MAJOR ARTICLE

# Laboratory-Confirmed Shigellosis in the United States, 1989–2002: Epidemiologic Trends and Patterns

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**During 1989–2002, a total of 208,368 laboratory-confirmed *Shigella* infections were reported to the Centers for Disease Control and Prevention. *Shigella sonnei* accounted for 71.7%, *Shigella flexneri* accounted for 18.4%, *Shigella boydii* accounted for 1.6%, and *Shigella dysenteriae* accounted for 0.7% of infections; for 7.6%, no serogroup was reported. National incidence rates ranged from 7.6 cases per 100,000 persons in 1993 to 3.7 cases per 100,000 persons in 1999. Incidence rates for *S. boydii, S. dysenteriae,* and *S. flexneri* decreased over the 14-year period by 81%, 83%, and 64%, respectively; *S. sonnei* rates only decreased by 8%. The highest rates were reported from western states (10.0 cases per 100,000 persons) and among children 1–4 years of age (20.6 cases per 100,000 persons). The female-male *S. sonnei* incidence rate ratio among 20–39-year-old adults decreased from 2.3 during 1989–1999 to 1.4 during 2000–2002. Approximately 1% of isolates were from extraenteric sources; 0.25% were from blood. *S. sonnei* remains an important cause of diarrhea in the United States. Prevention efforts that target high-risk groups are needed.**

*Shigella* species are a common cause of bacterial gastroenteritis. It is an important cause of morbidity among young children and is challenging to control, particularly in day-care settings [1]. Clinical illness may vary from asymptomatic infection to severe dysentery [2]. There are 4 major subgroups of *Shigella (Shigella boydii, Shigella dysenteriae, Shigella flexneri,* and *Shigella sonnei)* and >40 serotypes identified on the basis of characteristics of the O antigen. Although all *Shigella* subgroups can cause dysentery, *S. sonnei* causes generally milder disease than do *S. dysenteriae* and *S. flexneri* [3, 4]. Life-threatening complications, such as bacteremia, hemolytic uremic syndrome, and toxic megacolon, and long-term sequelae, such as reactive arthritis, can occur. Unlike non-Typhi *Salmonella* or *Escherichia coli* O157:H7, humans are the only natural host for *Shigella* species. On the basis of national laboratory-based surveillance data for *Shigella* for 1967–1988, the annual isolation rates ranged from 5.0 cases per 100,000 persons in 1985 to 10.1 cases per 100,000 persons in 1988 (average annual isolation rate, 6.5 cases per 100,000 persons) [5] (Centers for Disease Control and Prevention [CDC], unpublished data). We reviewed surveillance data for laboratory-confirmed cases of shigellosis in the United States for 1989–2002 to identify recent epidemiologic patterns and trends.

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## MATERIALS AND METHODS

Since 1964, the Foodborne and Diarrheal Diseases Branch at the CDC has maintained a national laboratory-based surveillance system for shigellosis. Data collected during the period of 1989–2002 were used. In

each state, isolation and identification of *Shigella,* serogrouping, and serotyping were performed at clinical microbiology and public health laboratories with commercially available and previously described procedures [6]. Data on culture-confirmed cases included subgroup, specimen collection date, reporting county and state, patient sex, patient age, patient race and ethnicity, type of residence, and clinical source of the isolate were reported weekly to the CDC by state health departments. During 1989–1999, California reported only the number of isolates of each subgroup identified each year. In 2000, California began reporting information on patient age, sex, and race.

US resident population data from the US Bureau of the Census were used to calculate nationwide isolation rates, rates of specific subgroups, and rates by census region [7, 8]. Midyear intercensal population estimates were used during noncensus years. US census regions were defined by standard US census definitions [8]. County-specific isolation rates were determined for 1990 and 2000 for counties stratified by selected county characteristics with 1990 and 2000 US census data [7]. All statistical analyses were performed with SAS software, version 8.22002 (SAS Institute).

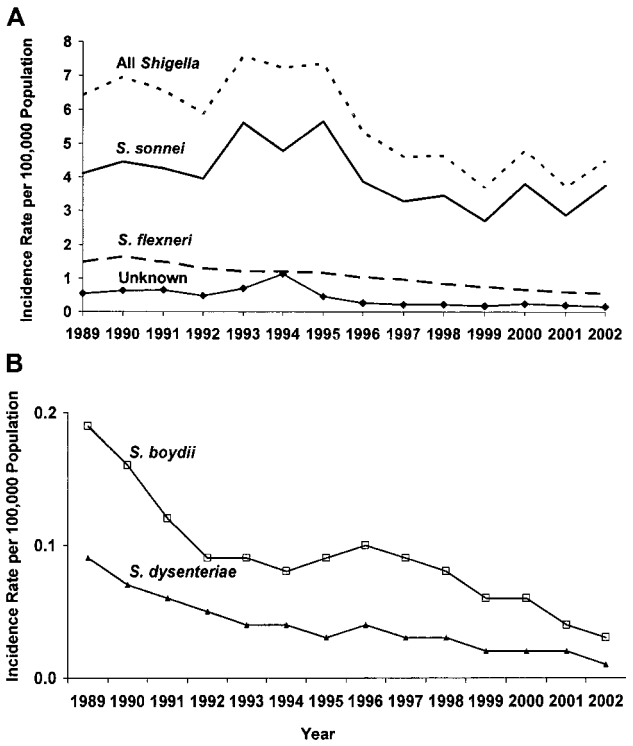


**Figure 1.** Incidence rates of *Shigella* species per 100,000 persons, by subgroup, United States, 1989–2002.

## RESULTS

During the period of 1989–2002, a total of 208,368 *Shigella* isolates were reported to the CDC. The distribution of isolates by subgroup was as follows: *S. sonnei,* 71.7%; *S. flexneri,* 18.4%; *S. boydii,* 1.6%; and *S. dysenteriae,* 0.7%; 7.6% were of an unknown subgroup (i.e., not reported, not further typed, or untypable). Nationwide incidence rates of *Shigella* infection varied during the study period, with an average total annual incidence rate of 5.6 cases per 100,000 US population (figure 1). Rates peaked in 1993 at 7.6 cases per 100,000 persons and decreased to a 14-year low of 3.7 cases per 100,000 persons in 1999. *Shigella* incidence rates were largely driven by *S. sonnei* (average annual isolation rate, 4.0 cases per 100,000 persons). *S. sonnei* accounted for an increasing proportion of all *Shigella* isolates: 64.1% in 1989 and 83.5% in 2002. Incidence rates per 100,000 population for *S. boydii, S. dysenteriae,* and *S. flexneri* decreased over the 12-year period by 81.4%, 82.8%, and 64.2%, respectively, whereas *S. sonnei* rates only decreased by 8%.

The average incidence rate of *Shigella* infection per 100,000 population was 10.0 cases (range, 5.2–14.9 cases) in the West, 4.6 cases (range, 2.5–8.4 cases) in the South, 4.5 cases (range, 3.0–6.8 cases) in the Midwest, and 3.9 cases (2.3–5.9 cases) in the Northeast (figure 2). During 1999–2002, the incidence of shigellosis in the West approached the incidence of other regions of the United States. Regional variations were often driven by large increases in *S. sonnei* infection in individual states. The peak incidence rate in the Northeast in 1991 was due to a large increase in *S. sonnei* infection in Massachusetts, and the peak incidence in the West in 1995 was due to an increase in *S. sonnei* infection in California. Although *S. sonnei* was the predominant subgroup overall, several states had a predominance of *S. flexneri* in specific years. Hawaii had more *S. flexneri* infections reported than *S. sonnei* infections in all years except 1994 and 1999. Nine other states and the District of Columbia also reported more *S. flexneri* than *S. sonnei* infections in more than a single year (data not shown).

In 1990, the highest isolation rates were reported from counties with relatively high proportions of urban, poor (20%–100% of residents with income below the poverty line), nonwhite residents (table 1). In 2000, compared with 1990, *Shigella* isolation rates decreased in urban, semiurban, and rural counties. *Shigella* isolation rates decreased most dramatically in counties with a relatively high proportion of Native American (5%–100%) or black residents (50%–100%). Decreases were also evident for rural and low-income counties. Isolation rates increased in counties with predominantly Hispanic residents, in counties that were 0%–89% white, and in counties that were 1%–49% black.

Patient age was reported for 140,927 isolates (68%). Children aged 1–4 years had the highest rates of shigellosis, ranging from 28.3 cases per 100,000 persons in 1994 to 12.5 cases per 100,000 persons in 1999 (average incidence rate, 20.6 cases per 100,000 persons) (figure 3). The median age of persons with *S. sonnei*

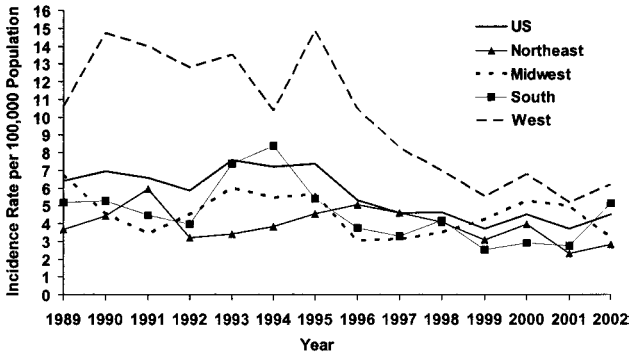


**Figure 2.** Incidence rates of *Shigella* species per 100,000 persons, by geographic region, United States, 1989–2002.

infection was 7 years, and the median ages for *S. boydii, S. flexneri,* and *S. dysenteriae* infections were 18, 18, and 25 years, respectively. Overall, 34.0% of all *Shigella* isolates were recovered from children aged <5 years, and 80.0% of these isolates were *S. sonnei.*

Patient sex was reported for 152,083 isolates (73.0%). The mean sex-specific annual incidence rates for *Shigella* infection were 4.3 cases per 100,000 women and 3.9 cases per 100,000 men, for a female-to-male incidence rate ratio of 1.1:1. By subgroup, the mean ratio was 1.2:1 for *S. sonnei,* 0.8:1 for *S. flexneri,* 1.2:1 for *S. boydii,* and 0.9:1 for *S. dysenteriae.* The differences in incidence rates by sex were greatest among adults aged 20–39 years for *S. sonnei* and *S. flexneri* infection. During 1989–1999, the incidence of *S. sonnei* infection was twice as high among women than among men in this age group (rate ratio range, 2.0–2.5). In 2000, a proportionately larger increase in male incidence rates (compared with female incidence rates) occurred, changing the female-to-male rate ratio to 1.4 in 2000, 1.1 in 2001, and 1.6 in 2002. In contrast, the ratio for *S. flexneri* infection among persons aged 20–39 years was 0.5–0.8 throughout the study period.

For all 4 subgroups, reporting of *Shigella* isolates demonstrated seasonality, with the largest percentage of reported isolates occurring between July and October and the smallest proportion occurring in January, February, and March.

The specific clinical source of the specimen was reported for 147,901 isolates (71%); 146,277 isolates (99%) were recovered from stool samples. The remaining 1624 isolates (1%) were recovered from the following specimens or sites: urine, 929 (0.63%); blood, 400 (0.27%); wound sites, 159 (0.11%); sputum, 102 (0.07%); gallbladder, 15 (0.01%); ear, 7 (0.005%); CSF, 6 (0.004%); and bone/joint, 6 (0.004%). Higher proportions of *S. dysenteriae* (0.74%), *S. flexneri* (0.69%), and *S. boydii* (0.58%) isolates were recovered from blood samples, compared with *S. sonnei* (0.19%) ($P < .01$). The highest blood isolation rates were among persons aged <1 year (0.28 cases per 1,000,000 persons), 1–4 years (0.25 cases per 1,000,000 persons), and ≥80 years (0.12 cases per 1,000,000 persons). Two percent of all *Shigella* isolates from persons aged >80 years were recovered from blood samples, compared with 0.4% of all *Shigella* isolates recovered from persons aged <1 year. Forty percent of the blood isolates were recovered from women. On average, 29 *Shigella* isolates recovered from blood samples were reported annually (range, 17–46 isolates). Among the 6 isolates recovered from CSF samples, 4 were *S. sonnei,* 1 was *S. flexneri,* and 1 was *S. boydii.* The ages of these persons were 0, 2, 5, 7, 33, and 42 years; 4 were men. Data on clinical presentation and outcome were not available.

## DISCUSSION

*Shigella* infection is the third most common cause of bacterial gastroenteritis in the United States, after *Campylobacter* infection and *Salmonella* infection and ahead of *E. coli* O157 infection. Unlike *Campylobacter, Salmonella,* and *E. coli* O157 in-

**Table 1. Reported incidence rates of *Shigella* species per 100,000 persons by selected United States county population characteristics for the census years 1990 and 2000.**

| | 1990 | | 2000 | |
|---|---|---|---|---|
| Characteristic, percentage of county[a] | No. of counties | Incidence rate | No. of counties | Incidence rate |
| Classified urban | | | | |
| 0 | 794 | 7.3 | 732 | 0.8 |
| 1–49 | 1332 | 6.7 | 1194 | 1.4 |
| 50–100 | 1015 | 12.9 | 1215 | 6.6 |
| Residents with income below poverty level | | | | |
| 0–9 | 553 | 3.1 | 883 | 3.4 |
| 10–19 | 1731 | 4.7 | 1758 | 4.8 |
| 20–100 | 857 | 8.4 | 500 | 4.8 |
| White residents | | | | |
| 0–49 | 126 | 12.2 | 158 | 15.4 |
| 50–89 | 1097 | 5.0 | 1308 | 6.0 |
| 90–100 | 1918 | 2.5 | 1675 | 2.5 |
| Black residents | | | | |
| <1 | 1454 | 4.4 | 1341 | 1.6 |
| 1–49 | 1599 | 4.4 | 1705 | 6.5 |
| 50–100 | 88 | 9.0 | 95 | 1.9 |
| Native American residents | | | | |
| 0–4 | 2955 | 4.3 | 2947 | 5.6 |
| 5–100 | 186 | 16.3 | 194 | 1.8 |
| Hispanic residents | | | | |
| 0–9 | 2810 | 4.1 | 2337 | 3.5 |
| 10–100 | 331 | 5.5 | 804 | 7.9 |

[a] The percentage ranges for demographic characteristics were based on how US census data are reported for counties.

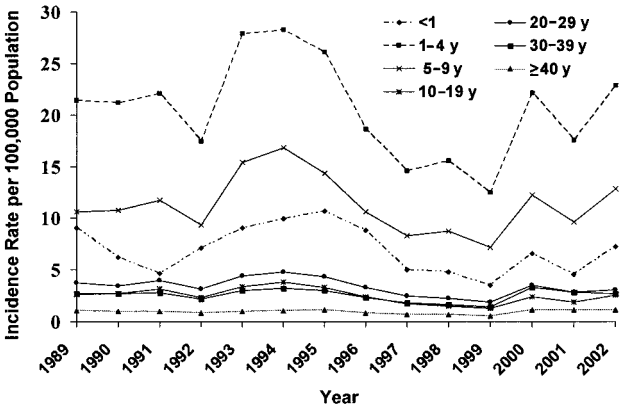


**Figure 3.** Incidence rates of *Shigella* species per 100,000 persons, by age, United States, 1989–2002.

fections, for which food-borne transmission predominates, an estimated 80% of *Shigella* infections are transmitted from person to person [9]. Approximately 10% of persons with reported culture-confirmed *Shigella* infections are hospitalized [10]. Our examination of laboratory-confirmed shigellosis identified an average annual incidence of 5.6 cases per 100,000 persons during 1989–2002, a 12% decrease from an average annual incidence rate of 6.4 cases per 100,000 persons during 1968–1988 [5, 11] (CDC, unpublished data). During the study period, the incidence of *S. dysenteriae, S. flexneri,* and *S. boydii* infections decreased substantially, but there was little decrease in the incidence of *S. sonnei* infection [5, 11]. The proportion of all *Shigella* isolates that were *S. sonnei,* therefore, increased steadily, continuing a trend evident since 1964, when national surveillance for *Shigella* began [5, 11, 12]. *S. sonnei* is the most common subgroup in other industrialized nations, whereas *S. flexneri* is the most common subgroup in developing nations [13].

During 1989–2002, children aged <5 years had the highest rates of shigellosis, followed by those aged 5–9 years. Approximately 80% of these infections were due to *S. sonnei.* High shigellosis rates in children are attributable to several factors. Young children are unable to practice good personal hygiene and have not yet acquired immunity to *S. sonnei.* The infectious dose is as low as 10–200 organisms [14], and person-to-person transmission is highly effective. Day-care centers play an important role in the person-to-person spread of shigellosis and its subsequent dissemination in communities [15, 16]. Inadequate hand washing, diapering practices, and fecal contamination of water-play areas, such as kiddie pools, have been associated with *S. sonnei* transmission in day-care centers [16, 17]. When outbreaks occur in day-care settings, attack rates are high (28%–73%) [18, 19], and secondary transmission of *S. sonnei* often exceeds 30% in households with young children [16, 20–22]. The high rates of *Shigella* in the West, particularly California, may be explained in part by the large numbers of young children and day-care centers in this state and a public health system that efficiently detects and reports laboratory-confirmed isolates [23].

Compared with 1990, shigellosis incidence rates decreased markedly among Native American persons and less so among black persons. There is no clear explanation for these findings. However, Native American populations and their health care providers, particularly those who serve in Indian Health Service facilities, have become much more aware of shigellosis during the past decade. In addition, water and sanitation infrastructure may have improved, and prevention measures, such as hand washing campaigns, have been conducted in some Native American communities [24, 25]. The change may also be part of the natural cycle of shigellosis in these communities.

During the period of 1989–1999, women 20–39 years of age were more than twice as likely as men in the same age group to have laboratory-confirmed *S. sonnei* infection, presumably reflecting the increased risk due to women being the primary caretakers of young children [26]. For 2000–2002, however, the female-to-male incidence rate ratio for *S. sonnei* among 20–39-year-old adults decreased to between 1.1 and 1.6. This occurred because of a proportionately larger increase in male incidence rates than in female incidence rates. This change occurred irrespective of the fact that California submitted age and sex data on patients with shigellosis for the first time in 2000 (data not shown). We believe that this change occurred, in part, because of increases in *S. sonnei* among men who have sex with men (MSM), among whom *S. flexneri* was previously more often reported [27]. It is not known why this subgroup shift has occurred in this population. In 2000–2001, a large outbreak of *S. sonnei* infection occurred among MSM in California [28]. Other outbreaks of *S. sonnei* infection in 2000–2001 among MSM were reported from Massachusetts (CDC, unpublished data), New York City (New York City Health Department, unpublished data), Canada, and Australia [29, 30]. Surveillance data from 2003 onward will indicate whether this is a continuing trend.

The most common extraenteric samples from which *Shigella* isolates were reported was urine. Although some of these isolates may have been fecal contaminants, *Shigella* has been reported as a cause of urinary tract infection [31]. Isolation of *Shigella* from blood and CSF specimens is rare [32, 33]. In studies of hospitalized patients with laboratory-confirmed shigellosis, reported prevalence rates of *Shigella* bacteremia were 0.4%–7.3% [32, 34]. Only 0.25% and 0.005% of *Shigella* isolate reports submitted to the CDC were from blood and CSF samples, respectively. *Shigella* septicemia is most common in infants and in persons with malnutrition or immunocompromising conditions, including AIDS [32, 35, 36]. Our demographic data identified infants and elderly patients (>80 years) as having the highest rates of *Shigella* bacteremia. *S. dysenteriae, S. flexneri,*

and *S. boydii* blood isolates were relatively more frequent than *S. sonnei,* suggesting that these subgroups are more invasive.

Our study has several limitations. Data were obtained from a passive surveillance system for laboratory-confirmed illnesses. Most cases of shigellosis are undiagnosed or diagnosed on clinical grounds alone and unreported. It is estimated that the true burden of shigellosis in the United States is ~440,000 infections annually [9]. Data on patient race and place of residence at the time of specimen culture were missing for ~90% of reports. We therefore relied on census data to model epidemiologic trends and patterns for race and ethnicity. In addition, patient sex and age were unknown for ~30% and 35% of reports, respectively.

During the past 14 years, progress has been made in reducing the incidence of shigellosis in the United States among non-*sonnei* subgroups; however, *S. sonnei* remains an important cause of gastroenteritis. Laboratory-based surveillance is important to identify trends in populations at particular risk for shigellosis and to inform priorities for vaccine development. A vaccine that provided protection from infection with *S. sonnei* and *S. flexneri* would be particularly useful. Although many approaches to *Shigella* vaccine development have been attempted, including live attenuated, killed whole-cell, conjugate, proteosome subunit, and ribosomal vaccines, to date, vaccine-induced immunity appears to be serotype specific [13, 37, 38]. No vaccines for *Shigella* are licensed in the United States. Interventions targeting high-risk groups, such as hand washing gels for preventing transmission in day-care centers and vaccines to protect children against infection with *S. sonnei,* have the potential to significantly reduce the incidence of shigellosis in the United States.

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