

**Syphilis Management  
for Clinicians**

**Satellite Conference and Live Webcast  
Wednesday, January 7, 2015  
8:30 – 10:30 a.m. Central Time**

Produced by the Alabama Department of Public Health  
Video Communications and Distance Learning Division

**Faculty**

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**Program Objectives**

- Upon completion of this content, the learner will be able to:
  - List the stages of syphilis
  - Describe the signs and symptoms of syphilis
  - Discuss the impression criteria for determining treatment and follow - up

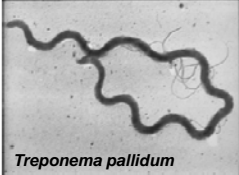
**Program Objectives**

- Describe clinical staging vs. surveillance DIS staging
- Explain the lab interpretation for reactive and non - reactive treponemal and non - treponemal test results

**Program Objectives**

- Describe the treatment for primary, secondary, early latent, late latent syphilis and contacts
- Explain required follow - up for symptomatic, asymptomatic, contacts and discordant lab results

**Syphilis Definition**

- Sexually acquired infection
- Etiologic agent: 
- Disease progresses in stages
- May become chronic without treatment

### Syphilis Transmission

- Sexual and vertical
- Most contagious to sex partners during the primary and secondary stages

### Microbiology

- Etiologic agent: *Treponema pallidum*, subspecies *pallidum*
  - Corkscrew - shaped, motile microaerophilic bacterium
  - Cannot be cultured in vitro
  - Cannot be viewed by normal light microscopy

### Stages of Syphilis

- Primary Syphilis: 2 to 4 weeks after exposure, chancre present, highly infectious
- Secondary Syphilis: 2 to 8 weeks after chancre disappears, highly infectious

### Stages of Syphilis

- Latent Syphilis – No signs and symptoms
  - Early Latent Syphilis <1 year duration
  - Late Latent Syphilis >1 year duration
  - Late Latent Syphilis of unknown duration

### Stages of Syphilis

- Neurosyphilis
  - Early neurosyphilis <1 year duration
  - Late neurosyphilis >1 year duration
- Tertiary Syphilis > 1 - 10 years
  - Neurosyphilis, cardiovascular and gummatous disease

### Stages of Syphilis

- Serofast state
  - After adequate therapy, VDRL / RPR decline, but always reactive

### Aspects of Syphilis Diagnosis

- Clinical history
- Physical examination
- Laboratory diagnosis

### Clinical History

- Assess
  - History of syphilis
  - Known contact to an early case of syphilis
  - Typical signs or symptoms of syphilis in the past 12 months
  - Most recent serologic test for syphilis

### Physical Examination

- Oral cavity
- Lymph nodes
- Skin of torso
- Palms and soles
- Genitalia and perianal area
- Neurologic examination
- Abdomen

### Laboratory Diagnosis

- The use of only one type of serologic test is insufficient for diagnosis
  - Darkfield (secretion from lesion)
  - Serologic Tests
    - Two types
      - Nontreponemal (qualitative and quantitative) VDRL, RPR, TRUST, USR

### Nontreponemal Serologic Tests

- Principles
  - Measure antibody directed against a cardiolipin - lecithin - cholesterol antigen
  - Not specific for *T. pallidum*

### Nontreponemal Serologic Tests

- Titers usually correlate with disease activity and results are reported quantitatively
- May be reactive for life, referred to as “serofast”

### Nontreponemal Serologic Tests

- Advantages
  - Rapid and inexpensive
  - Easy to perform and can be done in clinic or office
  - Quantitative
  - Used to follow response to therapy
  - Can be used to evaluate possible reinfection

### Nontreponemal Serologic Tests

- Disadvantages
  - May be insensitive in certain stages
  - False - positive reactions may occur
  - Prozone effect may cause a false - negative reaction (rare)

### Causes of False-Positive Reactions in Serologic Tests for Syphilis

Disease	RPR/VDRL	FTA-ABS	TP-PA
Age		Yes	
Autoimmune Diseases	Yes	Yes	
Cardiovascular Disease		Yes	Yes
Dermatologic Diseases	Yes	Yes	--
Drug Abuse	Yes	Yes	
Febrile illness	Yes		
Glucosamine/chondroitin sulfate		Possibly	
Leprosy	Yes	No	--
Lyme disease		Yes	
Malaria	Yes	No	
Pinta, Yaws	Yes	Yes	Yes
Recent Immunizations	Yes	--	--
STD other than Syphilis		Yes	

Source: Syphilis Reference Guide, CDC/National Center for Infectious Diseases, 2002

### Laboratory Diagnosis

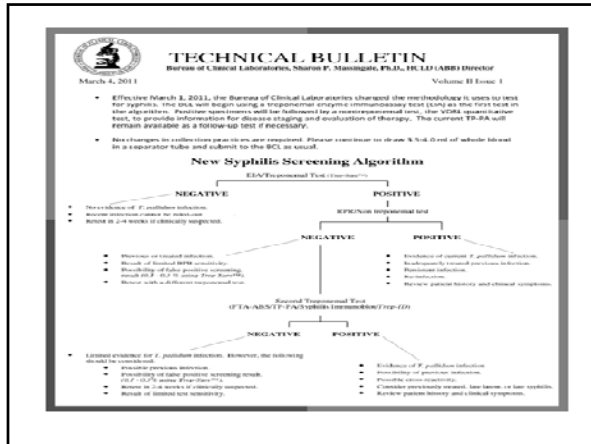
- Treponemal (qualitative) EIA, TP - PA, FTA - ABS, CIA

### Treponemal Serologic Tests

- Principles
  - Measure antibody directed against *T. pallidum* antigens
  - Qualitative
  - Usually reactive for life
  - Titers should not be used to assess treatment response

### Syphilis Screening at ADPH

- EIA
- VDRL
- TP - PA



**Managing Discordant Syphilis Test Results**

- Asymptomatic contact to early syphilis with non - reactive EIA
  - No further testing or clinical follow - up is required

**Managing Discordant Syphilis Test Results**

- Symptomatic patient / contact with non - reactive EIA or VDRL
  - Offer treatment as early syphilis
  - Repeat test within 2 - 4 weeks after treatment or upon return to the clinic

**Managing Discordant Syphilis Test Results**

- No history of previous adequate treatment with EIA or TP - PA reactive and VDRL non - reactive
  - Offer treatment
  - Repeat the test within 2 - 4 weeks or upon return to the clinic

**Managing Discordant Syphilis Test Results**

- Repeat VDRL non - reactive
  - No further testing or clinical follow - up required

**Clinical vs. Surveillance DIS Staging**

- Clinical
  - Purpose: Identify possible infection early and treat promptly to prevent spread
  - Key Points:
    - Clinical manifestations
    - EIA: ±

**Clinical vs. Surveillance  
DIS Staging**

- VDRL: ±
- TP - PA: ±
- **No clinical Manifestations**
- EIA: +
- VDRL: ±
- TP - PA: ±

**Clinical vs. Surveillance  
DIS Staging**

- **Surveillance DIS**
- **Purpose: Report to CDC and contact tracing**
- **Key Points:**
  - EIA: ±
  - VDRL: Tittered
  - TP - PA: +

**Impression Criteria:  
Primary Syphilis**


- **Consistent Clinical Exam Findings:**
  - **Genital or non-genital single or multiple, painless, rubbery ulcer(s)**
  - **or lesion(s) that is highly suspicious for syphilis chancre**

**OR**

**Impression Criteria:  
Primary Syphilis**


- **Darkfield positive lesion (If a Lab. Tech. is available in STD dedicated clinics)**

**Primary Syphilis  
Penile Chancre**



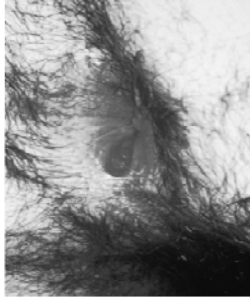
Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

**Primary Syphilis  
Labial Chancre**



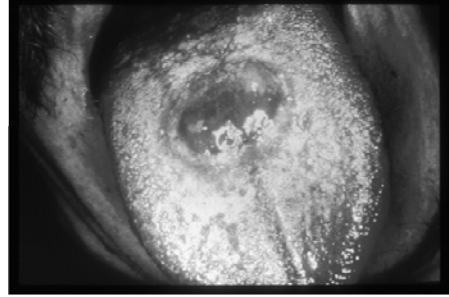
Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

### Primary Syphilis Perianal Chancre



Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

### Primary Syphilis Chancre of the Tongue



Source: CDC/ NCHSTP/ Division of STD Prevention /STD Clinical Slides

### Impression Criteria: Secondary Syphilis

- Any of the Following Clinical Exam Findings:
  - Generalized or localized cutaneous eruption without explanation, generalized lymphadenopathy
  - Palmar and / or plantar rash

### Impression Criteria: Secondary Syphilis

- Mucous patches on the tongue, oral cavity or lips
- Condyloma lata (moist, whitish - gray wart - like lesions)
- Alopecia
- Darkfield positive material from cutaneous or mucous membrane lesion

### Secondary Syphilis Papulosquamous Rash



Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

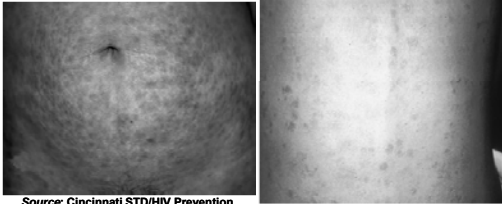
### Secondary Syphilis Palmar / Plantar Rash



Source: Seattle STD/HIV Prevention Training Center at the University of Washington, UW HSCER Slide Bank

Source: CDC/NCHSTP/Division of STD Prevention, STD Clinical Slides

### Secondary Syphilis Generalized Body Rash



Source: Cincinnati STD/HIV Prevention Training Center

Source: CDC/NCHSTP/Division of STD Prevention, STD Clinical Slides

#### Clinical Manifestations

### Secondary Syphilis Papulo - pustular Rash



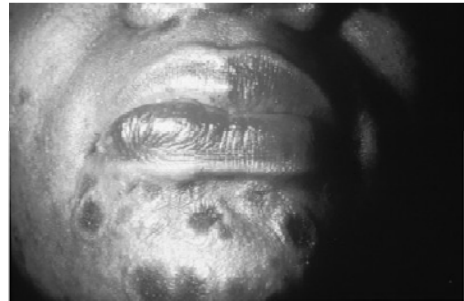
Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

### Secondary Syphilis Condylomata lata



Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

### Secondary Syphilis Nickel / Dime Lesions



Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

### Secondary Syphilis Alopecia



Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

### Impression Criteria: Latent Syphilis

- May occur between primary and secondary stages, between secondary relapses, and after secondary stage
- No symptoms or findings consistent with primary or secondary syphilis



**Impression Criteria:  
Latent Syphilis**

- **Categories:**
  - Early latent: <1 year duration
  - Late latent: ≥1 year duration

**Impression Criteria:  
Early Latent Syphilis**

- **Laboratory Findings:**
  - Reactive Syphilis - EIA and / or TP-PA, with / without reactive VDRL or RPR
- PLUS**
- **No symptoms or findings consistent with primary or secondary syphilis**
- PLUS**

**Impression Criteria:  
Early Latent Syphilis**

- **Any of the following within the past 12 months**
  - History of symptoms consistent with primary or secondary syphilis
  - OR Documented Serologic conversion

**Impression Criteria:  
Early Latent Syphilis**

- OR A >4 - fold increase in RPR or VDRL titer in a person who has previously received adequate treatment for a syphilis infection
- OR History of exposure to primary, secondary, or early latent syphilis
- OR Only possible exposure has been within the past 12 months

**Impression Criteria:  
Late Latent Syphilis**

- **Laboratory Findings:**
  - Reactive Syphilis - EIA and / or TP-PA with/without reactive VDRL or RPR
- PLUS**
- **No symptoms or findings consistent with primary or secondary syphilis**
- PLUS**

**Impression Criteria:  
Late Latent Syphilis**

- **Any of the following greater than 12 months in the past**
  - History of symptoms consistent primary or secondary syphilis
  - OR Documented serologic conversion

**Impression Criteria:  
Late Latent Syphilis**

- OR A >4 - fold rise in RPR / VDRL titer in a person who has previously received adequate treatment for a syphilis infection
- OR History of exposure to primary, secondary, or early latent syphilis
- OR No possible exposure within the past 12 months

**Latent Syphilis of Unknown Duration**

- Reactive Syphilis - EIA or TP - PA with / without reactive VDRL or RPR

PLUS

- No signs or symptoms consistent with primary or secondary syphilis

AND

**Latent Syphilis of Unknown Duration**

- No history of exposure to primary, secondary, or early latent syphilis or treatment in the past

AND

- Insufficient information to determine the duration of infection or the most likely time of exposure

**Neurosyphilis**

- Occurs when *T. pallidum* invades the central nervous system (CNS)
- May occur at any stage of syphilis
- Can be asymptomatic

**Neurosyphilis**

- Early neurosyphilis
  - Clinical manifestations can include acute syphilitic meningitis, meningovascular syphilis, and ocular involvement

**Neurosyphilis**

- Late neurosyphilis
  - Clinical manifestations can include general paresis, tabes dorsalis, and ocular involvement

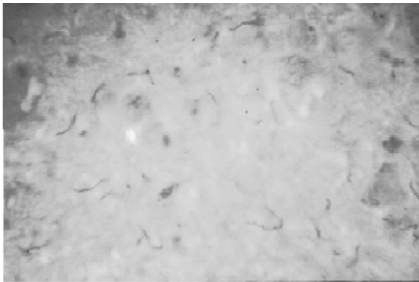
### Indications for CSF Examination

- 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)

### Indications for CSF Examination

- Treatment failure
- HIV infection with a CD4 count  $\leq 350$  and / or a nontreponemal serologic test titer of  $\geq 1:32$

### Neurosyphilis Spirochetes in Neural Tissue



Silver stain, 950x

Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

### Tertiary (Late) Syphilis

- Approximately 30% of untreated patients progress to the tertiary stage within 1 to 20 years
- Rare because of the widespread availability and use of antibiotics

### Tertiary (Late) Syphilis

- Manifestations
  - Gummatous lesions
  - Cardiovascular syphilis
  - Neurosyphilis

### Late Syphilis - Serpiginous Gummata of Forearm



Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

### Late Syphilis Ulcerating Gumma



Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

### Late Syphilis Cardiovascular



Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

### Syphilis Treatment

Syphilis	Recommended Regimens / Dose / Route	Alternative Regimens
Primary, Secondary, Early Latent and Sex Partners	Benzathine penicillin G 2.4 million units IM in a single dose.	
Not pregnant with True Penicillin Allergy		Doxycycline 100 mg PO BID x 14 days OR Tetracycline 500 mg PO QID x 14 days
Late latent/latent of unknown duration	Benzathine penicillin G 2.4 million units IM x 3 weeks	
Not pregnant with True Penicillin Allergy		Doxycycline 100 mg PO BID x 28 days OR Tetracycline 500 mg PO QID x 28 days

### Syphilis Treatment

Syphilis / Pregnant	Recommended Regimens / Dose / Route	Alternative Regimen
Primary, Secondary, Early Latent and Sex Partners	Benzathine penicillin G 2.4 million units IM in a single dose	
Late latent/latent of unknown duration	Benzathine penicillin G 2.4 million units IM x 3 weeks	
True Penicillin Allergy	<b>MUST BE REFERRED TO A HOSPITAL FOR DESENSITIZATION</b>	

### Referral for Management

- All pregnant patients with “true penicillin” allergy for desensitization
- Patients with suspected neurosyphilis, tertiary syphilis or congenital syphilis for treatment

### When to Offer Presumptive Treatment

- Symptomatic Patients
- Asymptomatic Patients
- Contacts

### **Treat Symptomatic Patients**

- With signs and symptoms consistent with primary or secondary regardless of the syphilis serologic test results should be treated

### **Treat Asymptomatic Patients**

- Who have reactive syphilis (EIA and / or TP - PA) with / without reactive (VDRL / RPR) plus any of the following should be treated based upon the stage of the disease:
  - History of symptoms consistent with primary or secondary syphilis
  - OR

### **Treat Asymptomatic Patients**

- History of recent exposure to primary or secondary syphilis or reinfection OR
- Inadequate serologic response to past treatment OR
- No history of past adequate treatment OR

### **Treat Asymptomatic Patients**

- No test results available to compare with previous test results OR
- $\geq 4$  - fold increase in VDRL / RPR titer in a patient with history of past adequate treatment

### **Treat Contacts**

- To Primary, Secondary, or Early Latent Syphilis should be treated regardless of the syphilis serologic test results
- With verbal history or DIS referral of a patient who is a contact to Primary, Secondary, or Early Latent Syphilis regardless of the syphilis serologic test results

### **Treat Contacts**

- To Late Latent Syphilis or Latent Syphilis of Unknown Duration if the treponemal test result (EIA and / or TP - PA) is reactive, with / without reactive non - treponemal (VDRL / RPR) test results

### **Syphilis Patient Follow-up**

- Evaluate signs and symptoms
- Weekly penicillin therapy
- Confirm syphilis infection
- Response to treatment

### **Follow-up for Treated Primary and Secondary Syphilis**

- Clinical evaluation: 2 Weeks
  - Clinical manifestation with doxycycline or tetracycline treatment
- Serological Testing:
  - At 6 and 12 months after treatment with penicillin therapy

### **Follow-up for Treated Primary and Secondary Syphilis**

- At 1, 3, 6, 9, 12 and 24 months after treatment with doxycycline or tetracycline treatment and HIV infected patients

### **Follow-up Treatment for Latent (Early or Late) Syphilis or Syphilis of Unknown Duration**

- Treatment:
  - Every week for three weeks for penicillin therapy
- Serological Testing:
  - At 6, 12, and 24 months after treatment

### **Response to Syphilis Treatment**

- Adequate response
  - Primary and secondary syphilis
    - Decline in VDRL / RPR titer 2 dilutions (4 fold) within 6 months after therapy

### **Response to Syphilis Treatment**

- Latent (early or late) syphilis
  - Decline in VDRL / RPR titer 2 dilutions (4 fold) within 6 months after therapy
- Inadequate response
  - Rise in VDRL / RPR titer 2 dilutions (4 fold) or greater rise since initiation of therapy

**Intervention for Inadequate Response**

- Consider reinfection if risk of re - exposure exists
  - Repeat therapy
- Consider treatment failure if oral therapy was used or patient is HIV Positive


**Intervention for Inadequate Response**

- Refer patient for CSF exam, if needed
- Re - treat all stages as late latent syphilis, if risk for re - exposure is low and the presence of neurosyphilis has been ruled out

**Conclusion**

- Syphilis Management:
  - Diagnosis
    - Clinical Manifestations
    - Lab test results
  - Staging
  - Treatment
  - Follow - up
  - Clinical and surveillance staff TEAM

**What Is On Your Mind?**



**Reference**

- Alabama Bureau of Clinical Laboratories, Alabama Department of Public Health (2011). New syphilis screening algorithm. Technical Bulletin(II)1
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- Centers for Disease Control and Prevention (2010). Sexually transmitted diseases treatment guidelines. Morbidity and Mortality Weekly Report, 59(12), 26-39.
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