Syphilis in Pregnancy

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Objectives

- Appreciate the prevalence of syphilis in the United States
- Explain the natural course and stages of syphilis in pregnancy
- Understand the effect of syphilis on pregnancy outcomes
- Outline the recommendations for syphilis screening
- Define the principles of medical management of syphilis
- Discuss methods to reduce vertical transmission

Background

Background

- Syphilis is a systemic infection from the spirochete *Treponema pallidum*
  - Transmitted sexually, hematogenously, vertical transmission
- It remains a public health threat and crisis
  - Congenital syphilis rates in the United States increased by 261% from 2013 to 2018
- Often referred to as “the great imitator”
- Several health disparities related to syphilis
  - Higher incidences in Black, American Indian, and Pacific Islander populations
  - Higher incidences in the Southern United States
- A correlation has been noted between primary and secondary syphilis and the rise of opioid and methamphetamine use in reproductive-aged women

Eppes CS, Stafford I, Rac M. Syphilis in pregnancy: an ongoing public health threat. AJOG 2022:822–38.

Kimball A, Torrone E, Miele K, et al. Missed opportunities for prevention of congenital syphilis - United States, 2018. MMWR Morb Mortal Wkly Rep 2020;69:661–5.

Kidd SE, Grey JA, Torrone EA, Weinstock HS. Increased methamphetamine, injection drug, and heroin use among women and heterosexual men with primary and secondary syphilis - United States, 2013-2017. MMWR Morb Mortal Wkly Rep 2019;68:144–8.

Missed Opportunities Leading to Congenital Syphilis

- Lack of timely prenatal care with no syphilis testing
- Lack of syphilis testing despite timely prenatal care
- Lack of adequate maternal treatment despite a timely diagnosis
- Late identification of seroconversion during pregnancy

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Clinical Manifestations

Clinical Manifestations in Pregnancy

- Similar course and presentation as those observed in non-pregnant patients
- **Primary Syphilis**
  - Painless ulcer within 3 weeks of exposure
- **Secondary Syphilis**
  - Systemic infection: skin rash, lymphadenopathy, alopecia, leukoplakia
  - 2-6 weeks after resolution of primary lesion
- **Latent Syphilis**
  - Lack of clinical symptoms despite (+) serologic testing
  - Carries risk of in utero transmission to the fetus
- **Tertiary Syphilis**
  - Cardiovascular infection, gummata, and neurosyphilis

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Clinical Manifestations in Pregnancy

- Delayed diagnosis of syphilis can occur due to:
  - Temporary nature of painless chancre
  - Vague symptoms that occur with secondary syphilis
  - Asymptomatic nature of latent syphilis
    - 50% of infected mothers who present with latent syphilis are discovered through routine testing rather than testing based on symptoms

Rac MW, Revell PA, Eppes CS. Syphilis during pregnancy: a preventable threat to maternal-fetal health. Am J Obstet Gynecol 2017;216:352–63.

TABLE 1

Clinical course and symptom presentation of syphilis

Stage of syphilis	Clinical findings	Location/characterization
Primary syphilis	Chancre lymphadenopathy	
Secondary syphilis	Rash (Figure 3, A)	Distributed widely, commonly involving palms and soles.Macular, papular, papulosquamous, pustular, and nonpruritic
	Patchy alopecia	Scalp hair or eyebrows
	Condyloma lata (Figure 3, B)	Warm/moist intertriginous areas such as vulva, inner thighs, axillae, perineum, skin under breasts
	Mucous patches	Mouth, throat, or genital areas
	Generalized symptoms	Fever, sore throat, weight loss, malaise, anorexia, meningismus
	Parenchymal effects (less common)	Hepatitis, gastrointestinal symptoms, nephrotic syndrome, arthritis, periostitis, optic neuritis
Tertiary syphilis	Granulomatous lesions	Skin, mucous membranes, skeleton
	Cardiovascular	Typically aortic lesions
Neurosyphilis	CNS	Cognitive dysfunction, motor or sensory deficits, auditory symptoms, cranial nerve palsies, meningitis, stroke, tabes dorsalis (syphilitic myelopathy)
	Opthalmologic	Uveitis, retinitis, optic neuritis, Argyll Robertson pupils

Reprinted from Rac et al[13].

CNS, central nervous system.

Eppes. Syphilis in pregnancy. Am J Obstet Gynecol 2022.

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Prenatal Ultrasound Findings

- *Treponema pallidum c*rosses the placenta during pregnancy
- Transmission of syphilis in utero starts with early placental infection→amniotic fluid infection→hematologic dysfunction→ascites→IgM production
- Vertical transmission occurs at all stages of syphilis and during all trimesters
  - Highest risk is noted in early syphilis
- Most common ultrasound findings:
  - Hepatomegaly (80%)
  - Fetal anemia with elevated MCA dopplers (33%)
  - Placentomegaly (27%)
  - Polyhydramnios (12%)
  - Ascites and fetal hydrops (10%)
  - Less commonly: splenomegaly and cardiomegaly
- After treatment, findings of late feta syphilis (Elevated MCA dopplers and hydrops) resolve first, and findings thought to occur early (placentomegaly and hepatomegaly) persist the longest.
- Important to remember that not all manifestations of fetal syphilis can be detected on ultrasound.

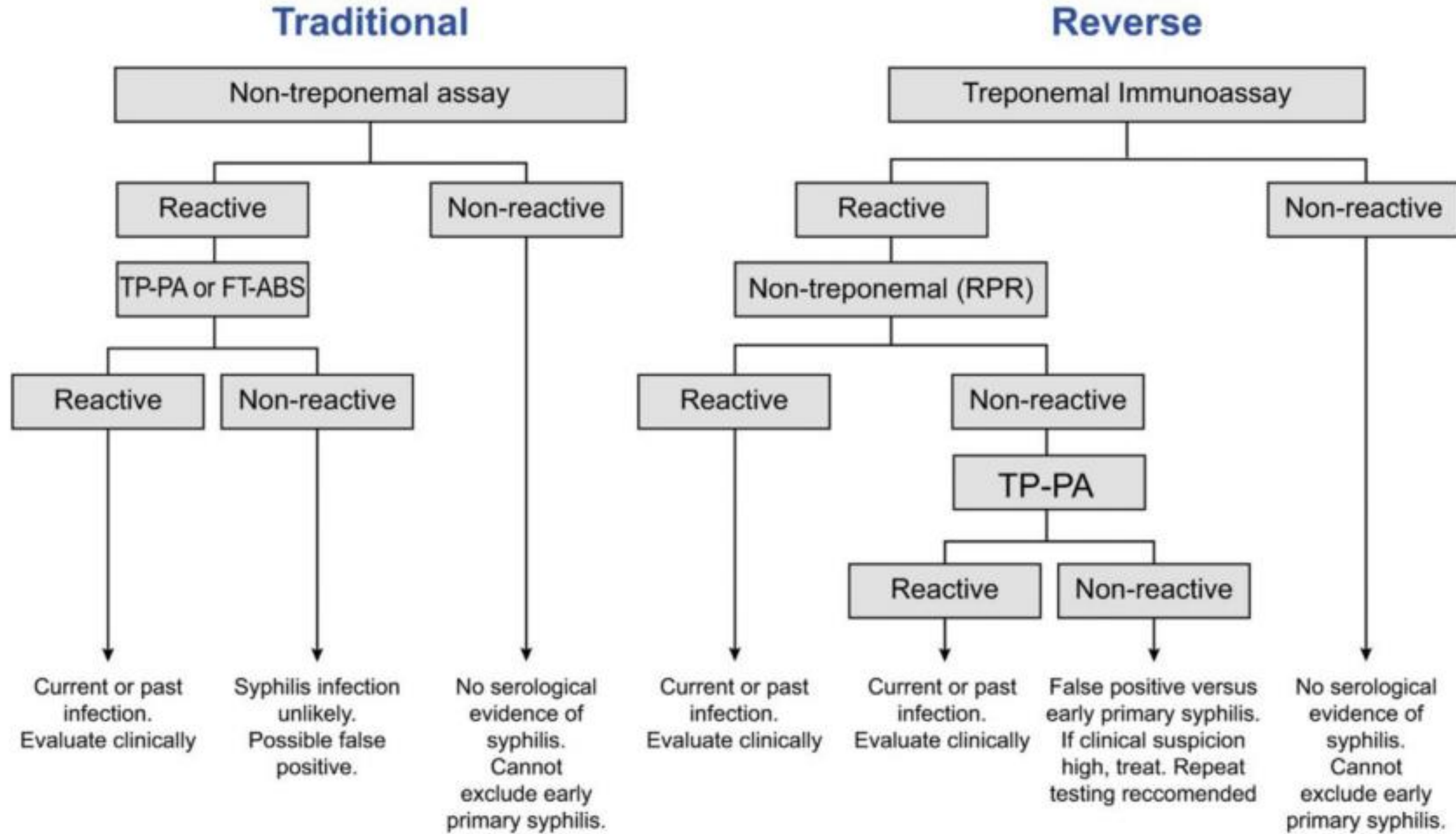
Weeks JW, Myers SR, Lasher L,
Goldsmith J, Watkins C, Gall SA. Persistence of

Diagnostic Testing

Diagnostic Testing

- In 2018, the USPSTF recommended testing for syphilis at the initiation of prenatal care
- CDC, AAP, ACOG affirmed this recommended and also added a repeated third trimester and at delivery screen for individuals in high prevalence areas.
- Diagnostic recommendations are complex and are misinterpreted.
- Major challenge that exists is that there is no test that distinguishes between newly acquired syphilis from a past infection

Kimball A, Torrone E, Miele K, et al. Missed opportunities for prevention of congenital syphilis - United States, 2018. MMWR Morb Mortal Wkly Rep 2020;69:661–5.



Eppes CS, Stafford I, Rac M. Syphilis in pregnancy: an ongoing public health threat.

Treatment

Treatment

- Treatment of Syphilis improves pregnancy outcomes.
- Untreated pregnant patients are more likely to experience:
  - Stillbirth (21%)
  - Preterm delivery (6%)
  - Congenital infection (50-80%)
  - Neonatal Death (9%)
- Treatment of Syphilis should occur as early in pregnancy as possible.
- Benzathine Penicillin G is the only recommended treatment for syphilis during pregnancy
  - It is 98.7% effective in treating maternal infection and preventing congenital syphilis.
  - If a pregnant patient is allergic to PCN, PCN desensitization with an allergy specialist is recommended.

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Treatment

- Currently, the CDC recommends that multiple doses of PCN G be administered within 9 days, and if this is not achieved, the entire treatment regimen should be restarted.
- After complete treatment, non-treponemal titers should be followed to ensure a 4-fold decline (e.g. 1:64→1:16).
    - The CDC suggests the following time intervals per stage of syphilis to observe a 4-fold decrease:
        - Early Syphilis: 6-12 months
        - Late Syphilis or unknown duration: up to 24 months
        - HIV (+): up to 24 months regardless of syphilis stage
- If a 4-fold decline is not observed after these time frames, then consider this to be treatment failure or reinfection.
- Some suggest checking titers every 4 weeks in order to appropriate identify with inappropriate titer decline.

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Jarisch-Herxheimer (JH) Reaction

- Acute systemic reaction that can occur during treatment for syphilis
- Occurs due to rapid killing of the spirochetes leading to rapid release of endotoxins, cytokines, and prostaglandins (acute inflammatory response)
- More likely to occur in early syphilis
- Clinical manifestations occur 2-8 hours after initiation of treatment
- Supportive treatment
- Limited evidence in pregnant population

Loveday C, Bingham JS. Changes in circulating immune complexes during the Jarisch Herxheimer reaction in secondary syphilis. Eur J Clin Microbiol Infect Dis 1993;12:185–91.

Treatment

- Don't forget treatment of the partner!
- Partner notification is often done by the infected pregnant patient
  - Limited knowledge about syphilis
  - Fear of Intimate Partner Violence
  - Lack of communication
  - Stigma associated with certain STIs
  - PCN G as an intramuscular injection requiring an in-person clinic visit

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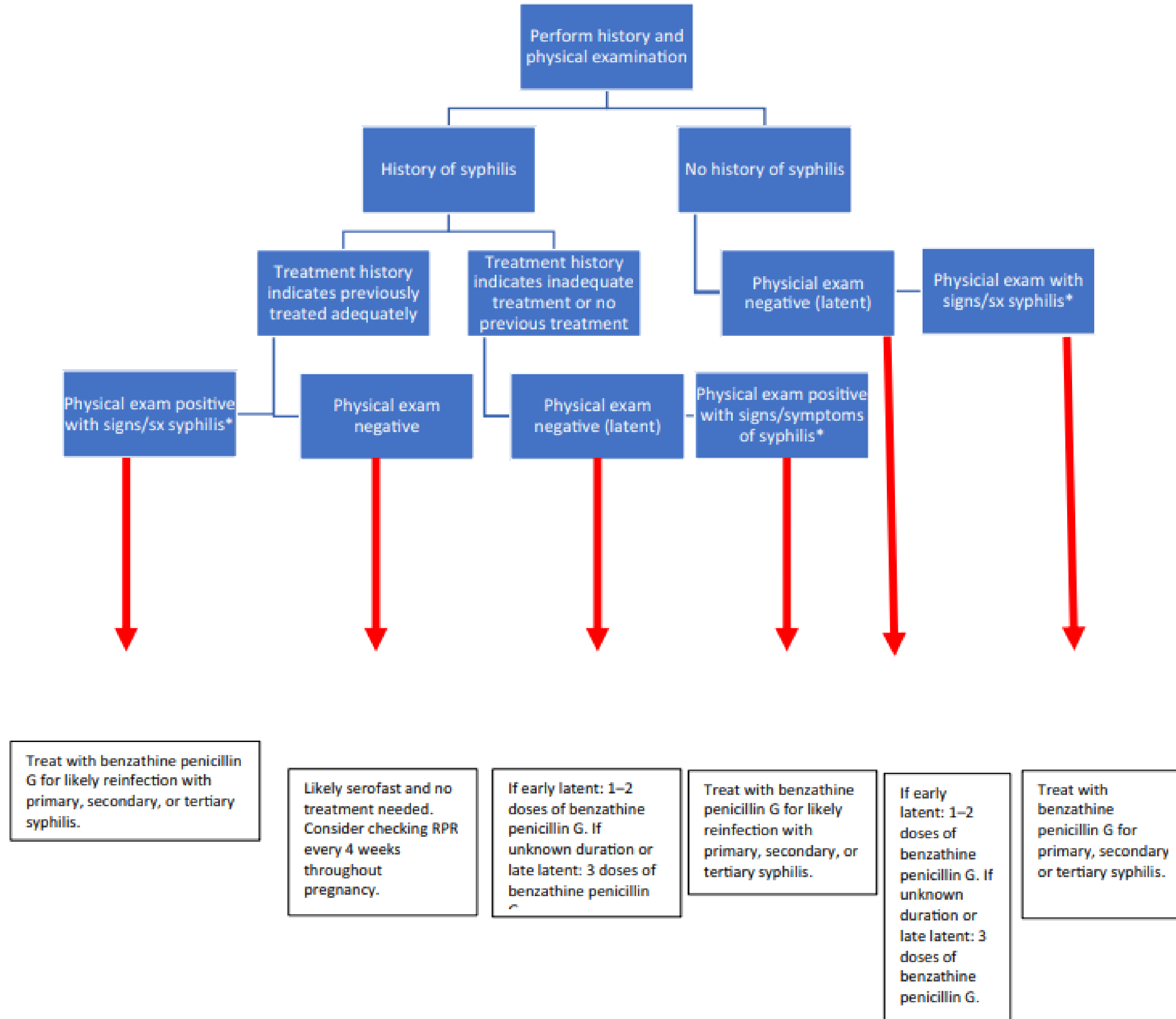
FIGURE 4
Management algorithm for patients with positive treponemal and nontreponemal antibodies



The *asterisk* represents that if at any point in the evaluation, clinical evidence of neurologic infection is observed, a cerebrospinal fluid examination to rule out neurosyphilis should be considered.

RPR, rapid plasma reagin.

Eppes. Syphilis in pregnancy. Am J Obstet Gynecol 2022.

Conclusions

Areas for Opportunity

- Alignment of syphilis screening and management across all States
- Improving clinician knowledge and increasing access to syphilis experts
- Reducing stigma through advocacy
- Increasing access to diagnostic testing
- Addressing health care disparities
- Acknowledging and improving access to timely prenatal care

Eppes CS, Stafford I, Rac M.
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