

Adult Syphilis Staging

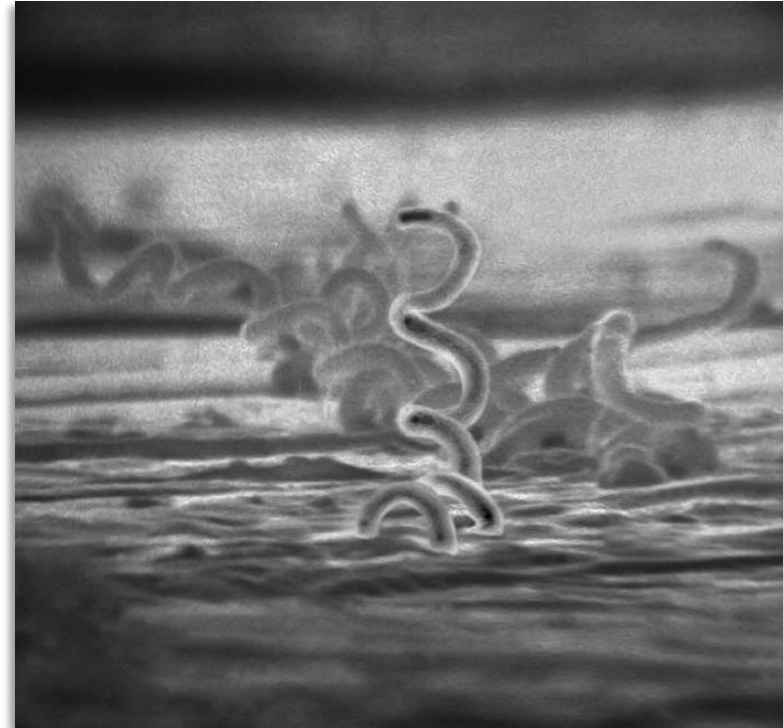
CSTE Webinar – December 2020

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Surveillance & Data Management Branch



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

A piece of torn, off-white paper with a black horizontal band across the middle. The band contains the text "#SyphilisIsHard" in a white, sans-serif font. Above the black band, there are three horizontal stripes of color: a green stripe on the left, a blue stripe in the middle, and an orange stripe on the right. The paper has a slightly textured appearance and some creases.

#SyphilisIsHard

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

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 - Otic Manifestations (verified/likely/possible/no/unknown)
 - Late Clinical Manifestations (verified/likely/no/unknown)
- **Definitions:**
 - <https://wwwn.cdc.gov/nndss/conditions/syphilis/case-definition/2018/>
- **Prior manifestations webinar:**
 - <https://cste.webex.com/cste/lsr.php?RCID=db2f5851d4533255108e747ba8190e91>

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:

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- Unknown duration or late

Manifestations:

- Neurologic
 - Verified
 - Likely
 - Possible
 - No
 - Unknown
- Ocular
 - Verified
 - Likely
 - Possible
 - No
 - Unknown
- Otic
 - 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
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- Otic
 - Verified
 - Likely
 - Possible
 - No
 - 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

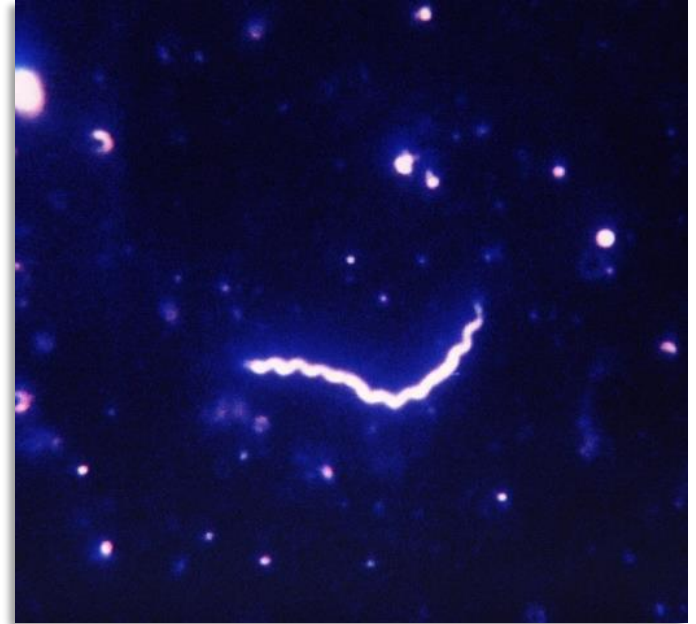
What is syphilis?

- Caused by the *Treponema pallidum* bacteria
- Corkscrew-shaped spirochete bacteria that can 'swim'



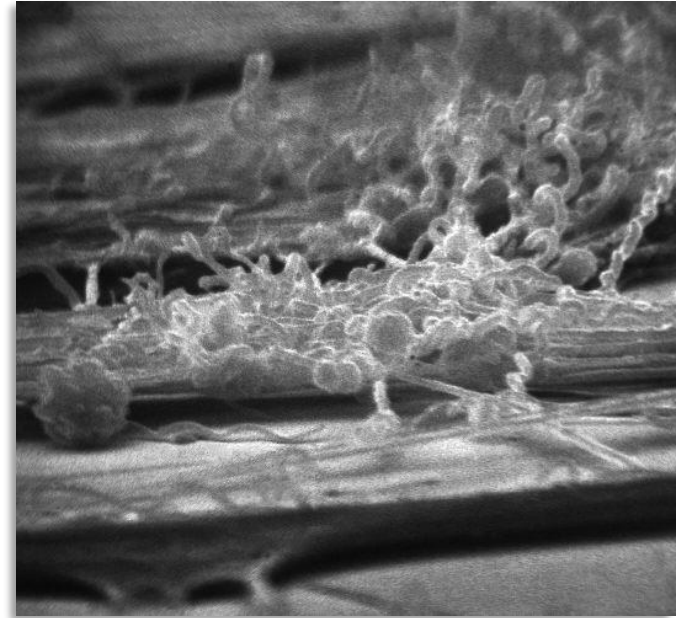
What is syphilis?

- 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

case identification & staging

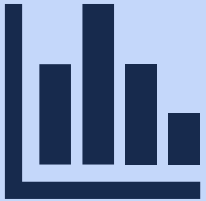
Clinical

case identification & staging



Surveillance

case identification & staging



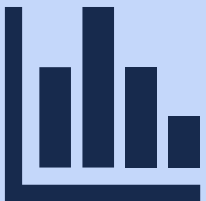
- Monitor burden & identify infectious cases
- Apply consistent criteria with high level of **specificity**
- Based on CSTE case definitions
- Leverages multiple data sources, including lab results and disease registries

Clinical

case identification & staging

Surveillance

case identification & staging



- Monitor burden & identify infectious cases
- Apply consistent criteria with high level of **specificity**
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Clinical

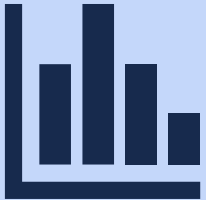
case identification & staging



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

Surveillance

case identification & staging



Overlaps most of the
time, but there may be
differences

Clinical

case identification & staging



Clinical Stages

Clinical Stages

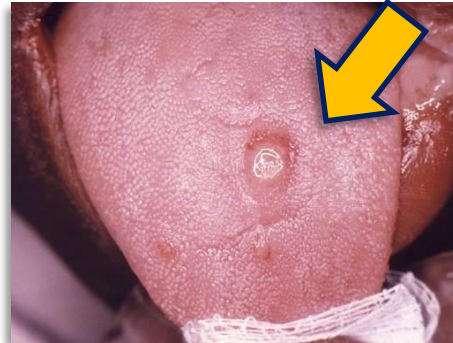
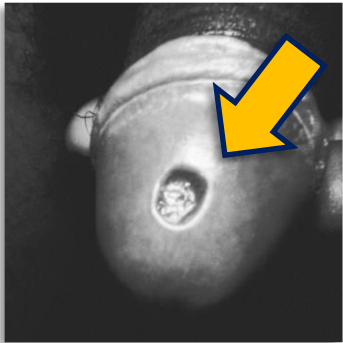
Primary

- 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)
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Tertiary

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Clinical Stages

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Latent

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

No signs or symptoms

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

Clinical Stages

Primary



Secondary



Early Latent

Late Latent

Tertiary

Primary

Secondary

Surveillance Stages

Clinical Stages

Primary



Secondary



Early Latent

≤1 Year

Late Latent

No signs or symptoms

Tertiary

Primary

Secondary

Early Non-
primary,
Non-
secondary

Surveillance Stages

Clinical Stages

Primary



Secondary



Early Latent

≤1 Year

Late Latent

> 1 Year

No signs or symptoms

Tertiary



Primary

Secondary

Early Non-
primary,
Non-
secondary

Unknown Duration or Late

Surveillance Stages

Syphilis Laboratory Testing

Syphilis Laboratory Tests



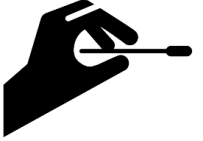
Syphilis Laboratory Tests



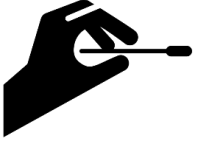
Syphilis Laboratory Tests



Direct Detection Methods

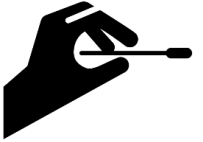


Direct Detection Methods

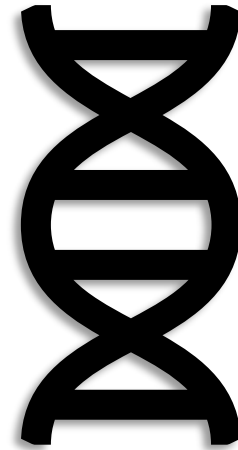


Darkfield microscopy

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



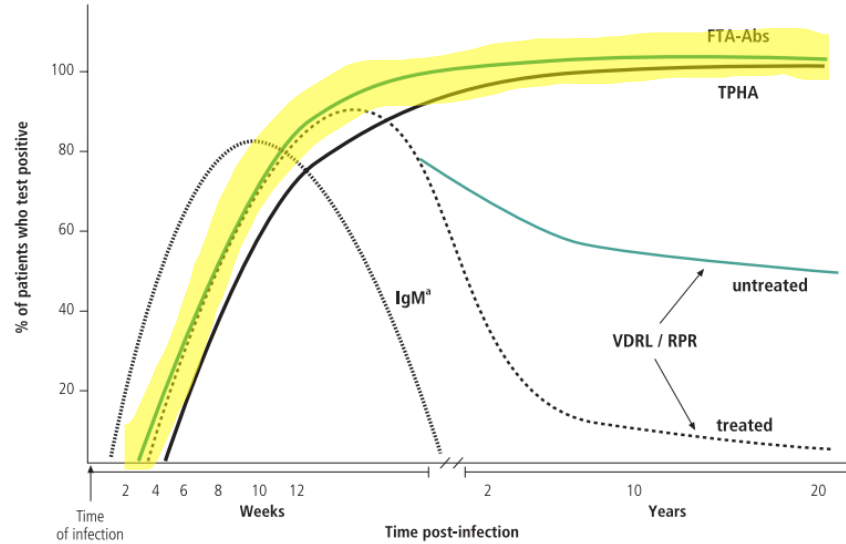
Treponemal

- 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

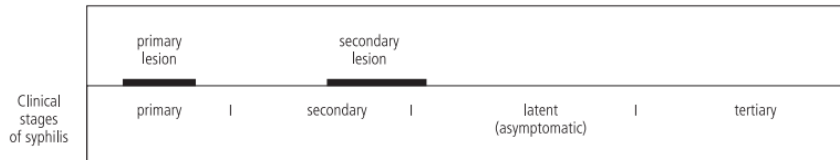


Fig. 1. Common patterns of serological reactivity in syphilis patients



Treponemal

- EIA, TPPA, FTA-ABS
- Detects specific antibodies against *T. pallidum*
- Qualitative
- Life-long reactivity (85%)



^a IgM by ELISA or FTA-ABS 195 or immunoblot

There are 2 types of serologic tests for syphilis



Non-treponemal

- RPR, VDRL
- Detects non-specific antibodies
- Quantitative: titers
- Reflect disease activity

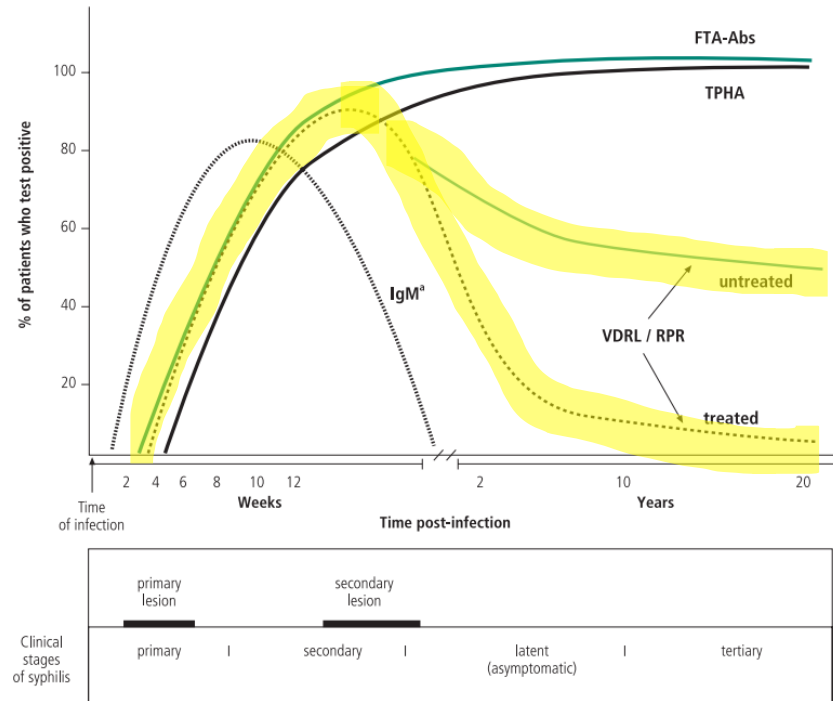
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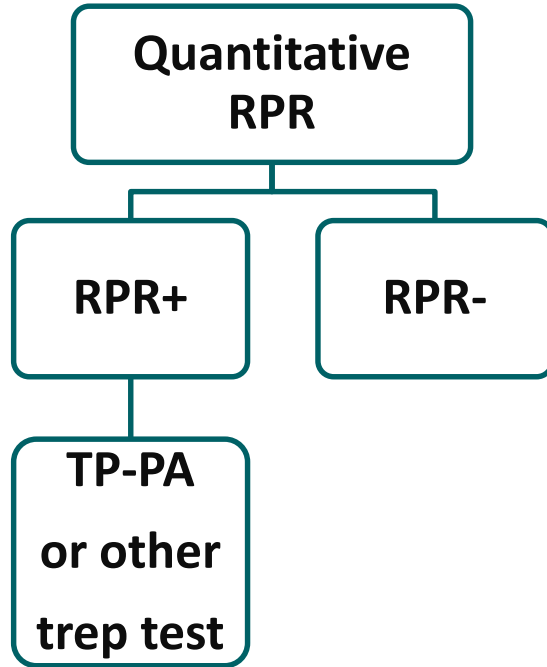
Fig. 1. Common patterns of serological reactivity in syphilis patients



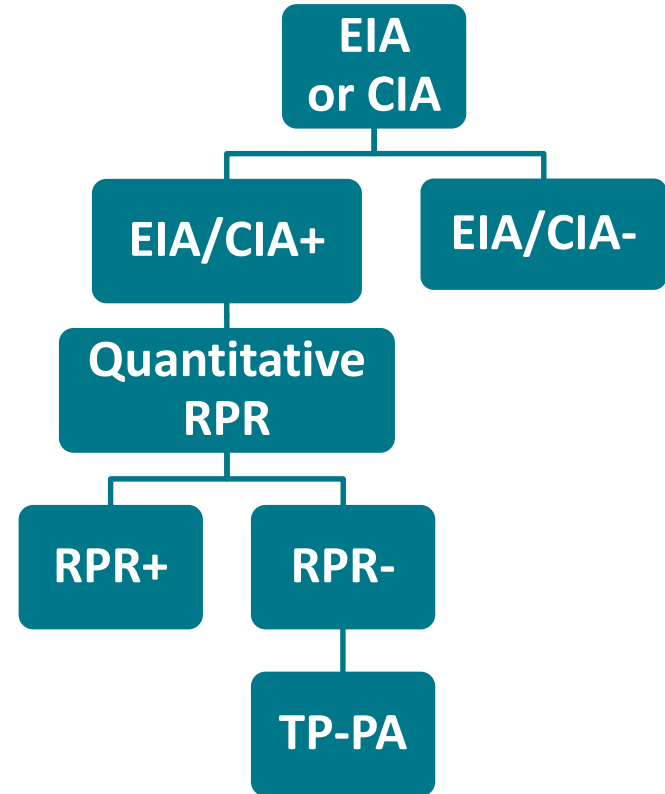
^a IgM by ELISA or FTA-ABS 195 or immunoblot

There are 2 syphilis screening algorithms

Traditional



Reverse Sequence



Surveillance Case Definitions

Surveillance Stages

Primary



Secondary



Early Non-
primary,
Non-
secondary

≤ 1 Year

Unknown Duration
or Late

> 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



■ 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**



■ 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

Secondary

Surveillance Stages



Secondary

Surveillance Stages



■ 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

Secondary

Surveillance Stages



■ 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

Early Non-
primary, Non-
secondary

Surveillance Stages

≤ 1 Year

No signs or
symptoms of
primary or
secondary

Early Non-
primary, Non-
secondary

Surveillance Stages

≤1 Year

No signs or
symptoms of
primary or
secondary

■ Clinical Description:

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

Early Non-
primary, Non-
secondary

Surveillance Stages

≤1 Year

- **Probable:**

A case with

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

AND

Early Non-
primary, Non-
secondary

Surveillance Stages

≤1 Year

■ Probable:

A case with

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

Early Non-
primary, Non-
secondary

Surveillance Stages

≤1 Year

■ 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

Early Non-
primary, Non-
secondary

Surveillance Stages

≤1 Year

■ 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

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)

Early Non-
primary, Non-
secondary

Surveillance Stages

≤1 Year

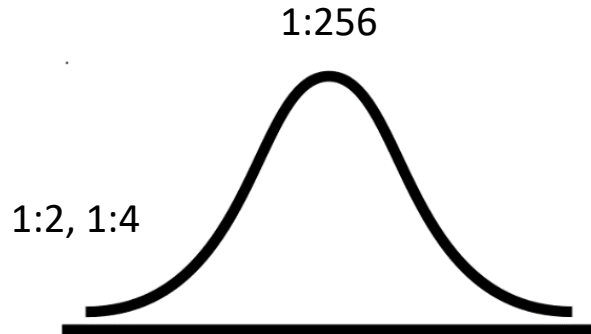
■ Probable:

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)

Early Non-
primary, Non-
secondary

Surveillance Stages

≤1 Year

■ 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**

Early Non-
primary, Non-
secondary

Surveillance Stages

≤1 Year

- **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



Determining the 4-fold increase



Determining the 4-fold increase

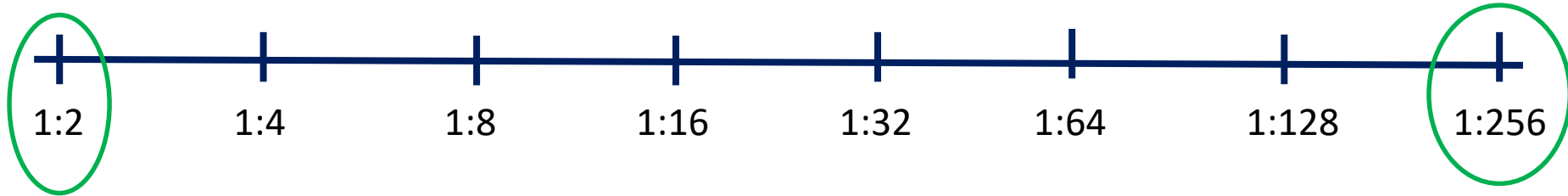


$$16/2=8$$

Determining the 4-fold increase



Determining the 4-fold increase



Unknown
Duration or
Late Syphilis

Surveillance Stages

>1 Year

No signs or
symptoms of
primary or
secondary

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

Unknown
Duration or
Late Syphilis

Surveillance Stages

>1 Year

■ 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 **≥ 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

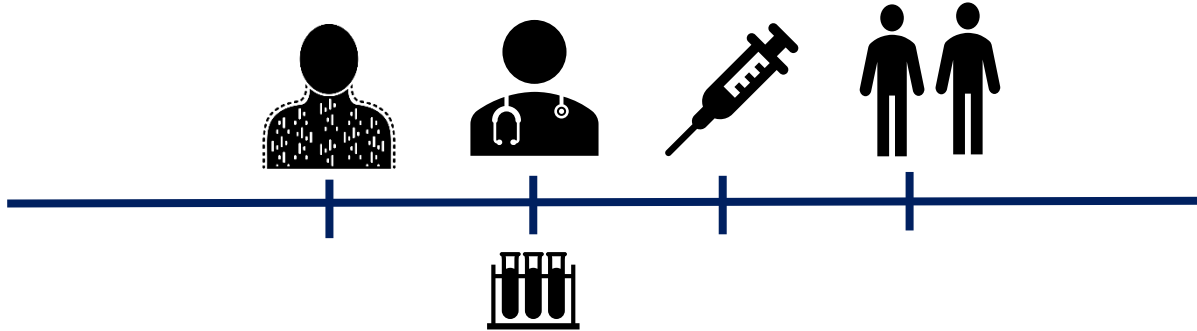


Syphilis cases should be categorized and reported by stage at the time of initial examination/diagnosis

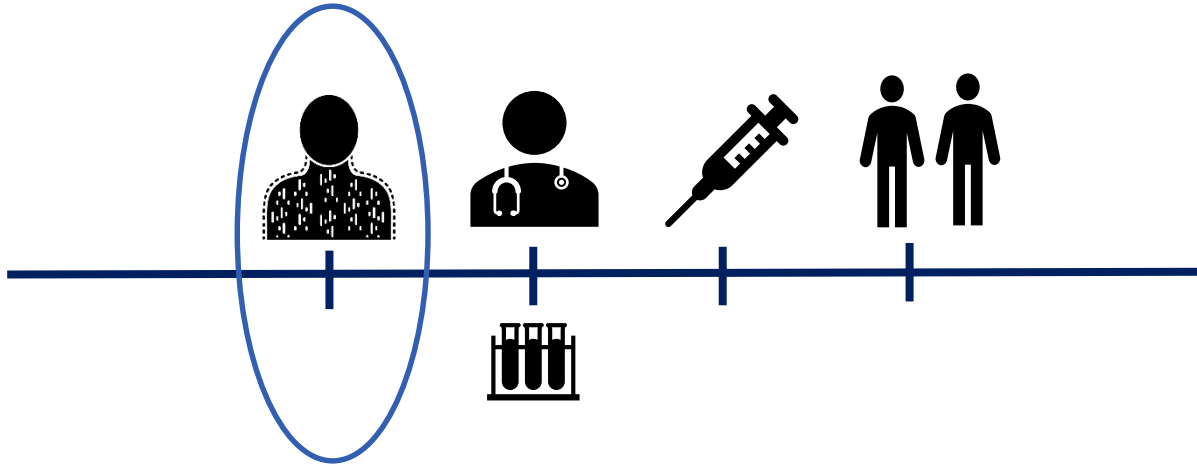
⚓ often the time of initial specimen collection

⚓ not at the time of treatment or interview

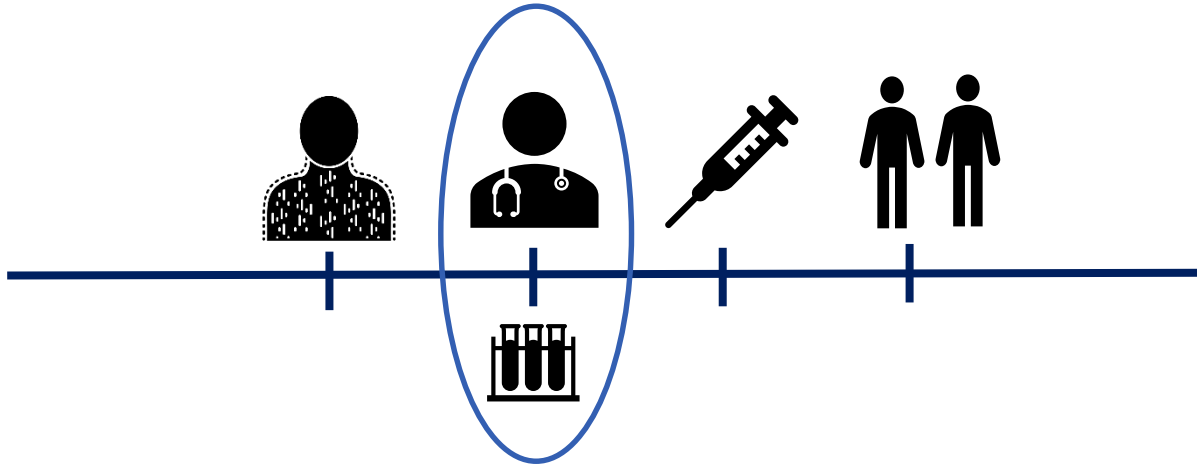
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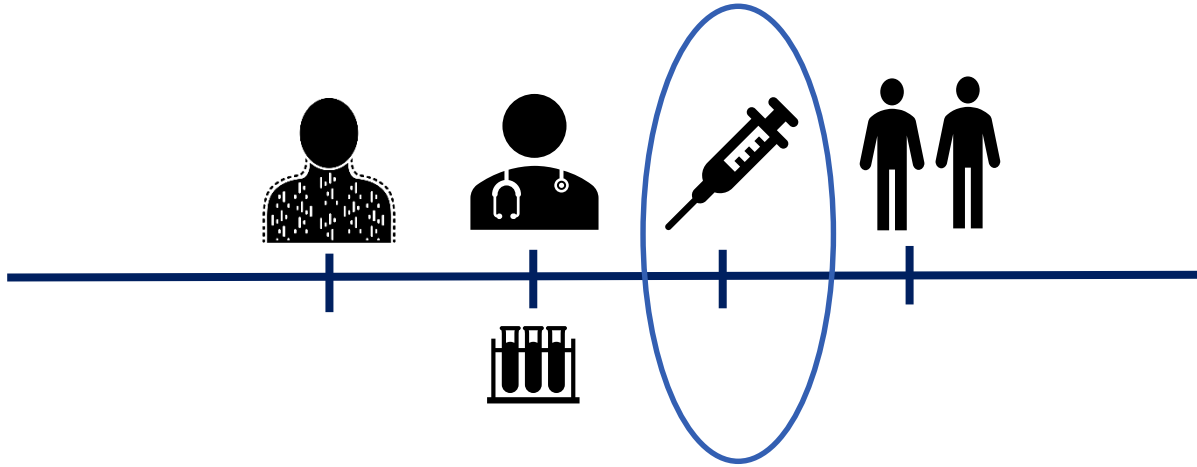
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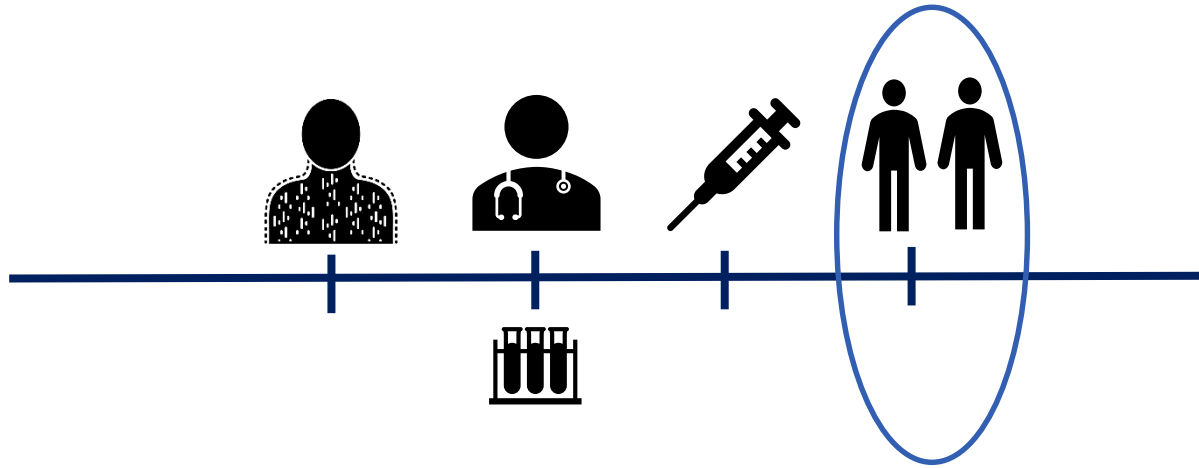
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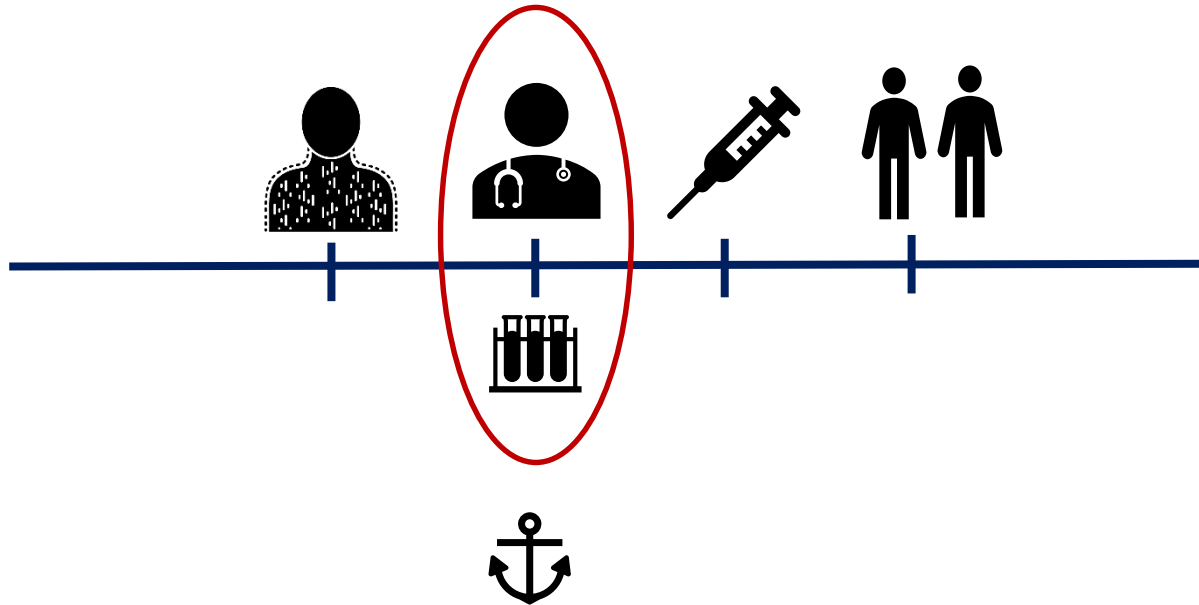
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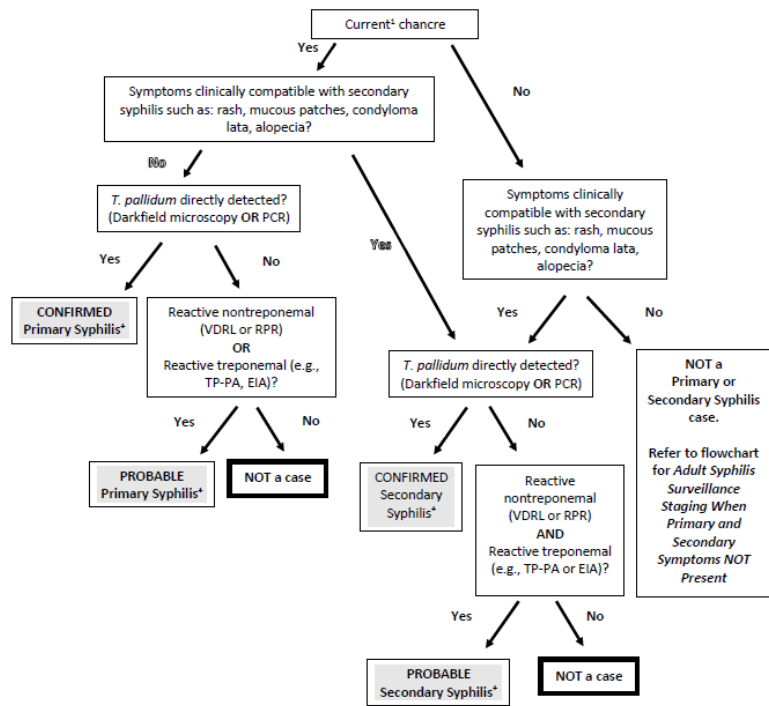
Syphilis cases should be categorized and reported by stage at the time of initial examination/diagnosis



A Systematic Approach

Adult Syphilis Surveillance Staging When Primary and Secondary Syphilis Symptoms Are Present

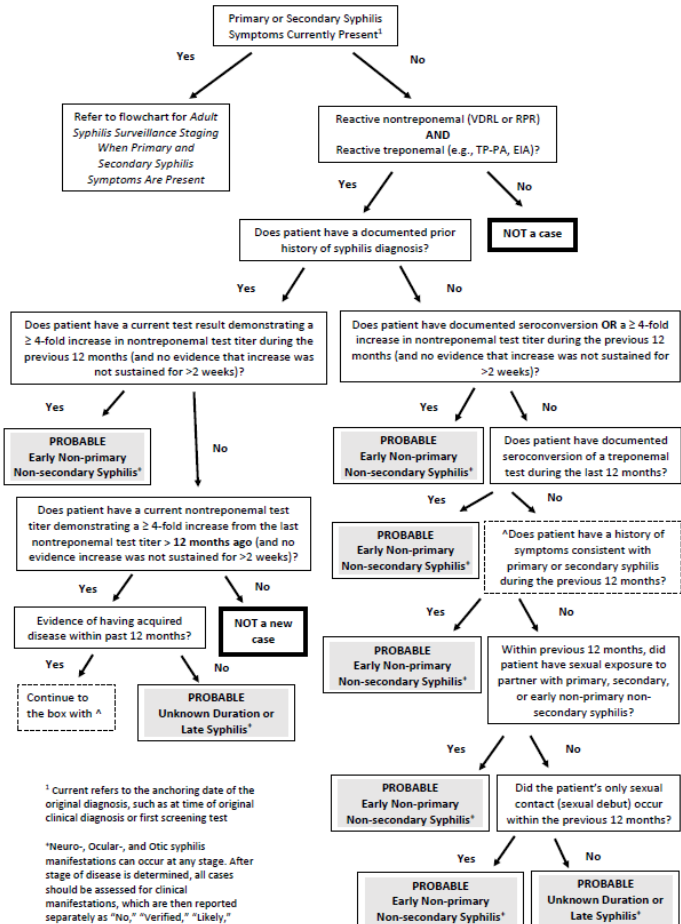
(Not to be used as guidance for treatment)



¹ Current refers to the anchoring date of the original diagnosis, such as at time of original clinical diagnosis or first screening test

*Neuro-, Ocular-, and Otic 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 "No," "Verified," "Likely," "Possible," or "Unknown."

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



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*Neuro-, Ocular-, and Otic 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 "No," "Verified," "Likely," "Possible," or "Unknown."

Start with primary syphilis assessment

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



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 (chancres)



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** (chancres)

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 (chancres)

**Probable
Primary
Syphilis**

No direct detection methods

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

--Nontreponemal (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



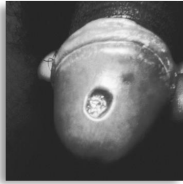
33-year-old



Case 1



33-year-old



6 weeks ago



Case 1



33-year-old

6 weeks ago



Case 1



33-year-old

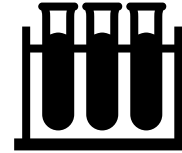
6 weeks ago



Case 1



33-year-old



RPR 1:64

TPPA Reactive

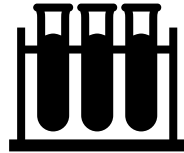
Case 1



33-year-old



6 weeks ago



RPR 1:64

TPPA Reactive

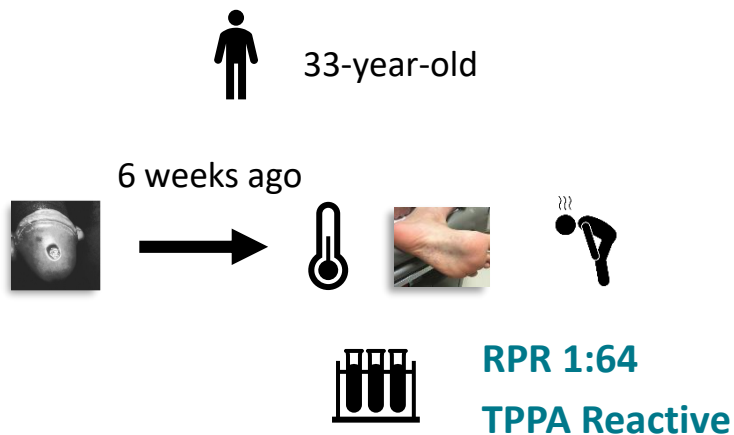
Please Vote:

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

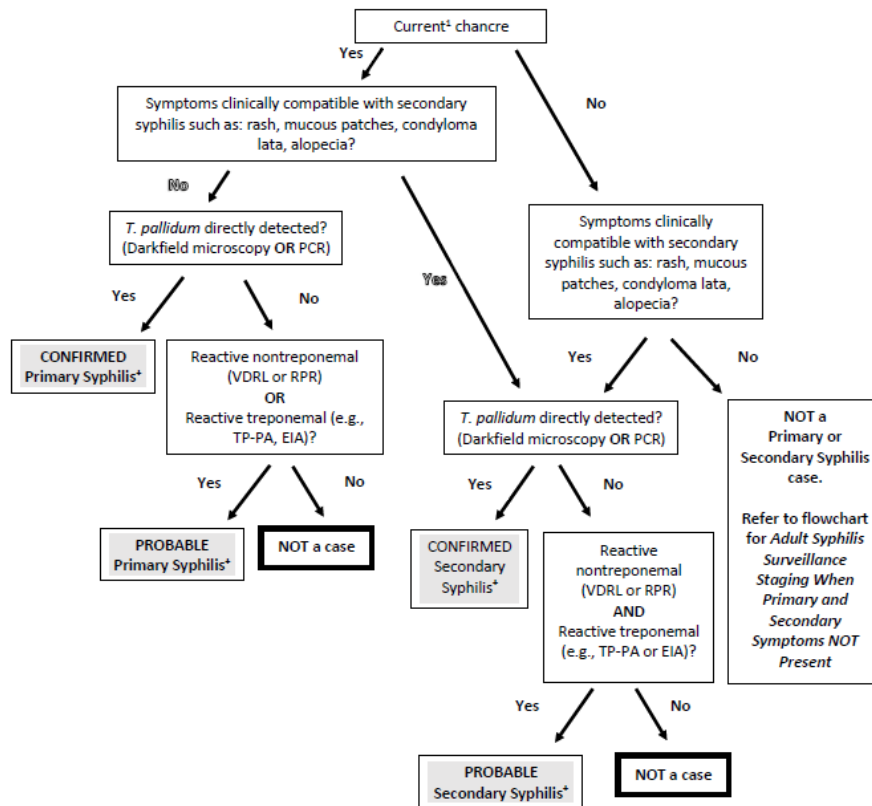
6 weeks ago



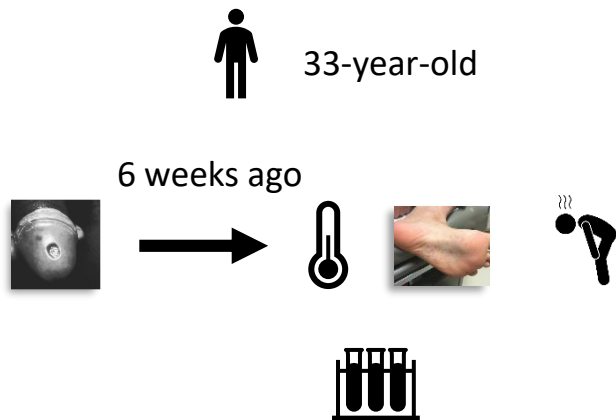
RPR 1:64
TPPA Reactive

Adult Syphilis Surveillance Staging When Primary and Secondary Syphilis Symptoms Are Present

(Not to be used as guidance for treatment)

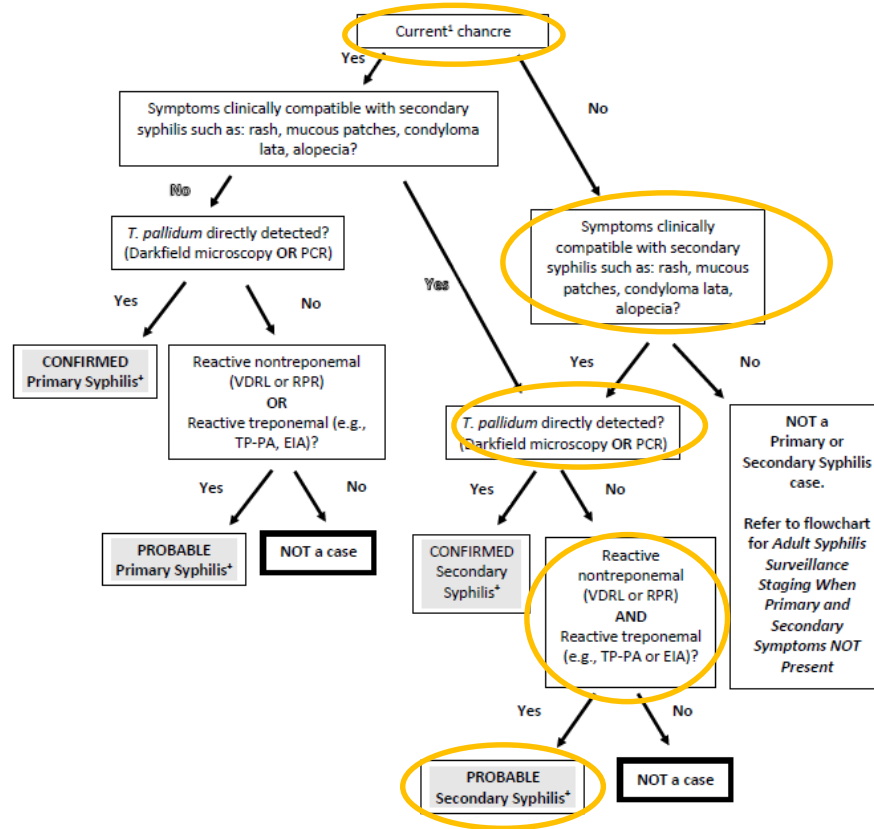


Case 1



Adult Syphilis Surveillance Staging When Primary and Secondary Syphilis Symptoms Are Present

(Not to be used as guidance for treatment)



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



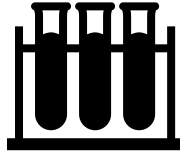
19 year old male
Penile chancre



Case 2



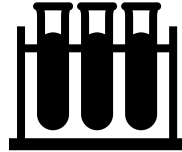
19 year old male
Penile chancre



Case 2



19 year old male
Penile chancre

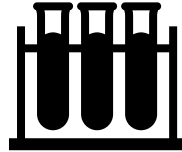


RPR nonreactive
TPPA nonreactive

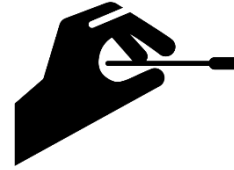
Case 2



19 year old male
Penile chancre



RPR nonreactive
TPPA nonreactive

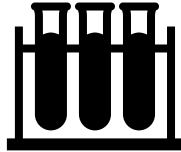


T. pallidum identified on
darkfield microscopy

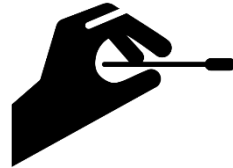
Case 2



19 year old male
Penile chancre



RPR nonreactive
TPPA nonreactive



T. pallidum identified on
darkfield microscopy

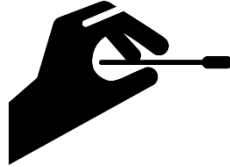
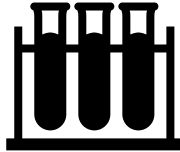
Please Vote:

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



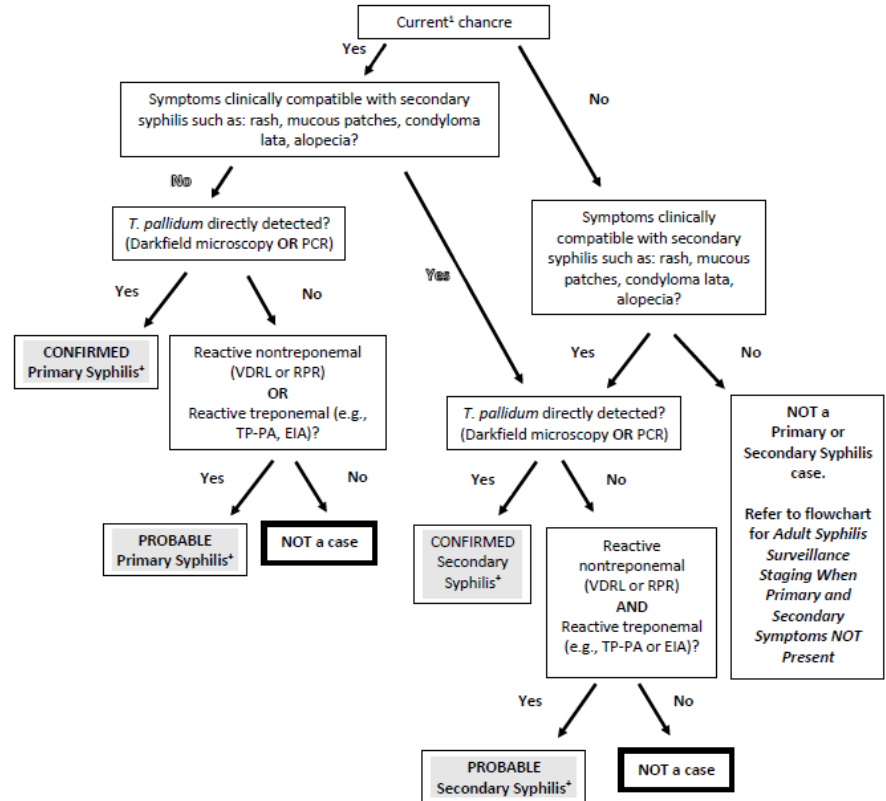
19 year old male
Penile chancre



RPR nonreactive
TPPA nonreactive

T. pallidum
identified on
darkfield
microscopy

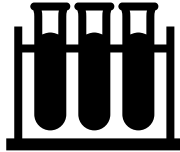
Adult Syphilis Surveillance Staging When Primary and Secondary Syphilis Symptoms Are Present (Not to be used as guidance for treatment)



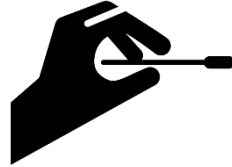
Case 2



19 year old male
Penile chancre

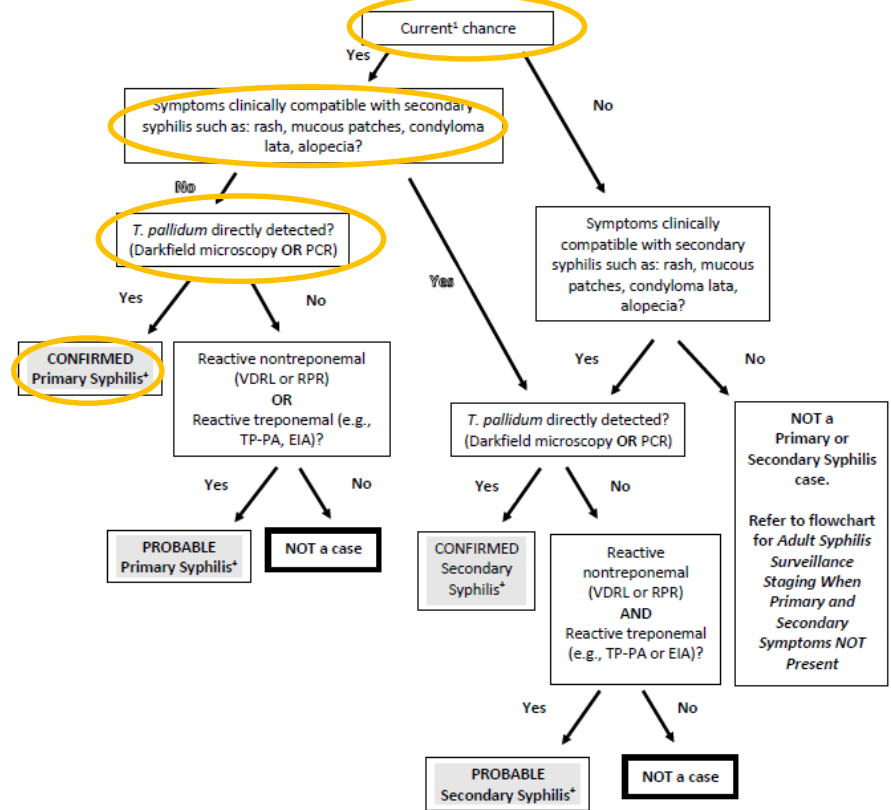


RPR nonreactive
TPPA nonreactive



T. pallidum
identified on
darkfield
microscopy

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



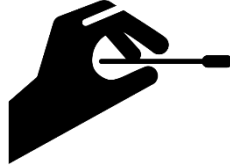
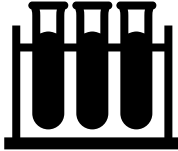
Case 2



19 year old male
Penile chancre



RPR nonreactive
TPPA nonreactive

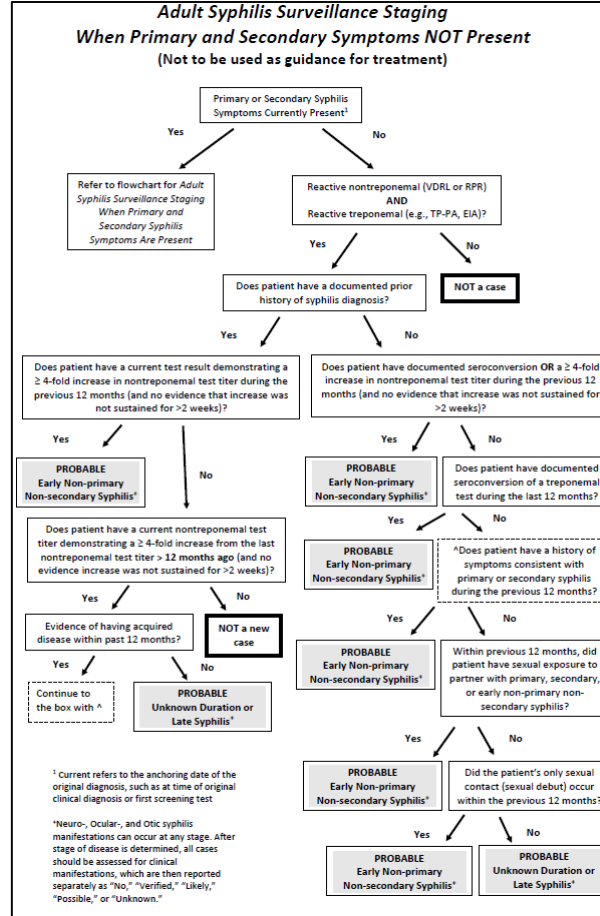


T. pallidum
identified on
darkfield
microscopy

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



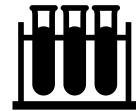
Case 3



22-year-old MSM
Asymptomatic



RPR 1:16
TPPA Reactive



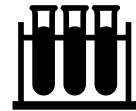
Case 3



22-year-old MSM



RPR 1:16
TPPA Reactive



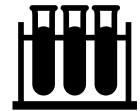
Case 3



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)

9 months ago
Nonreactive RPR



3 months ago
resolved
anal ulcer



RPR 1:16
TPPA Reactive



1 month ago
resolved
rash



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 3



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

9 months ago
Nonreactive RPR



3 months ago
resolved
anal ulcer



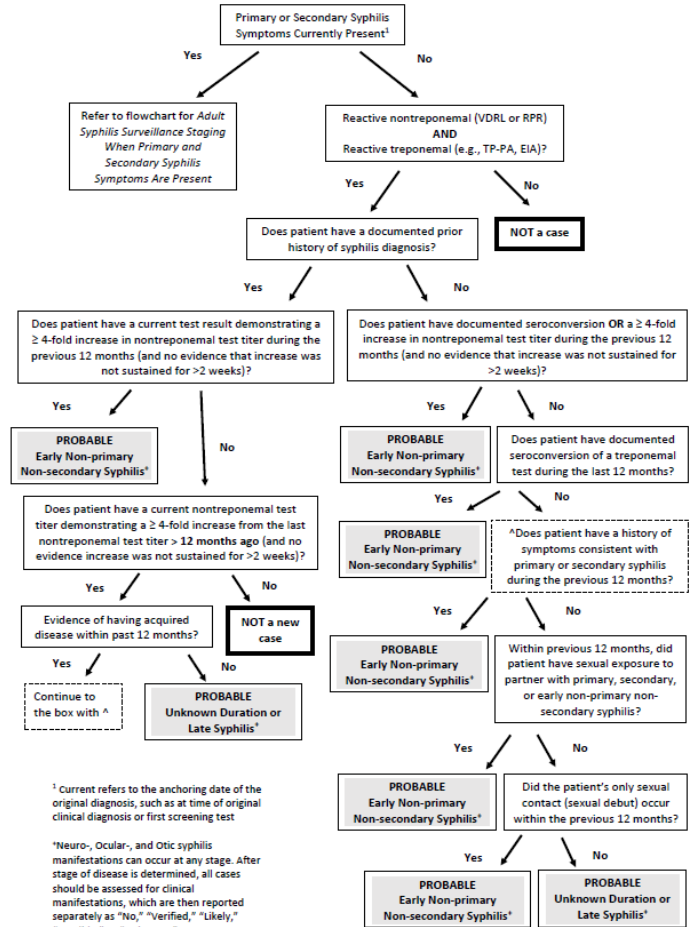
RPR 1:16
TPPA Reactive



1 month ago
resolved
rash



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



Case 3



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

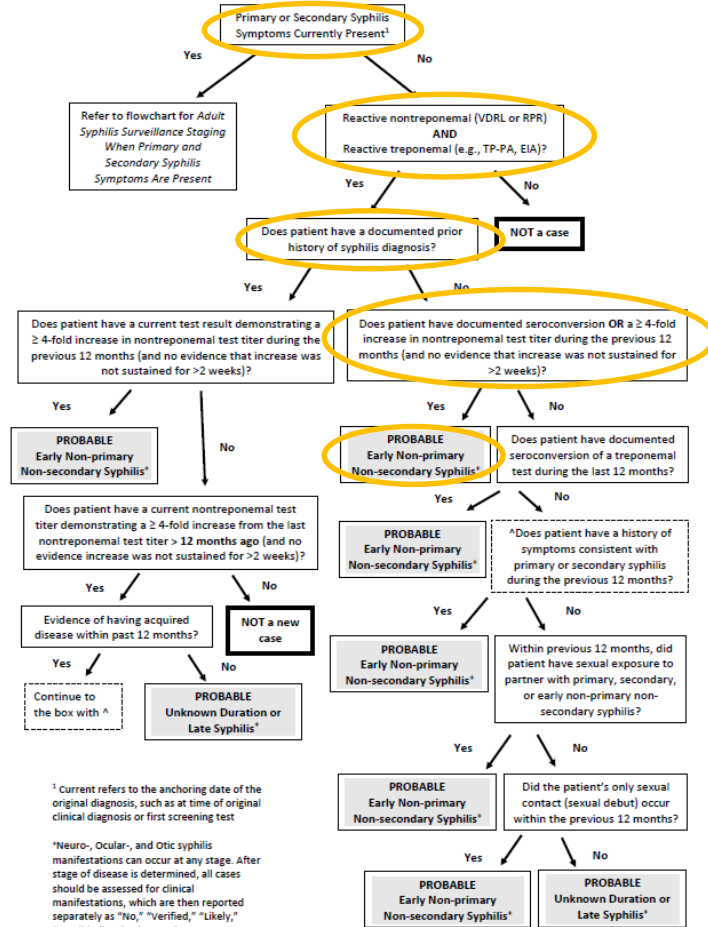
9 months ago
Nonreactive RPR



RPR 1:16
TPPA Reactive



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



Case 3



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

9 months ago
Nonreactive RPR



RPR 1:16
TPPA Reactive



Case: Early non-primary,
non-secondary

- No primary/secondary symptoms at time of diagnosis
- Seroconversion in past 12 months

Case 3



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

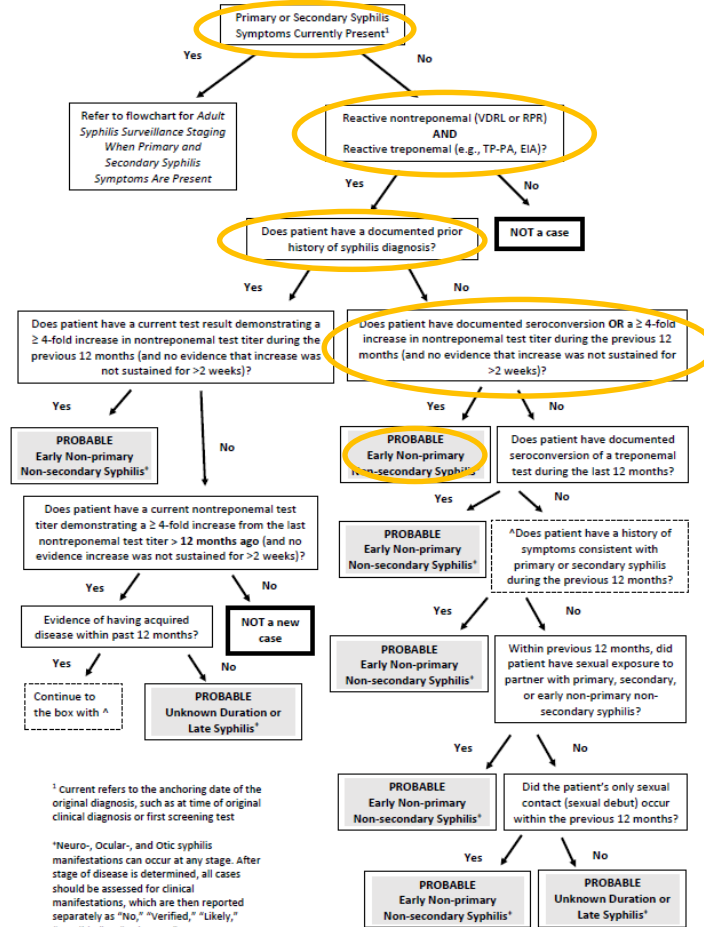
9 months ago
Nonreactive RPR



RPR 1:16
TPPA Reactive



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



¹ Current refers to the anchoring date of the original diagnosis, such as at time of original clinical diagnosis or first screening test

² "Neuro-, Ocular-, and Otic 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 "No," "Verified," "Likely," "Possible," or "Unknown."

Case 3



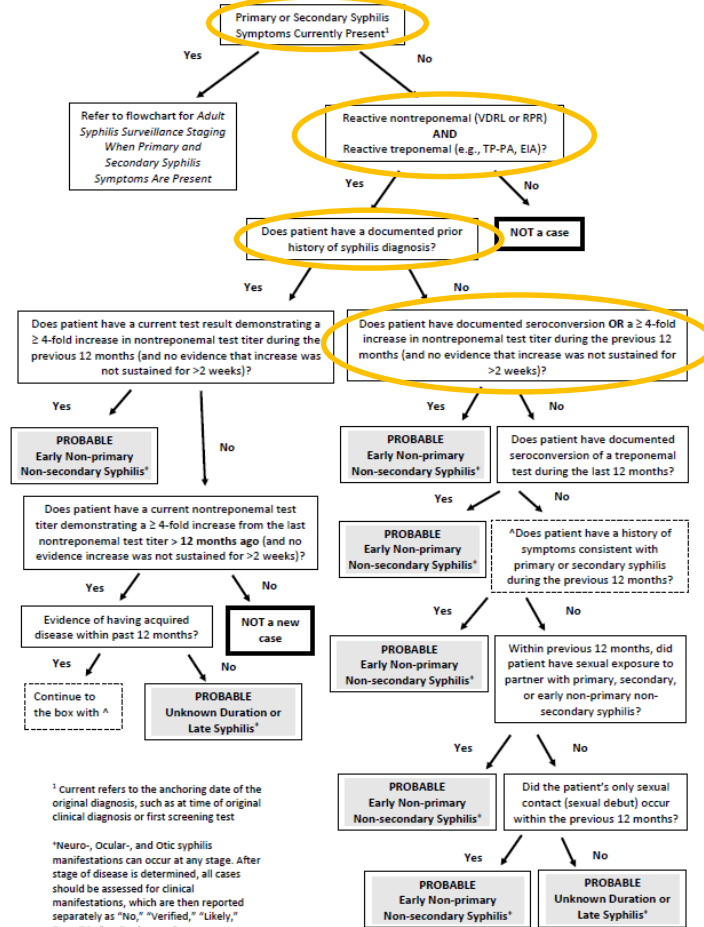
22-year-old MSM
Asymptomatic (At
time of testing)



RPR 1:16
TPPA Reactive



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



¹ Current refers to the anchoring date of the original diagnosis, such as at time of original clinical diagnosis or first screening test

*Neuro-, Ocular-, and Otic 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 "No," "Verified," "Likely," "Possible," or "Unknown."

Case 3



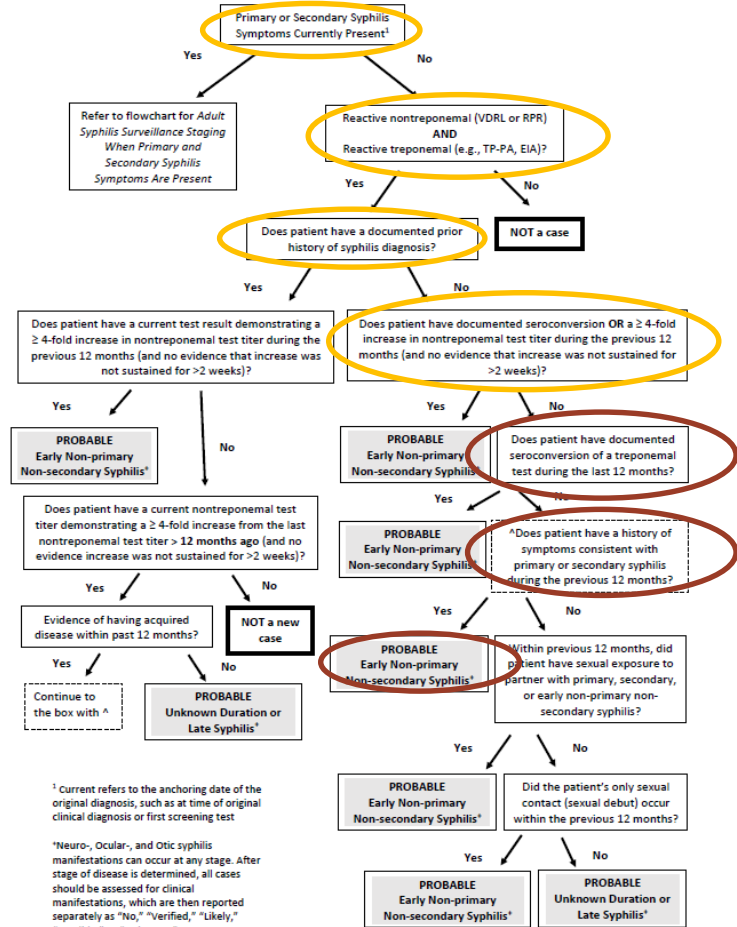
22-year-old MSM
Asymptomatic (At
time of testing)



RPR 1:16
TPPA Reactive



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



¹ Current refers to the anchoring date of the original diagnosis, such as at time of original clinical diagnosis or first screening test

² "Neuro-, Ocular-, and Otic 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 "No," "Verified," "Likely," "Possible," or "Unknown."

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

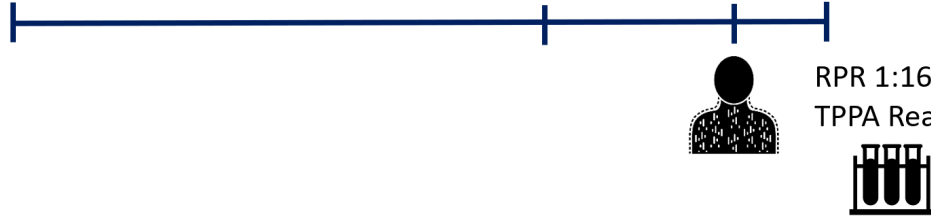
If patient has **NO history of syphilis**, and you **could NOT** prove ENPNS

**Probable unknown
duration or late syphilis**

Case 3

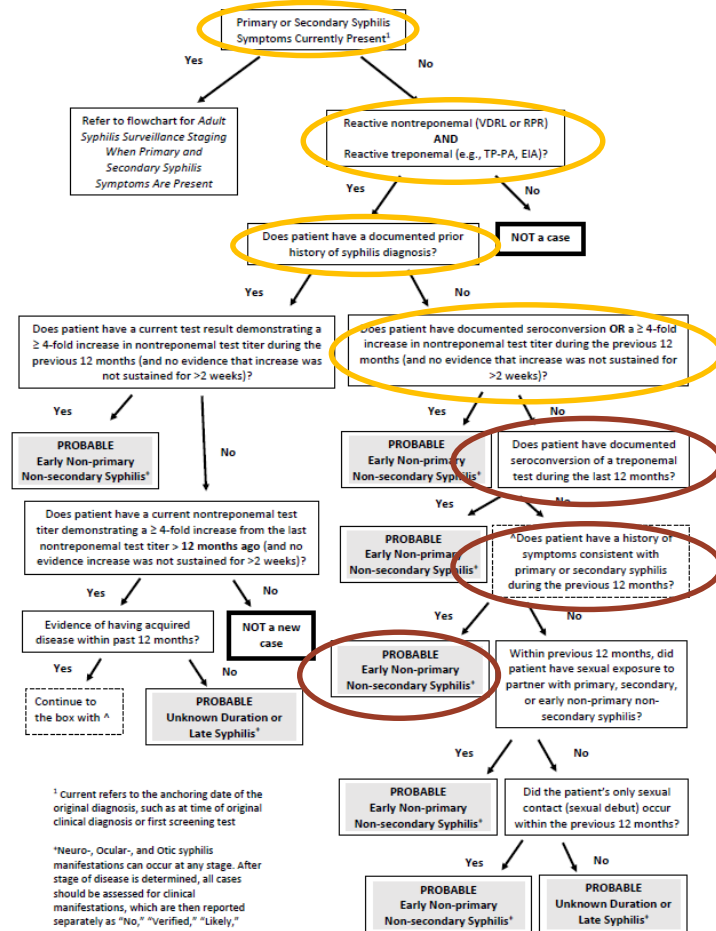


22-year-old MSM
Asymptomatic (At
time of testing)



RPR 1:16
TPPA Reactive

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



Case 3



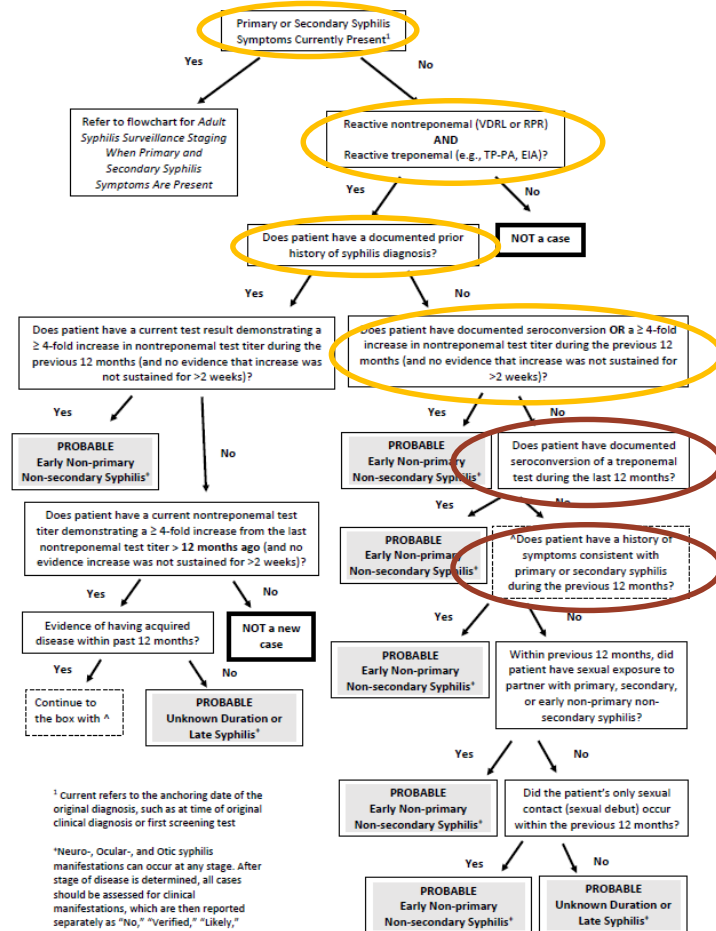
22-year-old MSM
Asymptomatic (At
time of testing)



RPR 1:16
TPPA Reactive



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



Case 3



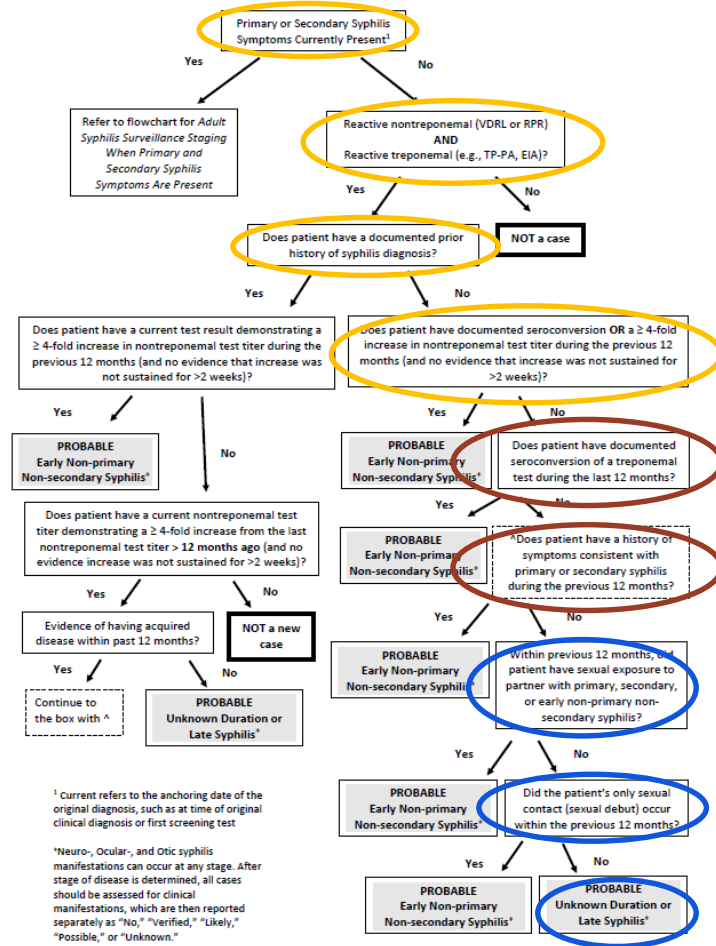
22-year-old MSM
Asymptomatic (At
time of testing)



RPR 1:16
TPPA Reactive



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



Case Scenarios

Case 4



Case 4



25-year-old
female



Asymptomatic

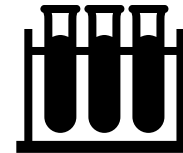
Case 4



25-year-old
female



Asymptomatic



RPR 1:16
TPPA Reactive

Case 4



25-year-old
female

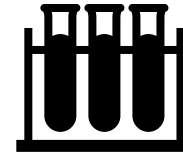
Nonreactive RPR



13 months



Asymptomatic



RPR 1:16
TPPA Reactive

Case 4



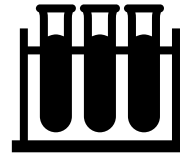
25-year-old
female



Nonreactive RPR



13 months



RPR 1:16
TPPA Reactive

- 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.

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 4



25-year-old female

Nonreactive RPR



13 months



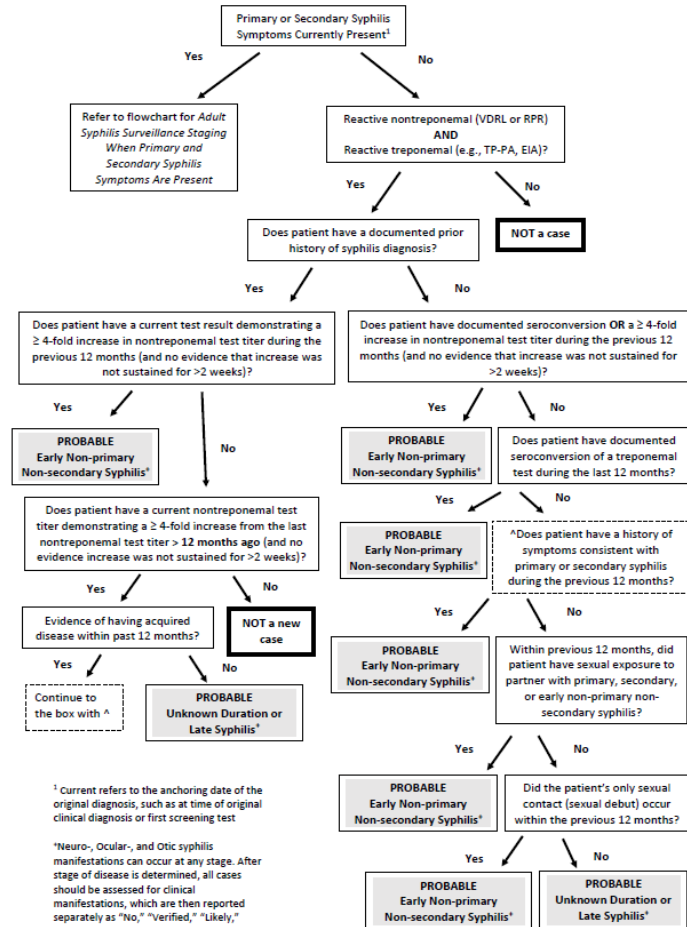
Asymptomatic



RPR 1:16
TPPA Reactive

- 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.

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



Case 4



25-year-old female

Nonreactive RPR



13 months



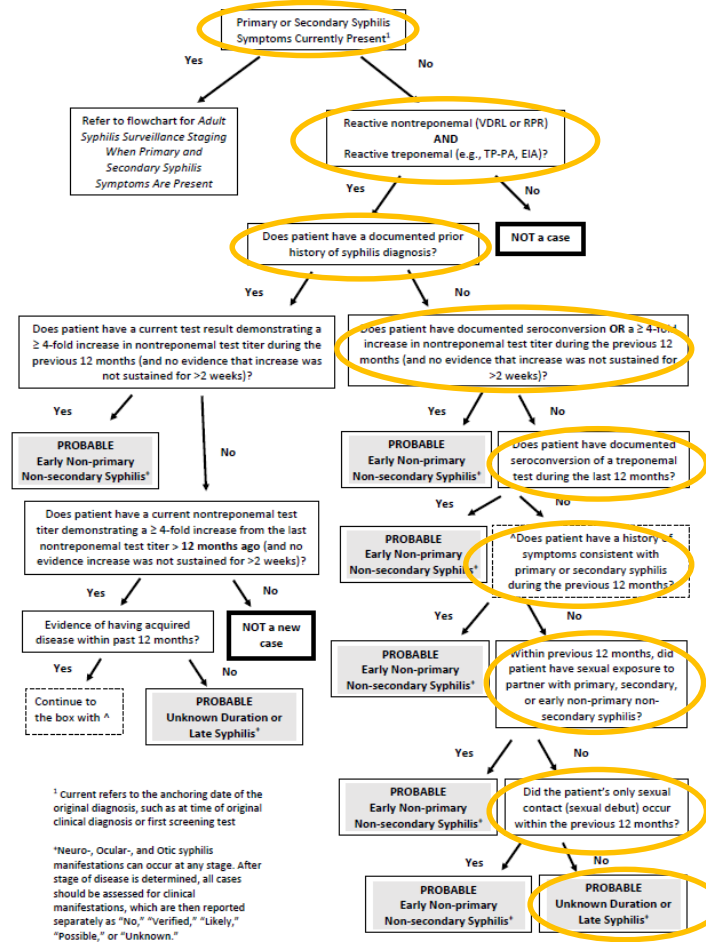
Asymptomatic



RPR 1:16
TPPA Reactive

- 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.

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



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² Neuro-, Ocular-, and Otic 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 "No," "verified," "likely," "possible," or "unknown."

Case 4



25-year-old
female

Nonreactive RPR



13 months



Asymptomatic



RPR 1:16
TPPA Reactive

Case: Unknown duration or late

- No primary/secondary symptoms
- Meets lab criteria
- No evidence of infection in last year

Case 5



Case 5



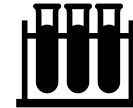
29-year-old
HIV+



Case 5



29-year-old
HIV+



RPR 1:32
TPPA Reactive

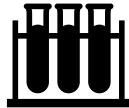
Case 5



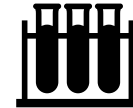
29-year-old
HIV+



6 months



RPR 1:2
TPPA Nonreactive



RPR 1:32
TPPA Reactive

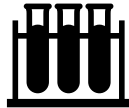
Case 5



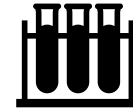
29-year-old
HIV+



6 months



RPR 1:2
TPPA Nonreactive



RPR 1:32
TPPA Reactive

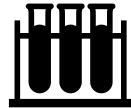
Case 5



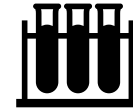
29-year-old
HIV+



6 months



RPR 1:2
TPPA Nonreactive



RPR 1:32
TPPA Reactive

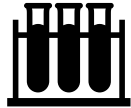
Case 5



29-year-old
HIV+

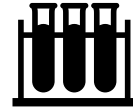


6 months



RPR 1:2

TPPA Nonreactive



RPR 1:32

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 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.

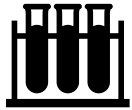
Case 5



29-year-old
HIV+

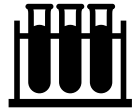


6 months



RPR 1:2

TPPA Nonreactive



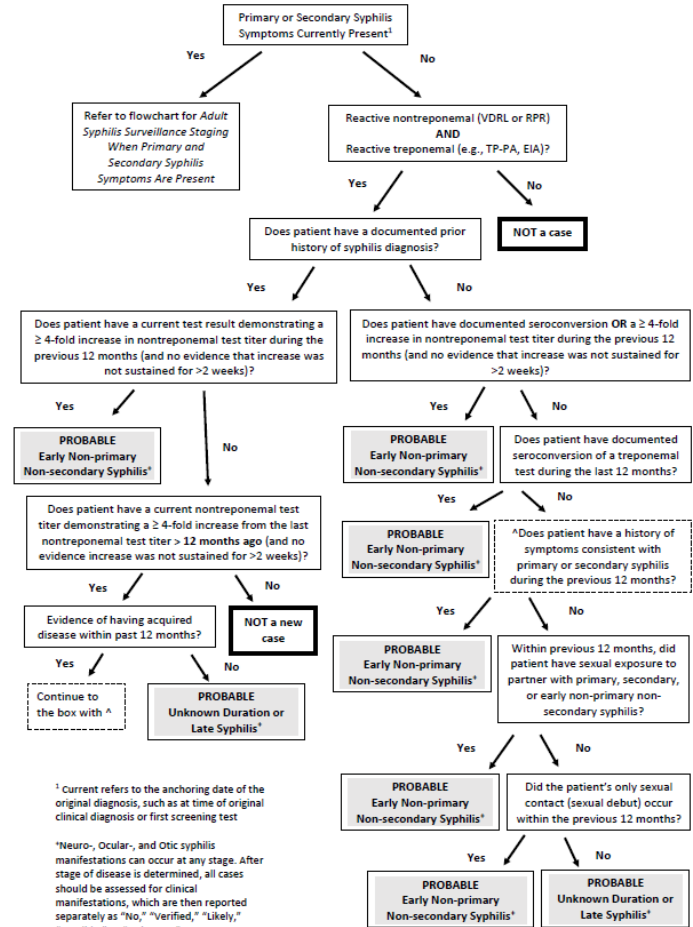
RPR 1:32

TPPA Reactive



- 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.

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



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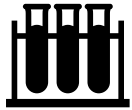
Case 5



29-year-old
HIV+

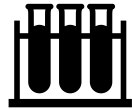


6 months



RPR 1:2

TPPA Nonreactive

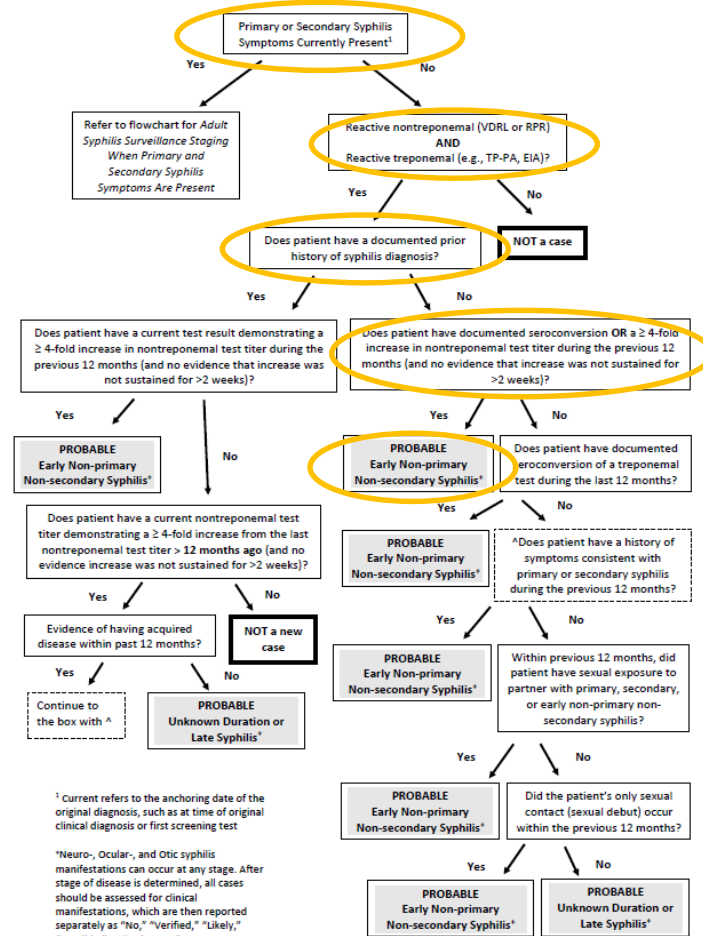


RPR 1:32

TPPA Reactive

- 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.

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

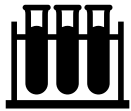


Case 5

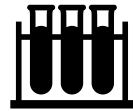


29-year-old
HIV+

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



Case 6



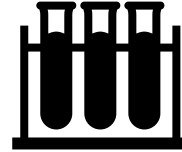
- 23 year old female
- chancre
- 1 new partner who denies syphilis



Case 6



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

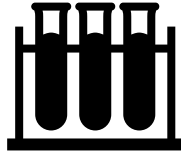


RPR 1:4
TPPA nonreactive

Case 6



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



RPR 1:4
TPPA nonreactive

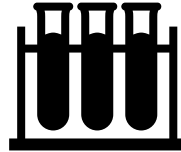
Please Vote:

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

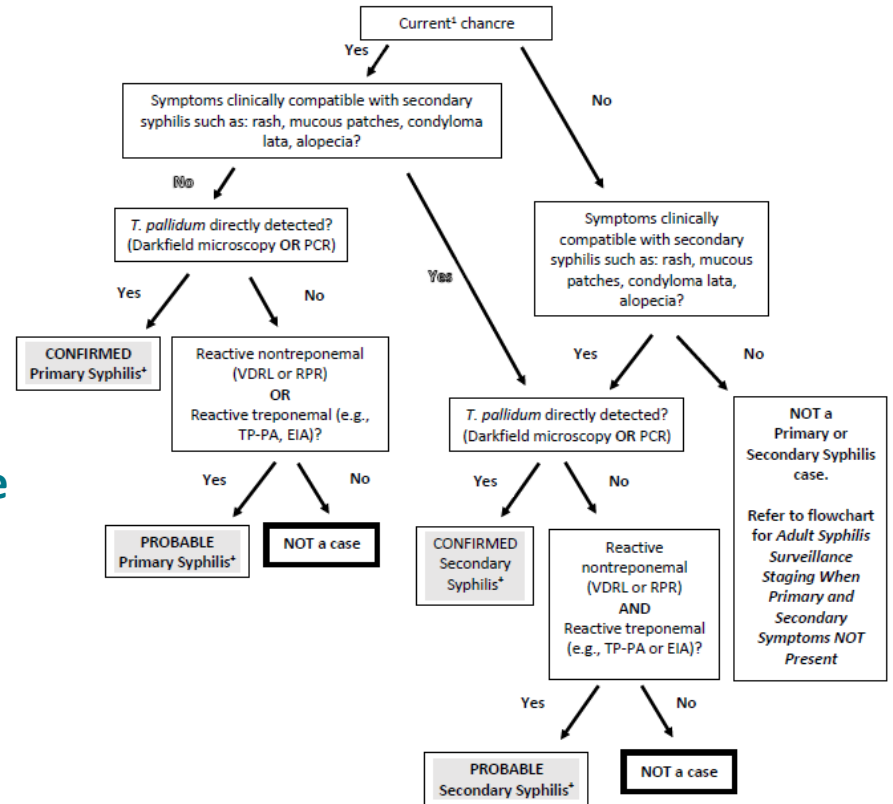


- 23 year old female
- chancre
- 1 new partner who denies syphilis



RPR 1:4
TPPA nonreactive

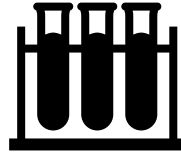
Adult Syphilis Surveillance Staging When Primary and Secondary Syphilis Symptoms Are Present (Not to be used as guidance for treatment)



Case 6

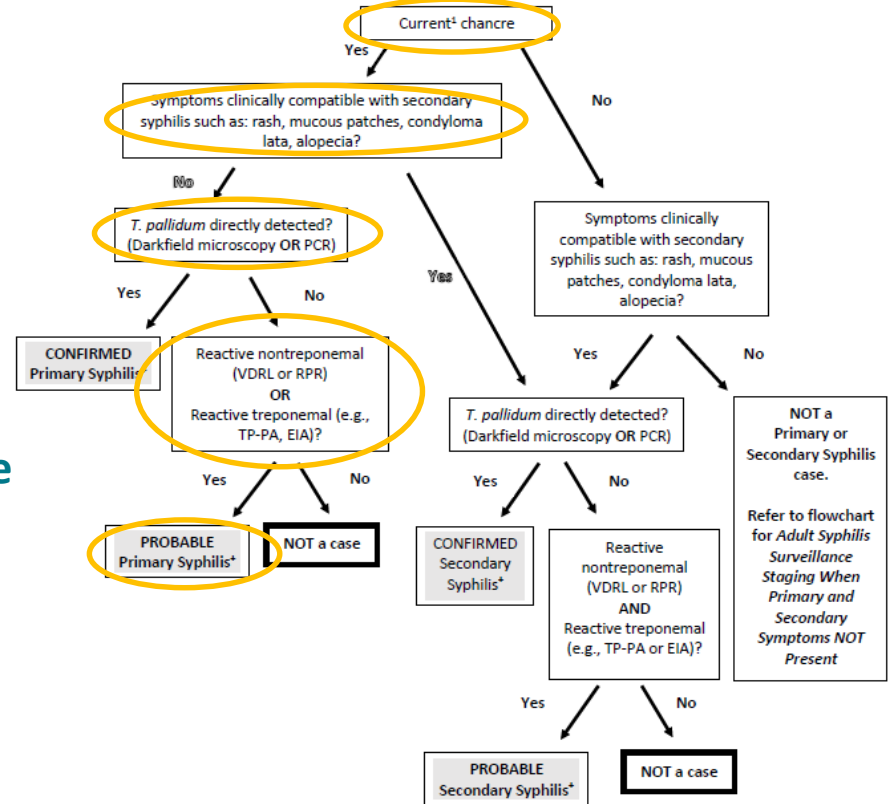


- 23 year old female
- chancre
- 1 new partner who denies syphilis



RPR 1:4
TPPA nonreactive

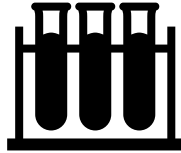
Adult Syphilis Surveillance Staging When Primary and Secondary Syphilis Symptoms Are Present (Not to be used as guidance for treatment)



Case 6



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



RPR 1:4
TPPA nonreactive

Case: Probable primary syphilis

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

Case 7



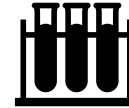
Case 7



48 year old
Past history of syphilis
No new sex partners



Asymptomatic

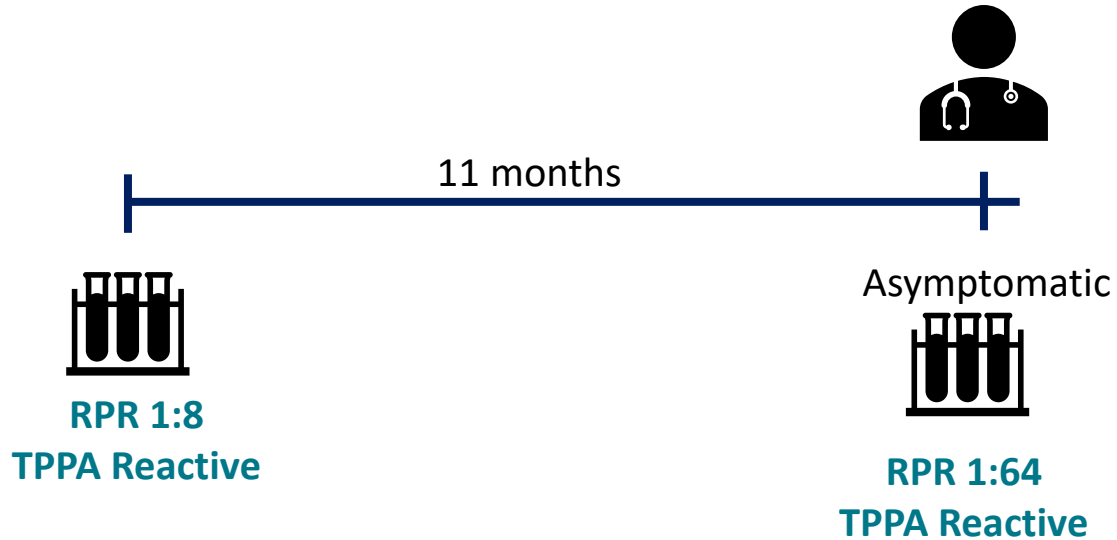


RPR 1:64
TPPA Reactive

Case 7



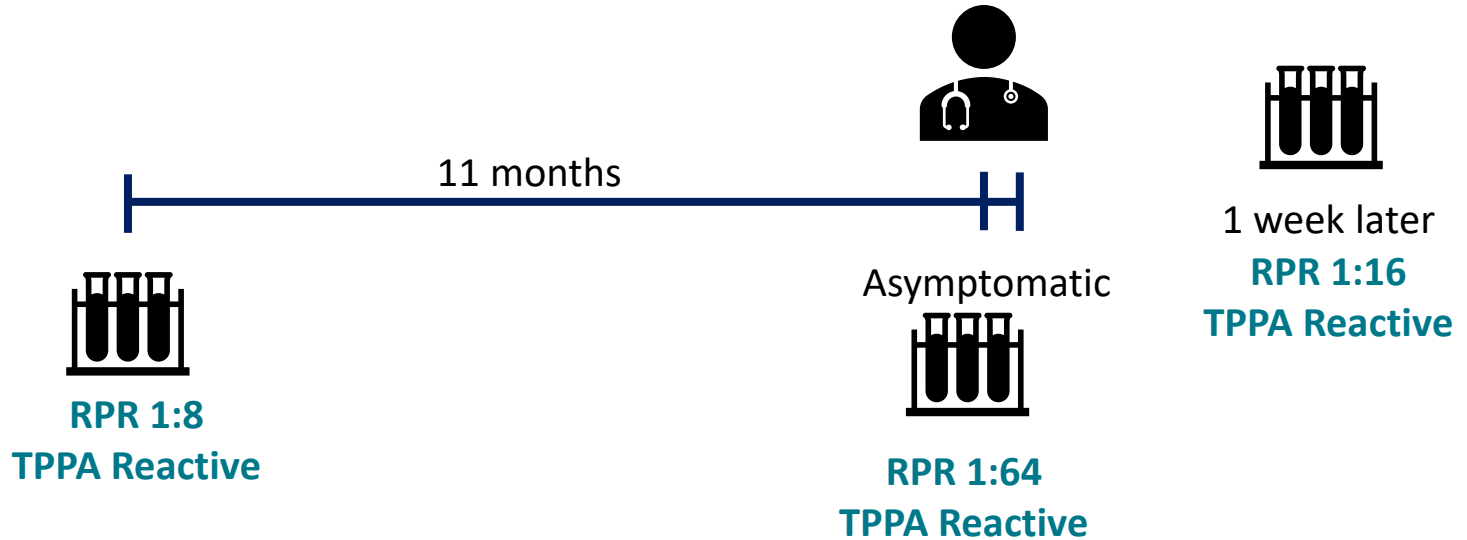
48 year old
Past history of syphilis
No new sex partners



Case 7



48 year old
Past history of syphilis
No new sex partners



Case 7



48 year old
Past history of syphilis
No new sex partners

Please Vote:

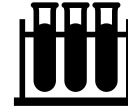
1. Confirmed Primary Syphilis
2. Probable Primary Syphilis
3. Confirmed Secondary Syphilis
4. Probable Secondary Syphilis
5. Early non-primary, non-secondary
6. Unknown duration or late
7. Not a case



11 months

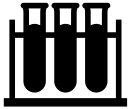


Asymptomatic



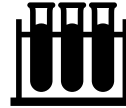
1 week later

RPR 1:16
TPPA Reactive



RPR 1:8

TPPA Reactive



RPR 1:64

TPPA Reactive

Case 7

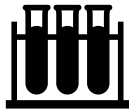


48 year old
Past history of syphilis
No new sex partners



1 week later
RPR 1:16
TPPA Reactive

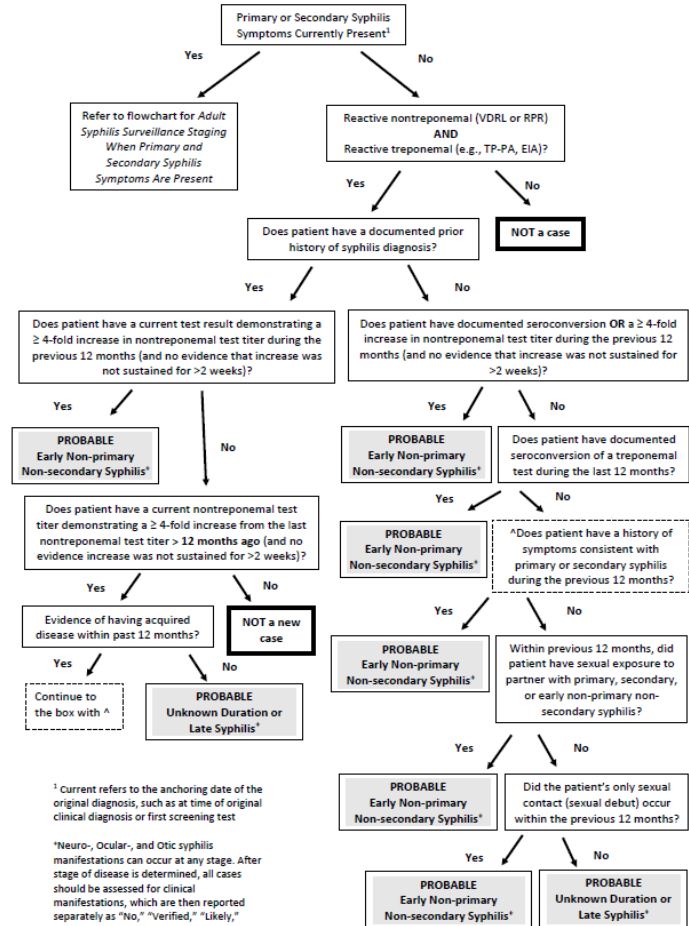
Asymptomatic
RPR 1:64
TPPA Reactive



RPR 1:8
TPPA Reactive



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



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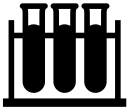
Case 7



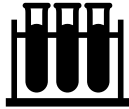
48 year old
Past history of syphilis
No new sex partners



1 week later
RPR 1:16
TPPA Reactive



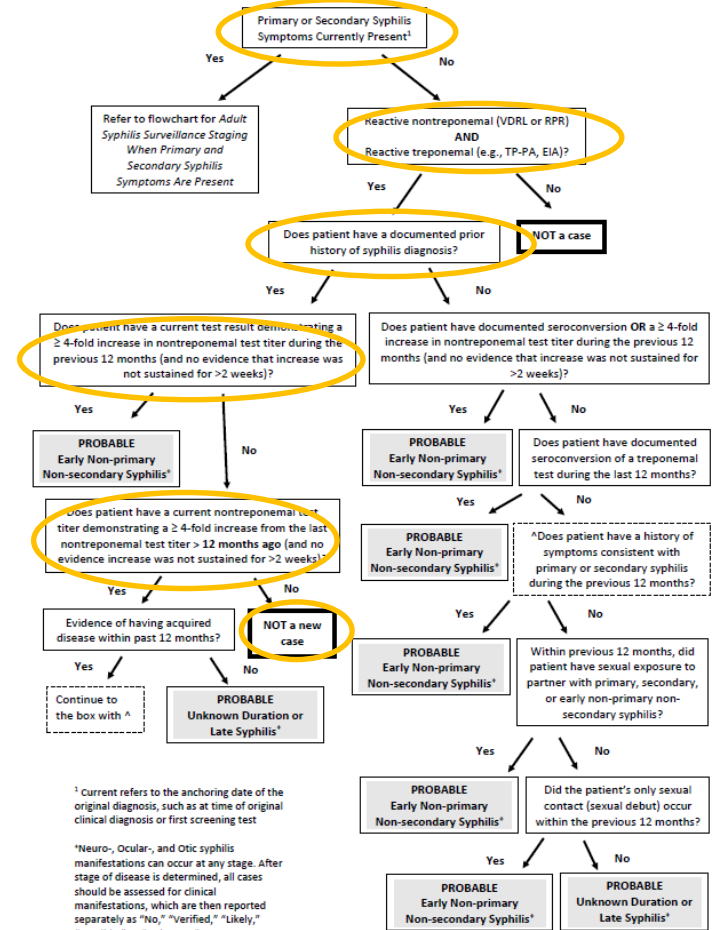
Asymptomatic
RPR 1:64
TPPA Reactive



RPR 1:8
TPPA Reactive
~baseline



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



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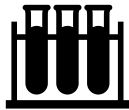
Case 7



48 year old
Past history of syphilis
No new sex partners

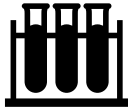


11 months



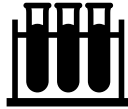
RPR 1:8

TPPA Reactive
~baseline



Asymptomatic

RPR 1:64
TPPA Reactive



1 week later
RPR 1:16
TPPA Reactive

Case: Not a case

- If test is repeated, needs to show increase is sustained > 2 weeks
- A repeat test is not required

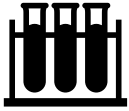
Case 7



48 year old
Past history of syphilis
No new sex partners

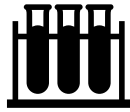


11 months



RPR 1:8

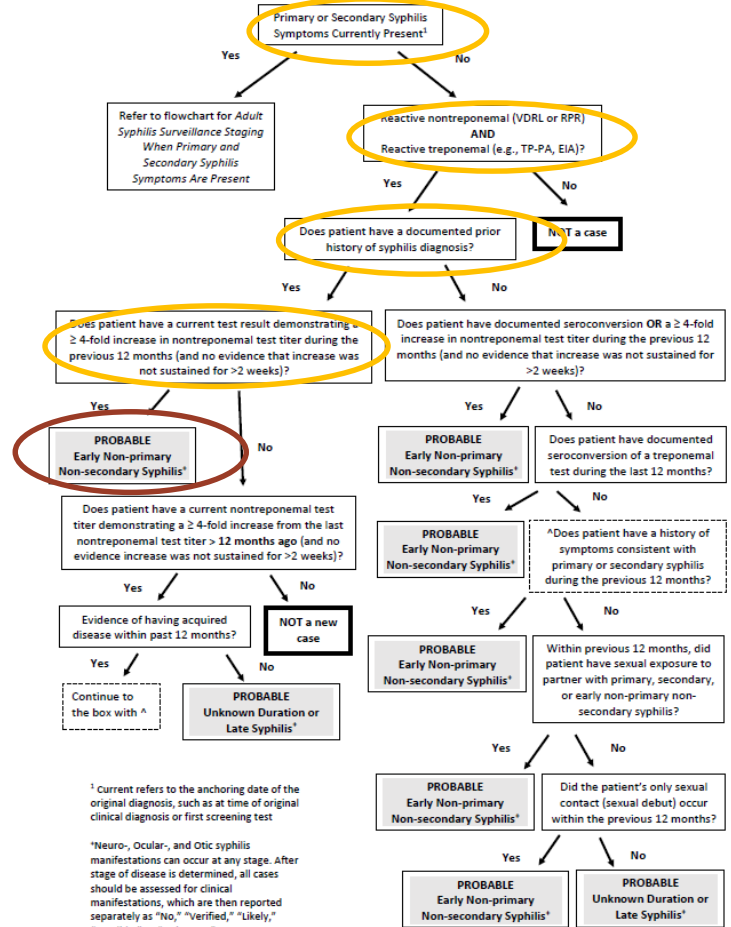
TPPA Reactive
~baseline



Asymptomatic

RPR 1:64
TPPA Reactive

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



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Case 8



Case 8

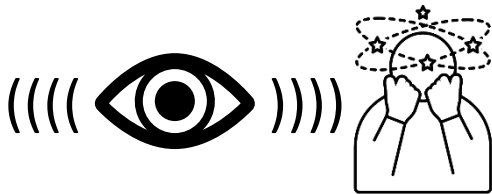
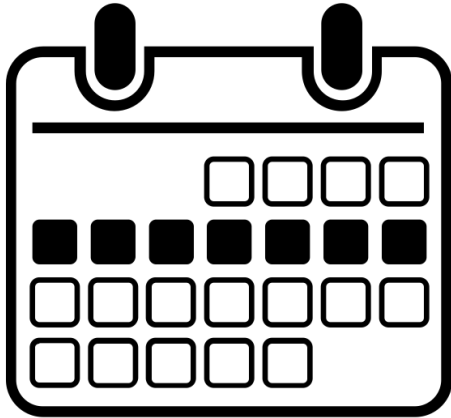


28 year old female
Sex worker

Case 8



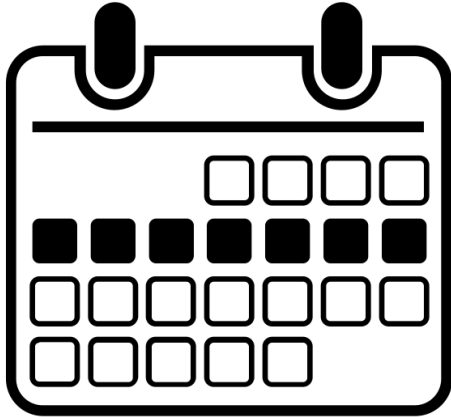
28 year old female
Sex worker



Case 8

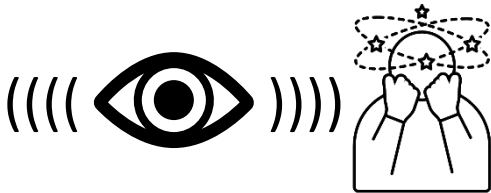


28 year old female
Sex worker



No history of genital
ulcers or rashes

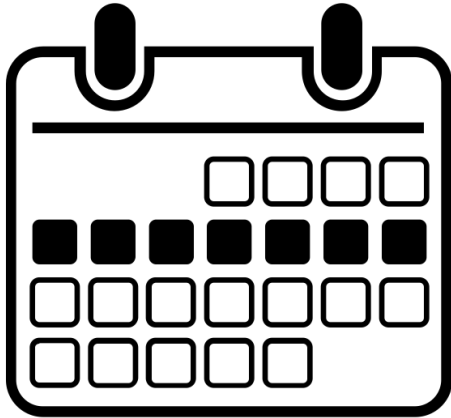
Syphilis testing negative
18 months ago



Case 8



28 year old female
Sex worker



No history of genital
ulcers or rashes

**Syphilis testing negative
18 months ago**

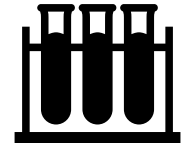
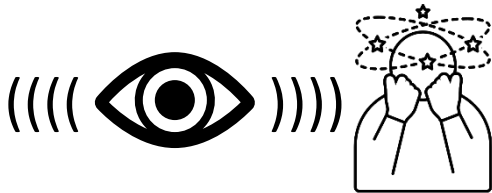
In ED:

RPR 1:64

TPPA reactive

Diagnosed Ocular Syphilis

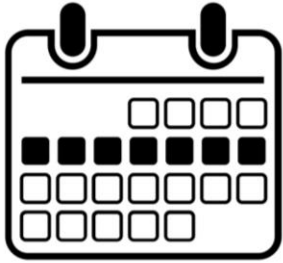
Treated with IV penicillin



Case 8



28 year old female
Sex worker



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



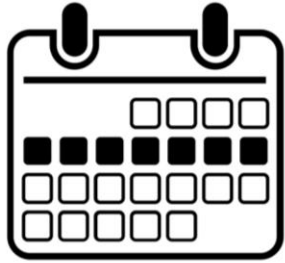
Please Vote:

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

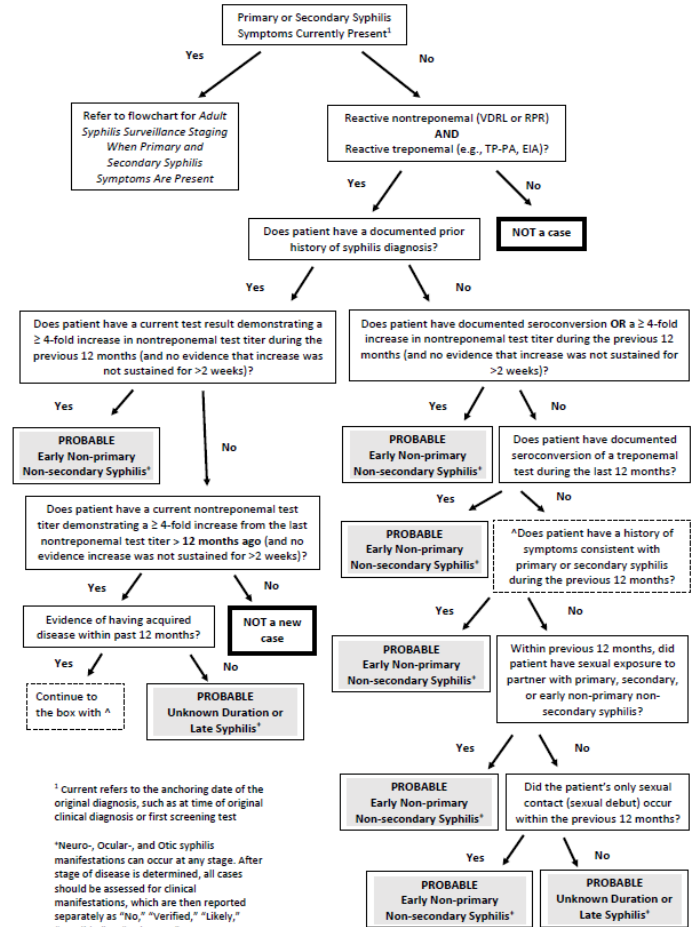
Syphilis testing negative
18 months ago



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



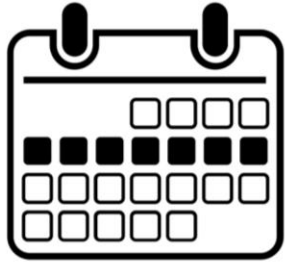
Adult Syphilis Surveillance Staging When Primary and Secondary Symptoms NOT Present (Not to be used as guidance for treatment)



Case 8



28 year old female
Sex worker



No history of genital
ulcers or rashes

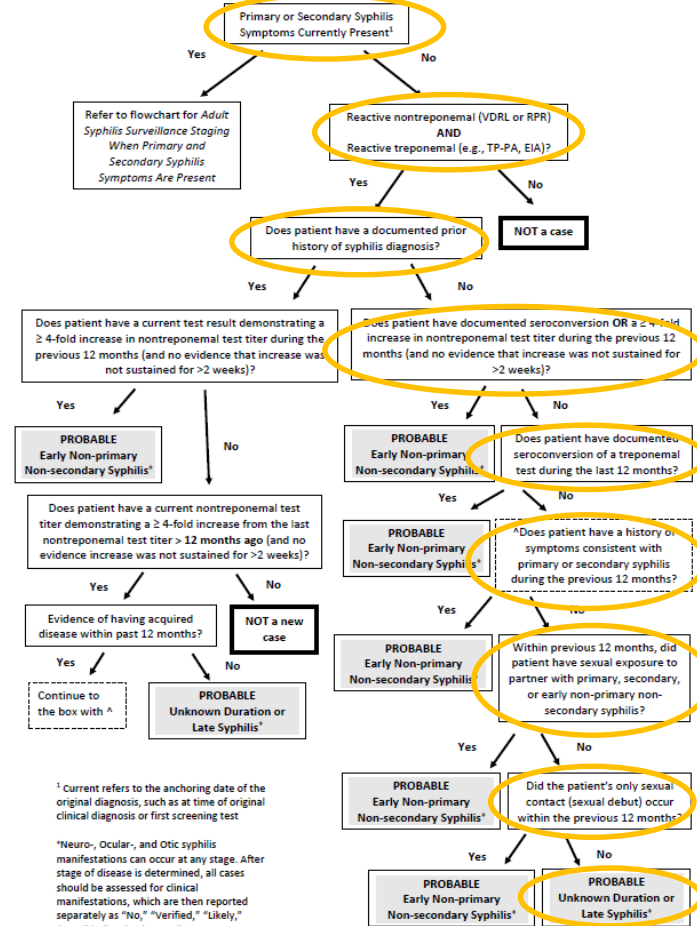
Syphilis testing negative
18 months ago



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



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



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:
Unknown duration or late
✓ Ocular manifestations



#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

ICON Credits: Noun Project

Tired – Gan Khoon

Rash – Priyanka

Hand rash – Veremeya

Dizziness – Priyanka

Week – Rohit Arun Rao

Swab – Luis Prado

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

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
Robert (Bobby) McDonald
BJX5@cdc.gov

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TTY: 1-888-232-6348 www.cdc.gov

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