Syphilis Strikes Back- Current Guidelines for an Age-Old Foe

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Presenter, MWAETC

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Disclosures

No conflicts or relationships to disclose

Disclaimer

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Learning Objectives

- Discuss the history and cyclical nature of syphilis epidemics
- Highlight the current trends in syphilis rates in the Dakotas and nationwide
- Explore the current clinical recommendations for identifying and treating primary and secondary syphilis in adults

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REVENGE OF THE SYPH

The Long Long History of Syphilis

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Historical Impact of Syphilis

- Syphilis-derived in archeological remains as far
- Cases explode s following Christopher Co s
  - Name first coi 'Syphilus, Sive Morbus Gallic e)
- Each country w med it on a neighboring kin
  - French name ussians assigned the name of 'F the German disease' etc.

Rothschild, B. M. (2005). History of syphilis. *Clinical Infectious Diseases*, *40*(10), 1454–1463. https://doi.org/10.1086/429626

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The Who's Who of STI's

- Many historical figures were confirmed to have or highly suspected of having Syphilis:
  - Christopher Columbus, Pope Alexander VI, Ivan the Terrible, Henry VIII, Hernan Cortes, Meriwhether Lewis, Friedrich Nietzche, Randolph Churchill (Winston Churchill's father), Al Capone, Franz Schubert, Charles VIII of France, Leo Tolstoy, Napoleon Bonaparte, Oscar Wilde, Ludwig van Beethoven, Vincent van Gogh, Isak Dinesen Gustave Flaubert, Charles Baudelaire, Guy de Maupassant, Eduoard Manet, Henri de Toulouse Lautrec, Paul Gaugin

Shorter, Edward. "The Famous, the Syphilitic." *Nature Medicine (Print)*, vol. 9, no. 8, 1 Aug. 2003, pp. 989–989, https://doi.org/10.1038/nm0803-989. Accessed 14 Apr. 2024.

CYCLICAL NATURE OF SYPHILIS EPIDEMICS

Syphilis is Back!

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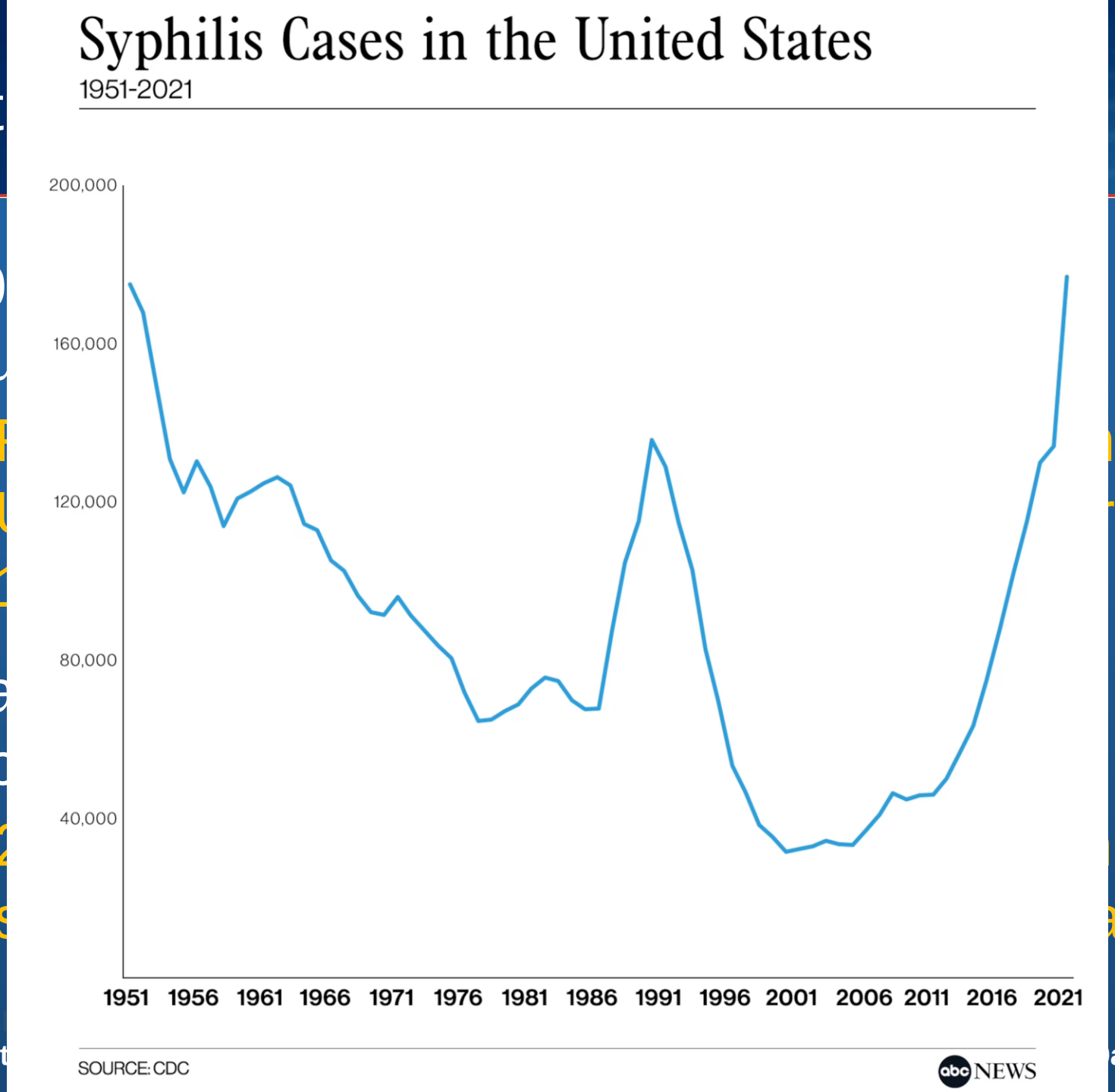

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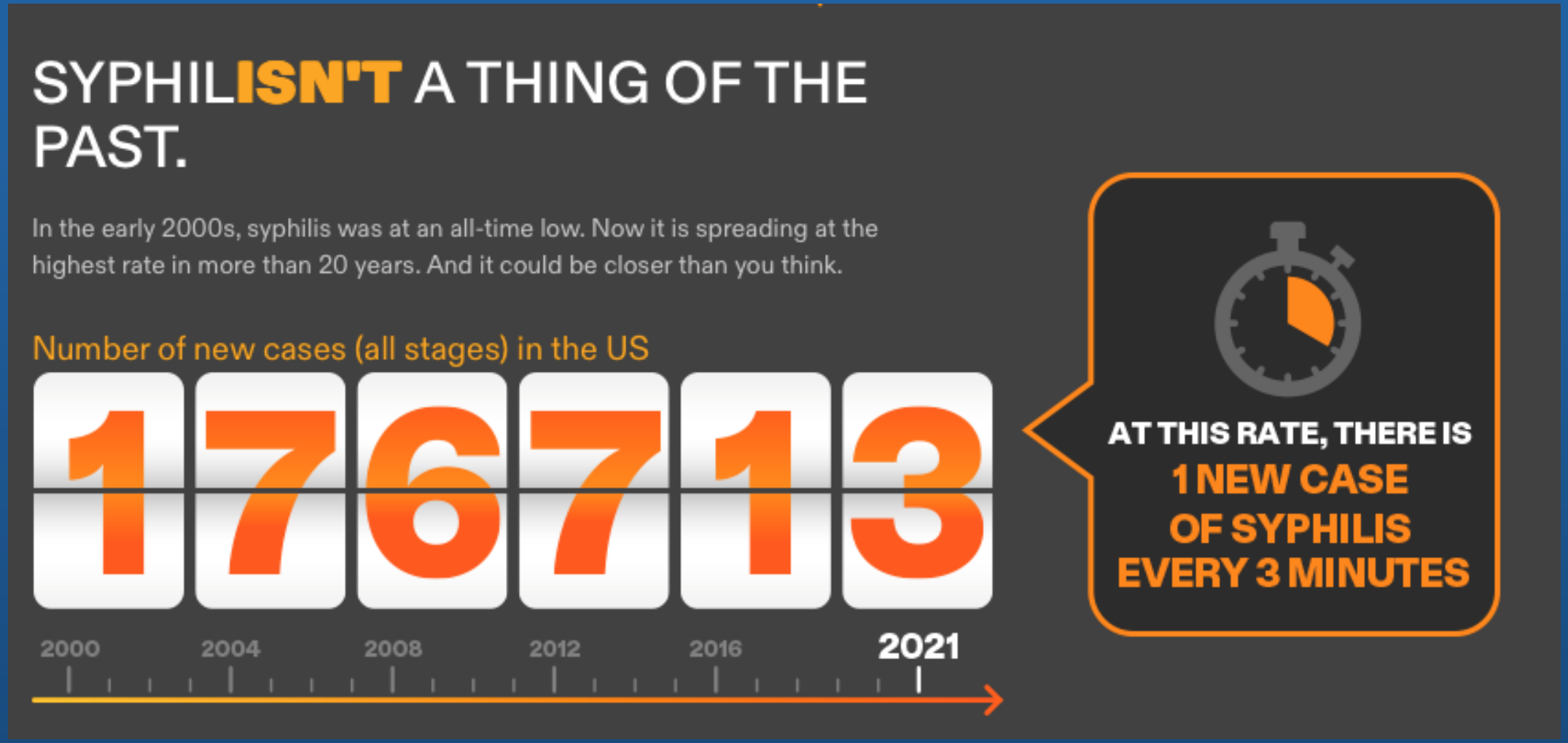

https://www.syphilisisback.com

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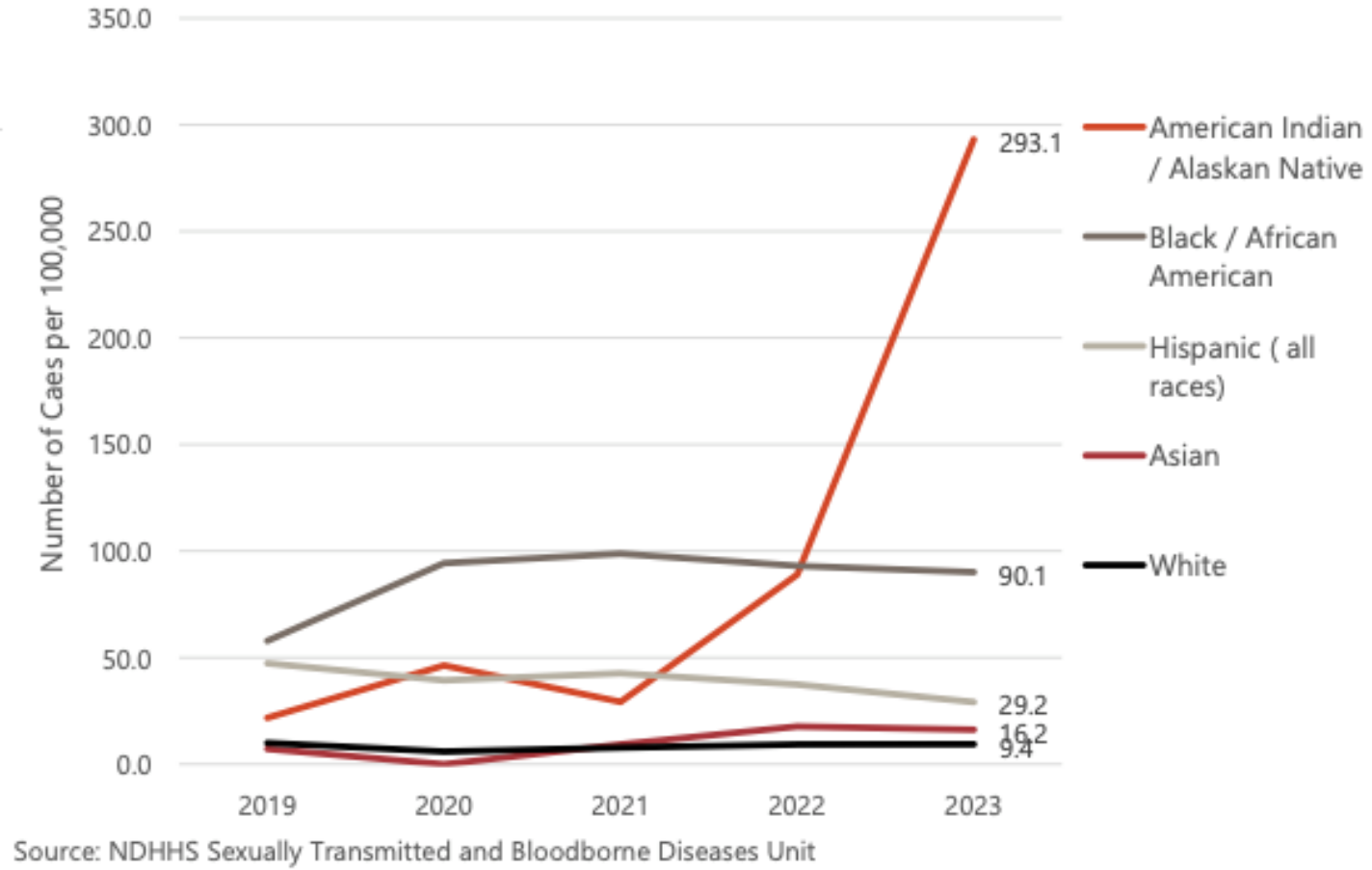
Syphilis Trends in the Dakotas

- North Dakota (Ranked 30th) Trends by Race



Source: NDHHS Sexually Transmitted and Bloodborne Diseases Unit

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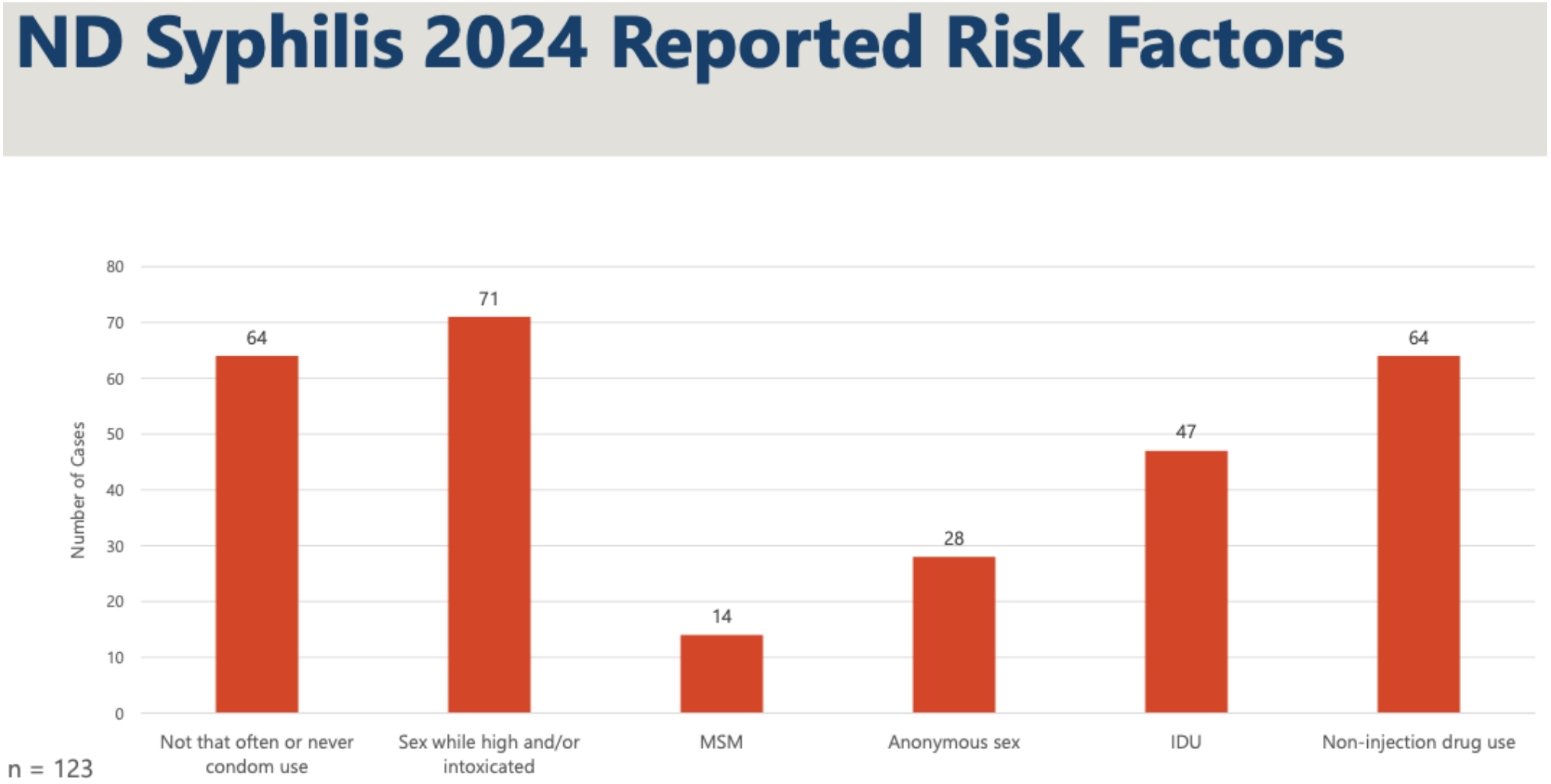
Syphilis Trends in the Dakotas

- North Dakota Trends by Risk Factors



Syphilis Trends in the Dakotas

- South Dakota Reported the HIGHEST rate of syphilis in the United States

SYPHILIS IN SOUTH DAKOTA

2022 DATA Data as of 8.22.23	
ADULT SYPHILIS	**CONGENITAL / SYPHILITIC STILLBIRTHS**
1,504 Cases Reported 90% Increase from 2021 **2,493%** Increase from 5-Year Median	40 Congenital and 3 Syphilitic Stillbirths 150% Increase from 2021 **1,233%** Increase in 5-Year Median

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Syphilis Trends in the Dakotas

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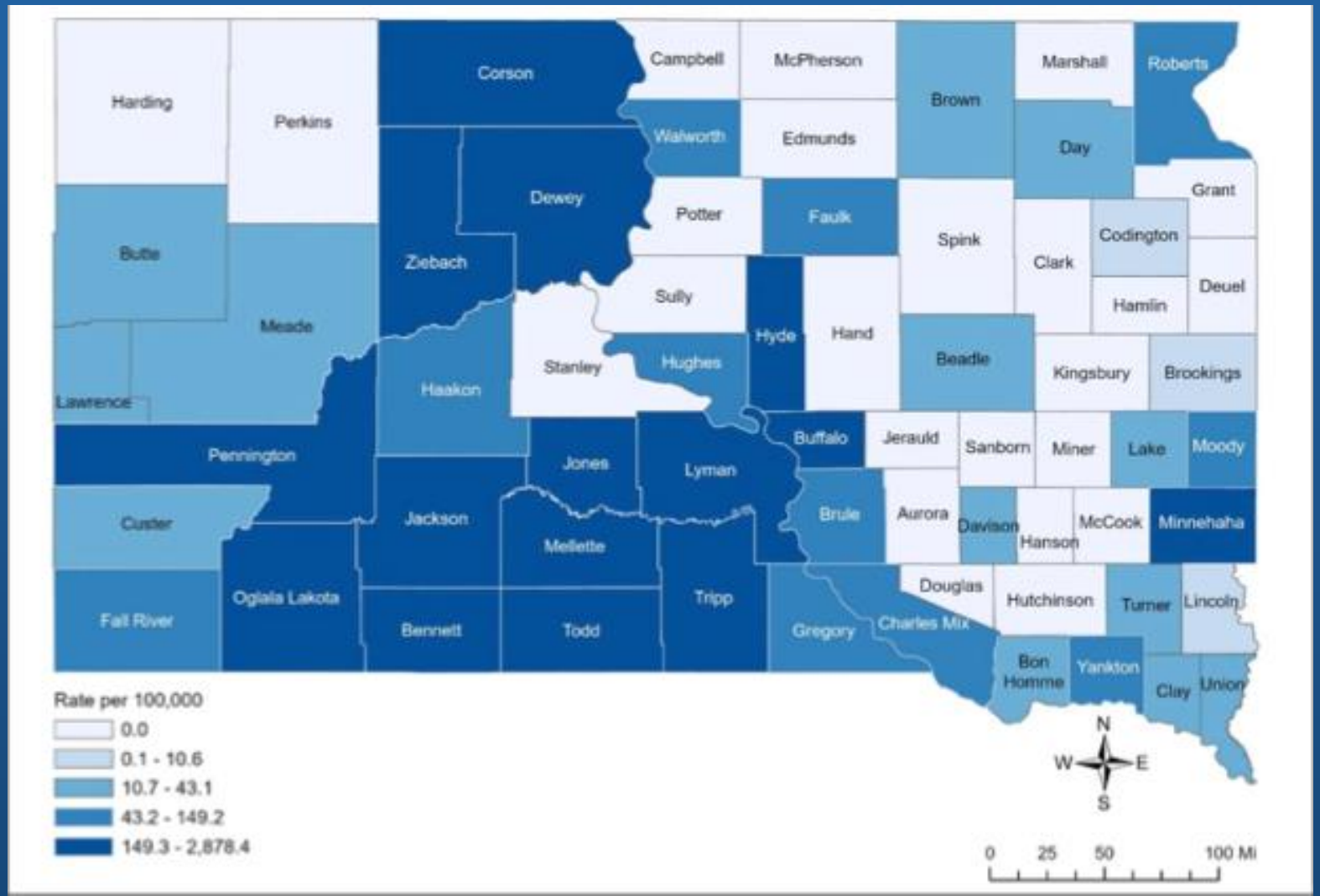
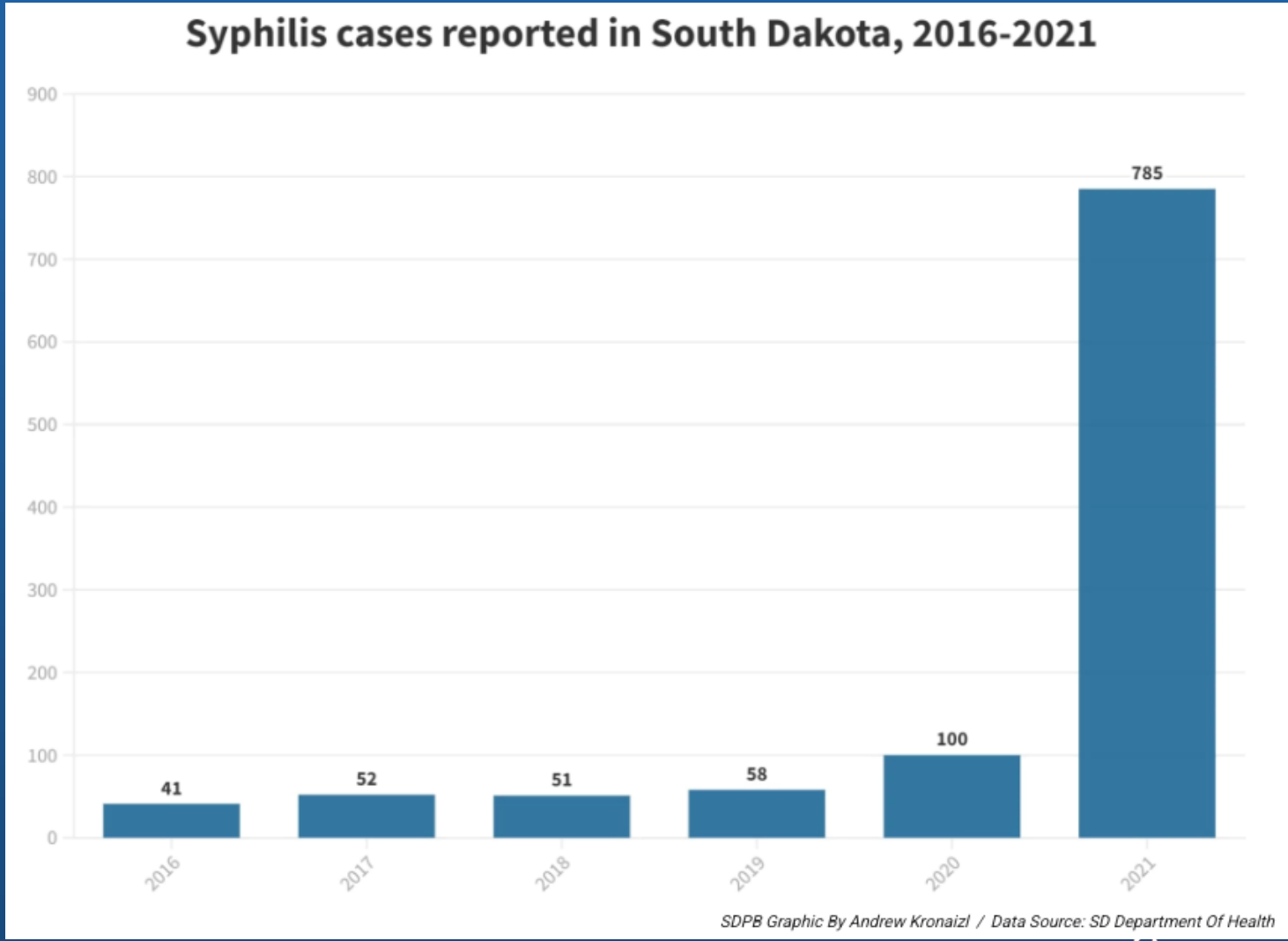


Syphilis Trends in the Dakotas

RISK FACTORS:
96% heterosexual exposure
62% history of other STIs
42% history of incarceration
81% American Indian
57% Reported age range of 25-39 years-old
33% sex while intoxicated
27% IV drug use



https://doh.sd.gov/media/gi1b4rwt/reducingsyphilis_2023.pdf

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GETTING TO KNOW YOUR PATHOGEN

Infectious Etiology and Progression of P/S Syphilis

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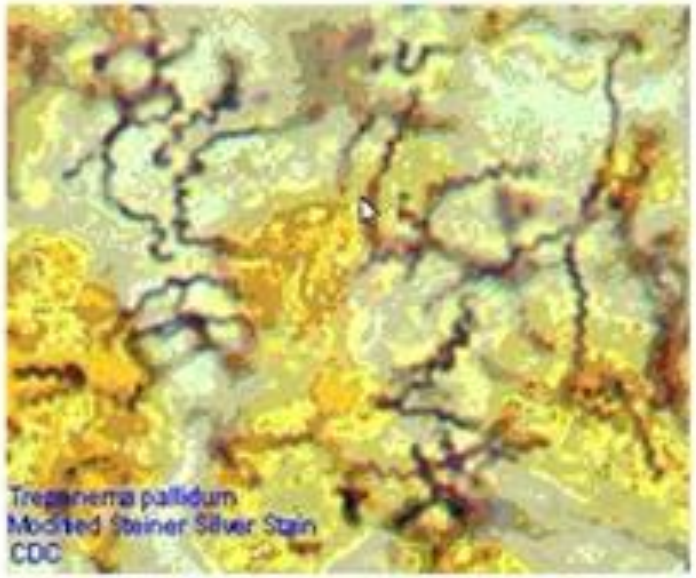
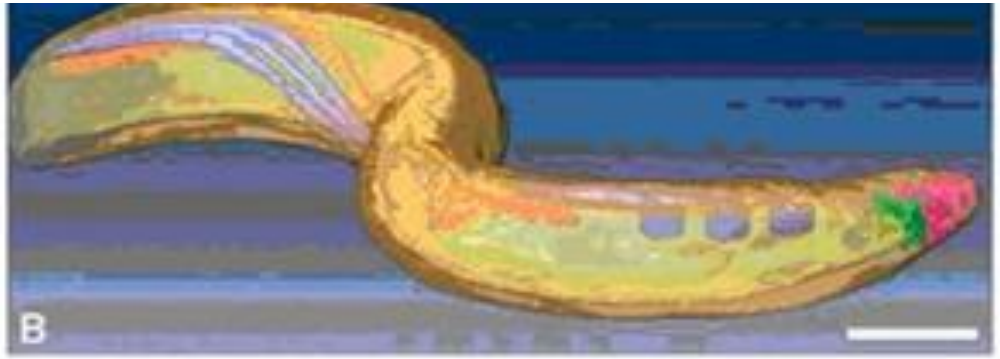
Treponema pallidum

- Spirochetal bacterial infection passed from one human to another (usually sexually)

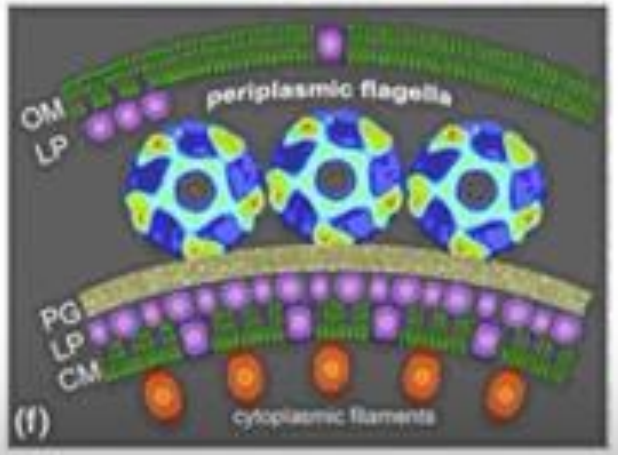
- Infection occurs in phases, involves multiple organ systems
  - Skin → internal organs → heart and brain

- Easily treated with penicillin (so far) if caught early





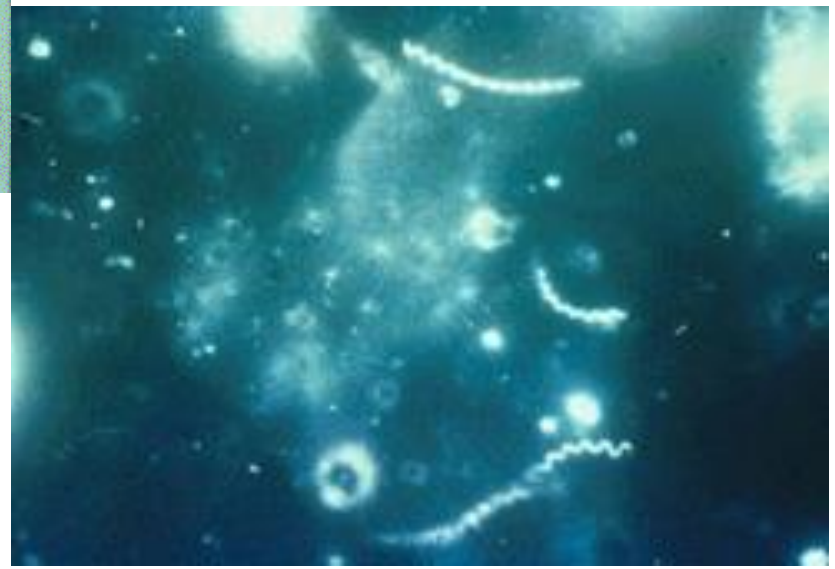
Izard, J. et al. 2009. J. Bacteriol. 191(24):7566-7580



Liu, J. et al. 2010. J Mol Biol.403(4):546-61

T. Pallidum cont.

Organism under dark field microscopy



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

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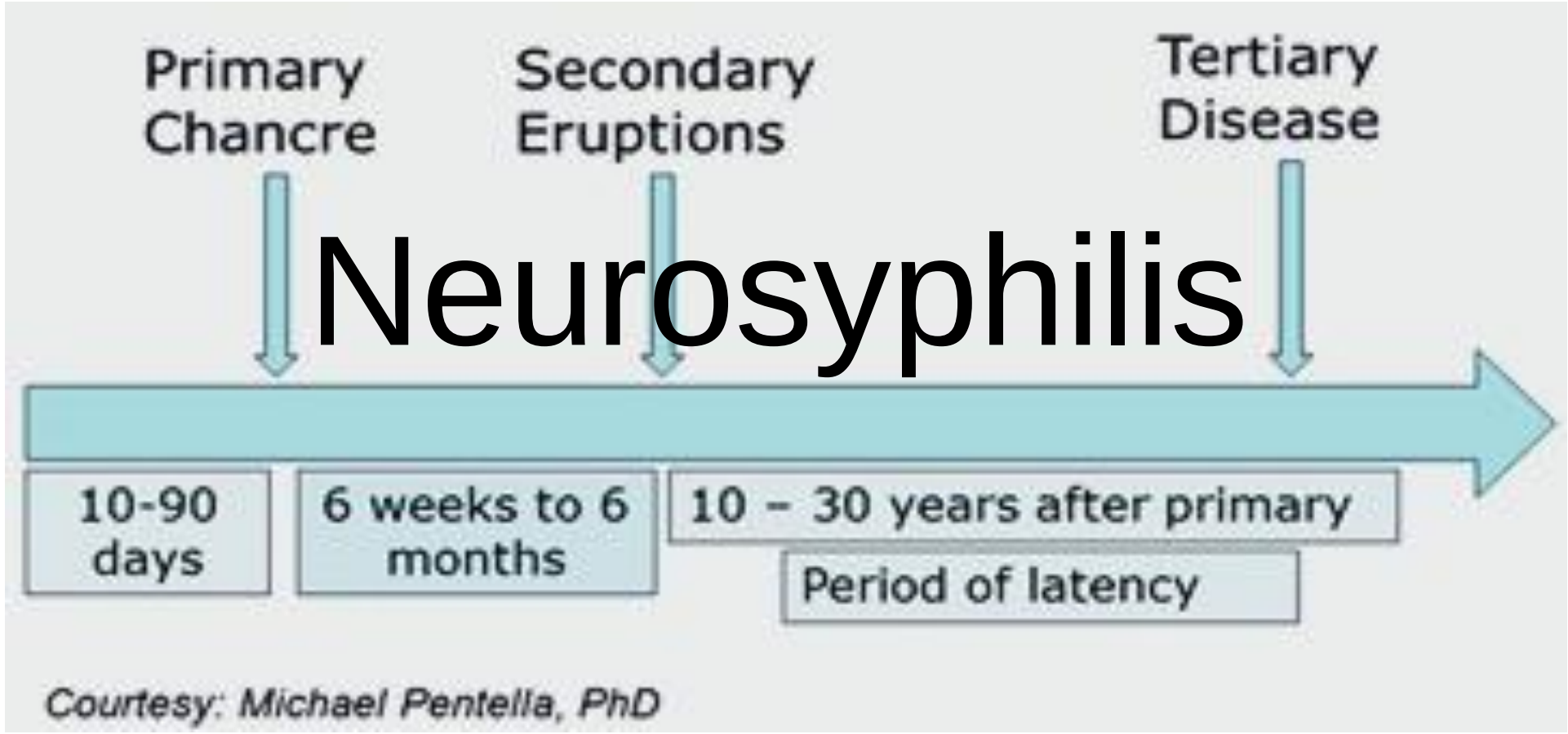
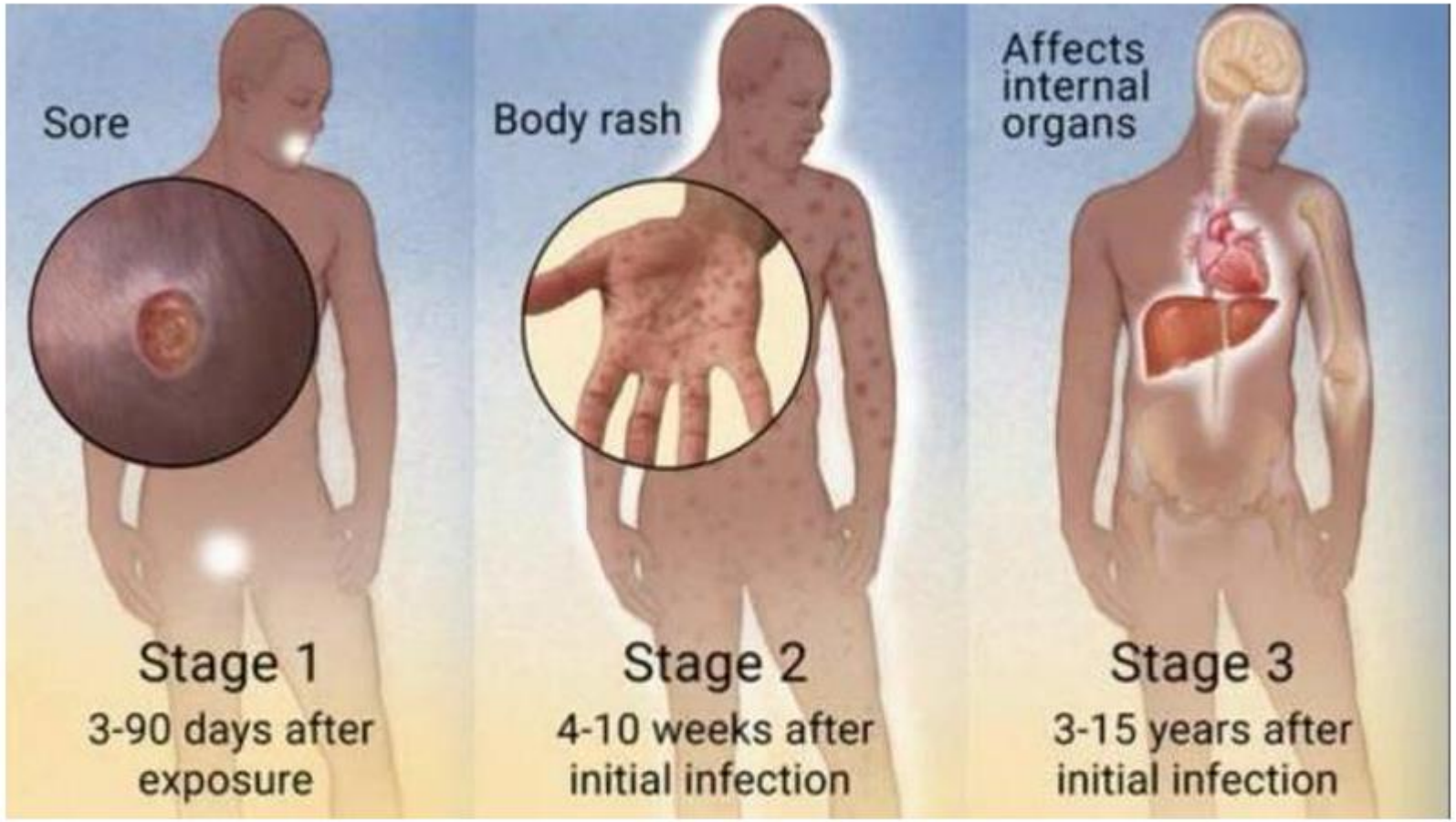
The Natural Course of Syphilis



Stages of Syphilis



Eye, meningitis, osteitis
Hepatitis, adenopathy

Gumma formation

Slide Courtesy of Dr. Lynn Besch

The Great Imitator

- Primary stage, when a painless sore marks the location where the infection entered the body.
  - May take up to 90 days after infection for the sore to appear, usually on or inside a person's genitals or mouth.
- The secondary stage is marked by a skin rash and sometimes other symptoms, including fever, headache, sore throat, swollen lymph glands, weight and hair loss, and fatigue.
- 15% of untreated syphilis resurfaces 10 to 20 years after the first infection, causing brain and muscle damage, paralysis, blindness, and even death

SORRY BUT IT HAS TO BE DONE

Brace yourself, genital ulcer pictures incoming

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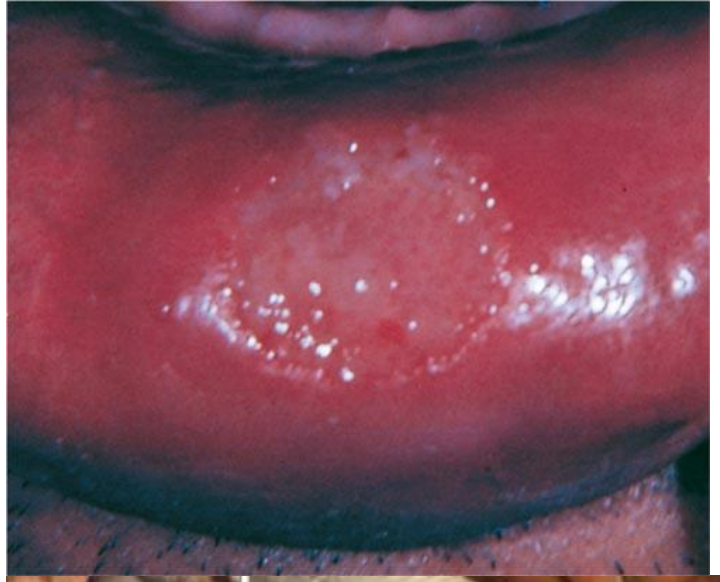
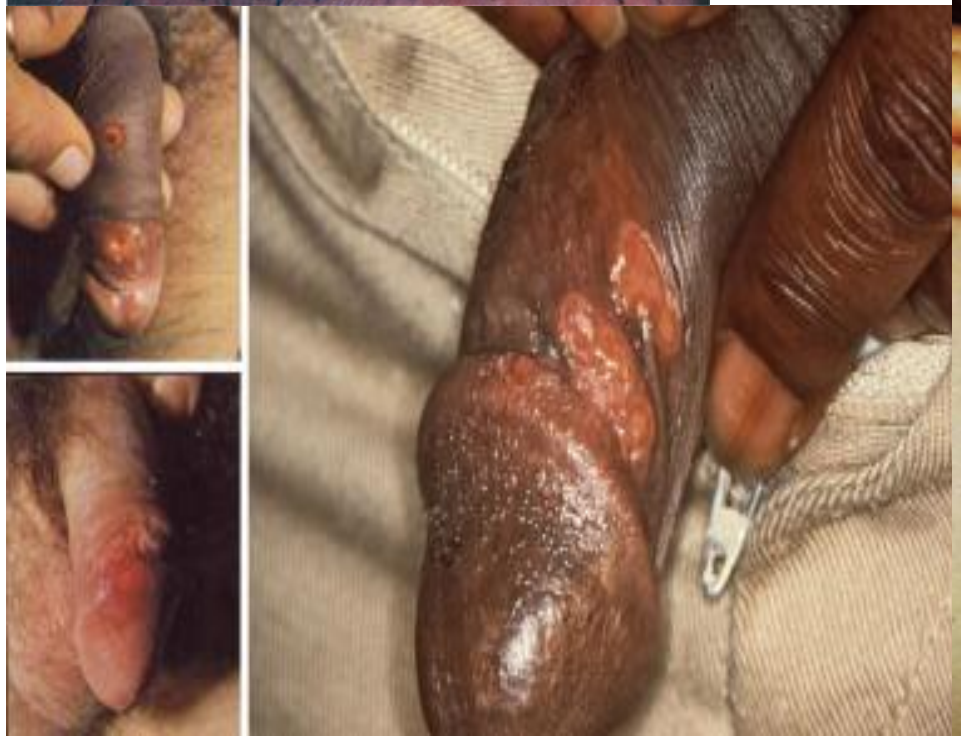
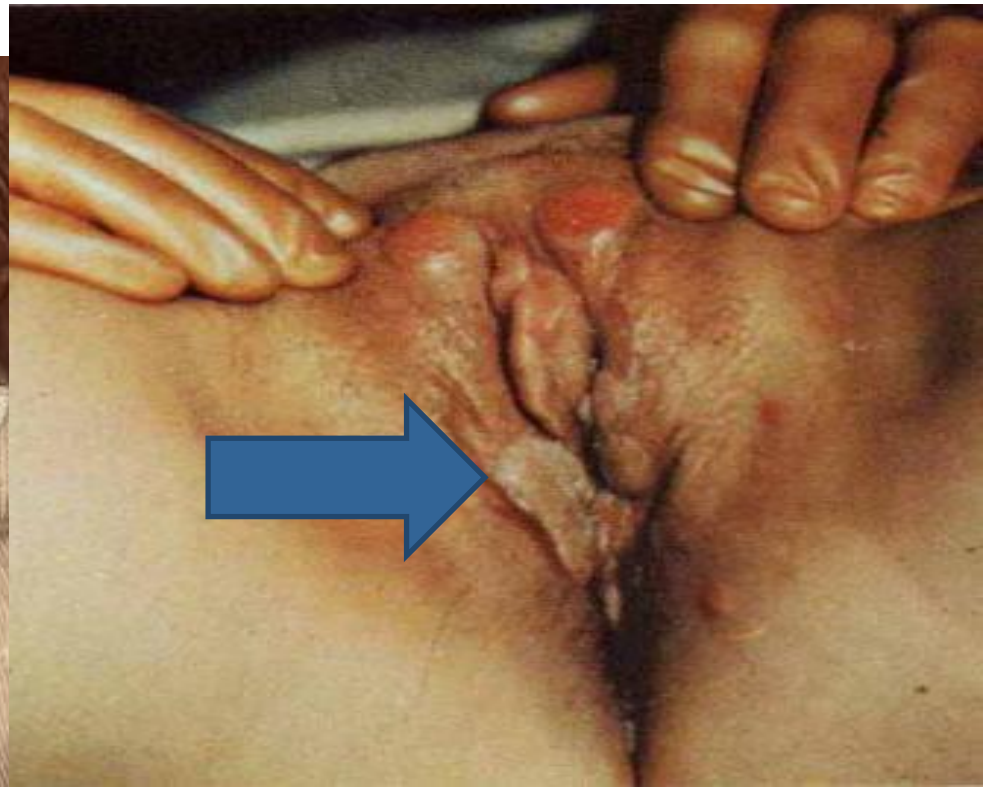


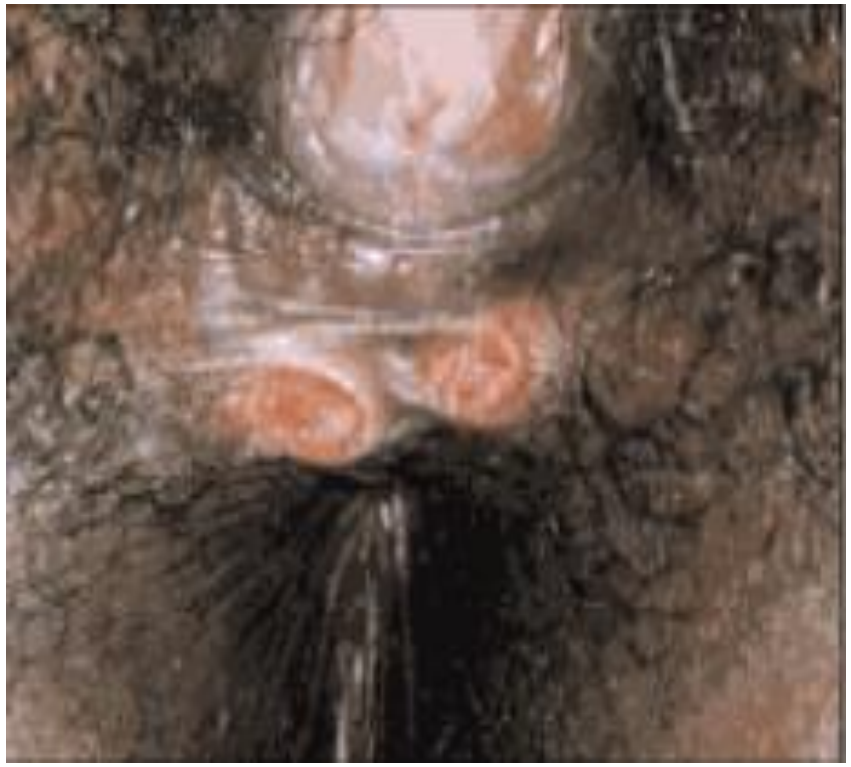
Primary Syphilis Chancre

"*Rarely seen…poorly described*"

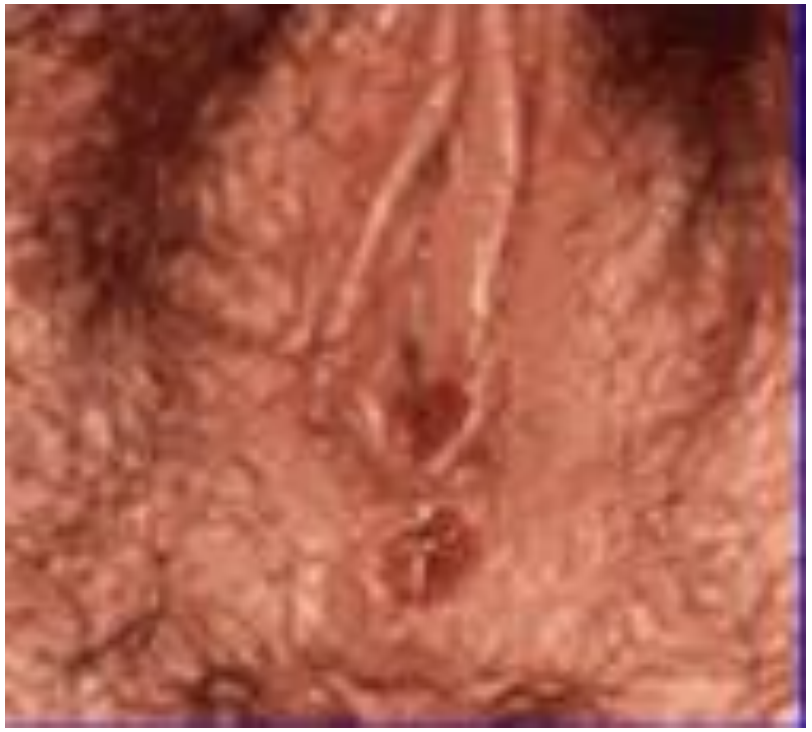




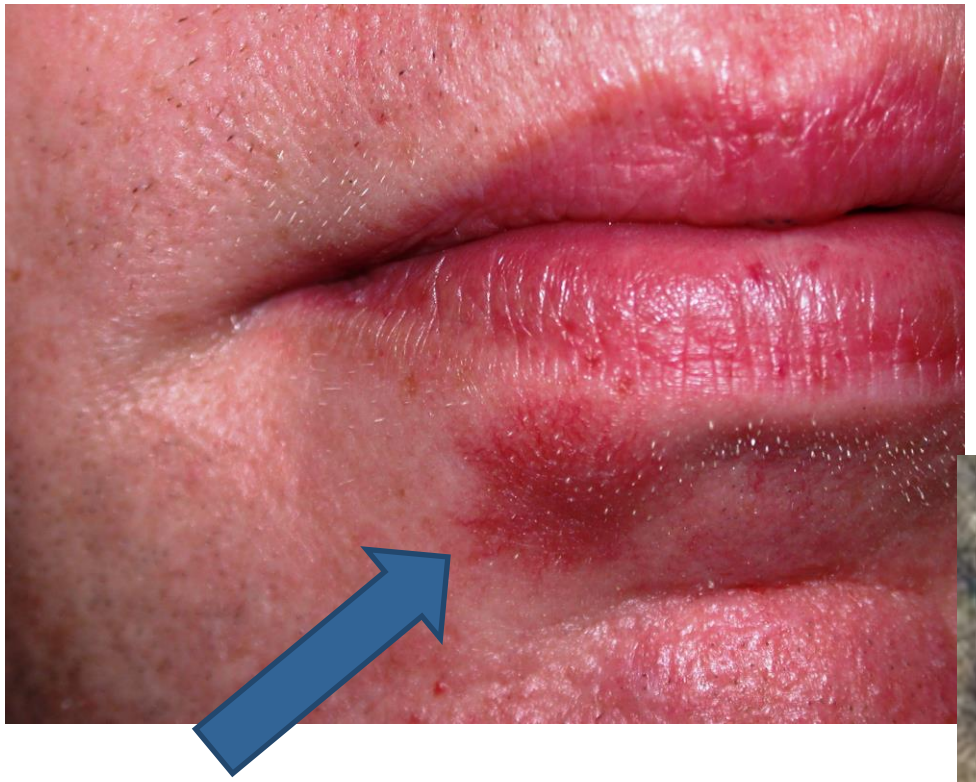
https://emedicine.medscape.com/article/229461-clinical

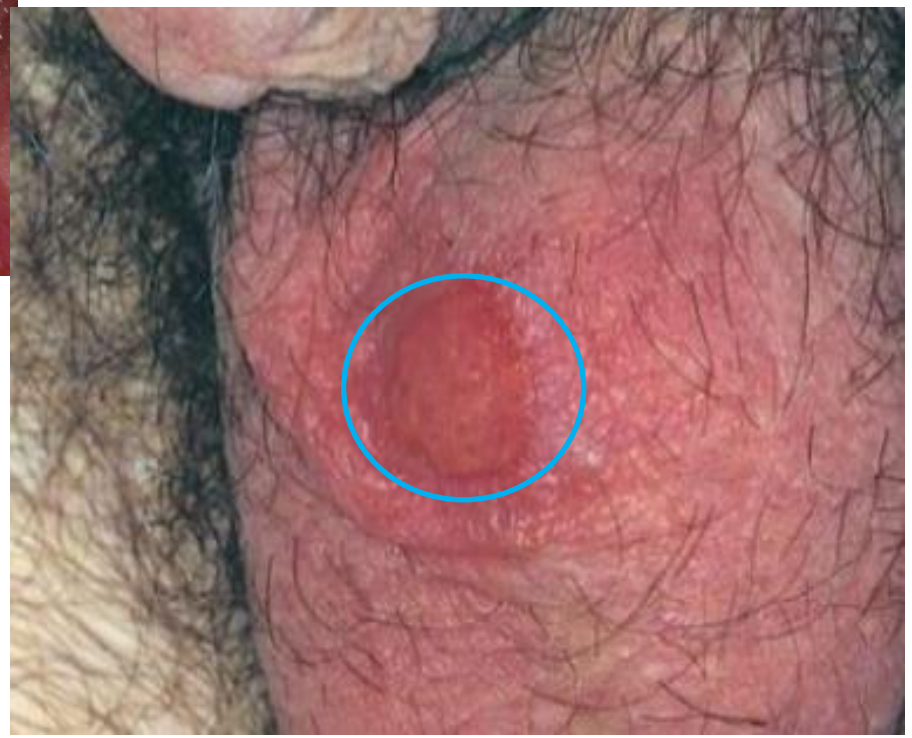


Kissing Chancre



Healed Primary Syphilis Chancre





http://chestersexualhealth.co.uk/syphilis-cases

Secondary Syphilis

"Frequently seen… frequently missed"

- **The Rash: Lesions are infectious**
  - Diffuse but symmetric
  - Usually start on trunk and move out
  - Seems very superficial (papulosquamous)
  - Can leave residual pigmentation or depigmentation
- **Condylomata Lata: Lesions are Highly infectious**
  - Clustering of large, pale, flat-topped papules (warts)
  - Occur in warm, moist areas such as the perineum
- **Mucosal lesions: Lesions are highly Infectious**
  - ~ 30% of untreated cases develop mucous patch
  - Slightly raised, oval area covered by a grayish white membrane, with a pink base that does not bleed
    - Similar to herpes lesion but no pain

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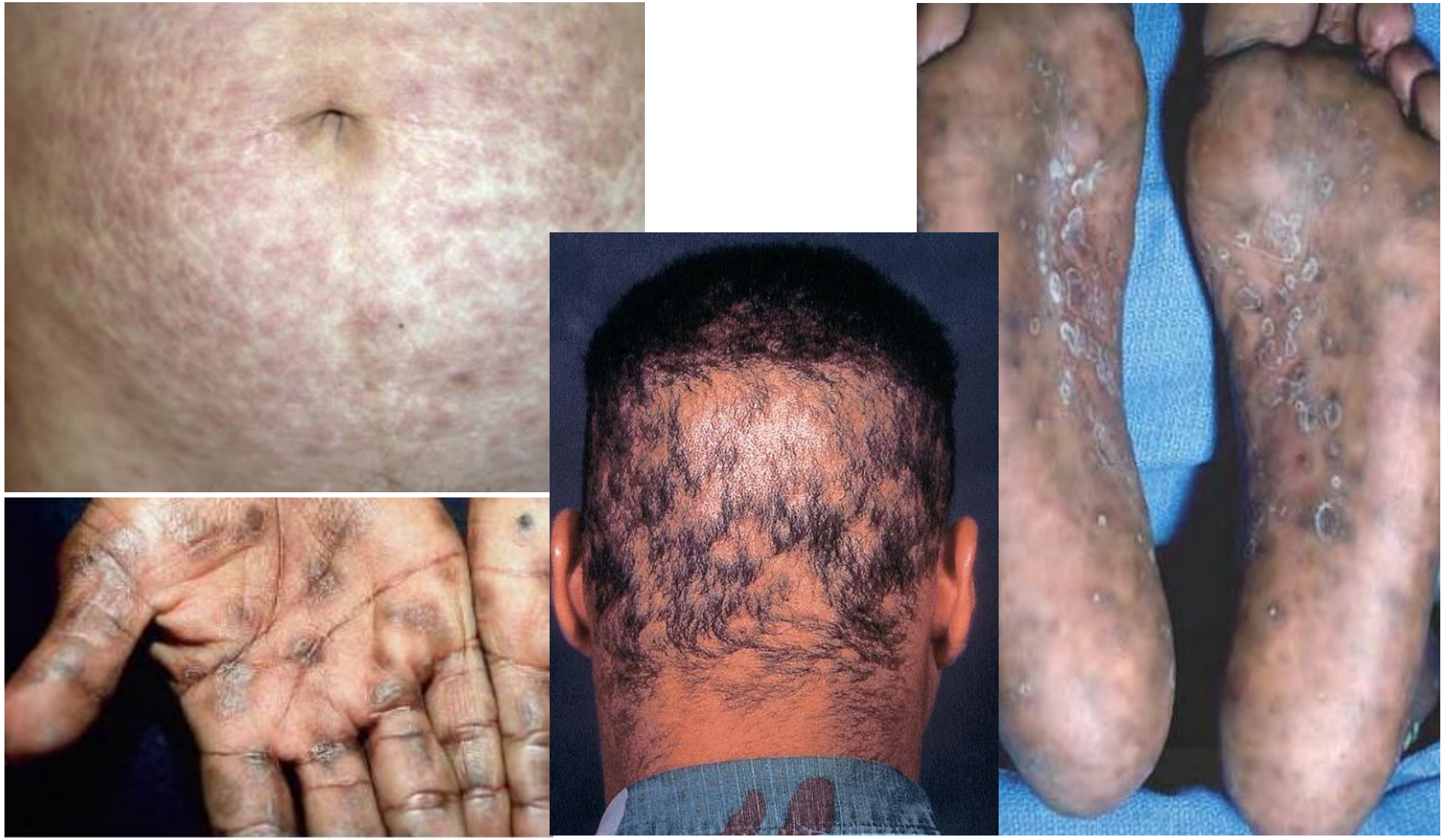
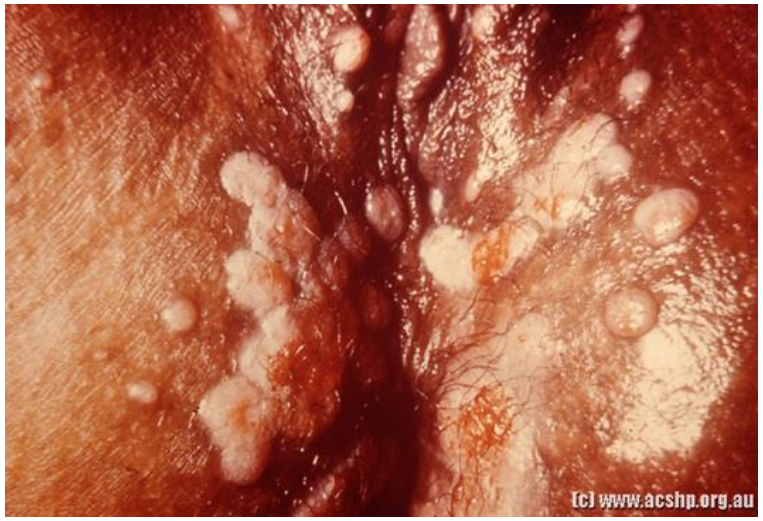
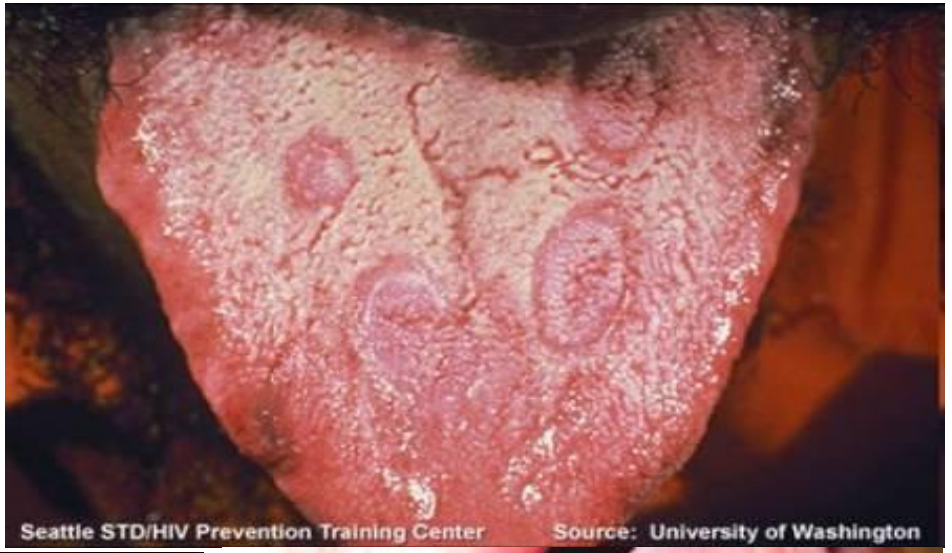
Secondary Syphilis: "*The Rash*"

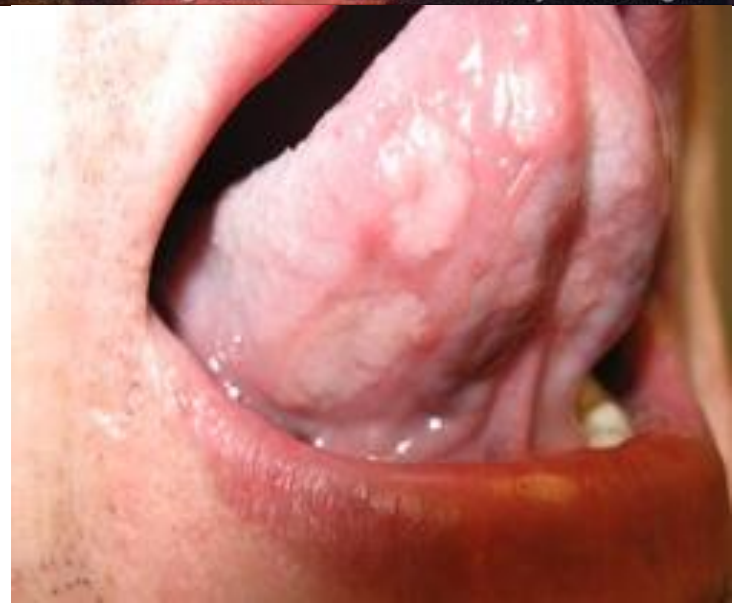




Mucous Patches



Condylomata Lata



http://www.stepwards.com/?glossary=condylomata-lata http://www.aafp.org/afp/2012/0901/p433.html

Latent Syphilis

- Period of time during syphilis infection when there are no symptoms
- Early latent (syphilis infection of <1 year duration)
  - The first year after the resolution of primary or secondary lesions, or
  - A reactive serologic test for syphilis in an asymptomatic individual who has had a negative serologic test within the preceding year
  - Can be infectious
- Late latent (syphilis infection of ≥1 year duration)
  - Usually not infectious, *except for pregnant women, who may transmit infection to the fetus*
- Syphilis of unknown length
  - When you cannot determine based on patient's recall/ history of symptoms

https://www.cdc.gov/std/treatment-guidelines/latent-syphilis.htm

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Screening Tests and Algorithms

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Who should I screen?

- The 2021 STI Treatment Guideline from the CDC refined the screening recommendations:
- **Men and Nonpregnant Women**
  - No routine recommendation for men who only have sex with women; nonpregnant women regardless of the genders of their partners
- **Gay, Bisexual, and other men who have sex with men**
  - Annual screening baseline recommendation, every 3-6 months for those with multiple partners

https://www.std.uw.edu/go/comprehensive-study/syphilis/core-concept/all#page-title

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Who Should I screen?

- The 2021 STI Treatment Guideline from the CDC refined the screening recommendations:
- **Pregnant Women**
  - ALL pregnant women should be tested at their first prenatal visit for each pregnancy and retested at 28 weeks. Retest at delivery for those with increased risk
- **Persons with HIV**
  - Annual screening baseline recommendation, every 3-6 months for those with multiple partners

https://www.std.uw.edu/go/comprehensive-study/syphilis/core-concept/all#page-title

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What Tests Should I Run?

- While there is a POC test for syphilis, the gold standard for screening is serologic testing
- **Treponemal tests**
  - Test for antibodies that are a direct result of the infection with Treponema pallidum (anti-treponemal IgG, IgM and to a lesser degree IgA),
- **Nontreponemal test**
  - Confirm the presence of biomarkers that are released during cellular damage that occurs from the damage of syphilis spirochete. They are an indirect method to test for syphilis infection.

Reverse Algorithm for Syphilis

- Start with specific Treponemal test

  - easier for labs with high volumes of testing
- RPR is done next to gauge infection ‘activity’
- If RPR negative, another confirmatory specific Treponemal test is done
- Still need to have treatment history and previous labs to fully interpret
- May pick up more early or latent untreated infections

Reverse Sequence Syphilis Screening: https://www.cdc.gov/std/syphilis/syphilis-webinar-slides.pdf

What Tests Should I Run?- Reverse Sequence

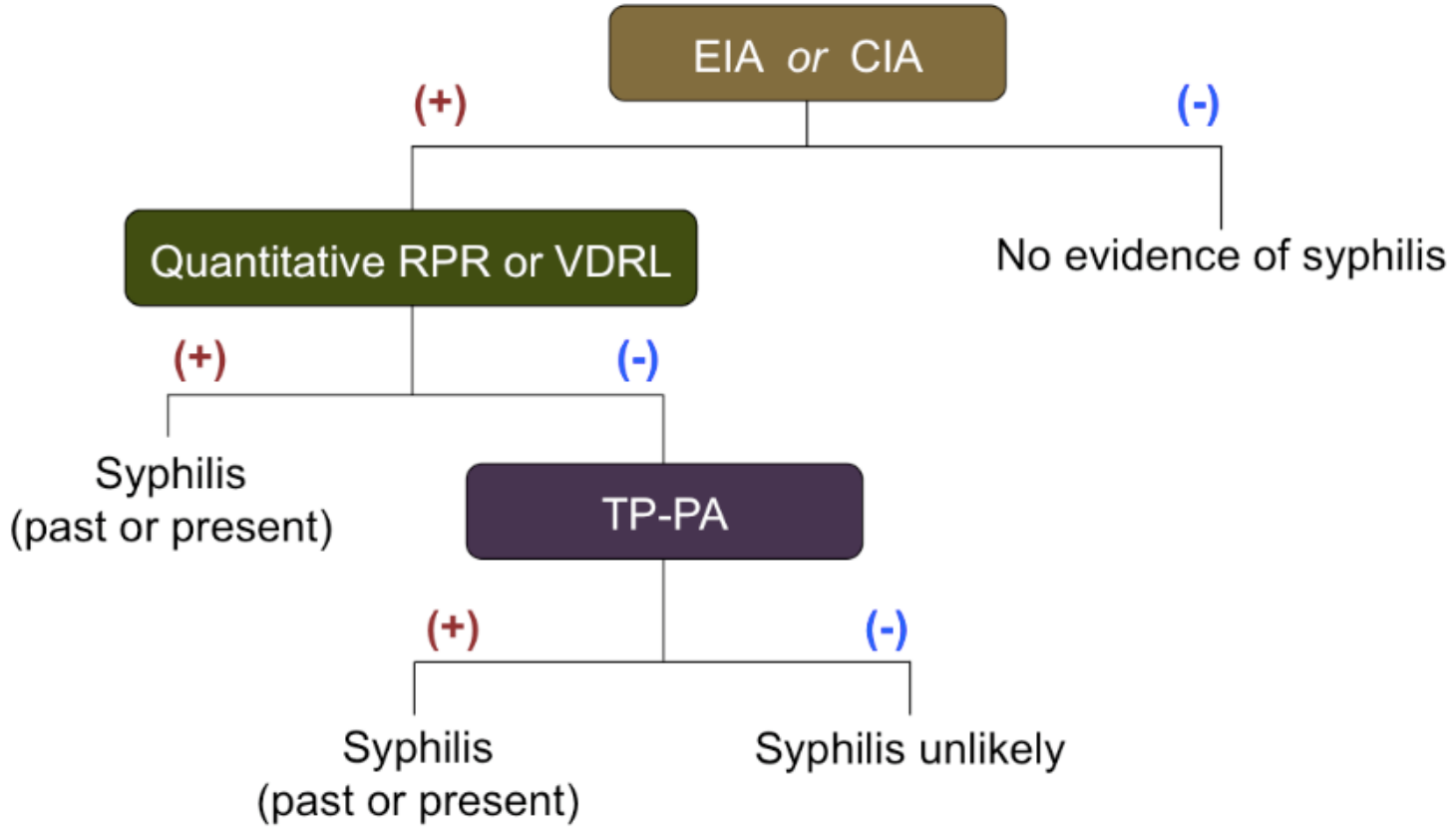

Figure 24 - Syphilis Serologic Screening—Reverse Sequence Algorithm
The reverse serologic screening algorithm uses an initial treponemal test for screening, followed by a nontreponemal test confirmation. A specimen with reactive EIA/CIA results should be tested reflexively with a quantitative nontreponemal test (RPR or VDRL).

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Syphilis Serology Interpretations

Non Treponemal Test	Treponemal Test	Possible Explanation
RPR/ VDRL	TP/PA FTA-Ab	
Measure "Activity " of Infection (Indirect test) May remain positive even after successful treatment	*Detect Antibodies to syphilis (Direct test) Remain positive even after treatment*	
+	+	Syphilis infection: recent or previous
+	-	No syphilis False positive Non Trep
-	+	Previous Treated or Untreated syphilis or early early infection
-	-	No infection detection, Not infected or too early to detect antibodies

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Syphilis Staging and Treatment

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You will need to stage the infection

- All patients with “new” positive syphilis serologic tests (a presumptive diagnosis of syphilis) must be staged to determine the recommended treatment regimen.
  - Sexual history, timing and type of sexual activity, activity that may have been point of exposure, use of condom
- If past positive test: hx of past syphilis treatment and response
  - State OPH/Disease Intervention Specialist (DIS) can help
- History to determine symptoms of infection: ulcer, rash, neurological changes, vision changes
- Physical exam to determine ulcer, rash, neurological symptoms, ocular lesions
- Sexual partner(s), potential source of infection or potential exposure
  - Most patients do care but are embarrassed to disclose.

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Adult probable syphilis surveillance definitions

Primary	Secondary
Presence of a chancre (sore) **and** a positive treponemal test **or** a positive nontreponemal (RPR) test.	Presence of secondary symptoms **and** a positive treponemal test **and** a positive nontreponemal (RPR) test.

See full detailed case definitions at https://ndc.services.cdc.gov/case-definitions/syphilis-2018/

Adult probable syphilis surveillance definitions

Early non-primary non-secondary

A positive treponemal test **and** a positive nontreponemal (RPR) test **and** no primary or secondary symptoms **and** one of the following criteria:

A negative test >12 months
A fourfold lower titer >12 months
A history of primary or secondary symptoms >12 months
Exposure to a partner with early syphilis >12 months

Unknown duration/late

A positive treponemal test **and** a positive nontreponemal (RPR) test **and** no primary or secondary symptoms **and** none of the early non-primary non-secondary criteria apply.

Neurosyphilis History

SYMPTOMS OF NEUROSYPHILIS

5)	Have you recently been having headaches?	☐ Yes	☐ No
6)	Have you had new weakness in any part of your body (including your arms, legs or face)?	☐ Yes	☐ No
7)	Have you had problems walking?	☐ Yes	☐ No
8)	Have you had problems with memory or confusion?	☐ Yes	☐ No
9)	Do you feel (or have you been told) that your personality has changed?	☐ Yes	☐ No

Consider evaluation and treatment for neurosyphilis in patients with new-onset of headaches (or headaches that are different from their usual headaches); new and persistent change in personality, memory or judgment; new numbness or weakness in the face, arms or legs; and/or new gait incoordination.

All persons with a positive serologic test for syphilis and any new neurologic signs or symptoms should have a lumbar puncture with cerebrospinal fluid (CSF) analysis. Patients with ONLY Optic/Otic symptoms do NOT need CSF analysis

CLINICAL ADVISORY: Ocular Syphilis in Maryland https://aaphysicians.org/pdf/ocular-syphilis.pdf

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Stage	Treatment	If penicillin allergic
Primary, secondary, and early latent*	Benzathine **penicillin G**, IM, 2.4 million units in a single dose	**Doxycycline** 100 mg po BID x 14 days OR **Tetracycline** 500 mg po QiD x14 days
Tertiary (late) * OR Late latent or latent syphilis of ?? duration *	Benzathine **penicillin G,** 2.4 million units X 3 (one a week)	**Doxycycline** 100 mg po BiD x 28 days OR **Tetracycline** 500 mg po QiD x 28 days
Neurosyphilis	**Aqueous crystalline penicillin G** 3–4 million units IV QiD 14 days	Penicillin desensitization require and treat as with IV AC Pen

*without neurologic involvement

Jarisch-Herxheimer Reaction

- **Manifestations**: general malaise, fever, headache, sweating, rigors, or a temporary exacerbation of the syphilitic lesions with treatment
- Usually seen in earlier stages, especially secondary syphilis
- Seen within 6 to 12 hours of initial treatment.
- Usually subsides within 24 hours and poses no danger but may produce anxiety
  - If in cases of neurospyphilis treatment (general paresis or a high CSF cell count) it can be more problematic and cause seizures or strokes
- OFTEN confused with allergic reaction to antibiotics
- Seen when patient treated with antibiotics for one condition/ not aware of syphilis infection as well
- Expect it every time so you will not be surprised
  - Patients should be warned before treatment to prevent anxiety

Jarisch-Herxheimer Reaction: https://patient.info/doctor/jarisch-herxheimer-reaction

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Follow up monitoring

Primary and Secondary Syphilis

- VDRL or RPR at 6 and 12 months
- Fourfold drop in titers generally expected after 3-6 months

Latent Syphilis

- VDRL or RPR at 6, 12 and 24 months
- A titer of **>** 1:32 should fall 4-fold within 12-24 months

Pregnancy

- VDRL or RPR in the third trimester and at delivery, monthly if at high risk of reinfection or area of high prevalence of syphilis. Response should be the same as for non-pregnant persons.

HIV infection

- VDRL or RPR at 3, 6, 19, 12 and 24 months for primary and secondary syphilis, and 6, 12, 18 and 24 months for latent syphilis.
- Expect a fourfold decrease within 6 to 12 months for primary and secondary syphilis, and within 12 to 24 months for latent syphilis

https://www.cdc.gov/std/treatment-guidelines/syphilis.htm

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