HHS Public Access

Author manuscript

Pediatrics. Author manuscript; available in PMC 2022 September 01.

Published in final edited form as:

Pediatrics. 2021 September ; 148(3): . doi:10.1542/peds.2020-049080.

Congenital Syphilis Diagnosed Beyond the Neonatal Period in the United States: 2014–2018

Anne Kimball, MD, MPH[a,b], **Virginia B. Bowen, PhD, MHS**[a], **Kathryn Miele, MD, MA**[a,c], **Hillard Weinstock, MD, MPH**[a], **Phoebe Thorpe, MD, MPH**[a], **Laura Bachmann, MD, MPH**[a], **Robert McDonald, MD, MPH**[a], **Aliza Machefsky, MD**[a,c], **Elizabeth Torrone, PhD, MSPH**[a]

[a]Division of STD Prevention; Centers for Disease Control and Prevention; Atlanta, GA

[b]Epidemic Intelligence Service, Centers for Disease Control and Prevention; Atlanta, GA

[c]CDC Foundation; Atlanta, GA

Abstract

Background and Objective: During 2014–2018, reported congenital syphilis (CS) cases in the United States increased 183% — from 462 to 1,306 cases. We reviewed infants diagnosed with CS beyond the neonatal period (>28 days) during this time.

Methods: We reviewed surveillance case report data for infants with CS delivered during 2014–2018 and identified those diagnosed beyond the neonatal period with reported signs or symptoms. We describe these infants and identify possible missed opportunities for earlier diagnoses.

Results: Of the 3,834 reported cases of CS delivered during 2014–2018, we identified 67 symptomatic infants diagnosed beyond the neonatal period. Among those with reported findings, 67% had physical exam findings of CS, 69% had abnormal long-bone radiographs consistent with CS, and 36% had reactive syphilis testing in the cerebrospinal fluid. The median serum nontreponemal titer was 1:256 (range: 1:1–1:2048). The median age at diagnosis was 67 days (range: 29–249 days). Among the 66 mothers included, 83% had prenatal care, 26% had a syphilis diagnosis during pregnancy or at delivery, and 42% were not diagnosed with syphilis until after delivery. Additionally, 24% had an initial negative test and seroconverted during pregnancy.

Conclusions: Infants with CS continue to be undiagnosed at birth and present with symptoms after 1 month of age. Pediatric providers can diagnose and treat infants with CS early by following guidelines, reviewing maternal records and confirming maternal syphilis status, advocating for maternal testing at delivery, and considering the diagnosis of CS regardless of maternal history.

Address Correspondence To: Anne Kimball, MD, MPH; Division of STD Prevention; Centers for Disease Control and Prevention; 1600 Clifton Road NE, US 12-2; Atlanta, GA 30329; 404-718-3642 opu7@cdc.gov.

Contributors' Statement Page

Dr. Kimball conceptualized and designed the study, performed the analysis, drafted the manuscript, and revised the manuscript.
Dr. Bowen contributed to the conceptualization of the study, reviewed the analysis in detail, and critically reviewed the manuscript.
Dr. Miele drafted sections of the manuscript, reviewed and formatted the manuscript.
Drs. Weinstock, Thorpe, and Bachmann critically reviewed the manuscript for important intellectual content.
Dr. McDonald reviewed the manuscript, wrote the cover letter, and facilitated manuscript submission paperwork.
Dr. Machefsky reviewed the manuscript and formatted the references.
Dr. Torrone contributed to the conceptualization of the study and critically reviewed the manuscript for important intellectual content.

Conflict of Interest Disclosures (includes financial disclosures): The authors have no conflicts of interest to disclose.

Table of Contents Summary:

This article describes infants reported to CDC with congenital syphilis diagnosed beyond the neonatal period in the United States during 2014–2018.

Introduction

In 1990, Dorfman and Glaser reported seven infants in New York City diagnosed with congenital syphilis (CS) beyond the newborn period after presenting to care with symptoms at 3–14 weeks of age. These infants were not diagnosed with CS at birth due to maternal acquisition of syphilis late in pregnancy and a lack of serologic testing at delivery.[1] After declines in U.S. rates of CS between 1991 and 2005, rates have increased steadily since 2013, with 1,306 CS cases reported to the Centers for Disease Control and Prevention (CDC) in 2018—a case count not seen since 1995.[2] In 2019, case reports of 4- and 6-month-old infants presenting with signs and symptoms of CS were published, demonstrating that CS diagnoses beyond the neonatal period occur today.[3,4] Pediatric providers are the frontline for diagnosis and management of infants with CS and should be aware of this reemerging threat.

Early signs and symptoms of CS can be present at birth or appear in the first two years of life and include rash, hepatosplenomegaly, copious nasal discharge known as “snuffles,” central nervous system abnormalities, and inflammation of the long bones with associated pain and fractures.[5] Late manifestations include intellectual disability, physical deformities, and Hutchinson’s triad (Hutchinson’s teeth, interstitial keratitis, and eighth nerve deafness), and can develop after two years of age as a result of persistent inflammation and scarring.[5,6] Infants with CS who appear normal at birth may later develop manifestations of CS if not treated.[5,7] The late manifestations can be prevented with early treatment, ideally in the first three months of age.[5] CS can be prevented by diagnosing and adequately treating maternal infection during pregnancy. The CDC recommends 1) universal screening for syphilis early in pregnancy with repeat screening—at 28 weeks’ gestation and at delivery—for pregnant people at increased risk for syphilis acquisition based on individual risk factors or high community prevalence, and 2) confirmation of maternal serologic status prior to discharge of mother and baby from the birth hospital at least once during pregnancy and again at delivery if at increased risk.[8]

We replicated Dorfman and Glaser’s 1990 analysis at the national level in the current CS epidemic by identifying infants delivered during 2014–2018 and reported to CDC as surveillance cases of CS with diagnoses beyond the neonatal period. We describe these infants and their birthing parents, who we refer to as “mothers,” and identify potential missed opportunities for early infant diagnoses, as well as how pediatric providers can intervene.

Methods

CS is a reportable condition in all 50 states and the District of Columbia, and CDC receives case report data through the National Notifiable Diseases Surveillance System. According

to the accepted Council of State and Territorial Epidemiologist's surveillance definition, CS cases include 1) liveborn infants with clinical evidence of CS through direct detection of *Treponema pallidum* or with reactive nontreponemal syphilis testing and findings on physical examination, radiographs, or cerebrospinal fluid (CSF) analysis, and 2) liveborn or stillborn infants delivered to mothers with untreated or inadequately treated syphilis.[9] A CSF white blood cell count (WBC) of >15 WBC/mm^3 or CSF protein >120mg/dL is considered elevated for infants ≤30 days old, and a CSF WBC of >5 WBC/mm^3 or CSF protein >40mg/dL is considered elevated for infants >30 days old, without other causes for elevation.[9] CS surveillance data include maternal and infant demographic and clinical information, with data collected by state or local health department staff through provider documentation, laboratory reports, and medical record reviews.

We reviewed infants delivered during 2014–2018 and reported to CDC as surveillance cases of CS; 2019 case report data were not available at the time of analysis. We included liveborn infants diagnosed with CS beyond the neonatal period (after 28 days of age) and with reported signs or symptoms consistent with CS ("symptomatic") to identify those with clinically relevant disease. Infants were defined as symptomatic if they had a reactive nontreponemal test and one of the following signs or symptoms reported: condyloma lata, snuffles, syphilitic rash, hepatosplenomegaly, jaundice due to syphilitic hepatitis, pseudoparalysis, edema, or other signs of CS on physical exam; long-bone radiographic findings consistent with CS; elevated protein or WBC in the CSF; or a reactive venereal disease research laboratory test (VDRL) in the CSF. We excluded infants with evidence of birth outside the United States as one of our objectives was to investigate possible intervention points during the birth hospitalization. For twins, the duplicate maternal record was excluded. Age at diagnosis was calculated by subtracting the infant's birthdate from the reported date of the infant's first reactive nontreponemal test.

Demographic and clinical characteristics of symptomatic infants with CS diagnosed beyond the neonatal period and their mothers were described. Possible missed opportunities for maternal diagnosis were described by calculating proportions of mothers reported to have received prenatal care, defined as ≥1 prenatal care visit, and syphilis testing during pregnancy and at delivery. Maternal seroconversion is defined as report of negative syphilis testing early in pregnancy followed by reactive syphilis testing later in pregnancy, around delivery, or up to 90 days after delivery.

Possible missed opportunities for infant diagnosis at birth were described by calculating the timing of maternal syphilis diagnoses. Timing of maternal syphilis diagnoses were categorized as during pregnancy (>3 days before infant's birthdate), at delivery (3 days before or after infant's birthdate), and after delivery (>3 days after infant's birthdate). These were calculated using maternal reactive nontreponemal and treponemal test dates compared to the infant's birthdate and the infant's reactive nontreponemal test date. Descriptive analyses were performed using Stata (version 16, Statacorp LP).

Results

During 2014–2018, the annual number of CS cases reported to CDC increased 183% (462 to 1,306 cases) (Figure 1). Of the 3,834 infants with CS delivered in this timeframe, 2,120 (55.5%) were reported as liveborn and asymptomatic at the time of identification, 1,455 (38.1%) were reported as liveborn and symptomatic, 245 (6.4%) were reported as stillborn, and 14 (0.4%) were reported with unknown or missing vital status.

Overall, 84 (2.2%) infants with CS were diagnosed beyond the neonatal period. Of these, two were reported as asymptomatic, 14 had incomplete data on signs and symptoms, and 68 were reported as symptomatic at the time of diagnosis. The 68 symptomatic infants diagnosed beyond the neonatal period included one set of twins and one infant with evidence of birth outside the United States. As a result, 67 infants and 66 mothers were included in analyses. While the number of liveborn, symptomatic infants with CS has increased over time, the proportion diagnosed beyond the neonatal period decreased from 5.9% in 2014 to 3.9% in 2018 (Figure 1). Seventeen (25%) of the 67 symptomatic infants diagnosed beyond the neonatal period were born in 2018 (Table 1). The median age at diagnosis was 67 days (interquartile range [IQR]: 46–100, range: 29–249 days). Twenty-one infants (31%) were diagnosed after three months of age, with four (6%) diagnosed after six months of age. Most of the 67 infants were born to non-Hispanic white (n=25, 37%) or non-Hispanic black (n=22, 33%) mothers but diagnoses beyond the neonatal period occurred among all racial and ethnic groups. Most infants were reported from the South (n=24, 36%) or West (n=21, 31%) U.S. census regions, but all four regions and 30 states were represented. The median gestational age at delivery was 38 weeks, and 78% were born full-term (≥37 weeks).

For the 67 infants diagnosed beyond the neonatal period, the median nontreponemal titer at diagnosis was 1:256 (IQR: 1:32–1:512, range: 1:1–1:2048) (Table 2). Forty-five (67%) were reported to have physical exam findings consistent with CS. The most commonly reported physical exam finding was rash (n=28, 42%), followed by snuffles (n=11, 16%) and hepatosplenomegaly (n=9, 13%), with 17 (25%) reported with other or unspecified signs of CS. The majority (n=55; 82%) of infants were reported to have radiographs performed, with 10 (15%) reported as not performed and two unknown. Among those with radiographs, 38 (69%) had abnormal long-bone radiographs consistent with CS. Among the 50 (75%) infants with reported CSF VDRL results, 18 (36%) were reactive. Eleven infants (16%) were reported as not having a CSF VDRL performed and six were unknown. Among the 44 (66%) infants with reported CSF counts, 22 (50%) had an elevated protein level and/or WBC count in the CSF. Seven infants had neither CSF VDRL nor cell counts performed. Most infants (n=61, 91%) were treated with the recommended 10-day course of intravenous or intramuscular penicillin, but six (9%) were treated with either a single dose of benzathine penicillin or another regimen.

Most of the 66 mothers (n=55, 83%) were reported to have had at least one prenatal care visit (Table 3). One-half (n=35, 53%) had early stages of syphilis, including primary, secondary, and early non-primary non-secondary (early latent) syphilis. Sixteen (24%) mothers had evidence of seroconversion during pregnancy, with twelve diagnosed with syphilis after delivery. Five mothers (8%) had no reported syphilis testing during pregnancy

or at delivery, although three had least one prenatal care visit. Nine (14%) mothers had evidence of syphilis diagnoses during pregnancy, with five diagnosed ≥30 days before delivery, and eight (12%) diagnosed at delivery. Thus, seventeen mothers (26%) had syphilis diagnoses during pregnancy or at delivery. Twenty-eight mothers (42%) did not have confirmed syphilis diagnoses until after delivery, of which 15 (23%) were diagnosed after the infant's diagnosis. The timing of syphilis diagnosis could not be determined for 21 (32%) mothers because maternal test results reported to CDC were missing or nonreactive. Three mothers were reported as having received syphilis diagnosis and treatment at least 30 days before delivery; reinfection, treatment failure, or inadequate spacing of doses might have contributed to their infants' diagnosis of CS at 36−100 days of age.

Discussion

In 1990, Dorfman and Glaser were "surprised" to identify seven infants diagnosed with CS after three weeks of age in New York City, given the attention placed on detecting and treating sexually transmitted infections at that time.[1] We identified 67 infants with symptomatic CS diagnosed beyond the neonatal period during 2014–2018, highlighting continued concerns for delayed diagnosis and treatment in the current CS epidemic.

While the 3,834 infants with CS in the United States during 2014–2018 represent failures of public health, clinicians, and healthcare systems,[2,5,10] the 67 infants diagnosed beyond the neonatal period and the 245 stillbirths are ultimate failures. CS diagnoses beyond the neonatal period occurred in all U.S. regions and among all racial and ethnic groups, representing widespread problems in provision of or access to recommended care for pregnant people and their infants in communities across the United States. While the declining proportion of symptomatic infants diagnosed with CS beyond the neonatal period suggests an improvement in early diagnoses over time, rates of female syphilis and CS continue to increase. Collaboration between public health and clinical sectors is needed to prevent further increases and to ensure that all infants with CS are identified and treated early.[5,10] Infants diagnosed beyond the neonatal period had high nontreponemal titers and a high prevalence of bone and central nervous system involvement. Infants with symptomatic CS at diagnosis and those diagnosed and treated later in life are at increased risk for developing sequelae.[5,7]

CDC's STD Treatment Guidelines contain specific instructions for evaluation, treatment, and follow-up of infants exposed to syphilis.[8] All neonates born to mothers with reactive nontreponemal and treponemal tests should be evaluated with a serum nontreponemal quantitative test, either a rapid plasma reagin (RPR) or VDRL, and be examined thoroughly for evidence of CS. Neonates with abnormal physical exams consistent with CS, with direct detection of *T. pallidum*, or with a nontreponemal titer that is four-fold higher than the mother's titer should, at a minimum, be evaluated with a complete blood cell count (CBC) and CSF analysis, including VDRL, and should be treated with 10 days of intravenous or intramuscular penicillin.[8] Neonates who appear normal but were born to mothers with untreated or inadequately treated syphilis should be evaluated with blood and CSF analyses and long-bone radiographs, and treated with 10-day or 1-dose penicillin therapy, depending on the results of the complete evaluation. Infants and children older than one month with

reactive syphilis serology should undergo a full evaluation, including CSF analysis, and 10 days of treatment with penicillin. Eleven infants in this analysis were reported with no CSF VDRL performed and six did not receive recommended treatment. Completing the recommended evaluation and treatment is necessary to identify complications and prevent sequelae of CS.

As rates of syphilis in adult females and CS continue to increase in every region of the United States, [2] pediatric providers should know how to identify, evaluate, and treat infants with CS. CS should be on the list of potential diagnoses for infants with any of the signs or symptoms of CS, such as rash, nasal secretions, hepatosplenomegaly, or more rare presentations like pseudoparalysis, perirectal mass, or isolated fever.[1,3–5,11] CS should be considered even if the mother does not have a known history of syphilis, as the majority of mothers in this analysis did not have known diagnoses of syphilis during pregnancy or at delivery.

Missed opportunities for earlier maternal and infant diagnosis were identified. Performing maternal and infant testing at delivery could have led to early diagnosis and treatment for the five infants whose mothers were not tested at all and the 12 infants whose mothers seroconverted and were diagnosed after delivery. The 17 infants whose mothers had evidence of syphilis diagnoses during pregnancy or at delivery should have been diagnosed and treated during the birth hospitalization. Pediatric providers can prevent these missed opportunities by confirming maternal syphilis status and advocating for maternal testing at delivery prior to discharging the newborn from the birth hospital. In order to accurately confirm maternal syphilis status, pediatric providers should be familiar with the types of syphilis screening tests and the syphilis screening algorithm used in the hospitals in their community.[5] Pediatric providers can partner with maternal care providers to ensure that syphilis testing is performed at delivery for mothers with no prior testing and for mothers with indications for repeat testing.[8] Pediatric providers can also partner with maternal care providers to identify missed prevention opportunities and work with local or statewide congenital syphilis case review boards to support systemic changes to prevent CS.[10,12]

Early diagnosis and treatment of the infant, especially for infants who are asymptomatic at birth, depends on identifying maternal syphilitic infection during pregnancy or at delivery. Although the majority of states (n=42) have laws that require universal syphilis screening at least once during pregnancy, as of 2018, less than one-half of these states (n=19) had legislation requiring screening in the third trimester and only eleven states required screening at delivery.[13] Pediatric providers should be familiar with the laws in their state around syphilis testing during pregnancy and at delivery, as well as the recommendations from CDC, American Academy of Pediatrics, American College of Obstetricians and Gynecologists, American Academy of Family Physicians, and the U.S. Preventive Services Task Force.[14–15] Pediatric providers should be aware of syphilis rates in their communities, per CDC's STD Surveillance Reports and Atlas,[2,16] and risk factors for syphilis acquisition in order to advocate for appropriate maternal testing at delivery. Individual risk factors may include a history of multiple sexually transmitted infections, homelessness, transactional sex, and substance misuse.[17,18] With rising rates of opioid use disorder among pregnant people and the intersection of heterosexual syphilis and drug use epidemics in the United

States, providers should assess for maternal substance misuse.[17,19] Only one-half of pregnant people with syphilis in 2012–2016 reported traditional individual risk factors, highlighting the limitations of risk factor-based screening and the importance of prevalence in the community and in sexual networks.[20]

This analysis is subject to limitations due to the nature of national CS surveillance data. First, an infant who meets the surveillance case definition may not always be considered a clinically relevant case of CS; however, all infants included in this analysis had CS-related signs or symptoms. Case report data may capture only 75% of signs or symptoms of CS among reported cases which could lead to under ascertainment of symptomatic infants and underestimates of all clinical characteristics (unpublished CDC data). Variability in provider documentation and in health department collection of clinical evidence may contribute to this under ascertainment of symptomatic infants. Additionally, CS case report data currently include only two sets of dates and results for maternal nontreponemal tests, which may lead to misclassification of timing of maternal syphilis diagnosis and underestimates of maternal seroconversion. CS case report data include only the first reactive infant nontreponemal test, but it is possible that a subsequent test date was reported, resulting in misclassification of timing of infant diagnosis, or that a prior nonreactive test result was obtained. Finally, CS case report data may not be complete or accurate due to the complex and time-consuming nature of CS investigations, especially for over-burdened health departments. CDC was unable to confirm the reported clinical information or identify additional clinical information, such as details on symptoms or treatment, through medical record review.

Conclusion:

As the number of symptomatic infants and infants diagnosed beyond the neonatal period in the United States continues to increase, the number of children with late manifestations of CS will likely increase. Pediatric providers can prevent physical and neurologic sequelae of CS through early diagnosis and treatment. Pediatric providers should be aware of recommendations for management of pregnant people with syphilis, follow the guidelines for evaluation and management of newborns exposed to syphilis in utero, and confirm maternal syphilis status prior to discharging newborns from the birth hospital. Pediatric providers should consider a diagnosis of CS in any infant with signs or symptoms regardless of maternal syphilis history. As the number of CS cases in the United States is higher than it has been in over 20 years, many pediatric providers may be evaluating and treating infants with CS for the first time in their careers and should be prepared to do so.

Funding/Support:

Supported by the U.S. Centers for Disease Control and Prevention. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Abbreviations:

CS	congenital syphilis

U.S.	United States
CDC	Centers for Disease Control and Prevention
STD	sexually transmitted disease
WBC	white blood cell
CSF	cerebrospinal fluid
VDRL	venereal disease research laboratory
RPR	rapid plasma reagin
IQR	inter-quartile range

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What's Known on This Subject:

Congenital syphilis cases continue to increase in the United States. Pediatric providers are the frontline for identifying and managing infants with congenital syphilis. The late manifestations of congenital syphilis can be prevented through early diagnosis and treatment.

What This Study Adds:

During 2014–2018, 67 symptomatic infants were diagnosed with congenital syphilis beyond the neonatal period. Pediatric providers should confirm maternal syphilis status prior to birth hospital discharge, advocate for appropriate maternal testing, and consider the diagnosis in symptomatic infants.

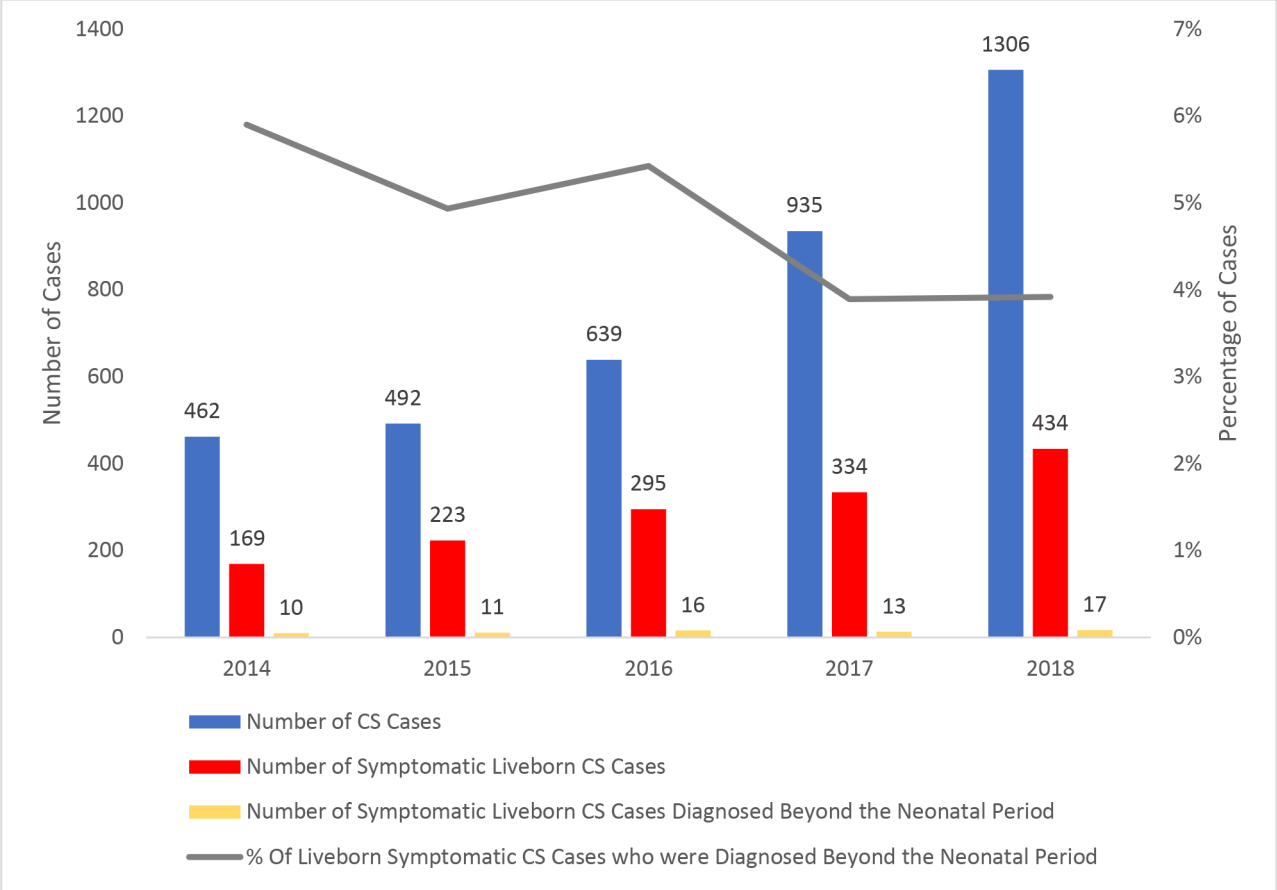

Figure 1.

Congenital syphilis (CS) cases in the United States, 2014–2018. The bars depict case counts (axis on left) by year, with the total number of CS cases reported to CDC shown in the first bar (blue), the number of symptomatic liveborn CS cases in the second bar (red), and the number of symptomatic liveborn CS cases diagnosed beyond the neonatal period in the third bar (yellow). The line depicts the percent of liveborn symptomatic CS cases who were diagnosed beyond the neonatal period (axis on right).

Table 1:

Demographic Characteristics of Symptomatic[a] Infants with Congenital Syphilis (CS) Diagnosed after 28 Days of Age — United States, 2014–2018 (N = 67)

Birthyear, n (%)	
2014	10 (15%)
2015	11 (16%)
2016	16 (24%)
2017	13 (19%)
2018	17 (25%)
Maternal Race/Ethnicity, n (%)	
White, non-Hispanic	25 (37%)
Black, non-Hispanic	22 (33%)
Hispanic	13 (19%)
American Indian/Alaskan Native	2 (3%)
Asian/Pacific Islander	1 (1%)
Other/Unknown	4 (6%)
U.S. Region, n (%)	
South	24 (36%)
West	21 (31%)
Midwest	15 (22%)
Northeast	7 (10%)
Age	
Median gestational age at delivery (IQR; range), weeks	38 (37–39; 31–41)
Born preterm (<37 weeks), n (%)	10 (15%)
Born full-term (≥37 weeks), n (%)	52 (78%)
Unknown gestational age	5 (7%)
Median post-natal age at diagnosis[b] (IQR; range), days	67 (46–100; 29–249)

IQR, inter-quartile range

[a] A symptomatic infant with CS is defined as an infant with a reactive nontreponemal test and documentation of any one of the following physical exam, radiographic, or laboratory signs: condyloma lata, snuffles, syphilitic rash, hepatosplenomegaly, jaundice due to syphilitic hepatitis, pseudoparalysis, edema or other signs on physical exam; findings consistent with CS on long-bone radiographs; elevated protein or white blood cell (WBC) count in the cerebrospinal fluid (CSF); or a reactive venereal disease research laboratory test (VDRL) in the CSF. For an infant in the first 30 days, a CSF WBC of >15 WBC/mm^3 or a CSF protein >120mg/dL is considered elevated. A CSF WBC of >5 WBC/mm^3 or a CSF protein >40mg/dL is considered elevated for an infant over 30 days of age.

[b] Calculated using date of infant's reactive nontreponemal test and infant's birthdate

Table 2:

Clinical Characteristics of Symptomatic[a] Infants with Congenital Syphilis (CS) Diagnosed after 28 Days of Age — United States, 2014–2018 (N = 67)

Infant Titer at Diagnosis of CS	
Median nontreponemal titer (IQR; range)	1:256 (32–512; 1–2048)
Physical Examination, n (%)	
Reported abnormal physical exam findings consistent with CS	45 (67%)
Rash	28 (42%)
Snuffles	11 (16%)
Hepatosplenomegaly	9 (13%)
Jaundice due to syphilitic hepatitis	5 (7%)
Pseudoparalysis	4 (6%)
Condyloma lata	3 (4%)
Edema	1 (1%)
Other[b]	17 (25%)
No reported physical exam findings consistent with CS[c]	22 (33%)
Long-Bone Radiographs, n (%)	
Performed	55 (82%)
Performed, findings consistent with CS	38/55 (69%)
Performed, normal	17/55 (31%)
Not Performed	10 (15%)
Unknown[d]	2 (3%)
CSF Studies, n (%)	
CSF VDRL	
Performed	50 (75%)
Performed, reactive	18/50 (36%)
Performed, nonreactive	32/50 (64%)
Not Performed	11 (16%)
Unknown[d]	6 (9%)
CSF Cell Counts	
Performed	44 (66%)
Performed, WBC and/or protein elevated	22/44 (50%)
Performed, WBC and protein normal	22/44 (50%)
Not Performed	12 (18%)
Unknown[d]	11 (16%)
Treatment, n (%)	
Treated with 10 days of intravenous or intramuscular penicillin	61 (91%)
Treated with 1 dose of benzathine penicillin	2 (3%)

Treated with another regimen	4 (6%)

IQR, inter-quartile range; CSF, cerebrospinal fluid; VDRL, venereal disease research laboratory; WBC, white blood cell

[a] A symptomatic infant with CS is defined as an infant with a reactive nontreponemal test and documentation of any one of the following physical exam, radiographic, or laboratory signs: condyloma lata, snuffles, syphilitic rash, hepatosplenomegaly, jaundice due to syphilitic hepatitis, pseudoparalysis, edema or other signs on physical exam; findings consistent with CS on long-bone radiographs; elevated protein or white blood cell (WBC) count in the cerebrospinal fluid (CSF); or a reactive venereal disease research laboratory test (VDRL) in the CSF. For an infant in the first 30 days, a CSF WBC of >15 WBC/mm^3 or a CSF protein >120mg/dL is considered elevated. A CSF WBC of >5 WBC/mm^3 or a CSF protein >40mg/dL is considered elevated for an infant over 30 days of age.

[b] "Other" includes nonspecific signs of CS and other signs not individually designated.

[c] Includes 7 infants with missing information for all physical exam findings.

[d] Includes unknown and missing, unclear whether the test was not performed or whether the results were not abstracted or reported.

Table 3:

Maternal Characteristics of Symptomatic[a] Infants with Congenital Syphilis (CS) Diagnosed after 28 Days of Age — United States, 2014–2018 (N = 66)

Prenatal Care, n (%)	
Received any prenatal care	55 (83%)
No reported prenatal care	11 (17%)
Maternal Stage of Syphilis, n (%)	
Primary or Secondary Syphilis	16 (24%)
Early Non-Primary, Non-Secondary (Early Latent)	19 (29%)
Unknown Duration or Late	31 (47%)
Seroconversion [b], n (%)	
Maternal seroconversion during pregnancy	16 (24%)
Diagnosis before or at delivery	4 (6%)
Diagnosis after delivery	12 (18%)
No evidence of maternal seroconversion during pregnancy	50 (76%)
Maternal Syphilis Testing During Pregnancy, n (%)	
Reported syphilis testing during pregnancy or at delivery	61 (92%)
No reported syphilis testing during pregnancy or at delivery	5 (8%)
Timing of Maternal Syphilis Diagnosis, n (%)	
>3 days before delivery (during pregnancy)	9 (14%)
≥30 days before delivery	5 (8%)
4–29 days before delivery	4 (6%)
+/− 3 days of delivery (at delivery)	8 (12%)
>3 days after delivery	28 (42%)
After delivery and before infant's reactive RPR	13 (20%)
After delivery and after infant's reactive RPR	15 (23%)
Unknown timing of maternal diagnosis[c]	21 (32%)

RPR, rapid plasma reagin

[a] A symptomatic infant with CS is defined as an infant with a reactive nontreponemal test and documentation of any one of the following physical exam, radiographic, or laboratory signs: condyloma lata, snuffles, syphilitic rash, hepatosplenomegaly, jaundice due to syphilitic hepatitis, pseudoparalysis, edema or other signs on physical exam; findings consistent with CS on long-bone radiographs; elevated protein or white blood cell (WBC) count in the cerebrospinal fluid (CSF); or a reactive venereal disease research laboratory test (VDRL) in the CSF. For an infant in the first 30 days, a CSF WBC of >15 WBC/mm^3 or a CSF protein >120mg/dL is considered elevated. A CSF WBC of >5 WBC/mm^3 or a CSF protein >40mg/dL is considered elevated for an infant over 30 days of age.

[b] Seroconversion is defined as documentation of negative syphilis testing early in pregnancy followed by reactive syphilis testing later in pregnancy, around the time of delivery, or up to 90 days after delivery.

[c] Maternal testing information submitted to CDC did not include treponemal and nontreponemal test results consistent with syphilitic infection during pregnancy or after delivery.