

Syphilis Clinical Training

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Kentucky Public Health
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TEAM 
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CABINET FOR HEALTH
AND FAMILY SERVICES

We will cover:

How to recognize syphilis

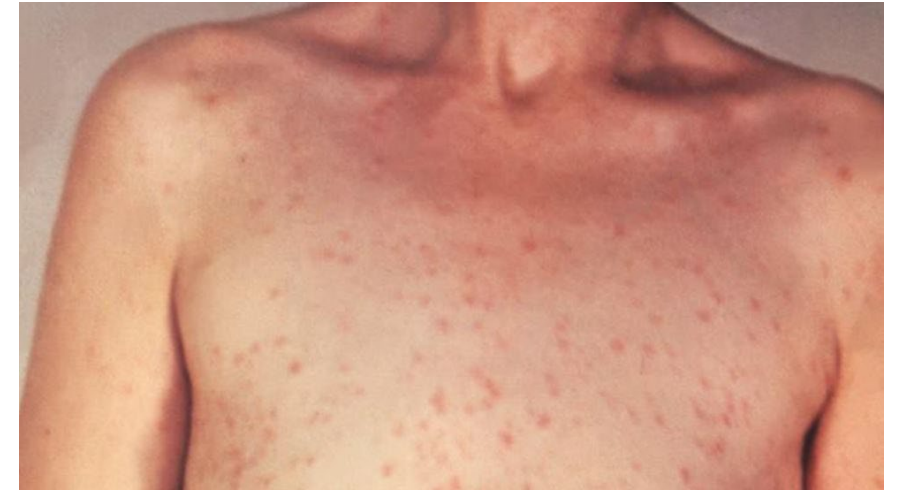
Interpretation of test results

Treatment decisions

Special considerations in pregnancy

Case 1

- 🛡️ A 44 year-old woman presents to her primary care physician with a rash.
- 🛡️ The rash developed a few days ago.
 - 🛡️ Reddish-copper macular rash
 - 🛡️ Diffuse, scaly
 - 🛡️ On trunk and extremities, palms and soles
- 🛡️ It is not itchy or painful.
- 🛡️ No one around her has had a similar rash.



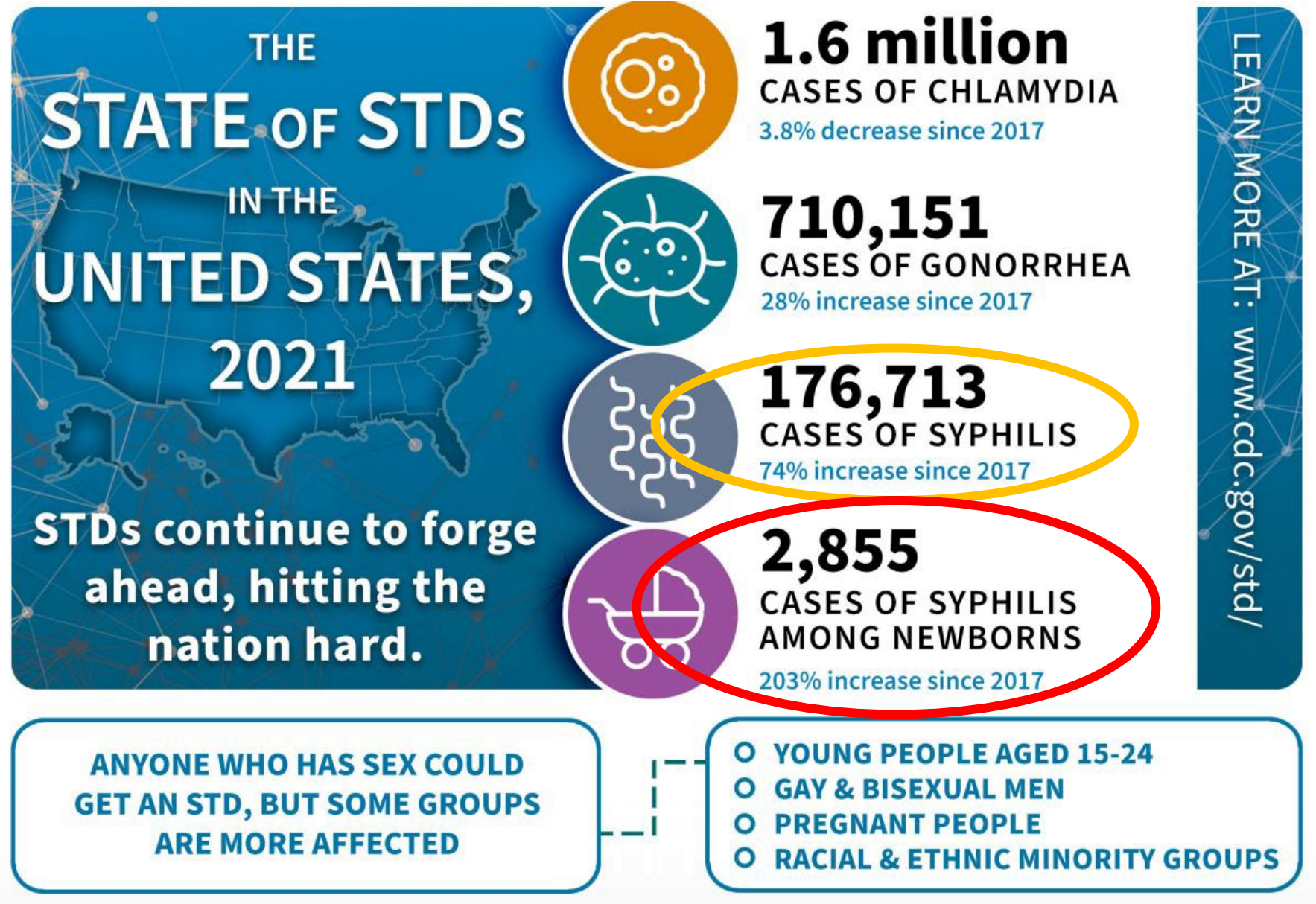
[CDC's Public Health Image Library](#)

What is the best next step?

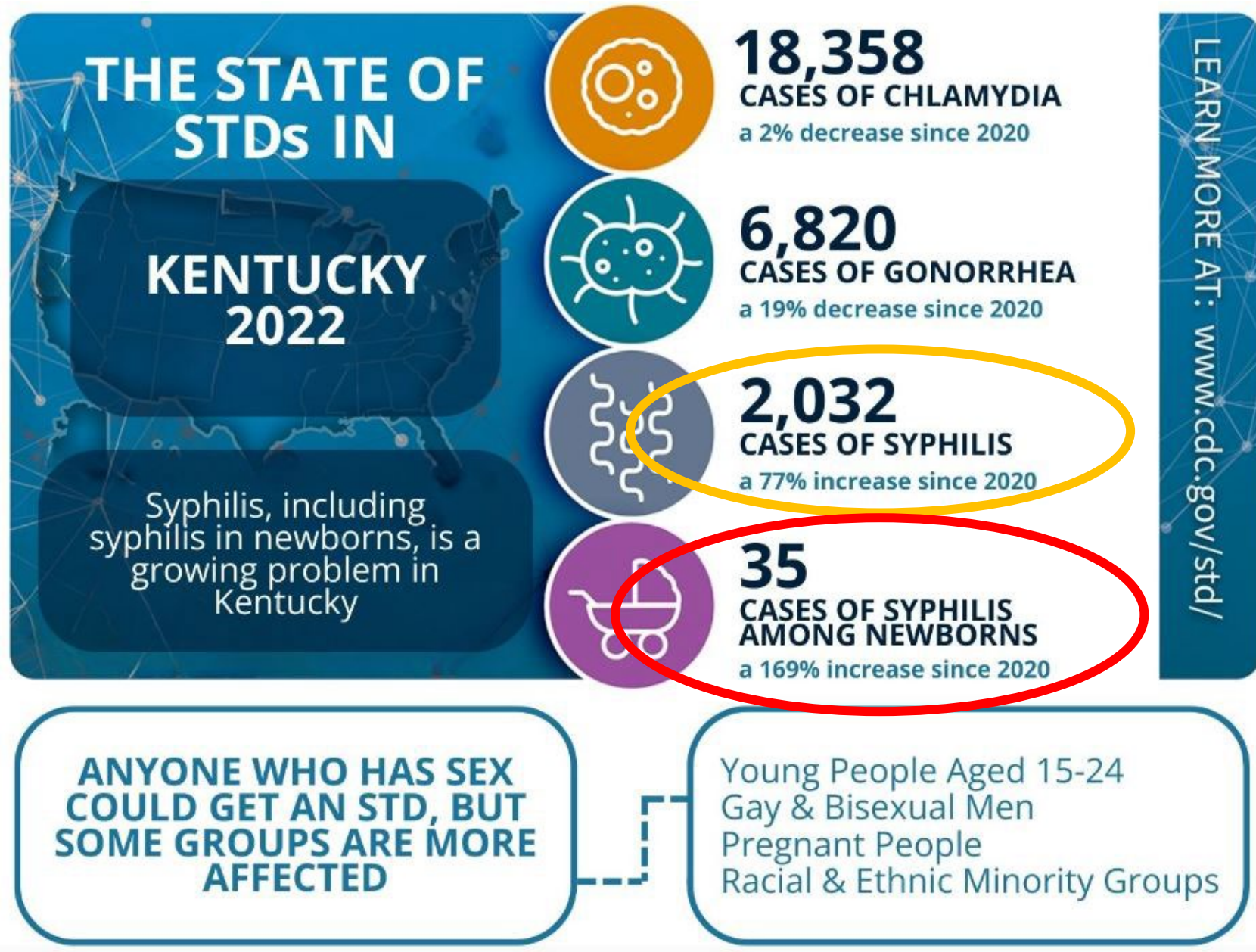
- A. Advise her to switch to a different laundry detergent.
- B. Give her an antiviral.
- C. Take a thorough sexual history.
- D. Prescribe a steroid cream and refer her to a dermatologist.

This looks like syphilis!

Syphilis in the US



Syphilis in Kentucky



Syphilis Rates in Kentucky

State/Territory	Cases					Rates per 100,000 Population				
	2017	2018	2019	2020	2021	2017	2018	2019	2020	2021
Iowa	290	286	359	501	763	9.2	9.1	11.4	15.7	23.9
Kansas	339	495	565	539	803	11.6	17.0	19.4	18.3	27.4
Kentucky	722	881	1,096	1,143	1,559	16.2	19.7	24.5	25.4	34.6
Louisiana	2,854	2,744	2,744	2,497	3,480	60.9	58.9	59.0	53.6	75.3
Maine	132	147	136	81	135	9.9	11.0	10.1	5.9	9.8

<https://www.cdc.gov/std/statistics/2021/tables/12.htm>

Stages of Syphilis

Primary

Early infection, single or multiple chancres



Secondary

Rash, systemic symptoms, weeks-months after infection



Syphilis

Early/Late Latent

Asymptomatic, can remain in this stage for years/decades
Still has positive labs

Early latent = less than 1 year duration

Late latent = over 1 year

Tertiary

Decades after primary infection

End-organ damage:

- Cardiovascular
- Neurological
- Bone/joint
- Other



Neurosyphilis, Ocular syphilis, Otosyphilis

- 🛡️ Means involvement of the central nervous system, eyes, or ears
- 🛡️ Can occur at any point after infection



Case 1 Learning Points

- 🛡️ Syphilis is present in Kentucky.
- 🛡️ Syphilis rates are increasing in Kentucky and nationwide.
- 🛡️ Syphilis has stages, and they each have different signs and symptoms.
- 🛡️ Neurosyphilis can occur at any point after infection, so you should evaluate anyone diagnosed with syphilis for neurological symptoms.

Case 2

- 🛡️ A 22 y.o. HIV-negative man presents to an STI clinic for screening. He was treated for primary syphilis 6 months ago and has since had anonymous sexual encounters with approximately 2 male partners per month.
- 🛡️ A syphilis test is sent to the lab. His EIA is positive, and the sample is reflexed to RPR, which results with a titer of 1:16.

What do you do next?

- A. Treat him again for primary syphilis, as this represents re-infection.
- B. Treat him with 3 doses of penicillin G, as this represents treatment failure.
- C. Do nothing, these are expected lab results in previously treated syphilis.
- D. Before making a treatment decision, look up his RPR titer from 6 months ago.

Syphilis Testing

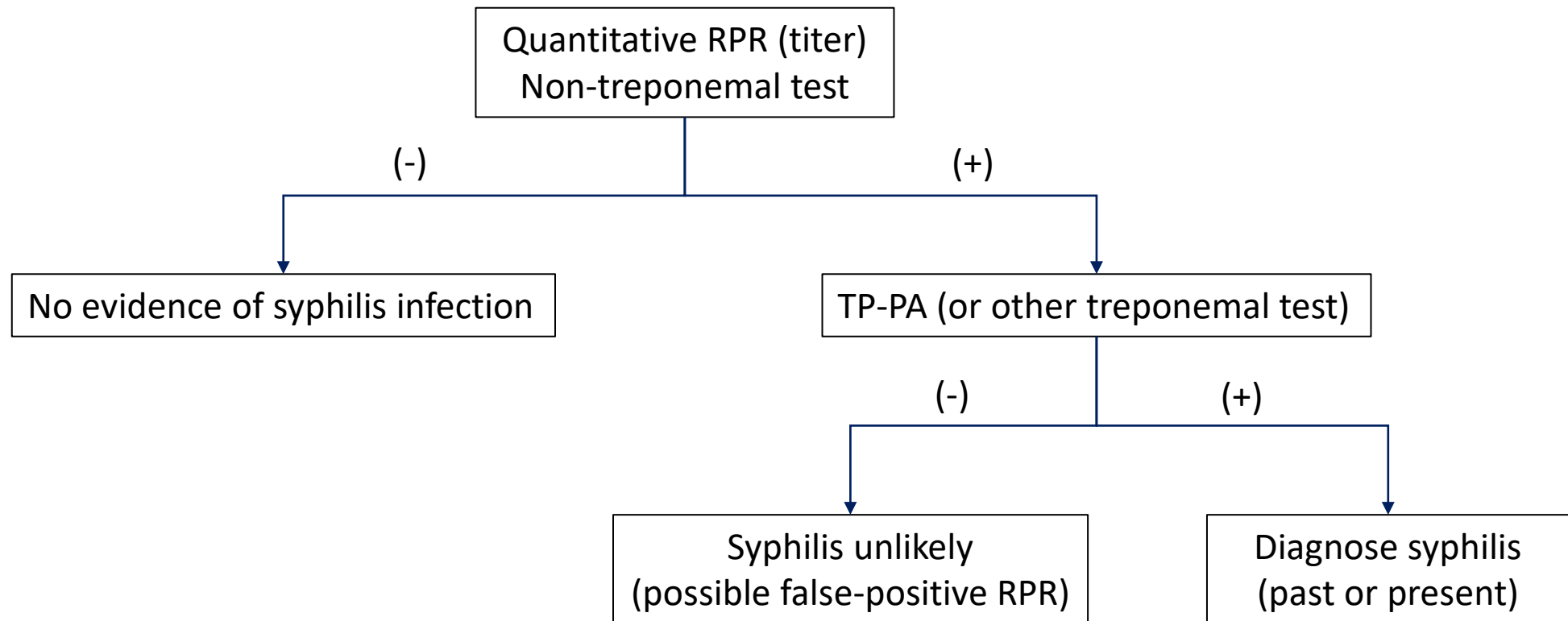
Treponemal Testing

- **EIA** (enzyme immunoassay)
- **TP-PA** (*Treponema pallidum* particle agglutination)
- Many others
- Detects antibodies against *Treponema pallidum* (and some other treponemal diseases)
- Usually remains positive even after treatment

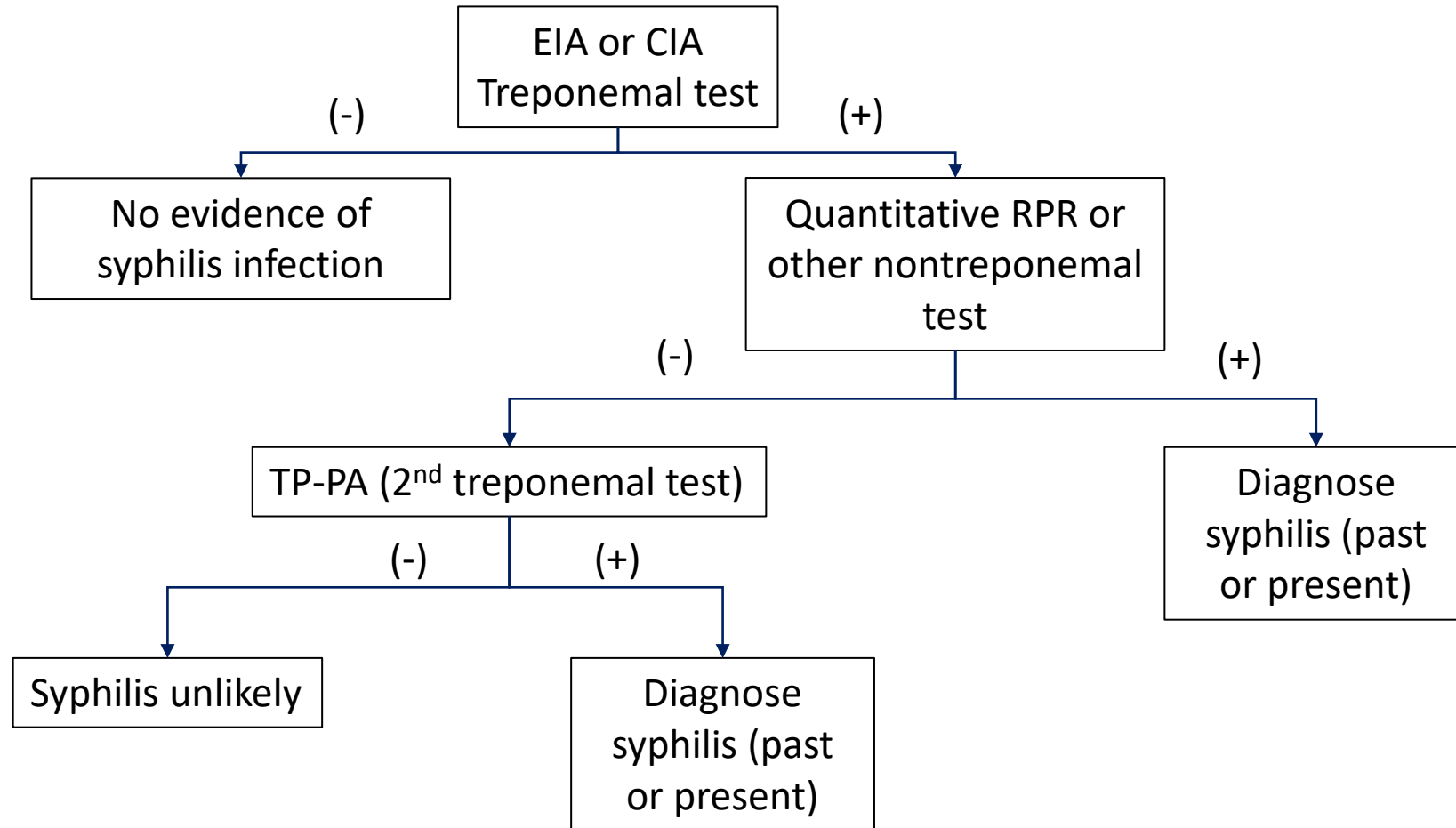
Non-treponemal Testing

- **RPR** (rapid plasma reagin)
- **VDRL** (Venereal Disease Research Laboratory test)
- Detect antibodies against cellular by-products of active infection
- Can follow a titer, which should decline and often reverts to negative after treatment

Syphilis Traditional Testing Algorithm



Syphilis Reverse Testing Algorithm



Case 2 Learning Points

- 🛡️ Syphilis testing involves treponemal (antibodies to syphilis) tests, and non-treponemal (antibodies to by-products of syphilis infection) tests.
- 🛡️ You need BOTH to diagnose syphilis, you can't just do one or the other.
- 🛡️ Treponemal testing can stay positive for life, non-treponemal testing usually reverts to negative eventually.

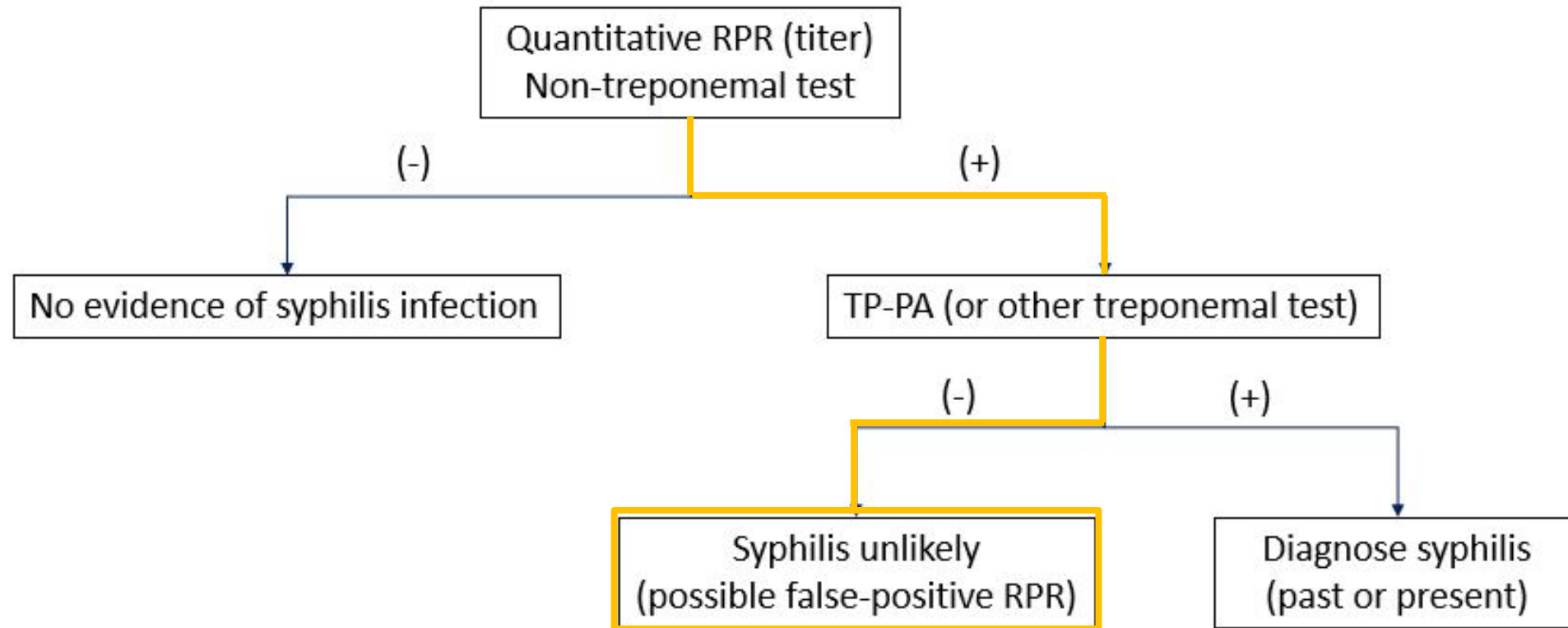
Case 3

- 🏥 A 55 year-old woman presents to her primary care physician for a routine appointment. She has a history of hypertension, high cholesterol, and rheumatoid arthritis. She recently began a new intimate relationship and requests STI testing.
- 🏥 You send an RPR, following the traditional 2-step testing protocol. The RPR comes back positive, but the EIA is negative.

How do you explain these results to the patient?

- A. This is likely a false positive RPR, though if you'd like we can recheck in a few weeks.
- B. You probably have syphilis.
- C. Were you treated for syphilis in the past? That's what it looks like.
- D. Sorry, the lab messed up the test, come back in today for another lab draw.

Syphilis Traditional Testing Algorithm



Positive RPR with Negative Treponemal Test

**Reasons
for This
Pattern**

Autoimmune disease

Pregnancy

Cancer

Viral infection

Recent immunization

Other treponemal disease

*If you see this pattern of results and you are still worried about syphilis, repeat treponemal testing (EIA, TP-PA, etc) after several weeks.

Case 3 Learning Points

- 🛡️ There are many reasons for a false-positive RPR.
- 🛡️ If you see a positive RPR but negative treponemal test, and you are still worried about syphilis, you can repeat testing in a few weeks.

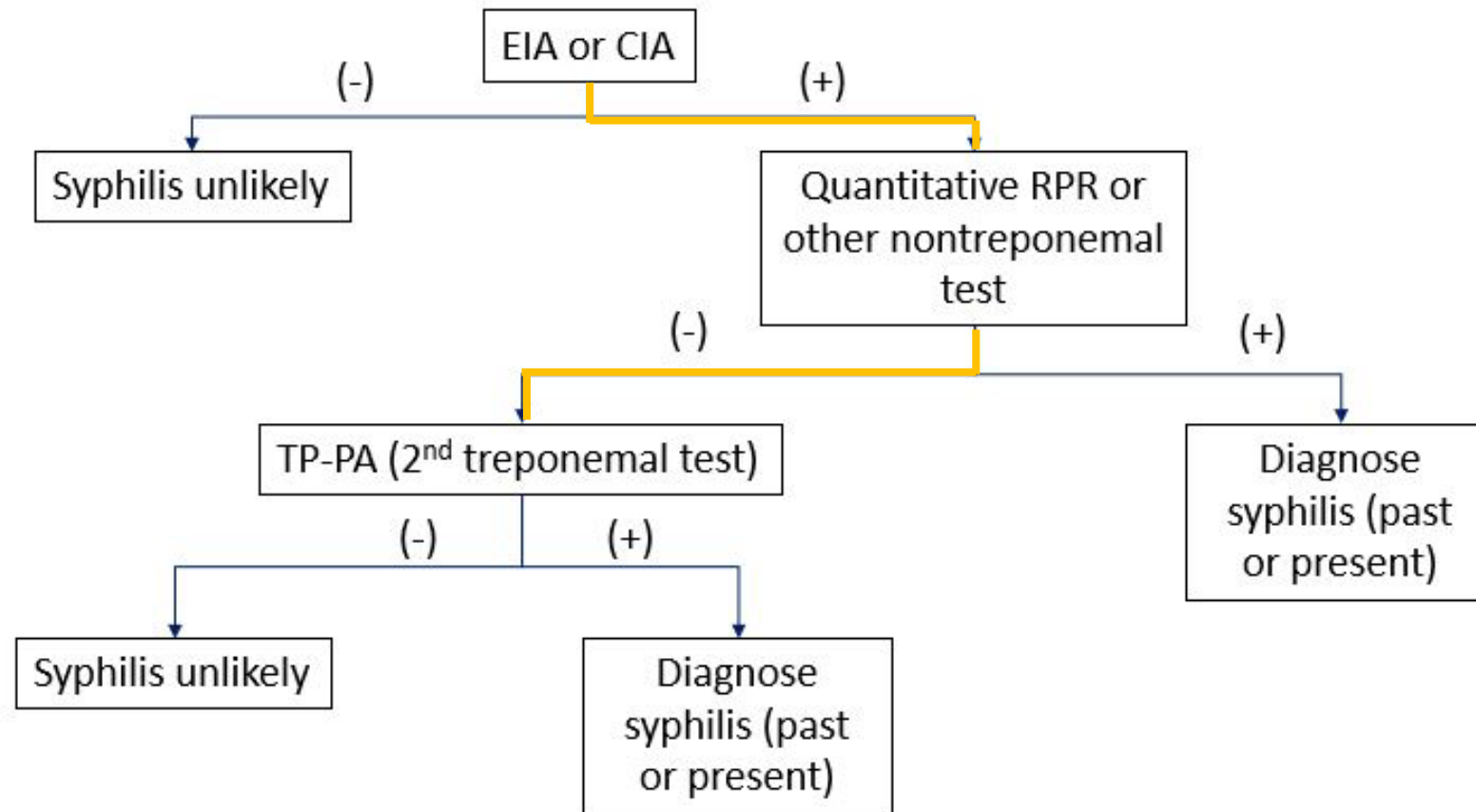
Case 4

- 🏥 A young man with poorly-controlled HIV presents with a rash suspicious for secondary syphilis. On further questioning, he also endorses floaters and flashes of light in his eyes starting about a week ago.
- 🏥 You are worried about ocular syphilis and make plans for an urgent ophthalmology examination.
- 🏥 In the meantime, you send blood for syphilis testing. His EIA is positive, but surprisingly, the RPR is negative.

What do you do next?

- A. No further testing, this is a false positive EIA caused by HIV infection.
- B. Call the lab and ask them to re-run an RPR titer on the same sample, diluting the specimen this time.
- C. Send the patient home and ask him to come back in 2 weeks for a repeat blood test.
- D. Send another EIA now in case it was a lab error.
- E. Send a TP-PA, a different treponemal test, as the tiebreaker.

Syphilis Reverse Testing Algorithm



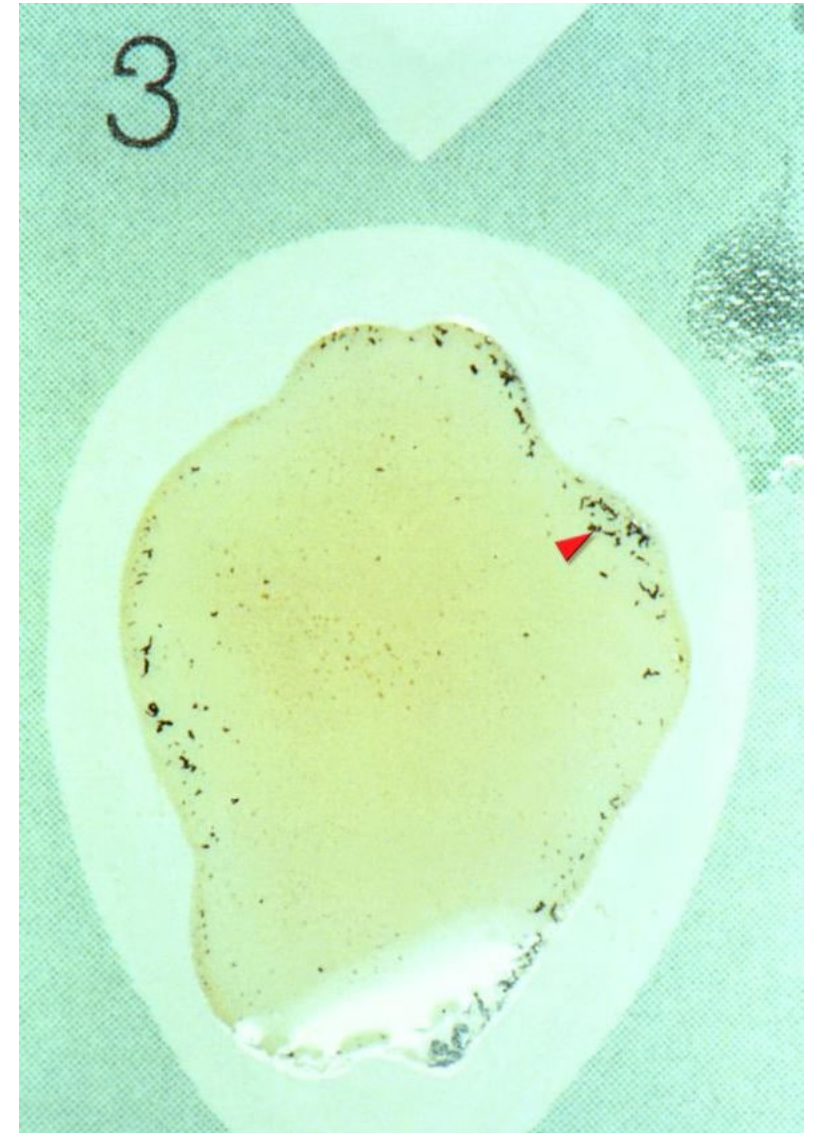
What is the prozone effect?

- ❖ Falsely negative RPR when a very high antibody titer interferes with the test
- ❖ Occurs most often in primary and secondary syphilis

Rapid Plasma Reagin (RPR) Test for the diagnosis of Syphilis



<https://microbiologyinfo.com>



[CDC's Public Health Image Library](#)

Positive treponemal test with negative RPR

Reasons for
Positive
Treponemal
Test with
Negative
RPR

Very early syphilis

Very late syphilis

Previously treated syphilis

Prozone effect

*If you see this pattern of results, there is probably syphilis somewhere, or there was in the past. How you handle it depends on the patient's individual history.

Case 4 Learning Points

- 🛡️ Positive treponemal test with negative RPR is the expected result in successfully treated syphilis but can also happen in very early or late active infection.
- 🛡️ The prozone effect results in a false negative when the RPR titer is very high.
 - Suspect if clinical suspicion for syphilis is very high, and RPR is negative
 - Solution is to talk to the lab, they can dilute the specimen and try again

Case 5

- 🛡️ A young male patient comes to your clinic to establish care. He says he last had STI testing ~1.5 years ago, all negative at that time. He is currently sexually active with a new partner, and requests repeat STI screening.
- 🛡️ His EIA and RPR come back positive. He does not recall a chancre or rash and has no signs or symptoms of neurosyphilis.
- 🛡️ You diagnose late latent syphilis and want to start him on treatment today.

What do you prescribe?

- A. Penicillin G, IM, x1 dose
- B. Penicillin G, IM, once weekly x3 doses
- C. Penicillin G, IV, 24 million units daily via continuous infusion
- D. Doxycycline 100mg, PO, twice daily for 14 days

Treat syphilis with penicillin.

Primary, Secondary, & Early Latent

- 2.4 million units of penicillin G (aka Bicillin) via intramuscular injection
- Single dose

Late Latent & Tertiary


- 2.4 million units of penicillin G via intramuscular injection
- Once weekly for 3 weeks
- If a dose is missed, need to start over

Neuro/Ocular/Oto syphilis

- 24 million units of penicillin daily via continuous intravenous infusion
- 10-14 days
- Usually requires hospitalization

There is a penicillin shortage.

Bicillin L-A® Shortage

The FDA has listed penicillin G benzathine injectable suspension products (Bicillin L-A®) on [their drug shortage webpage](#) , noting limited supply due to increased demand. The FDA website includes an expected duration for the shortage. CDC continues to monitor the situation and will post updates as needed.

Bicillin L-A® is the first-line recommended treatment for syphilis and the only recommended treatment option for some patients.

During this time, programs can see [Clinical Reminders during Bicillin L-A® Shortage](#) for priority actions they can take.

[Syphilis - STI Treatment Guidelines \(cdc.gov\)](#)

You can also treat syphilis with doxycycline.

Primary & Secondary	Early Latent	Late Latent
<ul style="list-style-type: none">• 100mg by mouth twice daily for 14 days	<ul style="list-style-type: none">• 100mg by mouth twice daily for 14 days	<ul style="list-style-type: none">• 100mg by mouth twice daily for 28 days

***Consider if your patient will be able to adhere to 2-4 weeks of twice daily pills.**

****There is not good evidence in neurosyphilis or tertiary syphilis.**

Syphilis Treatment in Pregnancy = **Penicillin**



NO EXCEPTIONS

Case 5 Learning Points

- 🛡️ Standard treatment for syphilis is with penicillin G, dose and timing is easy to look up.
- 🛡️ Doxycycline is an oral option appropriate for some patients.
- 🛡️ Pregnant patients **MUST** be treated with penicillin.
- 🛡️ Late latent syphilis requires longer treatment.

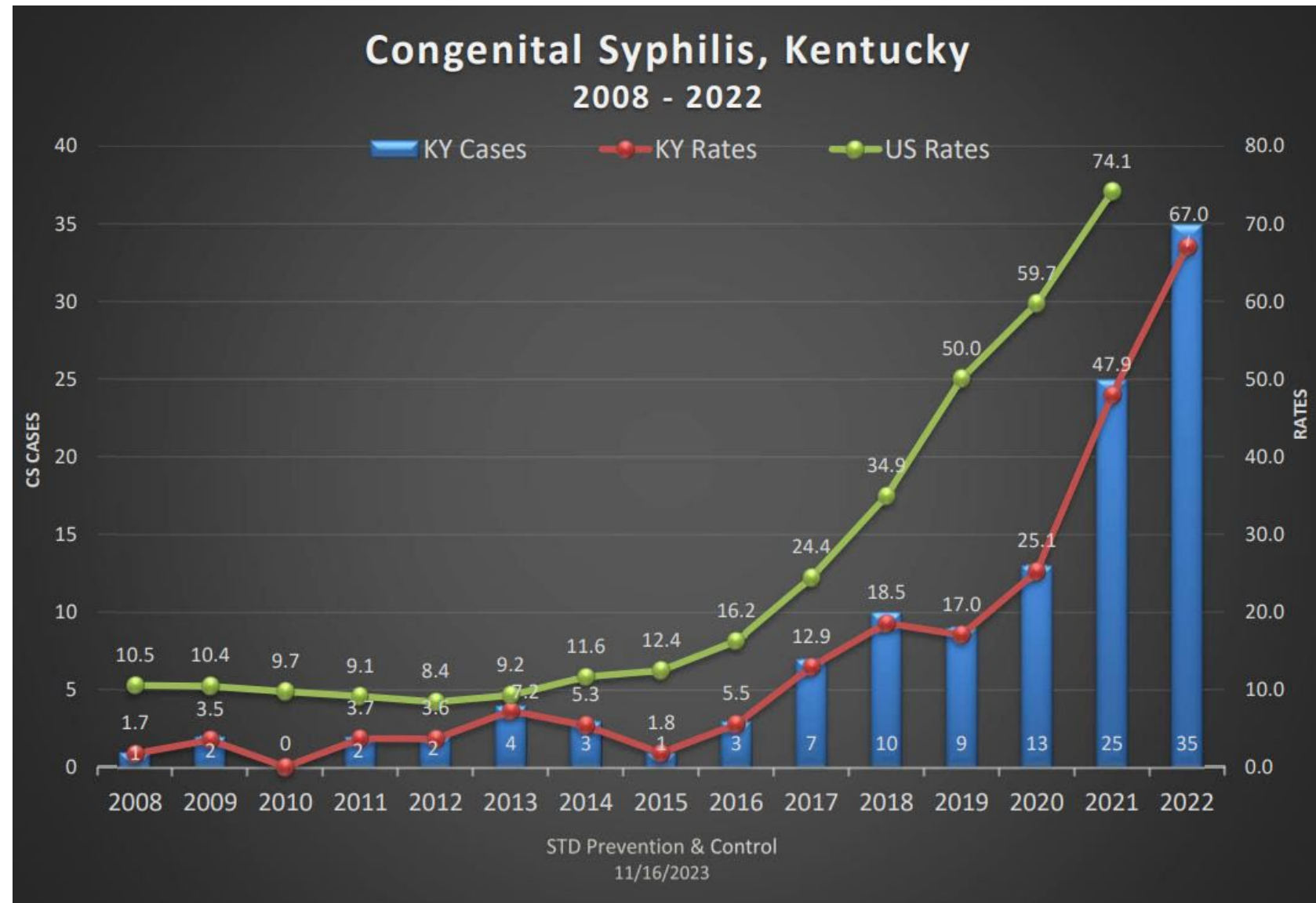
Case 6

- 🛡️ A patient presents to her obstetrician's office for an initial prenatal visit.
- 🛡️ She undergoes routine STI screening, and her syphilis EIA is positive, with an RPR of 1:64.
- 🛡️ She denies transactional sex but reports 4 male partners over the last 18 months. She hasn't had STI testing since her last pregnancy 5 years ago.

What do you do next?

- A. Treat her for primary syphilis, with penicillin since she is pregnant.
- B. Treat her for late latent syphilis, with penicillin since she is pregnant.
- C. Do not treat, she is asymptomatic and you should avoid exposing the baby to unnecessary antibiotics.
- D. Repeat testing with TP-PA instead of EIA, as this could be a false positive caused by her pregnancy.

Congenital Syphilis in Kentucky



Source: KY STD Prevention and Control

Kentucky Law

214.160 Blood specimen of pregnant women to be taken

- (1) Every physician and every other person legally permitted to engage in attendance upon a pregnant woman in this state shall take or cause to be taken from the woman a specimen of blood for serological test for syphilis as soon as he is engaged to attend the woman and has reasonable grounds for suspecting that pregnancy exists.

<https://apps.legislature.ky.gov/>

When do you test?

A syphilis test should be performed...

At the first prenatal visit

At 28 weeks in those at high risk

At delivery in those at high risk

Before hospital discharge in those with inadequate prenatal care/no testing prior to delivery

Anyone with a fetal death after 20 weeks gestation

Who is “high risk”?

**High
Risk:**

Multiple sex partners

Transactional sex

Late or no prenatal care

Methamphetamine or heroin use

Incarceration of woman or her partner

Unstable housing/homelessness

Case 6 Learning Points

- 🛡️ Congenital syphilis rates are rising in Kentucky.
- 🛡️ Congenital syphilis can have severe consequences for the child, and can cause stillbirth.
- 🛡️ Assessing for syphilis risk and testing is everyone's responsibility, not just the obstetrician's.
- 🛡️ Don't treat syphilis as a one-time-per-pregnancy checkbox.

Case 7

- 🛡️ A 24-year-old woman who engages in sex work presents to a local health department requesting routine STI screening. She seeks out STI testing every 3-6 months, and her last screening was negative. She has never had syphilis before and is negative for HIV.
- 🛡️ This time, her syphilis EIA is positive, and her RPR is 1:32. She has no current signs or symptoms of syphilis. You diagnose early latent syphilis and treat her with a dose of IM penicillin.
- 🛡️ She asks you how she will know if the antibiotics worked.

How many months should you wait before checking a repeat RPR titer?

- A. 1 month
- B. 3 months
- C. 6 months
- D. 12 months

When should you re-test?

Without
HIV

Primary and
Secondary

- 6 and 12 months

Latent

- 6, 12, and 24 months

With
HIV

Primary and
Secondary

- 3, 6, 9, 12, 24 months

Latent

- 6, 12, 18, and 24 months

Look for a four-fold decrease in titer by 12 months.

RPR

won't go
down?

Re-infection

Treatment failure

Neurosyphilis

Serofast state

Case 7 Learning Points

- 🛡️ You should repeat an RPR to confirm it is declining after treatment.
- 🛡️ Timing of the repeat depends on the patient's HIV status.
- 🛡️ If the titer goes UP, the patient probably needs retreatment.
- 🛡️ Some people have a persistent low titer, called “serofast”, this is ok.

Case 8

- 🏥 It's 4:45pm, and your last patient of the day comes into clinic with a painless penile lesion after a sexual encounter with a new partner 2 weeks ago. Last STI screening was negative 6 months ago. You suspect primary syphilis, and sure enough, his rapid syphilis screen is positive. You treat with 1 dose of IM penicillin, tell him to avoid sexual contact for 7 days, and send him on his way.
- 🏥 The next morning at 8:00 am the patient calls into clinic complaining of fever of 101F, headache, and muscle aches that began suddenly at 3:00 am.

What do you do?

- A. Prescribe ibuprofen and tell him he should feel better soon.
- B. Put a penicillin allergy flag in his chart, and tell him if he ever gets syphilis again, he should be treated with doxycycline.
- C. Order a test for flu and COVID – it's probably unrelated to the syphilis.
- D. Do a lumbar puncture, he may have neurosyphilis.

Jarisch-Herxheimer Reaction

- 🛡️ DON'T PANIC.
- 🛡️ Begins within 24 hours of first antibiotic dose.
- 🛡️ Usually resolves within 24 hours.
- 🛡️ Can happen after treatment of an infection with spirochetes (syphilis, Lyme, leptospirosis, etc).
- 🛡️ Caused by the body's reaction to the dying bacteria.
- 🛡️ Treatment is mostly time, anti-inflammatories like ibuprofen can help.
- 🛡️ Biggest concern is low blood pressure, monitor for this.

Jarisch-Herxheimer in Pregnancy

- 🛡️ Fetal monitoring is recommended.
- 🛡️ Has been associated with pre-term labor.
- 🛡️ The condition is still rare, and it is brief and self-limited in most cases.
- 🛡️ Concern for Jarisch-Herxheimer reaction is NOT a reason to avoid treating a pregnant patient for syphilis.

Case 8 Learning Points

- 🛡️ Jarisch-Herxheimer reaction can occur after syphilis treatment, usually within hours of receiving antibiotics.
- 🛡️ **THIS IS NOT AN ALLERGY.** It is a transient reaction that should self-resolve.
- 🛡️ Jarisch-Herxheimer can have more severe consequences in pregnancy, so pregnant patients should be monitored closely if they develop this reaction.

Case 9

- 🏥 A 30 year old woman is at her obstetrician's office discussing her positive prenatal syphilis test result. She is worried about the health of her baby and agrees to start treatment right away.
- 🏥 The OB offers to give a dose of penicillin G today in the office. The patient says "Wait, I can't have penicillin, I'm allergic!"
- 🏥 Upon further questioning, she says she was hospitalized for anaphylaxis when she had amoxicillin for a sinus infection in her 20s.

What do you do?

- A. Treat her with doxycycline instead.
- B. Treat her with ceftriaxone.
- C. Direct admit her to the ICU for penicillin desensitization.
- D. Challenge her with oral amoxicillin in the office.

What is an allergy?

Concerning

- Rash/hives
- Low blood pressure
- Trouble breathing
- Liver/kidney injury
- Angioedema
- Hospital admission

Less Concerning

- Nausea
- Diarrhea (as isolated symptom)
- Headache
- Family history of allergy
- “I don’t know my mom told me I’m allergic”




What percent of adults who report a penicillin allergy have a true allergy?

A. 10%

B. 25%

C. 50%

D. 75%

-  Many penicillin allergies in childhood will have resolved by adulthood.
-  Allergies with a mild reaction, especially if years in the past, may be a candidate for an amoxicillin challenge.
-  These are good questions for a pharmacist or an allergist – ask for help!

Penicillin Allergy in Pregnancy

- 🛡️ You must desensitize and treat with penicillin.
- 🛡️ This usually takes place in a hospital setting, often ICU for close monitoring.
- 🛡️ Doxycycline is an alternative for non-pregnant patients with true penicillin allergy, but **NOT FOR PREGNANT PATIENTS**.

Case 9 Learning Points

- 🛡️ If someone with syphilis reports a penicillin allergy, ask more questions to evaluate the allergy.
- 🛡️ Refer to a specialist if needed.
- 🛡️ Doxycycline is an alternative, but NOT in pregnancy.
- 🛡️ Pregnant people with syphilis and a penicillin allergy must be desensitized.

Case 10

- 🏥 A 19 year old woman walks in to a local health department, very distressed. Her boyfriend just told her he was diagnosed with syphilis.
- 🏥 She is generally healthy and feels well. She has not noticed a chancre.
- 🏥 She asks what this means for her health. Does she need to be treated?

What do you tell her?

- A. No, you don't need treatment unless you have symptoms.
- B. No, syphilis is not very contagious, so it is unlikely you have it.
- C. Maybe, but we have to wait for syphilis test results first.
- D. We will send blood tests, but if you want, we can start treatment while we wait for results.

Partner Treatment

- Persons who have had sexual contact with a person who receives a diagnosis of primary, secondary, or early latent syphilis <90 days before the diagnosis should be treated presumptively for early syphilis, even if serologic test results are negative.
- Persons who have had sexual contact with a person who receives a diagnosis of primary, secondary, or early latent syphilis >90 days before the diagnosis should be treated presumptively for early syphilis if serologic test results are not immediately available and the opportunity for follow-up is uncertain. If serologic tests are negative, no treatment is needed. If serologic tests are positive, treatment should be based on clinical and serologic evaluation and syphilis stage.

[Syphilis - STI Treatment Guidelines \(cdc.gov\)](https://www.cdc.gov/std/treatment-guidelines)

Case 10 Learning Points

- 🛡️ Consider presumptive treatment of sexual partners of those diagnosed with primary, secondary, or early latent syphilis.
- 🛡️ If testing comes back negative but the exposure was within the last 90 days, finish the treatment course anyway.

Thank you!

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