Epidemiologic Summary of Typhoid Fever in California, 2013 - 2019



Key Findings

Typhoid fever is a potentially life-threatening infectious disease caused by *Salmonella* Typhi bacteria. These bacteria are found only in humans and are passed to others when someone eats or drinks something that is contaminated with *S.* Typhi bacteria. These bacteria can spread from someone infected with *S.* Typhi who does not wash their hands properly after using the toilet. Symptoms include a prolonged high fever, weakness, and stomach pain. Without treatment, typhoid fever can be severe and cause death. Typhoid fever is not common in the United States. Most cases of typhoid fever in the United States and California are reported in people who were infected while traveling internationally in areas with poor water or sanitation systems where the disease is common, including in Asia, Africa, and Latin America.

Typhoid Fever in California from 2013 through 2019

Total Cases: There were a total of 514 typhoid fever cases from 2013 through 2019. Of these cases, four were reported to have died with typhoid fever.

Rate: The average annual rate of new typhoid fever cases during 2013-2019 was less than 1 case per 100,000 people in California.

- **By County**: There were 8 counties in California that reported at least 1 case of typhoid fever each year during 2013-2019, each with an average rate of less than 1 case per 100,000 people.
- **By Sex:** The average rates for males and females were similar, with rates less than 1 case per 100,000 people for both groups.
- **By Age Group**: The average rates were highest in children aged 1 to 4 years and adults aged 25 to 34 years, but rates in all groups were less than 1 case per 100,000 people.
- **By Race/Ethnicity**: For cases where race and ethnicity information was available, the highest percentage of cases was in people who reported non-Hispanic Asian/Pacific Islander race/ethnicity (71%).

To help prevent typhoid fever, people planning to travel in areas where typhoid fever is common should talk to their doctor about getting a typhoid fever vaccine. Whether or not you've been vaccinated, it's important to avoid risky food and drinks while traveling, including foods from street vendors and flavored ices. While traveling, drink only bottled water or boil water for one minute before drinking and eat only foods that have been thoroughly cooked.

For more information about typhoid fever in California, please visit the <u>CDPH Typhoid fever</u> <u>webpage</u>. For details about key infectious diseases in California, please visit the <u>CDPH IDB</u> <u>Surveillance and Statistics Section webpage</u>.

Background

Typhoid fever is caused by *Salmonella* Typhi, an uncommon but important bacterial pathogen, with more than 350 reported cases of culture-confirmed typhoid fever per year in the United States, mostly among travelers. While uncommon in the U.S. and other industrialized regions such as Canada, Western Europe, Australia, and Japan, typhoid fever is highly endemic in low and middle-income countries with limited access to safe drinking water, and where sanitation infrastructure and hygiene practice is poor, including in South Asia and parts of East and Southeast Asia, Africa, the Caribbean, and Central and South America. Most cases (estimated 85%) in the U.S. are in travelers returning from endemic areas (such as India, Pakistan, and Bangladesh). *S.* Typhi infection is restricted to humans (does not occur in animals), and consumption of food or water contaminated by the feces or urine of persons with typhoid fever are the leading sources of exposure.²

Typhoid fever is an acute systemic illness with an incubation period usually between 9 and 20 days but can vary from 3 to over 60 days depending on size of the inoculum and host factors.³ Illness onset is often insidious and non-specific, characterized by fever, malaise, chills, myalgia, headache, and abdominal pain.⁴ Most cases in the U.S. are associated with hospitalization. Without therapy, typhoid fever can be a life-threatening disease, with historical death rates before antibiotics ranging between 12% and 30%. Among untreated patients with acute illness, 10% shed bacteria for three months after initial onset of symptoms. Even when treated, up to 2.0-5.0% can become chronic typhoid carriers and bacteria can persist in the biliary tract even after symptoms have resolved.^{5, 6} A chronic carrier state may follow acute illness, even mild or subclinical infections.

S. Typhi isolates have shown increasing antimicrobial resistance globally and threaten the ability to treat disease and prevent severe infection. By the 1990s, multi-drug resistant (MDR) S. Typhi resistant to first-line drugs (chloramphenicol, ampicillin, and cotrimoxazole) became so common that fluoroquinolones became the drugs of choice for treatment. However, S. Typhi with decreased susceptibility or resistance to fluoroquinolones also began to circulate and are now widespread in South Asia. In 2016, an ongoing outbreak of extensively drug-resistant (XDR) S. Typhi, resistant to fluoroquinolones as well as to third generation cephalosporins (e.g., ceftriaxone) was reported in Pakistan. Between February 2018 and August 2019, 33 XDR S. Typhi cases were detected in the U.S. among recent travelers to Pakistan and Iraq. Emergence of this XDR S. Typhi strain (and XDR-variant strains that also carry third-generation cephalosporin resistance, but are distinct from the Pakistan XDR strain) has been particularly concerning because it leaves only one oral antibiotic, azithromycin, available for treatment. Recently, multiple reports of azithromycin resistance have also emerged from Pakistan, Bangladesh, and India. Entered in the U.S. and India. Entered in the U

Two typhoid vaccines are currently available in the U.S.; one is an injectable vaccine and the other is an oral vaccine. Both vaccines confer about 50-80% protection in children and adults. Notably, vaccine-induced immunity provides little protection against large challenge doses and protection decreases over time, requiring a booster.¹¹

This report describes the epidemiology of confirmed and probable typhoid fever cases in California from 2013 through 2019. Due to multiple factors that can contribute to underreporting, data in this report are likely underestimates of actual disease incidence. For a complete discussion of the definitions, methods, and limitations associated with this report, please refer to the *Technical Notes*. 12 The epidemiologic description of typhoid fever for earlier

surveillance periods can be found in the *Epidemiologic Summary of Typhoid fever in California*, 2001-2008 and 2009-2012.^{13, 14}

California Reporting Requirements and Surveillance Case Definition

California Code of Regulations (CCR), Title 17, Section 2500 requires health care providers to report suspected cases of typhoid fever and carriers of *S*. Typhi to their local health department within one working day of identification or immediately by telephone if an outbreak is suspected. Fer CCR, Title 17, Section 2505, clinical and reference laboratories are also required to report laboratory testing results suggestive of *S*. Typhi to either the California Reportable Diseases Information Exchange (CalREDIE) (via electronic laboratory reporting) or the local health department; notification should occur within one working day after the health care provider has been notified of the laboratory testing result. 16

California regulations require cases of typhoid fever and carriers of *S*. Typhi to be reported to CDPH. CDPH officially counted typhoid fever cases that satisfied the U.S. Centers for Disease Control and Prevention (CDC)/Council of State and Territorial Epidemiologists surveillance case definition including confirmed and probable classifications. From 2013 through 2018, a confirmed case of typhoid fever was defined as a case with a compatible clinical syndrome in which *S*. Typhi was cultured from a clinical specimen. A probable case was defined as one with clinically compatible illness and an established epidemiologic link to a laboratory-confirmed case during an outbreak.¹⁷ In 2019, the definition for a confirmed case was updated to require only isolation of *S*. Typhi culture from a clinical specimen, reflecting the high specificity of culture for this disease. A probable case was updated to include cases with clinically compatible illness and detection of *S*. Typhi in a clinical specimen using a culture-independent diagnostic test (CIDT). Cases with clinically compatible illness and an established epidemiologic link to a laboratory-confirmed case during an outbreak remained probable cases.¹⁸

CDPH defined a convalescent typhoid carrier as a person who shed typhoid bacilli for three or more months after onset of typhoid fever. A chronic typhoid carrier was defined as: (a) a person who continued to excrete typhoid bacilli for more than 12 months after onset of typhoid fever or (b) (i) a person who gave no history of typhoid fever or who had the disease more than one year previously, and (ii) whose feces or urine were found to contain typhoid bacilli on two separate examinations at least 48 hours apart, confirmed by the CDPH Microbial Diseases Laboratory. CDPH defined other typhoid carriers as persons who had typhoid bacilli isolated from surgically removed tissues, organs, or draining lesions and continued to excrete typhoid bacilli for more than 12 months.

Epidemiology of Typhoid Fever in California, 2013-2019

CDPH received reports of 514 total cases (511 confirmed and 3 probable) of typhoid fever with estimated symptom onset dates from 2013 through 2019. This corresponds to an average annual incidence rate of 0.2 cases per 100,000 population [Figure 1]. Deaths were reported among four (0.8%) case-patients at the time of case report.

The first XDR typhoid fever case was reported in 2018; a total of seven cases of XDR or ceftriaxone-resistant typhoid fever were reported during 2018-2019.

During the surveillance period, 450 (90.4%) of the total typhoid fever case-patients reported travel outside of the United States. Of these, case-patients most frequently reported travel to India (280 case-patients) and Mexico (42 case-patients).

Statewide from 2013 through 2019, eight counties reported at least one case for each year of the surveillance period: Alameda, Los Angeles, Orange, Sacramento, San Bernardino, San Diego, San Mateo, and Santa Clara counties. Cases from these 8 counties made up 73.0% of the total typhoid fever cases reported. Among these 8 counties, the highest average annual rate was in Santa Clara County (0.8 per 100,000; 105 total cases). Sutter County (0.9 per 100,000; 6 total cases) also reported high average annual rates, but low case counts [Figure 2]. By region (see *Technical Notes*), the average annual incidence rate for the surveillance period was higher in Northern California (0.3 per 100,000; 325 total cases) than Southern California (0.1 per 100,000; 189 cases total). The Bay Area region reported the highest average annual incidence rate in California (0.4 per 100,000; 239 total cases).

From 2013 through 2019, average annual incidence rates were similar in males (0.2 per 100,000; 264 total cases) and females (0.2 per 100,000; 249 cases); 51.4% of case-patients were male and 48.4% were female.

By age group, the average annual incidence rate during the surveillance period was highest in children aged 1 to 4 years (0.4 per 100,000 population in this age group; 49 cases) followed by adults aged 25 to 34 years (0.3 per 100,000; 118 cases) and children 5 to 14 years (0.3 per 100,000; 49 cases) [Figure 3].

For typhoid fever cases with complete race/ethnicity information (see *Technical Notes*), the highest percentage of cases was among those who reported non-Hispanic Asian/Pacific Islander race/ethnicity (71.0%), which is disproportionally higher than the percentage of the non-Hispanic Asian/Pacific racial/ethnic population in California during the same time period (71.0% vs. 15.0%, respectively) [Figure 4].

From 2013 through 2019, CDPH did not receive any reports of typhoid fever outbreaks.

During 2013-2019, ten persons were reported as chronic typhoid carriers. Chronic carriers were more likely than acute typhoid cases to be older (median age 48 years vs. 27 years).

Figure 1. Typhoid Fever Cases and Incidence Rates by Year of Estimated Illness Onset, California, 2013-2019

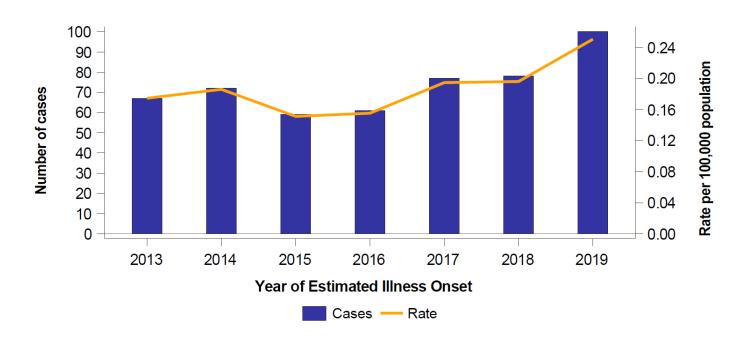


Figure 2. Typhoid Fever Average Annual Incidence by County, California, 2013-2019

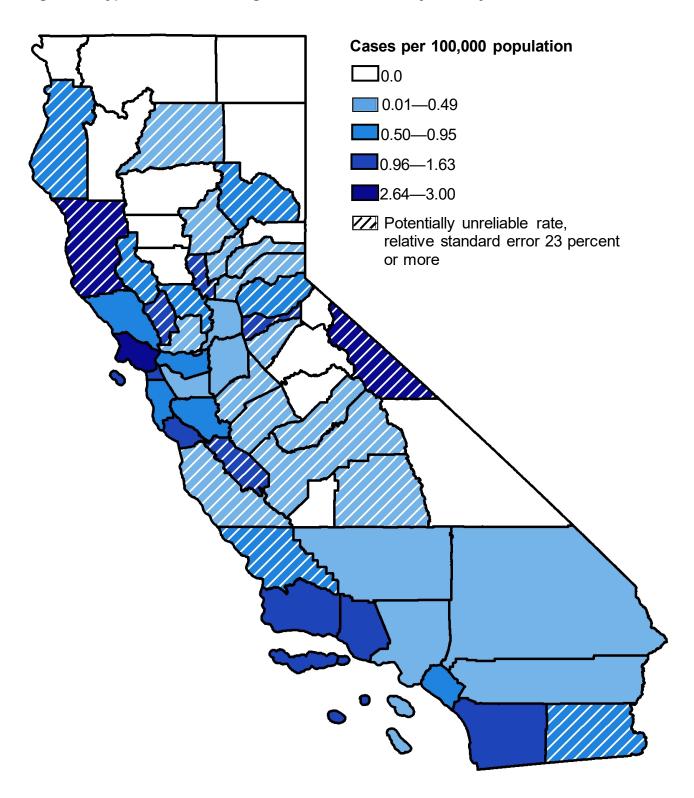
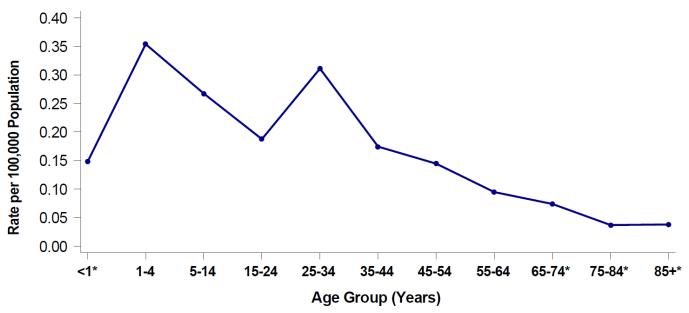
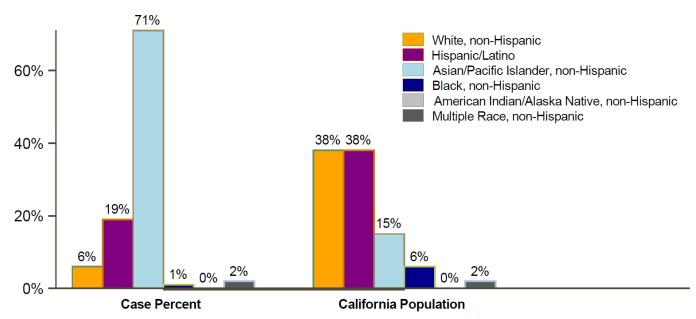


Figure 3. Typhoid Fever Average Annual Incidence Rates by Age Group, California, 2013-2019



^{*}Potentially unreliable rate: relative standard error 23 percent or more.

Figure 4. Typhoid Fever Cases and Population by Race/Ethnicity, California, 2013-2019



6% (n=31) of reported incidents of Typhoid Fever did not identify race/ethnicity and 6.8% (n=35) of incidents identified as 'Other' race/ethnicity and are not included in the Case Percent calculation. Information presented with a large percentage of missing data should be interpreted with caution.

Comments

The average annual incidence of typhoid fever in California during the 2013-2019 surveillance period (0.2 per 100,000; 514 total cases) was similar to that of the 2009-2012 surveillance period (0.2 cases per 100,000; 330 total cases). Incidence rates were also similar in trend between the two surveillance periods for age group, sex, and race/ethnicity.

Notably, the first case of XDR typhoid fever was reported in California in 2018, with seven cases of XDR or XDR-variant third-generation cephalosporin-resistant S. Typhi reported by end of 2019.

Vaccination against typhoid is recommended for international travelers to destinations where the risk of contracting typhoid fever is high. ¹⁹ Persons traveling to areas where water and/or sanitation infrastructure is inadequate (including South Asia) should be vaccinated against typhoid fever before travel, and should avoid risky food and drinks while traveling, including foods from street vendors and flavored ices. While traveling, persons should drink only bottled, canned, or properly treated/filtered drinks, and eat only foods that have been thoroughly cooked. While a typhoid vaccine confers some degree of protection, ensuring the safety of food and water is still the most important protective measure as typhoid immunization provides no protection against infection with *S.* Paratyphi and other potentially food- and water-borne enteric pathogens.

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