HOSPITAL

DIAGNOSIS AND MANAGEMENT OF SYPHILIS DURING PREGNANCY

ANTIMICROBIAL STEWARDSHIP PROGRAM

Background

- Since 2013, rates of syphilis have increased substantially. Click on links to see a CDC infographic and data table.
- Congenital syphilis rates also continue to climb. Click here for a recent summary of these data and a 2019 JAMA commentary.
- Screening women during pregnancy is recommended to identify untreated syphilis to prevent complications from syphilis including congenital syphilis among their infants.
- Consequences are severe for pregnant women with syphilis[1]
    - 69% of untreated infected pregnant women will have an adverse pregnancy outcome (serious birth defects, low birth weight, and prematurity)
    - 25% of in utero infections result in late-term miscarriage or stillbirth
    - 11% will have neonatal death
    - Surviving infants may have lifelong paralysis, hearing loss, blindness, skeletal deformities, and brain damage

Clinical Findings with Syphilis

TABLE

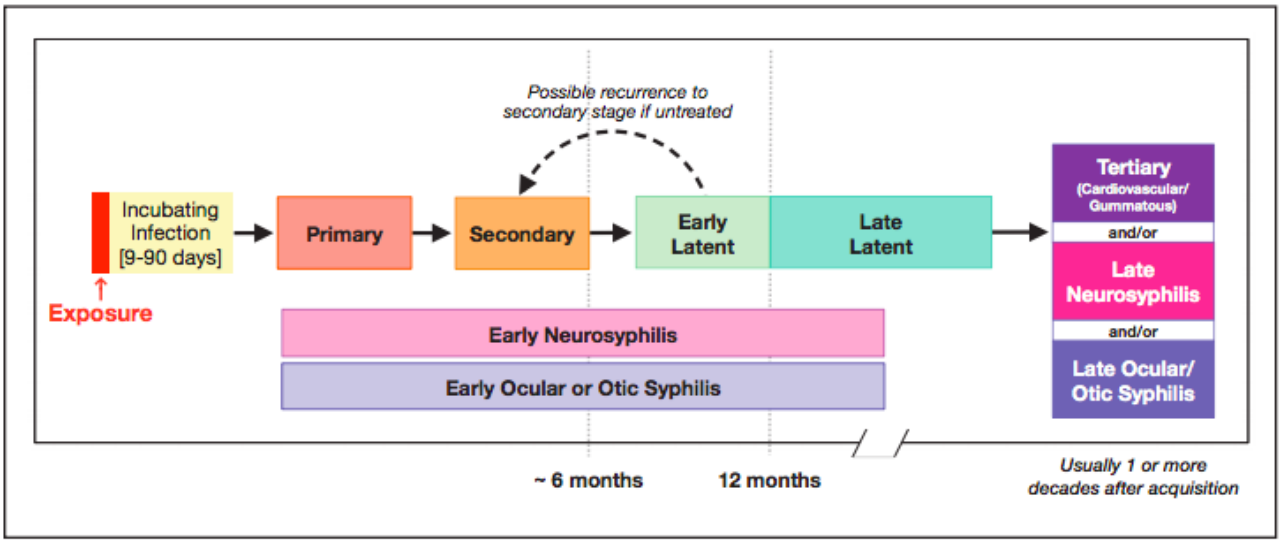
The 4 stages of syphilis[2]

Stage	Characteristics
Primary syphilis (stage of initial inoculation with *Treponema pallidum*) • Primary lesion appears 3 weeks to 3 months following exposure	• Chancre (typically painless, although it may be painful) usually on or around the genitals, anus, or mouth
Secondary syphilis • Begins 6 weeks to 6 months following exposure	• Diffuse rash that often involves the palms and soles • May entail a broad range of manifestations, including swollen lymph nodes and fever
Early latent stage of syphilis • Occurs within one year of exposure	• Few or no symptoms • Relapse of secondary syphilis can occur
Late latent stage of syphilis • Occurs 12 or more months following exposure	
Tertiary syphilis (final stage) • Occurs 3 or more years following exposure	• Gummas (large sores) • Neurologic or cardiac symptoms

Source

Need pictures or a thorough clinical resource? See the NYC DHMH 2019 Syphilis Guide for ulcers and rashes, treatment guidelines, testing interpretation and more here.

Figure 2. The Natural History of Untreated Syphilis



Screening for pregnant women

- **All** pregnant women should be screened for syphilis at:
  - First prenatal visit (i.e., as early in pregnancy as possible) AND
  - Third trimester (between 28-32 weeks of gestation) AND
  - Delivery
- *Any woman with an intrauterine fetal death > 20 weeks should be tested for syphilis*
- *Treponema pallidum* antibody (TPAB) testing can be ordered by prenatal providers at routine prenatal visits OR at an OB Triage encounter or emergency/urgent care encounter
- NOTE: Do not delay glucose testing for TPAB testing

NOTE: Women at higher risk for syphilis who may warrant more frequent screening include, but are not limited to the following:

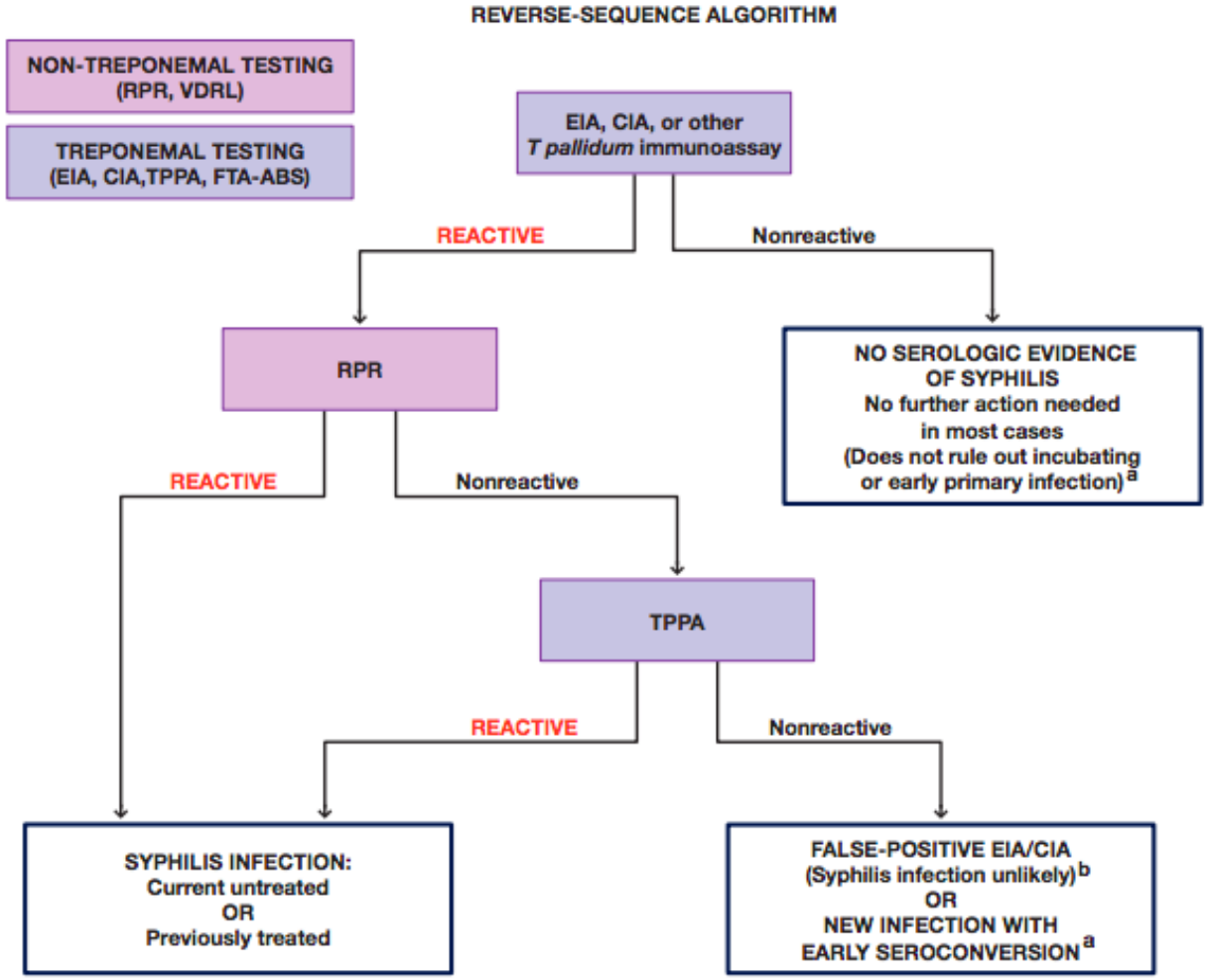
- Is a person who injects drugs or whose partner injects drugs
- Has an HIV-infected partner
- Has had new or multiple sex partners during pregnancy
- Has symptoms suggesting acute syphilis infection (see table above)
- Has recently been incarcerated
- Has been diagnosed with another sexually transmitted infection (STI) in past year

Primary provider/nurse is responsible to report new syphilis cases (both mothers and infants, if pertinent) including treatment to New Mexico Dept of Health via case report form:

- The case report form can be found here. Give as much information as you have.
- For questions about the form, call (505) 476-3636 or (505) 476-3611

Testing algorithm - Diagnosis

- **Reverse sequence algorithm for diagnosis of syphilis is now most common** (see figure below) and includes TriCore. This algorithm starts with treponeme-specific testing followed by nontreponemal tests (e.g., RPR).
- *Treponema pallidum* antibody; Cerner name: Syphilis-Screen; TriCore test name: TPAB
    - If first test (Treponema pallidum antibody [TPAB]) is positive, this will reflex automatically to RPR.
    - If TPAB is positive but RPR is negative, this will automatically reflex to the Treponema pallidum agglutination assay [TPPA].
    - Draw serology on or near the day of treatment to have an accurate baseline RPR value.
    - TPABs are performed daily at Tricore and automatically reflexed to RPR. These results should be available in 24 – 48 hours.
    - If needed, the TPPA is a lab that is sent out AND takes a minimum of 3 – 4 days for turnaround time.



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Interpretation of Results

Treponemal (TpAb)	Nontreponemal (RPR)	Meaning
Negative	Negative	No syphilis **Exception**: very early infection
Positive	Negative	Previously treated syphilis OR Untreated syphilis OR False positive (history and exam helpful to determine which applies)
Negative	Positive	Likely "biologic false positive," consider retest or consultation
Positive	Positive	Must presume syphilis (may be treated or untreated)

Please see in-depth table from NYC Syphilis guide here (page 16-17).

Treatment Recommendations for Adult Women (based on syphilis stage)

- Advise patients receiving multiple doses that there must not be a gap of more than 9 days between doses. **If they miss a dose they will have to start over.**

Syphilis Stage	**Treatment**
Primary, Secondary, **or** Early Latent (< 1 year)	Benzathine penicillin G 2.4 million units IM in a single dose* ***Note:** There is some evidence that pregnant women should receive 1 additional dose 1 week after the initial dose.
Latent Syphilis of Unknown Duration, or Tertiary Syphilis with Normal CSF Examination	Benzathine penicillin G as 3 doses of 2.4 million units IM each at 1-week intervals **Note:** Missed doses are not acceptable in pregnant women; women who miss any doses must restart until all 3 doses are given at correct interval.
Neurosyphilis or Ocular Syphilis	Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion, for 10–14 days
Additional Considerations for Treatment for Syphilis in Pregnant Women	Additional doses of penicillin may be indicated if evidence of fetal syphilis on ultrasound. Consult ID and MFM to determine if additional doses are required

Risk of Jarisch-Herxheimer reaction:

- Treatment of syphilis can result in the Jarish-Herxheimer reaction (fever, heachache, mayalgia, and rash). Reaction typically begins within 2 hours after treatment and resolves in 24-48 hours. Treatment is supportive.

- Treatment should NOT be delayed despite concern for this reaction. This needs to be distinguished from an allergic reaction.
- In pregnancy, JH reaction can cause fetal distress and preterm labor. Greatest risk is within 48 hours of treatment. Patients >24 wks gestational age should be counseled that JH reaction can precipitate preterm labor, preterm contractions and non-reassuring fetal heart tracings and therefore should be counseled to present to OB triage on signs and symptoms of preterm labor following treatment.

Does my patient report a penicillin allergy?

- If a patient reports a penicillin allergy, then ask the questions in toolkit A to determine if a penicillin allergy is likely or unlikely.
- If there is a more severe penicillin allergy (e.g., anaphylaxis), contact (Antimicrobial stewardship (975-2041, M-F 7:30 – 4pm) **or** Adult Infectious Diseases) **and** MFM on call via PALS.
- Consider early involvement of MICU attending if fetal monitoring is needed. Need for fetal monitoring will depend on gestational age as fetal monitoring may be needed and only certain beds in all adult ICUs have this capacity.
    - For MICU admissions, contact L&D RN Supervisor to ensure that L&D staff will be able to coordinate remote fetal monitoring (more common after 24 weeks gestational age) (L&D phone: 272-2603)

Did my patient have treatment for syphilis already (recent or distant past)?

- NM DOH may have a record for past testing and treatment, if completed and reported in New Mexico. If patient was treated in another state, DOH can help access this information.
- Contacts:
    - Louis Smith, telephone (505) 476-3636 (NM DOH, Syphilis Surveillance)
    - Cari Riley, STD Surveillance Coordinator (505) 476-3611
    - Janine Waters, STD Program Manager (505) 476-1778
- If the patient had prenatal care elsewhere, contact that clinic to obtain records of testing and treatment.

Assessing fetal health:

- If syphilis is diagnosed in the second half of pregnancy, ultrasound is recommended. Further evaluation or treatment may be needed if there are signs of fetal infection.

Response to treatment and other considerations:

- Serology should be repeated to ensure adequate response to treatment and no reinfection. For pregnant women, this should be done monthly and at delivery.
- Test to monitoring response after treatment:
    - Cerner name: Syphilis Monitoring (RPR titer)
- Expected response to therapy is a 4-fold decrease in titers. This may take several months. Patients with an initially low titer may not have a 4-fold decrease.
- Women diagnosed with syphilis should be rescreened for HIV at that time and again in 2 months.

Referrals to MFM:

- All women diagnosed with syphilis in the second or third trimester should have a detailed anatomy scan to look for signs of congenital syphilis (hepatomegaly, ascites, hydrops, fetal anemia, or a thickened placenta). Sonographic evidence of secondary syphilis may require additional treatment in consultation with MFM and ID. (Request ultrasound via Cerner ad hoc form and specify syphilis diagnosis in comments)
- Pregnant patients with primary or secondary syphilis AND >24 wks gestational age may require inpatient fetal monitoring for 12-24 hours after treatment. Contact MFM on call via PALs to determine if inpatient monitoring is warranted and to coordinate admission.

If other questions regarding treatment or management of the pregnant woman with syphilis, please contact adult infectious disease and/or MFM via PALS line. Examples include:

- Mother's diagnosis, staging, treatment history, or recommended management is not clear.
- Possible Penicillin allergy
- Patient who may have difficulty returning for all treatments
- Mother with possible nervous system or ocular involvement

For management of possible congenital syphilis, please see associated *Congenital Syphilis Pathway*. (Anticipate availability in Feb 2020).

Other key resources

Patient information sheet about congenital syphilis (from CDC)
Clinician pocket guide – Syphilis (from CDC)
The Diagnosis, Management, and Prevention of Syphilis (from New York City Department of Health and Mental Hygiene, Bureau of Sexually Transmitted Infections, 2019)

References

1. Clinical Microbiology Newsletter Dec 2014, author: Soreng K et al.
2. MMWR, CDC: https://www.cdc.gov/nchhstp/newsroom/2018/2018-std-prevention-conference.html
3. Soreng K, Levy R, Fakile Y. Serologic Testing for Syphilis: Benefits and Challenges of a Reverse Algorithm. J Clin Micro News 2014. Link to article.
4. CDC Syphilis website.
5. CDC – Syphilis during Pregnancy. (2015 STD Guidelines)
6. CDC – Congenital syphilis. (2015 STD Guidelines)
7. NM Dept of Health Public Health Order – Increased Screening of Syphilis in All Pregnant Women to Prevent Congential Syphilis, Jan 10, 2020.
8. Shenoy ES et al. Evaluation and Management of Penicillin Allergy: A Review. JAMA. 2019; 321(2):188-199. doi:10.1001/jama.2018.19283