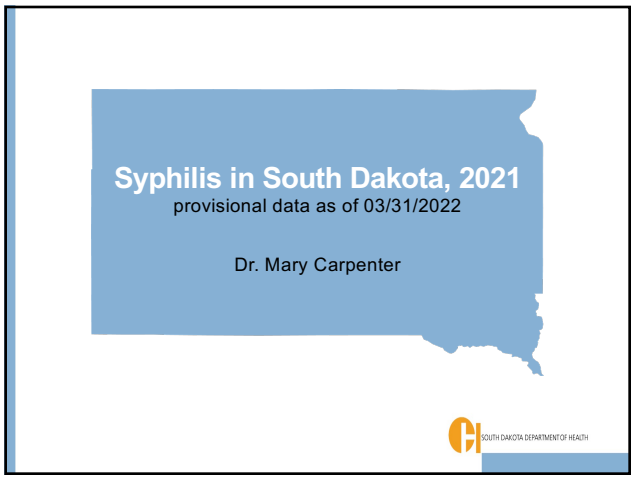
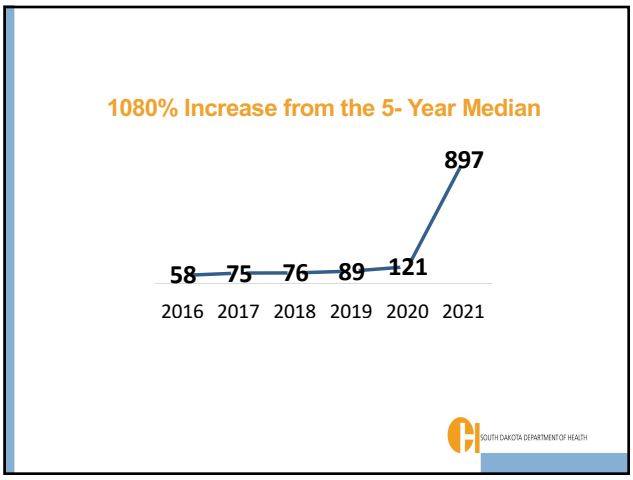
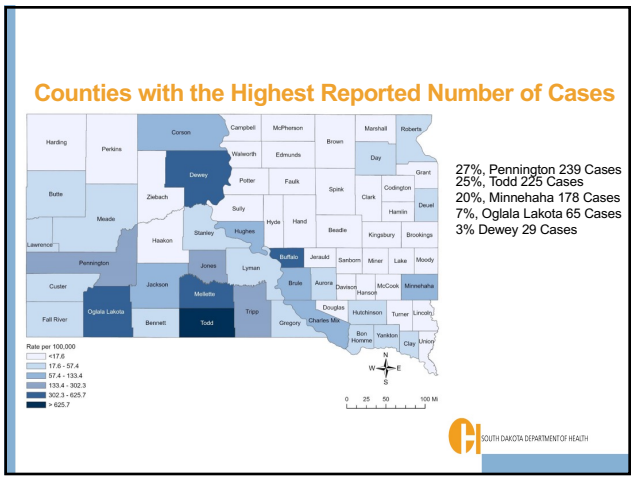

Syphilis in South Dakota, 2021
provisional data as of 03/31/2022
Dr. Mary Carpenter
SOUTH DAKOTA DEPARTMENT OF HEALTH

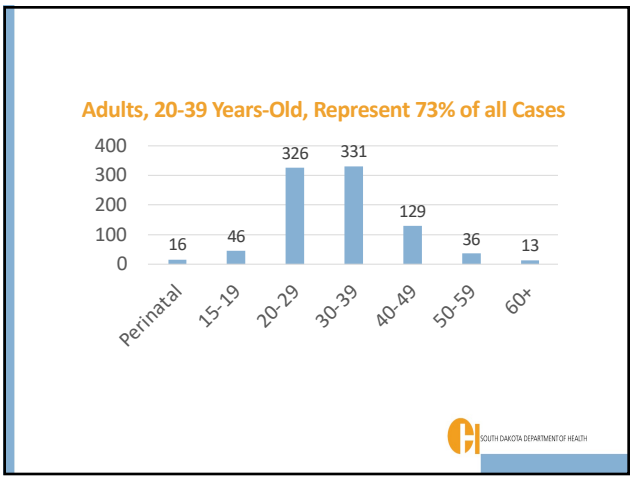
1


1080% Increase from the 5- Year Median
58
75
76
89
121
897
2016
2017
2018
2019
2020
2021
SOUTH DAKOTA DEPARTMENT OF HEALTH

2

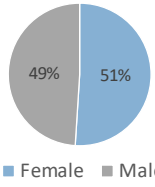

Counties with the Highest Reported Number of Cases
27%, Pennington 239 Cases
25%, Todd 225 Cases
20%, Minnehaha 178 Cases
7%, Oglala Lakota 65 Cases
3% Dewey 29 Cases
SOUTH DAKOTA DEPARTMENT OF HEALTH

3


Adults, 20-39 Years-Old, Represent 73% of all Cases
400
300
200
100
0
16
46
326
331
129
36
13
Perinatal
15-19
20-29
30-39
40-49
50-59
60+
SOUTH DAKOTA DEPARTMENT OF HEALTH

4

Females and Males are Proportionately Affected



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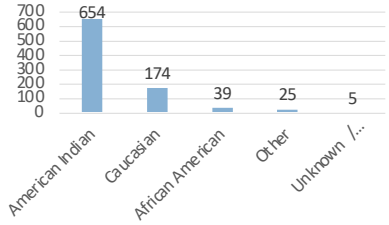
Native Americans are Disproportionately Affected, Equaling 73% of all Cases



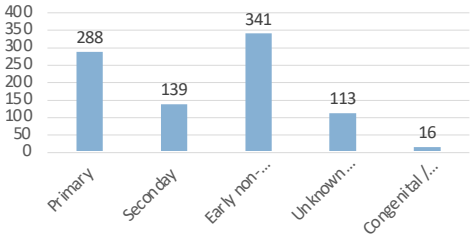
6

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

7

Syphilis Stages, >85% Infected within Previous 12 Months



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South Dakota's Congenital Syphilis Data will be Presented on April 14th Training

SOUTH DAKOTA DEPARTMENT OF HEALTH

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UNIVERSITY OF WASHINGTON
STD Prevention Training Center

Syphilis: Deeper Dive Part 2 of 3

Tara Reid, MD/PhD
Acting Instructor, University of Washington
Division of Infectious Diseases

Slides courtesy: Meena Ramchandani, Matt Golden, Julie Dombrowski, Sue Szabo, Sheila Lukehart

Updated April 2022

uwptc@uw.edu | uwptc.org | 206-685-9850

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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.*

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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*

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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.

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Who to screen and when

	Risk Criteria	Frequency
MSM	• "Lower risk" – Sexually active men outside of mutually monogamous relationships • "Higher risk" (based on RFs in past year) - Bacterial STI - Methamphetamine use - Condomless anal sex with HIV+/unknown status partner - >10 sex partners - On PrEP	Annually Every 3 months
Pregnant individuals	*ALL*	Testing should be performed three times; at the first prenatal visit, at 28 -36 weeks gestation and at delivery
Persons with bacterial STIs	Focus on MSM and gonorrhea	
Persons living homeless or unstably housed	Any sex outside of long-term mutually monogamous relationship	Annually
People who use methamphetamines & sex workers	Any sex outside of long-term mutually monogamous relationship	Every 3 months

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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

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Syphilis contacts & Partner management

- Syphilis transmission is high in early stages
- Contact to 1ry, 2ry, 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

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Syphilis Treatment

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*

Efficacy of alternative therapies not well-studied in HIV patients

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Follow up (HIV-negative patients)

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

Stage	Retest	4 fold decline by:
P&S, early latent	6, 12 mo	**12 mo**
Late latent/unk duration	6, 12, 24 mo	**24 mo**

- Public Health Seattle & King County practice is to retest at 3 months (or sooner), reinfection risk is high
  - Assure continued engagement with care
  - Rescreen for all STIs, including HIV!

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Monitoring 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

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Monitoring response to treatment

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)

Seña AC et al, BMC ID 2015; Romanowski B et al, Ann Int Med 1991

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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

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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.

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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?

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Audience poll!

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General approach to syphilis management

Question or Task	Rationale
1) Does the patient have evidence of complicated syphilis?	Determine need for additional work-up
2) What is the syphilis stage?	Determines therapy
3) Test for other STIs (HIV, GC/CT, Trich) & pregnancy. Vaccinate for HPV?	Define need for other therapy or special follow-up
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

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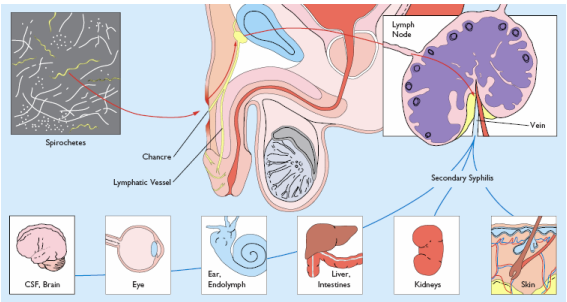
Rapid dissemination of syphilis via the lymphatics and blood



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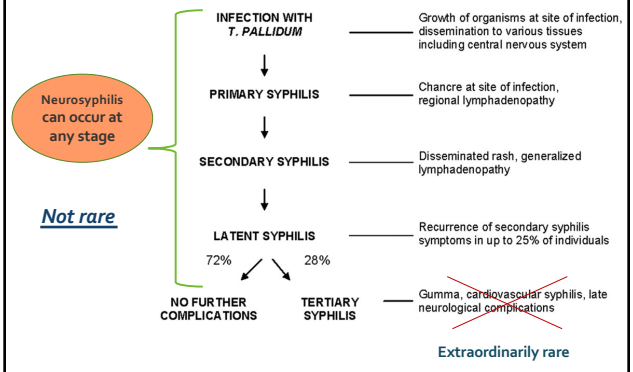
Neurosyphilis can occur at any stage



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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

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 70 / No. 4 July 23, 2021

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Neurosyphilis or complicated syphilis

- Invasion of central nervous system by *T. pallidum*
- Increased protein, WBC in CSF; or reactive CSF VDRL
- Untreated, can progress to meningovascular 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

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Complicated syphilis – screening questions

- Changes in vision? (blurry vision)
- Changes in hearing?
- Tinnitus?

Negative LP does not rule out ocular or otosyphilis

- Headaches?
- Stiff neck?
- Photophobia?

Ophthalmologic & Otologic (ENT) referrals

- Discomfort, redness or burning of eyes?
- Other concerning changes: gait changes, sensorimotor deficits, cranial nerve abnormalities, *cognitive dysfunction*

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Screening for complicated syphilis

Questions	
Symptoms of Otosyphilis	
1) Have you recently had new trouble hearing?	□ Yes – refer to ENT □ No
2) Do you have ringing in your ears?	□ Yes – refer to ENT □ No
Symptoms of Ocular syphilis	
3) Have you recently had a change in vision?	□ Yes – refer to ophthalmology □ No
4) Do you see flashing lights?	□ Yes – refer to ophthalmology □ No
5) Do you see spots that move or float by in your vision?	□ Yes – refer to ophthalmology □ No
6) Have you had any blurring of your vision?	□ Yes – refer to ophthalmology □ No
Symptoms of neurosyphilis	
7) Are you having headaches?	□ Yes □ No
8) Have you recently been confused?	□ Yes □ No
9) Has your memory recently gotten worse?	□ Yes □ No
10) Do you have trouble concentrating?	□ Yes □ No
11) Do you feel that your personality has recently changed?	□ Yes □ No
12) Are you having a new problem walking?	□ Yes □ No
13) Do you have weakness or numbness in your legs?	□ Yes □ No

Consider evaluation & treatment for neurosyphilis in patients with any of the following:
1) New persistent headache moderate or greater
2) New change in vision – loss, blurring, seeing spots or flashing lights
3) New change in hearing – loss, muffling or tinnitus
4) New and persistent change in personality, memory or judgement
5) New numbness of both legs or gait incoordination

http://www.kingcounty.gov/healthservices/health/communicable/hiv.aspx

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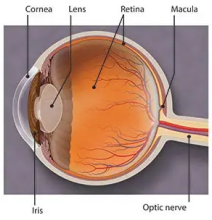
Ocular syphilis

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



aao.com

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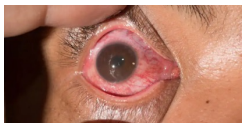
Evaluation of ocular syphilis

- 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



Panuveitis, retinal vasculitis, CN II-VI dysfunction, etc.

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Proportion of Syphilis Cases with Clinical Ocular Involvement

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

*Iritis only

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

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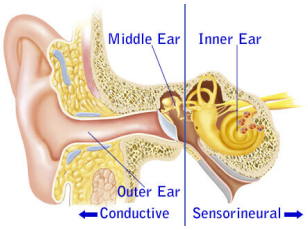
Otosyphilis (syphilitic labyrinthitis)

- 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



audicus.com

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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***

audicus.com

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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

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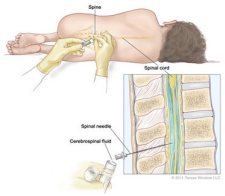
CSF in diagnosis of complicated syphilis

- 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



- CSF-VDRL is specific, but not sensitive
- CSF FTA-ABS is sensitive, but not specific

Marra CM, et al. Interpreting cerebrospinal fluid pleocytosis in HIV in the era of potent antiretroviral therapy. *BMC Infect Dis.* 2007;7:37.

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Management of complicated syphilis

Neurosyphilis (includes oto- 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*

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

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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.

* 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

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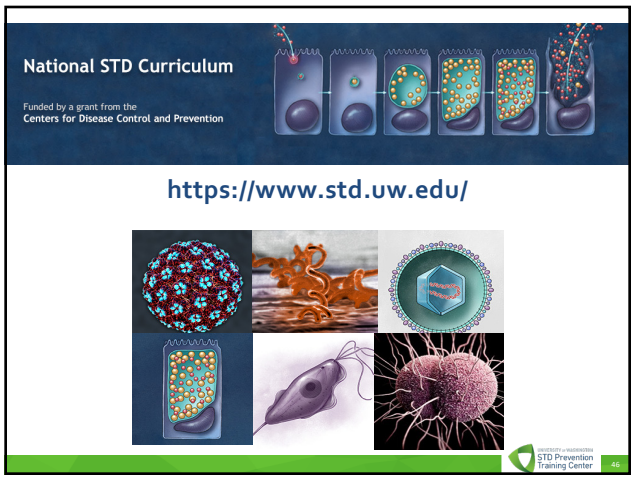
National STD Curriculum
Funded by a grant from the
Centers for Disease Control and Prevention
https://www.std.uw.edu/
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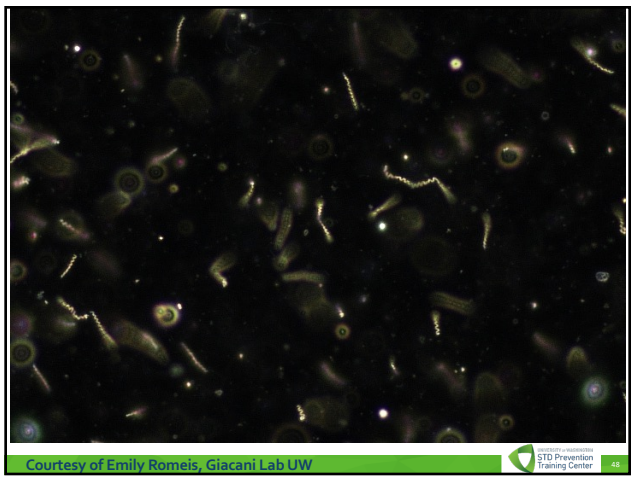
Courtesy of Emily Romeis, Giacani Lab UW
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