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Increase in Reported Coccidioidomycosis — United States, 1998–2011

Coccidioidomycosis, also known as valley fever, is an infection caused by inhalation of *Coccidioides* spp. spores. This soil-dwelling fungus is endemic to arid regions of Mexico, Central and South America, and the southwestern United States (*1*). Symptomatic patients typically experience a self-limited influenza-like illness, but some develop severe or chronic pulmonary disease, and less than 1% of patients experience disseminated disease (*1*). Coccidioidomycosis can be costly and debilitating, with nearly 75% of patients missing work or school because of their illness, and more than 40% requiring hospitalization (*2*). Previous publications have reported state-specific increases in coccidioidomycosis in Arizona and California during 1998–2001 and 2000–2007, respectively (*3,4*). To characterize long-term national trends, CDC analyzed data from the National Notifiable Diseases Surveillance System (NNDSS) for the period 1998–2011. This report describes the results of that analysis, which indicated that the incidence of reported coccidioidomycosis increased substantially during this period, from 5.3 per 100,000 population in the endemic area (Arizona, California, Nevada, New Mexico, and Utah) in 1998 to 42.6 per 100,000 in 2011. Health-care providers should be aware of this increasingly common infection when treating persons with influenza-like illness or pneumonia who live in or have traveled to endemic areas.

In collaboration with the Council of State and Territorial Epidemiologists (CSTE), CDC compiles data on selected diseases through NNDSS. Data are reported to CDC from various state and territorial surveillance systems and reporting mechanisms. Coccidioidomycosis has been nationally notifiable since 1995; however, it was not nationally notifiable in 2010. Although the CSTE case definition includes both laboratory and clinical criteria, Arizona uses a laboratory-only case definition because of its large number of cases and the high predictive value of a positive laboratory result (*2*); since 2008, the laboratory component of the CSTE definition has included cases with a single positive serologic test. California uses the CSTE case definition, requiring both laboratory and clinical evidence of infection, but some counties with large numbers of cases use a laboratory-only definition.

State and regional annual incidence rates were calculated by dividing the number of cases by U.S. Census Bureau population estimates for each year. Crude, sex-specific, age-specific, and age-adjusted incidence rates (aIR) were calculated for Arizona, California, and other endemic states where coccidioidomycosis is reportable (Nevada, New Mexico, and Utah, combined). Rates were age adjusted using the 2000 U.S. standard population. Negative binomial regression was performed to assess statistical significance of incidence trends during 1998–2011. This model adjusts for changes in population size and age and sex distribution over time.

During 1998–2011, a total of 111,717 coccidioidomycosis cases were reported to CDC from 28 states and the District of Columbia: 66% from Arizona, 31% from California, 1% from other endemic states, and <1% from nonendemic states. In Arizona, California, Nevada, New Mexico, and Utah combined, the number of cases increased from 2,265 in 1998 (aIR: 5.3 per 100,000 population) to 8,806 in 2006 (18.0 per 100,000); a decrease occurred in 2007 and 2008 before

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an increase in 2009 (12,868 cases; 25.3 per 100,000), which continued into 2010 and 2011 (42.6 per 100,000) (Table 1).

Incidence in endemic states increased among all age groups during 1998–2011 (Figure). During this period, incidence typically was highest among the 40–59 year age group in California but was consistently highest among persons aged ≥60 years in Arizona and other endemic states. Incidence during 2011 was 381.1 per 100,000 among persons aged 60–79 years and 385.2 per 100,000 among persons aged ≥80 years in Arizona (Table 2).

During 1999–2008, most (56%) Arizona cases occurred among males, but beginning in 2009, a higher proportion (55%) of cases occurred among females. Incidence in 2011 in Arizona was substantially higher among females (286.9 per 100,000) than males (215.7 per 100,000). In contrast, only 35% of California cases occurred among females during 1998–2011, and 2011 incidence among California males (20.5 per 100,000) was more than double that among females (9.7 per 100,000).

The increase in the number of Arizona cases, from 1,474 in 1998 to 16,467 in 2011, was statistically significant by negative binomial regression (aIR: 30.5 per 100,000 in 1998; 247.7 per 100,000 in 2011, p<0.001). Adjusting for changes in population demographics, this corresponds to an increase in coccidioidomycosis incidence of approximately 16% each year during the study period. The number of California cases increased from 719 in 1998 (aIR: 2.1 per 100,000) to 5,697 in 2011 (aIR: 14.9 per 100,000) (average annual increase of 13%, p<0.001). The number of cases reported in Nevada, New Mexico, and Utah combined increased from 72 in 1998 (aIR: 1.4 per 100,000) to 237 in 2011 (aIR: 3.1 per 100,000) (p<0.001). Cases reported in nonendemic states increased from six in 1998 to 240 in 2011.

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Editorial Note

This report describes statistically significant increases in the incidence rate of reported coccidioidomycosis in endemic states during 1998–2011 after adjusting for changes in population size and in age and sex distribution. Although the number of cases decreased in Arizona during 2007–2008 and in California during 2007–2009, incidence dramatically increased in 2010 and 2011. In 2011, coccidioidomycosis was the second most commonly reported nationally notifiable condition in Arizona and the fourth most commonly reported in California (5).

The reasons for the increases described in this report are unclear. *Coccidioides* exists in the soil and is sensitive to environmental changes; factors such as drought, rainfall, and temperature might have resulted in increased spore dispersal,

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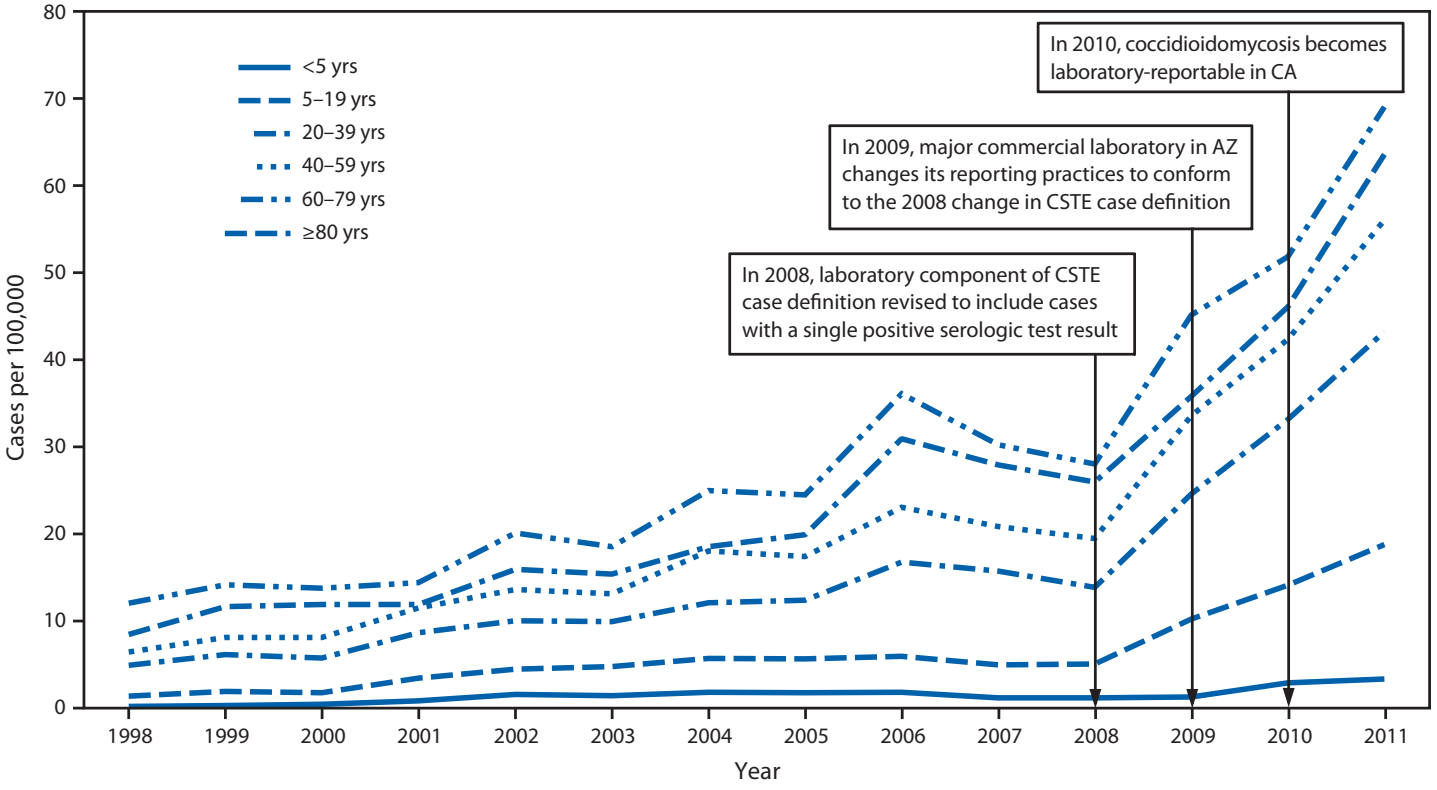
TABLE 1. Number and age-adjusted incidence per 100,000 population of coccidioidomycosis cases, by region — Arizona, California, Nevada, New Mexico, and Utah, 1998–2011

	Arizona		California		Nevada, New Mexico, and Utah		Total endemic area*	
Year	No.	Incidence	No.	Incidence	No.	Incidence	No.	Incidence
1998	1,474	30.5	719	2.1	72	1.4	**2,265**	**5.3**
1999	1,812	37.6	939	2.8	55	0.9	**2,806**	**6.6**
2000	1,917	36.6	840	2.5	67	1.1	**2,824**	**6.4**
2001	2,301	43.1	1,538	4.4	63	1.0	**3,902**	**8.6**
2002	3,133	57.2	1,727	4.9	63	1.0	**4,923**	**10.7**
2003	2,695	47.8	2,091	5.9	55	0.9	**4,841**	**10.4**
2004	3,667	62.9	2,641	7.4	110	1.5	**6,418**	**13.5**
2005	3,516	58.3	2,885	7.8	108	1.7	**6,509**	**13.4**
2006	5,535	88.6	3,131	8.6	140	2.1	**8,806**	**18.0**
2007	4,832	75.0	2,991	8.1	163	2.4	**7,986**	**16.0**
2008	4,768	72.5	2,597	7.0	99	1.4	**7,464**	**14.8**
2009	10,233	154.4	2,488	6.7	147	2.1	**12,868**	**25.3**
2010	11,883	182.0	4,622	12.2	159	2.1	**16,664**	**32.2**
2011	16,467	247.7	5,697	14.9	237	3.1	**22,401**	**42.6**

* Coccidioidomycosis is endemic but not reportable in Texas.

FIGURE. Coccidioidomycosis incidence per 100,000 population, by age group — Arizona, California, Nevada, New Mexico, and Utah, 1998–2011



Abbreviations: CSTE = Council of State and Territorial Epidemiologists; AZ = Arizona; CA = California.

and disruption of soil by human activity, such as construction, also might be a contributing factor.

Changes in surveillance methodology might have resulted in artifactual increases. California transitioned to a laboratory-based reporting system during 2010, which facilitated reporting and might account for the increase in reported cases in 2011. However, some highly endemic counties, such as Kern County, already had been using laboratory-based systems, so this cannot fully explain the recent increase. The observed increase in Arizona might be partially attributable to a 2009 change by a major commercial laboratory to conform its reporting practices to the 2008 CSTE case definition,

TABLE 2. Number and incidence per 100,000 population of coccidioidomycosis cases, by region, age group, and sex — Arizona, California, Nevada, New Mexico, and Utah, 2011

Area and age group (yrs)	Male		Female		Total*	
	No.	Incidence	No.	Incidence	No.	Incidence
Arizona						
<5	38	16.5	25	11.3	**63**	**14.0**
5–19	621	89.4	796	120.3	**1,428**	**105.3**
20–39	1,671	187.1	2,707	319.4	**4,422**	**254.1**
40–59	2,239	276.4	3,223	386.5	**5,509**	**335.1**
60–79	1,919	382.4	2,078	372.8	**4,037**	**381.1**
≥80	424	445.4	461	334.8	**897**	**385.2**
All ages	6,954	215.7	9,349	286.9	**16,467**	**254.0**
California						
<5	35	2.7	22	1.8	**57**	**2.2**
5–19	340	8.5	263	6.9	**605**	**7.7**
20–39	1,329	24.0	561	10.6	**1,897**	**17.6**
40–59	1,513	30.0	583	11.4	**2,098**	**20.6**
60–79	509	21.4	337	12.4	**848**	**16.7**
≥80	88	18.5	75	9.8	**163**	**13.1**
All ages	3,839	20.5	1,844	9.7	**5,697**	**15.1**
Nevada, New Mexico, and Utah						
<5	0	0.0	0	0.0	**0**	**0.0**
5–19	8	0.9	5	0.6	**13**	**0.8**
20–39	15	1.4	17	1.7	**32**	**1.5**
40–59	49	5.2	29	3.0	**77**	**4.1**
60–79	62	12.2	38	7.2	**100**	**9.6**
≥80	10	11.6	4	3.2	**14**	**6.6**
All ages	143	3.8	93	2.5	**237**	**3.1**
Total endemic area†						
<5	**73**	**4.0**	**47**	**2.7**	**120**	**3.3**
5–19	**969**	**17.4**	**1,064**	**20.0**	**2,046**	**18.8**
20–39	**3,015**	**40.1**	**3,286**	**45.8**	**6,352**	**43.2**
40–59	**3,801**	**55.8**	**3,834**	**55.5**	**7,684**	**56.0**
60–79	**2,491**	**73.4**	**2,455**	**90.2**	**4,988**	**69.1**
≥80	**522**	**79.4**	**540**	**52.3**	**1,074**	**63.6**
All ages	**10,398**	**40.3**	**11,288**	**43.4**	**22,401**	**43.2**

* Categories might not sum to totals because of missing age and sex data.
† Coccidioidomycosis is endemic but not reportable in Texas.

whereby positive enzyme immunoassay (EIA) results were reported as cases without confirmation by immunodiffusion. One commercially available EIA test (Meridian Bioscience) commonly used to diagnose coccidioidomycosis has been described to have false-positive results in some instances (*6*), but the contribution of this phenomenon, if any, to the overall increase in cases is unknown.

Improved awareness of coccidioidomycosis might have resulted in increased diagnostic testing (and thus reporting) in endemic and nonendemic states. *Coccidioides* has been found to be the etiologic agent in an estimated 15%–29% of community-acquired pneumonias in highly endemic areas (*7*). However, a 2006 study demonstrated that only a small proportion (2%–13%) of patients with compatible illness in an endemic area were tested for coccidioidomycosis (*7*), suggesting that the disease is greatly underreported. Further study is needed to understand if testing practices have changed. Despite the increase in reported cases, overall U.S. coccidioidomycosis mortality rates have remained fairly stable at approximately 0.6 per 1 million person-years during 1990–2008 (*8*).

The findings in this report are subject to at least four limitations. First, NNDSS data might underrepresent the actual burden of disease because coccidioidomycosis is not reportable in every state, even in known endemic areas such as Texas, and because state reporting of cases to CDC is voluntary. In particular, the number of cases reported in 2010 might underestimate the actual number of infections because coccidioidomycosis was not notifiable in 2010 (but became notifiable again in 2011). Second, minor discrepancies between the findings in this report and those presented in *MMWR*'s annual *Summary of Notifiable Diseases* reports likely exist because the summary does not include cases from states where the disease was not reportable. Third, minor discrepancies might exist between this report and state-specific reports because of delays in case reporting. Finally, because nearly 70% of cases were missing race/ethnicity data, incidence rates by race and ethnicity were not calculated. This is an important consideration because high rates among Asians and blacks have been documented previously, and black race has been shown to be an independent risk factor for disseminated coccidioidomycosis (*9*).

Further investigation is needed to determine how much of the observed increase in coccidioidomycosis incidence is artifactual. Nevertheless, health-care providers should be alert for coccidioidomycosis among patients of all ages who live in or have traveled to endemic areas. Persons in endemic areas should consider trying to reduce exposure to dusty air, which might contain *Coccidioides* spp. spores. However, because there are currently no proven preventive measures

What is already known on this topic?

Coccidioidomycosis is an infection that results from inhalation of *Coccidioides* spp. fungal spores. It is endemic in the southwestern United States, with the highest number of cases occurring in Arizona and California, and constitutes a substantial public health burden in these areas, particularly among older persons.

What is added by this report?

Reported coccidioidomycosis cases have increased dramatically in recent years. The age-adjusted incidence was 5.3 cases per 100,000 population in the endemic area in 1998 and 42.6 per 100,000 in 2011. Among persons aged 60–79 years in the endemic area, incidence was 69.1 cases per 100,000 in 2011.

What are the implications for public health practice?

The number of reported cases of coccidioidomycosis is increasing. Health-care providers should be alert for this infection among persons with influenza-like illnesses who live in or have traveled to endemic areas. Further research on strategies to reduce the morbidity of coccidioidomycosis is needed.

for coccidioidomycosis, additional research into strategies that reduce the incidence or morbidity of this infection is warranted. Specifically, the role of antifungal treatment for primary pulmonary disease remains controversial and deserves further exploration (*10*), although treatment is recommended in certain patient groups, particularly those at high risk for severe disease (*1*). Because the symptoms of coccidioidomycosis mimic those of other community-acquired respiratory illnesses, patients often experience delays in testing and diagnosis and receive unnecessary antibiotics; however, patients who know about coccidioidomycosis are more likely to request testing and receive a diagnosis sooner than those who are not familiar with the disease (*2*). Therefore, promoting increased community and health-care provider awareness of this infection continues to be an important role for public health officials.

Acknowledgments

National Notifiable Diseases Surveillance System. Div of Notifiable Disease Surveillance, Public Health Surveillance Program Office, Office of Surveillance, Epidemiology, and Laboratory Services, CDC.

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Two Measles Outbreaks After Importation — Utah, March–June 2011

Before licensure of a measles vaccine in 1963, more than 500,000 measles cases on average were reported in the United States each year during 1951–1962 (*1*). By 1993, through measles vaccination and control efforts, only 312 cases were reported nationwide (*1*). In 2000, the last year in which an outbreak had occurred in Utah, measles was declared "not endemic in the United States," (*2*) but measles importations continue to occur, leading to outbreaks, especially among unvaccinated persons (*3*). Many U.S. health-care personnel have never seen a measles patient, which might hamper diagnosis and delay reporting. During March–June 2011, local health departments collaborated with the state health department in Utah to investigate two measles outbreaks comprising 13 confirmed cases. The first outbreak, with seven confirmed cases, was associated with an unvaccinated U.S. resident who traveled internationally; the second, with six confirmed cases, had an undetermined source. The genotype D4 sequences obtained from these two outbreaks differed by a single nucleotide, suggesting two separate importations. Health-care providers should remind their patients of the importance of being current with measles, mumps, and rubella (MMR) vaccination; this is especially important before international travel. Measles should be considered in the differential diagnosis of febrile rash illness, especially in unvaccinated persons with recent international travel. Reporting a confirmed or suspected case immediately to public health authorities is critical to limit the spread of measles.

Outbreak 1. On April 5, 2011, a health-care provider notified the Salt Lake Valley Health Department (SLVHD) of an unvaccinated Salt Lake County resident aged 16 years with generalized rash (onset April 4) and a 3-day history of sore throat and fever (101.7°F [38.7°C]) (Table). When investigated by public health officials on April 6, the patient had a morbilliform rash, cough, coryza, conjunctivitis, and Koplik spots, and reported no recent travel or contact with ill persons. Serum collected on April 5 was positive for measles immunoglobulin M (IgM). On April 7, SLVHD announced that a measles case had been confirmed. On April 8, a health-care provider notified SLVHD that an unvaccinated Salt Lake County patient aged 15 years had sought care in late March with generalized rash (onset March 21), fever (103.7°F [39.8°C]), cough, coryza, and conjunctivitis. The patient had traveled in Europe during March 3–17. No measles testing was performed during the acute illness. Serum collected on April 8 was measles IgM-positive. This patient had attended a school class on March 21 with the patient reported previously. Five additional Salt Lake County residents were confirmed to have measles, with the last rash onset on April 17, 2011 (Figure).

Outbreak 2. On May 24, 2011, a Cache County resident notified the Bear River Health Department that her unvaccinated child aged 7 years had signs and symptoms compatible with measles, including generalized rash (onset May 23) and fever (101.5°F [38.6°C]) (Table, Figure). She reported no recent travel outside Utah or contact with any person with a rash illness; the source was not identified. Serum collected on May 26 was measles IgM-positive. On May 31, the Bear River Health Department announced that a measles case had been identified. Two unvaccinated siblings of the patient, for whom the parents declined postexposure vaccination, were home-quarantined and developed measles, with rash onsets June 1 and 2, respectively. Additionally, two Cache County residents and one Millard County resident, all family members of the two siblings, were identified as having measles; the last reported rash onset was June 16, 2011.

During the two measles outbreaks, local health departments collaborated with the state health department in investigating and initiating active surveillance and outbreak response. Confirmed cases were defined using the 2010 Council of State and Territorial Epidemiologists measles case definition (*4*). Case-finding efforts included e-mail messages to health-care providers, press releases, syndromic surveillance for febrile rash illness, urgent-care facility admission data, and communications with hospital infection control practitioners. Laboratory methods included testing serum specimens for measles IgM and immunoglobulin G (IgG) at commercial and CDC laboratories, viral culture, polymerase chain reaction, genotyping, and testing for parvovirus B19 IgM. Public health investigators assessed patients and contacts for symptoms, vaccination history, and presumptive evidence of measles immunity.* Contacts without presumptive evidence of immunity were offered MMR vaccine or immunoglobulin, as appropriate, or placed in voluntary home quarantine.

In the two outbreaks, separated by 36 days, 13 persons were confirmed to have measles; nine (69%) were unvaccinated and had personal belief exemptions,† one had a documented history of 2 doses of measles antigen–containing vaccine, and

* Presumptive evidence of measles immunity is defined as documented receipt of 2 doses of live measles virus–containing vaccine, laboratory evidence of measles immunity, documentation of physician-diagnosed measles, or birth before 1957.

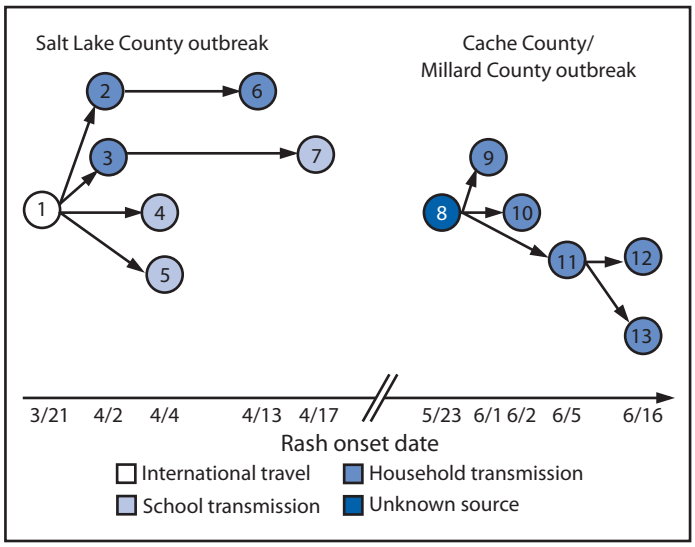
† Immunizations required – Exceptions – Grounds for exemption from required immunizations. Utah Code 53A-11-302 (2010). Available at http://le.utah.gov/~code/title53a/htm/53a11_030200.htm.

TABLE. Characteristics of confirmed measles cases, by date of rash onset — Utah, March–June 2011

Location	Case no.	Date of rash onset	Age at onset (yrs)	Previous MMR vaccine doses	Symptoms				Transmission setting	Genotype	Total contacts*
					Fever	Cough	Coryza	Conjunctivitis			
Salt Lake County											
	1	3/21/2011	15	0	+	+	+	+	International travel	NA	**1,418**
	2	4/2/2011	18	0	+	+	+	+	Household	NA	**3,702**
	3	4/2/2011	12	0	+	+	+	+	Household	NA	**1,022**
	4	4/4/2011	18	0	+	+	+	+	School	NA	**98**
	5†	4/4/2011	16	0	+	+	+	+	School	D4	**2,100**
	6	4/13/2011	22	0	+	+	+	+	Household	NA	**1,409**
	7	4/17/2011	13	2	+	+	+	+	School	NA	**985**
Cache County/Millard County											
	8†	5/23/2011	7	0	+	+	+	+	Unknown	D4	**5**
	9	6/1/2011	11	0	+	+	+	+	Household	D4	**105**
	10	6/2/2011	5	0	+	+	+	+	Household	D4	**105**
	11	6/5/2011	44	1§	+	+	+	+	Household	NA	**405**
	12	6/16/2011	44	2§	–	–	+	+	Household	NA	**5**
	13	6/16/2011	48	1§	+	+	+	–	Household	D4	**905**

Abbreviations: MMR = measles, mumps, and rubella; NA = not available.
* Contacts are not mutually exclusive.
† Cases 5 and 8 were the first cases in the respective outbreaks to be reported to the local public health departments.
§ Vaccination history based on verbal reporting only.

FIGURE. Timeline demonstrating chain of measles transmission in 13 cases, by date of rash onset and transmission setting — Utah, March–June 2011



three adult patients reported a history of vaccination, although vaccination records were not available (Table, Figure). Patients were aged 5–48 years. Measles genotype D4 was identified from the clinical samples obtained in both outbreaks (Table). Two unvaccinated patients were hospitalized; one for 3 days for respiratory complications and another overnight in an emergency department for observation. Among the 12 cases where the source of infection was known, measles infections were acquired during international travel (one case) and in households (eight) and schools (three). During the Salt Lake County outbreak, seven additional patients who initially tested positive or equivocal by commercial measles IgM testing were suspected of having measles but were not confirmed at CDC. Five of these had a history of vaccination, no direct epidemiologic link to the Salt Lake County cases, and were confirmed as parvovirus B19 cases by additional serologic testing. The sixth patient suspected of having measles was epidemiologically linked to the school and the seventh was a household contact of that patient; neither showed evidence of measles infection in samples tested by CDC.

For both outbreaks, approximately 13,000 contacts of patients were notified by visit, phone, letter, or e-mail. Health officials reviewed vaccination records of approximately 8,700 exposed persons, conducted 253 measles IgG antibody tests, and administered 484 MMR vaccine and 28 measles immunoglobulin doses as postexposure prophylaxis. Voluntary home quarantine of 192 exposed persons without presumptive evidence of immunity was requested.

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Editorial Note

Because measles remains endemic in many regions of the world, the United States continues to be at risk for measles importations and outbreaks. In 2011, a total of 220 measles cases were reported in the United States, the highest number of reported measles cases since 1996; 89% were associated with importations (*2*). The outbreaks in Utah and elsewhere during 2011 highlight the critical need for appropriate vaccination of U.S. residents, particularly those who travel internationally. The Salt Lake County outbreak began when an unvaccinated traveler from the United States developed measles on returning to the United States and infected four other unvaccinated persons.

The genotype D4 sequences obtained from the two Utah outbreaks differed by a single nucleotide. Each of the Utah sequences was identical to one of two predominant sequence variants of genotype D4 that were circulating in Europe during 2011 (*5,6*). This, together with the interval of 5 weeks without cases between the two outbreaks, suggests the second outbreak likely was the result of a separate importation from an unknown source, rather than a continuation of the first outbreak.

In the Salt Lake County outbreak, three of the patients were adolescents who acquired the disease in school. In 2010, an estimated 96.4% of children attending public school in Utah were vaccinated with 2 doses of MMR vaccine (*7*). The high level of vaccination coverage among schoolchildren likely helped contain this outbreak. None of the three patients infected by the index patient at school transmitted the disease to other students. Ensuring high vaccination rates among schoolchildren is important to limit measles transmission.

For patients with risk factors for measles (e.g., unvaccinated status, recent travel history, or known epidemiologic link to a confirmed measles case), health-care providers and public health officials should consider measles in the differential diagnosis of febrile rash illness and should consider other potential exposures, including parvovirus, when ordering laboratory tests. Because measles now occurs so rarely in the United States, interpretation of measles tests can be challenging, especially during outbreaks, and confirming and correctly classifying measles in vaccinated persons can be particularly difficult. False-positive measles IgM results might be obtained in response to infections caused by parvovirus (*8,9*) and other viruses, including enteroviruses, Epstein-Barr virus, and varicella zoster virus. The capture IgM assay methodology available at CDC's Measles Virus Laboratory[§] generally is less prone to nonspecific reactions; however, the low prevalence of measles in the United States results in a low positive predictive value regardless of the IgM assay used. Serum and respiratory specimens both should be collected from suspected patients at first contact, because serological testing coupled with molecular testing provides the best opportunity for laboratory confirmation (*10*).

Measles cases and outbreaks can have considerable impact on communities in the United States and often require substantial resources for public health response. Recognition of suspected measles cases by health-care providers and immediate reporting to public health officials can help limit illness and associated costs. For the two Utah outbreaks combined, those costs were estimated from multiple sources to exceed $330,000 for public health personnel time at state and local levels, vaccine administration, laboratory testing, and outbreak control efforts. Unvaccinated persons put themselves and their communities at risk for measles. Maintaining high vaccination coverage and rapid public health response is critical to ensuring continued measles elimination in the United States.

What is already known on this topic?

Since introduction of the measles vaccine in 1963, the incidence of measles has declined significantly, such that measles is no longer endemic in the United States, and many U.S. health-care providers currently practicing have never seen a patient with measles. Measles remains common in parts of the world, however, and international travel–related outbreaks are becoming more common.

What is added by this report?

During March–June 2011, Utah investigated two measles outbreaks comprising 13 confirmed cases. One outbreak was associated with an unvaccinated U.S. resident who traveled internationally; the source was unknown for the second outbreak. Genotype D4 sequences obtained from the two outbreaks differed by a single nucleotide, suggesting separate importations; each of the sequences was identical to one of two predominant sequence variants of genotype D4 circulating in Europe during 2011.

What are the implications for public health practice?

Health-care providers should remind their patients of the importance of being current with measles, mumps, and rubella vaccination, especially before international travel. Recognition of suspected measles cases by health-care providers and immediate reporting to public health officials can help prevent illness and associated costs. False-positive measles serologic test results can be obtained in infections caused by parvovirus and other viruses, including enteroviruses, Epstein-Barr virus, and varicella zoster virus.

[§] Additional information available at http://www.cdc.gov/measles/lab-tools/measles-virus-lab.html.

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Three Cases of Congenital Rubella Syndrome in the Postelimination Era — Maryland, Alabama, and Illinois, 2012

Infection with rubella virus during pregnancy, especially during the first trimester, can result in congenital rubella syndrome (CRS). Serious manifestations of CRS include deafness, cataracts, cardiac defects, mental retardation, and death (*1*). In the last major rubella epidemic in the United States, during 1964–1965, an estimated 12.5 million rubella virus infections resulted in 11,250 therapeutic or spontaneous abortions, 2,100 neonatal deaths, and 20,000 infants born with CRS (*2*). In 2004, after implementation of a universal vaccination program, elimination of endemic rubella virus transmission was documented in the United States; evidence also suggests that endemic rubella has been eliminated in the entire World Health Organization (WHO) Region of the Americas (*3,4*). However, rubella virus continues to circulate elsewhere in the world, especially in regions where rubella vaccination programs have not been established (e.g., the African Region), placing the United States at risk for imported cases of rubella and CRS. During 2004–2012, 79 cases of rubella and six cases of CRS were reported in the United States (Figure); all of the cases were import-associated or from unknown sources. Of the three cases of CRS that occurred in 2012, conditions included cardiac defects, cataracts, hearing impairment, and pericardial effusion in one infant; patent ductus arteriosus, cardiomegaly, thrombocytopenia, and pneumonitis in a second infant; and cataracts, thrombocytopenia, and cardiac defects in a third infant. All three mothers had been in Africa early in their pregnancies. While rubella remains endemic elsewhere in the world, imported CRS will continue to be a public health concern in the United States.

Case Reports

Infant A. In February 2012, an infant born in Maryland at 36 weeks' gestation and weighing 4.2 lbs (1,910 g) was noted at birth to have congenital heart defects, hyperpigmented skin lesions, cataracts, cerebral edema, and pericardial effusion. Hearing impairment was suspected after the infant failed a hearing screening test before hospital discharge in February, and bilateral profound hearing impairment was diagnosed by an audiologist in June. Surgical procedures for correction of congenital heart defects and cataracts were performed in February and June, respectively. During eye surgery, the infant experienced breathing difficulties and went into cardiac arrest. Following stabilization, the infant was admitted to the pediatric intensive-care unit for observation and was later discharged.

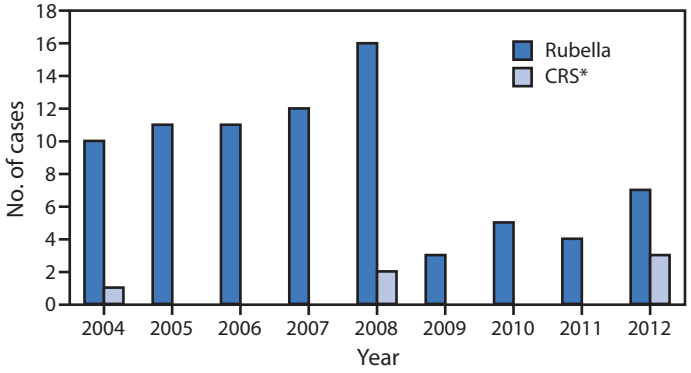
CRS diagnosis initially was confirmed at a commercial laboratory by a positive test for rubella immunoglobulin M (IgM) from serum collected on the second day of life. Serum collected on the sixth day of life tested positive for rubella IgM and immunoglobulin G (IgG) at the Maryland State Public Health Laboratory and CDC. A throat swab collected the same day tested positive by real-time reverse transcription–polymerase chain reaction (rRT-PCR) for rubella RNA, and rubella virus genotype 1G was identified by sequencing at CDC. The viral nucleotide sequences from this CRS patient were similar to those obtained from eastern African countries bordering Tanzania. Because CRS was suspected early, appropriate specimens were collected in a timely manner, and the diagnosis was laboratory confirmed.

The mother, in her late 20s, was from urban Tanzania. She reported having a rash around the time of her first missed menstrual period in June 2011 while in Tanzania. At the time, she did not know that she was likely a few weeks pregnant. The mother's generalized, erythematous, maculopapular rash lasted 2–3 days. She also reported swollen eyes. She reported having received all of her childhood vaccinations in Tanzania, but rubella-containing vaccine had not been part of the routine vaccination schedule. She had no prenatal care in Tanzania.

The mother arrived in the United States in December 2011, and approximately 46 days later she developed a varicella-like rash. She stated that this rash was dissimilar to the rash she had had in Tanzania. She went to a local hospital for evaluation of what appeared to be a varicella-like rash 3 days later, but laboratory testing for varicella was not performed. She went to a different hospital 13 days after rash onset with abdominal pain and concern that she had not felt the baby kick for 2 days. Fetal ultrasonography indicated breech presentation, a small abdominal circumference, and marked oligohydramnios. The next day she went to a third hospital for a prenatal visit. She still had the varicella-like rash at this visit, and it was noted that the rash was crusted over. Varicella was suspected, but testing for varicella was not performed. However, routine tests in pregnancy as described by the American College of Obstetricians and Gynecologists* include a serum test for rubella antibody, which was positive in this case (immunoglobulin type not specified) at the hospital laboratory.

* Available at http://www.acog.org/~/media/for%20patients/faq133.pdf?dmc=1&ts=20130228t1231184484.

FIGURE. Reported cases of rubella and congenital rubella syndrome (CRS) — National Notifiable Diseases Surveillance System, United States, 2004–2012



* By year of birth.

Infant B. In March 2012, an infant was born in Alabama by cesarean delivery at 33 weeks' gestational age. At birth, the infant had generalized hemorrhagic purpura (a blueberry muffin rash) over the entire body, patent ductus arteriosus, cardiomegaly, thrombocytopenia, pneumonitis, anemia, and liver dysfunction. Approximately 1 month later, the infant was transferred to a pediatric hospital, where the infant died in April 2012. Cause of death was recorded as CRS.

Diagnosis initially was confirmed by a positive rubella IgM test result. Serum drawn from the infant on the day of birth tested positive for rubella IgM at the hospital laboratory. Serum drawn 4 days later tested positive for rubella IgM at the Alabama Bureau of Clinical Laboratories, and serum drawn 11 days after birth tested positive for rubella IgM and IgG at CDC. A throat swab and urine specimen, collected 7 days after birth, as well as a nasopharyngeal swab, collected 10 days after birth, tested positive by rRT-PCR for rubella RNA at CDC. Nucleotide sequencing identified the virus as belonging to genotype 1G and having the closest similarity to virus sequences obtained from countries neighboring Nigeria in western Africa. Because CRS was suspected at birth, appropriate specimens were collected early, enabling the diagnosis to be laboratory confirmed.

The mother was a woman in her late 20s from Nigeria. She began prenatal care in Nigeria at 9 weeks' gestation and had a total of nine visits. Receipt of a rubella-containing vaccine, which is not part of the routine vaccination schedule in Nigeria, was not recorded at any time. She received 2 doses of tetanus toxoid and antimalarial prophylaxis at 20 and 24 weeks, respectively, but further prophylaxis was not reported. In Nigeria at 28 weeks, the baby was noted to be small for that gestational age. At 29 weeks' gestation, the baby was noted to have asymmetric intrauterine growth retardation. No abnormal prenatal laboratory results were reported in Nigeria; however, rubella testing was not performed.

The mother arrived in the United States in early March 2012 in approximately week 32 of pregnancy. In the United States, her pregnancy was complicated with oligohydramnios and severe growth retardation. She did not recall having had a rash illness during her pregnancy. Maternal serum collected 3 days after she had given birth tested negative at CDC for rubella IgM and positive for rubella IgG with a high avidity index. Documents indicated that all members of her U.S. household (i.e., an aunt, uncle, two adolescents, and a child aged 2 years) had been vaccinated with a rubella-containing vaccine.

Infant C. In September 2012, an infant was born in Illinois by cesarean delivery at approximately 32.5 weeks' gestational age, weighing 1.4 lbs (650 g). Conditions noted after birth included cataracts, Dandy-Walker syndrome (discovered on antenatal ultrasound), intrauterine growth retardation, thrombocytopenia, chorioretinitis, coarctation of the aorta (which was repaired), mild liver dysfunction, mildly elevated transaminases, mild direct hyperbilirubinemia, and persistent elevation of C reactive protein. The child was discharged in February 2013.

CRS diagnosis was initially confirmed by a positive rubella IgM test result. Serum collected from the infant 44 days after birth tested positive for rubella IgM and IgG at CDC. Also at CDC, the throat swab specimen collected the same day as the serum was positive by rRT-PCR, but the nasal wash and urine specimens were negative. Nucleotide sequencing identified a genotype 1E virus, most similar to a 2011 virus from a region of Uganda bordering South Sudan and a 2008 virus from Yemen.

The mother was an immigrant from Sudan in her late 20s. Her rubella vaccination status was unknown; however, rubella vaccine is not part of the routine vaccination schedule in Sudan. The mother reported not having had a rash or fever after December 2011. She reported having had her last menstrual period in mid-January 2012. In late February, she, along with her husband and two daughters (aged 3 and 5 years), traveled by airplane to the United States via Cairo, Egypt.

The mother sought prenatal care in Illinois. Serum was drawn in early April 2012, and the rubella IgG result was positive. On the same day, the physician estimated her pregnancy at approximately 10 weeks. At the mother's second visit, at 18 weeks, a screening test for birth defects was performed with measured levels of alpha-fetoprotein, human chorionic gonadotropin, estriol, and inhibin A; the results suggested an increased risk for Down's syndrome. A follow-up ultrasound showed fetal abnormalities, and she was hospitalized for additional evaluation. She reported no health problems in the United States. The two daughters in the household had documented receipt of measles, mumps, and rubella vaccine, but the father's vaccination status was unknown.

Reported by

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Editorial Note

Since 2004, when rubella and CRS elimination were documented in the United States, six cases of CRS have been reported, including the three cases described here. In five cases, infection of the mother in a foreign country was thought highly probable, given travel history (i.e., Nigeria, Tanzania, Sudan, Ivory Coast, and either India, China, or Singapore). In one case, the mother did not report international travel. Although few cases of CRS have been reported in the United States, rubella continues to circulate in many other parts of the world, and the risk remains for severe effects from CRS, including death. In this report, one of the three infants with CRS died.

In 2011, a total of 130 countries, comprising approximately 41% of the world's birth cohort, included rubella-containing vaccine in their national childhood immunization program (*5*). However, in the African Region, only three countries have introduced rubella-containing vaccine into their routine childhood vaccination program.[†] In 2009, the Region of the Americas reached its 2010 rubella and CRS elimination goal (*4*). The European Region and Western Pacific Region have rubella control or elimination goals, but rubella continues to circulate in these regions (*6*). The African, Eastern Mediterranean, and South-East Asia regions do not have a regional rubella or CRS control or elimination goal at this time because of the additional cost of the rubella component and competing priorities (e.g., polio eradication) (*6*).

Health-care providers should consider CRS if the mother of an infant with compatible congenital birth defects traveled during her pregnancy to an area where rubella circulates or was exposed to someone who traveled to such an area. As a nationally notifiable condition, all suspected cases of CRS should be reported immediately to the local health department, which, in turn, reports them to CDC via the state health department. Both serum and throat swab specimens should be collected as soon as CRS is suspected. Either serum positive for rubella IgM antibody or a throat swab positive for rubella RNA is confirmatory for CRS in a patient with compatible signs.

At this time, during maintenance of CRS elimination in the United States, confirmation at CDC of all laboratory results that support diagnoses of CRS cases is recommended. Molecular characterization of the virus is critical because the viral genotype can substantiate the suspected source of the virus or suggest one if the source is unknown, because some of the circulating genotypes are associated with specific geographic areas. Heightened awareness, gathering of pertinent information, and collection of appropriate specimens are required of the health-care provider and public health department to diagnose and investigate a case of CRS; however, these surveillance efforts are crucial to maintaining elimination in the United States.

As long as rubella remains endemic in any area of the world, imported CRS will continue to be a public health concern in the United States. Residents or foreign visitors entering the

What is already known on this topic?

Congenital rubella syndrome (CRS) is caused by fetal infection with rubella virus from the mother and characterized by birth defects. During the 1964–1965 rubella epidemic in the United States, an estimated 12.5 million rubella cases occurred, and an estimated 20,000 infants were born with CRS. As a result of universal childhood vaccination, rubella and CRS elimination were documented in the United States in 2004; however, rubella still circulates in other areas of the world.

What is added by this report?

With the elimination of rubella, cases of CRS are a rare occurrence in the United States. This report describes three infants with CRS born in the United States in 2012; all had severe defects, and one died. In all three cases, the mother likely was exposed to rubella in Africa and had no documentation of vaccination against the virus.

What are the implications for public health practice?

Although CRS occurs infrequently in the United States, health-care providers and public health officials should consider CRS in an infant with compatible birth defects whose mother was in a rubella-endemic country during her pregnancy. Heightened awareness is critical for obtaining appropriate specimens early for laboratory confirmation of CRS and for initiation of a thorough epidemiologic investigation. In addition, health-care providers should know the vaccination status of women of childbearing age who are planning to travel internationally.

[†] Information available at http://www.who.int/entity/immunization_monitoring/data/year_vaccine_introduction.xls.

United States from rubella-endemic areas can introduce the virus. In addition, infants born with CRS can shed infectious virus for several months; therefore, care must be taken to avoid contact with others who are susceptible to rubella (e.g., unvaccinated infants in day-care settings) (*7*). Although levels of vaccination with rubella-containing vaccine are high in the United States, a small proportion of persons are not vaccinated for medical or personal reasons (*8*). Those who are not vaccinated against rubella virus can become infected if exposed. If a pregnant woman is infected with rubella virus, the fetus also can become infected. Fetal infection with rubella virus, especially early during pregnancy, often leads to CRS. The risk for CRS in the unborn child of a mother with rubella infection might be as high as 90% for infections occurring through week 10 of pregnancy (*9*). Clusters of unvaccinated persons are at high risk for an outbreak, as in the Netherlands and Canada in 2009 (*10*). Health-care providers and public health workers should remain vigilant for imported cases of CRS.

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Notes from the Field

Outbreak of Severe Respiratory Illness in an Assisted-Living Facility — Colorado, 2012

On May 28, 2012, the Colorado Department of Public Health and Environment (CDPHE) was notified of six cases of severe respiratory illness among 12 residents of an assisted-living facility (ALF) specializing in the care of elderly persons with dementia or memory loss. During May 22–27, 2012, five residents were hospitalized, and two developed invasive disease with *Streptococcus pneumoniae* (pneumococcal) bacteremia. *S. pneumoniae* is spread by airborne droplets and causes an estimated 175,000 hospitalizations and 50,000 cases of pneumococcal bacteremia each year. The case-fatality rate of pneumococcal bacteremia can be as high as 60% among the elderly.

CDPHE and CDC conducted an investigation to determine the extent of the outbreak and to assess the infection control capabilities at the facility. A probable case of pneumococcal disease was defined in a resident or staff member who received a diagnosis of pneumonia by a health-care provider during May 15–June 3, 2012. Confirmed cases met criteria for probable infection and also had *S. pneumoniae* isolated from a normally sterile site. CDPHE performed serotyping of culture isolates from confirmed cases.

Two confirmed and five probable cases of pneumococcal disease were identified; six patients (two with confirmed and four with probable pneumococcal disease) were residents, and one patient with probable pneumococcal disease was a staff member. Three of the six resident patients died. Median age of the seven patients was 80 years (range: 39–97 years) and all had received the 23-valent pneumococcal polysaccharide vaccine, consistent with guidelines from the Advisory Committee on Immunization Practices (*1*). The staff member had received pneumococcal polysaccharide vaccine because of a history of asthma.

All patients shared common areas in the ALF; the staff member's responsibilities required close contact with all residents at the facility. Patients had symptom onset during May 19–27. The staff member had the earliest onset of respiratory symptoms and continued to work while symptomatic, raising concerns that the staff member might have introduced the infection into the facility. Although the ALF had an employee sick leave policy, staff members might not have been aware of the policy and its role in infection control. Additionally, the facility did not have a written infection control policy for maintaining minimum stocks of personal protective equipment such as gowns and face masks, and staff members were not aware such equipment should be worn to prevent person-to-person transmission of an unknown respiratory illness (*2*).

Isolates from both confirmed cases were identified as *S. pneumoniae* serotype 3 with indistinguishable antimicrobial resistance patterns. All residents were offered empiric postexposure chemoprophylaxis to reduce nasopharyngeal colonization with *S. pneumoniae*. All residents also were offered 13-valent pneumococcal conjugate vaccine (*3*). After careful consideration, public health officials did not identify additional benefits that could be gained from extending either prophylaxis or vaccination recommendations to the entire facility staff.

ALFs are community-based residential facilities that offer 24-hour supervision and also can provide supportive services such as medication management and dementia care (*4*). Considered the fastest-growing segment of long-term care, approximately 730,000 persons currently reside in the 31,000 licensed ALFs in the United States (*5*). Whereas hospitals and skilled-nursing facilities have federal regulatory standards for infection control and prevention programs (*6*), similar requirements currently do not exist for ALFs. Infection control requirements for ALFs vary among states, and ALF staff members might not have training in infection prevention and control. This outbreak in a vulnerable elderly population in a nonacute health-care setting highlights the importance of infection prevention training, guidance, and oversight for ALFs and their staffs.

To prevent future outbreaks of communicable illness in the Colorado ALF, CDC and CDPHE provided recommendations to increase support and awareness of existing sick-leave policies among staff members (e.g., not reporting to work when ill), and to develop and implement written infection control policies that include staff education, adequate availability and appropriate use of personal protective equipment, and recognition and reporting of disease outbreaks to public health authorities.

Reported by

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Announcement

Autism Awareness Month and World Autism Day — April 2013

April is Autism Awareness Month, and April 2 is World Autism Day. Nearly one in 88 children has been identified with an autism spectrum disorder (ASD), according to estimates from CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network (*1*). ASDs are a group of developmental disabilities that can result in major social, communication, and behavioral challenges. Onset of symptoms usually occurs between a child's first and third birthdays (*1*). Early identification and intervention can help a child access services and learn new skills; however, most children are not identified until after they reach age 4 years (*1*).

ADDM Network surveillance data serve as a guide for CDC's own autism research as well as the research of other scientists throughout the United States. To identify the causes of ASDs, the scientific community first needs to better understand the factors that put children at risk for ASDs. CDC currently is conducting the Study to Explore Early Development to help identify these risk factors (*2*).

CDC's "Learn the Signs, Act Early" program (http://www.cdc.gov/actearly) has tools to help parents and early childhood-care and education providers track children's developmental milestones and provides information about what to do if there is a concern. This program also offers resources for health-care providers, including the Autism Case Training course, which is available online for individual continuing education credit and as a classroom-based curriculum for pediatric residency programs. Additional information is available at http://www.cdc.gov/autism.

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Notice to Readers

NNDSS Tables Have Updated 'N' Indicators for 2011–2013

Because of delays in the collection, processing, and analysis of data from the 2011 Council of State and Territorial Epidemiologists (CSTE) State Reportable Conditions Assessment (SRCA), 2011 SRCA data could not be applied to the National Notifiable Diseases Surveillance System (NNDSS) data in the *MMWR* NNDSS Tables I and II for 2011 or 2012. CSTE performed a major redesign of the SRCA application in 2011, which delayed CSTE's data collection efforts. Additionally, CDC's data quality control and assessment efforts and analysis of 2011 SRCA data were prolonged, in part because of challenges experienced in analyzing the data.

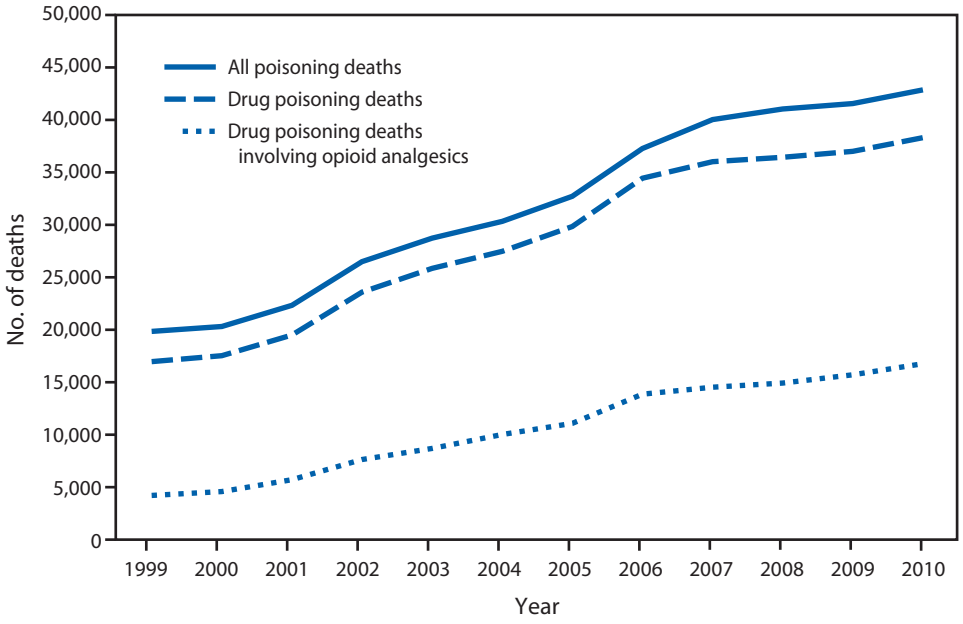
SRCA data are analyzed annually to create "not reportable" ("N") indicators for *MMWR* Tables I and II, to denote when a nationally notifiable disease is not reportable in a specific reporting jurisdiction. As a temporary measure to update the "N" indicators applied to *MMWR* NNDSS Tables I and II, reporting jurisdictions informed CDC of which nationally notifiable infectious conditions were not reportable in their jurisdictions for years 2011 and again for year 2012. Thus, the *MMWR* NNDSS Tables I and II use 2011 and 2012 "N" indicators reported directly to CDC and not from the CSTE's SRCA. The 2012 "N" indicators from CDC are being used for both the 2012 and 2013 NNDSS data. The 2011 "N" indicators from CDC are being used for the 2011 NNDSS data. NNDSS reporting exceptions ("N" indicators) for 2006 through 2012 can be found at http://wwwn.cdc.gov/nndss/script/downloads.aspx.

SRCA data CSTE currently displays on its web query page (http://www.cste2.org/izenda/entrypage.aspx) reflect the State Reportable Conditions Assessment results from 2007 through 2010 only. SRCA results for 2011 will be available on CSTE's web site via a new web query tool being developed by CSTE.

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Number of Deaths From Poisoning,* Drug Poisoning,† and Drug Poisoning Involving Opioid Analgesics§ — United States, 1999–2010



* Poisoning deaths include those resulting from drugs, and those associated with solid or liquid biologics, gases or vapors, or other substances. Poisoning deaths are from all manners, including unintentional, suicide, homicide, and undetermined intent.

† Drug poisoning deaths include unintentional or intentional poisoning deaths resulting from overdoses of a drug, being given the wrong drug, taking the drug in error, or taking a drug inadvertently.

§ Among deaths with drug poisoning as the underlying cause, the *International Classification of Diseases, 10th Revision* codes T40.2–T40.4 were used to indicate whether opioid analgesics were involved.

From 1999 to 2010, the number of U.S. drug poisoning deaths involving any opioid analgesic (e.g., oxycodone, methadone, or hydrocodone) more than quadrupled, from 4,030 to 16,651, accounting for 43% of the 38,329 drug poisoning deaths and 39% of the 42,917 total poisoning deaths in 2010. In 1999, opioid analgesics were involved in 24% of the 16,849 drug poisoning deaths and 20% of the 19,741 total poisoning deaths.

Sources: National Vital Statistics System. Mortality data. Available at http://www.cdc.gov/nchs/deaths.htm.

Warner M, Chen LH, Makuc DM, Anderson RN, Miniño AM. Drug poisoning deaths in the United States, 1980–2008. NCHS data brief, no 81. Hyattsville, MD: US Department of Health and Human Services, CDC, National Center for Health Statistics; 2011. Available at http://www.cdc.gov/nchs/data/databriefs/db81.pdf.

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