SYPHILIS

"The Great Pretender"

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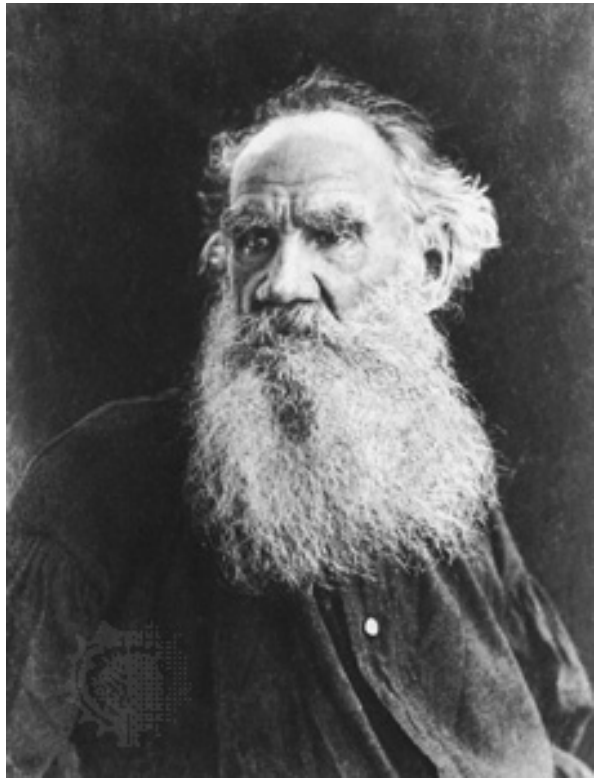
I AM NOT HEARTLESS
I JUST LEARNED HOW
TO USE MY HEART LESS

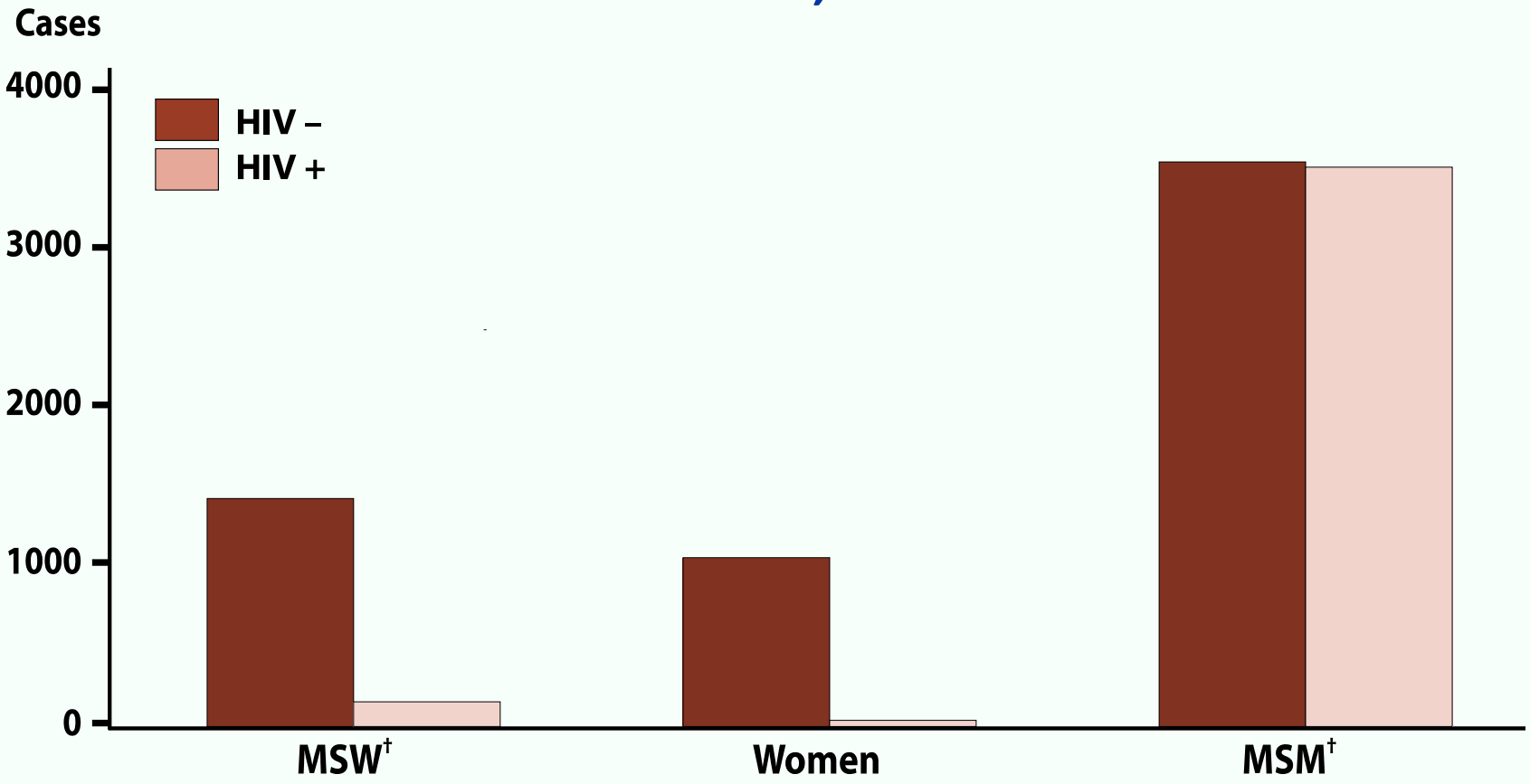


Learning Objectives

At the end of this presentation, the participants will be able to

1. Describe the epidemiology of syphilis in the United States
2. Describe the pathogenesis of Treponema pallidum
3. Discuss the clinical manifestations of syphilis.
4. Identify the methods used in diagnosis of syphilis
5. Discuss the CDC recommended treatment regimens for syphilis
6. Describe public syphilis prevention strategies

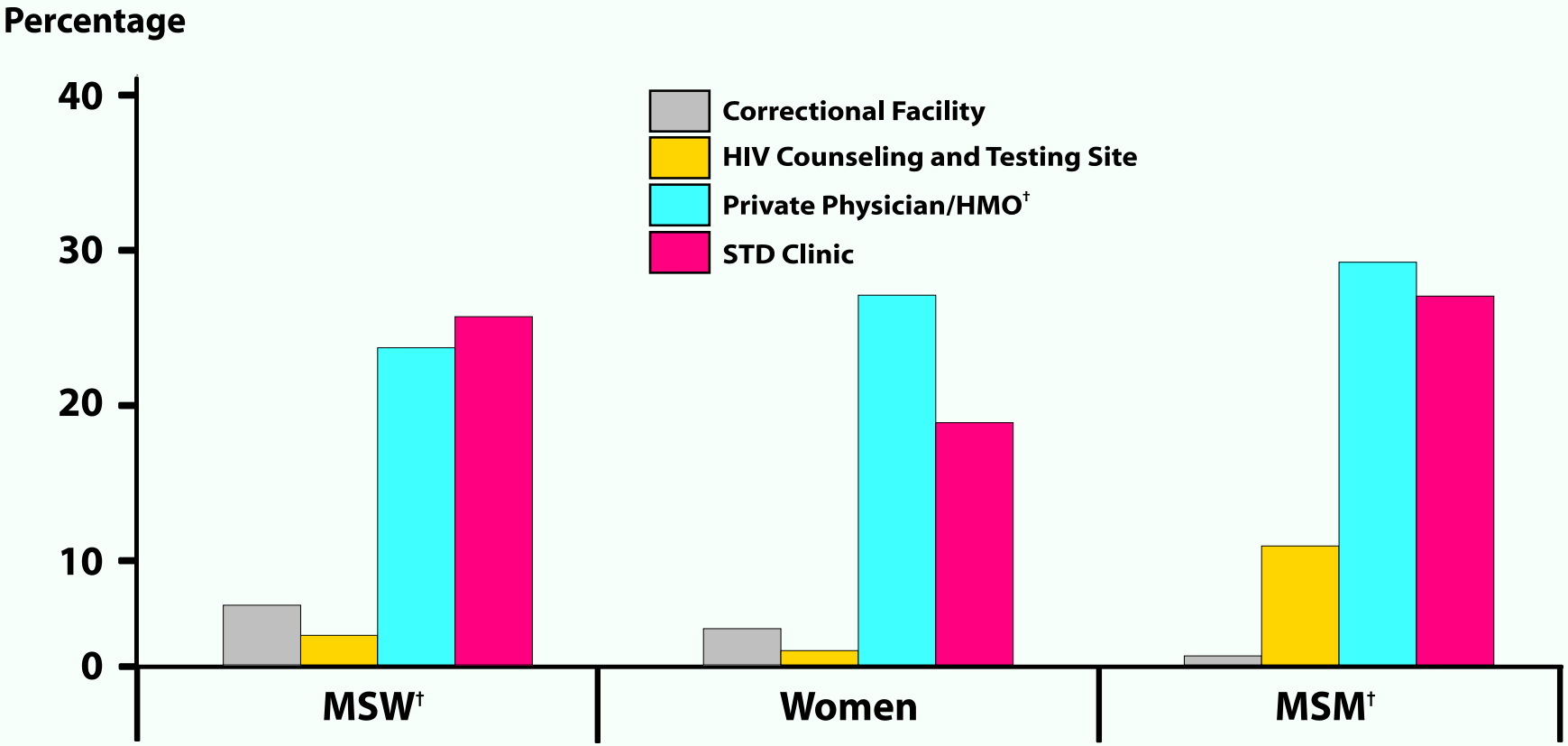
Primary and Secondary Syphilis — Reported Cases by Sex, Sexual Behavior, and HIV Status, 31 States*, 2015



* 31 states were able to classify ≥70% of reported cases of primary and secondary syphilis as MSW †, MSM †, or women and ≥70% of cases as HIV-positive or HIV-negative during 2015.

† MSM = men who have sex with men; MSW = men who have sex with women only.

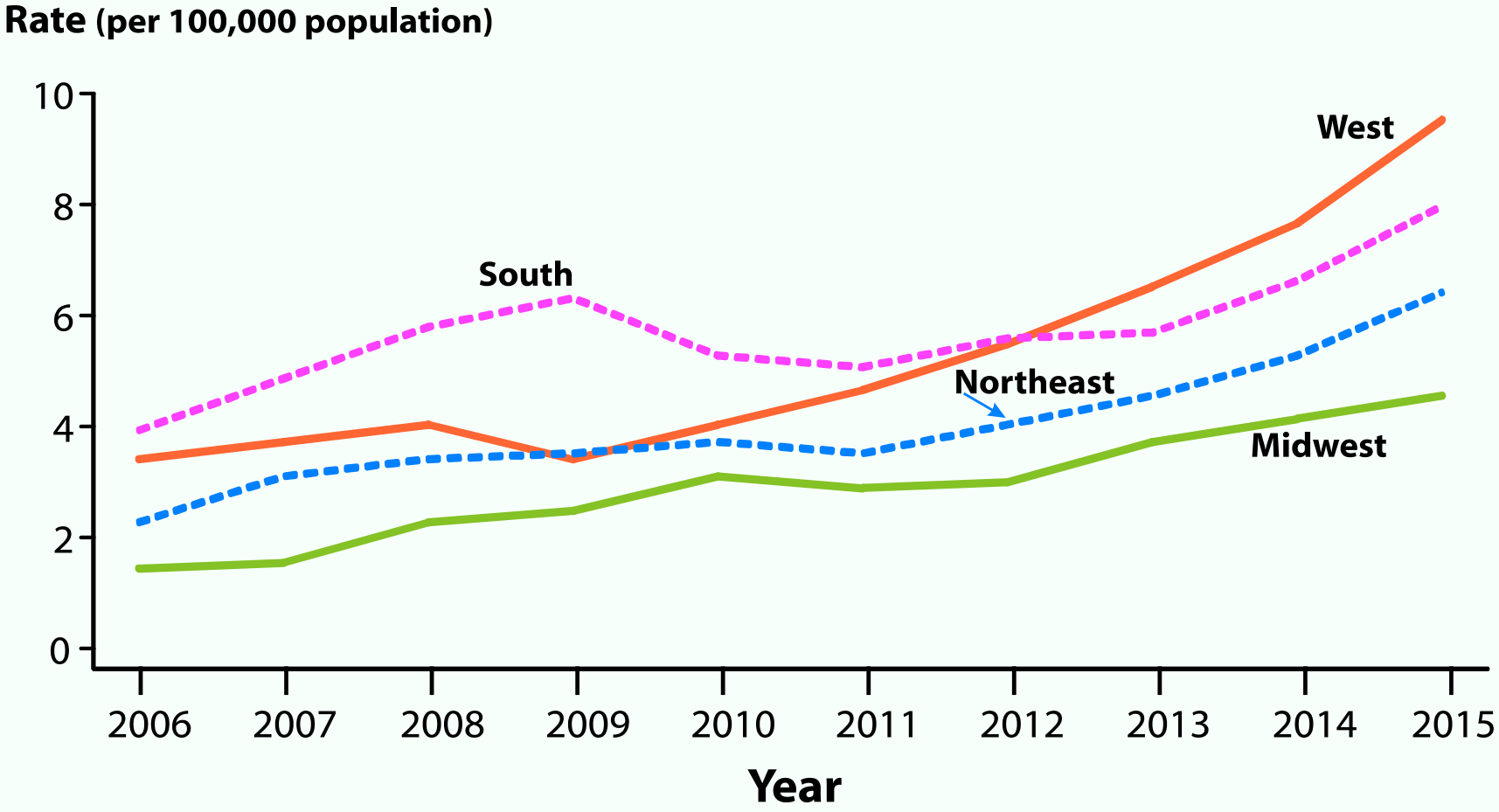
Primary and Secondary Syphilis — Percentage of Reported Cases* by Sex, Sexual Behavior, and Selected Reporting Sources, 2015



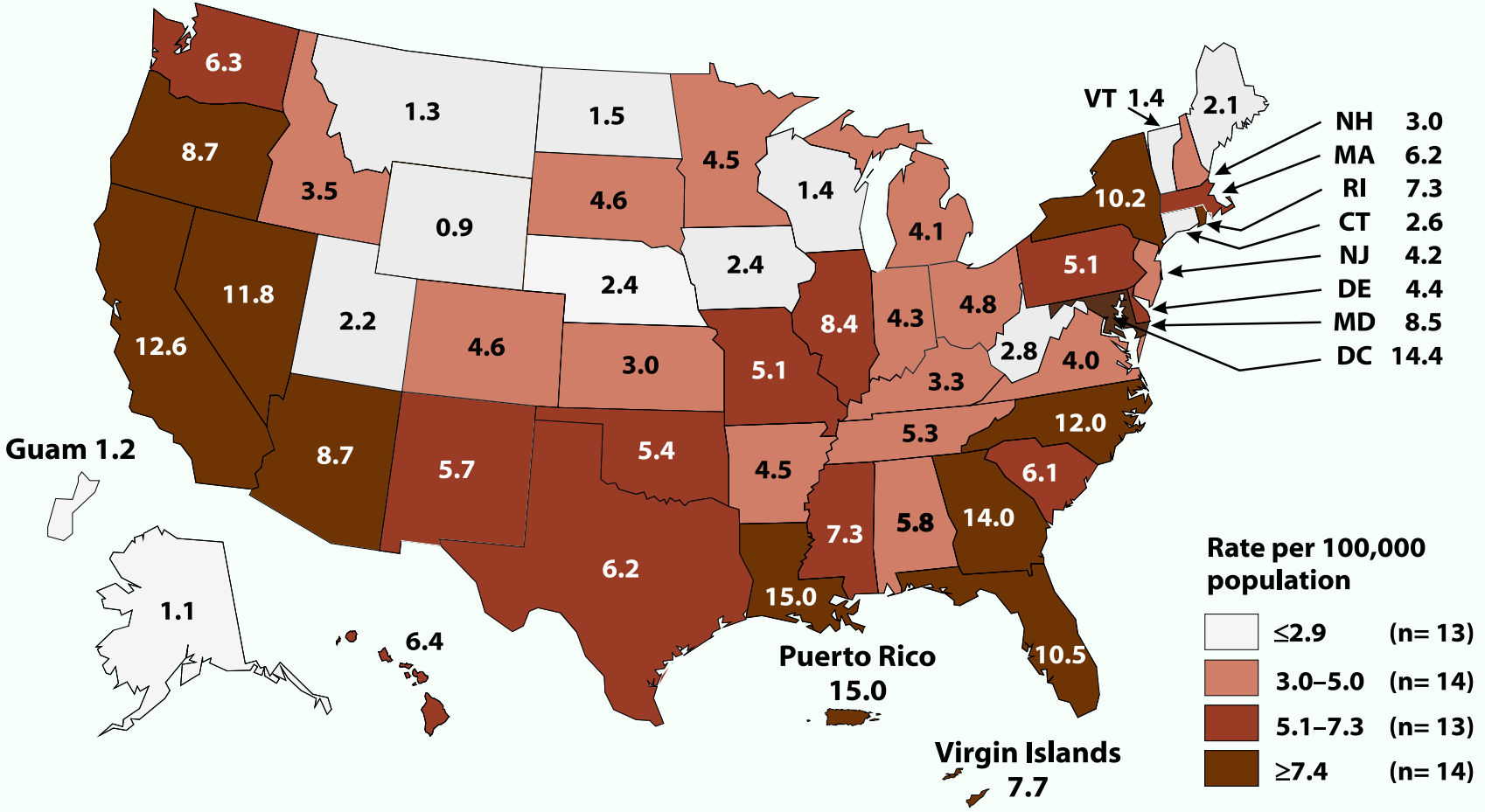
* Of all primary and secondary syphilis cases, 7.4% had a missing or unknown reporting source. Among all cases with a known reporting source, the reporting source categories presented represent 57.8% of cases; 42.2% were reported from sources other than those shown.

† HMO = health maintenance organization; MSM = Gay, bisexual, and other men who have sex with men (collectively referred to as MSM); MSW = Men who have sex with women only.

Primary and Secondary Syphilis — Rates of Reported Cases by Region, United States, 2006–2015



Primary and Secondary Syphilis — Rates of Reported Cases by State, United States and Outlying Areas, 2015



NOTE: The total rate of primary and secondary syphilis for the United States and outlying areas (Guam, Puerto Rico, and Virgin Islands) was 7.6 cases per 100,000 population.

Trends in Syphilis cases in the United States

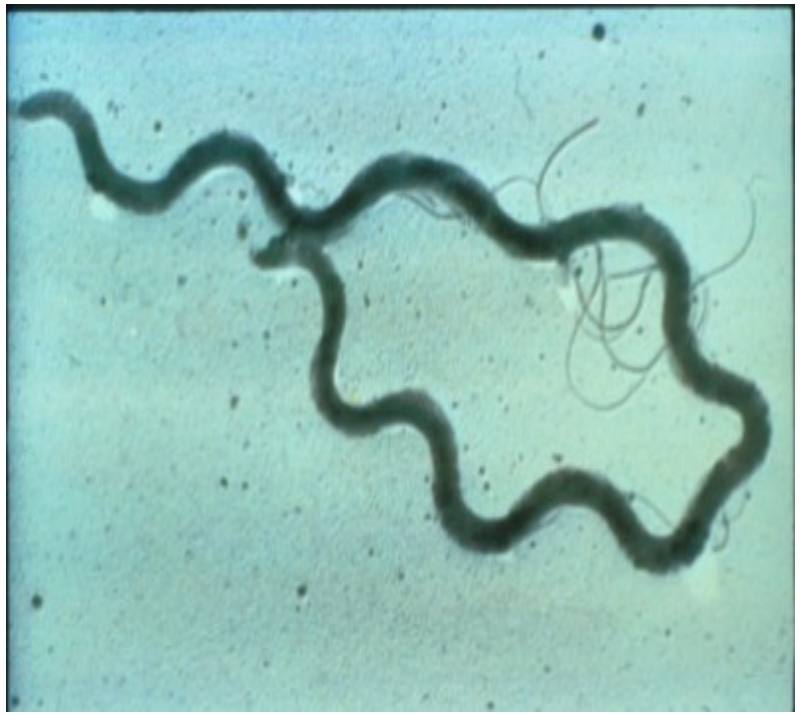
- In 1940s, syphilis was wildly distributed in the united states
- After the 1940s, there was a rapid decline with introduction of penicillin and public health prevention programs
- 1986 -90: 83% increase in incidence of primary and secondary syphilis
- 1990s: reported cases of syphilis declined 89.7% to an all-time low in 2000
- There were 23,872 new cases of P & S syphilis reported in 2015 and a 19 percent increase over 2014 and a record high

Current Trends in Syphilis Cases

- Remains a Public Health problem in the U.S
- High incident rate in the West Coast and Southern States
- MSM is an important high risk population
- Disproportionately affects ethnic minorities, especially African Americans
- Men and women ages 20 -30 are in high risk group

Syphilis

- Sexually transmitted infection
- Etiologic agent: Treponema pallidum
- Long thin spirochete
- Cannot culture in vitro
- Diagnosis is by serology or dark field microscopy
- Disease progresses in stages
- May become chronic without treatment



Pathogenesis / Transmission

- Penetration

  -T. pallidum enters the body via the skin and mucous membrane during sexual contact.

  -Transmitted from mother to fetus via the placenta during pregnancy

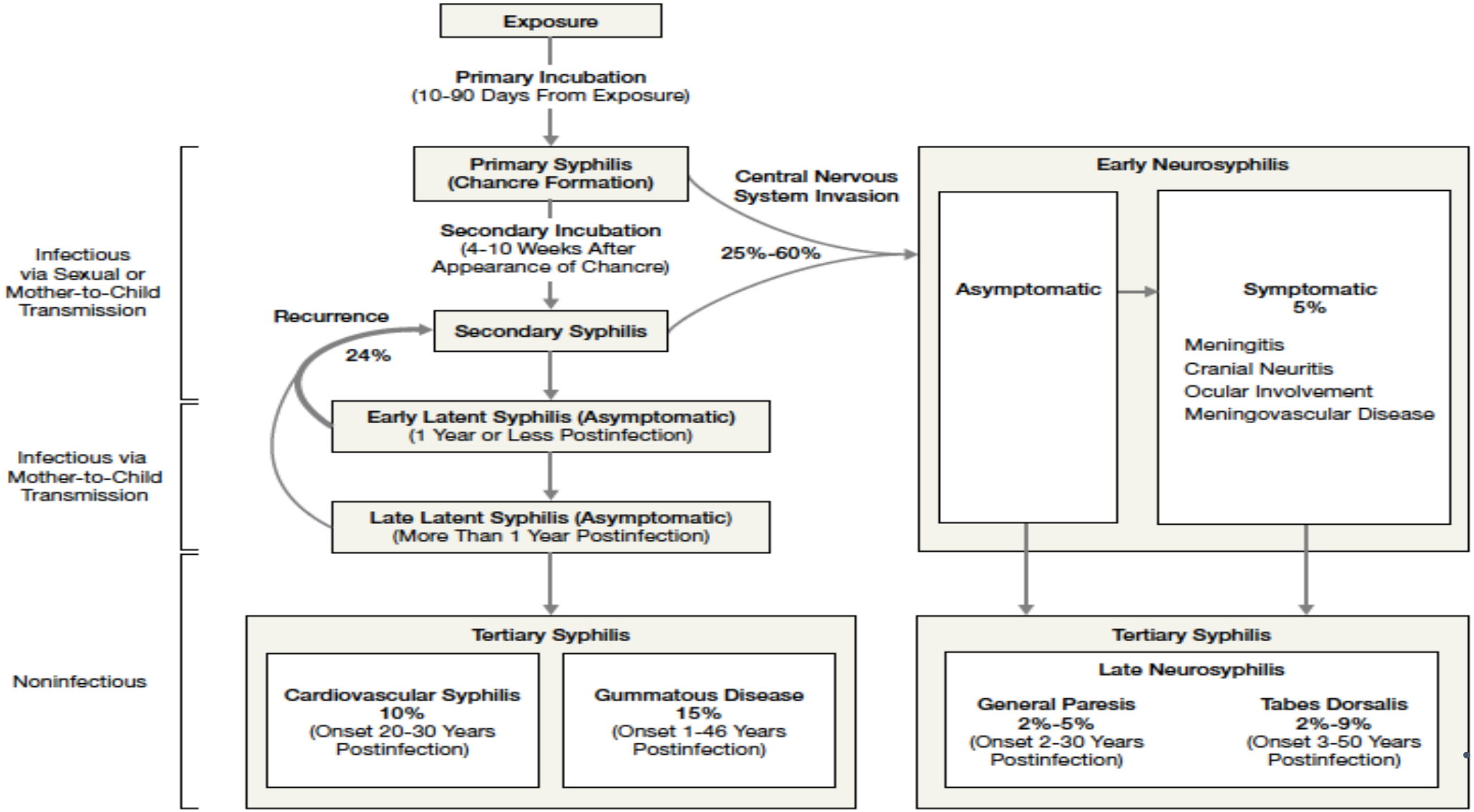
- Dissemination:

  -Travels via the circulatory system, including the lymphatic system and regional nodes

  -Invasion of the central nervous system can occur during any state of the disease

Most contagious during the primary and secondary stages

Natural History of Untreated Syphilis



Golden, MR et al
JAMA 2003; 290(11)
1510-1514

Primary Syphilis

Onset of the first symptom can range from 10 to 90 days, averaging 21 days.

The chancre is usually firm, round, small, and painless

The chancre lasts 3 to 6 weeks, and it heals without treatment.

Regional adenopathy –painless and bilateral

Serologic tests for syphilis may not ne positive during early primary stage

If adequate treatment is not administered, the infection progresses to the secondary stage.

Source: CDC: Public image Library

Secondary Syphilis

- Secondary lesions occur several weeks after the primary chancre appears; and may persist for weeks to months.
- Primary and secondary stages may overlap
- Mucocutaneous lesions most common
- Clinical Manifestations:
  - Rash (75%–100%)
  - Lymphadenopathy (50%–86%)
  - Malaise
  - Mucous patches (6%–30%)
  - Condylomata lata (10%–20%)
  - Alopecia (5%)
  - Liver and kidney involvement can occur
  - Splenomegaly is occasionally present
- Serologic tests are usually highest in titer during this stage.

Secondary Syphilis

Latent Syphilis

- Infection is suppressed.
- No lesions are clinically apparent
- Positive serologic test
- May occur between primary and secondary stages

Categories:

- Early latent <1 year duration
- Late latent > 1 year duration

Case study

- Jose is a 31 year old HM that was treated was diagnosed with HIV and secondary syphilis in 3/2014. His baseline RPR was RPR was 1:128.

He had rash on his palms, sole of his feet and inguinal LAD.

He was treated with Bicillin 2.4MU IM weekly for 3 weeks.

At 3, 6 and 9 months follow-up, his RPR was 1:64. He was retreated with Bicillin 2.4 MU weekly for 3 weeks.

His RPR was rechecked at 12 months was unchanged.

He c/o depression and mood swings. He was recently fired from his job.

Question

What do you think is happening to Jose and how will you address his syphilis titer result and depression

1. He is depressed. Refer him to the psychiatrist.
2. He may be suffering from neurosyphilis. Treat him again with Bicillin LA 2.4MU IM weekly for 3 weeks
3. He has signs of neurosyphilis and refer him for LP
4. Do nothing. Just watch him and repeat his RPR in 24 months

Neurosyphilis

- Occurs when Treponema pallidum invades the CNS
- May occur at any stage of syphilis
- Can be asymptomatic
- Early neurosyphilis – few months to few years following infection

  - clinical manifestations- acute syphilic meningitis, meningovascular syphilis (strokes), mental status changes, and ocular and auditory involvement
- Other neurologic manifestations may occur decades after infection.

  - general paresis, tabes dorsalis and ocular involvement

Neurosyphilis Criteria

- CSF WBC ≥ 20 cells/microliter + reactive CSF VDRL
- No single test can be used alone to diagnose neurosyphilis.
- VDRL-CSF: highly specific, but insensitive
- Diagnosis usually depends on the following factors:
  - Reactive serologic test results
  - Abnormalities of CSF cell count or protein
  - A reactive VDRL-CSF with or without clinical manifestations
- The VDRL-CSF is the standard serologic test., and when reactive in the absence of contamination of the CSF with blood, it is considered diagnostic for neurosyphilis. However, in early syphilis it can be of unknown prognostics significance.

Indication for CSF Exam

- Patients with syphilis who demonstrate any of the following criteria should have a prompt CSF evaluation:
- Neurologic or ophthalmic signs or symptoms
- Evidence of active tertiary syphilis (e.g., gummatous lesions)
- Treatment failure
- HIV infection with a CD4 count ≤350 and/or a nontreponemal serologic test titer of ≥1:32

Tertiary (Late) Syphilis

- Estimated 30% of untreated patients progress to tertiary stage in 1 to 20 years
- This is rare because of widespread availability and use of antibiotics.

Manifestations

-Gummatous lesions

-Cardiovascular syphilis

Question

Janice is a 23 year old female and 16 weeks gestation.

She is mother of one- 2 year old son. She is incarcerated for prostitution. She is in the clinic today for prenatal visit.

What labs would you order ?

1. HIV antibody test
2. Treponemal test and with reflex to RPR or RPR with reflex to TP-PA
3. UA and culture
4. Gonorrhea / chlamydia by DNA
5. All of the above

Congenital Syphilis

- Occurs when T. pallidum is transmitted from pregnant mother to her fetus
- May lead to stillbirth, neonatal death, deafness, neurologic impairment and bone deformities
- Transmission can occur at any stage of syphilis
- Fetal infection can occur during any trimester
- All pregnant women – screen 1St and early 3rd trimester.
- If no record of prior test, screen after delivery and prior to leaving the hospital. Screen all women with still births.

Source: CDC STD Awareness Month; 2017

Ocular Syphilis

- Screen for visual complaints in any patient at risk for syphilis
- Can involve almost any eye structure
- Can occur at any stage of syphilis
- All patients with syphilis and ocular complaints should receive urgent eye exam by an Eye specialist
- Can be associated with neurosyphilis
- CSF exam (LP) for any patient with syphilis and ocular complaints

Syphilis Testing

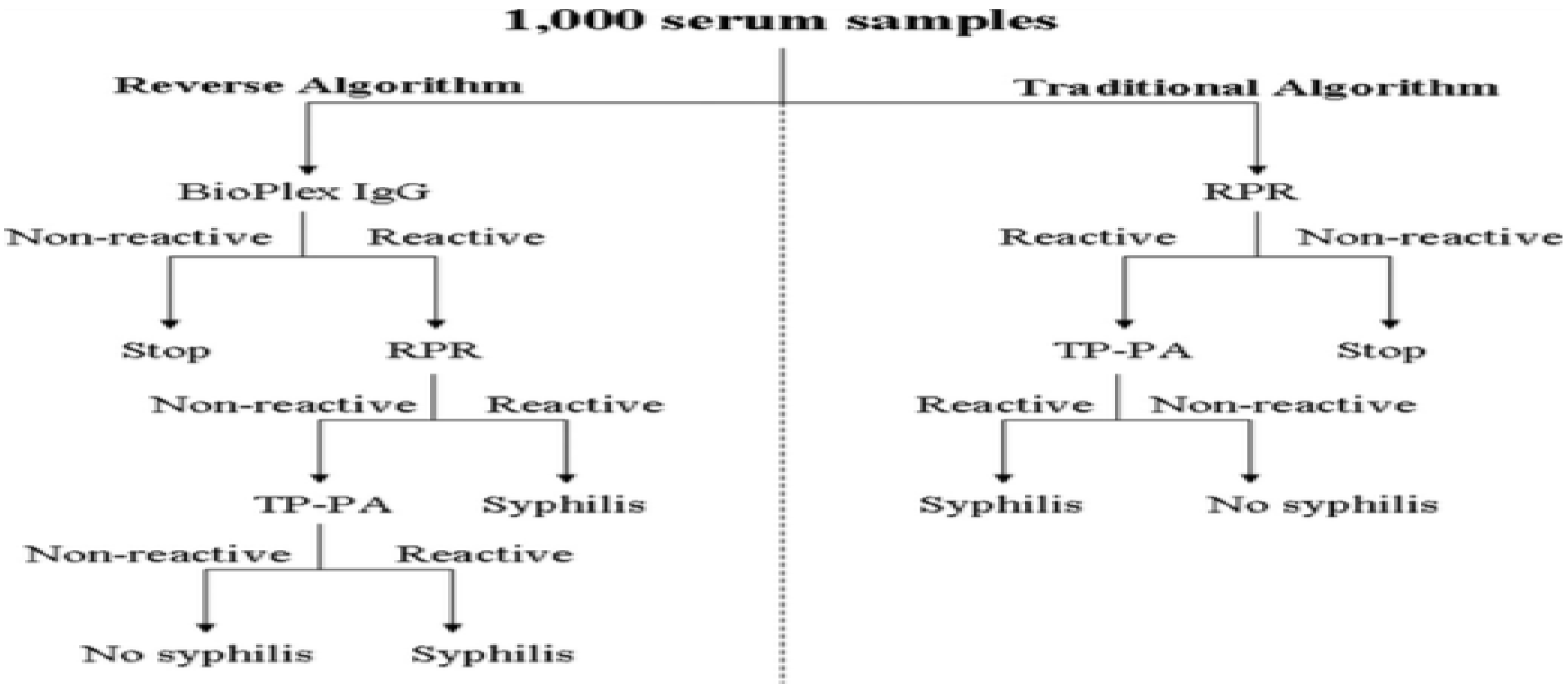
Nontreponemal testing

- VDRL- Veneral disease Research Laboratory
- RPR -Rapid Plasma Reagin
- TRUST – Toluidine red unheated serum test

Treponemal Testing

- FTA-ABS -Fluorescent Treponenal Absorbed Test
- TP-PA- T. Pallidum particle agglutination assay
- Various EIAs - Enzyme Immunoassays
  - -Trep-Chek
  - - Trep-sure
- CIAs Chemiluminenscence Immunoassays
  - - Liaison
  - -Architect

Traditional and Reverse Sequence Algorithms



Treatment of Syphilis.

Primary, Secondary or Early Latent Syphilis

- Benzathine penicillin G 2.4 million units intramuscularly in a single dose (Bicillin L-A®)
- **Late latent syphilis or syphilis of unknown duration**
  - Benzathine penicillin G 2.4 million units IM once weekly for 3 weeks
- **Tertiary syphilis with normal CSF examination**
  - Benzathine penicillin G 2.4 million units IM once weekly for 3 weeks

- If penicillin allergic
  - Doxycycline 100 mg orally twice daily for 14 days, or
  - Tetracycline 500 mg orally 4 times daily for 14 days

Therapy for Neuro Syphilis and ocular syphilis

- Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units intravenously every 4 hours or continuous infusion for 10 to14 days intravenously

- Alternative regimen (if compliance can be ensured)
  - Procaine penicillin 2.4 million units intramuscularly once daily

    PLUS
  - Probenecid 500 mg orally 4 times a day, both for 10 to14 days

Case Study: Remember Janice?

Her HIV test was positive: CD4 450 /28% and HIV VL 58,000 copies/ml

Treponemal IGG pos and RPR NR. Last Treponemal IGG was neg in 08/2015. MHA-TP is also positive. She is Pregnant and allergic to penicillin

How will you manage Janice ?

1. Janice is false positive for syphilis because she is pregnant.
2. Janice has early primary syphilis and should be treated with Doxy 100mg po bid for 14 days because she is allergic to PCN
3. Janice should be treated for presumptive syphilis. She needs to be desensitized and treated with PCN –G 2.4MU IM once

Therapy for Syphilis in Pregnancy

- Penicillin G is the only therapy with documented efficacy in pregnancy
- Treat based on the stage of infection.
- **Pregnant women who are skin-test-reactive to penicillin should be desensitized in the hospital and treated with penicillin G.**

Prozone Phenomenon

- False negative to HIV resting due to very high anti-body titer.
- An agglutination or precipitation reaction (antigen and antibody)
- Most often associated with secondary syphilis,

  HIV co-infection and Pregnancy

- Incidence of Prozone phenomenon estimated @ 0.2 to 2 percent and higher in HIV positive patients

Jarisch – Herxheimer Reaction

- Self-limited reaction to antitreponemal therapy
  - Fever, malaise, nausea/vomiting; may be associated with chills and exacerbation of secondary rash
- Occurs within 24 hours after therapy
- Not an allergic reaction to penicillin
- More frequent after treatment with penicillin and treatment of early syphilis
- Antipyretics can be used to manage symptoms, but they have not been proven to prevent this reaction.
- Pregnant women should be informed of this possible reaction, that it may precipitate early labor

Follow-Up after Treatment

- Primary or secondary syphilis
  - Clinical and serologic evaluation at 6 and 12 months.
  - Follow-up titers should be compared to the maximum or baseline nontreponemal titer obtained on day of treatment.
- Latent syphilis
  - Reexamine at 6, 12, and 24 months.
- HIV-infected patients
  - 3, 6, 9, 12 and 24 months for primary or secondary syphilis
  - 6, 12, 18, and 24 months for latent syphilis
- Neurosyphilis
  - Serologic testing as above
  - Repeat CSF examination at 6-month intervals until normal

Follow-up and Treatment Failure

- Persistent symptoms, or persistent titer elevation (less than 4 fold drop)
- Retest for HIV, if HIV negative initially
- Consider lumbar puncture
- Re-treat with benzathine penicillin G 2.4 million units IM once weekly for 3 weeks
- Neurosyphilis: if initial CSF pleocytosis, repeat LP at 6 months

Management of sexual contacts primary, secondary and early latent syphilis

Partners within 90 days of Diagnosis

- All sex partners within 90 days of diagnosis should be treated presumptively for early syphilis, even if serologic tests results are negative

Partners >90 days before Diagnosis

- Treat presumptively for early syphilis if serologic test results are not immediately available and follow-up is uncertain
- If serologic tests are positive- stage and treat based on clinical evaluation

CDC : 2015 Treatment Guidelines

Partner Notification

- Screen and examine long term partners of persons diagnosed syphilis
- Confidential notification for the following partners;

- For Primary syphilis
 -- contact 3 months plus the duration of symptoms
- For Secondary Syphilis
 -- contact within 6 months plus the duration of symptoms
- For Early Latent Syphilis
 -- Contact one year prior to diagnosis
-

Patient Counseling and Education

- Nature of the disease
- Transmission
- Treatment and follow-up
- Risk reduction

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Finally, I wish to thank everyone present for this presentation this morning.