

Addressing the Syphilis Crisis in Oklahoma: A Provider Call to Action

Syphilis in Pregnancy

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Goals



- How to diagnose syphilis
- Treatment of syphilis in pregnancy
- Discuss missed opportunities
- Highlight action items

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Polling Question 1
I treat or manage syphilis in my clinical practice:



- A. Less than 5 times a month
- B. Less than 5 times a week
- C. ≥ 5 times a week
- D. ≥ 10 times a week
- E. I have not treated or managed syphilis in my practice

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Case 1: Mother



- 20 year old G1 P0
- First prenatal appointment @ 7wks gestation
 - RPR non-reactive, GC/CT negative, HIV negative
- 28 weeks
 - RPR non-reactive
- Delivered at 39 weeks gestation due to gestational hypertension
 - **Did not have RPR tested at delivery**

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Case 1: Neonate




- Normal newborn physical exam other than weak palmar grasp
 - Bilirubin - 9.8 treated with less than 24hrs of phototherapy
- Discharged home after 48hr observation due to maternal GBS + with inadequate antibiotic treatment

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Case 1: Neonate

- DOL 30: Presents to rural emergency department due to worsening skin peeling that began to worsen 4 days prior to ER visit, perioral rash and bloody diarrhea for the last several days
 - Physical Exam:
 - Temp 102 F, BP 85/39 Wt 3700 grams
 - Lethargic, hypotonic
 - Optic nerve edema
 - Pericardial effusion
 - Generalized desquamating rash
 - Labs:
 - Hemoglobin 4.8 Hematocrit 24, Platelets 26
 - RPR Result: 1:1,024
 - CSF VDRL reactive 1:4; CSF WBC 1; CSF Protein 71; CSF glucose 5.4
 - **Diagnosis: Congenital Syphilis**
 - Treated with 18500units of IV Penicillin every 6hrs for 21 days

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Case 1: Mother

- After baby's diagnosis mom went to ER for evaluation
- Palmar/plantar rash present
- RPR 1:128; TPPA reactive
- Diagnosed with Secondary Syphilis
- Treated with 2.4 Million Units of Benzathine Penicillin G IM x1

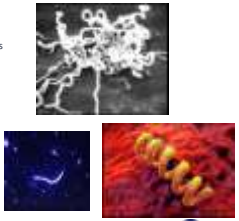


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What is Syphilis?

Treponema pallidum

- Spirochete 5 to 15 um
- Dark field microscopy for direct visualization
- Outer membrane relatively devoid of protein targets
- Entirely dependent on mammalian host for sustained growth
- Acquired sexually, hematogenously, or via vertical transmission
- Can cross skin with only microabrasions and intact mucous membranes
- Sexual transmission efficacy 30%
- Effective treatment has been available for over 70 years



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How to diagnose syphilis - "The Great Imitator"

Identify patients at risk

- All pregnant patients
- Sexual health history
- Substance use history
- Physical examination

Diagnostic challenges:

- Temporary nature of painless chancre
- Vague symptomatology of secondary syphilis
- Asymptomatic nature of latent syphilis
- Absence of a test that distinguishes newly acquired infection from past infection
- Confusing serologic test results

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Why take a sexual health history?

Essential part of health

Testing/labs

Avoids Assumptions

Exam components

Care about health

Provide appropriate services

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Hi! I'm Allison - I'm a nurse practitioner and I'll be helping you out today. My pronouns are she/her/hers.

At this clinic we ask a lot of questions - about your medical and sexual history, as well as about drug and alcohol use. Everything we discuss is confidential.

I ask these questions to everyone, and it helps determine what testing you need and from what places on your body you may need them.

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Sexual history: What are the 6Ps?

Partners	Sexual Practices	Past History of STIs
Pregnancy	Protection from STIs	Plus: Problems, Pleasure, Pride

Source: National Coalition for Sexual Health
<https://www.nationalcoalitiononstis.org/sexual-history>
<https://www.cdc.gov/sti/sexual-history/>

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Partners

- Gender identity of each partner
- Number of partners in past # months
- Partner info

Examples		
Are your partners male, female (trans-female, trans-male) or both?	Some people have sex with men, some with women, and some both. Who do you have sex with?	What gender are your partners?

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Sexual Practices

Vaginal sex	• Use of condoms with vaginal sex: never, sometimes, most of the time, or always?
Oral sex	• Give? Receive? • Condom use with oral sex: never, sometimes, most of the time, always?
Anal sex	• Give? Receive? • Condom use with anal sex: never, sometimes, most of the time, always?

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Past History of STIs

What STIs have you had in the past?			
When?	How were you treated?	What places on your body?	Partners treated?
<p>What STIs have your partners had in the past?</p> <p>When and where do? Symptoms? How were you treated? Did you have follow up testing after treatment? Partners treated?</p>			
<p>When was your last HIV test?</p> <p>What were the results?</p>			

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Clinical Stages of Syphilis

The flowchart illustrates the clinical stages of syphilis. It starts with 'Asymptomatic Infection (seronegative)', followed by 'Primary', 'Secondary', 'Early Latent', and 'Late Latent' stages. 'Tertiary' syphilis is shown as a separate path. A blue double-headed arrow at the bottom indicates 'Congenital Syphilis' which can occur at any stage from primary to tertiary.

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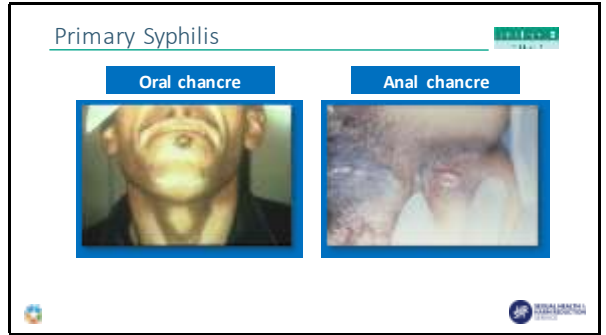
Physical Exam: Primary Syphilis

- Skin lesion at site of infection
- 1-2 cm **painless** ulcer with raised, indurated margin
- Will heal spontaneously over 3-6 weeks
- Can appear in any sites of sexual contact
- *Oral exam is very important*
- *May go unnoticed if in anus, vagina or cervix*

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Physical Exam: Secondary Syphilis

- Occurs 2-6 weeks after resolution of the primary lesion
- Represents disseminated systemic process
- Generalized maculopapular rash often involving palms and soles
 - characterized by brown discoloration
- Generalized lymphadenopathy

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Secondary rash

Condyloma lata

Papulo-pustular rash

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Secondary Syphilis

Mucous patches

Patchy Alopecia

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Latent/Unknown Duration Syphilis


- 2-3 months after resolution of secondary symptoms
- No visible signs or symptoms
- Can relapse to secondary syphilis
- **Early latent**
 - **Criteria met during the 12 months preceding the diagnosis:**
 - Documentation of a negative RPR or VDRL within the past year
 - Documented sustained $\geq 4x$ increase in RPR
 - Unequivocal symptoms of primary or secondary syphilis
 - Sex partner with primary, secondary, or early latent syphilis
 - Person whose only possible exposure occurred ≤ 12 months
- **Late Latent or Unknown duration (>12 months)**

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Tertiary Syphilis

- One or more decades after acquisition
- Slowly progressive signs and symptoms
- Gumma formation
- Neurological, cardiovascular, ophthalmologic, bone damage



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Ocular Syphilis


- Often presents as panuveitis
- Can involve structures in the anterior and posterior segment of the eye including:
 - Conjunctivitis
 - Anterior uveitis
 - Posterior interstitial keratitis
 - Optic neuropathy
 - Retinal vasculitis
- Can be permanent

Otosyphilis

- Typically presents with cochleo-vestibular symptoms including
 - Tinnitus
 - Vertigo
 - Sensorineural hearing loss
 - Unilateral or bilateral
 - Can be sudden onset
 - No one 'classic' presentation
- Can be permanent

Neurosyphilis

- Severe Headache, nausea and vomiting
- Neck stiffness
- Photophobia
- Visual changes
- Cranial nerve deficits
- Seizures
- New weakness in arms, legs or face
- Unsteady gait/balance issues
- Argyll Robertson pupils
- Parosmia
- Bladder dysfunction



Screen for ocular, otic and neurosyphilis in ALL patients being treated for syphilis

2023 ST Treatment Guidelines, CDC
Reberstein, et al (2023). *Diagnosis: A review of Infectious Disease Seminars*. *Disease*, Vol.4(3), Mar2023.

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Polling Question 2

What syphilis screening algorithm does your clinic/organization use?

- Traditional
- Reverse
- I don't know
- I don't know but I'm going to find out.

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Diagnosing Syphilis: Serologic Testing

Screening Tests

Non-Treponemal (RPR or VDRL)

- Detects non-specific antibodies caused by damage to the cell wall after infection (lecithin, cholesterol, cardiolipin)
- Rapid plasma reagin (RPR)
- Venereal disease research laboratory (VDRL) test

Treponemal

Detects specific IgG and/or IgM antibodies against *T. Pallidum*

- Enzyme immunoassay (EIA)
- Chemiluminescence immunoassay (CIA)
- *Treponema pallidum* particle agglutination (TPPA) test
- Indirect fluorescent antibody (IFA-ABS)

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Diagnosing Syphilis: Serologic testing

Non-treponemal (RPR or VDRL)

- Reported as a titer (1x)
- Fluctuates according to disease activity
- Highest sensitivity in secondary syphilis
- Higher false negative in primary and tertiary syphilis
- After appropriate treatment will usually become negative but can have low level positive (serofast)
- False positive (1-2% in general population)

Treponemal

- Reported as reactive or non-reactive
- After infection, these antibodies usually exist for life
 - *Cannot differentiate previously treated infection from active disease*
- Better sensitivity for early primary syphilis

Cases of False Positives on RPR

Chronic infection	Proteins	Other infections	Autoimmune diseases	Drugs
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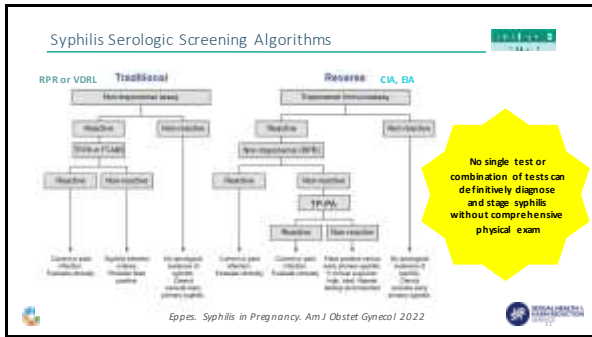
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Diagnosing Syphilis: Serologic testing

Nature Reviews, 2017

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Case 2

- 20 year old G2P1 presents at 10 weeks of gestation for new OB visit.
- Medical History: tobacco use current
- OB History: one prior vaginal delivery without complication
- Past Surgical History: none
- Allergies: none
- Sexual History: None. New partner this pregnancy.
- **New OB visit labs:**
 - CIA immunoassay reactive
 - RPR nonreactive
 - TPPA nonreactive

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Polling Question 3

Case 2: What should you as the provider do?

- Counsel her this result is nothing to be worried about, and plan to repeat test in the third trimester according to state law
- Initiate treatment for syphilis because the patient is high risk
- Complete history and physical exam including pelvic exam, and if low risk repeat the CIA in 4 weeks**
- Complete history and physical exam including pelvic exam, and if low risk repeat the CIA at delivery

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What should you as the provider do?

- Counsel her this result is nothing to be worried about, and plan to repeat test in the third trimester according to state law
- Initiate treatment for syphilis because the patient is high risk
- Complete history and physical exam including pelvic exam, and if low risk repeat the CIA in 4 weeks**
- Complete history and physical exam including pelvic exam, and if low risk repeat the CIA at delivery

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Case 2: Next steps

- **History and physical exam negative; repeat the CIA in 4 weeks**
- @ 14 weeks pt returns for repeat CIA
 - CIA immunoassay reactive
 - **RPR 1:16**

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Polling Question 4

Case 2: What are next steps as a provider?

- Complete history and physical exam including pelvic exam
- STI counseling, offer full STI panel if not recently completed
- Contact local health department and request partner services
- Contact the lab to request TPPA test result
- Initiate treatment for early stage syphilis
- F. A, B, C, D
- G. A, B, C, E

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Case 2: What are next steps as a provider?

- A. Complete history and physical exam including pelvic exam
- B. STI counseling, offer full STI panel if not recently completed
- C. Contact local health department and request partner services
- D. Contact the lab to request TPPA test result
- E. Initiate treatment for early stage syphilis
- F. A, B, C, D
- G. A, B, C, E**

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Syphilis in pregnancy

- Course and presentation is no different than in non-pregnant individuals

50% of pregnant women with latent syphilis are discovered through routine serologic testing

- Maternal syphilis at ALL stages is a risk to the fetus

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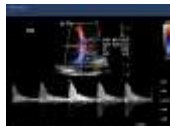

Untreated syphilis: Adverse pregnancy outcomes

Outcome	Primary and secondary syphilis
Stillborn or CHD*	10.0% (9.0-11.0)
Stillborn or CHD†	10.0% (9.0-11.0)
Stillborn or CHD‡	10.0% (9.0-11.0)
Stillborn or CHD§	10.0% (9.0-11.0)
Stillborn or CHD¶	10.0% (9.0-11.0)
Stillborn or CHD	10.0% (9.0-11.0)
Stillborn or CHD&	10.0% (9.0-11.0)
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Stillborn or CHD)	10.0% (9.0-11.0)

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Syphilis in pregnancy: Fetal complications

- Frequency of vertical transmission *increases* with advancing gestational age and with early stage disease
- risk of vertical transmission with early syphilis is 50%
- Fetal manifestations more likely with infection AFTER 20 weeks gestation due to low fetal immune response in the first half of pregnancy

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Congenital Syphilis

- Risk of congenital infection *increases* with recent maternal infection
 - 50% risk with primary and untreated secondary disease
 - 40% risk with untreated early latent disease
 - 10% risk with untreated late latent disease
- Risk of congenital infection also increases with higher titers
 - 26% risk if titer >8 versus 4% risk if titer <8
- Short interval treatment prior to delivery (<30 days) increases risk of treatment failure
 - If delivery occurs less than 30 days after completing treatment the baby is automatically diagnosed with congenital syphilis

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Congenital Syphilis

- Bone deformities
- Anemia
- Enlarged liver and spleen
- Jaundice
- Brain injury (blindness and deafness)
- Meningitis
- Rashes




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Syphilis in Pregnancy: Treatment

Benzathine Penicillin G

- The only recommended treatment in pregnancy
- Effective in treating maternal and fetal infection and preventing congenital syphilis



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Treatment of syphilis during pregnancy

Stage of syphilis	Treatment
Primary syphilis	BPG 2.4 million units IM once
Secondary syphilis	
Early latent syphilis	14-day regimen (recommended): a second dose of BPG of 2.4 million units IM, 1 month after the first dose; (also of 4.8 million units)
Late latent syphilis	BPG of 7.2 million units total, given as 3 doses of 2.4 million units IM, each at 1-week intervals
Syphilis of unknown duration	2.4 million units IM, each at 1-week intervals

Per CDC multiple doses need to be administered within 9 days

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Management algorithm after positive serologic screen with no history of syphilis

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    graph TD
      A[Physical exam s/sx syphilis +] --> B[Treat for primary, secondary, or tertiary syphilis]
      C[Physical Exam negative (latent)] --> D[If early Latent: 1-2 doses of Benzathine PCN]
      C --> E[If late latent or unknown duration: 3 doses of Benzathine PCN]
    
```

* If neurologic symptoms must consider LP to evaluate for neurosyphilis

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Management algorithm after positive serologic screen with history of syphilis

```

    graph TD
      A[History of disease treatment] --> B[Physical exam s/sx syphilis +]
      A --> C[Physical exam negative]
      B --> D[Treat with Benzathine PCN for the type of infection]
      C --> E[Physical exam negative]
      C --> F[Physical exam s/sx syphilis +]
      E --> G[If early latent]
      E --> H[If late latent or unknown duration]
      F --> I[Treat with Benzathine PCN for the type of infection]
      G --> J[1 dose benzathine penicillin]
      H --> K[3 doses benzathine penicillin]
      I --> L[1 dose benzathine penicillin]
    
```

* If neurologic symptoms must consider LP to evaluate for neurosyphilis

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Penicillin Allergies

Questions to ask

- What medication were you taking when the reaction occurred?
- What kind of reaction occurred?
- How long ago did the reaction occur?
- How was the reaction managed?
- What was the outcome?

Characteristics of an IgE-mediated (Type 1) reaction:

- Reactions that occur immediately or within one hour
- Hives: multiple pink/red areas of skin that are intensely itchy
- Angioedema: localized edema without hives affecting the abdomen, face, extremities, genitalia, oropharynx, or larynx
- Wheezing and shortness of breath
- Anaphylaxis



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Penicillin Allergies

- If PCN allergy:
 - Skin testing
 - Dose challenge with oral PCN
 - Desensitization

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Special Considerations: Jarisch Herxheimer reaction

- Most common with treatment of primary and secondary syphilis
 - Acute systemic reaction
 - Due to release of large amounts of treponemal lipopolysaccharide from dying spirochetes and increase in circulating cytokine levels
- Acute febrile reaction
 - HA, myalgia, rash, hypotension
 - Can precipitate preterm labor and fetal heart rate decelerations
- Symptoms appear 2-8 hours after treatment initiation and abate by 24 hours
- Educate pregnant patients to go to the hospital if decreased fetal movement, fevers, or preterm labor symptoms

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Management of syphilis in pregnancy

- Treatment should be initiated as soon as possible following diagnosis
- Treatment of partners
- Ultrasound evaluation of the fetus if diagnosed in the second half of the pregnancy
 - Fetal anemia
 - Fetal hepatomegaly
 - Fetal ascites
 - Fetal hydrops
 - Placentomegaly

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Evaluation of treatment

- 4 fold decline in titer OR absence of a 4 fold increase if initial titer is low ($\leq 1:8$)
- Expected time frame for decline
 - Early syphilis: 6 to 12 months
 - Late latent or unknown duration: up to 24 months
 - HIV positive: up to 24 months regardless of stage of syphilis

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Case 3

28yo G2P0010 8 2/7 weeks gestation


- RPR 1:64; TPPA(+)
- No previous syphilis diagnosis
- No signs or symptoms of infection

Treatment for syphilis of unknown duration initiated with Long acting bicillin (LAB) 2.4 mU

LAB #1: 9/3
LAB #2: 9/10
LAB #3: 9/24

12 weeks after treatment initiated: RPR 1:32

Delivery 7 months after treatment initiated: RPR 1:16




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Polling Question 5

Case 3: Was the mother's treatment adequate?

A. Yes
B. No
C. I need more information




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2021 STI Treatment Guidelines

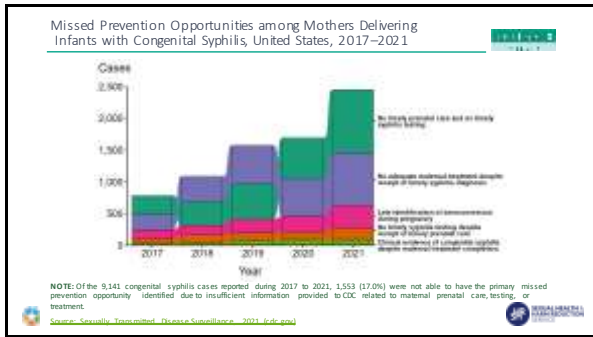
Syphilis Treatment During Pregnancy

Latent Syphilis of Unknown Duration or Late Latent Syphilis



- interval between injections CAN NOT exceed 9 days
- If 10 or more days, must restart the series

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Oklahoma Legislation: SB 292 Effective November 2023

Every physician, physician assistant, or Advanced Practice Registered Nurse attending a pregnant woman in Oklahoma this state during gestation shall, in the case of each woman so attended, take or cause to be taken a sample of blood of such woman at the time of first examination, and shall submit such sample to an approved laboratory for a standard serological test for syphilis, when indicated by current guidance of the Centers for Disease Control and Prevention first prenatal visit and twice during the third trimester (28 weeks and delivery) for women with risk factors AND women who live in communities with high rates of syphilis

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- ### Congenital Syphilis in OK: Action Items
- Educate patients regarding risks of untreated syphilis in pregnancy and signs of syphilis
 - Primary: 1-2 cm painless ulcer with raised, indurated margin
 - NOT ALL GENITAL/ORAL ULCERS are HSV**
 - Secondary: Generalized maculopapular rash involving palms and soles
 - Obtain complete sexual history on all patients
 - Follow current CDC recommendations for syphilis testing in pregnant women
 - Initial OB visit, third trimester, and at delivery
 - ACOG Practice Advisory from April 2024 also recommends universal syphilis screening at this interval rather than risk based screening

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Congenital Syphilis in OK: Action Items

- Ensuring that patients who test positive are reported to the health department and that they *and their partners* get appropriate treatment AS SOON AS POSSIBLE

All positive syphilis cases should be reported within 24 hours to PHEDCO or by fax at 405-980-1506.

For any questions or concerns about this matter please contact the Oklahoma State Department of Health, Sexual Health and Harm Reduction Service at 405-438-8480 or shh@health.ok.gov

To request enrollment to facilitate reporting, please contact electronicreporting@health.ok.gov

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What if you don't know what to do/need help?

Disease Intervention Specialists

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- ### Congenital Syphilis in OK: Action Items
- Identify ways to ensure pregnant patients who have no prenatal care but present for non-pregnancy related healthcare get tested and treated
 - Increase access to prenatal care/testing
 - Benzathine PCN shortage
 - prioritizing pregnant women
 - Increase public advocacy
 - Address social determinants of health
 - Prioritize community outreach
 - Increase education for providers

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