larger and more widespread outbreak occurred

Table 1. *Characteristics of 128 patients with household-acquired measles and 1004 patients with community-acquired measles, Milwaukee, May 1989–June 1990*

Case-patient characteristic	Total no.	Household-acquired	Community-acquired	<i>P</i>
		no. (%)	no. (%)	
Hospitalized for measles	290	34 (27)	256 (26)	0.79*
Age				
0–15 months	290	28 (22)	262 (26)	0.49*
16–59 months	398	50 (39)	348 (35)	
≥ 60 months	444	50 (39)	394 (39)	
Gender				
Male	566	62 (48)	504 (50)	0.71*
Female	566	66 (52)	500 (50)	
Race				
Black	597	71 (55)	526 (52)	0.80*
Non-black	105	11 (9)	94 (9)	
Unknown	430	46 (36)	384 (38)	
Low SES†	271	39 (32)†	232 (24)†	0.04*
Vaccinated against measles‡	291	24 (19)	267 (27)	0.06*
Date of rash onset				
May–Jul 1989	32	1 (1)	31 (3)	0.27§
Aug–Oct 1989	97	12 (9)	85 (8)	
Nov–Dec 1989	464	43 (34)	421 (42)	
Jan–Feb 1990	302	45 (35)	257 (26)	
Mar–Apr 1990	195	25 (20)	170 (17)	
May–Jun 1990	42	2 (2)	40 (4)	

* Mantel–Haenszel Chi-square test.

† Census tract specific median annual household income < \$13000; includes 122 patients with household-acquired and 980 patients with community-acquired measles for whom census tract median annual household income was available.

‡ After the first birthday and ≥ 15 days prior to rash onset.

§ Chi-square for trend.

during August 1989–June 1990 and involved many unvaccinated preschool age children [16, 17].

The case-patients ranged in age from 29 days to 36 years (median 40 months). Of 702 case-patients of known racial/ethnic background, 597 (85%) were black; 72 (10%), white; 20 (3%), hispanic; 12 (2%), Asian; and 1 (0.1%) native American. By comparison, 30% of the total population of Milwaukee is black [17]. Documentation of at least one vaccination against measles after the first birthday and ≥ 15 days prior to rash onset was obtained from 291 (26%) case-patients. The median value census tract specific median household income (MAHI) was \$16520 (range: \$7041–\$35145), and 271 (25%) of 1102 case-patients for whom data were available resided in a census tract with a MAHI of under \$13000.

Hospitalization

The risk of hospitalization was similar for case-patients with household- and community-acquired measles (Table 1). Additionally, case-patients with household-acquired measles did not differ significantly from those with community-

Table 2. Case-patients hospitalized by date of rash onset

Date of rash onset	Total no.	Hospitalized
		no. (%)
May-Jul 1989	32	1 (3)
Aug-Oct 1989	97	42 (43)
Nov-Dec 1989	464	113 (24)
Jan-Feb 1990	302	85 (28)
Mar-Apr 1990	195	39 (20)
May-Jun 1990	42	10 (24)

acquired measles regarding age, race, and date of rash onset. Case-patients with household-acquired measles were significantly more likely to live in a census tract with MAHI of < \$13000 than those with community-acquired infection (Table 1). A slightly lower proportion of case-patients with household-acquired measles were vaccinated against measles than those with community-acquired disease ($P = 0.06$).

The risk of hospitalization did not differ for case-patients with household- and community-acquired infection when the analysis was restricted to children < 24 months old or to black children. Of 404 children < 24 months old with measles, 18 of 42 (43%) with household-acquired cases compared to 136 of 362 (38%) with community-acquired cases were hospitalized ($P = 0.50$). Among 597 black case-patients, 19 of 71 (27%) with household-acquired cases compared to 134 of 526 (25%) with community-acquired measles were admitted to a hospital ($P = 0.82$).

Measles-related illness resulted in hospitalization of 290 (26%) case-patients. One hundred and eight (37%) of 290 case-patients < 15 months old, 110 (28%) of 398 case-patients 16 through 59 months old, and 72 (16%) of 444 case-patients age ≥ 60 months old were hospitalized (trend chi square $P < 0.0001$). Two hundred and fifty-three (30%) of 841 case-patients lacking documentation of measles vaccination were hospitalized compared to 37 (13%) of 291 case-patients vaccinated against measles (RR = 2.4, 95% CI 1.7, 3.3). The proportion of case-patients hospitalized was similar when compared by race/ethnic category. Proportions hospitalized included 153 (26%) of 579 black case-patients, 23 (22%) of 105 non-black case-patients, and 114 (27%) of 430 case-patients of unknown racial/ethnic background. Fifty-seven (21%) of 271 case-patients residing in census tracts with MAHI < \$13000 were hospitalized compared to 222 (27%) of 831 case-patients residing in census tracts with MAHI $\geq$ \$13000 (RR = 0.8, 95% CI 0.6, 1.0).

Table 2 shows the number of non-hospitalized and hospitalized case-patients during each of six time intervals during the study period. When patients with rash onset between May 1989 and July 1989 (the period of the first, smaller outbreak) are excluded from analysis, patients with rash onset during the first 3 months of the second outbreak were more likely to be hospitalized than patients with rash onset later in the study period, 42 (43%) of 97 patients with rash onset during August to October 1989 were hospitalized, compared to 247 (25%) during November 1989 to June 1990 (RR = 1.8, 95% CI 1.4, 2.3).

A logistic regression model was used to evaluate the association between

Table 3. *Characteristics associated with hospitalization based on a logistic regression model for 1102 measles case-patients, Milwaukee, May 1989–June 1990*

Case-patient characteristic	No.	Estimated odds ratio	95% Confidence interval	P value
Case classification				
Community-acquired	122	Reference		
Household-acquired	980	0.9	0.6, 1.5	0.79
Age				
0–15 months	278	Reference		
16 months–4 years	389	0.7	0.5, 1.0	0.05
≥ 5 years	435	0.4	0.3, 0.7	< 0.01
Race				
Black	582	Reference		
Non-black	102	1.8	0.8, 4.0	0.15
Unknown	418	1.0	0.7, 1.4	0.94
Census tract MAHI*				
< \$13000	271	Reference		
≥ \$13000	831	1.4	1.0, 2.0	0.04
Vaccinated against measles				
Yes	563	Reference		
No	539	2.3	1.5, 3.5	< 0.01
Date of rash onset				
May–Jul 1989	30	Reference		
Aug–Oct 1989	90	2.1	0.8, 6.0	0.14
Nov–Dec 1989	458	1.3	0.5, 3.6	0.64
Jan–Feb 1990	292	1.5	0.5, 4.4	0.45
Mar–Apr 1990	190	0.9	0.3, 2.9	0.91
May–Jun 1990	42	0.5	0.0, 4.8	0.51

* Median annual household income.

household-acquisition of measles and measles-related hospitalization while controlling for potential confounding case-patient characteristics (Table 3). Only the 1102 patients for whom census tract MAHI was available were included in the model. Case-patients with household-acquired measles were no more likely to be hospitalized than those with community-acquired infection after controlling for patient age, race, census tract MAHI, measles vaccination status, and date of rash onset. Hospitalization was more likely among younger patients, those of higher SES, and those with no history of measles vaccination.

Mortality

Measles-related illness resulted in death for three (0.3%) case-patients. Each of the three case-patients who died of measles was black, lacked a history of vaccination against measles, and resided in a census tract with a MAHI of ≥ \$13000. Ages at time of rash onset for the three who died were 7, 13, and 20 months. Two of the three fatal cases were classified as household acquired; however, because the number of measles-related deaths is small, meaningful statistical interpretation of these data is obviated.

DISCUSSION

Our findings suggest that during the measles outbreaks that occurred in Milwaukee during 1989 and 1990, household-acquired measles was not more severe than community-acquired measles. While this result contrasts with conclusions from studies conducted in developing countries [5–10], it is in agreement with a recent study conducted among the Amish in Pennsylvania [18]. Most studies of household-acquisition in developing countries used death rather than hospitalization as the marker of severe illness. A review of children evaluated for measles in the out-patient departments at one Milwaukee hospital between August 1989 and April 1990 showed that hospital admission was independently associated with greater severity of illness, the presence of measles-related complications, younger age, and illness onset earlier during the outbreak period [19]. Therefore, hospitalization should be a suitable marker for illness severity after controlling for patient age and the interval of onset during the outbreak.

One possible explanation for the disparity between findings from developing countries and the United States is the role of factors that may be associated with household crowding such as nutritional status. Anthropometric indices or other measures of nutritional status were not available for the case-patients in this study. Additionally, the intensity of measles exposure among patients with household-acquired infection in our study may have differed from that of patients in developing countries due to differences in household structure. There may be more opportunity for isolation of household members in an American home. However, any protective effect from isolation within the home is likely to be minimal since measles is highly infectious for non-immune persons, airborne transmission without direct person-to-person contact has been reported, and the period of greatest infectivity occurs during the prodromal phase of the illness [20–22].

The lower risk of hospitalization for patients living in poor census tracts (defined as the lowest quartile of MAHI) was unexpected. The difference may reflect less access to medical care for those living in poorer areas. This finding should be interpreted with caution since census tract MAHI may not accurately reflect the actual household income of patients. The association between the lack of vaccination and hospitalization may reflect attenuation of measles illness severity among those who have been vaccinated [23].

The findings of this study are based on public health surveillance records and therefore are subject to biases inherent to passive surveillance systems. During urban measles outbreaks in St Louis in the early 1970s and New York City during 1989–91, it is estimated that 55–85% of cases were not reported to public health authorities [24, 25]. The degree of under-reporting of cases during the Milwaukee outbreaks has not been assessed. It is likely that cases requiring medical evaluation were more likely to be reported. Subsequent cases occurring within the household may have been less likely to result in medical evaluation and thus be reported. Therefore, there may have been a selection bias favouring the reporting of household-acquired cases that were more severe relative to community-acquired cases. Such selection bias would be expected to exaggerate the proportion of patients with household-acquired measles that were hospitalized; however, this

effect may have been minimal since no difference in hospitalization was observed when patients with household-acquired infection were compared to those with community-acquired illness. The appropriate classification of cases as household- or community-acquired is dependent on the quality of data collected. Records with missing or incomplete home address or rash onset date were excluded from the analysis to minimize misclassification of cases.

Appropriate classification by reporting clinicians of patients with febrile illness and rash as having measles or another childhood exanthem is also critical to the quality of these data. While Koplik spots are characteristic of measles, other symptoms of measles may be similar to those of rosela, scarlatina, and rubella. The reliability of case report of measles is probably higher than that for most other infectious diseases [4], particularly during large outbreaks among unvaccinated children. Studies accessing the sensitivity and specificity of the clinical diagnosis of measles in outbreak and non-outbreak settings are warranted.

During the 1989–90 measles outbreaks in Milwaukee, 11 % of measles cases appear to have been acquired in the home. Of measles cases with known setting of exposure reported to the CDC during 1988 and the first half of 1989, 16 and 25 % were attributed to household-acquisition, respectively [26, 27]. While our study did not find measles to be more severe among patients with household-acquired infection, it did demonstrate the considerable role that household transmission plays in outbreak propagation and highlights the need for preventing transmission within the home. The Immunization Practices Advisory Committee (ACIP) to the Public Health Service and the American Academy of Pediatrics Committee on Infectious Diseases recommend administration of measles vaccine within 72 h of exposure to non-immune immunocompetent household contacts over 12 months of age to prevent infection [28, 29]. Adherence to these recommendations requires rapid reporting of newly identified measles cases to public health officials and speedy delivery of preventive services. Timely post-exposure vaccination of household contacts may not only prevent transmission of measles within the household but will also increase vaccine coverage in the population during any future outbreak. One recently published study of the 1989–90 measles outbreaks in Milwaukee demonstrated that measles attack rates were highest in census tracts with the lowest mean immunization rates and that even modest improvements in immunization coverage among young children confer substantial protection against measles outbreaks [17]. Increasing the level of vaccine coverage is imperative to prevention of measles-related morbidity and mortality [17, 28, 30].

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