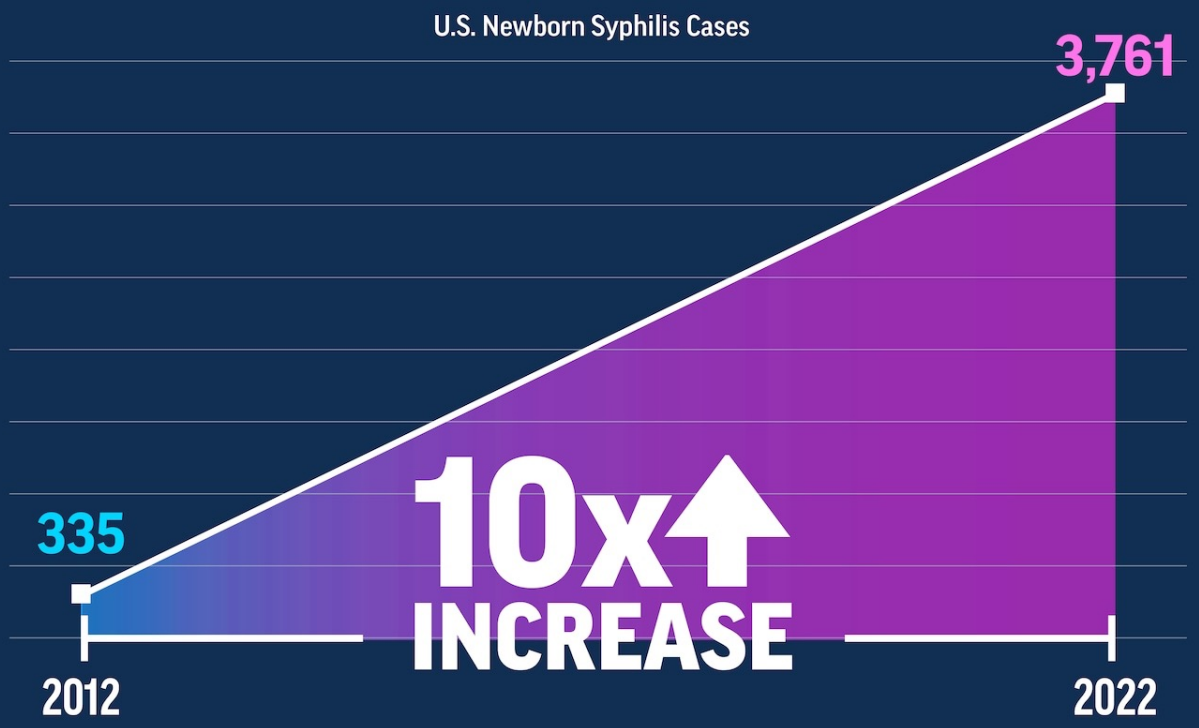
Connecticut STI Series: Congenital Syphilis

Ian C. Michelow, MD

May 9, 2024

U.S. Newborn Syphilis Cases Surge Over 10 Years



Vitalsigns™

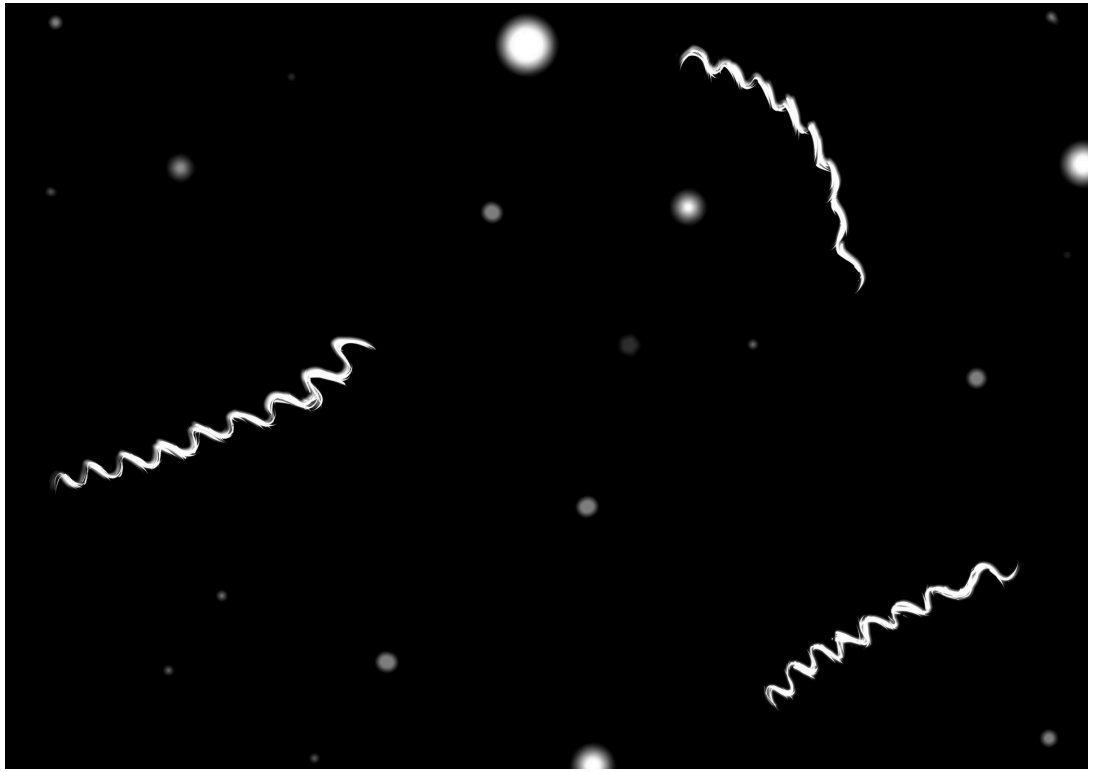
Source: November 2023 *Vital Signs*

CS341746

Disclosures

Dr. Michelow has no financial disclosures or conflicts of interest to report.

No unapproved/investigative use of commercial products or devices will be discussed



A Case of Congenital Syphilis

A **32-week** female born via uncomplicated NVD transferred to NICU

PE

Gen: SGA, generalized edema, pale, icteric, mild RDS

Lung: crackles

CVS: normal

Abdomen: liver 6cm; spleen tip palpated

Skin: desquamating reddish rash-trunk, palms and soles

M/S: not moving right arm

The Washington Post

U.S. syphilis numbers are at their highest since the 1950s, CDC report says

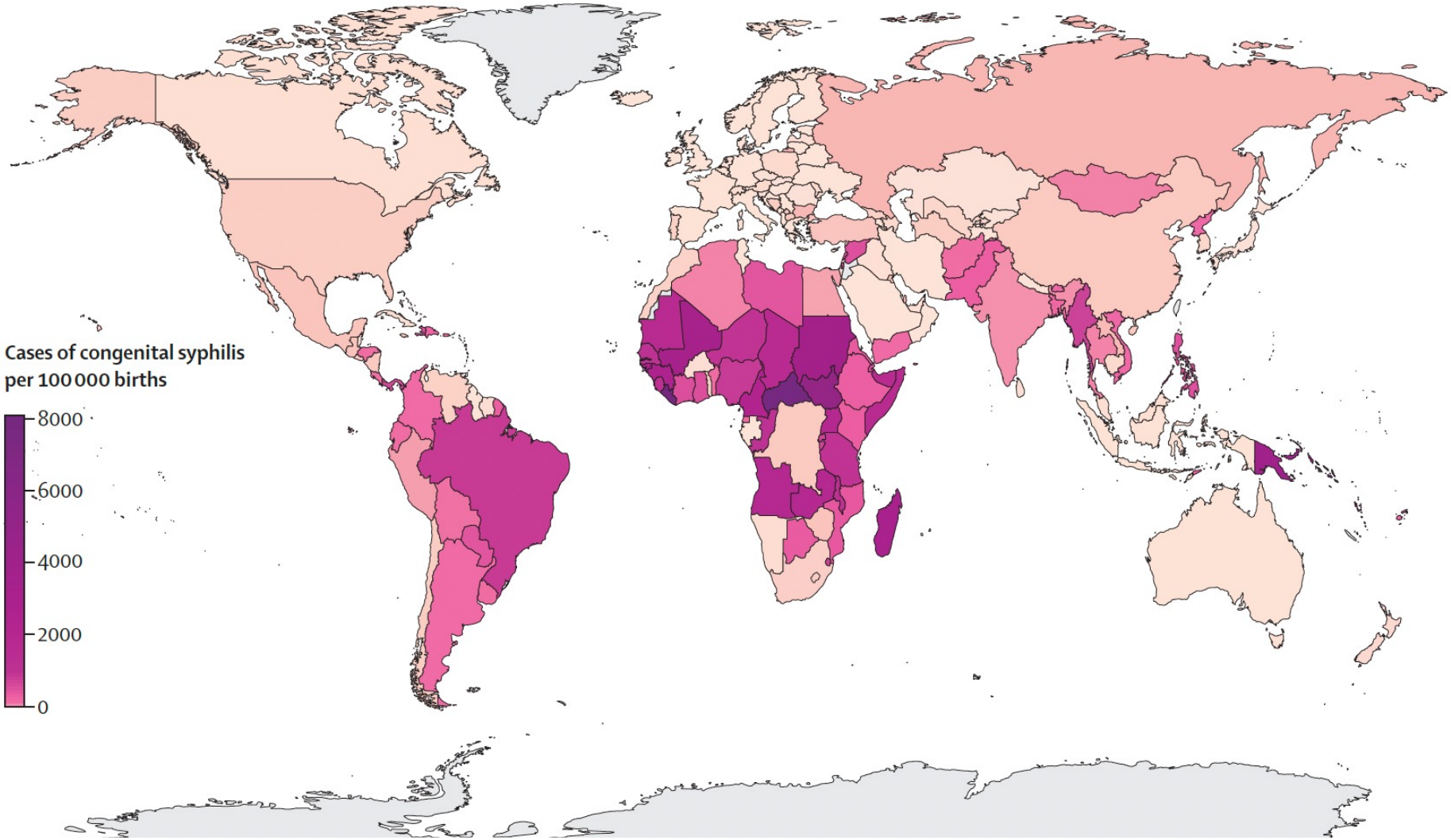
By Kelly Kasulis Cho

February 1, 2024

- lack of funding →less screening, treatment and partner services
- opioid epidemic
- decreased condom use
- socioeconomic disparities, homelessness, incarceration
- penicillin shortage (April 2023-early 2025)

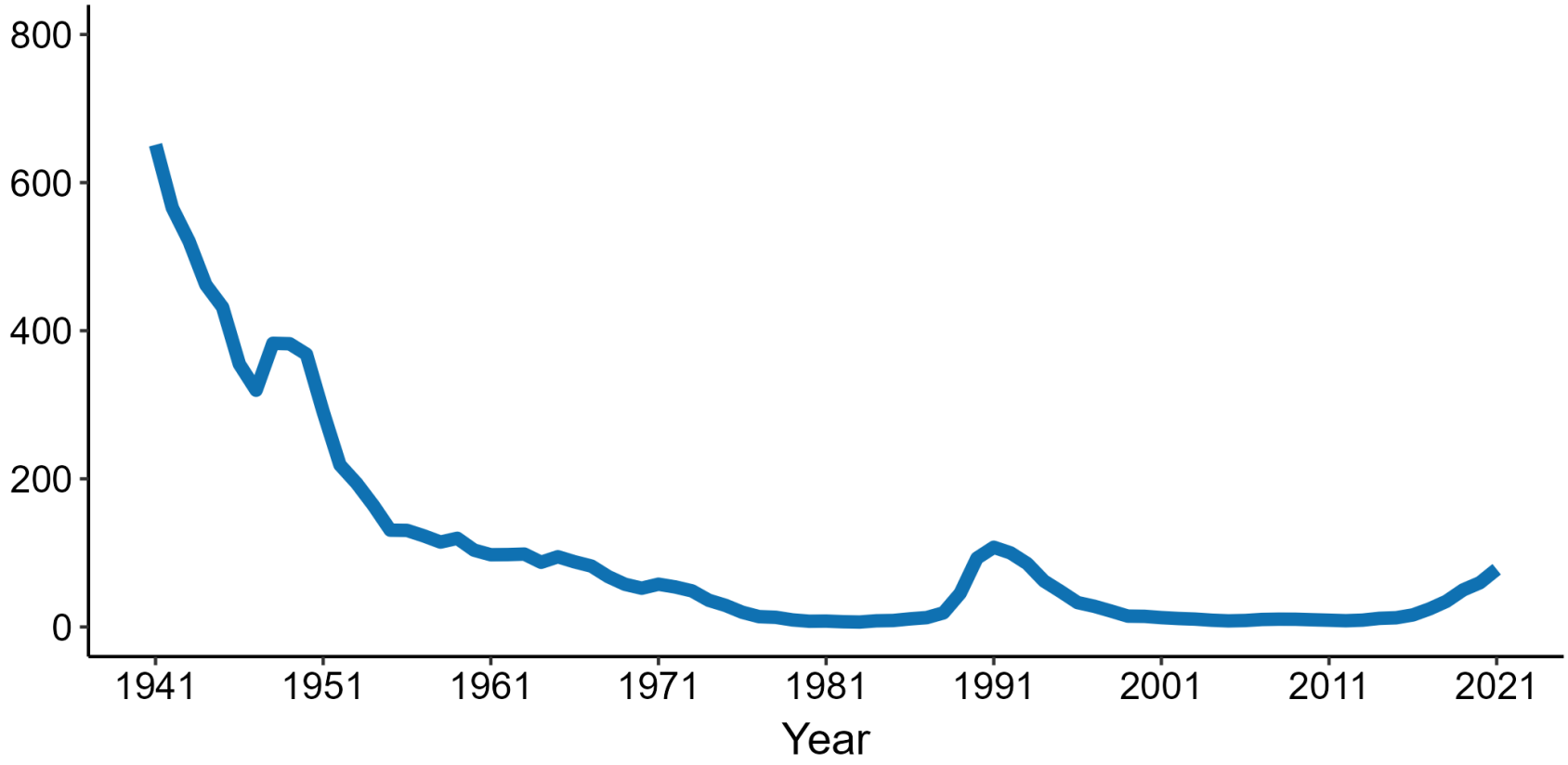
World map of congenital syphilis cases per 100,000 live births

Additional: ≤40% of untreated infections in pregnancy cause stillbirths

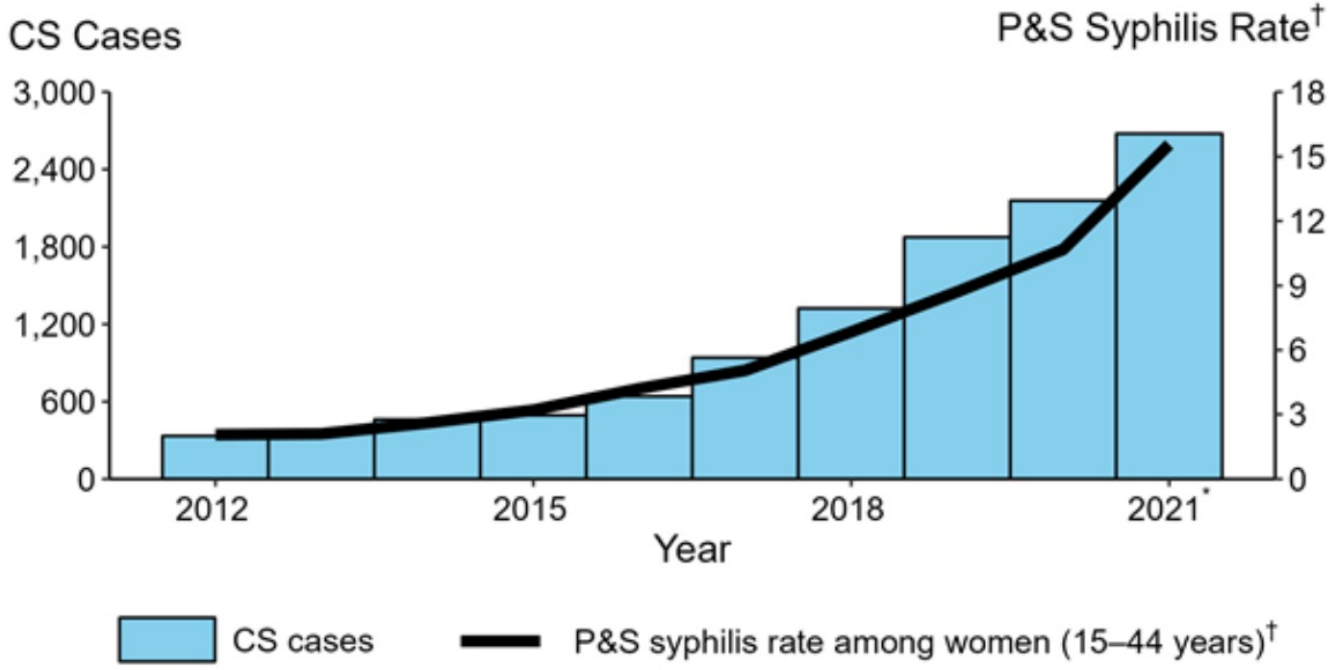


Congenital Syphilis: Rates of Reported Cases by Year of Birth, United States, 1941–2021

* Per 100,000 live births



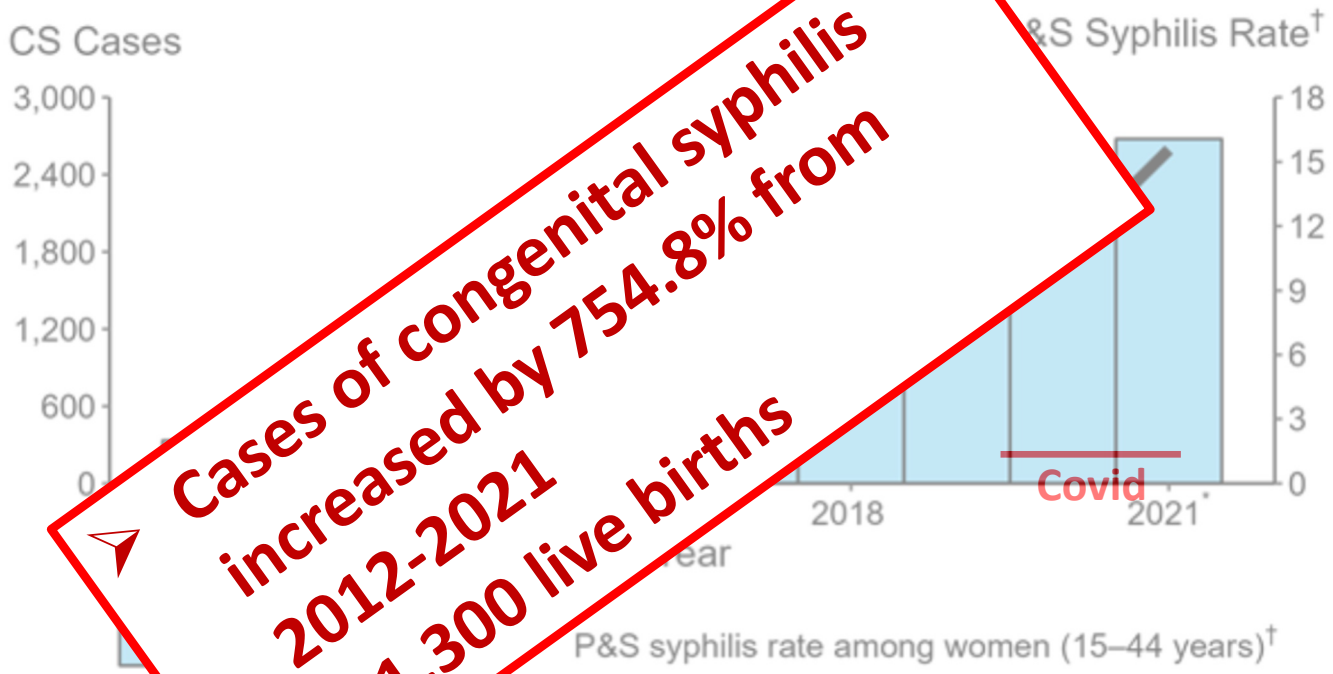
U.S. trends in congenital syphilis and maternal primary and secondary syphilis: 2012-2021



† Per 100,000

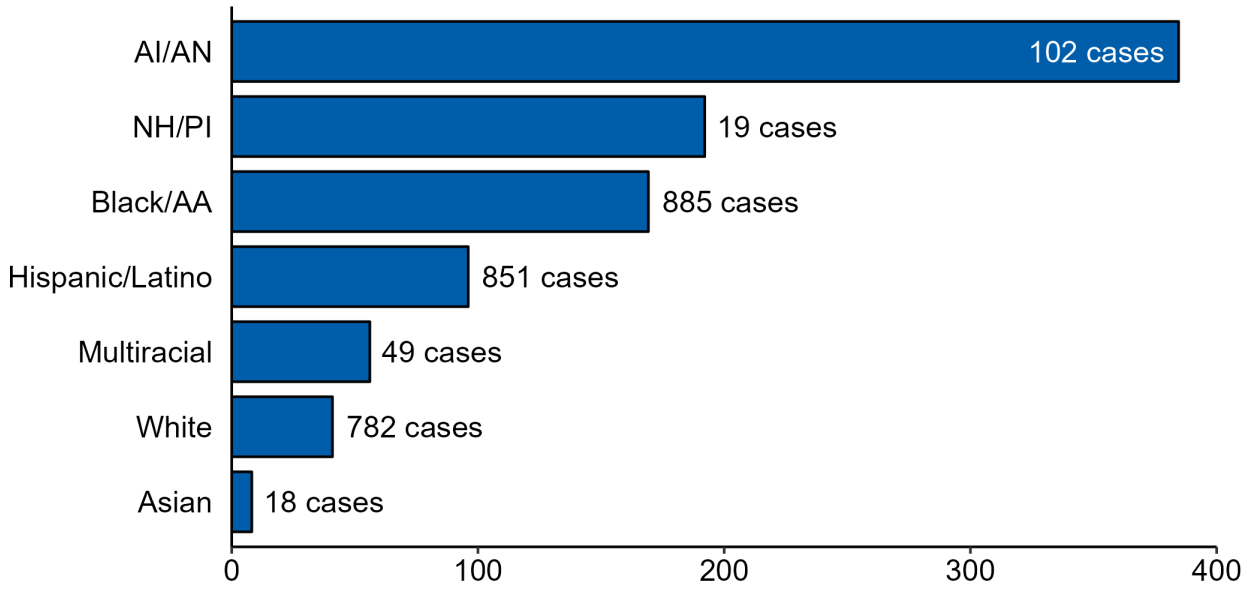
ACRONYMS: CS = Congenital syphilis; P&S = Primary and secondary syphilis

U.S. trends in congenital syphilis and maternal primary and secondary syphilis: 2012-2021



- Cases of congenital syphilis increased by 754.8% from 2012-2021
- 1:1,300 live births

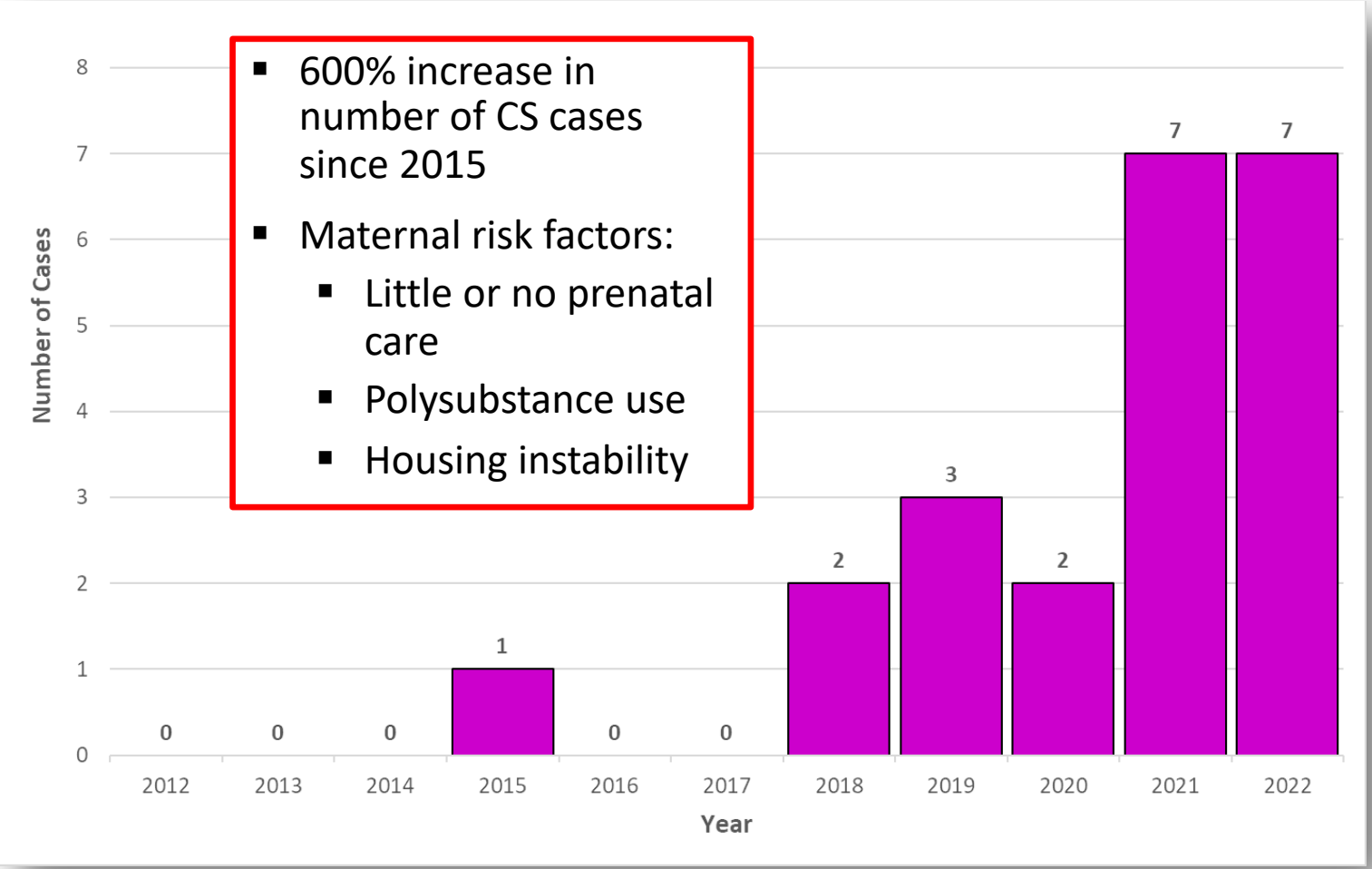
Congenital syphilis: case counts and rates by race/ethnicity of mother, 2021



*** Per 100,000 live births**

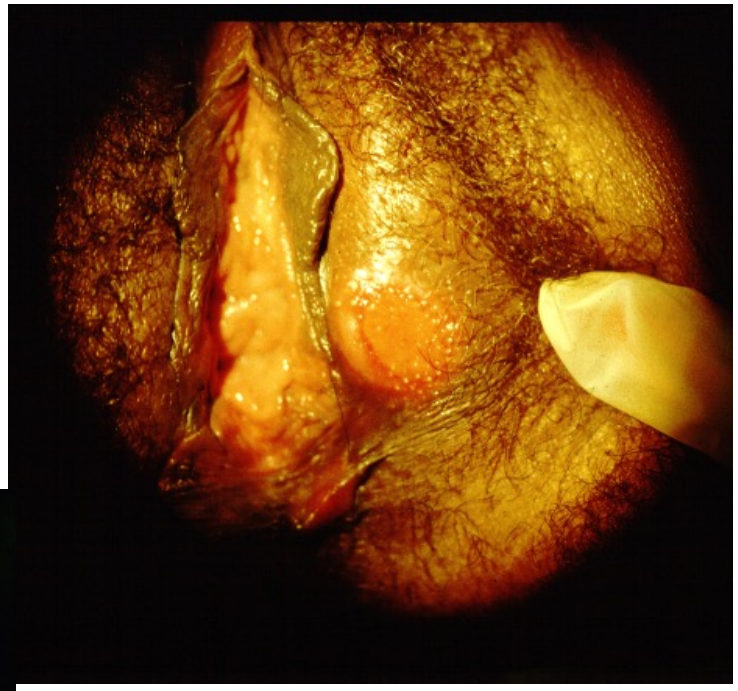
ACRONYMS: AI/AN = American Indian or Alaska Native; Black/AA = Black or African American; NH/PI = Native Hawaiian or other Pacific Islander

Congenital syphilis: reported cases by year of birth—Connecticut, 2012-2022



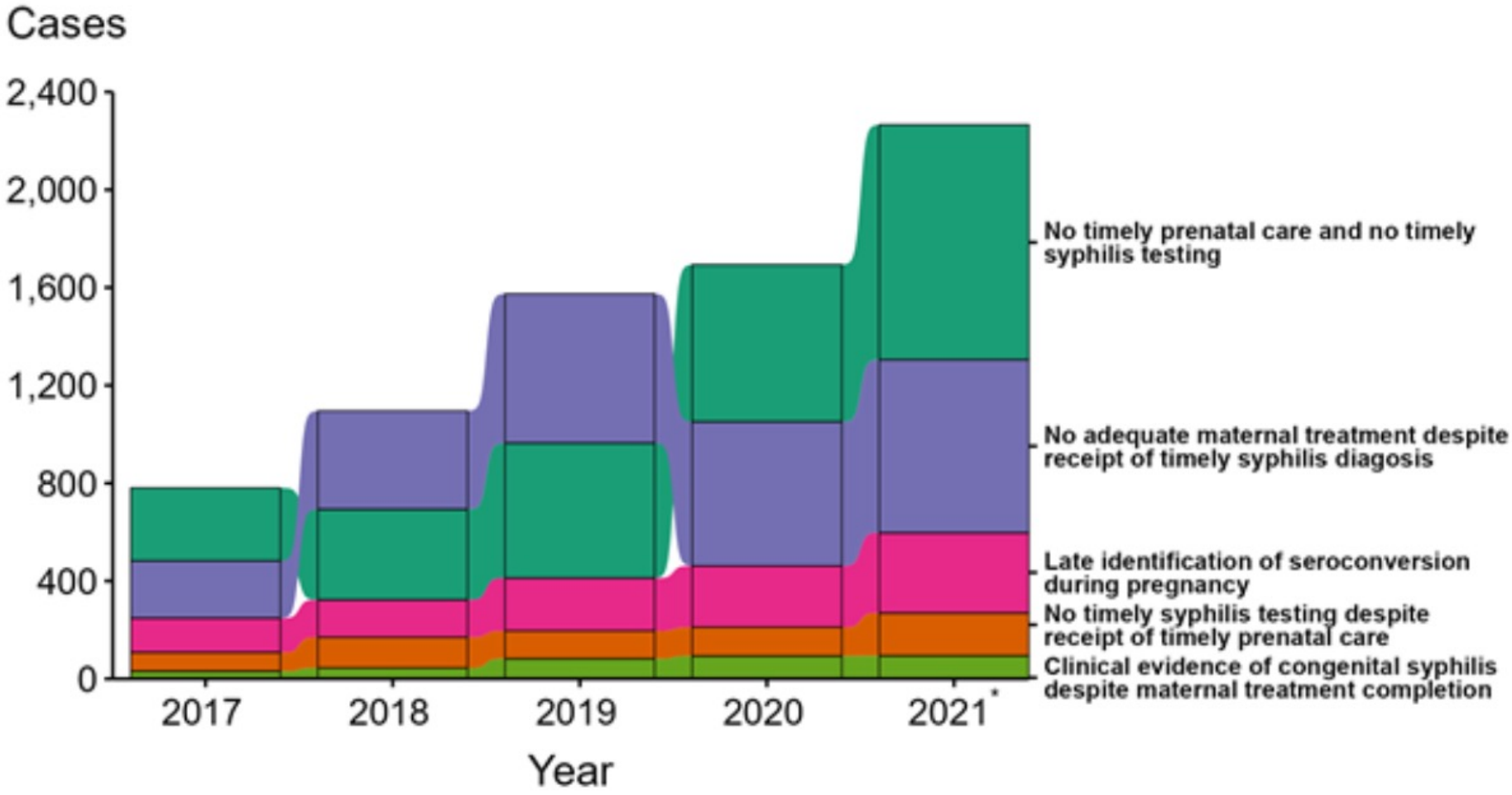
Courtesy Dr. Lynn Sosa, CT DPH

The only way to prevent congenital syphilis is to prevent, test, and treat maternal syphilis



Courtesy of Katherine Hsu, MA DPH

Missed prevention opportunities among mothers delivering infants with congenital syphilis, 2017-2021



CDC. STI Surveillance 2023

Transmission of Congenital Syphilis

- **Transplacental**
  - ≥9 wks gestation
  - **primary** or **secondary** syphilis: 60%-100% transmission
  - **early latent syphilis**: 40% transmission
  - **late latent syphilis**: <8% transmission
  - risk of transmission **increases as gestational age increases** at the time of maternal infection
- **Perinatal** via genital lesion at delivery
- **Untreated**
  - spontaneous abortion, stillbirth or perinatal death in ≤**40%** of pregnancies

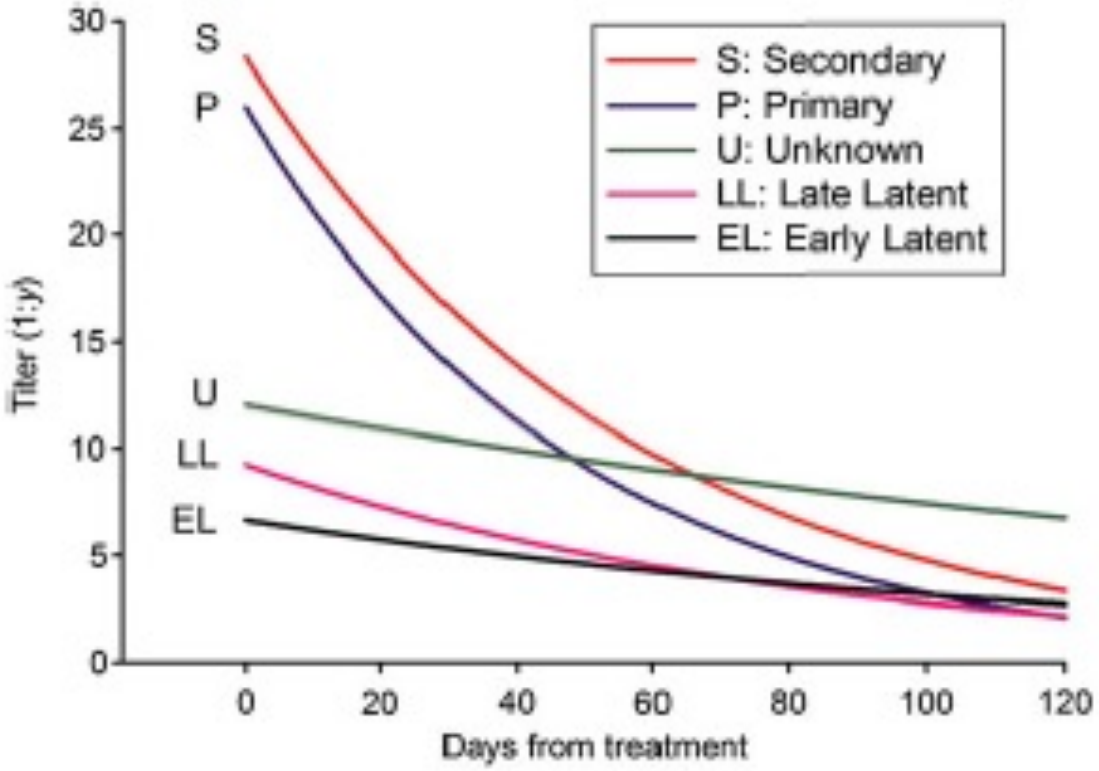
Remington & Klein

CDC: 2021 Syphilis Guidelines

Treatment: benzathine penicillin G is the only effective treatment during pregnancy

- primary, secondary, or early latent syphilis: **2nd dose** of benzathine penicillin G 2.4 million units IM can be administered 1 week after the initial dose to ensure adequate serum levels
- if Rx for late latent syphilis delayed **>9 days** between doses →restart Rx

Nontreponemal Titers Decline Following Maternal Treatment



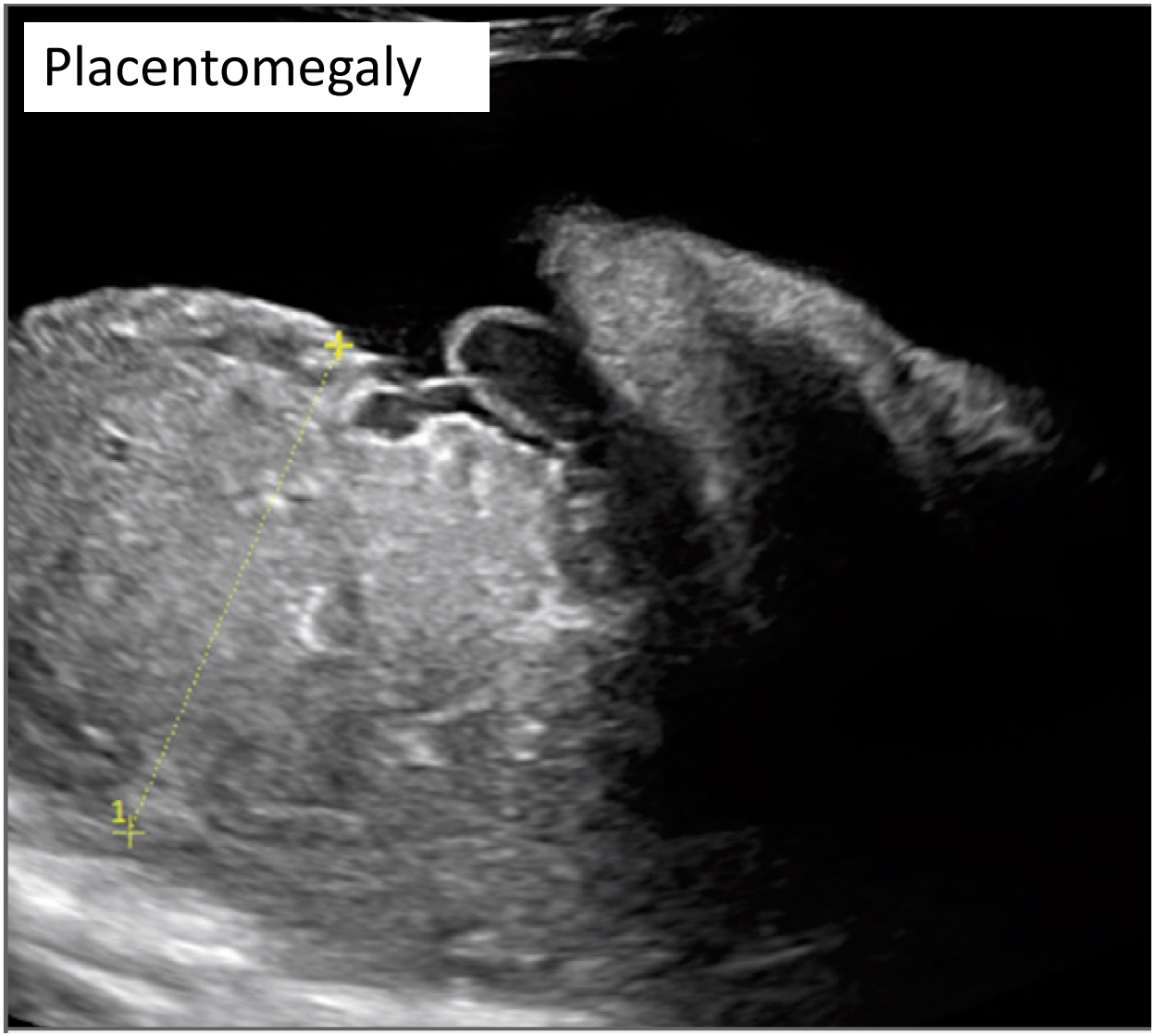
Rac MW et al CID 2015:60

Ultrasound:
monitor fetus in infected mothers

N ENGL J MED 390;3

JANUARY 18, 2024

- fetal hepatomegaly
- non-immune hydrops
- polyhydramnios
- anemia (peak flow in MCA)



Complications of syphilis in pregnancy

- spontaneous abortion
- stillbirth
- preterm delivery
- IUGR and SGA
- congenital infection
- infant mortality

Clinical, hematologic and radiographic features

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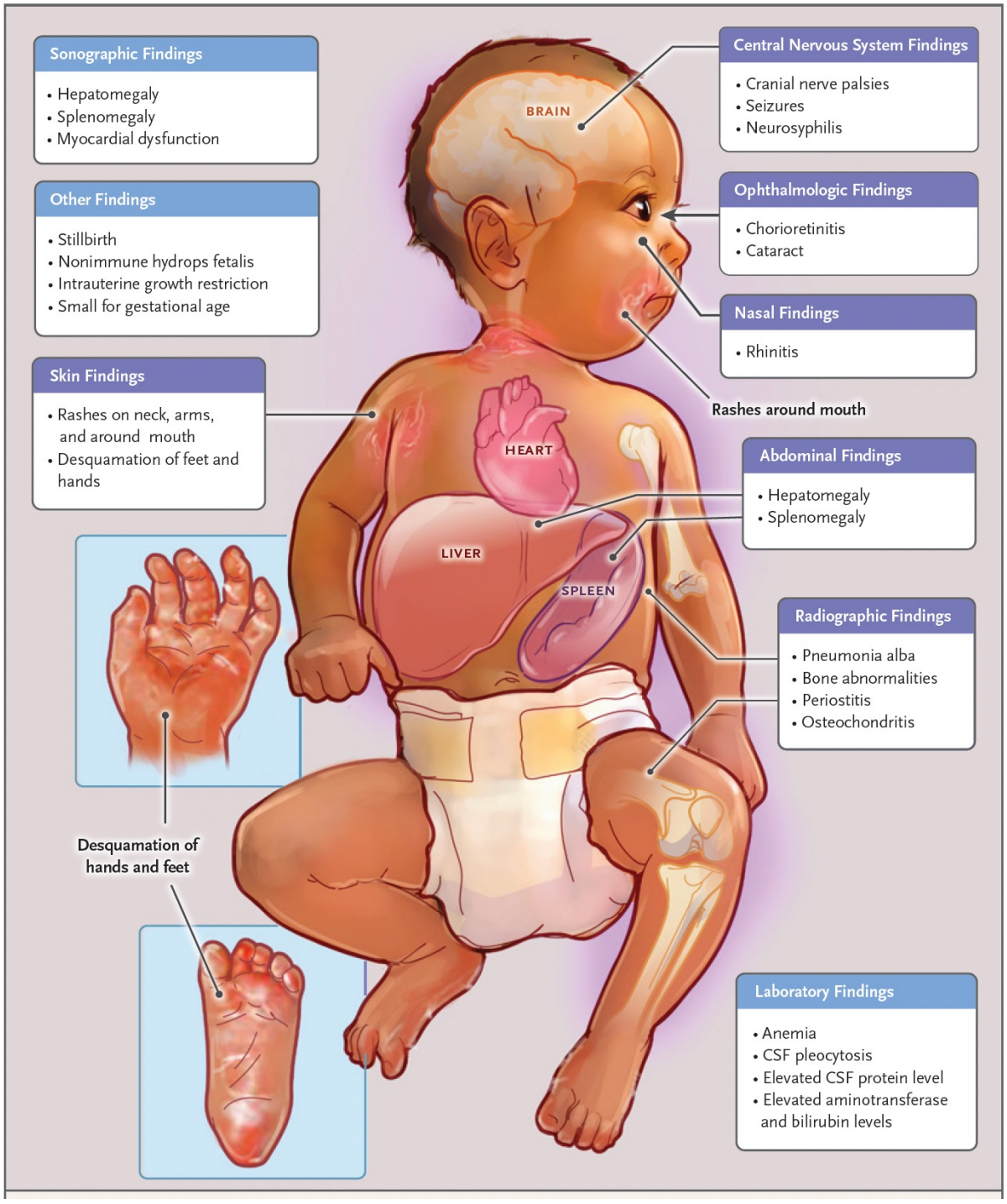
“ the great imitator”



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Copper-red maculopapular lesions

American Academy of Pediatrics

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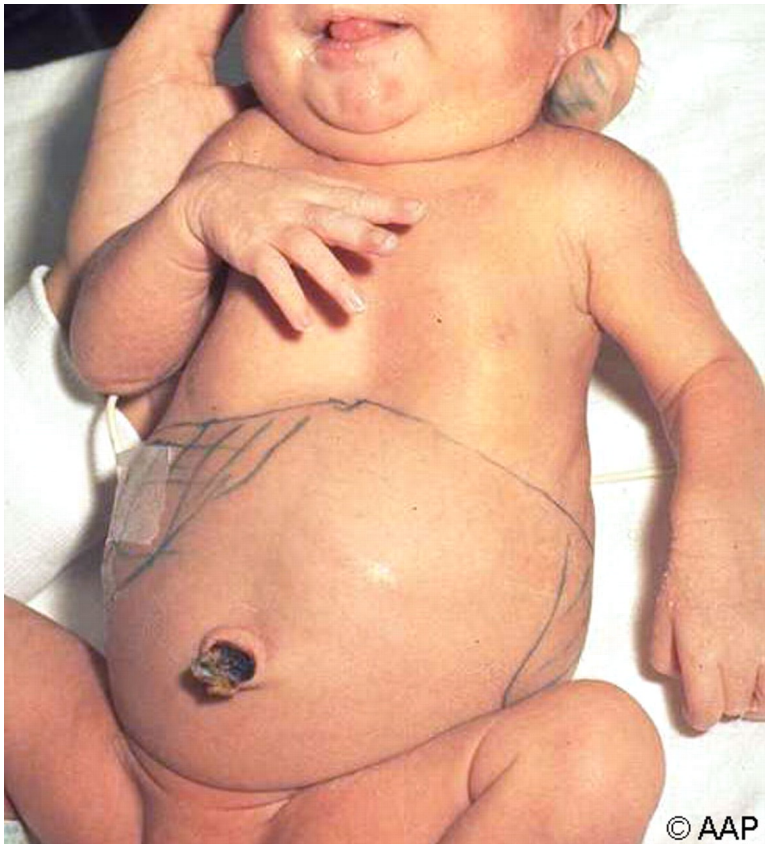
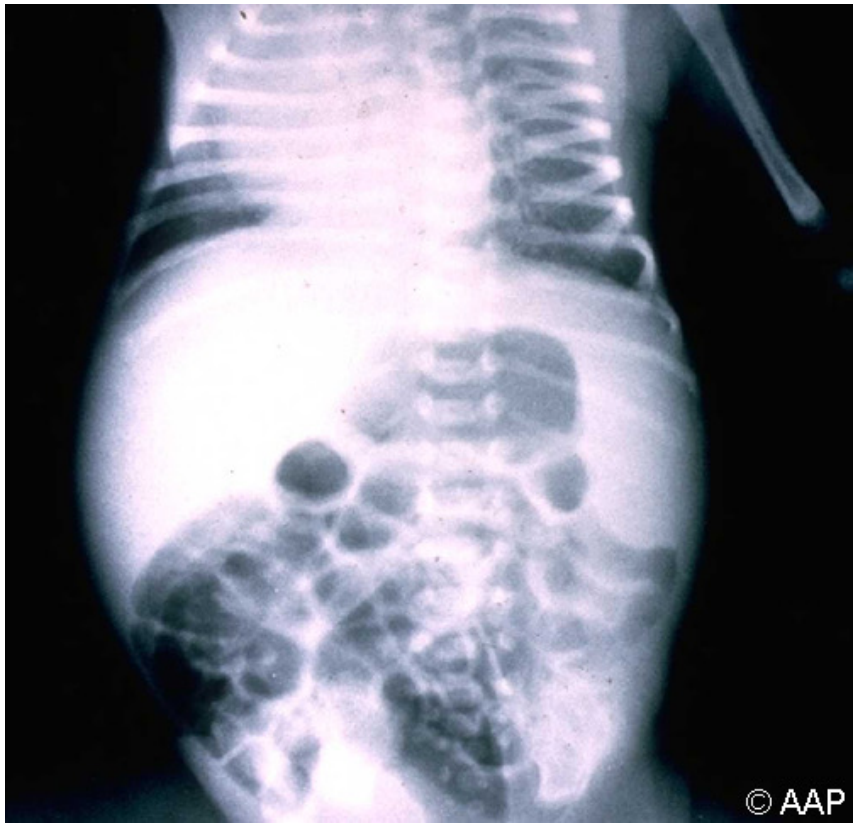
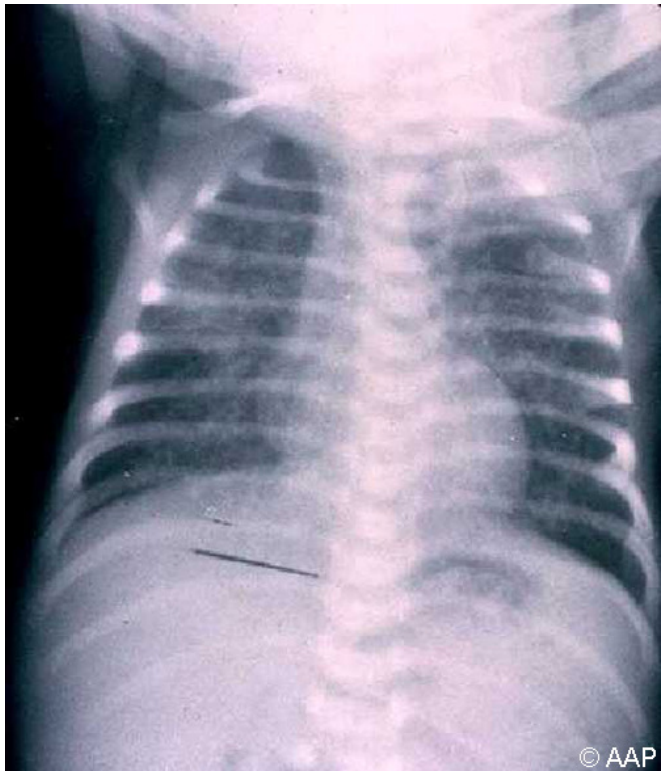
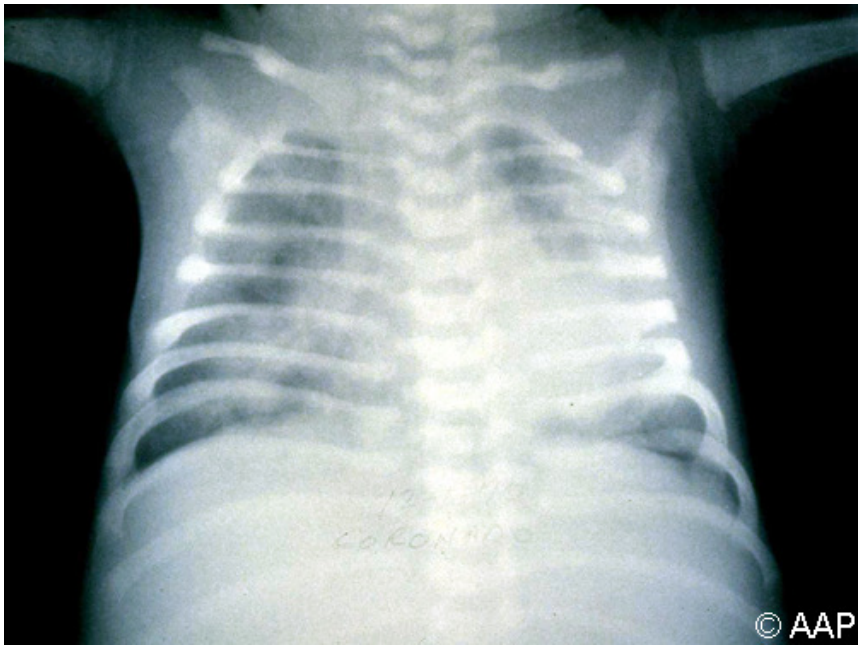
Mucous membrane and skin lesions







Pneumonia alba



A 3-day-old with severe luetic pneumonia.

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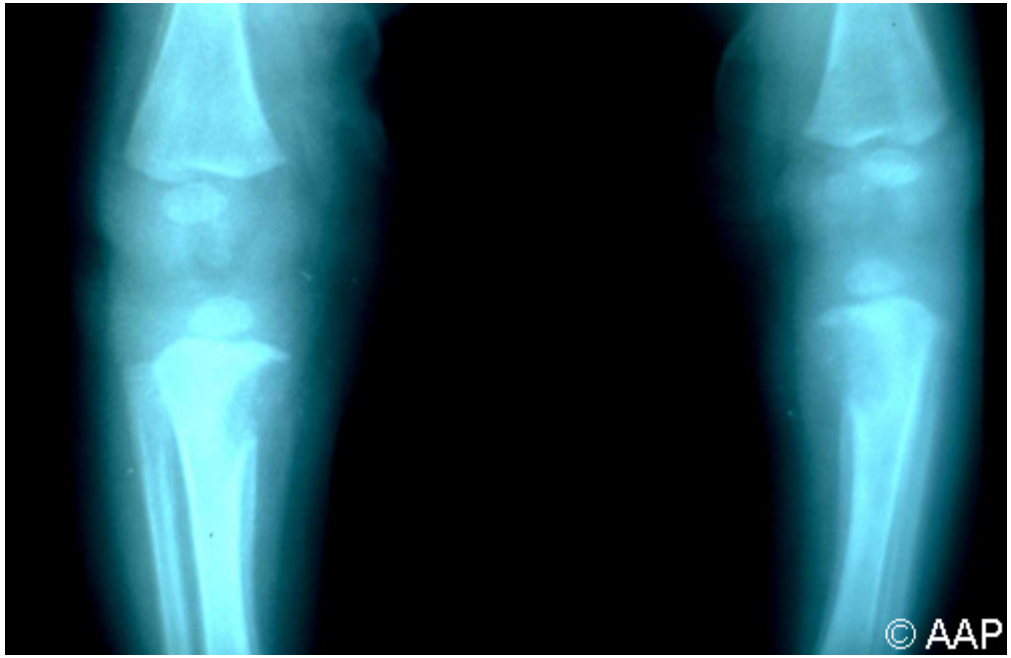
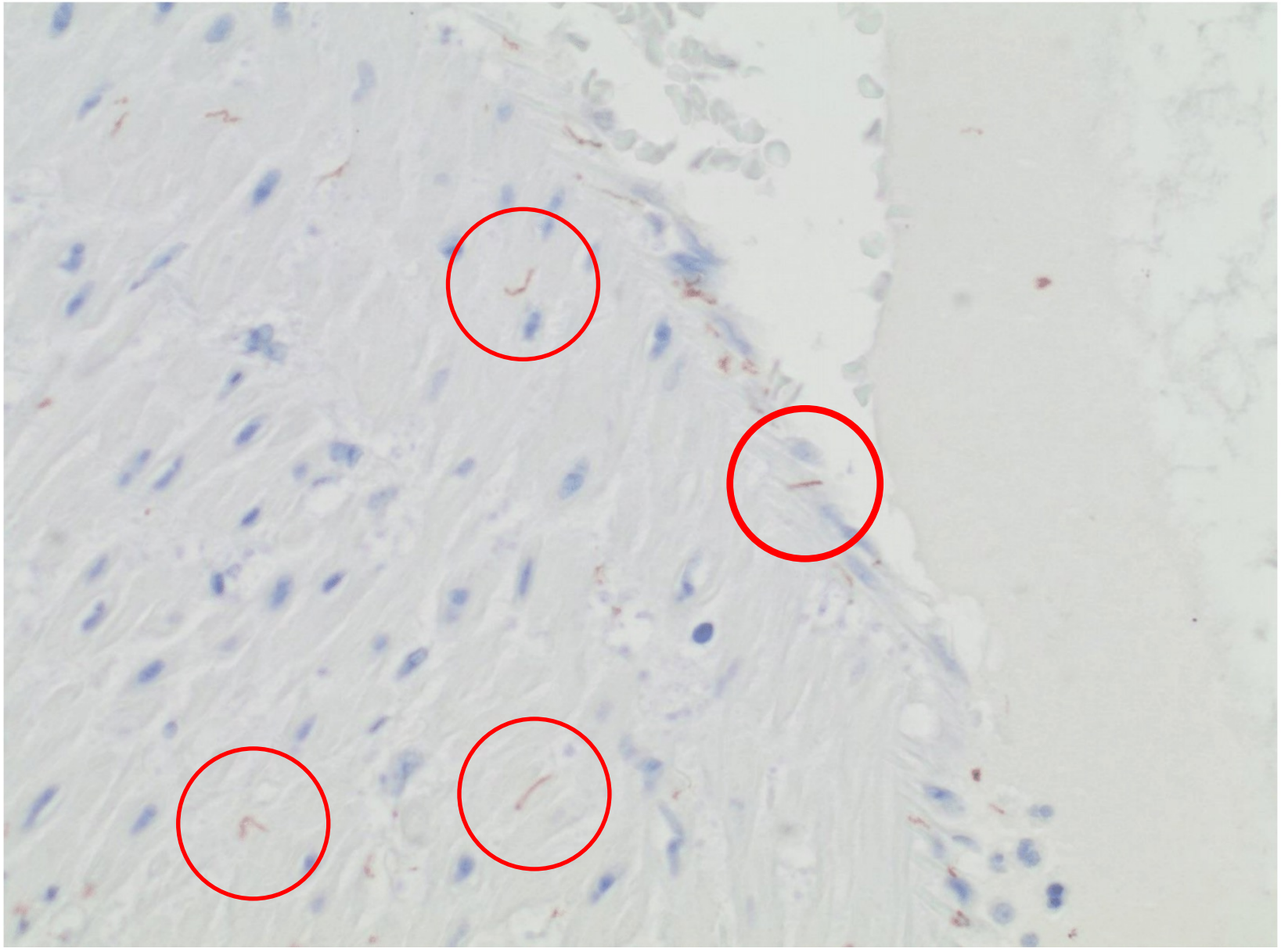


Proximal tibial metaphysitis (Wimberger sign)

Pathologic fracture of the proximal humerus and the distal femur.

Umbilical cord vein (400X): spirochetes caught in the act of infiltrating endothelial lining



Timing of Clinical Presentation

- ~80% infected infants are asymptomatic at birth
- in 2/3 of untreated cases, signs of congenital syphilis begin to appear at 3-8 weeks of life
- almost all cases have symptoms within 3 months

Courtesy Dr Katherine Hsu

Evaluation of Neonate

- RPR must be done on serum (not cord blood)
  - Maternal blood can contaminate cord blood→false positives (5-10%)
  - Wharton's jelly can inhibit test →false negatives (5-20%)
- CBC/diff
- LFT
- CSF including VDRL
- Xray long bones
- ± CXR
- placenta pathology
- test mother for HIV & other STIs

The New England Journal of Medicine

CENTRAL NERVOUS SYSTEM INFECTION IN CONGENITAL SYPHILIS

IAN C. MICHELOW, M.B., B.CH., D.T.M.&H., GEORGE D. WENDEL, JR., M.D., MICHAEL V. NORGARD, PH.D., FIKER ZERAY, R.N., N. KRISTINE LEOS, B.S., RAJIHA ALSAADI, M.S., AND PABLO J. SÁNCHEZ, M.D.

- 22% (17/76) neonates born to untreated mothers had cong neurosyphilis based on identification of treponemes in CSF by rabbit infectivity testing
- 94% (16/17) had ≥1 abnormal finding on PE, labs or x-ray
- only 82% (14/17) had abnormal CSF WBC, protein or pos CSF VDRL

Michelow et al. *NEJM* 2002

Syphilis management guideline: 2021

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

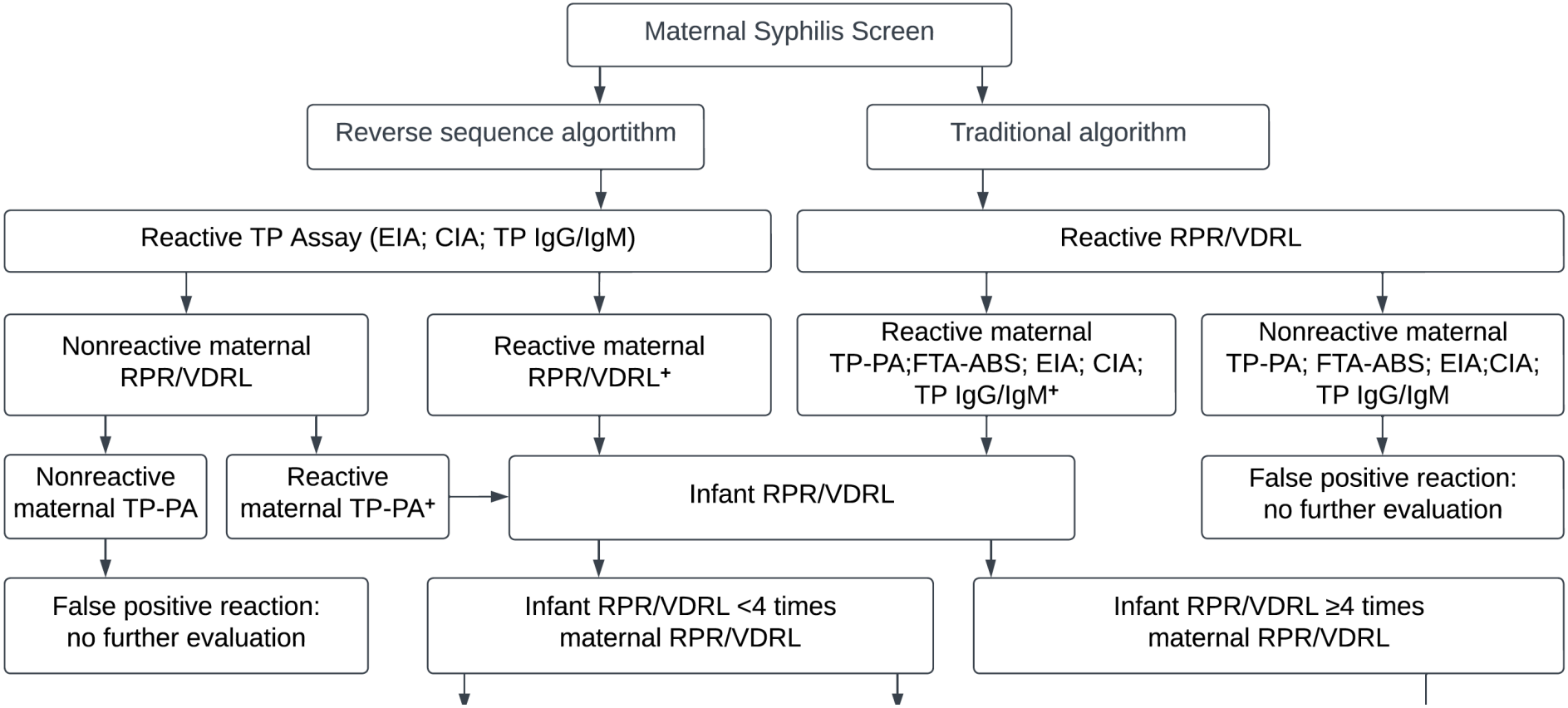
Evaluation and treatment of neonates born to women with reactive non-treponemal (RPR) and treponemal (EIA, TPPA) serologic tests during pregnancy

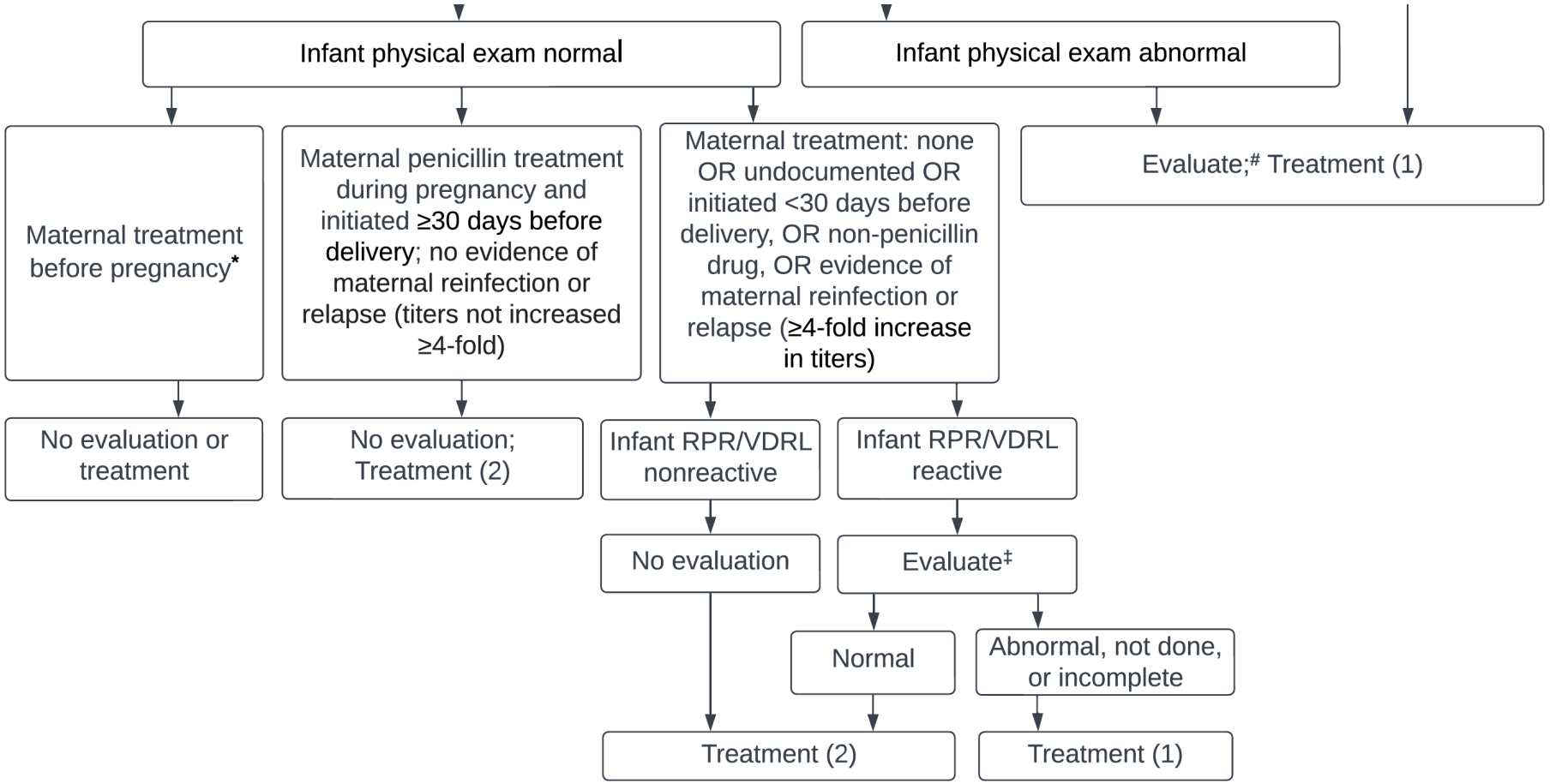
Scenario 1: Confirmed or highly probable CS
Scenario 2: Possible CS
Scenario 3: CS Less Likely
Scenario 4: CS Unlikely

CS, congenital syphilis

Screening algorithm for mothers

- **traditional** (1st RPR) vs **reverse** (1st treponemal EIA)
- traditional algorithm: less sensitive (more false negatives) for early or late latent syphilis
- reverse algorithm: less specific (more false positives) in low-prevalence settings
- **99% agreement** between the two approaches
- **both algorithms are acceptable according to CDC**


Maternal Syphilis Screen
Reverse sequence algortithm
Traditional algorithm
Reactive TP Assay (EIA; CIA; TP IgG/IgM)
Reactive RPR/VDRL
Nonreactive maternal RPR/VDRL
Reactive maternal RPR/VDRL+
Reactive maternal TP-PA;FTA-ABS; EIA; CIA; TP IgG/IgM+
Nonreactive maternal TP-PA; FTA-ABS; EIA;CIA; TP IgG/IgM
Nonreactive maternal TP-PA
Reactive maternal TP-PA+
Infant RPR/VDRL
False positive reaction: no further evaluation
False positive reaction: no further evaluation
Infant RPR/VDRL <4 times maternal RPR/VDRL
Infant RPR/VDRL ≥4 times maternal RPR/VDRL



TREATMENT:
(1) Aqueous penicillin G 50,000 U/kg IV q 12 hr (≤1 wk of age), q 8 hr (>1 wk), or procaine penicillin G 50,000 U/kg IM single daily dose, x 10 days
(2) Benzathine penicillin G 50,000 U/kg IM x 1 dose

Report to CT DPH within 12 hrs by fax or mail

Reportable Laboratory Findings
Diseases Relating to Public Health - Form OL-15C
For information or to order forms call (860) 509-7994. (rev. 01/01/2022)

Connecticut Department of Public Health
410 Capitol Avenue, MS #11FDS
P.O. Box 340308
Hartford, CT 06134-0308

Patient Last Name:_____ First:_____ D.O.B._____ Age: _____
Street Address:_____ City:_____ State/Zip Code: _____
Patient Phone:_____ Gender: ☐ Male ☐ Female ☐ Intersex Hispanic/Latino: ☐ Yes ☐ No ☐ Unk. ☐ Refused
Race: ☐ White ☐ Black/African Amer. ☐ Asian ☐ Amer. Indian/Alaska Nat. ☐ Nat. Hawaiian/Other Pacific Islander
☐ Other specify: _____ ☐ Unknown ☐ Refused If patient resides in a LTC facility please check: ☐ Yes
Occupation: _____ Name and address of workplace: _____
Attending Physician Last Name: _____First: _____
Address:_____ Phone: _____

Person Reporting: _____
Lab Phone: _____
Submitting Laboratory: (name/address or label)

Specimen collection date: _____
Date laboratory finding reported to physician: _____
Date OL-15C completed: _____
Hospital Chart No:_____Lab Specimen No: _____
Source/Type specimen: _____
Submitted to state lab: (see reverse) ☐ Yes ☐ No

☐ *Anaplasma phagocytophilum* by PCR only
☐ *Babesia* ☐ IFA IgM (titer) _____IgG (titer) _____
☐ Blood smear ☐ PCR ☐ Other _____
☐ *microti* ☐ *divergens* ☐ *duncani* ☐ Unspeciated
☐ *Bordetella pertussis* (titer) _____
☐ Culture [1] ☐ Non-pertussis *Bordetella* [1] (specify) _____
☐ DFA ☐ PCR
☐ *Borrelia burgdorferi* [2]
☐ *Borrelia miyamotoi*
☐ California group virus [3] spp_____
☐ *Campylobacter* [3] spp _____ ☐ Culture ☐ PCR ☐ EIA
☐ *Candida auris* [report samples from all sites] [1]
☐ *Candida* spp, [blood isolates only]: _____ [1,3]
☐ Carbapenem-resistant *Acinetobacter baumannii* (CRAB) [1,4]
☐ Carbapenem-resistant Enterobacteriaceae (CRE) [1,3,4]
Genus _____ spp _____
☐ Carboxyhemoglobin ≥ 5% [2] _____% COHb
☐ Chikungunya virus
☐ *Chlamydia trachomatis* (test type) _____
☐ *Clostridium difficile* [5]
☐ *Corynebacterium diphtheria* [1]
☐ *Cryptosporidium* spp [3] _____ ☐ PCR ☐ DFA ☐ EIA
☐ Microscopy ☐ Other: _____
☐ *Cyclospora* spp [3]
☐ PCR ☐ Microscopy ☐ Other:_____
☐ Dengue virus
☐ Eastern equine encephalitis virus
☐ *Ehrlichia chaffeensis* ☐ PCR ☐ IgG ≥1:128 only ☐ Culture
☐ Enterotoxigenic *Escherichia coli* (ETEC) ☐ Culture ☐ PCR
☐ *Escherichia coli* O157 [1] ☐ Culture ☐ PCR
☐ *Giardia* spp [3] _____
☐ Group A *Streptococcus*, invasive [1,4] ☐ Culture ☐ Other_____
☐ Group B *Streptococcus*, invasive [1,4] ☐ Culture ☐ Other_____
☐ *Haemophilus ducreyi*
☐ *Haemophilus influenzae*, invasive [1,4] ☐ Culture ☐ Other _____
☐ Hepatitis A virus (HAV): ☐ IgM anti-HAV [6] ☐ NAAT Positive [6]
ALT _____ Total Bilirubin _____ ☐ Not Done
☐ Hepatitis B HBsAg ☐ Positive ☐ Negative [7]
☐ IgM anti-HBc ☐ HBeAg [2] ☐ HBV DNA [2]
anti-HBs [7] ☐ Positive (titer) _____ ☐ Negative
☐ Hepatitis C virus (HCV) [8] ☐ Antibody _____
☐ PCR/NAAT/RNA _____ ☐ Genotype:_____
☐ Herpes simplex virus (infants ≤ 60 days of age)
☐ Culture ☐ PCR ☐ IFA ☐ Ag detection
☐ HIV Related Testing (report only to the State) [9]
☐ Detectable Screen (IA)
Antibody Confirmation (WB/IFA/Type-diff) [9]
HIV 1 ☐ Positive ☐ Negative/Ind HIV 2 ☐ Positive ☐ Negative/Ind
☐ HIV NAAT (or qualitative RNA) ☐ Detectable ☐ Not Detectable
☐ HIV Viral Load (all results) [9] _____ copies/mL
☐ HIV genotype [9]
☐ CD4 count: _____ cells/uL; _____% [9]
☐ HPV (report only to the State) [10]
Biopsy proven ☐ CIN2 ☐ CIN3 ☐ AIS
or their equivalent, (specify) _____
☐ Influenza virus (report only to the State) ☐ Rapid antigen [2] ☐ RT-PCR
☐ Type A ☐ Type B ☐ Type Unknown
☐ Subtype: _____
☐ Lead poisoning (blood lead ≥10 µg/dL <48 hrs; 0-9 µg/dL monthly) [11]
☐ Finger stick lead level _____µg/dL
☐ Venous lead level _____µg/dL

☐ *Legionella* spp [1] _____
☐ Culture ☐ DFA ☐ Ag positive ☐ PCR
☐ Four-fold serologic change (titers) _____
☐ *Listeria monocytogenes* [1] ☐ Culture ☐ PCR
☐ Mercury poisoning
☐ Urine ≥ 35 µg/g creatinine _____µg/g
☐ Blood ≥ 15 µg/L _____µg/L
☐ Monkeypox virus ☐ PCR ☐ IgM anti-MPXV ☐ Sequencing
☐ Orthopoxvirus ☐ PCR ☐ IHC ☐ Sequencing
☐ Non-variola orthopoxvirus ☐ PCR
☐ Mumps virus [12] (titer) _____ ☐ PCR
☐ *Mycobacterium leprae*
☐ *Mycobacterium tuberculosis* Related Testing [1]
AFB Smear ☐ Positive ☐ Negative
If positive ☐ Rare ☐ Few ☐ Numerous
NAAT ☐ Positive ☐ Negative ☐ Indeterminate
Culture ☐ *Mycobacterium tuberculosis*
☐ Non-TB mycobacterium (specify *M.*) _____
☐ *Neisseria gonorrhoeae* (test type) _____
☐ *Neisseria meningitidis*, invasive [1,4] (Call DPH with these results)
☐ Culture ☐ Other _____
☐ Neonatal bacterial sepsis [3,13] spp_____
☐ *Plasmodium* [1,3] spp_____
☐ Poliovirus
☐ Powassan virus
☐ Rabies virus
☐ *Rickettsia rickettsii* ☐ PCR ☐ IgG ≥1:128 only ☐ Culture
☐ Respiratory syncytial virus [2]
☐ Rubella virus [12] (titer) _____
☐ Rubeola virus (Measles) [12] (titer) _____ ☐ PCR
☐ St. Louis encephalitis virus
☐ *Salmonella* [1,3] (serogroup & type) _____ ☐ Culture ☐ PCR
☐ SARS-CoV [1] ☐ IgM/IgG
☐ PCR _____ (specimen) ☐ Other _____
☐ SARS-CoV-2 [15] ☐ PCR/NAA test ☐ Antigen test
☐ Positive ☐ Negative
☐ Shiga toxin [1] ☐ Stx1 ☐ Stx2 ☐ Type Unknown
☐ PCR ☐ EIA
☐ *Shigella* [1,3] (serogroup/spp) _____ ☐ Culture ☐ PCR
☐ *Staphylococcus aureus*, invasive [4] ☐ Culture ☐ Other _____
☐ methicillin-resistant ☐ methicillin-sensitive
☐ *Staphylococcus aureus*, vancomycin MIC ≥ 4 µg/mL [1]
MIC to vancomycin _____µg/mL
☐ *Staphylococcus epidermidis*, vancomycin MIC ≥ 32 µg/mL [1]
MIC to vancomycin _____µg/mL
☐ *Streptococcus pneumoniae*
☐ Culture [1,4] ☐ Urine antigen ☐ Other [4] _____
☐ *Treponema pallidum*
☐ RPR (titer) _____ ☐ FTA ☐ EIA
☐ VDRL (titer)_____ ☐ TPPA
☐ *Trichinella*
☐ Varicella-zoster virus, acute
☐ Culture ☐ PCR ☐ DFA ☐ Other _____
☐ *Vibrio* [1,3] spp _____ ☐ Culture ☐ PCR
☐ West Nile virus
☐ Yellow fever virus
☐ *Yersinia*, not *pestis* [1,3] spp _____ ☐ Culture ☐ PCR
☐ Zika virus

BIOTERRORISM at first clinical suspicion [14]
☐ *Bacillus anthracis* [1] ☐ *Brucella* spp [1]
☐ *Burkholderia mallei* [1] ☐ *Burkholderia pseudomallei* [1]
☐ *Clostridium botulinum* ☐ *Coxiella burnetii*
☐ *Francisella tularensis* ☐ Ricin
☐ *Staphylococcus aureus*-enterotoxin B
☐ Variola virus [1]

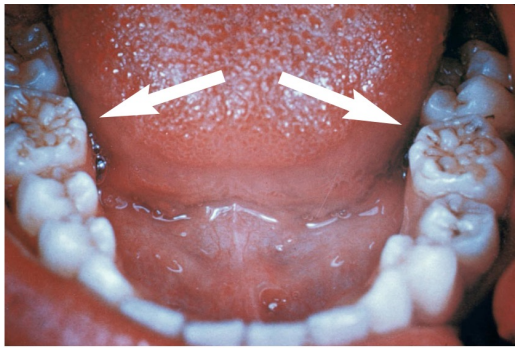
1. Send isolate/specimen to DPH Laboratory. Send laboratory report (electronic or paper) on first identification of an organism. For CRE/CRAB, send laboratory report if carbapenem resistance is suggested by laboratory antimicrobial testing and include antibiogram with report. For GBS, send isolate for cases <1 year of age. For *Salmonella*, *Shigella*, *Vibrio*, and *Yersinia*, (not pestis) tested by non-culture methods, send isolate if available;
(lymph node, brain, heart, liver, spleen, kidney, pancreas, or ovary), or other normally sterile site including muscle. For CRE and CRAB, also include urine or sputum; for CRAB also include wounds.
5. Upon request from the DPH, report all *C. difficile* positive stool samples.
6. Report peak ALT and Total Bilirubin results if conducted within one week of HAV positive test, if
sequence) and all CD4 results are only reportable by electronic file.
10. Upon request from the DPH, send fixed tissue from the diagnostic specimen for HPV typing.
11. Report results ≥ 10 µg/dL within 48 hours to the Local Health Department and DPH; submit ALL lead results at least monthly to DPH only.
12. Report all IgM positive titers, only report IgG titers

Treatment of confirmed or highly probable congenital syphilis

- aqueous penicillin G IV x 10 days
- if >1 day of penicillin is missed, the entire course should be restarted.
- no data to support other antibiotics (eg, ampicillin)

Late congenital syphilis

- Untreated infants (a/symptomatic)
- >2 years of age
- CNS, bones, joints, teeth, eyes, and skin
- Some signs develop many years later
  - interstitial keratitis, 8th nerve deafness, Hutchinson teeth, anterior bowing of the shins, frontal bossing, mulberry molars, saddle nose, rhagades (perioral fissures), and Clutton joints (painless swelling of knees)



Breastfeeding

- *T pallidum* is not transmitted through human milk
- transmission may occur if infectious lesion (chancre) on her breast

Follow-up

- No newborn should be discharged without mother's syphilis result
- PE at 2, 4, 6, and 12 months of age.
- RPR every 2-3 months until nonreactive
- RPR typically decrease by 3 months and should be nonreactive by 6 months of age

ACOG

The American College of Obstetricians and Gynecologists

News Releases | Apr 18, 2024 Share

ACOG Recommends Obstetrician-Gynecologists Increase Syphilis Screening for Pregnant Individuals

New Practice Advisory: screen all preg
individuals for syphilis at:

1) **1st prenatal care visit**
2) **rescreening during 3rd trimester**
3) **at birth**

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CDC (at least once): PNC visit, 28 wks and delivery if high risk

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