Revisions to the Syphilis Surveillance Case Definitions, 2018

Sarah Kidd, MD, MPH
Medical Epidemiologist
Division of STD Prevention
Centers for Disease Control and Prevention

November 16, 2017
Objectives of Syphilis Surveillance

- Monitor syphilis transmission (new syphilis infections)
  - Count Primary & Secondary (or all Early) cases

- Monitor total syphilis diagnoses
  - Count total (all stages) syphilis cases

- Monitor important clinical manifestations of syphilis
  - E.g., neurosyphilis
Current (2014–2017) Syphilis Case Reporting

- Must report a case as one of the following surveillance stages
  - Primary
  - Secondary
  - Early Latent
  - Late Latent
  - Late with Clinical Manifestations

- Additional variable for all cases: “Neurologic involvement?”
  - Refers to Neurosyphilis case definition
  - Answered as “Yes, confirmed,” “Yes, probable,” “No,” or “Unknown”
Why Make Revisions?

- Inability to track Ocular Syphilis and other important clinical manifestations
- Inconsistencies in the current (2014) guidance for reporting “Neurologic Involvement” (Neurosyphilis)
Syphilis Surveillance Case Definition Revisions 2018

- Revisions related to reporting surveillance stages
- Revisions related to reporting clinical manifestations
  - New clinical manifestations variables
Syphilis Case Definition Revisions for 2018: Stages

- "Secondary Syphilis" still requires BOTH reactive treponemal test AND reactive nontreponemal test, but no longer requires a titer $\geq 1:4$

- Nomenclature changes to remove "latent" from surveillance stages
  - "Early Latent Syphilis" $\rightarrow$ "Early Non-Primary, Non-Secondary Syphilis"
  - "Late Latent Syphilis" $\rightarrow$ "Unknown Duration or Late Syphilis"

- "Late Syphilis with Clinical Manifestations" omitted
  - Report these cases as "Unknown Duration or Late Syphilis"
  - Report the late clinical manifestations in the case report data with the new variables
New Clinical Manifestation Variables in 2018

- Any case can be reported with one or more of the following
  - Neurologic Manifestations (verified/likely/possible/no/unknown)
  - Ocular Manifestations (verified/likely/possible/no/unknown)
  - Otic Manifestations (verified/likely/possible/no/unknown)
  - Late Clinical Manifestations (verified/likely/no/unknown)

- Definitions/guidance in the Position Statement
Review of Syphilis Stage Definitions
Primary Syphilis: Clinical Description

- A stage of infection with *Treponema pallidum* characterized by one or more ulcerative lesions (e.g., chancre), which might differ considerably in clinical appearance
Primary Syphilis: Case Classification

- **Probable:**
  - A case that meets the **clinical description** of primary syphilis with a **reactive serologic test**

- **Confirmed:**
  - A case that meets the **clinical description** of primary syphilis with demonstration of *T. pallidum* in a clinical specimen by **darkfield microscopy** or by PCR or equivalent direct molecular methods
Secondary Syphilis: Clinical Description

- A stage of infection with *Treponema pallidum* characterized by localized or diffuse mucocutaneous lesions (e.g., rash), often with generalized lymphadenopathy. Other signs can include mucous patches, condyloma lata, and alopecia. The primary ulcerative lesion may still be present.
Secondary Syphilis: Case Classification

- **Probable:**
  - A case that meets the **clinical description** of secondary syphilis with a **reactive nontreponemal test** AND a **reactive treponemal test**

- **Confirmed:**
  - A case that meets the **clinical description** of secondary syphilis with demonstration of *T. pallidum* in a clinical specimen by **darkfield microscopy** or by PCR or equivalent direct molecular methods
Early Non-Primary, Non-Secondary Syphilis: Clinical Description

- A stage of infection with *Treponema pallidum* in which initial infection has occurred within the previous 12 months, but there are no signs or symptoms of primary or secondary syphilis.
Early Non-Primary, Non-Secondary Syphilis: Case Classification (Paraphrased)

- **Probable:**
  - A case with
    1. No signs/symptoms of primary or secondary syphilis
    2. Evidence of current infection*
    3. Evidence of having acquired infection within last 12 months (see next slide)

*Evidence of current infection:
- No prior history of syphilis AND current reactive nontreponemal test AND current reactive treponemal test
- A prior history of syphilis with a current nontreponemal titer demonstrating a ≥4-fold increase from the last titer, unless there is evidence that this increase was not sustained >2 weeks
Evidence of Having Acquired Infection within Last 12 Months:

- Documented seroconversion of nontreponemal or treponemal test in last 12 months
- ≥4-fold increase in nontreponemal titer within last 12 months (unless increase is not sustained)
- History of symptoms of primary or secondary syphilis within last 12 months
- History of sex partner with primary, secondary, or early non-primary non-secondary syphilis within last 12 months
- Sexual debut within last 12 months
Unknown Duration or Late Syphilis: Clinical Description

- A stage of infection with *Treponema pallidum* in which initial infection has occurred >12 months previously OR in which there is insufficient evidence to conclude that infection was acquired during the previous 12 months.
Unknown Duration or Late Syphilis: Case Classification (Paraphrased)

- **Probable:**
  - A case with
    - (1) No signs/symptoms of primary or secondary syphilis  
      AND
    - (2) Evidence of current infection*
      AND
    - (3) **No** evidence of having acquired infection within last 12 months

*Evidence of current infection:
- No prior history of syphilis AND current reactive nontreponemal test AND current reactive treponemal test  
  OR
- A prior history of syphilis with a current nontreponemal titer demonstrating a $\geq 4$-fold increase from the last titer, unless there is evidence that this increase was not sustained $>2$ weeks  
  OR
- Clinical signs/symptoms/labs that meet the likely or verified criteria for neurologic, ocular, otic, or late clinical manifestations
New Clinical Manifestations Variables
New Clinical Manifestations Variables

- Variables
  - Neurologic Manifestations
    - Verified, Likely, Possible, No, Unknown
  - Ocular Manifestations
    - Verified, Likely, Possible, No, Unknown
  - Otic Manifestations
    - Verified, Likely, Possible, No, Unknown
  - Late Clinical Manifestations
    - Verified, Likely, No, Unknown

- Any case can report 1 or more of these manifestations
Clinical Manifestations Variables: General Principles

- Must have evidence of syphilitic infection
  - Reactive treponemal AND nontreponemal tests

- Must have signs/symptoms (or lesions) consistent with clinical description without other known causes for these abnormalities
  - Clinical judgement, somewhat subjective

- “Possible” classification only requires the above 2 criteria be met

- “Likely” and “Verified” classifications require additional evidence
Neurologic Manifestations: Summary

- Serologic tests + signs/symptoms → POSSIBLE
- Serologic tests + signs/symptoms + elevated CSF protein or WBCs → LIKELY
- Serologic tests + signs/symptoms + positive CSF VDRL → VERIFIED
Ocular Manifestations: Summary

- Serologic tests + signs/symptoms $\rightarrow$ POSSIBLE

- Serologic tests + signs/symptoms
  + diagnosis by ophthalmologist $\rightarrow$ LIKELY

- Serologic tests + signs/symptoms
  + ocular fluid positive by darkfield or PCR $\rightarrow$ VERIFIED
Otic Manifestations: Summary

- Serologic tests + signs/symptoms $\rightarrow$ POSSIBLE

- Serologic tests + signs/symptoms
  + diagnosis by otolaryngologist $\rightarrow$ LIKELY

- Serologic tests + signs/symptoms
  + inner ear fluid positive by darkfield or PCR $\rightarrow$ VERIFIED
LATE Clinical Manifestations: Clinical Description

- Inflammatory lesions of
  - Cardiovascular system
  - Skin
  - Bone
  - Other tissue

- Certain neurologic manifestations
  - General paresis
  - Tabes dorsalis
LATE Clinical Manifestations: Summary

- Serologic tests + characteristic lesions → LIKELY

- Serologic tests + characteristic lesions
  + special stains/PCR/histology → VERIFIED
LATE Clinical Manifestations: Summary

- Serologic tests + characteristic lesions $\rightarrow$ LIKELY

- Serologic tests + characteristic lesions
  + special stains/PCR/histology $\rightarrow$ VERIFIED

- Serologic tests + signs/symptoms of late neurosyphilis
  + meets criteria for likely neuro manifestations $\rightarrow$ LIKELY

- Serologic tests + signs/symptoms of late neurosyphilis
  + meets criteria for verified neuro manifestations $\rightarrow$ VERIFIED
Summary of Clinical Manifestations Variables

- Must have reactive serologic tests + signs/symptoms (or lesions)
Summary of Clinical Manifestations Variables

- Must have reactive serologic tests + signs/symptoms (or lesions)
- Things that might indicate “VERIFIED”
  - CSF: VDRL positive (Neuro)
  - Ocular fluid: detection of *T. pallidum* by darkfield or PCR (Ocular)
  - Inner ear fluid: detection of *T. pallidum* by darkfield or PCR (Otic)
  - Tissues/lesions: detection of *T. pallidum* by stains or PCR (Late)
Summary of Clinical Manifestations Variables

- Must have reactive serologic tests + signs/symptoms (or lesions)
- Things that might indicate “VERIFIED”
  - CSF: VDRL positive (Neuro)
  - Ocular fluid: detection of *T. pallidum* by darkfield or PCR (Ocular)
  - Inner ear fluid: detection of *T. pallidum* by darkfield or PCR (Otic)
  - Tissues/lesions: detection of *T. pallidum* by stains or PCR (Late)
- Things that might indicate “LIKELY”
  - CSF: elevated protein or WBC (Neuro)
  - Ophthalmologist diagnosis of Ocular Syphilis
  - Otolaryngologist diagnosis of Otosyphilis
  - Characteristic lesions of Late Syphilis
Syphilis Surveillance Case Definitions, 2018

- Must report a case as one of the following surveillance stages
  - Primary
  - Secondary
  - Early Non-Primary, Non-Secondary
  - Unknown Duration or Late

- For Neurosyphilis, Ocular Syphilis, Otosyphilis, or Late Clinical Manifestations (Tertiary Syphilis)
  - Report case as one of the above surveillance stages
  - Note the clinical manifestations using the new variables
Questions and Discussion

Sarah Kidd
skidd@cdc.gov

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
From CDC’s 2003 Recommendations on Public Health Surveillance of Syphilis in the U.S.:

“Syphilis cases should be categorized and reported by stage at the time of initial examination (which is often the time of initial specimen collection), not at the time of treatment or interview.”
Infection of the central nervous system with *T. pallidum*, as evidenced by manifestations including syphilitic meningitis, meningovascular syphilis, general paresis, including dementia, and tabes dorsalis
Neurologic Manifestations – Verified

- Reactive nontreponemal and treponemal serologic tests
  AND
- Clinical signs/symptoms consistent with neurosyphilis without other known causes for these clinical abnormalities
  AND
- Reactive VDRL in CSF in the absence of grossly bloody contamination of the CSF
Neurologic Manifestations - Likely

- Reactive nontreponemal and treponemal serologic tests
  
  AND

- Clinical signs/symptoms consistent with neurosyphilis without other known causes for these clinical abnormalities
  
  AND

- Elevated CSF protein (>50 mg/dL²) or CSF leukocyte count (>5 white blood cells/cubic mm) in the absence of other known causes for these abnormalities
Neurologic Manifestations – Possible

- Reactive nontreponemal and treponemal serologic tests
  
  AND

- Clinical signs/symptoms consistent with neurosyphilis without other known causes for these clinical abnormalities

- *No CSF criteria*
Neurologic Manifestations: Summary

- Serologic tests + signs/symptoms → POSSIBLE

- Serologic tests + signs/symptoms + elevated CSF protein or WBCs → LIKELY

- Serologic tests + signs/symptoms + positive CSF VDRL → VERIFIED
OCULAR Manifestations: Clinical Description

- Infection of any eye structure with *T. pallidum*, as evidenced by manifestations including posterior uveitis, panuveitis, anterior uveitis, optic neuropathy, and retinal vasculitis. Ocular syphilis may lead to decreased visual acuity including permanent blindness.
Ocular Manifestations – Verified

- Reactive nontreponemal and treponemal serologic tests

  AND

- Clinical signs/symptoms consistent with ocular syphilis without other known causes for these clinical abnormalities

  AND

- Demonstration of *T. pallidum* in aqueous or vitreous fluid by darkfield microscopy, or by PCR or equivalent direct molecular methods.
Ocular Manifestations – Likely

- Reactive nontreponemal and treponemal serologic tests

  AND

- Clinical signs/symptoms consistent with ocular syphilis without other known causes for these clinical abnormalities

  AND

- Findings on exam by an ophthalmologist that are consistent with ocular syphilis in the absence of other known causes for these abnormalities
Ocular Manifestations – Possible

- Reactive nontreponemal and treponemal serologic tests

AND

- Clinical signs/symptoms consistent with ocular syphilis without other known causes for these clinical abnormalities

- No additional criteria
Ocular Manifestations: Summary

- Serologic tests + signs/symptoms → POSSIBLE

- Serologic tests + signs/symptoms + diagnosis by ophthalmologist → LIKELY

- Serologic tests + signs/symptoms + ocular fluid positive by darkfield or PCR → VERIFIED
Infection of the cochleovestibular system with *T. pallidum*, as evidenced by manifestations including sensorineural hearing loss, tinnitus, and vertigo.
Otic Manifestations – Verified

- Reactive nontreponemal and treponemal serologic tests

AND

- Clinical signs/symptoms consistent with otosyphilis without other known causes for these clinical abnormalities

AND

- Demonstration of *T. pallidum* in inner ear fluid by darkfield microscopy, or by PCR or equivalent direct molecular methods
Otic Manifestations – Likely

- Reactive nontreponemal and treponemal serologic tests
  
  AND

- Clinical signs/symptoms consistent with otosyphilis without other known causes for these clinical abnormalities
  
  AND

- Findings on exam by an otolaryngologist that are consistent with otosyphilis in the absence of other known causes for these abnormalities
Otic Manifestations – Possible

- Reactive nontreponemal and treponemal serologic tests

AND

- Clinical signs/symptoms consistent with otosyphilis without other known causes for these clinical abnormalities

- No additional criteria
Otic Manifestations: Summary

- Serologic tests + signs/symptoms → POSSIBLE

- Serologic tests + signs/symptoms
  + diagnosis by otolaryngologist → LIKELY

- Serologic tests + signs/symptoms
  + inner ear fluid positive by darkfield or PCR → VERIFIED
LATE Clinical Manifestations: Clinical Description

- Inflammatory lesions of
  - Cardiovascular system
  - Skin
  - Bone
  - Other tissue

- Certain neurologic manifestations
  - General paresis
  - Tabes dorsalis
Late Clinical Manifestations – Verified (Part 1 – For Late Non-Neurologic Manifestations)

- Reactive nontreponemal and treponemal serologic tests
  AND
- Characteristic abnormalities or lesions of the cardiovascular system, skin, bone, or other tissue in the absence of other known causes of these abnormalities
  AND
- Demonstration of *T. pallidum* in late lesions by special stains or equivalent methods, or by PCR or equivalent direct molecular methods or by demonstration of pathologic changes that are consistent with *T. pallidum* infection on histologic examination of late lesions
Late Clinical Manifestations – Verified (Part 2 – For Late Neurologic Manifestations)

- Reactive nontreponemal and treponemal serologic tests

  AND

- Clinical signs and symptoms consistent with late neurologic manifestations of syphilis (e.g., general paresis, including dementia, or tabes dorsalis) in a case that meets the criteria for verified neurologic manifestations
Late Clinical Manifestations - Likely

- Reactive nontreponemal and treponemal serologic tests
  AND EITHER

- Characteristic abnormalities or lesions of the cardiovascular system, skin, bone, or other tissue in the absence of other known causes of these abnormalities
  OR

- Clinical signs and symptoms consistent with late neurologic manifestations of syphilis (e.g., general paresis, including dementia, or tabes dorsalis) in a case that meets the criteria for likely neurologic manifestations