PROVIDENCE
Children's Health

Congenital & Maternal Syphilis

Pediatric Grand Rounds
Mark Tomlinson, MD (OB) &
Genevieve Buser, MD (Peds ID)
October 17, 2023

Conflicts of interest

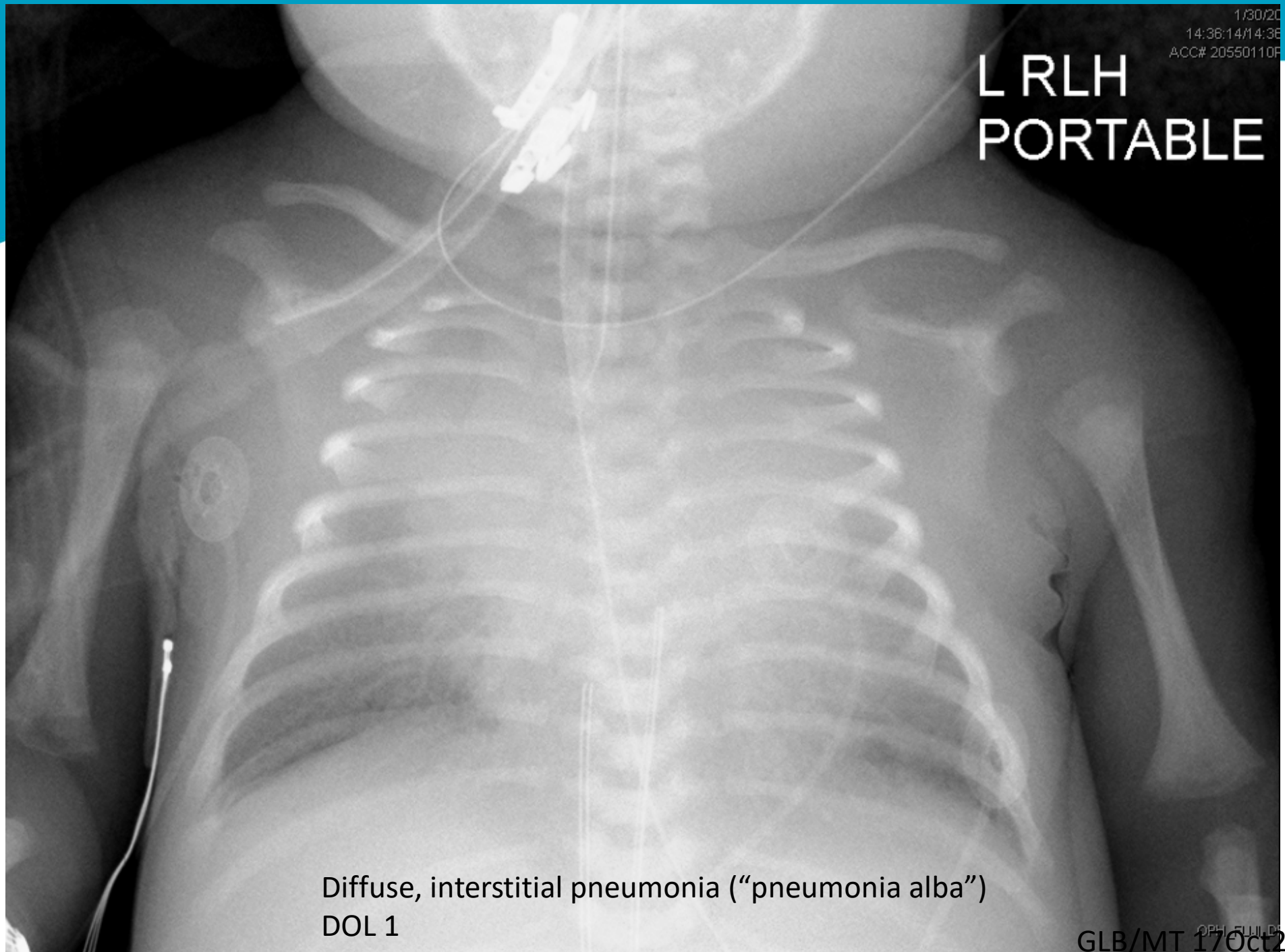
- Dr. Tomlinson and Dr. Buser received funding from the Gilead Foundation for hepatitis C screening study of women presenting for delivery

Objectives for congenital & maternal syphilis

- Discuss the epidemiology of syphilis in Oregon emphasizing dramatic increase in rates
- Review maternal & congenital syphilis screening, laboratory interpretations, diagnosis, treatment

Why is this Important?

- Ex-33w female, pre-term labor, abnormal exam
  - 20yo G1P1 mother, without prenatal care, +substance use
  - Mother known chronic hepatitis C, trichomonas positive, rapid HIV negative
  - Cloudy amniotic fluid
  - APGAR 3, 7, s/p surfactant x 2
  - Pneumonia, copious secretions
  - Hepatosplenomegaly, spleen 4cm BCM
  - Anasarca
  - Desquamating rash DOL 0 including hands and feet
  - Additional maternal and infant labs sent



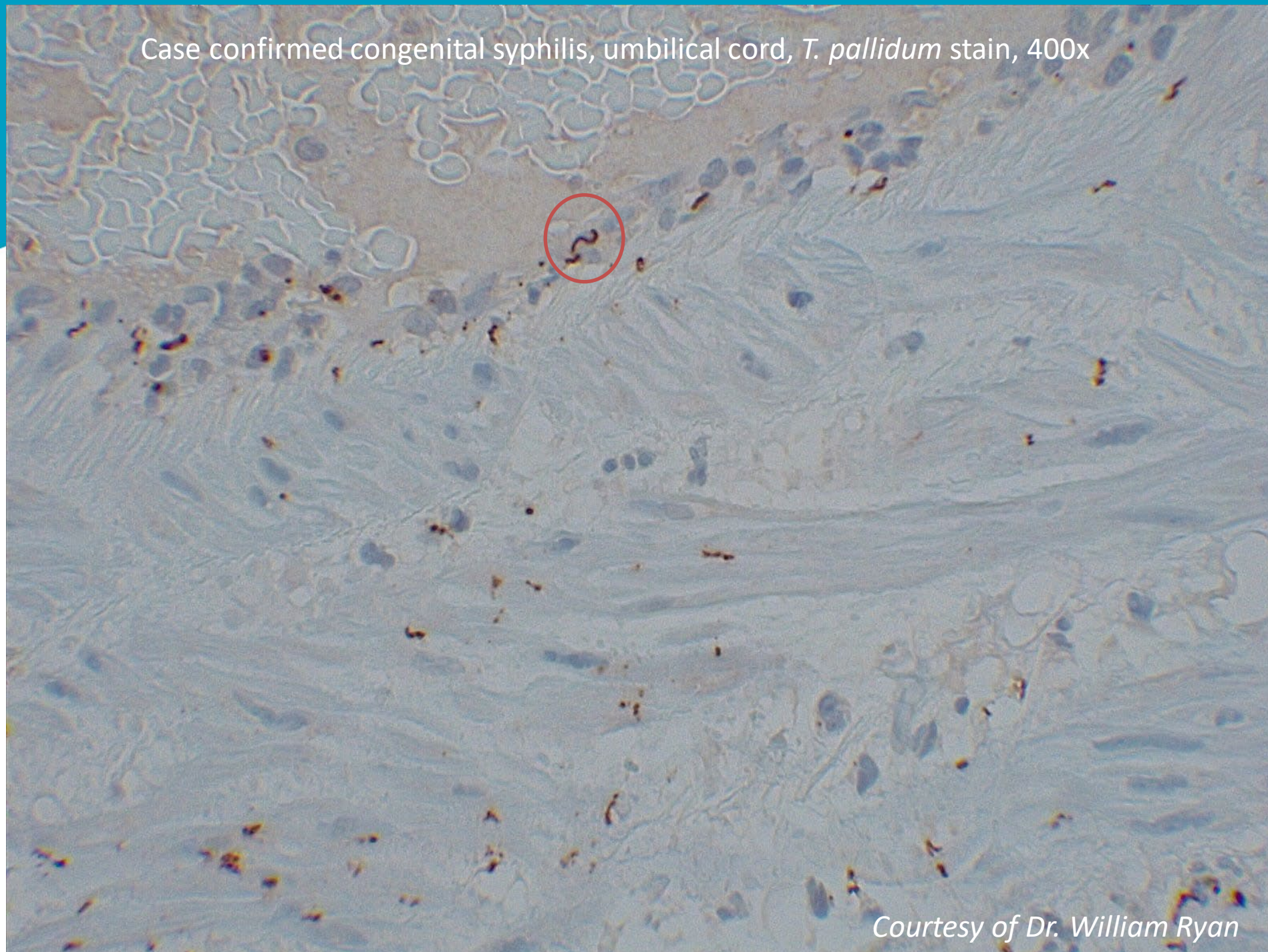
Diffuse, interstitial pneumonia (“pneumonia alba”)
DOL 1

Differential: Congenital infections

- LymP ToRCHESZ
  - Lymphocytic choriomeningitis, Lyme, Leishmaniasis
  - Parvovirus B19
  - *Toxoplasmosis gondii*
  - Rubella
  - CMV, Chickenpox (VZV), Coxsackie, Chagas
  - HIV, HSV
  - Enterovirus
  - Syphilis
  - Zika

Investigations

- Ex-33w female, PTL, abnormal exam
  - Hepatosplenomegaly, desquamating rash, anasarca, interstitial pneumonia
- On admit:
  - Maternal RPR 1:32, new dx
  - Infant RPR: 1:1024
  - Bili 8.29, direct bili 2.8, ALT 9, AST 63
  - WBC 15.5, Platelets 256, Hgb 13.7
- CSF: WBC 3, RBC 55, Mono/Macro 55%, Pro 65, VDRL 1:1
- Long bone x-ray: periostitis, severe
- Head US, MRI: normal
- Placental stains: positive *Treponema pallidum* stains


Case confirmed congenital syphilis, umbilical cord, *T. pallidum* stain, 400x
Courtesy of Dr. William Ryan

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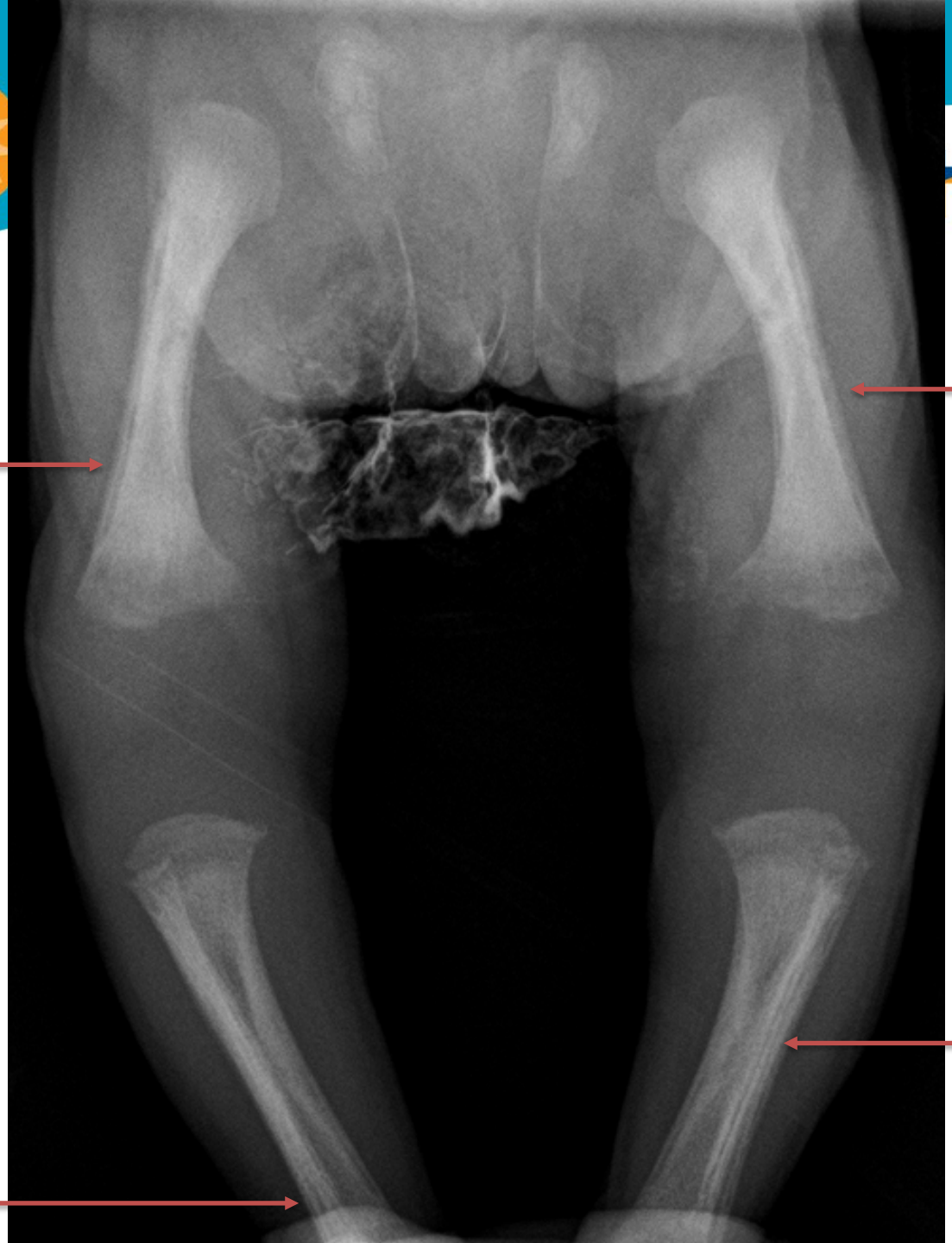

Diffuse periostitis of long bones DOL 18

"celery stick" appearance

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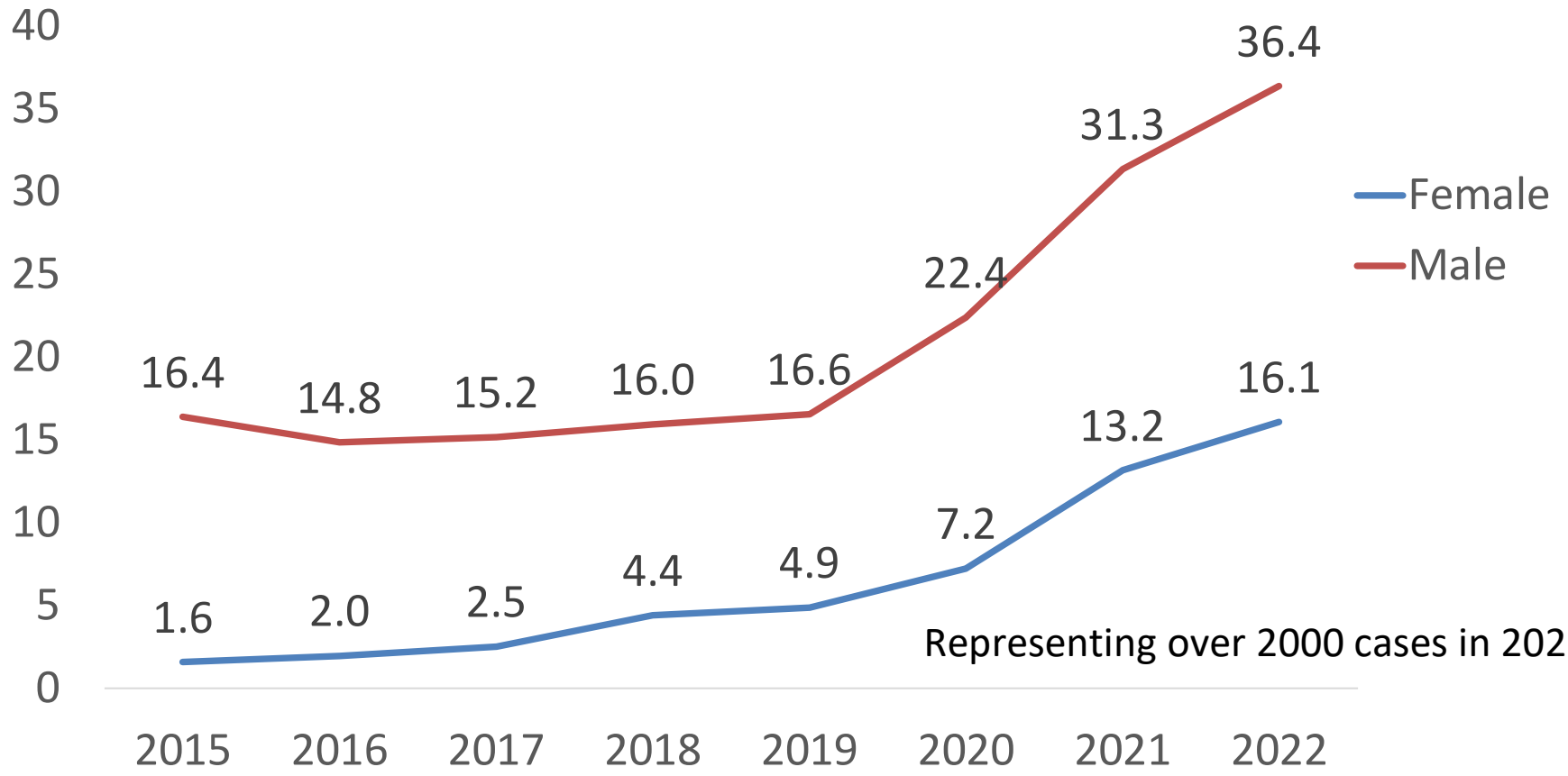
Confirmed congenital syphilis

- Pre-term labor (almost fetal demise)
- Pemphigus syphiliticus (rash)
- Pneumonia alba (classic syphilitic newborn pneumonia, often fatal)
- Severe, diffuse periostitis
- Hepatosplenomegaly, cholestasis with hepatitis
- Neurosyphilis
- Nephrotic syndrome
- ?Adrenal insufficiency
- Villitis, spirochetes on placenta
- Received 21 days of IV Aqueous penicillin G
- Retreated x 10d IV at 11mo for persistently positive RPR;
- RPR NR at 18m, 26m

Rate of primary and secondary syphilis by sex at birth, Oregon, 2015-2022



Representing over 2000 cases in 2021

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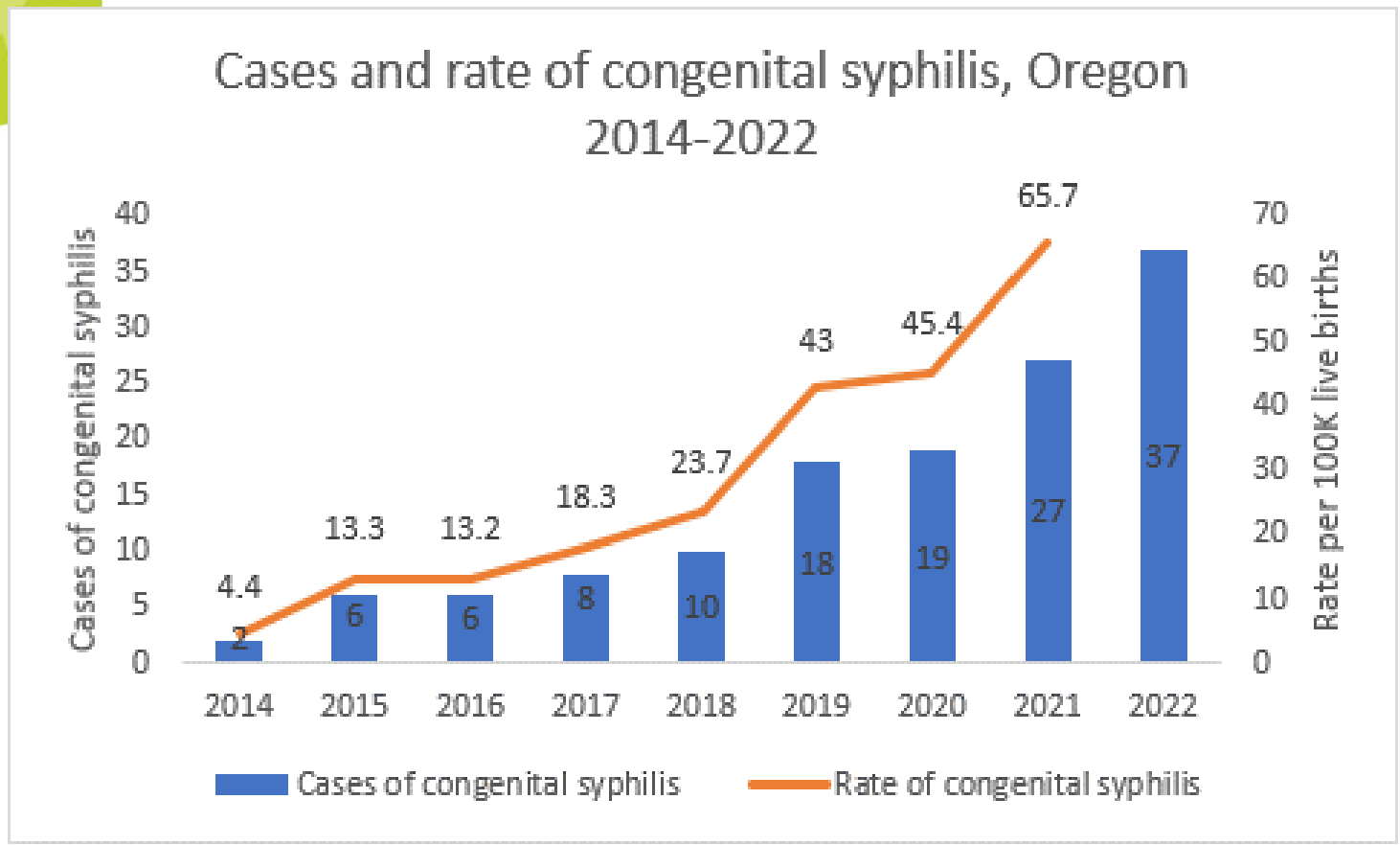
Syphilis in pregnancy

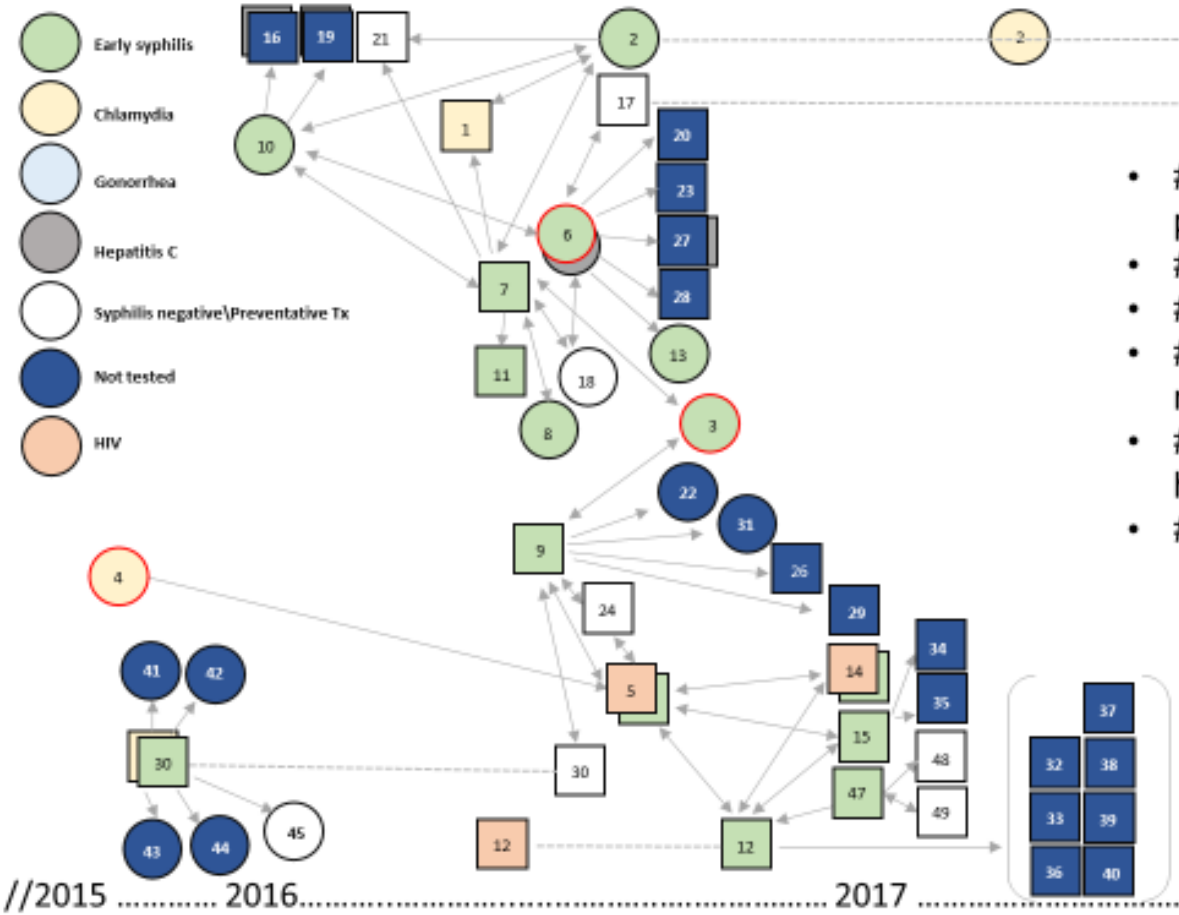
- 422 cases of syphilis in pregnancy from 2014 through 2022
  - 3 cases/10,000 pregnancies (15/45,557) in 2014
  - 21 cases/10,000 pregnancies (86/40931) in 2021*
- 133 (32%) of pregnant people with syphilis were associated with a case of congenital syphilis
  - 2/15 (13%) cases in 2014
  - 37/88 (42%) cases in 2022

*Oregon vital statistics data have not yet been updated for 2022



0-2 cases per year prior to 2014 → 37 per year in 2022

Syphilis contact network



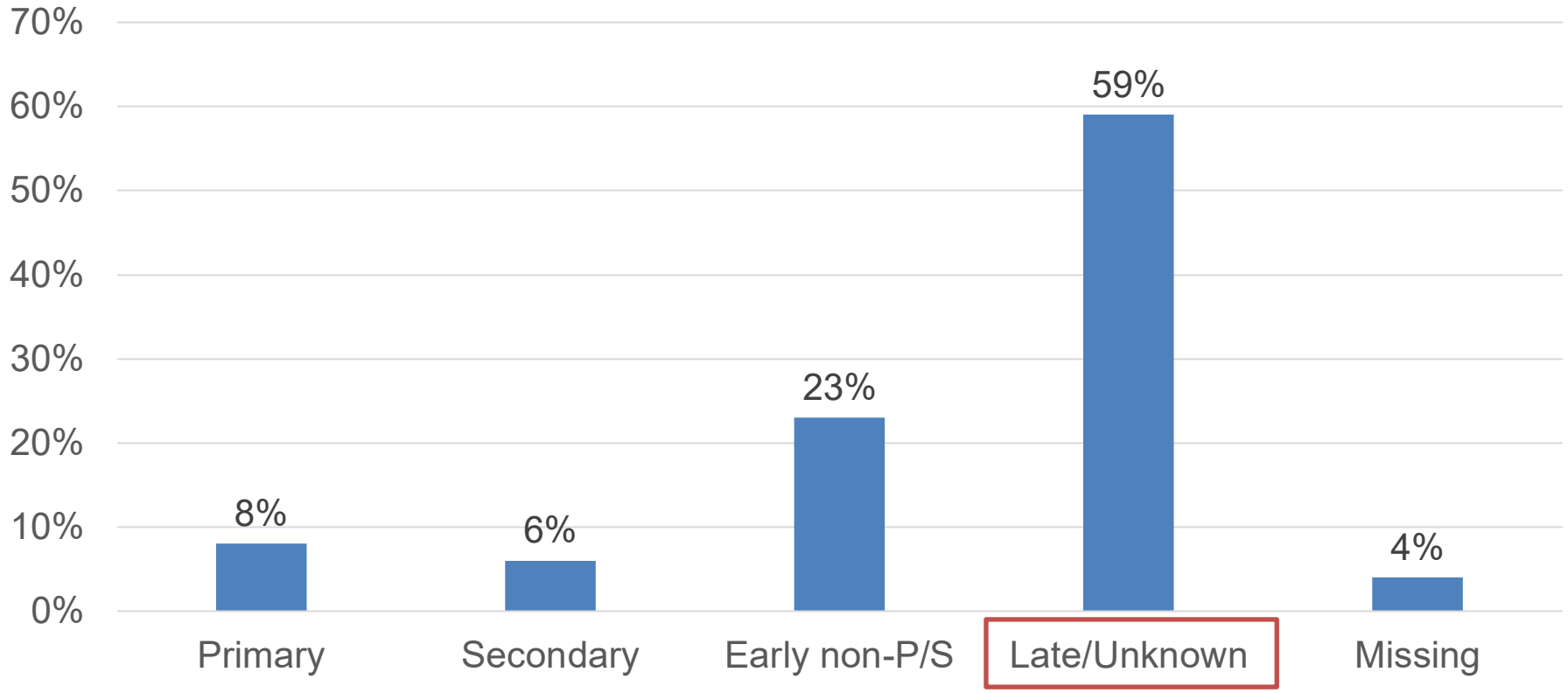
- #10 with ES, came to care for HIV/STI and pregnancy testing
- #6 ES in pregnancy, CS case
- #3 ES in pregnancy
- #4 CT in pregnancy, tested HIV- after naming #5 who was HIV+
- #9 and #3 bridged MSM/IDU and heterosexual/IDU networks
- #9 tested HIV- in early 2018

Clinical staging of syphilis

- Early:
  - Primary
  - Secondary
  - Early latent

  Highest risk of maternal to infant transmission 50-60%
- Syphilis of unknown duration
- Late latent
- Congenital

Syphilis stage at diagnosis, Oregon, 2014-2022



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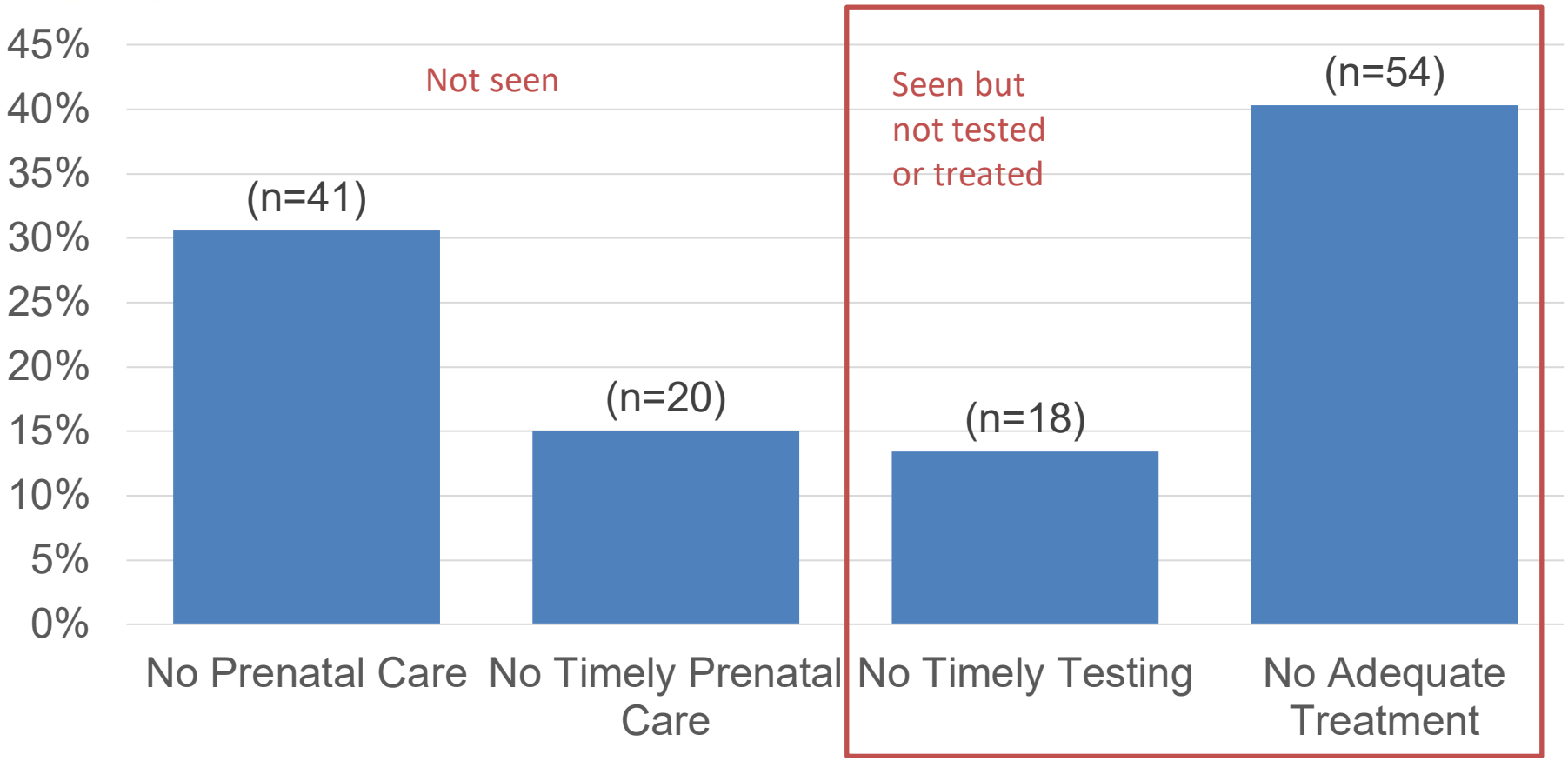
Missed CS Prevention Opportunities



OHA considers all visits are prenatal visits: ER/urgent care, carceral settings, substance use disorder treatment when syphilis/prenatal care status is unknown

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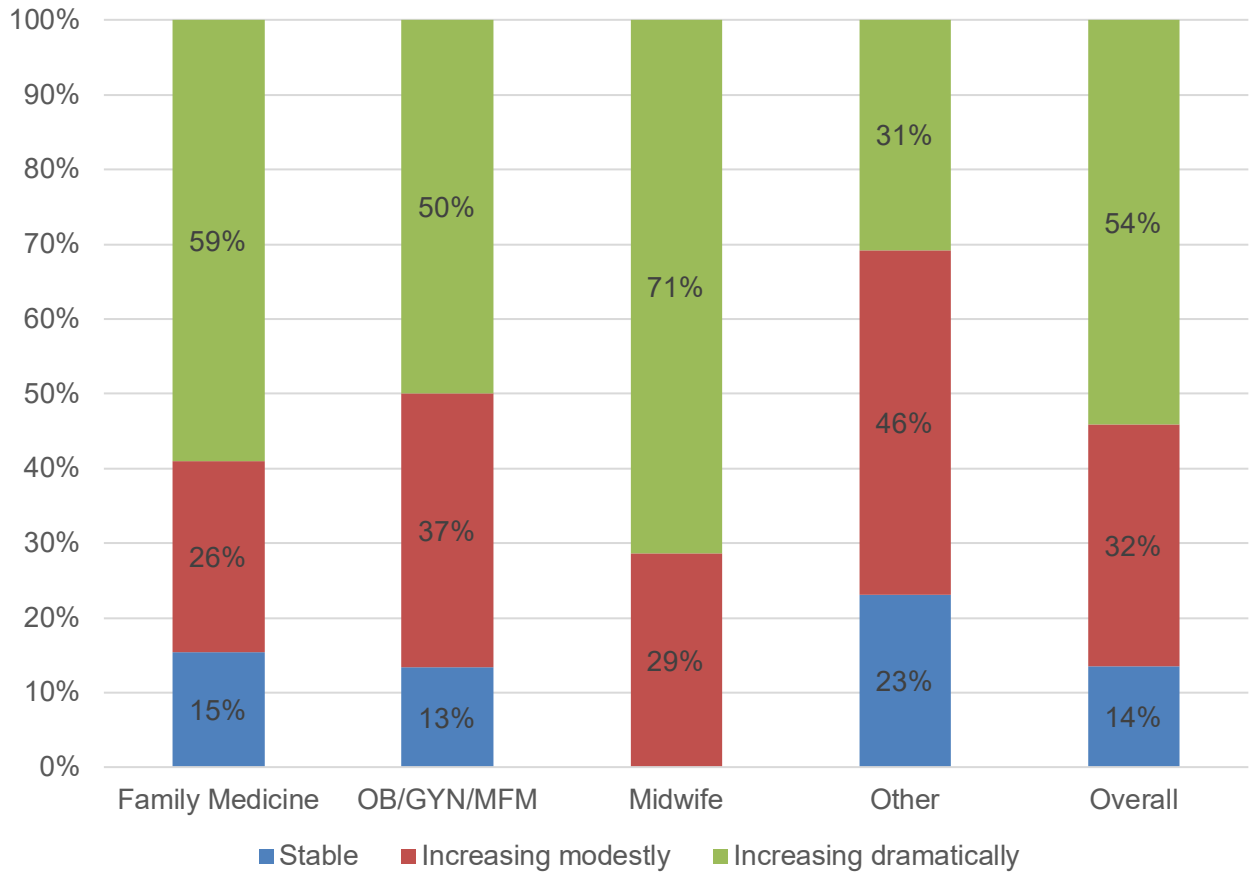
Recommendations for Syphilis Screening in Pregnancy in Oregon, 2023

- Screen at first prenatal visit
- Screen again in early third trimester (24-28 wks)
  - Allows enough time to arrange for treatment
  - Detects seroconversion and re-infection
  - Only 69% of providers are screening at this time
- Screen at delivery
- No discharge without syphilis result documentation

Perception of Current Syphilis Trends in Pregnancy



Laboratory

- Non-treponemal test: RPR, VDRL
  - False positives possible, ↑ other inflammatory diseases
  - Non-specific serum reactivity to cardiolipin-cholesterol-lecithin Ag
  - Should return to non-reactive after successful treatment
  - "Traditional algorithm" begins with these
- Treponemal antibody test: Trep EIA, CIA, TP-PA, TrepSure, FTA-ABS
  - Sensitive and specific
  - Remains positive long-term despite adequate treatment
  - "Reverse" algorithm begins with these
- MAY BE NON-REACTIVE early in infection so retesting indicated if suspicion high

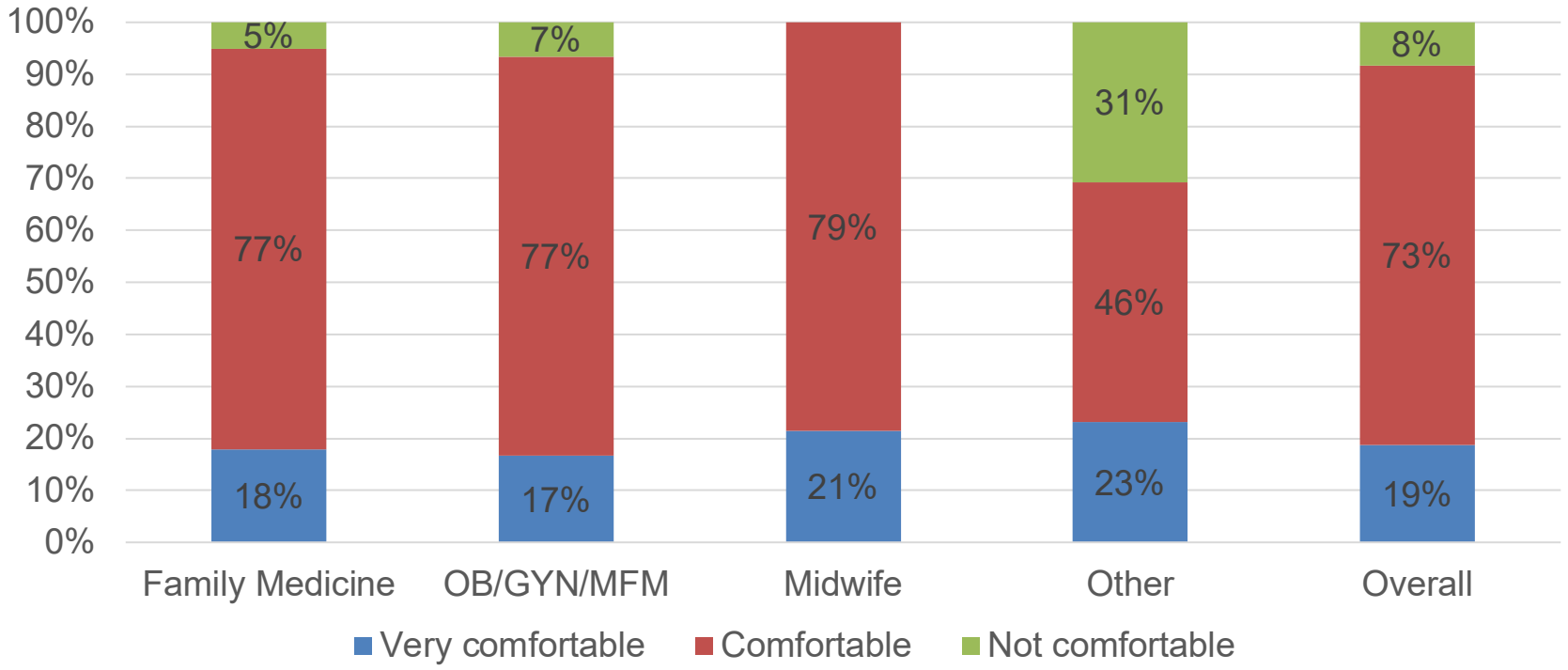
Laboratory details

- Tricky test
- Know which algorithm your lab uses
- Providence uses “reverse” algorithm
  - Starts with more sensitive treponemal test (EIA) in-house
  - If EIA positive, reflexes to RPR in-house
  - If RPR positive, reflexes to titer in-house
  - If RPR negative, reflexes to second treponemal test send-out

Fast TAT

- Understand your available test results and plan prior to discharge
- Phone a friend if unsure
  - Health department for contact tracing and long term follow up
  - ID or MFM

Comfort with interpreting syphilis serologies by provider type

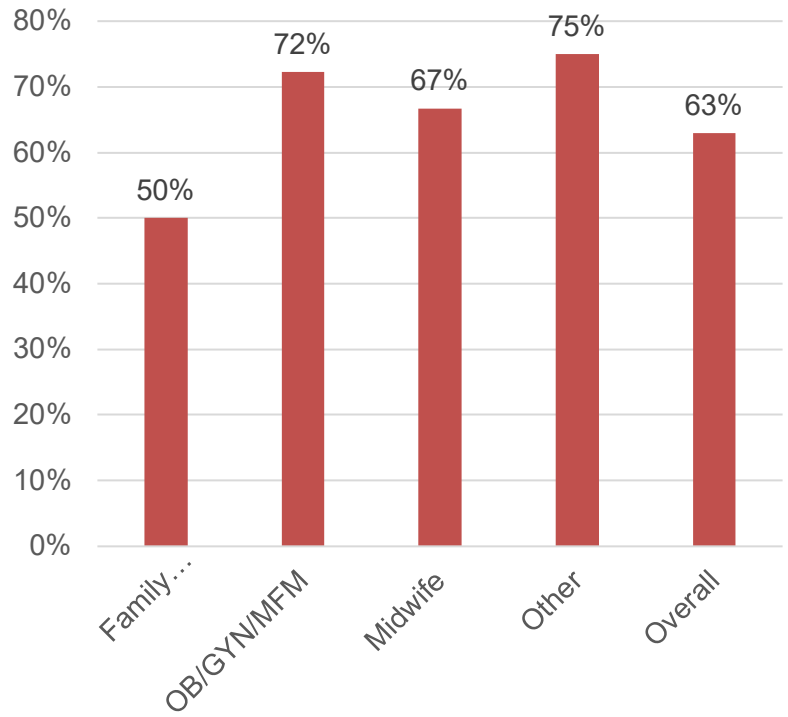


Treatment in Pregnancy

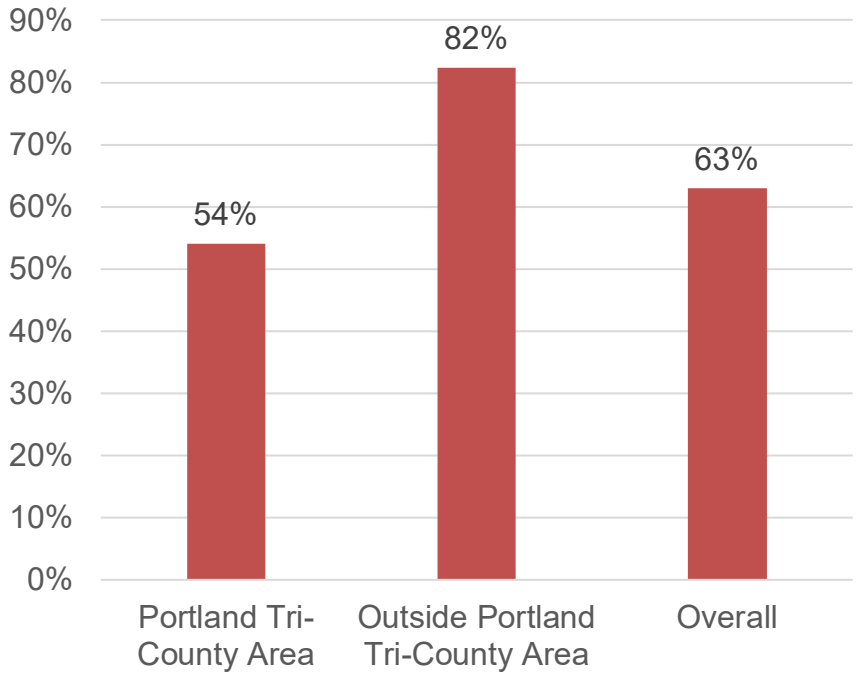
- Penicillin is the only effective therapy in pregnancy
  - Allergic patients require desensitization
- Benzathine penicillin 2.4 million units IM
  - Single dose for primary, secondary, and early latent
    - 2 doses preferred by OHA during pregnancy
  - 3 weekly doses for late latent or unknown duration
- It is hard to get IM penicillin in community practices, worsened by current shortage
  - Involve the health department

Health Department Involvement

By provider type



By practice geography



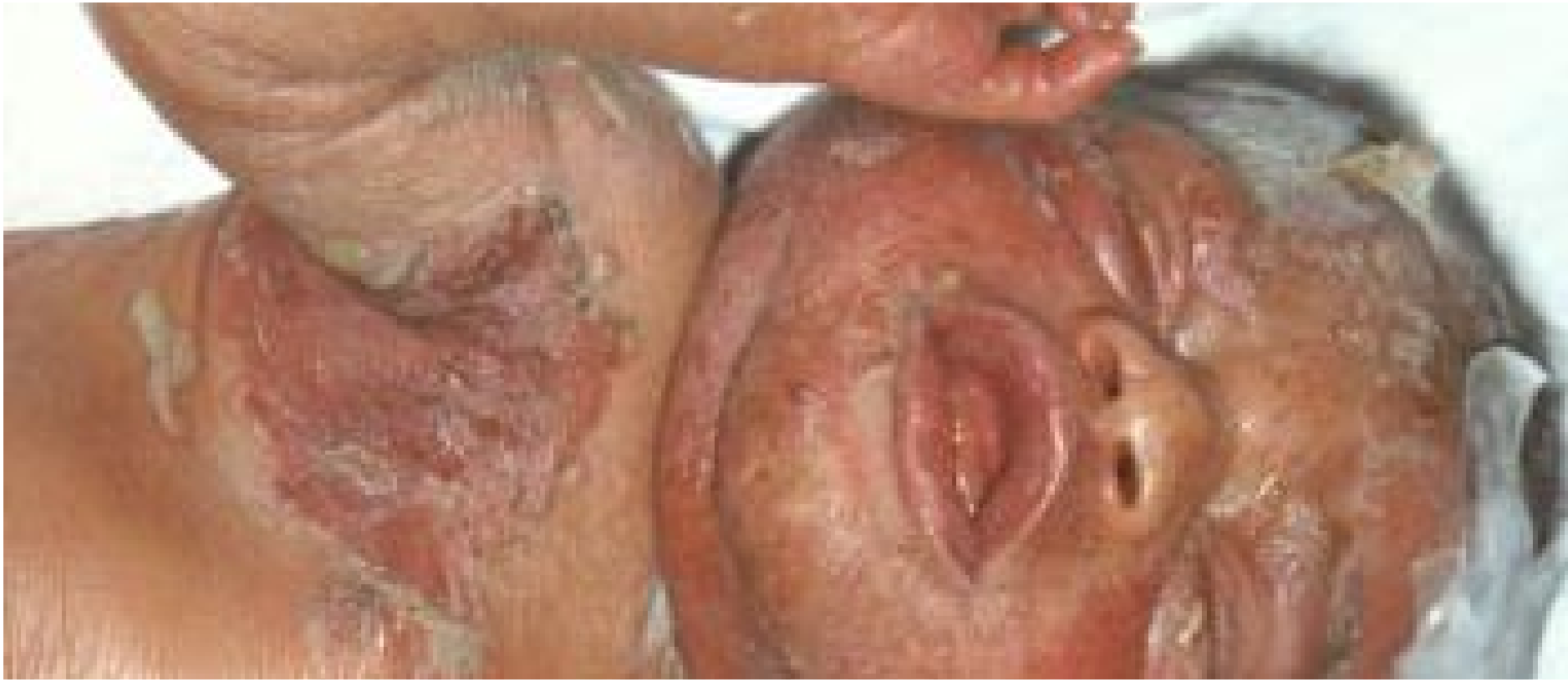
Transmission risk and Natural history of CS

- Maternal stage of syphilis assoc w/ CS (1988-1989 Sheffield et al)
  - Primary: 29%
  - Secondary: 59%
  - Early latent: 50%
  - Late, latent infection: 13%
- Infant outcomes of untreated 1°/2° maternal syphilis (1951 Ingraham et al)
  - Among mothers with untreated syphilis <4 yrs duration
    - 25% stillborn
    - 14% neonatal death
    - 41% live but infected
    - Only 20% live and uninfected infant
  - Among mothers with late latent syphilis (≥4yr): 2% live but infected, 77% uninfected

Clinical features of congenital syphilis

- None
- Preterm delivery, SGA, IUGR, poor weight gain
- Pneumonia, respiratory distress
- Non-immune hydrops, edema
- Mucocutaneous lesions or rashes, rhinitis
- Persistent jaundice
- Lymphadenopathy
- Hepatosplenomegaly
- Pseudoparalysis of Parrot (periostitis)
- Cranial nerve palsy, adrenal, hypopituitary

Rashes carry infectious treponemes!



Pemphigus syphiliticus

Courtesy of Dr. Dianne Glover

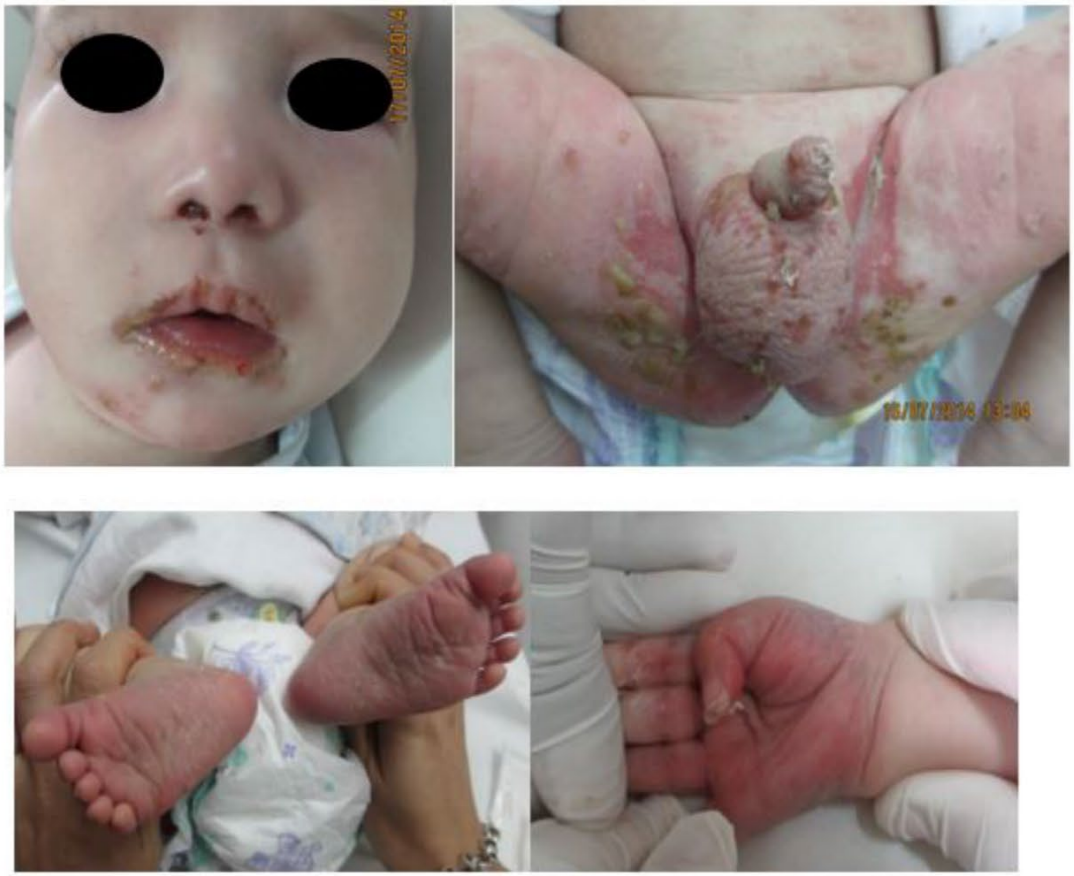
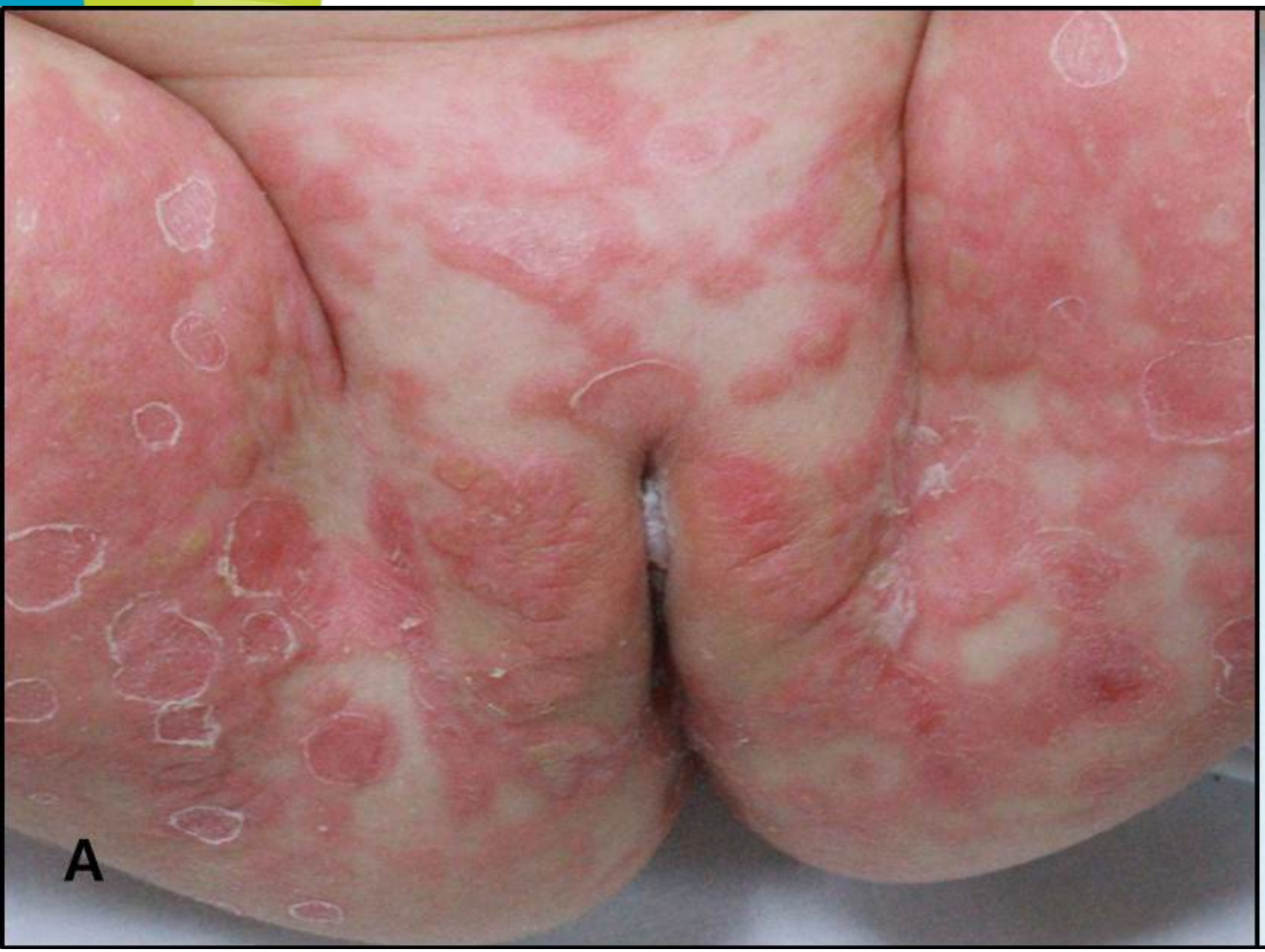
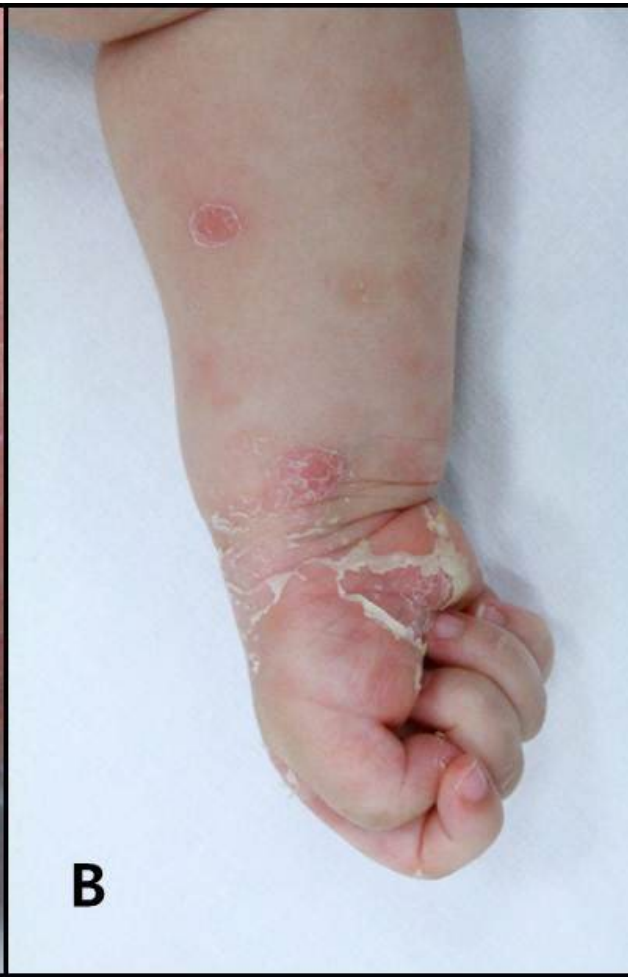


Figure 1. *Congenital syphilis. Patient 1: A) Periorificial secretions. B) Erythematous, scaly and macerated lesions in the diaper area. C) ana D) Skin flaps on palms and soles.*

Dermatol Res Skin Care 2018 Volume 2 Issue 1





Collarette de Biett

Thick skin peeling, skin flaps

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Laboratory & Radiographic findings of CS

Laboratory

- Anemia, hemolytic
- Thrombocytopenia
- Conjugated hyperbilirubinemia, hepatitis

} Consider other congenital infections

- Nephrotic syndrome, hypopituitarism, hypoadrenalism

Radiology

- Periostitis, osteochondritis
- Meningitis
- Pneumonia
- Necrotizing ileitis

Courtesy of Frank Bel

Data to collect to determine diagnosis

Mother

- Maternal treponemal test (EIA/CLIA) and non-treponemal test results (RPR with titer)
- Maternal stage, if known
- Maternal treatment history
- medicine, dose, dates, intervals
- Partner treatment
- Maternal HIV, other prenatal labs, placental pathology

Infant

- Infant RPR and titer
- Infant exam, hearing screen (+/- ophthalmologic)
- Based on story: CBC+diff, CMP, CSF (cell count, protein, diff, VDRL), limited long-bone films, etc

Diagnosis of congenital syphilis

- Diagnosis under consideration:
  - Symptomatic patient: IV penicillin and await testing
  - Asymptomatic patient: await testing, then treat prior to discharge
- Confirmed, highly probable
  - Exam c/w CS, infant RPR titer ≥4x maternal RPR, +spirochetes
- Possible
  - Inadequate treatment at any time
- Less Likely
  - Adequate treatment during pregnancy
- Unlikely
  - Adequate treatment before pregnancy

*Full algorithm RedBook

https://www.cdc.gov/std/treatment-guidelines/congenital-syphilis.htm

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Treatment of congenital syphilis

- Confirmed, highly probable
  - Exam c/w CS, infant RPR titer ≥4x maternal RPR, +spirochetes
  - IV aqueous penicillin G 50,000 IU/kg/dose at least 10 days
- Possible
  - Inadequate treatment
  - IV aqueous penicillin G 50,000 IU/kg/dose x 10 days
- Less Likely
  - Adequate treatment during pregnancy
  - IM Benzathine penicillin G 50,000 IU/kg x 1
- Unlikely
  - Adequate treatment before pregnancy
  - +/- IM Benzathine penicillin G 50,000 IU/kg x 1
  - Must follow titer to NR if no Rx.

*Full algorithm RedBook

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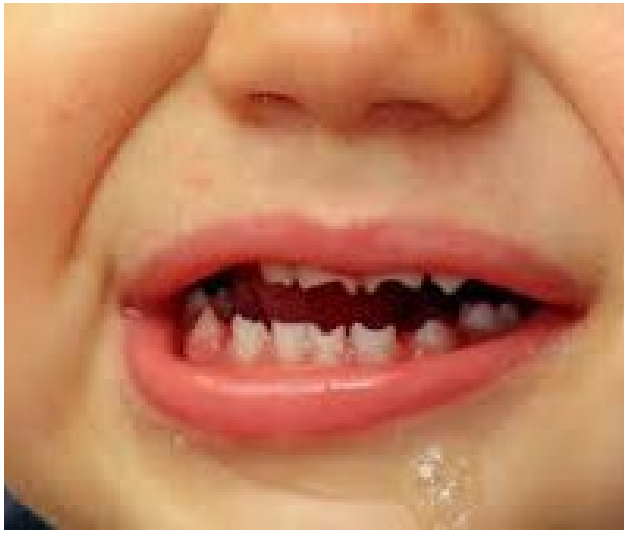
Late (untreated) congenital syphilis



- Sequelae of prolonged periosteal reaction
  - Olympian brow, saber shin, Clutton joints
  - Perforation of hard palate
  - Hutchinson teeth*, mulberry molar
  - Saddle nose
  - Deafness*, developmental delay
  - Interstitial keratitis*, corneal scarring, uveitis, glaucoma
- *Screen as part of AAP recommendations for international adoptees/refugees/immigrants/arrivals*
  - Cheap test, one-time treatment, benefits a lifetime

Courtesy of Dr. Dianne Glover

*Hutchinson Triad

Follow-up (even when treated)

- F/u RPR q2-3 months until non-reactive.
- Refer if not non-reactive by 6 months old
  - Neurosyphilis: consider repeat LP @ 6m; recommend f/u RPR through 12m
- Eye exam for chorioretinitis
- Hearing exams through school age
- Neurodevelopmental milestones
- Dental exams

Take Home Points

Mother

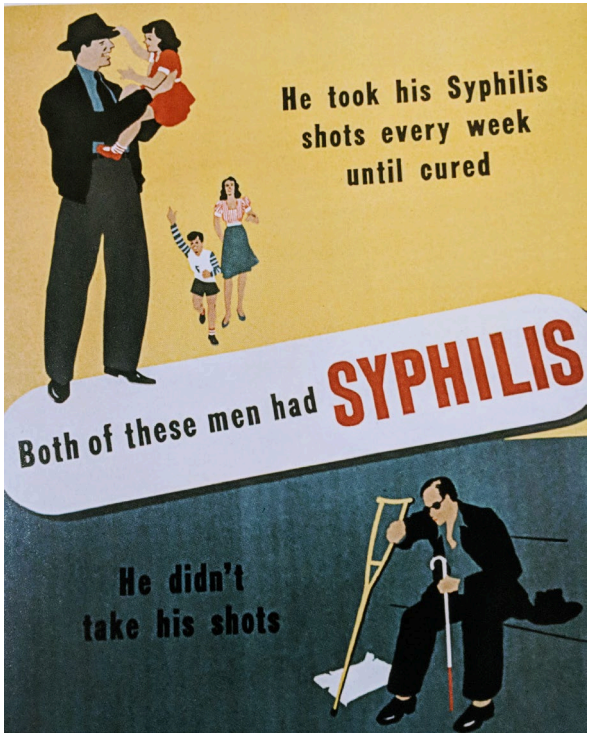
- Prefer penicillin for women of child-bearing age or uncertain follow-up
- Screen moms at least 1st visit, 3rd trimester delivery
  - Reverse algorithm more sensitive
- Highest transmission during secondary syphilis
- No discharge without syphilis result documentation (& HCV, HIV)
- Every visit for a pregnancy is a "pre-natal visit"

Infant

- Many newborns with CS are asymptomatic
- Blind spots: No prenatal care, home births, fetal demise, incomplete tests
- Unless infant ill, gather data and determine diagnostic category
- Update EMR problem list with follow-up actions
- Phone a Public Health or ID friend when in doubt

Questions?

- MFM: page on-call
- Peds ID clinic: 503-216-6050 or page on-call or e-consult
- Include any key information you want sent with the referral



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SYPHILIS IS INCREASING IN THE U.S.

BUT IT IS 100% PREVENTABLE

Early 2021 data show an **increase** in primary and secondary syphilis among adults

- **Women up 34%** — **10,620** cases*
- **Men up 9%** — **36,614** cases*

Syphilis in **newborns is up 6% in 2021; 2,268** cases already reported*

33 states report increases

If you are sexually active:

- Ask your provider about how to prevent syphilis
- Talk to your partner(s) about STIs and safer sex
- Get tested, especially if you are pregnant or planning to get pregnant

If you are a healthcare provider:

- Know the syphilis burden in your community and talk to patients about sexual health
- Test patients at first prenatal visit; repeat at 28 weeks if at risk of infection**
- Treat syphilis immediately

*COVID-19 affected 2021 reporting; these data points reflect what is known as of March 2022

**See STI Treatment Guidelines

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References

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