Syphilis in South Dakota, 2021
provisional data as of 03/31/2022

Dr. Mary Carpenter

1080% Increase from the 5-Year Median

58 75 76 89 121

Counties with the Highest Reported Number of Cases

27%, Pennington 239 Cases
25%, Todd 225 Cases
20%, Minnehaha 178 Cases
7%, Oglala Lakota 65 Cases
3%, Dewey 29 Cases

Adults, 20-39 Years-Old, Represent 73% of all Cases

Perinatal: 16 46 326 331
15-19: 36 36 36 36
20-29: 36 36 36 36
30-39: 36 36 36 36
40-49: 36 36 36 36
50-59: 36 36 36 36
60+: 36 36 36 36
Females and Males are Proportionately Affected

- 49% Female
- 51% Male

Native Americans are Disproportionately Affected, Equaling 73% of all Cases

Risk Factors
- 93% reported heterosexual exposure
- 45% had a history of other STIs
- 45% had a history of incarceration
- 36% had sex while intoxicated
- 27% had a history of IV drug use
- 15% Pregnant at time of syphilis test

Syphilis Stages, >85% Infected within Previous 12 Months
South Dakota’s Congenital Syphilis Data will be Presented on April 14th Training

Disclosures

• Tara Reid does not have relationships with a commercial interest related to the content of this educational activity.

• Caveat: Language is evolving, and though our aim is to change accordingly, we acknowledge that CDC guidelines are written using binary language with respect to gender.

Overview

• Part 1
  • Clinical manifestations of syphilis
  • Staging of disease
  • Lab testing
  • Treatment

• Part 2: Deeper dive into complicated syphilis
  • Screening
  • Treatment follow up and failure
  • Ocular/Otic/Neuro syphilis
  • Part 3: Congenital syphilis
Part 1: Take home points

- Maintain high suspicion for syphilis – any person who is sexually active in high incidence/prevalence areas
- Diagnosis is clinical (P&S) or serologic (latent)
- Low threshold for presumptive treatment
  - Clinical symptoms c/w possible case
  - All contacts to bacterial STI (treat before test results)
- Understand the syphilis screening algorithms
- Phone a friend! UW STD PTC, local PHD, etc.

Who to screen and when

<table>
<thead>
<tr>
<th>Risk Criteria</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSM</td>
<td></td>
</tr>
<tr>
<td>• “Lower risk” – Sexually active men outside of mutually monogamous relationships</td>
<td></td>
</tr>
<tr>
<td>• “Higher risk” (based on RFs in past year)</td>
<td></td>
</tr>
<tr>
<td>- Bacterial STI</td>
<td></td>
</tr>
<tr>
<td>- Methamphetamine use</td>
<td></td>
</tr>
<tr>
<td>- Condomless anal sex with HIV+/unknown status partner</td>
<td></td>
</tr>
<tr>
<td>- &gt;10 sex partners</td>
<td></td>
</tr>
<tr>
<td>- On PrEP</td>
<td></td>
</tr>
<tr>
<td>Pregnant individuals</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td></td>
</tr>
<tr>
<td>Persons with bacterial STIs</td>
<td></td>
</tr>
<tr>
<td>Focus on MSM and gonorrhea</td>
<td></td>
</tr>
<tr>
<td>Persons being homeless or unstably housed</td>
<td>Any sex outside of long-term mutually monogamous relationship</td>
</tr>
<tr>
<td>People who use methamphetamines &amp; sex workers</td>
<td>Any sex outside of long-term mutually monogamous relationship</td>
</tr>
</tbody>
</table>

Syphilis screening: Who is at risk?

- Be aware of prevalence in your community
  - Heterosexual population, meth use, sexual minority men, people of pregnancy potential
- History of incarceration
- Commercial sex workers or people who exchange sex
- Certain racial/ethnic groups
  - Disparities among African Americans, Alaska Natives, Native Americans, NHOPI
- Men 20-35 years old, history of prior syphilis
- Highest case rates in West and South US

Syphilis contacts & Partner management

- Syphilis transmission is high in early stages
- Contact to 1st, 2nd, EL stage infection within 90 days; screen for syphilis and treat for early syphilis -- you can do it or refer to DOH
- Contact to LL/UD syphilis or > 90 days
  - Option 1: Treat presumptively based on exposure, prior tests
  - Option 2: Test and have contact return if positive
- No EPT for syphilis
Syphilis Treatment

<table>
<thead>
<tr>
<th>Stage</th>
<th>Retest</th>
<th>4 fold decline by:</th>
</tr>
</thead>
<tbody>
<tr>
<td>P&amp;S, early latent</td>
<td>6, 12 mo</td>
<td>12 mo</td>
</tr>
<tr>
<td>Late latent/unk duration</td>
<td>6, 12, 24 mo</td>
<td>24 mo</td>
</tr>
</tbody>
</table>

**Primary, Secondary or Early Latent**
- 2.4 million units benzathine PCN IM x 1
- PCN Allergy: Doxy 100mg bid x 14 days (or tetracycline 500 mg QID x 14 days)

**Late Latent or unknown duration**
- 2.4 million units benzathine PCN IM weekly for 3 weeks
- PCN Allergy: Doxy 100mg bid x 28 days (or tetracycline 500 mg QID x 28 days)
- Ceftriaxone IM/IV daily x10d? – consult an ID specialist

Follow up (HIV-negative patients)

- Quantitative nontreponemal titers used to follow response. Fourfold change (two dilutions) is an appropriate response within 12 months*

**Efficacy of alternative therapies not well studied in HIV patients**

Monitor response (HIV-positive patients)

- Evaluated clinically and serologically at
  - 3, 6, 9, 12, and 24 months after therapy (Early syphilis)
  - 6, 12, 18, and 24 months after therapy (Latent syphilis)
- Careful neurologic exam at time of diagnosis
- Most respond appropriately to the recommended treatment regimen for syphilis
- Those who meet the criteria for treatment failure should be managed similarly to HIV-negative patients

Factors associated with adequate serologic response: age, early stage, initial NTT titer

- Earlier stages are more likely to decline and become negative
- Lower initial nontreponemal titers are less likely to decline than higher titers
- Younger age
- High serofast (> 1:16) titers raise questions of treatment failure vs re-infection
- HIV+ (more likely to be serofast; may be higher titer)

Monitoring response to treatment: Failure

Suspect treatment failure (or reinfection) if:

• Recurrent signs and symptoms
• 2-titer (4-fold) rise in nontreponemal titer
  • Consider repeating test
  • Retreat and evaluate for HIV
  • Consider CSF evaluation
• Failure to achieve 2 titer (4-fold) decline in titer within 12-24 months
  • Consider retreatment
  • Consider CSF evaluation
  • ~ 15% of persons may not have decline, even in the absence of neurosyphilis

Actual or suspected treatment failure

• Clinical and serologic follow-up, test for HIV!

• Management of treatment failure:
  • Benzathine penicillin G 2.4 MU weekly x 3.
  • Consider LP to evaluate for neurosyphilis:
    • Many experts suggest, in the absence of neurological sx, re-treating with Bicillin LA x 3, and performing LP if titers fail to decrease after the re-treatment.
    • Patients should be aware of their serofast titers.

Patient Case

• 30 y/o man presents with diffuse rash and “floaters” in the right eye over the past few days.
• Recent labs show a syphilis IgG+ and RPR 1:256.
• How does his history of vision loss affect your treatment plan?
Audience poll!

### General approach to syphilis management

<table>
<thead>
<tr>
<th>Question or Task</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Does the patient have evidence of complicated syphilis?</td>
<td>Determine need for additional work-up</td>
</tr>
<tr>
<td>2) What is the syphilis stage?</td>
<td>Determines therapy</td>
</tr>
<tr>
<td>3) Test for other STIs (HIV, GC/CT, Trich) &amp; pregnancy. Vaccinate for HPV?</td>
<td>Define need for other therapy or special follow-up</td>
</tr>
</tbody>
</table>
| 4) Define HIV treatment or prevention plan | - If HIV positive: Is patient on ART and suppressed?  
- If HIV negative: Recommend PrEP |
| 5) Define follow-up plan | Assure >2 titer (4-fold) decline over 12-24 months, or sooner if MSM, pregnant or HIV+ |
| 6) Report to health department | Helps assure partner treatment, decrease transmission, optimizes care |

### Rapid dissemination of syphilis via the lymphatics and blood

Neurosyphilis can occur at any stage.

- NOT RARE
- Extraordinarily rare

- Growth of organisms at site of infection, dissemination to various tissues including central nervous system
- Chance at site of infection, regional lymphadenopathy
- Disseminated rash, generalized lymphadenopathy
- Recurrence of secondary syphilis symptoms in up to 25% of individuals
- Ocular, cerebral, pulmonary, carditis, late neurological pain, mental

Extraordinarily rare

- NOT RARE
2021 CDC STI Treatment Guidelines

- Incorporation of new data/evidence
- More focus on challenges in syphilis management
- Enhanced discussion about algorithms
- Ocular syphilis
- CSF follow-up
- Expanded risk factors for testing in pregnant people

Neurosyphilis or complicated syphilis

- Invasion of central nervous system by *T. pallidum*
- Increased protein, WBC in CSF; reactive CSF VDRL
- Untreated, can progress to meningo-vascular syphilis (stroke), other late neurologic complications
- Ocular syphilis can lead to permanent blindness
- Otosyphilis can lead to permanent hearing loss
- Imperative to screen everyone diagnosed with syphilis

This is an EMERGENCY

Complicated syphilis — screening questions

- Changes in vision? (blurry vision)
- Changes in hearing?
- Tinnitus?
- Headaches?
- Stiff neck?
- Photophobia?
- Discomfort, redness or burning of eyes?
- Other concerning changes: gait changes, sensorimotor deficits, cranial nerve abnormalities, cognitive dysfunction

Screening for complicated syphilis

- Negative LP does not rule out ocular or otosyphilis
- Ophthalmologic & Otologic (ENT) referrals

Questions

<table>
<thead>
<tr>
<th>Symptom of Syphilis</th>
<th>Yes</th>
<th>Refer to ENT</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>New persistent headache severe or greater</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>New change in vision — yes, blurring, seeing spots or flashing lights</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>New change in hearing — loss, muffling or distortion</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>New and persistent change in personality, memory or judgement</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>New numbness of both legs or gait incoordination</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Consider evaluation & treatment for neurosyphilis in patients with any of the following:
- New persistent headache severe or greater
- New change in vision — yes, blurring, seeing spots or flashing lights
- New change in hearing — loss, muffling or distortion
- New and persistent change in personality, memory or judgement
- New numbness of both legs or gait incoordination
Ocular syphilis

- *T. pallidum* infection of ANY eye structure
- Presents as
  - Uveitis, iritis, neuroretinitis, optic neuritis, scleritis, vasculitis
- Vision threatening

Evaluation of ocular syphilis

- Urgent ophthalmology
  - Slit-lamp exam
- May or may not involve CNS
  - Thorough neurologic exam
  - CN 2, 3, 4, 5, 6
- If isolated ocular sx that are confirmed on exam + reactive serology = CSF exam is unnecessary before treatment
- CSF may be helpful if ocular sx + reactive serology and normal exam

Proportion of Syphilis Cases with Clinical Ocular Involvement

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Population</th>
<th>Ocular Involvement/Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stokes (1945)*</td>
<td>Syphilis Cooperative Clinical Group</td>
<td>91/3244 (2.8%)</td>
</tr>
<tr>
<td>Moore (1930)*</td>
<td>Johns Hopkins</td>
<td>111/2413 (4.5%)</td>
</tr>
<tr>
<td></td>
<td>Early secondary</td>
<td>29/309 (9.3%)</td>
</tr>
<tr>
<td></td>
<td>Recurrent secondary</td>
<td>109/3420 (3.1%)</td>
</tr>
<tr>
<td>Balba (2006)</td>
<td>HIV Clinic</td>
<td>3/33 (9%)</td>
</tr>
<tr>
<td>Dombrowski (2015)</td>
<td>King County 2012</td>
<td>15/567 (2.6%)*</td>
</tr>
</tbody>
</table>

*Iritis only

3.5% had confirmed complicated syphilis (including oto- and neuro) & 7.9% had confirmed or possible complicated syphilis

Otosyphilis (syphilitic labyrinthitis)

- Treponeme infection of the inner ear
- Can present as
  - Tinnitus, vertigo, sensorineural hearing loss
  - Unilateral or bilateral
- Sudden onset, rapid progression
- Can cause permanent hearing loss
Evaluation of otosyphilis

- Urgent ENT referral
- CN 8 exam
- Auditory acuity, Nystagmus, balance, sensorineural hearing
- If isolated auditory abnormalities + reactive serology, **CSF is almost always normal and not of any additional diagnostic benefit**

Who really needs an LP? (2021 updates)

- Neurologic signs or symptoms or ocular sx + reactive serology with a normal exam
- Evidence of active tertiary disease – (aortitis, gumma, general paresis, tabes dorsalis)
- Treatment failure
  - Sustained 2-titer (4-fold) increase in VDRL/RPR
  - High titer (RPR >1:32) syphilis that does not decline 2 titers (4-fold) over 6-12 months (1º or 2º syphilis) or 12-24 months (latent syphilis) – soft indication
- Expert opinion: Anyone with RPR titer ≥1:32, HIV patients off ART or with CD4 ≤350

CSF in diagnosis of complicated syphilis

- Pleocytosis
  - >5 WBC/µl if HIV-negative
  - More complicated if HIV-positive
  - >20 WBC/µl is definitive
  - HIV itself can also cause asymptomatic, mild pleocytosis – more likely if not on ART, CD4 >200 and detectable plasma VL
- Protein concentration
  - >45 mg/dL

**Management of complicated syphilis**

For LL/UD syphilis:
- Consider additional 1-3 Bicillin doses after NS tx
- Steroids not proven to be of any benefit
- Always screen for HIV! If negative, offer PrEP
- Monitor for improvement of abnormal signs/sx
- Follow serologies according to initial stage of infection

**Neurosyphilis (includes otos- or ocular)**

- Aqueous crystalline PCN G 3-4 MU IV q4 or as continuous infusion x 10-14d
  - or -
- Procaine PCN 2.4 million units IM + probenecid 500mg po qid x 10-14 days
- Ceftriaxone 2 gm IV daily x 10-14 days

**Follow-up LP after treatment?**

For those who are immunocompetent or who have HIV and on effective ART, normalization* of the serum RPR titer predicts normalization of CSF parameters after NS tx.

* Repeat CSF exams not necessary in setting of serologic and clinical response to therapy.

* A 4-fold decrease or reversion to nonreactive vs >8-fold decrease in serum RPR

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**Patient case, cont.**

- Patient should be treated promptly with benzathine penicillin G (Bicillin LA) for secondary stage infection
- Loss to follow-up without tx = transmission potential
- Don’t delay treatment to arrange LP
- Urgent evaluation by Ophthalmology

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**Part 2: Take home points**

- Maintain high suspicion for syphilis – any person who is sexually active in high incidence/prevalence areas
- Low threshold for presumptive treatment
  - Clinical symptoms c/w possible case
  - All contacts to bacterial STI (treat before test results)
- Treatment failure: give Benzathine penicillin G 2.4 MU weekly x 3
- Complicated/neurosyphilis can occur at any stage. LP is no longer recommended for everyone!
- Phone a friend! UW STD PTC, local PHD, etc.

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**Resources**

- University of WA STD Prevention Training Center  
  - www.uwptc.org
- National Network of STD/HIV Prevention Training Centers  
  - www.nnptc.org
- 2021 CDC STI Treatment Guidelines  
  - www.cdc.gov/std/treatment-guidelines
- American Social Health Association (ASHA) booklets, books, handouts, the Helper  
  - www.ashastd.org
  - (800) 230-6039
- NNPTC National STD Curriculum  
  - www.std.uw.edu