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Pediatrics 2010;125;747

DOI: 10.1542/peds.2009-1653 originally published online March 22, 2010;

The online version of this article, along with updated information and services, is located on the World Wide Web at:

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American Academy of Pediatrics

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Measles Outbreak in a Highly Vaccinated Population, San Diego, 2008: Role of the Intentionally Undervaccinated

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KEY WORDS

measles vaccine, disease outbreaks, vaccine-preventable diseases, vaccine refusal, vaccination coverage

ABBREVIATIONS

CDC—Centers for Disease Control and Prevention
PBE—personal-beliefs exemption

Preliminary results of this study were presented at the 57th annual Epidemic Intelligence Service conference; April 18, 2008; Atlanta, Georgia.

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention, US Department of Health and Human Services.

www.pediatrics.org/cgi/doi/10.1542/peds.2009-1653

doi:10.1542/peds.2009-1653

Accepted for publication Oct 20, 2009

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*



WHAT'S KNOWN ON THIS SUBJECT: In the relative absence of measles, public attention has increasingly focused on vaccine adverse events, raising concerns that vaccination refusal might decrease coverage to the point at which an imported case could reestablish ongoing viral transmission.



WHAT THIS STUDY ADDS: Despite high community vaccination coverage, measles outbreaks can occur among clusters of intentionally undervaccinated children, at major cost to public health agencies, medical systems, and families. Rising rates of intentional undervaccination can undermine measles elimination.

abstract

OBJECTIVE: In January 2008, an intentionally unvaccinated 7-year-old boy who was unknowingly infected with measles returned from Switzerland, resulting in the largest outbreak in San Diego, California, since 1991. We investigated the outbreak with the objective of understanding the effect of intentional undervaccination on measles transmission and its potential threat to measles elimination.

METHODS: We mapped vaccination-refusal rates according to school and school district, analyzed measles-transmission patterns, used discussion groups and network surveys to examine beliefs of parents who decline vaccination, and evaluated containment costs.

RESULTS: The importation resulted in 839 exposed persons, 11 additional cases (all in unvaccinated children), and the hospitalization of an infant too young to be vaccinated. Two-dose vaccination coverage of 95%, absence of vaccine failure, and a vigorous outbreak response halted spread beyond the third generation, at a net public-sector cost of \$10 376 per case. Although 75% of the cases were of persons who were intentionally unvaccinated, 48 children too young to be vaccinated were quarantined, at an average family cost of \$775 per child. Substantial rates of intentional undervaccination occurred in public charter and private schools, as well as public schools in upper-socioeconomic areas. Vaccine refusal clustered geographically and the overall rate seemed to be rising. In discussion groups and survey responses, the majority of parents who declined vaccination for their children were concerned with vaccine adverse events.

CONCLUSIONS: Despite high community vaccination coverage, measles outbreaks can occur among clusters of intentionally undervaccinated children, at major cost to public health agencies, medical systems, and families. Rising rates of intentional undervaccination can undermine measles elimination. *Pediatrics* 2010;125:747–755

Measles is a highly infectious viral illness that is associated with fever and rash but occasionally produces serious complications including pneumonia and encephalitis, which may lead to death.¹ Before introduction of vaccination in the United States in 1963, measles caused an estimated 4 million cases, with 48 000 hospitalizations and 500 deaths reported annually.¹ Because of high 2-dose vaccine coverage, endemic transmission of measles was declared eliminated from the United States in 2000.² Lack of personal experience with measles has led certain parents to question the need for vaccination and to focus on vaccine adverse events.³ However, measles remains endemic in other countries,^{4,5} and the risk of imported disease persists. The number of measles cases in the United States for 2008 (140) was the largest since 1996 (508), before measles transmission had been eliminated (CDC, unpublished data). Existing data suggest that patients in almost all cases were US residents and that a majority of them were unvaccinated because of philosophical or religious beliefs.⁶

In January 2008, an intentionally unvaccinated 7-year-old boy who was unknowingly infected with measles returned to San Diego, California, from Switzerland.⁷ The resulting outbreak was the largest in San Diego County since 1991. To understand the role of intentional undervaccination and its threat to measles elimination, we examined measles-transmission patterns, vaccination rates, outbreak costs, and beliefs/characteristics of parents who decline vaccination for their children.

METHODS

Definitions

A case-patient was defined as a person with symptoms that met the standard clinical definition of measles⁸ and

whose infection was confirmed by a laboratory or who was epidemiologically linked to a patient with laboratory-confirmed infection. Laboratory confirmation was defined as serum positivity for anti-measles immunoglobulin M or cell-culture isolation of measles virus. Molecular typing was performed by using protocols recommended by the World Health Organization.⁹ The outbreak period was defined as a 14-day incubation period before the index patient's rash onset through 1 incubation period after the last patient's rash onset (January 11 through February 29, 2008). Patients were considered infectious from 4 days before to 4 days after rash onset.¹⁰ A person-day exposure was defined as the exposure of a person without measles, at some point during the course of a calendar day, to a person who was infectious with measles or to the closed environments visited by that person (for up to 2 hours after leaving).¹¹

Patients and Exposures

We interviewed all case-patients to obtain information about demographic characteristics, the likely transmission event, and persons they potentially exposed. Immunization status was verified by review of individual, provider, or school vaccination records.

Vaccination and Vaccination-Exemption Rates

The 2006 National Immunization Survey provided data on preschool vaccination rates in San Diego County, California, and the United States.¹² The California Department of Health Services Kindergarten Assessment provided rates of 2007 kindergarten-entry vaccination for San Diego County and California. In California, children can be exempted from school vaccination requirements if their parents/guardians sign the California School Immunization Record and claim a personal-

beliefs exemption (PBE) that indicates philosophic or religious opposition to vaccination. The Centers for Disease Control and Prevention (CDC) School Entry Immunization Assessment Report provided data on 2006–2007 national school-entry vaccination rates.¹³ To evaluate the association of income with vaccination-exemption rates, we obtained San Diego census-tract and zip-code-specific 2008 median income data from the San Diego Association of Governments (<http://datawarehouse.sandag.org>).

Attitudes of Persons Who Declined/Delayed Vaccination for Their Children

To characterize the attitudes of San Diego parents who chose not to vaccinate their children during the outbreak, we implemented a rapid mixed-method strategy¹⁴ that involved discussion groups and a network survey. Parents of patients with measles, unvaccinated quarantined families, and concerned parents from San Diego County were invited to participate in discussion groups (60- to 90-minute sessions facilitated by 2 behavioral scientists). Seventeen persons participated, of whom 11 reported declining or delaying vaccination for their children, and their views were included in the analysis. Major themes were derived from systematic review of the audio transcripts. Parents did not report affiliation with a common religious/secular organization but said that they accessed 2 Web-based parenting discussion sites. Although these parenting Web sites were not focused on vaccination issues, and the proportion of persons accessing the Web sites who had intentionally undervaccinated children was unknown, discussion-group participants reported that the sites were used by many parents with intentionally undervaccinated children to exchange views and information. With the assistance of discussion-

group participants, we conducted an online, anonymous survey regarding immunization perceptions and practices of this informal network. The content of the survey instrument was guided by the themes elicited in the discussion groups but included opportunities for open-ended responses. Discussion-group participants aided in recruitment of respondents. Included in this convenience sample were persons who responded during the collection period (June 10 through July 16, 2008), reported living in San Diego, and declined, or planned to decline, some or all vaccinations for their youngest child. Surveys were sent to 1642 e-mail accounts in the online parenting networks, and 256 surveys were returned during the collection period; a San Diego County residence was reported by 194 respondents, of whom 83 reported intentional under-vaccination and were included in our analysis.

Statistical Analysis

Bivariate associations of dichotomous variables were statistically evaluated by using Pearson's χ^2 and Fisher's exact test. For continuous variables, the Wilcoxon rank-sum test was used. Correlations of 2 continuous variables were quantified by using Spearman's rank-order correlation coefficient. Statistical analyses were performed by using SAS 9.1.3 (SAS Institute, Inc, Cary, NC).

RESULTS

Case Identification

We identified 12 case-patients with measles. All had a morbilliform rash and at least 2 of the following symptoms: fever, cough, coryza, or conjunctivitis. Ten were laboratory-confirmed (5 immunoglobulin M–positive, 5 with measles virus isolations), and 2 were epidemiologically linked to a laboratory-confirmed case. Three

measles virus specimens isolated from 3 different patients had the same genotype (D5) and identical molecular sequences (MVi/California.USA/6.08 [GenBank No. EU715978]), most closely resembling sequences isolated from a concurrent Swiss outbreak.⁴

Case-Patient Characteristics

Patient age ranged from 10 months to 9 years. Of the 12 case-patients, 11 were white and 6 were female. All were unvaccinated: 9 had parents who had signed PBEs, and 3 were below the minimum age for vaccination. All had parents who were college-educated and lived in middle- to upper-income neighborhoods (zip code median household income: \$44 521–\$72 806). Five patients required urgent outpatient care, and an infant aged 10 months (too young to be vaccinated) was hospitalized for 72 hours and received intravenous hydration for diarrhea. No deaths or long-term complications occurred.

Transmission Patterns

First Generation (1 Case Spread to 8)

On January 13, 2008, the 7-year-old male index patient returned from Switzerland, asymptomatic but incubating measles. He transmitted infection to his 9-year-old unvaccinated sister and 3-year-old unvaccinated brother. On January 24, 2008, after 2 days of fever and conjunctivitis, the index patient attended charter school A. Forty-one of the 377 students (11%) at charter school A were unvaccinated for measles because of personal beliefs, and 2 children became infected. The next day, the index patient developed a rash and was taken to an internist who diagnosed an upper-respiratory infection and prescribed amoxicillin. No airborne-infection isolation precautions were taken; adults in the waiting room were exposed, but none of them became infected. Later the same day,

the index patient was taken to pediatric clinic A, where scarlet fever was diagnosed; again, amoxicillin was prescribed. No respiratory precautions were taken, 6 children were exposed, 5 were unvaccinated, and 4 were infected (3 infants too young for vaccination and a 2-year-old whose parents had intentionally delayed measles vaccination). The next day, after telephone consultation with a pediatrician, the child was taken for measles serology testing. No respiratory precautions were taken in the clinical laboratory, and no records were kept to permit identification of potentially exposed persons. With worsening fever, the index patient was taken to a children's hospital emergency department, where measles was clinically diagnosed. The patient was triaged, placed in a negative-airflow waiting room, and then examined in a room with curtain-separated beds and no negative airflow, all without wearing a mask. Thirteen children were potentially exposed, and 5 were unvaccinated infants; none of them were infected (Fig 1).

Second Generation (8 Cases Spread to 3)

By February 1, 2008, when the San Diego Immunization Branch was notified of the index patient's positive measles serology, 4 of the 8 secondary case-patients were already infectious. The index patient's sister infected 2 schoolmates and exposed an unknown number of children at a dance studio. One infected classmate of the index patient infected his own younger brother and exposed 10 children at a pediatric clinic, 18 children and adults at a clinical laboratory, and an unknown number at 2 grocery stores and a circus. Another infected classmate of the index patient exposed an unknown number at an indoor amusement facility. Four secondary patients from clinic A returned to the same clinic while

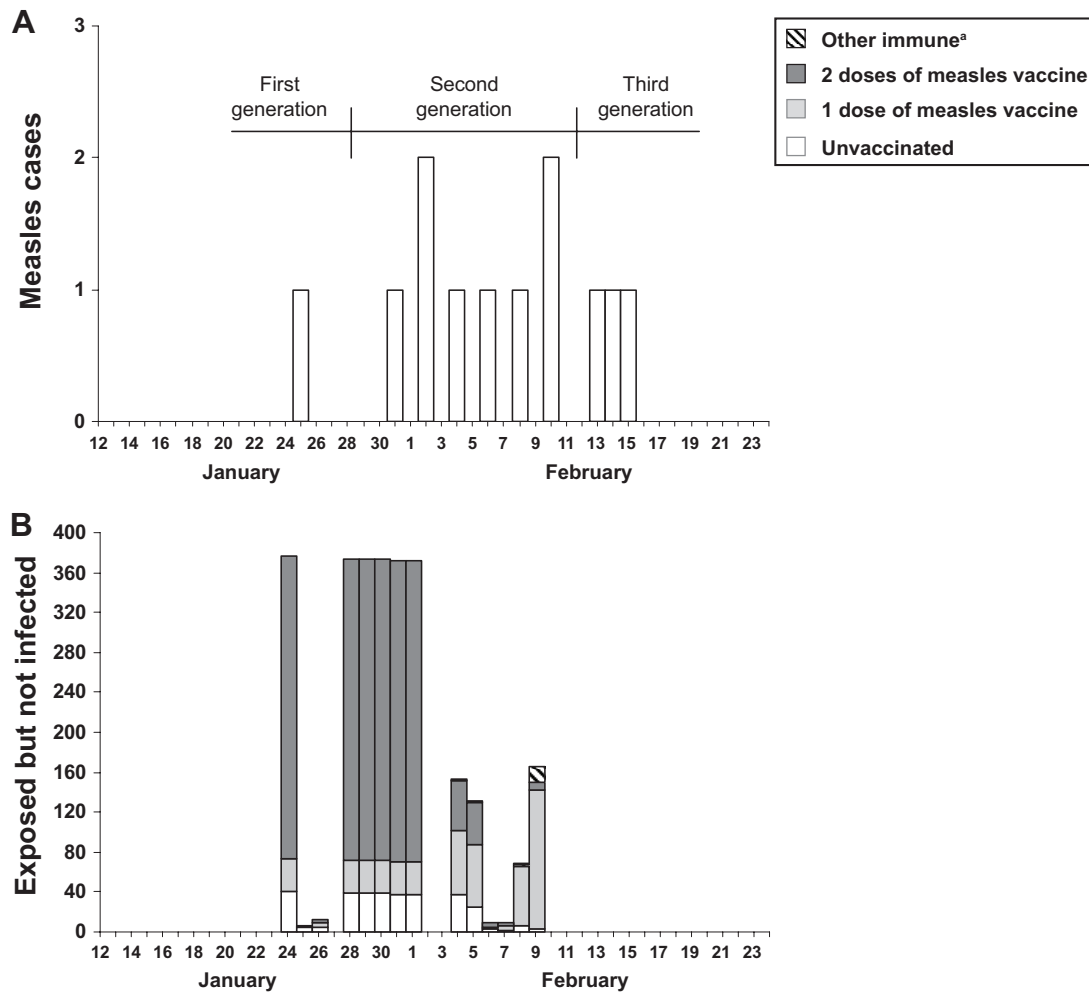


FIGURE 1 Case-patients and exposed persons according to status of immunity. A, The 12 patients with measles. B, The 2800 potential measles person-day exposures among 839 persons. ^a Otherwise immune according to Advisory Committee on Immunization Practice standards.¹⁵

symptomatic on 4 separate days before adequate airborne-infection isolation was implemented, thus exposing 37 children. Of these same 4 patients, 1 exposed an additional 95 children in a preschool on 2 consecutive days, 6 patients at an outpatient laboratory, and 47 children at a swimming-instruction facility; the second patient exposed children in the same swimming class; the third patient exposed 55 students in a school and 10 persons at an outpatient laboratory; and the fourth patient potentially exposed 166 passengers on an airplane flight to Hawaii.

Third Generation (3 Cases Spread to 0)

One patient had already been quarantined before symptom onset, and the 2 other case-patients were isolated before transmitting the virus.

Containment Measures

A total of 839 persons were identified who were exposed to measles (involving 2800 person-day exposures). Of the 839, 106 (13%) (all children) lacked proof of measles immunity according to the standards of the Advisory Committee on Immunization Practices.¹⁵ Twenty were considered to have had minimal exposure be-

cause of the extremely short case-patient contact times or the use of airborne-infection isolation precautions in health care facilities. Of the remaining 86, 38 (44%) had parents who had declined (36) or intentionally delayed (2) vaccination. Of these, 32 (84%) were still eligible to receive postexposure measles vaccination prophylaxis, of whom 13 (41%) accepted the vaccine. The remaining 73 unvaccinated children (25 [34%] children whose parents declined vaccination and 48 [66%] children who were too young to be vaccinated) were placed under 21-day quarantine.

TABLE 1 Estimated Cost of Personnel, Time, and Materials: San Diego Measles Outbreak, 2008

	San Diego County Health and Human Services Agency	California Department of Public Health	Total	%
Personnel directly involved, <i>n</i>	31	10	41	100.0
Time spent per activity, h ^a				
Investigation	399	11	410	23.5
Emergency response	479	136	615	35.2
Laboratory work	81	241	322	18.4
Vaccination	32	0	32	1.8
Other	366	2	368	21.1
Total time, h ^b	1355	390	1745	100.0
Percentage of overtime	15.9	6.1	15.7	—
Selected materials ^c				
Measles/mumps/rubella vaccine, No. of doses	5	0	5	—
Travel, mi	273	0	273	—
Estimated costs, US\$				
Wages and salaries ^d	92 552	8039	100 591	80.8
Overhead	17 766	608	18 375	14.8
Laboratory ^e	501	4750	5251	4.2
Measles/mumps/rubella vaccine ^f	163	0	163	0.1
Mileage ^g	138	0	138	0.1
Total costs, US	111 120	13 397	124 517	100.0

All costs are in 2008 US dollars. Estimated total response costs were obtained by adding the cost of gross wages, fringe benefits, overhead, and inputs and materials. Em dashes indicate that no data were reported or estimated for those entries.

^a Activities included in the investigation were tracking of cases, case interview, contact notification, and screening of suspected cases; in emergency response were information to the public, quarantine follow-up, treatment of cases, prophylaxis of contacts, enhanced surveillance, and isolation or quarantine.

^b The total number of hours included regular business hours used by the personnel and overtime nonbusiness hours (ie, during weekends or evenings).

^c The number of doses of measles/mumps/rubella vaccine reported by the San Diego Health Department used during the outbreak and quarantine.

^d Fringe benefits and overhead costs were included when reported or calculated by following the specific accounting method of each involved institution.

^e Cost for materials and laboratory work.

^f The unitary cost used is \$32.50 for 1 dose of measles/mumps/rubella vaccine.

^g Mile costs were calculated by multiplying \$0.51 by the total number of miles.

Costs

County and state personnel reported spending 1745 person-hours on investigation and containment efforts, producing a public-sector cost of \$124 517, or \$10 376 per case. Direct medical charges for the case-patients and exposed infants totaled \$16 163 (\$14 458 for the hospitalized infant), or \$1347 per case. Quarantined families reported average direct and indirect costs of \$775 per quarantined child. Total outbreak costs were \$176 980 (Table 1).

Vaccination Coverage

For preschool-aged children, first-dose measles vaccination coverage in San Diego was high and had overlapping confidence intervals with state and national coverage: 91.4% ± 4.0% (San Diego),

92.8% ± 2.7% (California), and 92.3% ± 0.6% (United States). For San Diego kindergarteners, aggregate coverage was higher: first dose, 97%; second dose, 95% (Fig 2A and 2B). However, among 643 surveyed schools, 56 (9%) enrolling 1858 students had first-dose coverage at <90%, among which 19 (3%) enrolling 399 students had coverage at <70%. Second-dose coverage at <90% was observed in 131 (20%) schools enrolling 5057 students, among which 31 (5%) enrolling 915 students had coverage at <70%.

PBEs to Vaccination

PBE Rates

Overall, 2.5% (972 of 39 132) of San Diego kindergarteners had parents who

had registered PBEs to vaccination. Compared with a 1.8% (587 of 33 405) aggregate exemption rate among children attending 404 general public schools, rates were significantly higher ($P < .001$) for children attending 34 public charter schools (11% [204 of 1870]) and 208 private schools (5% [181 of 3857]). The highest exemption rates (>40%) were observed in 10 schools with a total kindergarten enrollment of 284 children: 6 private (50%–100%), 2 public charter (55%–56%), and 2 general public (42%–50%). Schools and districts with high refusal rates tended to cluster. A group of 4 contiguous school districts (Fig 3 inset) had significantly higher kindergarten exemption rates than those of the rest of the county (168 of 1862 [9.0%] vs 804 of 37 270 [2.2%]; $P < .001$). Charter school A, with a 30% (12 of 40) kindergarten rate, was located in a district with a 2.2% exemption rate (Fig 3).

PBE and Measles Vaccination

Of the 377 total enrollees in charter school A, the parents of 65 (17%) children had signed PBEs. Of these, 28 (43%) children had received at least 1 antigen of the school-recommended vaccinations before the outbreak, including 24 (37%) who had received at least 1 dose of measles vaccine and 3 (5%) who had received 2 doses. Across all surveyed kindergartens, higher PBE rates correlated strongly with lower measles vaccination rates ($r = -0.87$; $P < .001$).

PBE and Income

In geographic analysis, higher general public school exemption rates correlated significantly ($P < .001$) with higher median income, examined either according to zip code ($n = 88$; $r = 0.48$) or census tract ($n = 325$; $r = 0.40$). Exemption rates for public charter and private schools, which lack prescribed catchment areas, tended

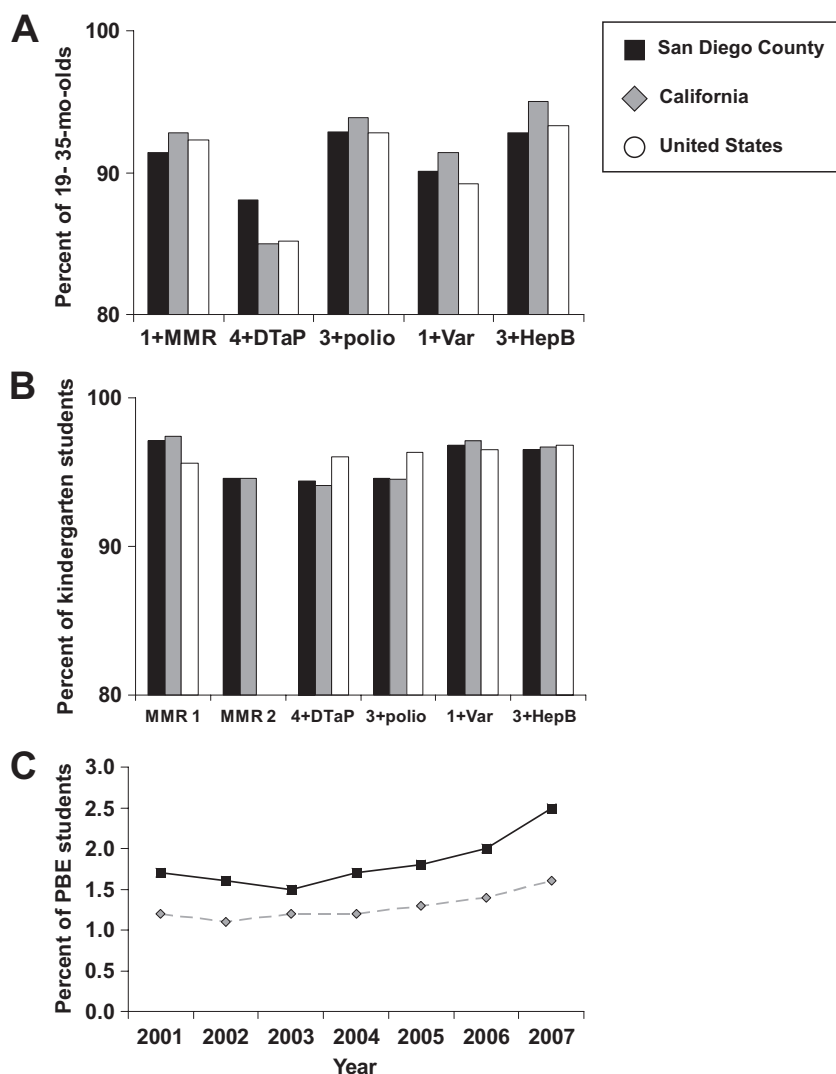


FIGURE 2 Vaccination rates. A, Percentage of coverage for children aged 19 to 35 months, according to the 2006 National Immunization Survey.¹² B, Percentage of coverage for children entering kindergarten, according to the 2007 California Department of Health Services Kindergarten Assessment and the 2006–2007 CDC School Entry Immunization Assessment Report.¹³ C, PBE rates according to the California Department of Health Services Kindergarten Assessment for 2001–2007.

to correlate with income, but the effect was not consistently significant. Compared with the rest of the county, the population living in census tracts within the group of 4 high-refusal districts (indicated by Fig 3 inset) was more likely to have high median household income (\$87 958 vs \$53 317; $P < .001$).

PBE Trends

For 7 years, San Diego PBE rates (1.1%–2.5%) have been higher than

California's average exemption rates overall (1.1%–1.6%). Both have been increasing (Fig 2C).

Attitudes of Parents With Intentionally Undervaccinated Children

Discussion Groups

Of the 11 participants who reported declining or delaying vaccination for 1 or more of their children, 3 were parents of 6 unvaccinated children with

measles (50% of case-families). Nearly all were white and college-educated, and 9 (82%) had incomes higher than \$100 000. They reported substantial skepticism of the government, pharmaceutical industry, and medical community. They believed vaccination was unnecessary, because most vaccine-preventable diseases had already been reduced to very low risk by improvements in water, sanitation, and hygiene and were best prevented by "natural lifestyles," including prolonged breastfeeding and organic foods. In contrast to the immunity produced by disease, they felt that vaccines could damage the immune system while producing a number of other immediate and long-term adverse health conditions, particularly those involving the child's neurologic system.

Online Parent Network Survey

Compared with the overall county population, survey respondents more often were non-Hispanic white (91% vs 50%), were college-educated (91% vs 34%), and had household incomes higher than \$100 000 (51% vs 19%). Two-thirds indicated that they would accept certain vaccinations, but three-quarters would not accept measles vaccination. Perceived adverse vaccine reactions, especially autism, were often cited by those who declined some or all vaccines (Table 2).

DISCUSSION

An intentionally unvaccinated 7-year-old unknowingly infected with measles returned from Switzerland, resulting in >800 known exposed persons and 11 additional cases. The outbreak was fueled by clusters of intentionally unvaccinated children and perpetuated by delayed clinical diagnosis and inadequate infection-control measures. Because of community vaccination rates of >90%, the outbreak began to subside before containment started, but

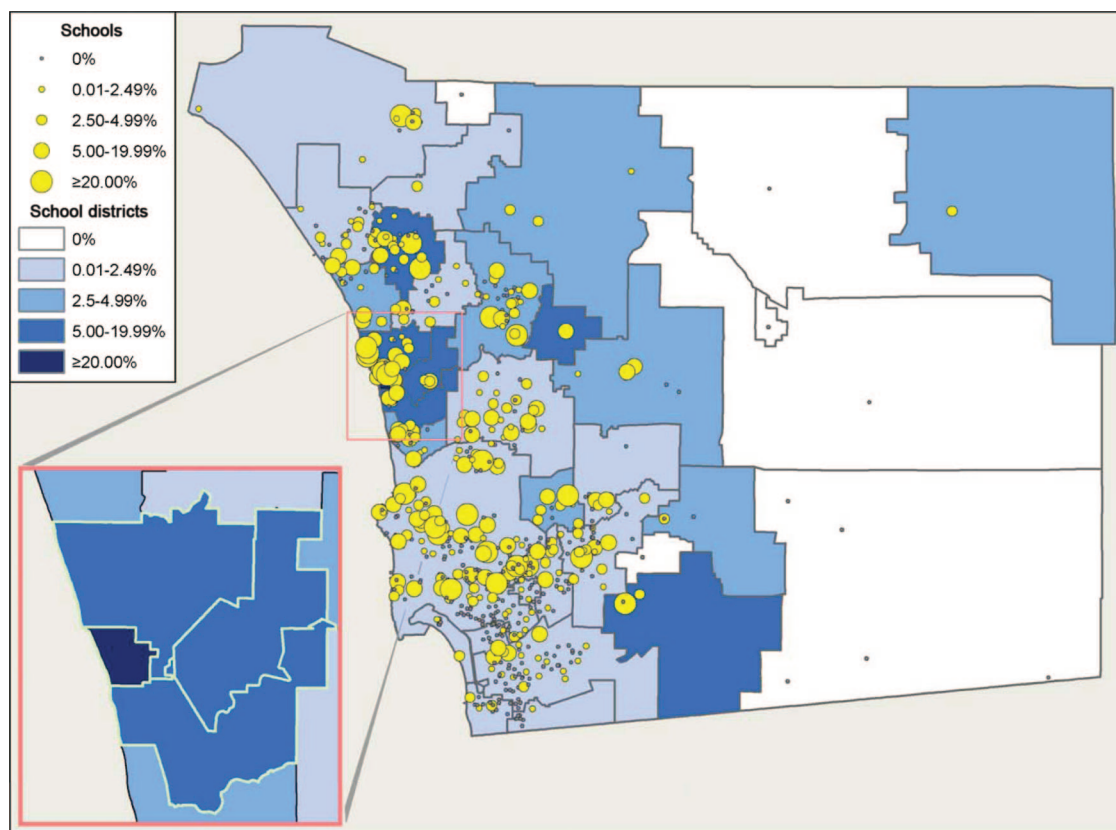


FIGURE 3

San Diego school PBE rates. Shown is a Geographic Information System (GIS) map of PBEs among San Diego County students entering kindergarten, according to school ($n = 643$) and public school district ($n = 19$) for 2007, according to the California Department of Health Services Kindergarten Assessment.

a vigorous public health response halted transmission beyond the third generation at a public-sector cost of more than \$10 000 per case. Results of discussion-groups and an online network survey suggested that parents of intentionally undervaccinated children tended to be white, college-educated, and of upper- and middle-income levels. The majority of them believed that a “natural lifestyle” protects children from vaccine-preventable diseases and that vaccines can cause multiple health conditions, especially autism.

During the 1980s and 1990s, undervaccination in the United States was primarily unintentional, associated with diminished access to health care, and was frequently observed among inner-city ethnic or racial minorities, inner-city families living in poverty,¹⁶ and

children whose mothers had limited education.¹⁷ Outbreaks attributable to vaccine refusal tended to be observed among religious groups with objections to vaccination (eg, Christian Scientists¹⁸ and the Amish¹⁹). In contrast, reluctance to vaccinate in the San Diego outbreak was associated with health beliefs, particularly among well-educated, upper- and middle-income segments of the population, similar to those seen in measles outbreak patterns elsewhere in 2008.⁶

Measles is among the most infectious viruses that affect humans.¹ The disease is communicable 4 days before onset of the characteristic rash,¹⁰ and delayed clinician recognition of measles is common in an era of elimination.²⁰ Fortunately, San Diego had preschool and school-aged measles vaccination rates that exceeded the commonly accepted

herd-immunity threshold for measles transmission.²¹ The school attended by the index patient had a 30% exemption rate among kindergarteners, but fortunately it was located in a school district with a 2% exemption rate. Of the 839 persons exposed, 87% were immune, and by the second generation, the spread rate had decreased to less than 1 per case. Although vaccine-induced antibody levels may wane in an elimination environment,²² no vaccine failures were detected.

However, if intentional undervaccination rates continue to rise, measles could again become an endemic disease, as has happened recently in the United Kingdom.²³ The clustering of vaccine refusal, as documented in San Diego and elsewhere,²⁴ is particularly worrisome, because foci of vaccine refusal can provide a reservoir of sus-

TABLE 2 Characteristics and Beliefs of Parents With Intentionally Undervaccinated Children: Respondents to the 2008 San Diego County Online Parent Network Survey

Demographic	Survey Respondents (N = 83)	
	n	%
Mother/stepmother	81	98.8
Age range, 25–44 y	71	86.6
White, non-Hispanic	70	90.9
College graduate or higher	74	91.4
Household Income		
Less than \$50 000	5	7.2
\$50 000–\$100 000	29	41.4
More than \$100 000	36	51.4
Practiced no religious faith	35	52.6
Refusal characteristic		
Level of refusal		
Refused all	27	32.5
Refused some	56	67.5
Refused measles-containing vaccine	63	75.9
Vaccination for international travel		
Accept	24	33.8
Refuse	23	32.4
Don't know	24	33.8
Family evolution of refusal ^a		
Decreasing level of refusal	0	0
No change in level of refusal	27	57.4
Increasing level of refusal	20	42.6
Moved from fully vaccinated to select or absolute refusal	11	55.0
Moved from select to absolute refusal	9	45.0
Concerning health condition		
Autism	63	79.8
ADD/ADHD	58	73.4
Asthma	58	73.4
Allergies	58	73.4
Inflammatory bowel disease	53	67.1
Source of information ^b		
Doctor	56	67.5
Internet sites	32	38.6
Alternative provider	27	32.5
CDC	25	30.1
Books	20	24.1
Influenced by provider (n = 49)		
Supported spacing or declining vaccines or offered an alternative schedule	25	51.0
Recommended spacing or declining vaccines	9	18.4
Aware of outbreak (n = 79)		
No change in vaccination practices	70	90.9
Reinforced ideas that vaccines are unnecessary	50	68.5

Not all variables were divided by the total survey respondents (n = 83) because of respondents answering “don't know” or “refuse.” ADD indicates attention-deficit disorder; ADHD, attention-deficit/hyperactivity disorder.

^a From oldest to youngest child in families with more than 1 child (n = 47).

^b Mentioned source at least once in top 3 sources.

ceptibility, enhancing spread of disease to the larger community, as occurred in the 2008–2009 measles resurgence in France.²⁵

Procedures that make claiming an exemption easier than providing

proof of vaccination have been associated with lower vaccination rates²⁶ and higher pertussis²⁷ and measles²⁸ incidence. California, where a child can be exempted with only a parent's signature, has among the easiest exemption processes in the nation.²⁸

The majority of parents in our network survey indicated that they took their health guidance from a mainstream health care provider and would accept vaccination under specific circumstances, yet many said their provider supported their decision not to vaccinate. It should be noted that 41% of the parents who had previously declined vaccination for their children accepted vaccination prophylaxis during the outbreak. Additional studies are needed to examine provider roles in intentional undervaccination.²⁹

This investigation was limited in multiple aspects. The total extent of community exposure to measles was unknown, because contact tracing was impractical at certain public venues. The discussion groups and network respondents were convenience samples. Containment costs were retrospectively measured with potential recall bias. Provider surveys were not conducted.

Despite these limitations, we believe that the San Diego measles outbreak illustrates the challenges of intentional undervaccination. Measles infects 20 million persons globally each year³⁰ and the risk for importation continues. Only maintenance of high vaccination coverage can prevent the return of endemic measles transmission in the United States.

ACKNOWLEDGMENTS

Personnel and other costs for investigation of the outbreak were provided by the County of San Diego Health and

Human Services Agency, the CDC, and the Council of State and Territorial Epidemiologists.

We thank Jennifer Nelson, MPH, Janaki Kari, MS, and Randall Young, MA, for Geographic Information System mapping; Allison Kennedy, MPH, for critically valuable input for the discussion group and survey design; Jane Seward, MBBS, for subject matter expertise and outbreak supervisory guidance; Kathleen Gallagher, DSc, Gregory Armstrong, MD, and Stephen Waterman, MD, MPH, for supervisory guidance; the CDC Measles, Mumps, Rubella, and Herpesvirus Laboratory (Jennifer Rota, MPH, William Bellini, PhD, and Luis Lowe, MS), the California Department of Public Health Viral and Rickettsial Disease Laboratory (David Schnurr, PhD, Carol Glaser, MD MPH, David Cottam, BS, Chris Preas, BS, Janice Louie, MD, MPH, and Sharon Messenger, PhD), and the San Diego County Public Health Laboratory (Jill Giesick, MS, MPH, Christopher Peter, PhD, and Thelma Deguzman, BS) for indispensable laboratory work; Christine Garcia, MPH, Dean Sidelinger, MD, MPH, Anne Hassidim, MSN, RN, Mary Beckhelm, RN, Suzanne Hunt, RN, Suzanne Bouveron, MPH, Yolanda Herlich, RN, Jacqueline Tate, PhD, Wilma Wooten, MD, MPH, Michele Ginsberg, MD, Mark Sawyer, MD, and Kathleen Harri-man, PhD, MPH, RN, for assistance during the outbreak; Teresa Lee, MPH, of the California Department of Public Health Immunization Branch for providing data on kindergarten-entry assessment reports; Emily Zielinski-Gutierrez, DrPH, CDC, and Mary Hayden, PhD, National Center for Atmospheric Research, for leading parent discussion groups; and Mark Lindstrom for coordinating collection of cost data from San Diego County employees.

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Pediatrics 2010;125;747

DOI: 10.1542/peds.2009-1653 originally published online March 22, 2010;

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