Adult Syphilis Staging
CSTE Webinar – December 2020

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Outline for Webinar

- *Treponema pallidum*
- Clinical vs surveillance staging
- Review of types of syphilis tests
- Review of syphilis stage definitions
- Fundamentals of staging
- Practice cases
Today’s Talk Will Not Review Clinical Manifestation Variables Implemented 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)
Today’s Talk Will Not Review Clinical Manifestation Variables Implemented 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:

▪ Prior manifestations webinar:
Today’s Talk Will Not Review Clinical Manifestation Variables Implemented in 2018

Stage:
- Confirmed Primary Syphilis
- Probable Primary Syphilis
- Confirmed Secondary Syphilis
- Probable Secondary Syphilis
- Early non-primary, non-secondary
- Unknown duration or late
Today’s Talk Will Not Review Clinical Manifestation Variables Implemented in 2018

Stage:
- Confirmed Primary Syphilis
- Probable Primary Syphilis
- Confirmed Secondary Syphilis
- Probable Secondary Syphilis
- **✓ Early non-primary, non-secondary**
- Unknown duration or late

Manifestations:
- **Neurologic**
  - Verified
  - Likely
  - Possible
  - No
  - Unknown
- **Otic**
  - Verified
  - Likely
  - Possible
  - No
  - Unknown
- **Ocular**
  - Verified
  - Likely
  - Possible
  - No
  - Unknown
- **Late (Clinical)**
  - Verified
  - Likely
  - No
  - Unknown
Today’s Talk Will Not Review Clinical Manifestation Variables Implemented in 2018

Stage:
- Confirmed Primary Syphilis
- Probable Primary Syphilis
- Confirmed Secondary Syphilis
- Probable Secondary Syphilis
- Early non-primary, non-secondary ✓
- Unknown duration or late

Manifestations:
- Neurologic
  - Verified
  - Likely
  - Possible ✓ No
  - Unknown

- Ocular
  - Verified
  - Likely
  - Possible ✓
  - No
  - Unknown

- Otic
  - Verified
  - Likely
  - Possible
  - Unknown

- Late (Clinical)
  - Verified
  - Likely
  - No ✓
  - Unknown
Syphilis Staging Subtypes

- Syphilis, primary
- Syphilis, secondary
- Syphilis, early non-primary non-secondary
- Syphilis, unknown duration or late
- Syphilis, congenital
- Syphilitic stillbirth
Treponema pallidum
What is syphilis?

- Caused by the *Treponema pallidum* bacteria
- Corkscrew-shaped spirochete bacteria that can ‘swim’
What is syphilis?

- Caused by the *Treponema pallidum* bacteria
- Corkscrew-shaped bacteria that can ‘swim’
- Cannot be easily cultured in a dish (*in vitro*)
- Not visible by normal light microscope
What is syphilis?

- Caused by the *Treponema pallidum* bacteria
- Corkscrew-shaped bacteria that can ‘swim’
- Cannot be easily cultured in a dish (*in vitro*)
- Not visible by normal light microscope
- We are almost always measuring the body’s *response* to syphilis, not the syphilis itself
How is it transmitted to others?

- Sexual contact
- Vertical transmission from mother to fetus
- Touching infectious lesions (rare)
- Blood transfusion (rare)
How does it enter and spread throughout the body?

- **Penetration (Entry)**
  - Enters via skin and mucous membranes through abrasions during sex
  - Transmitted across the placenta from mother to fetus during pregnancy

- **Dissemination (Spread)**
  - Travels via lymphatic system to regional lymph nodes
  - Then travels throughout body via blood stream
  - Invasion of Central Nervous System can occur at any time
Review of Stages of Syphilis
Surveillance

Clinical

case identification & staging
Surveillance

- Monitor burden & identify infectious cases
- Apply consistent criteria with high level of specificity
- Based on CSTE case definitions
- Leverages multiple data sources, including lab results and disease registries
Surveillance

case identification & staging

- Monitor burden & identify infectious cases
- Apply consistent criteria with high level of **specificity**
- Based on CSTE case definitions
- Leverages multiple data sources, including lab results and disease registries

Clinical

case identification & staging

- Ensure appropriate treatment
- Apply criteria with high level of **sensitivity**
- Leverages multiple data sources—often what is available at time of clinical care
Surveillance

Case identification & staging

Clinical

Case identification & staging

Overlaps most of the time, but there may be differences
Clinical Stages

No signs or symptoms
Primary

• Ulcer or chancre at site of infection
Clinical Stages

Primary

- Ulcer or chancre at site of infection

- Appears about 3 weeks (range: 10-90 days) after infection
- Sore goes away even if person is not treated
Clinical Stages

Primary
- Ulcer or chancre at site of infection

Secondary
- Skin rash
- Mucocutaneous lesions
- Generalized lymphadenopathy

- Usually occurs 3-6 weeks after primary
- Symptoms go away even if not treated
Clinical Stages

Primary
- Ulcer or chancre at site of infection

Secondary
- Skin rash
- Mucocutaneous lesions
- Generalized lymphadenopathy
Clinical Stages

Primary
- Ulcer or chancre at site of infection

Secondary
- Skin rash
- Mucocutaneous lesions
- Generalized lymphadenopathy

Mucus patches
Condyloma lata
Clinical Stages

Primary
- Ulcer or chancre at site of infection

Secondary
- Skin rash
- Mucocutaneous lesions
- Generalized lymphadenopathy

Alopecia
Clinical Stages

Primary
- Ulcer or chancre at site of infection

Secondary
- Skin rash
- Mucocutaneous lesions
- Generalized lymphadenopathy

Systemic symptoms can include:
- Generalized lymphadenopathy
- Fever
- Headache
- Malaise
- Anorexia
- Sore throat
- Myalgia
Clinical Stages

Primary
• Ulcer or chancre at site of infection

Secondary
• Skin rash
• Mucocutaneous lesions
• Generalized lymphadenopathy

P&S Syphilis
• Most infectious stages
• Recent acquisition
• Leading edge of syphilis epidemic
Clinical Stages

Primary
- Ulcer or chancre at site of infection

Secondary
- Skin rash
- Mucocutaneous lesions
- Generalized lymphadenopathy

Latent
- No visible signs/symptoms
- Early latent (≤1 year)
- Late latent (>1 year)

No signs or symptoms
Clinical Stages

Primary
- Ulcer or chancre at site of infection

Secondary
- Skin rash
- Mucocutaneous lesions
- Generalized lymphadenopathy

Latent
- No visible signs/symptoms
- Early latent (≤1 year)
- Late latent (>1 year)

Tertiary
- Cardiovascular
- Gummatous lesions
- Central nervous system

aortic aneurysm
Clinical Stages

**Primary**
- Ulcer or chancre at site of infection

**Secondary**
- Skin rash
- Mucocutaneous lesions
- Generalized lymphadenopathy

**Latent**
- No visible signs/symptoms
- Early latent (≤1 year)
- Late latent (>1 year)

**Tertiary**
- Cardiovascular
- Gummatous lesions
- Central nervous system

No signs or symptoms
Clinical Stages

**Primary**
- Ulcer or chancre at site of infection

**Secondary**
- Skin rash
- Mucocutaneous lesions
- Generalized lymphadenopathy

**Latent**
- No visible signs/symptoms
- Early latent (≤1 year)
- Late latent (>1 year)

**Tertiary**
- Cardiovascular
- Gummatous lesions
- Central nervous system

***Neuro/ocular/otic syphilis at any time period during infection***
Clinical Stages

Primary

Secondary

Early Latent

Late Latent

Tertiary

Surveillance Stages

Primary

Secondary

Early Non-primary, Non-secondary

No signs or symptoms

≤1 Year
Clinical Stages

Primary

Secondary

Early Latent

Late Latent

≤1 Year

> 1 Year

No signs or symptoms

Tertiary

Primary

Secondary

Early Non-

Primary, Non-

Secondary

Unknown Duration or Late

Surveillance Stages
Syphilis Laboratory Tests
Syphilis Laboratory Tests
Syphilis Laboratory Tests
Direct Detection Methods
Direct Detection Methods

Darkfield microscopy
Direct Detection Methods

Darkfield microscopy

Polymerase chain reaction (PCR)
There are 2 types of serologic tests for syphilis

Non-treponemal
- RPR, VDRL

Treponemal
- EIA, TPPA, FTA-ABS
There are 2 types of serologic tests for syphilis

Treponemal

- EIA, TPPA, FTA-ABS
There are 2 types of serologic tests for syphilis

**Treponemal**
- EIA, TPPA, FTA-ABS
- Detects specific antibodies against *T. pallidum*
- Qualitative (yes/no)
- Life-long reactivity (85%)
There are 2 types of serologic tests for syphilis

**Treponemal**
- EIA, TPPA, FTA-ABS
- Detects specific antibodies against *T. pallidum*
- Qualitative
- Life-long reactivity (85%)
There are 2 types of serologic tests for syphilis

Non-treponemal

- RPR, VDRL
- Detects non-specific antibodies
- Quantitative: titers
- Reflect disease activity
There are 2 types of serologic tests for syphilis

Non-treponemal
- RPR, VDRL
- Detects non-specific antibodies
- Quantitative: titers
- Reflect disease activity
There are 2 syphilis screening algorithms

Traditional

Quantitative RPR

RPR+

RPR-

TP-PA

or other
trep test

Reverse Sequence

EIA or CIA

EIA/CIA+

EIA/CIA-

Quantitative RPR

RPR+

RPR-

TP-PA
Surveillance Case Definitions
Surveillance Stages

- Primary
- Secondary
- Early Non-primary, Non-secondary
- Unknown Duration or Late

- ≤1 Year
- > 1 Year
Primary

Surveillance Stages
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.
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Probable:
- Case that meets clinical description of primary syphilis with a reactive nontreponemal OR treponemal serologic test
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

Probable:
- Case that meets clinical description of primary syphilis with a reactive nontreponemal OR treponemal 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
Clinical Description:

- **Mucocutaneous lesions**, often with generalized **lymphadenopathy**. Other signs can include **mucous patches**, **condyloma lata**, and alopecia. The primary ulcerative lesion may still be present.
Clinical Description:

- Mucocutaneous lesions, often with generalized lymphadenopathy. Other signs can include mucous patches, condyloma lata, and alopecia. The primary ulcerative lesion may still be present.

Probable:

Confirmed:
Clinical Description:

- Mucocutaneous lesions, often with generalized lymphadenopathy. Other signs can include mucous patches, condyloma lata, and alopecia. The primary ulcerative lesion may still be present.

Probable:

- Case that meets clinical description of secondary syphilis with a reactive nontreponemal AND treponemal serologic test.

Confirmed:
Clinical Description:

- Mucocutaneous lesions, often with generalized lymphadenopathy. Other signs can include mucous patches, condyloma lata, and alopecia. The primary ulcerative lesion may still be present.

Probable:

- Case that meets clinical description of secondary syphilis with a reactive nontreponemal AND treponemal serologic 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.
Surveillance Stages

Early Non-primary, Non-secondary

≤1 Year

No signs or symptoms of primary or secondary

≤1 Year
Clinical Description:

- *T. pallidum* initial infection has occurred within the previous 12 months, but there are no signs/symptoms of primary or secondary syphilis.
Probable:

A case with

- **No signs/symptoms** of primary or secondary syphilis

AND

**Early Non-primary, Non-secondary**
Probable:

A case with

- **No signs/symptoms** of primary or secondary syphilis
  AND
- Evidence of **current infection**
Probable:

A case with

- No signs/symptoms of primary or secondary syphilis
  AND
- Evidence of current infection

No history of syphilis:
- a current reactive nontreponemal AND
- current reactive treponemal test

OR
Probable:

A case with

- No signs/symptoms of primary or secondary syphilis
  
- Evidence of current infection

No history of syphilis:
- A current reactive nontreponemal test AND current reactive treponemal test

History of syphilis:
- A current nontreponemal test titer demonstrating fourfold or greater increase from the last nontreponemal test titer (unless there is evidence that this increase was not sustained for > 2 weeks)
### Probable:

A case with

- No signs/symptoms of primary or secondary syphilis
  AND
- Evidence of current infection

**History of syphilis:**

- A current **nontreponemal** test titer demonstrating **fourfold or greater** increase from the last nontreponemal test titer (unless there is evidence that this increase was not sustained for > 2 weeks)
Probable:
A case with
- No signs/symptoms of primary or secondary syphilis
  AND
- Evidence of current infection
  AND
- Evidence of having acquired infection within the last 12 months
Evidence of having acquired infection within the last 12 months

- Documented *seroconversion* of nontreponemal or treponemal test in last 12 months
- *≥ 4-fold increase* in titer of a nontreponemal test during the previous 12 months (unless there is evidence that this increase was not sustained for >2 weeks)
- History of *symptoms* consistent with primary or secondary syphilis during the previous 12 months
- History of *sex partner* with primary, secondary, or early non-primary non-secondary syphilis within the previous 12 months
- *Sexual debut* was within the previous 12 months.
Determining the 4-fold increase
Determining the 4-fold increase

1:2
Determining the 4-fold increase
Determining the 4-fold increase

\[ \frac{16}{2} = 8 \]
Determining the 4-fold increase
Determining the 4-fold increase
Clinical Description:

- A stage of infection with *T. 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
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
  current reactive nontreponemal AND reactive treponemal tests
  OR

- Prior History of syphilis
  current nontreponemal titer demonstrating $\geq 4$-fold increase from 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
There is a need to anchor the diagnosis to a moment in time, allowing for a consistent surveillance definition

**Syphilis cases should be categorized and reported by stage at the time of initial examination/diagnosis**

- Often the time of initial specimen collection
- Not at the time of treatment or interview
Syphilis cases should be categorized and reported by stage at the time of initial examination/diagnosis
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Syphilis cases should be categorized and reported by stage at the time of initial examination/diagnosis
A Systematic Approach
Start with primary syphilis assessment

- Does the patient have clinical evidence of primary syphilis?
  - This includes one or more ulcerative lesions (chancre
  - They should have no symptoms of secondary syphilis
Start with primary syphilis assessment

- Does the patient have clinical evidence of primary syphilis?
  - This includes one or more ulcerative lesions (chancre)s

Has *T. pallidum* been directly detected?

--Can include darkfield microscopy of a specimen NOT from oropharynx or potentially contaminated by stool

OR

--PCR or equivalent molecular method
Start with primary syphilis assessment

- Does the patient have clinical evidence of primary syphilis?
  - This includes one or more ulcerative lesions (chancre)

Has *T. pallidum* been directly detected?

--Can include **darkfield microscopy** of a specimen NOT from oropharynx or potentially contaminated by stool
  OR
--**PCR** or equivalent molecular method

**Confirmed Primary Syphilis**
Start with primary syphilis assessment

- Does the patient have clinical evidence of primary syphilis?
  - This includes one or more ulcerative lesions (chancre)

No direct detection methods

Does the patient have at least ONE reactive serologic test?

  --Nontreponemal (RPR/VDRL)  
  OR  
  --Treponemal (EIA/CIA/TPPA/FTA-Abs)
Start with primary syphilis assessment

- Does the patient have clinical evidence of primary syphilis?
  - This includes **one or more ulcerative lesions** (chancre)

No direct detection methods

**Probable Primary Syphilis**

Does the patient have **at least ONE reactive serologic test**?

-- Nonreponemal (RPR/VDRL)
  OR
-- Treponemal (EIA/CIA/TPPA/FTA-Abs)
Move to secondary syphilis assessment

- Does the patient have clinical evidence of secondary syphilis?
  - This can include any of the following: localized or diffuse mucocutaneous lesions (e.g., rash), often with generalized lymphadenopathy; mucous patches, condyloma lata, alopecia
Move to secondary syphilis assessment

- Does the patient have clinical evidence of secondary syphilis?
  - This can include any of the following: localized or diffuse mucocutaneous lesions (e.g., rash), often with generalized lymphadenopathy; mucous patches, condyloma lata, alopecia

Has *T. pallidum* been directly detected?

--Can include darkfield microscopy of a specimen NOT from oropharynx or potentially contaminated by stool
OR
--PCR or equivalent molecular method
Move to secondary syphilis assessment

- Does the patient have clinical evidence of secondary syphilis?
  - This can include any of the following: localized or diffuse mucocutaneous lesions (e.g., rash), often with generalized lymphadenopathy; mucous patches, condyloma lata, alopecia

Has *T. pallidum* been directly detected?

--Can include **darkfield microscopy** of a specimen NOT from oropharynx or potentially contaminated by stool

OR

--**PCR** or equivalent molecular method

**Confirmed Secondary Syphilis**
Move to secondary syphilis assessment

- Does the patient have clinical evidence of secondary syphilis?
  - This can include any of the following: localized or diffuse mucocutaneous lesions (e.g., rash), often with generalized lymphadenopathy; mucous patches, condyloma lata, alopecia

Does the patient have **TWO reactive serologic tests**?

--Nontreponemal (RPR/VDRL)

AND

--Treponemal (EIA/CIA/TPPA/FTA-Abs)
Move to secondary syphilis assessment

- Does the patient have clinical evidence of secondary syphilis?
  - This can include any of the following: localized or diffuse mucocutaneous lesions (e.g., rash), often with generalized lymphadenopathy; mucous patches, condyloma lata, alopecia

Probable Secondary Syphilis

Does the patient have **TWO reactive serologic tests**?

--Nontreponemal (RPR/VDRL)

AND

--Treponemal (EIA/CIA/TPPA/FTA-Abs)
Case 1

33-year-old
Case 1

33-year-old

6 weeks ago
Case 1

33-year-old

6 weeks ago
Case 1

33-year-old

6 weeks ago
Case 1

33-year-old

RPR 1:64
TPPA Reactive
Case 1

33-year-old

6 weeks ago

RPR 1:64
TPPA Reactive

Please Vote:
1. Confirmed Primary Syphilis
2. Probable Primary Syphilis
3. Confirmed Secondary Syphilis
4. Probable Secondary Syphilis
5. Early non-primary, non-secondary
6. Unknown duration or late
7. Not a case
Case 1

33-year-old

6 weeks ago

RPR 1:64
TPPA Reactive
Case 1

33-year-old

6 weeks ago
Case 1

33-year-old

6 weeks ago

Case: Probable Secondary Syphilis
- No active chancre
- Symptoms of secondary syphilis
- BOTH serologic tests
Case 2

19 year old male
Penile chancre
Case 2

19 year old male
Penile chancre
Case 2

19 year old male
Penile chancre
Case 2

19 year old male
Penile chancre

RPR nonreactive
TPPA nonreactive
Case 2

19 year old male
Penile chancre

RPR nonreactive
TPPA nonreactive

*T. pallidum* identified on darkfield microscopy
Case 2

19 year old male
Penile chancre

RPR nonreactive
TPPA nonreactive

T. pallidum identified on darkfield microscopy

Please Vote:
1. Confirmed Primary Syphilis
2. Probable Primary Syphilis
3. Confirmed Secondary Syphilis
4. Probable Secondary Syphilis
5. Early non-primary, non-secondary
6. Unknown duration or late
7. Not a case
Case 2

19 year old male
Penile chancre

RPR nonreactive
TPPA nonreactive

*T. pallidum* identified on darkfield microscopy
Case 2

19 year old male
Penile chancre

RPR nonreactive
TPPA nonreactive

*T. pallidum* identified on darkfield microscopy
Case 2

19 year old male
Penile chancre

RPR nonreactive
TPPA nonreactive

T. pallidum identified on darkfield microscopy

Case: Confirmed Primary Syphilis
• Chancre
• No symptoms of secondary syphilis
• Direct detection of *T. pallidum*
Move to ‘early non-primary non-secondary’ (ENPNS) assessment
Move to ‘early non-primary non-secondary’ (ENPNS) assessment

Confirm no signs or symptoms of primary/secondary
Move to ‘early non-primary non-secondary’ (ENPNS) assessment

Confirm **no signs or symptoms** of primary/secondary

Confirm positive on **BOTH** types of **serologic tests**
Move to ‘early non-primary non-secondary’ (ENPNS) assessment

Confirm no signs or symptoms of primary/secondary

Confirm positive on BOTH types of serologic tests

If patient has NO history of syphilis, stage as ENPNS if you can prove the infection occurred in the past 12 months:

• Patient lost his/her virginity (sexual debut) in past 12 mos. OR
• Patient exposed to sexual partner with primary, secondary, or ENPNS in past 12 mos. OR
• History of primary or secondary symptoms in past 12 mos. OR
• Documented seroconversion in past 12 mos. (negative test in past 12 mos.)
Move to ‘early non-primary non-secondary’ (ENPNS) assessment

Confirm *no* signs or symptoms of primary/secondary

Confirm positive on BOTH types of serologic tests

If patient has NO history of syphilis, stage as ENPNS
if you can prove the infection occurred in the past 12 months:

**Probable early non-primary non-secondary syphilis**
Case 3
Case 3

22-year-old MSM
Asymptomatic
Case 3

22-year-old MSM
Asymptomatic

RPR 1:16
TPPA Reactive
Case 3

22-year-old MSM

RPR 1:16
TPPA Reactive
Case 3

22-year-old MSM

RPR 1:16
TPPA Reactive
Case 3

22-year-old MSM

9 months ago
Nonreactive RPR

RPR 1:16
TPPA Reactive
Case 3

22-year-old MSM
Asymptomatic (At time of testing)

Please Vote:
1. Confirmed Primary Syphilis
2. Probable Primary Syphilis
3. Confirmed Secondary Syphilis
4. Probable Secondary Syphilis
5. Early non-primary, non-secondary
6. Unknown duration or late
7. Not a case

9 months ago
Nonreactive RPR

3 months ago
resolved anal ulcer

3 months ago
resolved rash

RPR 1:16
TPPA Reactive

1 month ago
resolved rash

1 month ago
resolved rash

resolved rash
Case 3

22-year-old MSM
Asymptomatic (At time of testing)

9 months ago
Nonreactive RPR

3 months ago
resolved anal ulcer

1 month ago
resolved rash

RPR 1:16
TPPA Reactive
Case 3

22-year-old MSM
Asymptomatic (At
time of testing)

9 months ago
Nonreactive RPR

RPR 1:16
TPPA Reactive
Case 3

22-year-old MSM
Asymptomatic (At
time of testing)

Case: Early non-primary,
non-secondary
• No primary/secondary
  symptoms at time of
diagnosis
• Seroconversion in past
  12 months

9 months ago
Nonreactive RPR

RPR 1:16
TPPA Reactive
Case 3

22-year-old MSM
Asymptomatic (At time of testing)

9 months ago
Nonreactive RPR

RPR 1:16
TPPA Reactive
Case 3

22-year-old MSM
Asymptomatic (At time of testing)
Case 3

22-year-old MSM
Asymptomatic (At time of testing)
Move to ‘unknown duration or late’ assessment
Move to ‘unknown duration or late’ assessment

Confirm *no signs or symptoms* of primary/secondary
Move to ‘unknown duration or late’ assessment

Confirm *no signs or symptoms* of primary/secondary

Confirm positive on *BOTH* types of serologic tests
Move to ‘unknown duration or late’ assessment

Confirm *no signs or symptoms* of primary/secondary

Confirm positive on **BOTH** types of serologic tests

If patient has *NO history of syphilis*, and you *could NOT prove ENPNS*
Move to ‘unknown duration or late’ assessment

Confirm *no signs or symptoms* of primary/secondary

Confirm positive on **BOTH** types of serologic tests

If patient has **NO history of syphilis**, and you **could NOT prove** ENPNS

**Probable unknown duration or late syphilis**
Case 3

22-year-old MSM
Asymptomatic (At
time of testing)
Case 3

22-year-old MSM
Asymptomatic (At time of testing)

Adult Syphilis Surveillance Staging
When Primary and Secondary Symptoms NOT Present
(Not to be used as guidance for treatment)

Primary or Secondary Syphilis Symptoms Currently Present?
Yes
No

Refer to flowchart for Adult Syphilis Surveillance Staging
When Primary and Secondary Syphilis Symptoms Are Present

Reactive nonreproval (USR or RPR) AND
Reactive treponemal (e.g., TP-PA, EIA)?
Yes
No

Does patient have a documented prior history of syphilis diagnosis?
Yes
No

Does patient have a current test result demonstrating a 2-4-fold increase in nonreproval test titer during the previous 12 months (and no evidence that increase was not sustained for >2 weeks)?
Yes
No

PROBABLE Early Non-primary Non-secondary Syphilis

Does patient have a current nonreproval test that demonstrates a 2-4-fold increase in the last nonreproval test titer >12 months age (and no evidence increase was not sustained for >2 weeks)?
Yes
No

PROBABLE Early Non-primary Non-secondary Syphilis

Does patient have evidence of having acquired disease within past 12 months?
Yes
No

NOT a case

PROBABLE Early Non-primary Non-secondary Syphilis

Within previous 12 months, did patient have sexual exposure to partner with primary, secondary, or early non-primary non-secondary syphilis?
Yes
No

PROBABLE Early Non-primary Non-secondary Syphilis

Did the patient only sexual contact (anal or oral) occur within the previous 12 months?
Yes
No

PROBABLE Early Non-primary Non-secondary Syphilis

RPR 1:16
TPPA Reactive

Current refers to the anchoring data of the original diagnosis, such as time of original clinical diagnosis or first screening test

Yes
No

NOT a case

PROBABLE Early Non-primary Non-secondary Syphilis

PROBABLE Unknown Duration or Late Syphilis

PROBABLE Early Non-primary Non-secondary Syphilis
Case 3

22-year-old MSM
Asymptomatic (At time of testing)

RPR 1:16
TPPA Reactive
Case Scenarios
Case 4
Case 4

25-year-old female

Asymptomatic
Case 4

25-year-old female

Asymptomatic

RPR 1:16
TPPA Reactive
Case 4

25-year-old female

Nonreactive RPR

13 months

Asymptomatic

RPR 1:16
TPPA Reactive
Case 4

25-year-old female

Nonreactive RPR

13 months

RPR 1:16
TPPA Reactive

Please Vote:
1. Confirmed Primary Syphilis
2. Probable Primary Syphilis
3. Confirmed Secondary Syphilis
4. Probable Secondary Syphilis
5. Early non-primary, non-secondary
6. Unknown duration or late
7. Not a case

- No history of sores, rashes, or being sick within the last year
- 3 sex partners in the last year; none reported syphilis
- Sexual debut was age 18
- Her doctor treated her with 1 dose of penicillin.
Case 4

- 25-year-old female
- No history of sores, rashes, or being sick within the last year
- 3 sex partners in the last year; none reported syphilis
- Sexual debut was age 18
- Her doctor treated her with 1 dose of penicillin.
Case 4

25-year-old female

- No history of sores, rashes, or being sick within the last year
- 3 sex partners in the last year; none reported syphilis
- Sexual debut was age 18
- Her doctor treated her with 1 dose of penicillin.
Case 4

25-year-old female

Case: Unknown duration or late
• No primary/secondary symptoms
• Meets lab criteria
• No evidence of infection in last year
Case 5
Case 5

29-year-old
HIV+
Case 5

29-year-old HIV+

RPR 1:32
TPPA Reactive
Case 5

29-year-old HIV+

6 months

RPR 1:2
TPPA Nonreactive

RPR 1:32
TPPA Reactive
Case 5

29-year-old HIV+

6 months

RPR 1:2
TPPA Nonreactive

RPR 1:32
TPPA Reactive
Case 5

29-year-old HIV+

6 months

RPR 1:2
TPPA Nonreactive

RPR 1:32
TPPA Reactive
Case 5

29-year-old HIV+

RPR 1:2
TPPA Nonreactive

RPR 1:32
TPPA Reactive

6 months

Please Vote:
1. Confirmed Primary Syphilis
2. Probable Primary Syphilis
3. Confirmed Secondary Syphilis
4. Probable Secondary Syphilis
5. Early non-primary, non-secondary
6. Unknown duration or late
7. Not a case

- No primary or secondary syphilis symptoms in past year
- No sexual partners have reported to him that they have syphilis
- His sexual debut was at age 19.
Case 5

29-year-old HIV+

- RPR 1:2
  - TPPA Nonreactive
  - No primary or secondary syphilis symptoms in past year
  - No sexual partners have reported to him that they have syphilis
  - His sexual debut was at age 19.

- RPR 1:32
  - TPPA Reactive

6 months
Case 5

- 29-year-old HIV+

- No primary or secondary syphilis symptoms in past year
- No sexual partners have reported to him that they have syphilis
- His sexual debut was at age 19.

RPR 1:2
TPPA Nonreactive

RPR 1:32
TPPA Reactive

6 months

**Adult Syphilis Surveillance Staging**
When Primary and Secondary Symptoms NOT Present
(Not to be used as guidance for treatment)

- Does patient have a documented prior history of syphilis diagnosis?
  - Yes
    - Refer to flowchart for Adult Syphilis Surveillance Staging When Primary and Secondary Syphilis Symptoms Are Present
  - No
    - Does patient have documented seroconversion OR a 4-fold increase in nonreactosomal test titer during previous 12 months (and no evidence that increase was not sustained for 3 weeks)?
      - Yes
        - PROBABLE Early Non-primary Non-secondary Syphilis*2
      - No
        - Evidence of having acquired disease within past 12 months?
          - Yes
            - PROBABLE Unknown Duration or Late Syphilis*
          - No
            - Did the patients' only sexual contact (sexual debut) occur within the previous 12 months?
              - Yes
                - PROBABLE Early Non-primary Non-secondary Syphilis*2
              - No
                - PROBABLE Unknown Duration or Late Syphilis*

*1 Current refers to the occurrence of the last diagnosis, such as time of original clinical diagnosis or first screening test

*2 "Early", "Late", and "TS" syphilis manifestations can occur at any stage. After stage of disease is determined, all cases should be assessed for clinical manifestations, which are then reported separately as "early", "verified", "likely", "possible", or "unknown."
Case 5

29-year-old HIV+

6 months

RPR 1:2
RPR 1:32
TPPA Reactive

Case: Early non-primary, non secondary
• Anchor the staging to the point in time when the diagnosis was first identified
Case 6

- 23 year old female
- chancre
- 1 new partner who denies syphilis
Case 6

- 23 year old female
- chancre
- 1 new partner who denies syphilis

RPR 1:4
TPPA nonreactive
Case 6

- 23 year old female
- chancre
- 1 new partner who denies syphilis

RPR 1:4
TPPA nonreactive

Please Vote:
1. Confirmed Primary Syphilis
2. Probable Primary Syphilis
3. Confirmed Secondary Syphilis
4. Probable Secondary Syphilis
5. Early non-primary, non-secondary
6. Unknown duration or late
7. Not a case
Case 6

- 23 year old female
- chancre
- 1 new partner who denies syphilis

RPR 1:4
TPPA nonreactive
Case 6

- 23 year old female
- chancre
- 1 new partner who denies syphilis

RPR 1:4
TPPA nonreactive
Case 6

- 23 year old female
- chancre
- 1 new partner who denies syphilis

Case: Probable primary syphilis
- Only 1 type of serologic test is needed when identifying probable primary syphilis

RPR 1:4
TPPA nonreactive
Case 7
Case 7

48 year old
Past history of syphilis
No new sex partners

Asymptomatic

RPR 1:64
TPPA Reactive
Case 7

48 year old
Past history of syphilis
No new sex partners

11 months

Asymptomatic

RPR 1:8
TPPA Reactive

RPR 1:64
TPPA Reactive
Case 7

48 year old
Past history of syphilis
No new sex partners

11 months

1 week later
RPR 1:16
TPPA Reactive

RPR 1:8
TPPA Reactive

Asymptomatic

RPR 1:64
TPPA Reactive
Case 7

48 year old
Past history of syphilis
No new sex partners

Please Vote:
1. Confirmed Primary Syphilis
2. Probable Primary Syphilis
3. Confirmed Secondary Syphilis
4. Probable Secondary Syphilis
5. Early non-primary, non-secondary
6. Unknown duration or late
7. Not a case
**Case 7**

48 year old

Past history of syphilis

No new sex partners

---

11 months

1 week later

RPR 1:16

TPPA Reactive

Asymptomatic

RPR 1:8

TPPA Reactive
Case 7

48 year old
Past history of syphilis
No new sex partners

<table>
<thead>
<tr>
<th>Time</th>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 months</td>
<td>RPR</td>
<td>1:64</td>
</tr>
<tr>
<td></td>
<td>TPPA</td>
<td>Reactive</td>
</tr>
<tr>
<td></td>
<td>~baseline</td>
<td></td>
</tr>
<tr>
<td>1 week later</td>
<td>RPR</td>
<td>1:16</td>
</tr>
<tr>
<td></td>
<td>TPPA</td>
<td>Reactive</td>
</tr>
</tbody>
</table>

RPR 1:8
TPPA Reactive
Asymptomatic
RPR 1:64
TPPA Reactive
Case 7

48 year old
Past history of syphilis
No new sex partners

Case: Not a case
• If test is repeated, needs to show increase is sustained > 2 weeks
• A repeat test is not required

11 months

1 week later
RPR 1:16
TPPA Reactive

RPR 1:8
TPPA Reactive
~baseline

Asymptomatic
RPR 1:64
TPPA Reactive
Case 7

48 year old
Past history of syphilis
No new sex partners

11 months

RPR 1:8
TPPA Reactive
~baseline

Asymptomatic
RPR 1:64
TPPA Reactive
Case 8

28 year old female
Sex worker
Case 8

28 year old female
Sex worker
Case 8

28 year old female
Sex worker

No history of genital ulcers or rashes

Syphilis testing negative 18 months ago
Case 8
28 year old female
Sex worker

No history of genital ulcers or rashes
Syphilis testing negative 18 months ago

In ED:
RPR 1:64
TPPA reactive
Diagnosed Ocular Syphilis
Treated with IV penicillin
Case 8

28 year old female
Sex worker

Please Vote:
1. Confirmed Primary Syphilis
2. Probable Primary Syphilis
3. Confirmed Secondary Syphilis
4. Probable Secondary Syphilis
5. Early non-primary, non-secondary
6. Unknown duration or late
7. Not a case
Case 8

28 year old female
Sex worker

No history of genital ulcers or rashes
Syphilis testing negative 18 months ago

In ED:
RPR 1:64
TPPA reactive
Diagnosed Ocular Syphilis
Treated with IV penicillin
Case 8

28 year old female
Sex worker

No history of genital ulcers or rashes
Syphilis testing negative 18 months ago

In ED:
RPR 1:64
TPPA reactive
Diagnosed Ocular Syphilis
Treated with IV penicillin
Case 8

28 year old female
Sex worker

Case:
Unknown duration or late
✓ Ocular manifestations

No history of genital ulcers or rashes
Syphilis testing negative 18 months ago

In ED:
RPR 1:64
TPPA reactive
Diagnosed Ocular Syphilis
Treated with IV penicillin
#SyphilisIsHard

- CDC
  https://www.cdc.gov/std/default.htm

- CSTE
  https://www.cste.org/members/group.aspx?id=87602

- National Network of STD Clinical Prevention Training Centers
  Self study STI modules www.std.uw.edu
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.
Thank You
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For more information, contact CDC
1-800-CDC-INFO (232-4636)

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