

Rising Cases of Congenital Syphilis: What Can We Do About It?

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Disclosure Statement

I have nothing to disclose and
no conflicts of interest.

Objectives

- Briefly describe the current epidemiology of syphilis, specifically congenital syphilis, in the US and in LA
- Determine potential options for areas of change to ensure we do not miss babies with congenital syphilis

Case #1:

- Term AGA male delivered via SVD to 25 year old female. Soon after birth, the infant is noted to have respiratory distress, hepatomegaly, and bluish macular-papular rash across his body, including his face.
- Social history: Mom denies any history of alcohol, smoking, or illegal drug use.
- Transferred to level 3-4 NICU for further evaluation and treatment

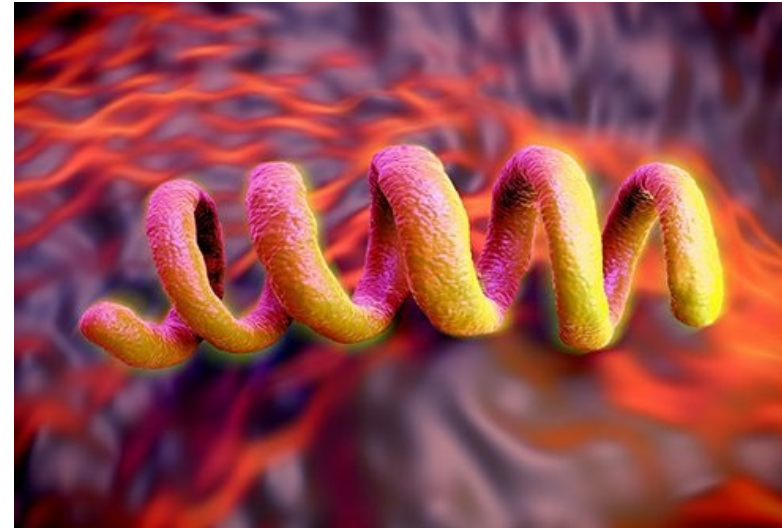
Case #1:



BACKGROUND & EPIDEMIOLOGY

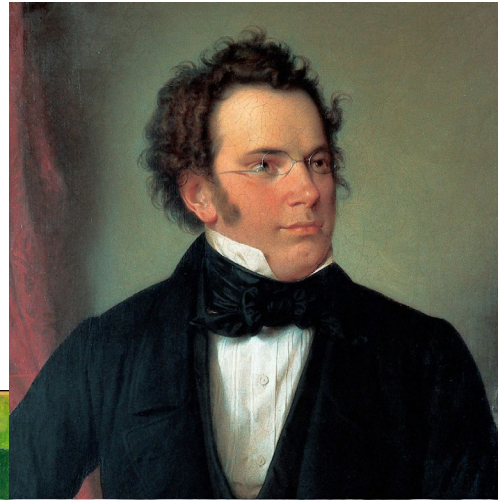
Syphilis

- Syphilis was recognized as early as the end of the 15th century
- In 1905, discovery made syphilis is caused by the gram negative spirochete bacterium, *Treponema pallidum*.
- Humans are the only natural host.



Background

- Famous individuals who acquired syphilis include:
 - Al Capone
 - Paul Gauguin
 - Benito Mussolini
 - Franz Schubert

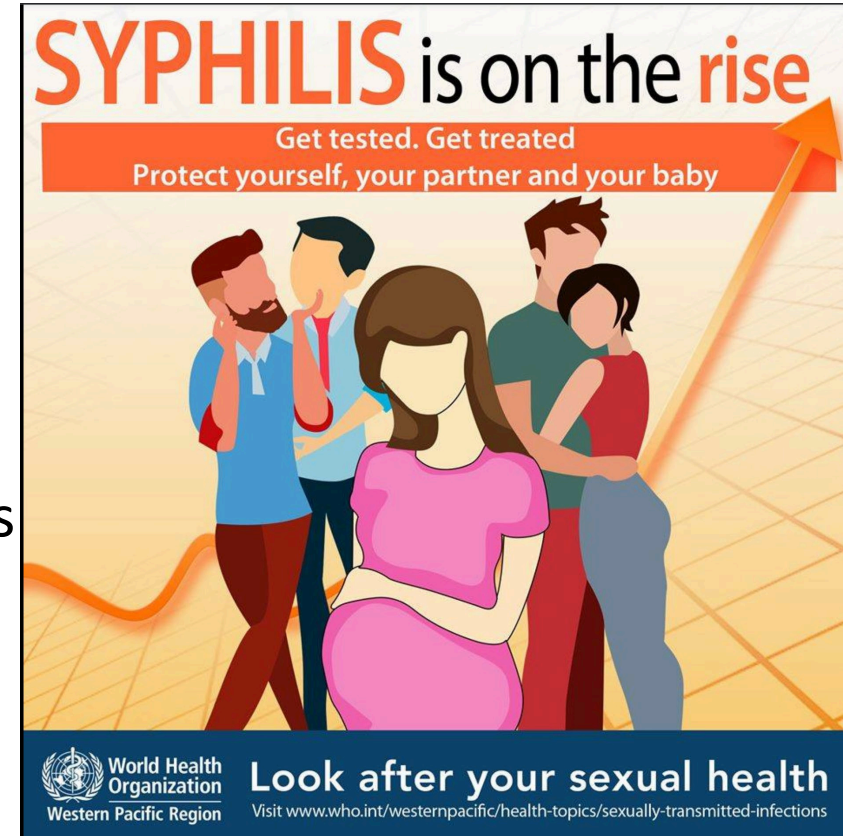


World Health Organization

~6 million new cases of syphilis globally in 2016.

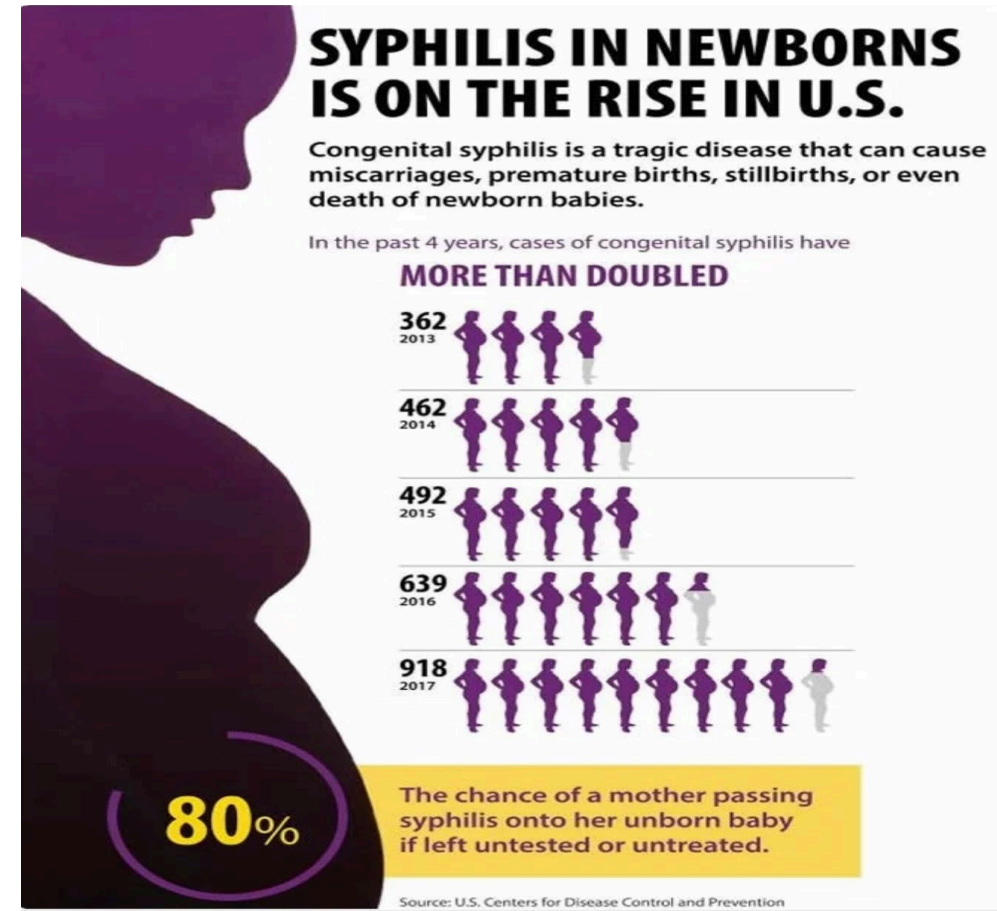
~ 1 million gravidae involved resulting:

- 661,000 congenital syphilis
- 200,000 fetal and neonatal deaths
- 41,000 preterm or LBW



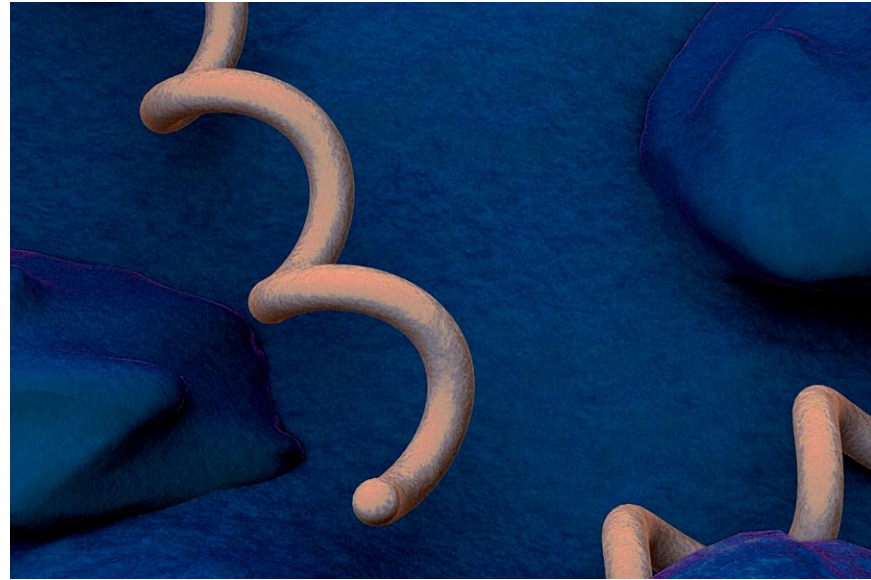
Worldwide Epidemiology: Syphilis

- Syphilis is the second leading cause of stillbirth in the world.
- Syphilis can be effectively and inexpensively treated with penicillin, making it a preventable disease



US Based Epidemiology: Acquired Syphilis

- Syphilis tracking started in the 1940's
 - Penicillin treatment became widely available in early 1950's
 - Lowest rate ever reported in the United States were in 2000- 2001
 - Since 2002, rates have increased again with 2018 rates equal to 1990's rates



US Based Epidemiology: Acquired Syphilis

- During 2014-2018, primary and secondary syphilis rates among *women* have almost tripled.
 - Increased 172.7% overall
 - Increased 165% among women during their reproductive years (15–44 years)
 - Rates of syphilis among women were highest in the *western* and *southern* regions.



RECENT HIGH-IMPACT PUBLICATIONS

CORRESPONDENCE



**High Congenital Syphilis Case Counts
among U.S. Infants Born in 2020**

As of July 29, 2021, a total of 2022 infants born in 2020 had been reported to the [CDC] as having congenital syphilis. This number already surpasses the 1870 cases reported in 2019, represents the highest case count since 1994, and is likely to continue to rise...”

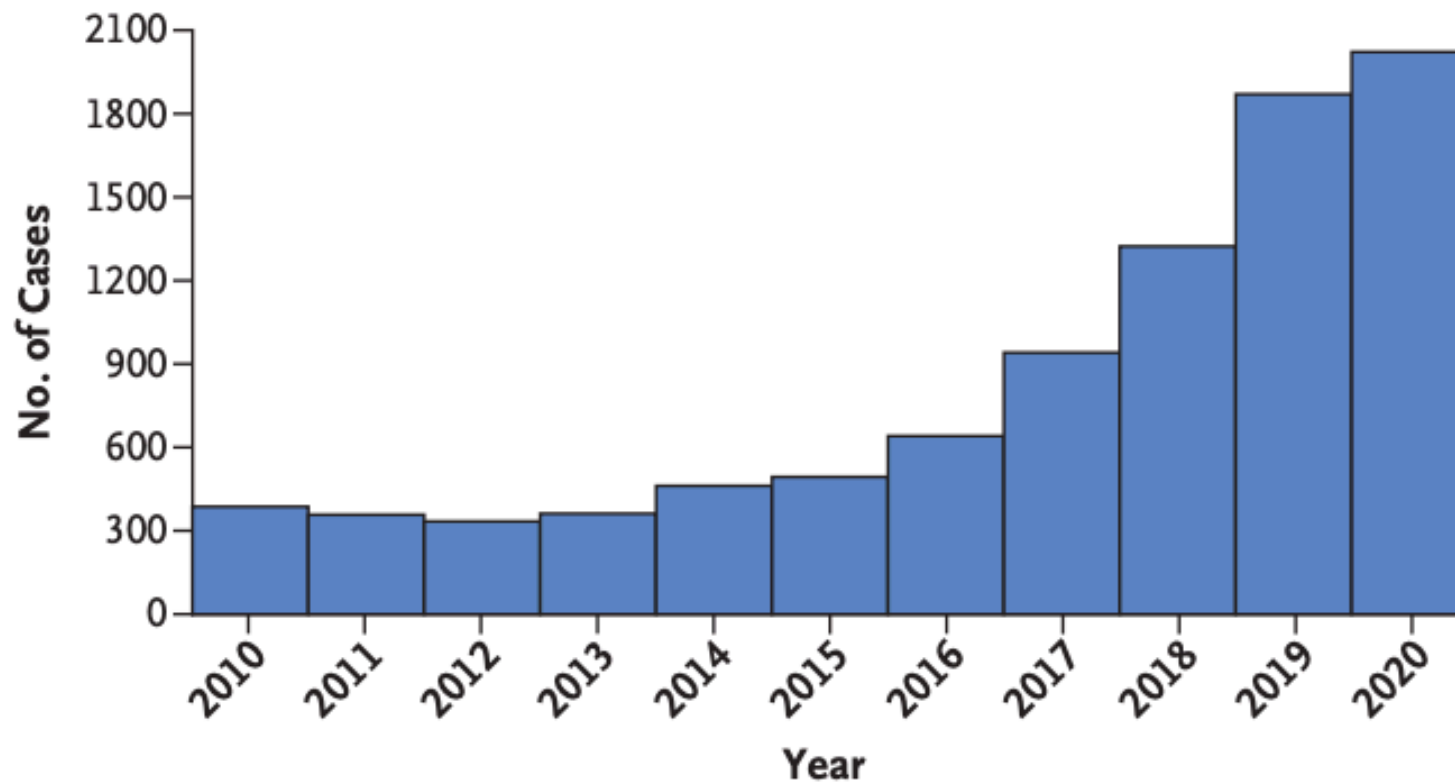
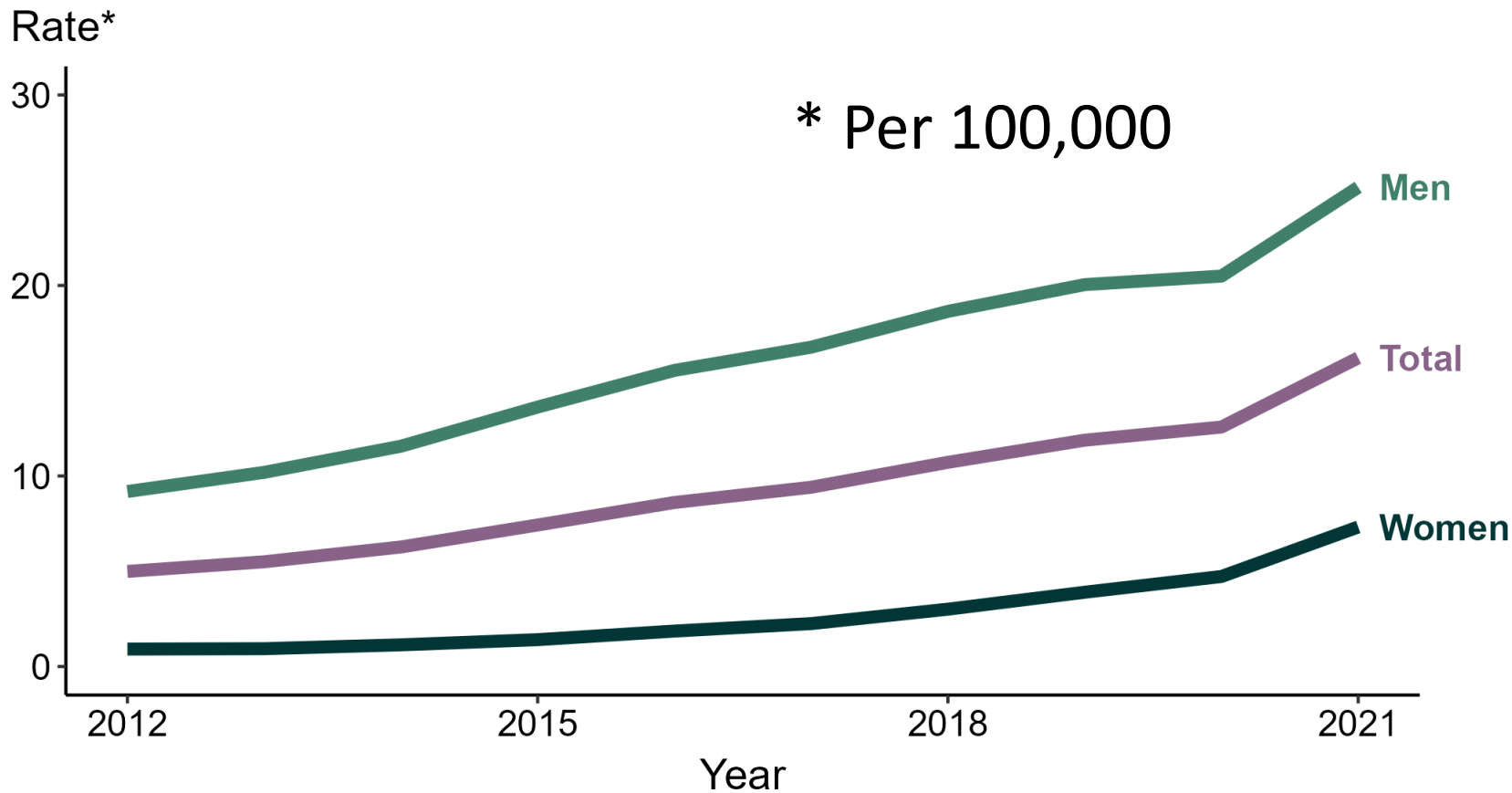


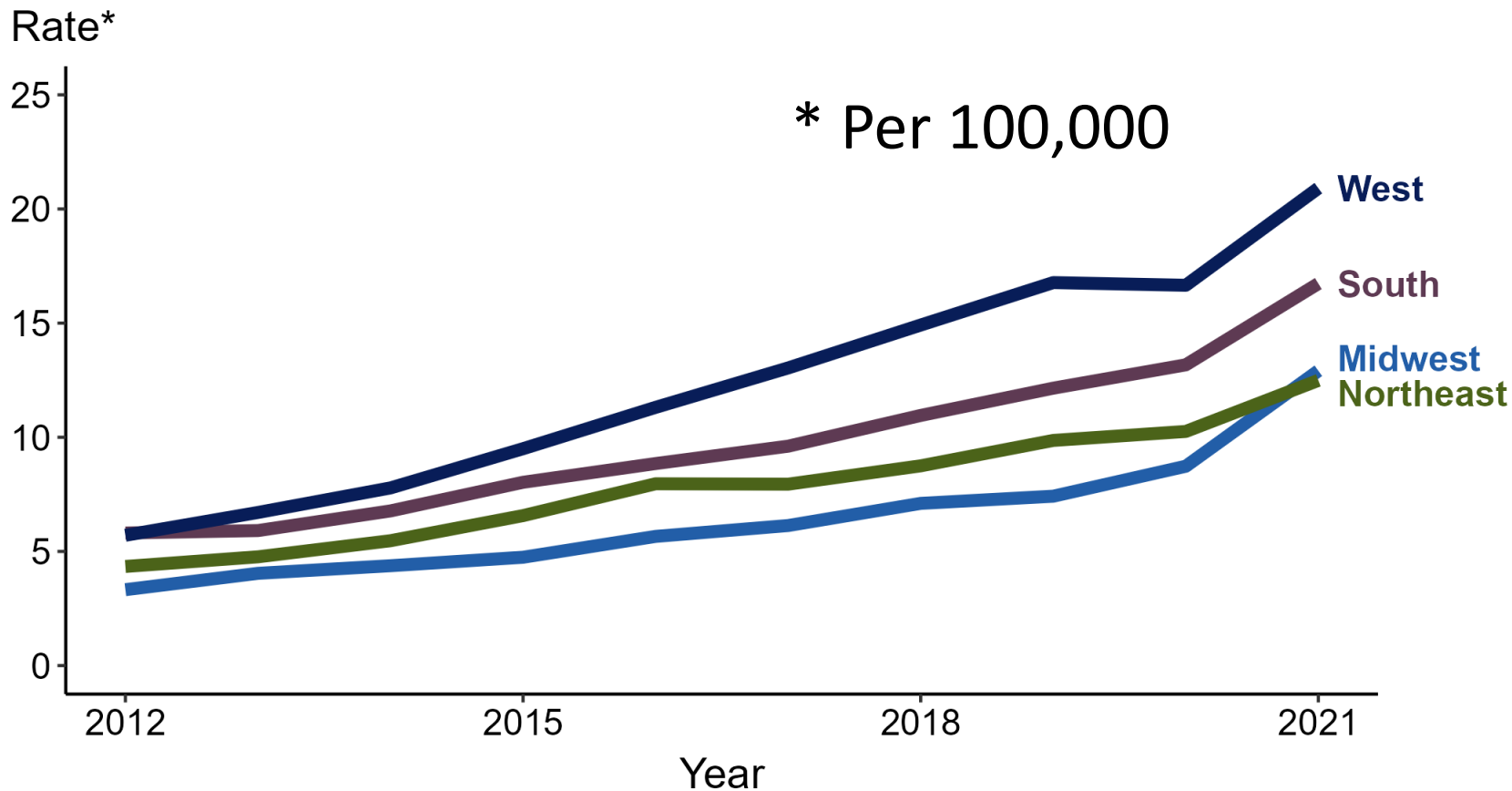
Figure 1. Reported Cases of Congenital Syphilis among U.S. Infants Born 2010–2020.

The case counts for congenital syphilis for 2010–2019 were previously published in the *2019 STD Surveillance Report*.² The case counts for 2020 include cases reported to Centers for Disease Control and Prevention as of July 29, 2021. The reporting period for 2020 cases ends in October 2021.

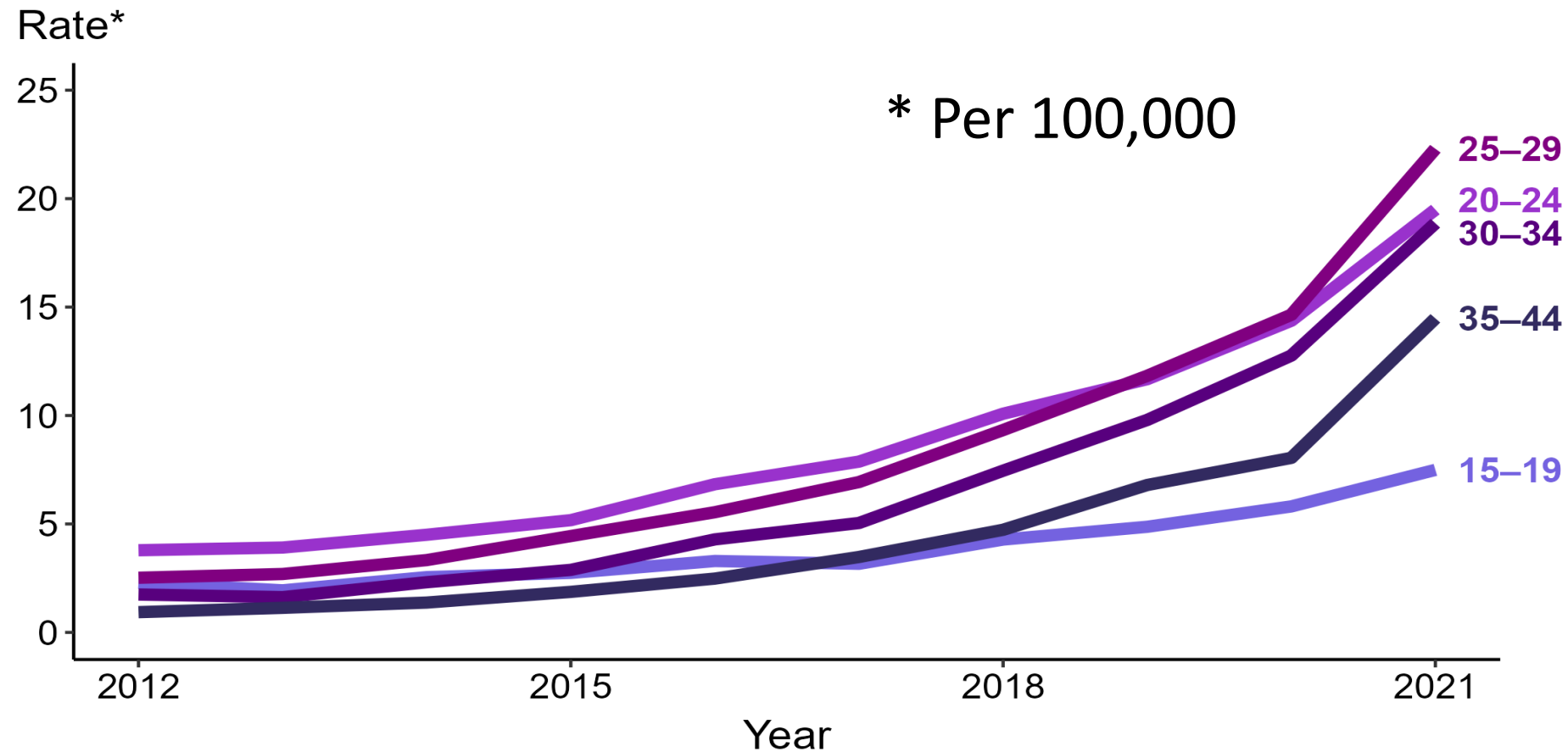
Primary and Secondary Syphilis — Rates of Reported Cases by Sex, United States, 2012–2021



Primary and Secondary Syphilis — Rates of Reported Cases by Region, United States, 2012–2021



Primary and Secondary Syphilis — Rates of Reported Cases Among Women Aged 15–44 Years by Age Group, United States, 2012–2021



Current Syphilis Rates and Louisiana (LA)

- Early syphilis increased in LA overall by 36% from 2020 -2021
- Early syphilis in LA disproportionately affected **women, people of color, and gay and bisexual men.**
 - 66% were people of color
 - 37% were gay and bisexual men
 - 47% were black men
- LA had 63 congenital syphilis cases (7th highest in US) in 2020
- LA had 110 congenital syphilis cases in 2021 (**75% increase**)
 - 65% of cases involved black women
 - 64% of cases involved women under 30 years of age

RISK-FACTOR BASED TESTING

Maternal and Congenital Risk Factors

- Lack of or inadequate prenatal care
- Lack of health insurance
- Mental health disorders
- Use of illicit drugs
- Unstable housing and lower socioeconomic status
- Having other sexually transmitted diseases (STD)
 - High prevalence of co-infection with human immunodeficiency virus (HIV)
 - Syphilis is a known risk factor for acquisition of HIV.
- More than 1 partner in the past year
- Residence in an area of high prevalence.

National Trends and Reported Risk Factors Among Pregnant Women With Syphilis in the United States, 2012–2016

Shivika Trivedi, MD, MSc, Charnetta Williams, MD, Elizabeth Torrone, PhD, Sarah Kidd, MD, MPH

CDC Foundation and the Division of STD Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia.

- Analyzed U.S> national case report data from 2012-2016 to assess trends among pregnant women with all stages of syphilis. Risk behavior data collected through case interviews during routine local health department investigation.

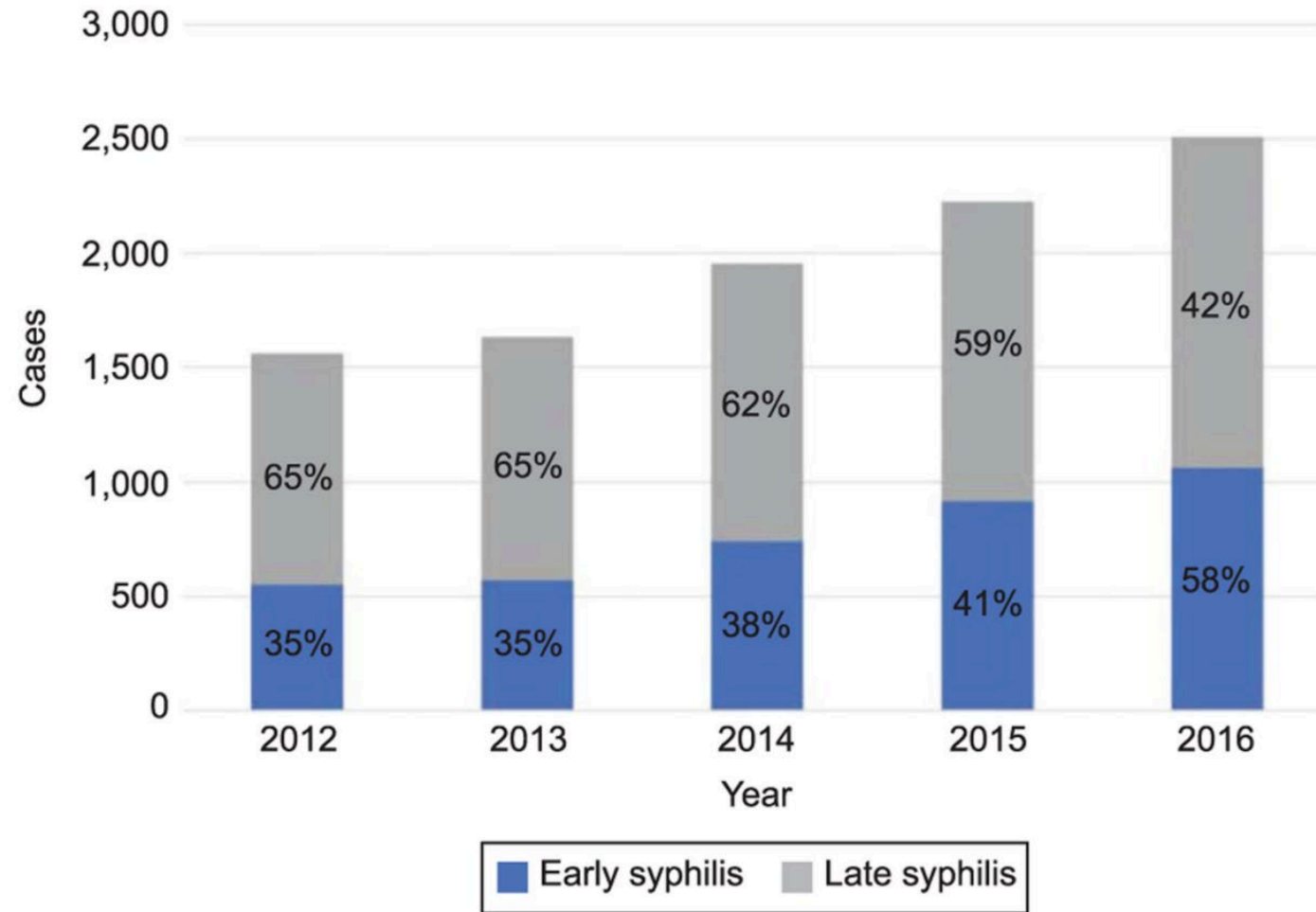


Fig. 1.
Reported cases of early and late latent syphilis among pregnant women. The increase in the proportion of cases that were early syphilis cases was statistically significant ($P<.001$).

Reported Risk Factors Among Pregnant Women With Syphilis (All Stages), 2012–2016

Reported Risk Factor [*]	2012 (n=1,561)	2013 (n=1,633)	2014 (n=1,955)	2015 (n=2,226)	2016 (n=2,508)	2012–2016 ^{*†} (n=9,883)
Prior STD ^{‡§}	452/1,135 (39.8)	512/1,196 (42.8)	581/1,410 (41.2)	673/1,544 (43.6)	831/1,740 (47.8)	3,049/7,025 (43.4)
More than 1 sex partner	387/1,258 (30.8)	421/1,301 (32.4)	457/1,570 (29.1)	495/1,784 (27.8)	656/2,063 (31.8)	2,416/7,976 (30.3)
Sex while intoxicated	177/1,165 (15.2)	178/1,200 (14.8)	212/1,455 (14.6)	272/1,629 (16.7)	301/1,873 (16.1)	1,140/7,322 (15.6)
Anonymous sex partner	98/1,152 (8.5)	94/1,187 (7.9)	117/1,466 (8.0)	157/1,622 (9.7)	177/1,873 (9.5)	643/7,300 (8.7)
Incarceration	87/1,157 (7.5)	86/1,198 (7.2)	104/1,463 (7.1)	114/1,627 (7.0)	171/1,865 (9.2)	562/7,310 (7.7)
Sex for drugs or money	49/1,173 (4.2)	48/1,213 (4.0)	52/1,460 (3.6)	62/1,651 (3.8)	61/1,907 (3.2)	272/7,404 (3.7)
Sex with persons known to inject drugs [§]	21/1,122 (1.9)	32/1,149 (2.8)	35/1,394 (2.5)	65/1,575 (4.1)	79/1,771 (4.5)	232/7,011 (3.3)
HIV-positive [‡]	13/1,071 (1.2)	18/1,080 (1.7)	13/1,330 (1.0)	26/1,420 (1.8)	31/1,877 (1.7)	101/6,788 (1.5)
Sex with MSM ^{//}	11/1,106 (1.0)	11/1,121 (1.0)	11/1,344 (0.8)	19/1,539 (1.2)	35/1,727 (2.0)	87/6,837 (1.3)
Methamphetamine use ^{//}	24/1,081 (2.2)	22/1,147 (1.9)	47/1,411 (3.3)	94/1,523 (6.2)	129/1,827 (7.1)	316/6,986 (4.5)
Cocaine use	30/1,083 (2.8)	22/1,147 (1.9)	41/1,409 (2.9)	37/1,524 (2.4)	43/1,812 (2.4)	173/6,975 (2.5)
Crack use	25/1,083 (2.3)	14/1,146 (1.2)	21/1,408 (1.5)	18/1,522 (1.2)	25/1,809 (1.4)	103/6,968 (1.5)
Heroin use	17/1,082 (1.6)	18/1,146 (1.6)	18/1,407 (1.3)	30/1,524 (2.0)	26/1,816 (1.4)	109/6,975 (1.6)
Injection drug use	24/1,136 (2.1)	29/1,155 (2.5)	27/1,434 (1.9)	51/1,567 (3.3)	50/1,733 (2.9)	181/7,025 (2.6)
Nitrates or poppers use	2/1,066 (0.2)	1/1,144 (0.1)	4/1,406 (0.3)	6/1,519 (0.4)	7/1,772 (0.4)	20/6,907 (0.3)
Other drug use	115/1,080 (10.7)	138/1,146 (12.0)	198/1,407 (14.1)	198/1,531 (12.9)	226/1,826 (12.4)	875/6,990 (12.5)
Any risk factor ^{§//}	747/1,561 (47.9)	828/1,633 (50.7)	987/1,955 (50.5)	1,095/2,226 (49.2)	1,340/2,508 (53.4)	4,997/9,883 (50.6)

Overall, 49% of women with diagnosed syphilis did not report any of the 15 surveyed risk factors for syphilis

MATERNAL ACQUIRED INFECTION

Maternal Acquired Infection

- Primarily transmitted through sexual contact with an infected person, as the spirochete enters the body through broken or intact skin.
- ~ 30% chance of infection resulting from sexual contact with an infected person.

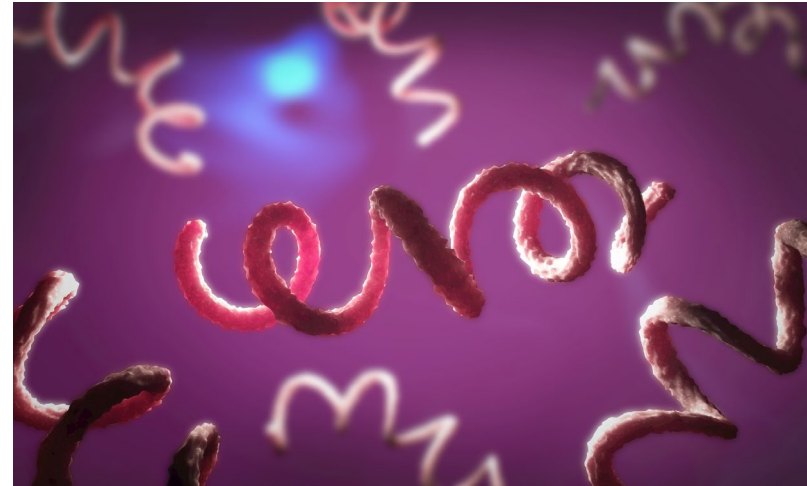


Table 1: Stages of Syphilis

Stage	Time Period	Symptoms
Primary	21 days after initial infection	Painless ulcer in mouth, genitals, rectum or skin
Secondary	4 – 8 weeks after primary infection ulcer appearance	Body rash, headache, fever, fatigue, lymphadenopathy
Tertiary	1 – 10 years after initial infection	Aortic insufficiency, aortic aneurysm, tabes dorsalis, loss of cortical function, altered mental status
Latent		
	<i>Early</i> First year after resolution of the primary or secondary lesions	Signs & symptoms usually disappear
	<i>Late</i> Unknown Duration	Cardiovascular syphilis, neurosyphilis, syphilitic meningitis

Table 2: Recommended Treatment Guidelines for Pregnant Patients

Stage	CDC STD Treatment Guidelines	WHO STI Guidelines
Primary/Secondary	2.4 MU benzathine penicillin G IM x1 once	2.4 MU benzathine penicillin G IM x1 once
Early Latent	2.4 MU benzathine penicillin G IM x1 once	2.4 MU benzathine penicillin G IM x1 once
Late Latent/Unknown Duration	2.4 MU benzathine penicillin G IM x1 per week for 3 weeks	2.4 MU benzathine penicillin G IM x1 per week for 3 weeks
Tertiary without evidence of neurosyphilis	2.4 MU benzathine penicillin G IM x1 per week for 3 weeks	No set recommendation
Neurosyphilis	Aqueous crystalline penicillin G 18-24 MU per day for 10–14 days; 3–4 MU IV every 4 hours or continuous IV for 10– 14 days	No set recommendation

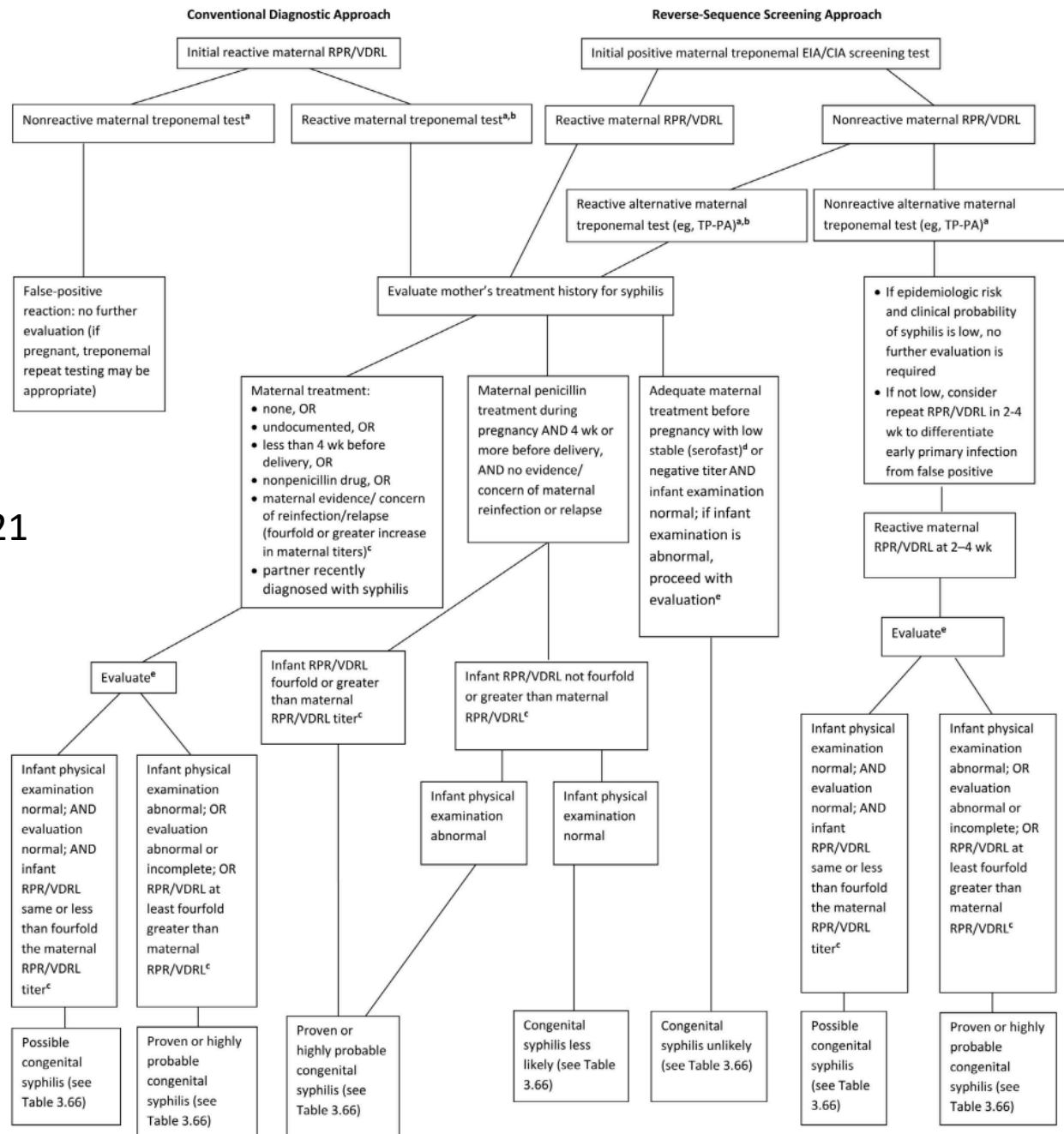
Maternal Screening

- The United States Preventive Services Task Force and CDC recommend that pregnant women should be screened for syphilis early in pregnancy.
- The CDC and joint guidelines from the AAP and the ACOG recommend screening be repeated at 28 to 32 weeks of gestation and at the time of delivery for *high-risk individuals*
- Per Louisiana Act 459, **all pregnant women residing in Louisiana are to be screened for syphilis at their first examination during pregnancy, at their first examination in their third trimester and at delivery.** (May 2, 2023)

Maternal Screening

- Current screening tests often include non-specific treponemal tests (i.e. PR/VDRL) and specific treponemal (i.e.: EIA, CIA, and FHA-TP)
- *Concern is* false negatives screens are possible due to early infection, infection acquired after testing, and late stages of disease (result of the prozone phenomenon)

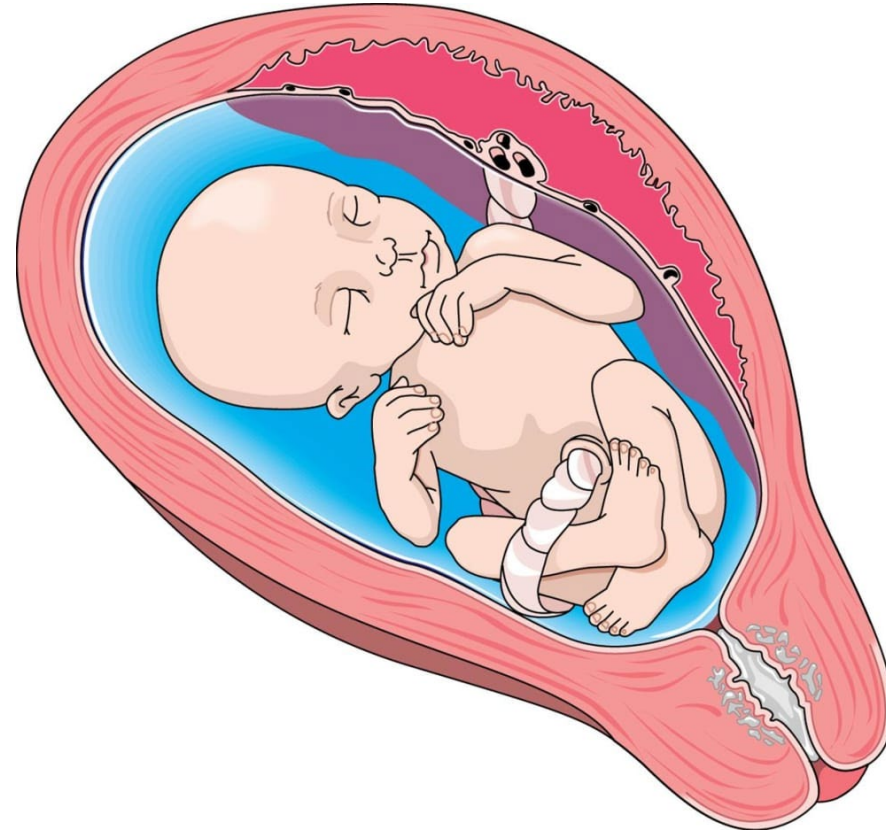
Redbook 2021



CONGENITAL SYPHILIS

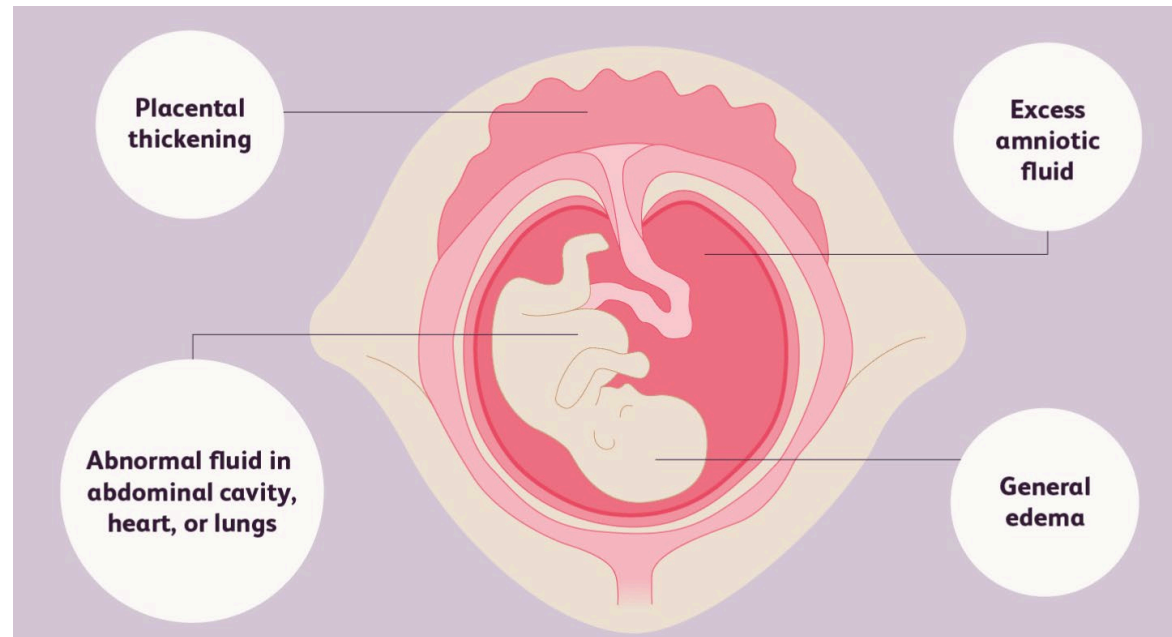
Congenital Syphilis

- Most commonly transmitted transplacentally
- Infection later in pregnancy higher risk for fetal infection
- Associated with larger placentas than expected



Congenital Syphilis – Symptomatic *in utero*

- Stillbirth
- Abortion
- Perinatal death
- Non-immune hydrops fetalis
- Preterm birth
- Low birthweight



Congenital Syphilis

- Majority of newborns are **asymptomatic** at birth
- Two types:
 - Early congenital syphilis (<2 years old)
 - Late congenital syphilis (>2 years old)



Congenital Syphilis

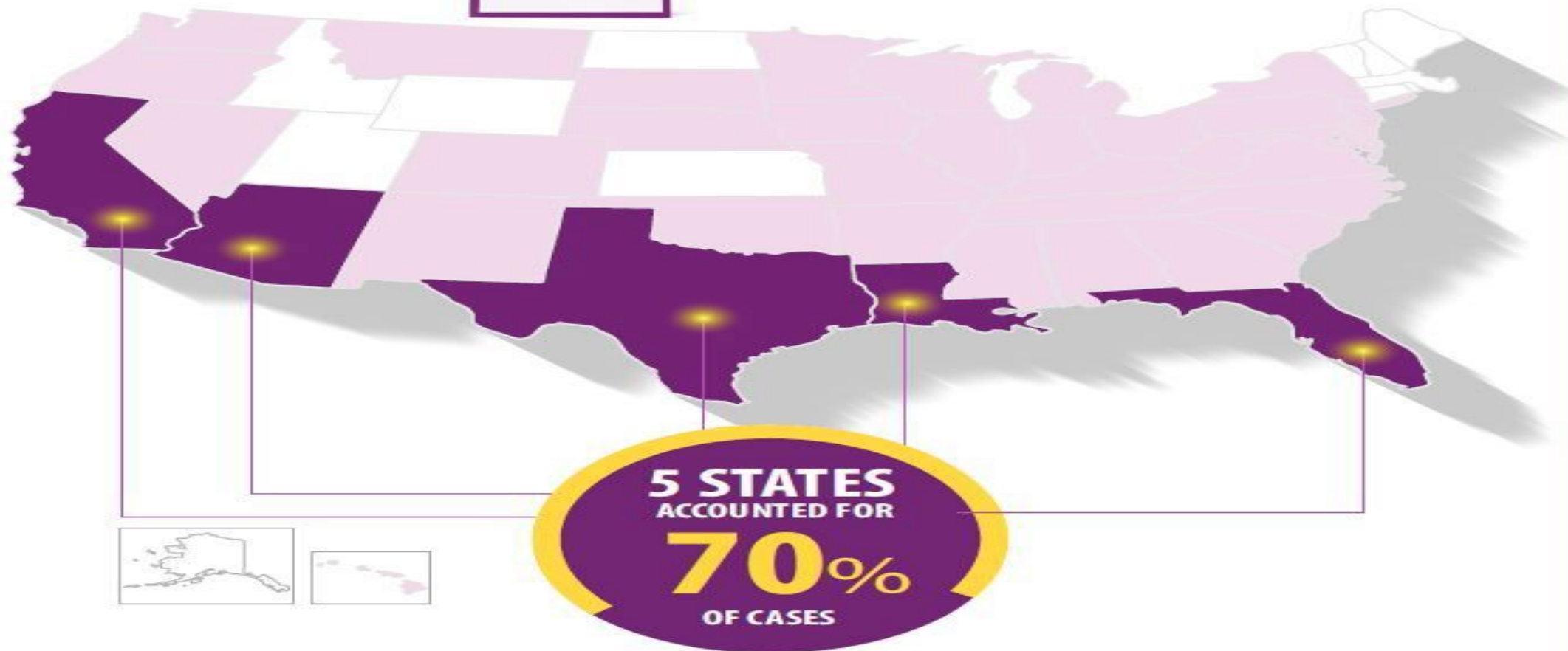
- Increased risk of transmission if mom co-infected with HIV
- More likely to transmit if in primary or secondary disease rather than latent disease
 - 60-90% vs 40% (latent) vs <10% (late latent)
- **NOT** in breastmilk!



SYPHILIS IN NEWBORNS: THE STATE OF THE NATION 2017

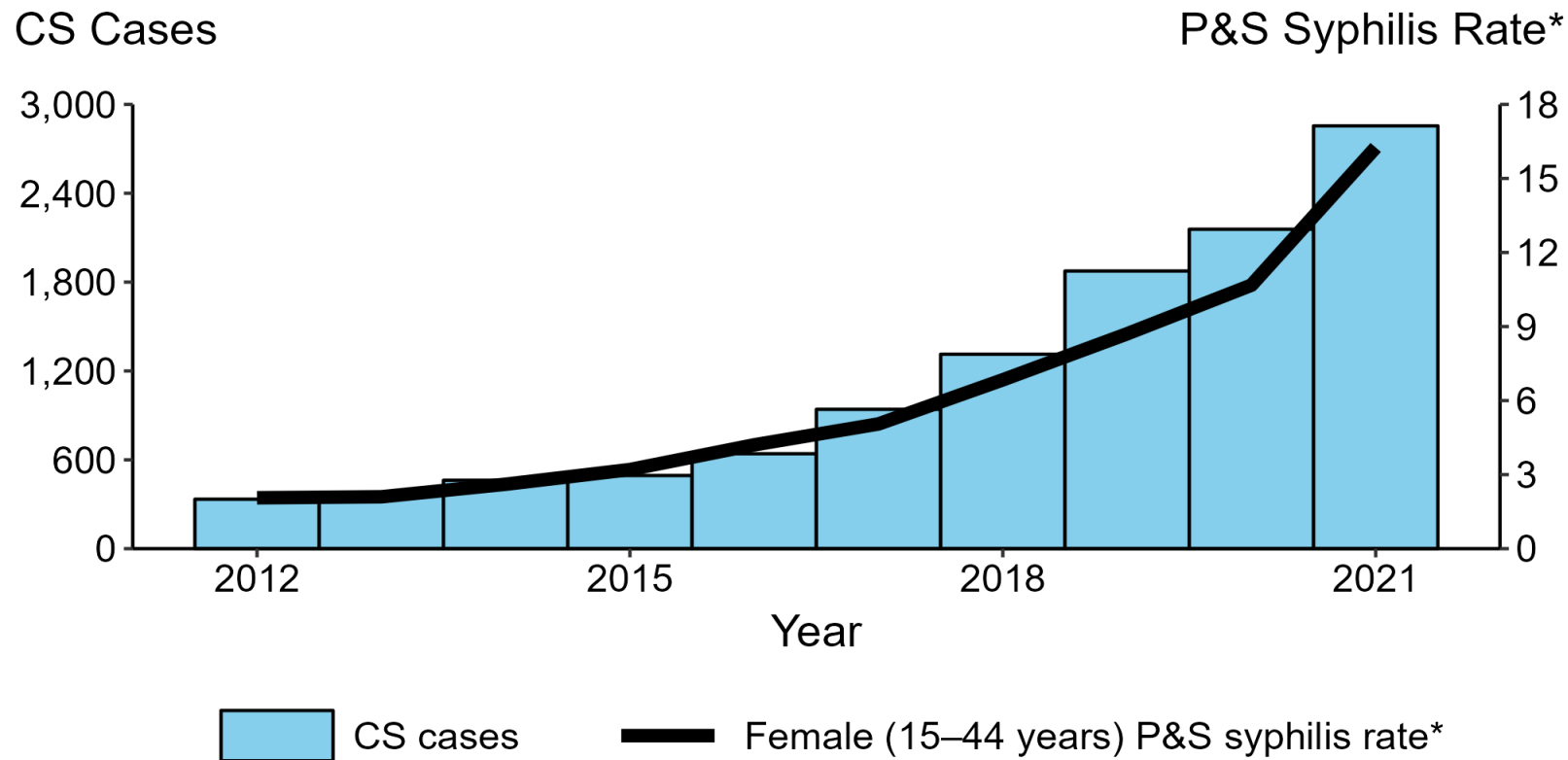
 **37**
STATES

Reported at least
ONE CASE
of congenital syphilis.



Source: U.S. Centers for Disease Control and Prevention

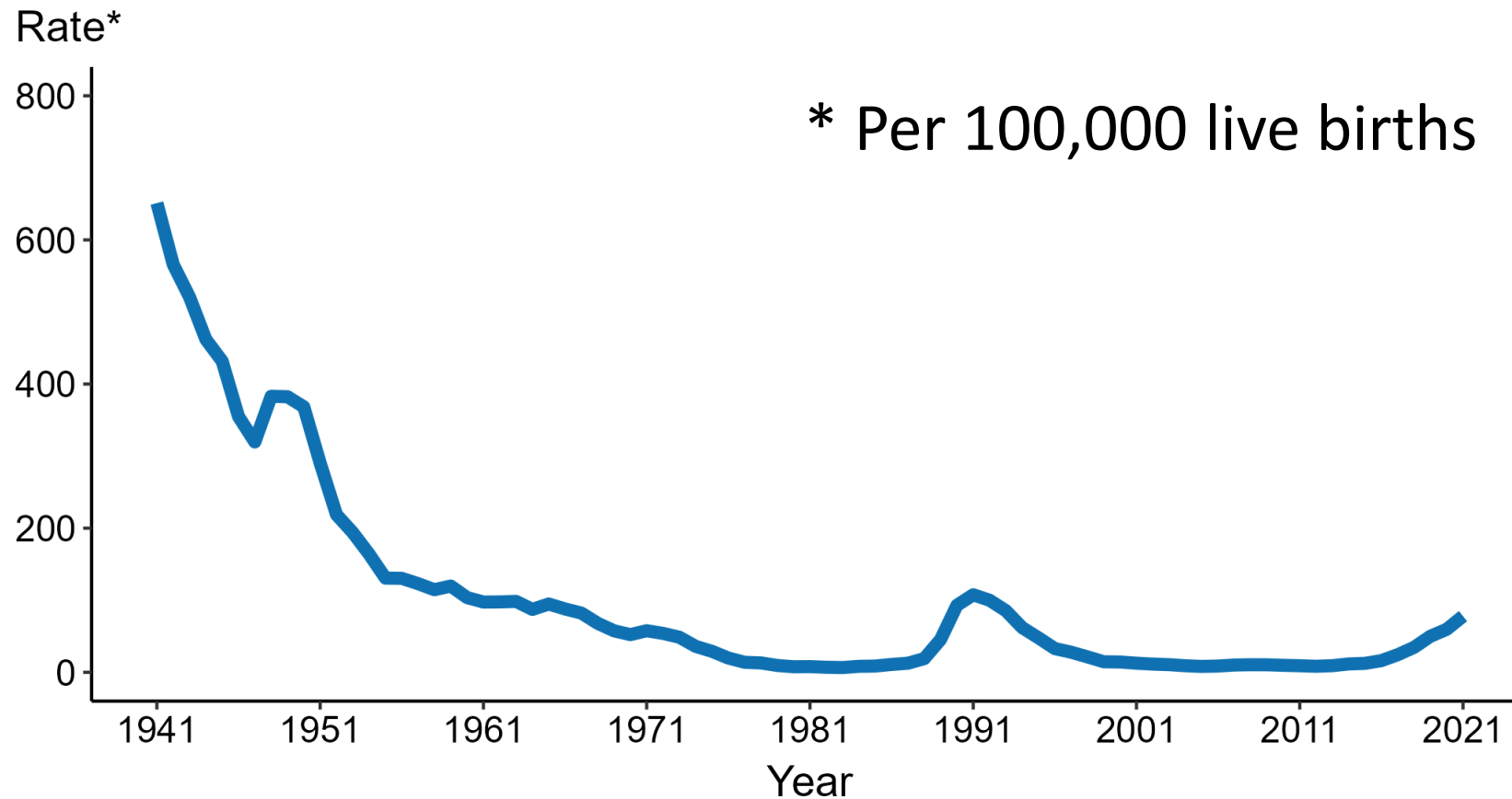
Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Women Aged 15–44 Years, United States, 2012–2021



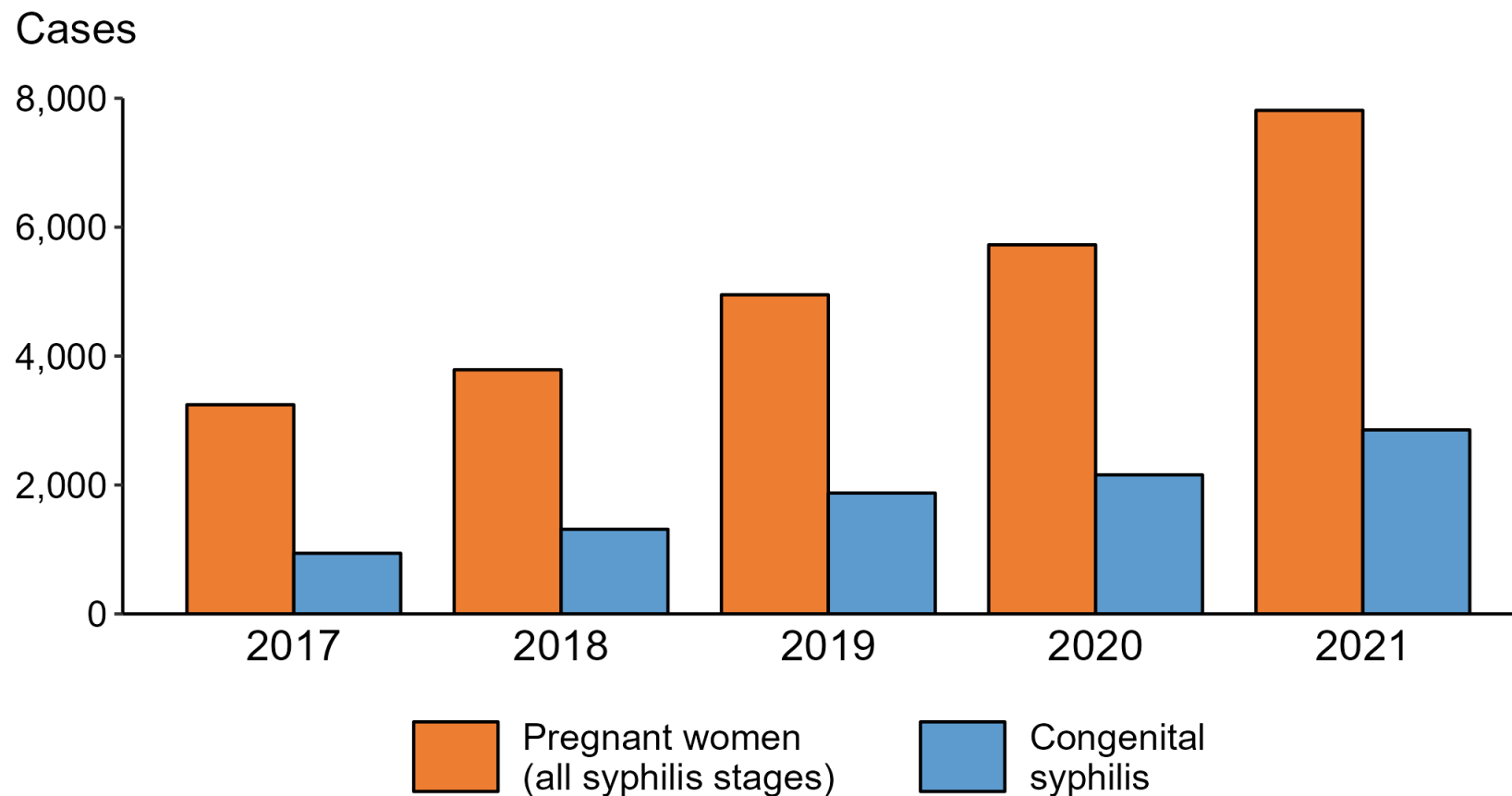
* Per 100,000

ACRONYMS: CS = Congenital syphilis; P&S Syphilis = Primary and secondary syphilis

Congenital Syphilis — Rates of Reported Cases by Year of Birth, United States, 1941–2021



Syphilis— Reported Cases of Syphilis (All Stages) among Pregnant Women and Reported Cases of Congenital Syphilis by Year of Birth, United States, 2017–2021



NOTE: The percent of cases missing information on pregnancy status decreased from 14.0% in 2017 to 9.3% in 2021.

Early Congenital Syphilis



Early Congenital Syphilis

- 60-90% asymptomatic at birth
- Clinical manifestations usually appear by 3 months of age
 - Most often by 5 weeks after birth

Early Congenital Syphilis

- Signs and Symptoms:
 - Snuffles (Contagious)
 - Maculopapular Rash (Contagious)
 - Lymphadenopathy
 - Thrombocytopenia
 - Hepatosplenomegaly with hepatitis
 - Anemia
 - Chorioretinitis
 - Meningitis
 - Osteochondritis
 - Sawtooth Metaphysis (Wegner Sign)

Late Congenital Syphilis



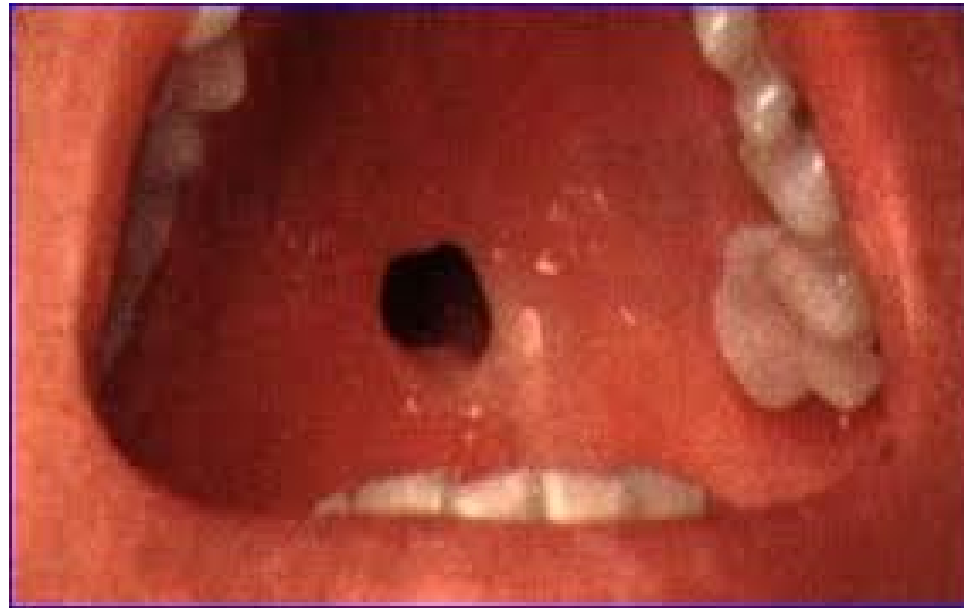
Late Congenital Syphilis



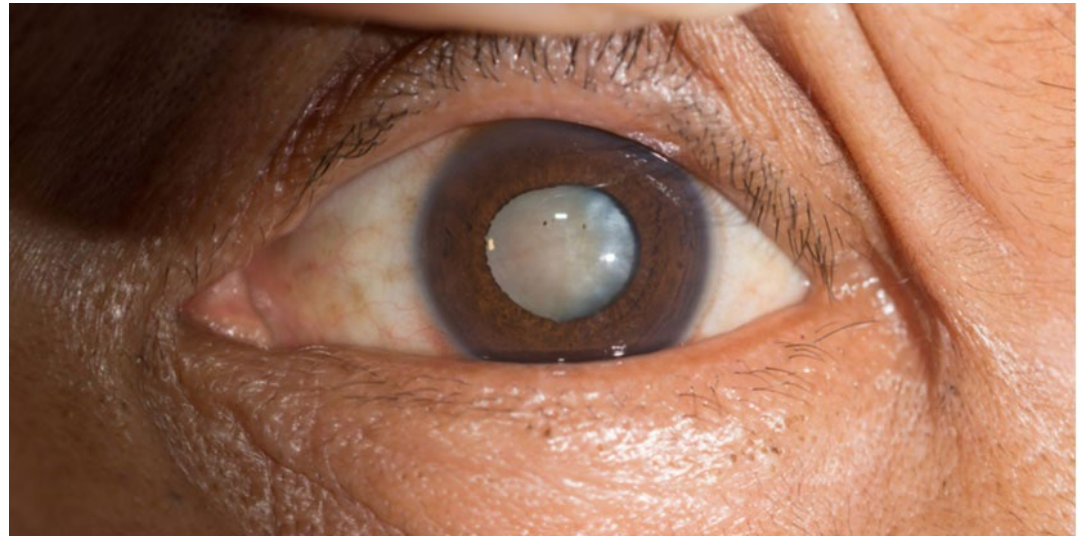
wiseGEEK



Late Congenital Syphilis

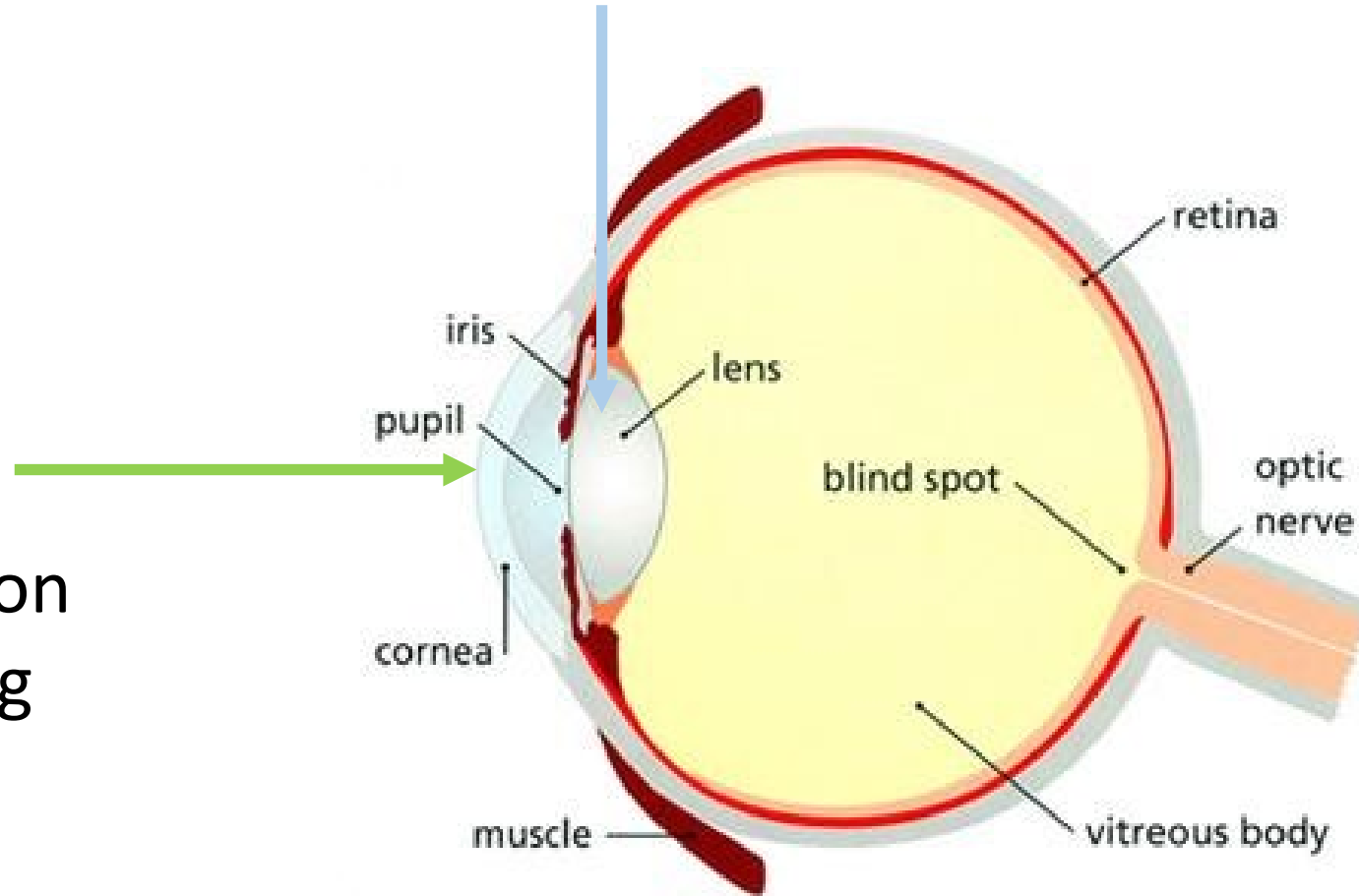


Interstitial Keratitis (Late Congenital Syphilis)



Cataract = Clouding of Lens

**Interstitial
Keratitis =**
Cornea
inflammation
and scarring



Late Congenital Syphilis

- Symptoms develop in ~40% of infants born to women with untreated syphilis during pregnancy
- Some manifestations (e.g. keratitis, saber shins) may occur or progress despite appropriate therapy

Late Congenital Syphilis

- Signs and Symptoms:

- Hutchinson Teeth
- Interstitial Keratitis
- Sensorineural Hearing Loss



**Hutchinson
Triad**

A blue rectangular box containing the text 'Hutchinson Triad'. Three blue arrows originate from the left side of this box and point to the three items in the list above: 'Hutchinson Teeth', 'Interstitial Keratitis', and 'Sensorineural Hearing Loss'.

- Perforated Hard Palate
- Mulberry Molars
- Saber Shins
- Saddle Nose
- Higoumenakis Sign
 - Enlargement of the Sternoclavicular portion of the clavicle

Syphilis Cases Can Present
in Differing Ways

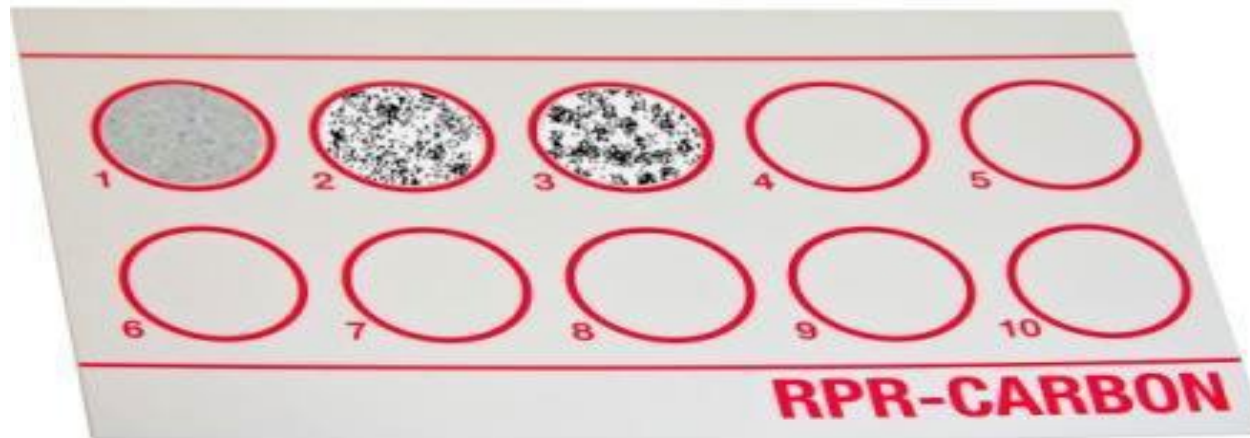
Differing Ways Syphilis Can Present

- Negative maternal testing in pregnancy
- Positive maternal testing without receiving treatment
- Positive maternal testing with treatment with reinfection
- Asymptomatic newborn at birth
- Hydrops with rapid deterioration after birth
- Clinical neonatal symptoms

INFANT SCREENING & TREATMENT

If suspicious for syphilis but unsure:

- Send RPR on baby, and ask OB to send on gravida
 - Obtain the same test on both to compare
- Placenta and umbilical cord should be sent for review on all suspected syphilis → path review



If Gravidae Positive for Syphilis

- Determine maternal treatment history (adequate or inadequate), timing of treatment: > or < 4 weeks from delivery, and possible relapse risk
- Obtain infant RPR and compare to mother
- Thorough physical exam (abnormal or normal)
- Consult Red Book and/or ID

If ANY of the following:

- Mother not treated, inadequately treated, or no documentation of receiving treatment
- Mother treated with regimen other than recommended in the guideline (ex: non-penicillin regimen)
- Mother received treatment <4 weeks before delivery

If Possible, Probable, or Confirmed Congenital Syphilis

- CSF analysis (CSF VDRL, cell count, protein)
- CBC
- Long-bone films
- Start penicillin treatment

Treatment

- Aqueous crystalline penicillin G
 - 50,000 U/kg IV every 12 hours (1 week or younger), then every 8 hours for infants older than 1 weeks for total of 10 days of therapy (preferred)
- OR
- Procaine penicillin G
 - 50,000 U/kg IM, single day dose x 10 days
- OR
- *Benzathine Penicillin G*
 - *50,000 U/kg IM, single dose (ONLY recommended by some experts, if all components of exam and labs normal and follow-up certain)*

Treatment

IF IV access is limited, make sure to give the correct treatment with IM dosing (i.e., Procaine Penicillin and NOT Benzathine Penicillin if abnormal findings) or you will have to restart the treatment all over...

Also, make sure to adjust treatment dosing on the 8th day after birth to Q8H for IV...

Any missed dose or wrong drug means treatment has to start all over

***New York Times*: Antibiotic **Shortage** Could Worsen Syphilis Epidemic (July, 2023)**

- The company cited significant increases in demand because of the *rising* rate of syphilis infections, as well as Bicillin's recent use as an *alternative to amoxicillin*, another antibiotic that has periodically been scarce and is prescribed for more general infections like strep throat.
- Pfizer rarely used pediatric version of Bicillin would soon *run out* because the company had begun using that drug's production line to increase the adult formula. Doctors turned to it in the last year in lieu of amoxicillin during an increase in the number of [strep throat cases](#).

Conclusion(s)

- Syphilis has increased significantly in the US, impacting women ages 15-44 years of age
- Congenital syphilis cases have significantly increased as maternal cases has increased
- US West and Southern states seemed most affected
- Early and more frequent maternal recognition with PCN can reduce # congenital syphilis and associated mortality/morbidities.
- Shortage of Benzathine Penicillin has created a further challenge