



All About Syphilis: Diagnosis, Treatment and Follow-Up

April Lunch and Learn

April 26, 2023



Health & Human Services

Topics of Discussion

- Identify the current impact of syphilis in North Dakota.
- Describe the process of diagnosing syphilis.
- Summarize CDC recommended treatment regimens and follow-up testing.



THE STATE OF STDs IN THE UNITED STATES, 2021

STDs continue to forge ahead, compromising the nation's health.

Note: These data reflect the effect of COVID-19 on STD surveillance trends.



1.6 million
CASES OF CHLAMYDIA
3.8% decrease since 2017



710,151
CASES OF GONORRHEA
28% increase since 2017



176,713
CASES OF SYPHILIS
74% increase since 2017



2,855
CASES OF SYPHILIS
AMONG NEWBORNS
203% increase since 2017

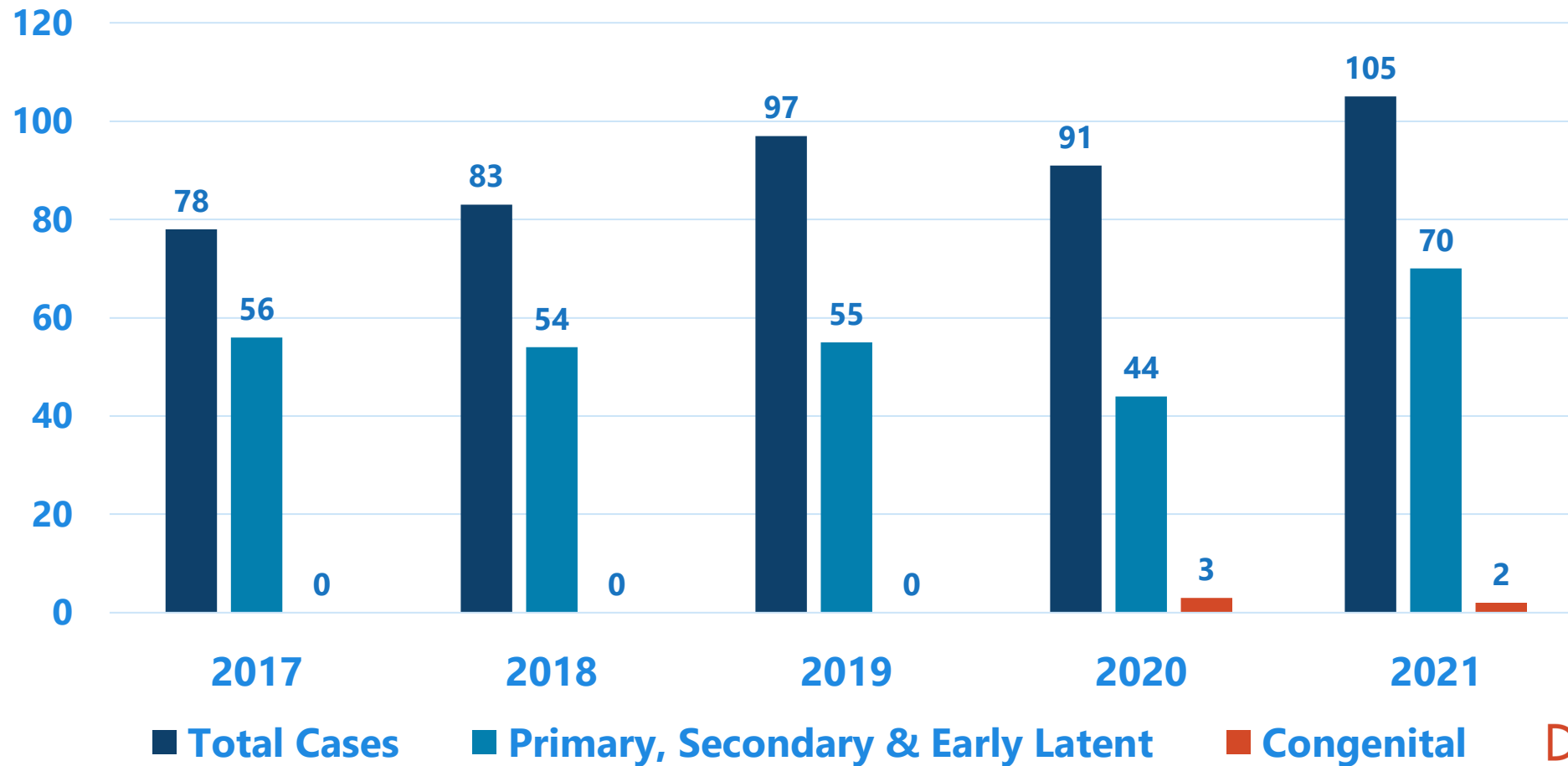
LEARN MORE AT: www.cdc.gov/std/

**ANYONE WHO HAS SEX COULD
GET AN STD, BUT SOME GROUPS
ARE MORE AFFECTED**

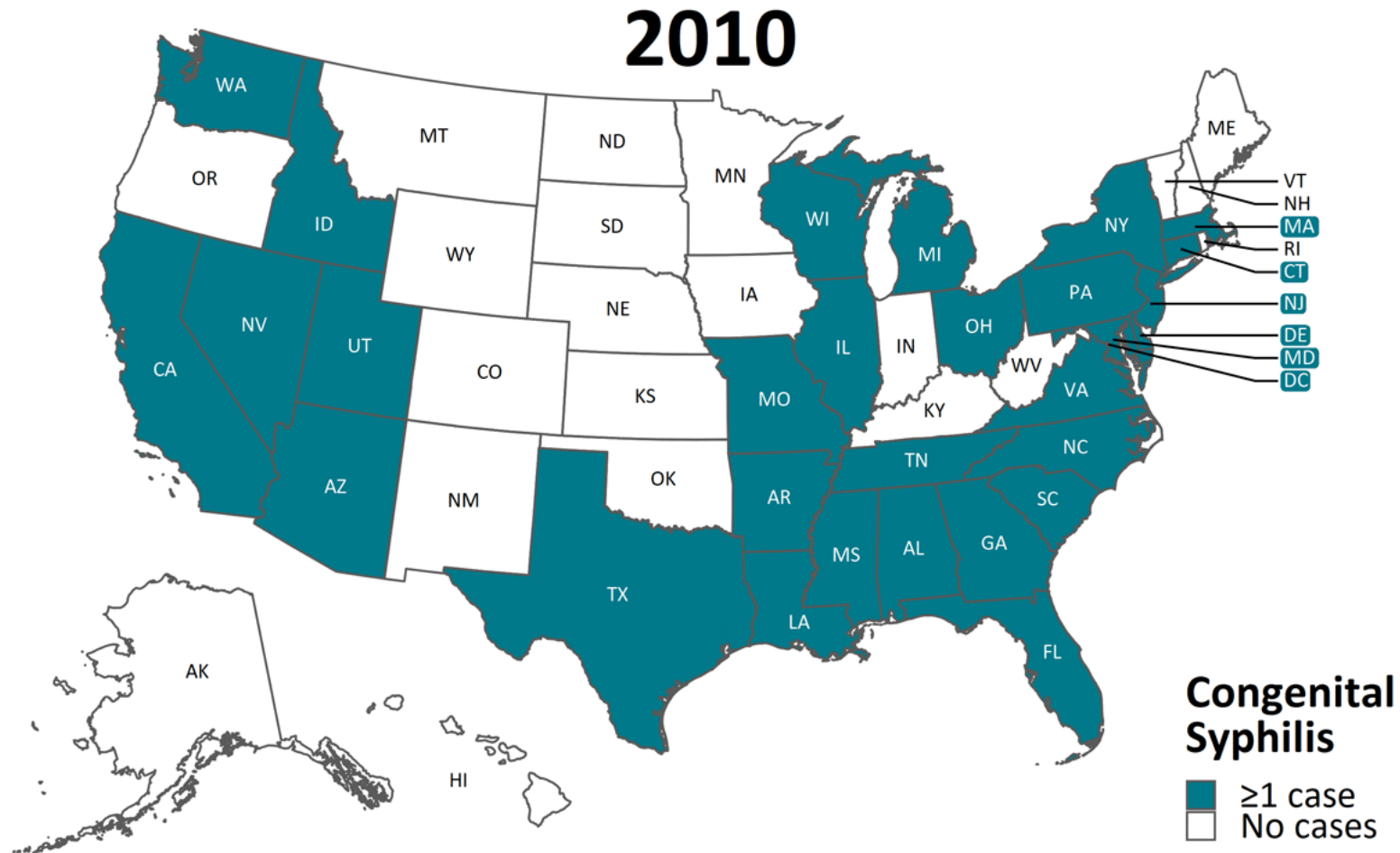
- YOUNG PEOPLE AGED 15-24
- GAY & BISEXUAL MEN
- PREGNANT PEOPLE
- RACIAL & ETHNIC MINORITY GROUPS

Syphilis Cases in ND Have Increased 35% from 2017 to 2021.

ND Syphilis Morbidity by Stage, 2017 -2021

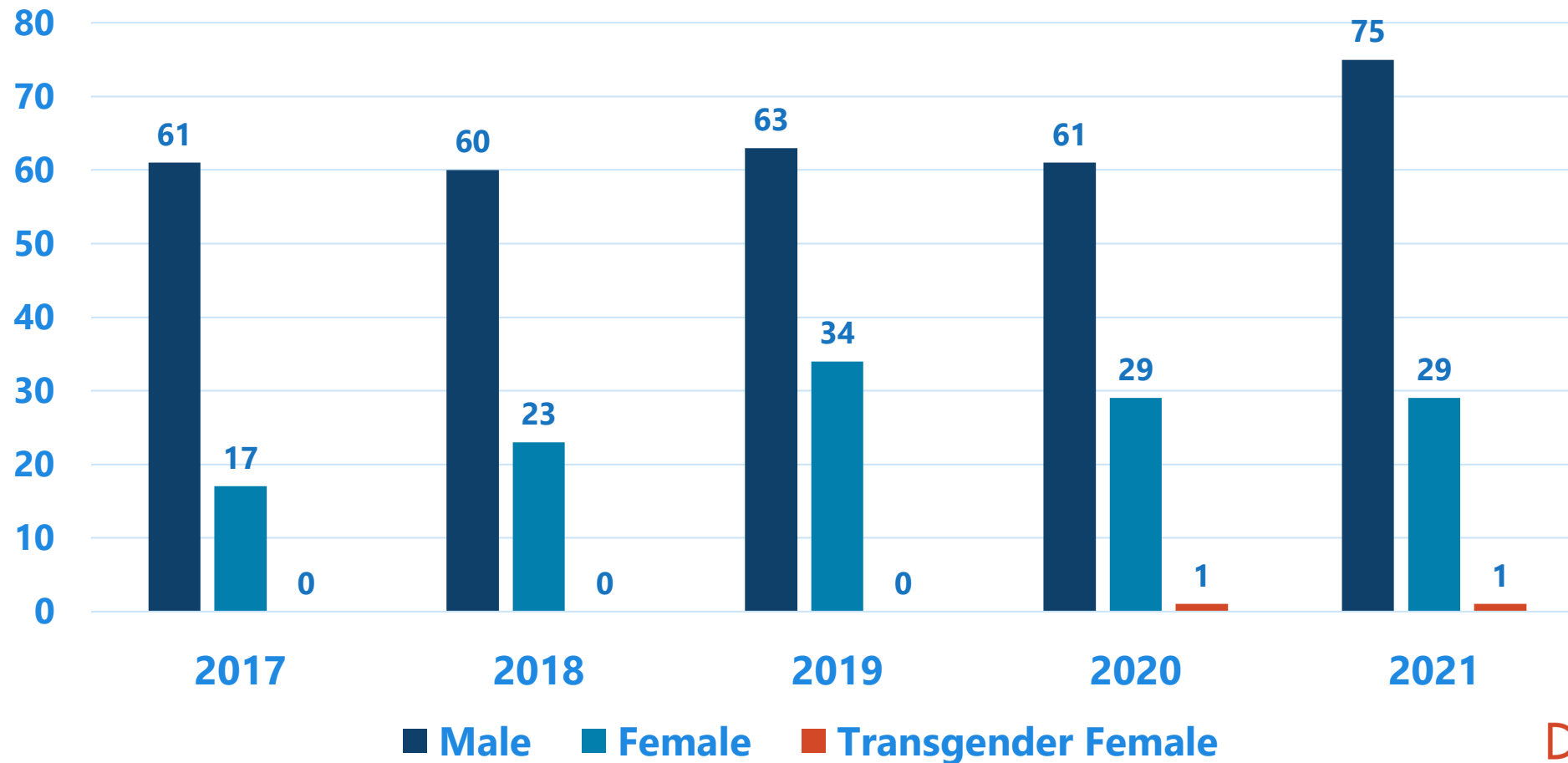


Congenital syphilis has spread across the nation in the last decade.



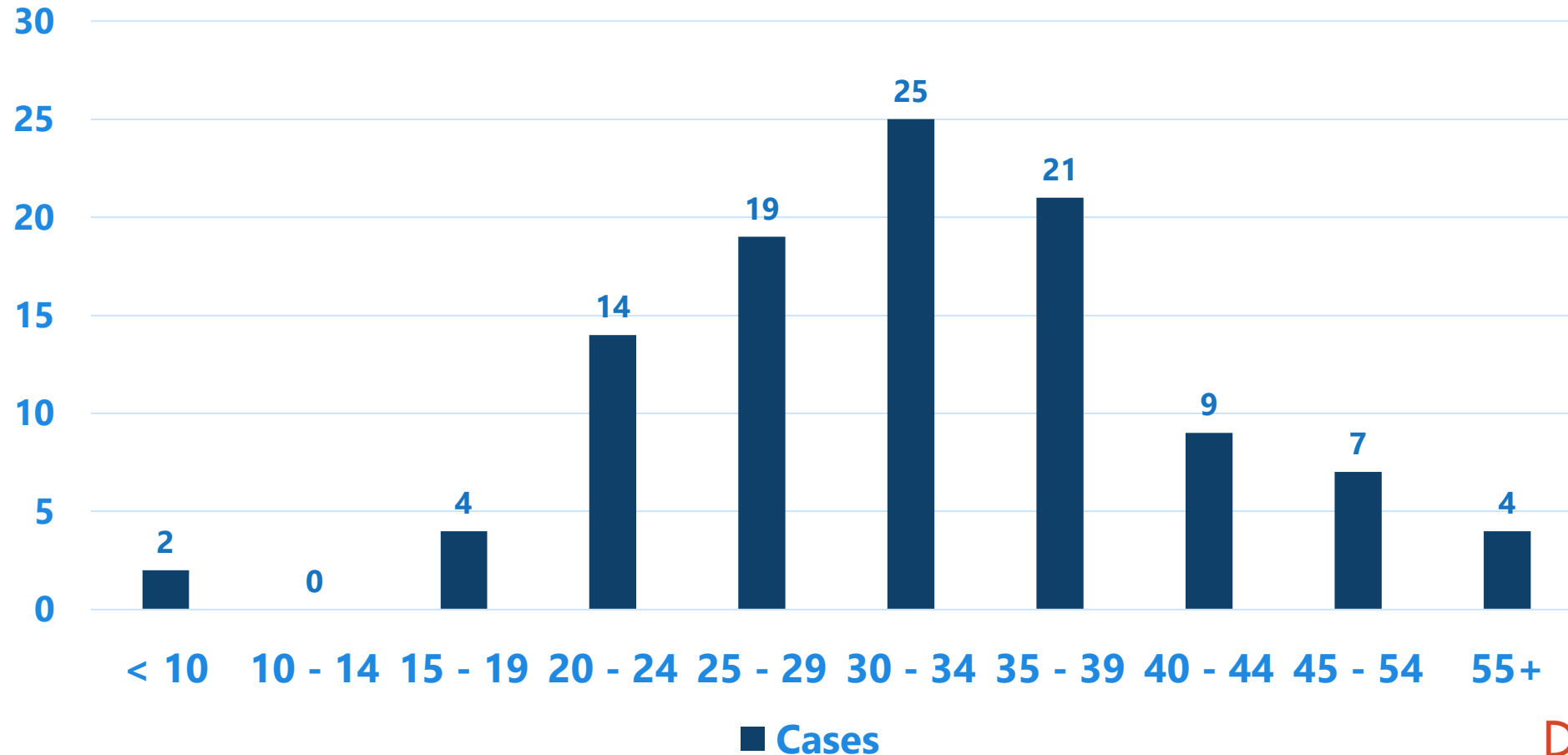
Syphilis Cases in ND Have Increased 70% Among Females from 2017 to 2021.

ND Syphilis Morbidity by Gender, 2017 -2021



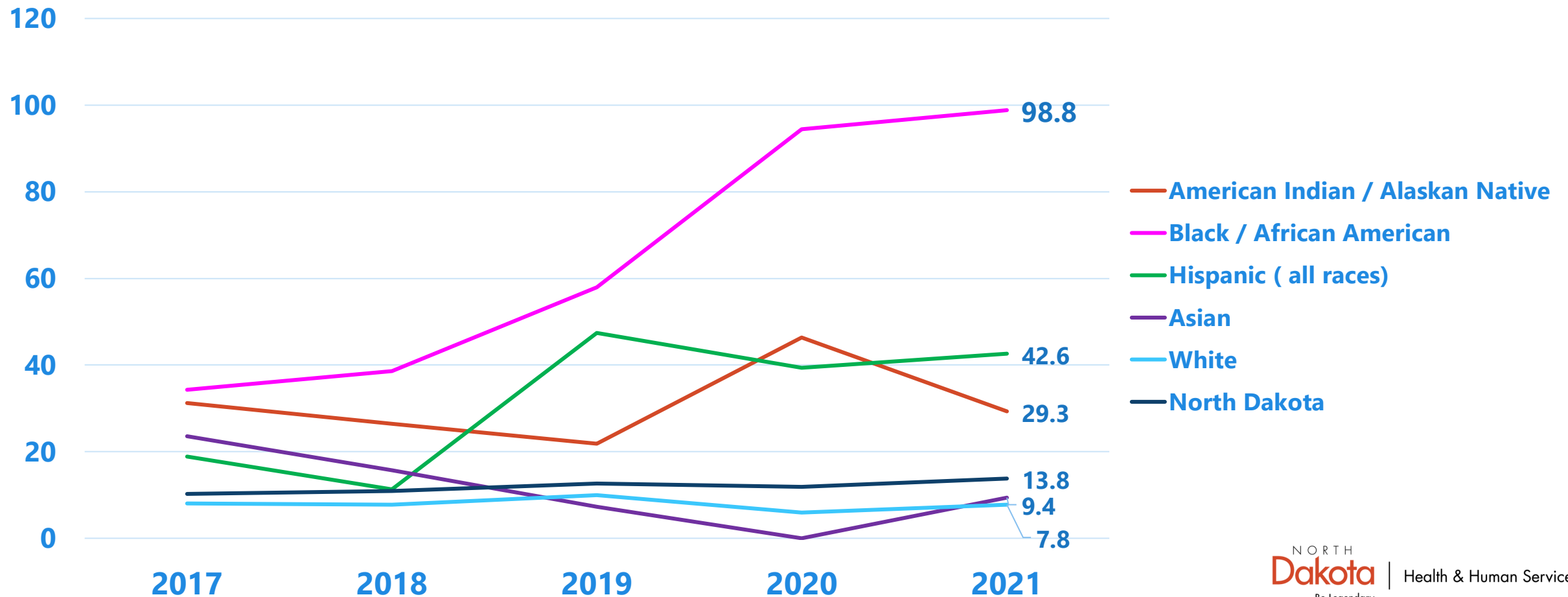
Most (62%) Syphilis Cases in ND were Between the Ages of 25 – 39 years in 2021.

ND Syphilis Morbidity by Age, 2021

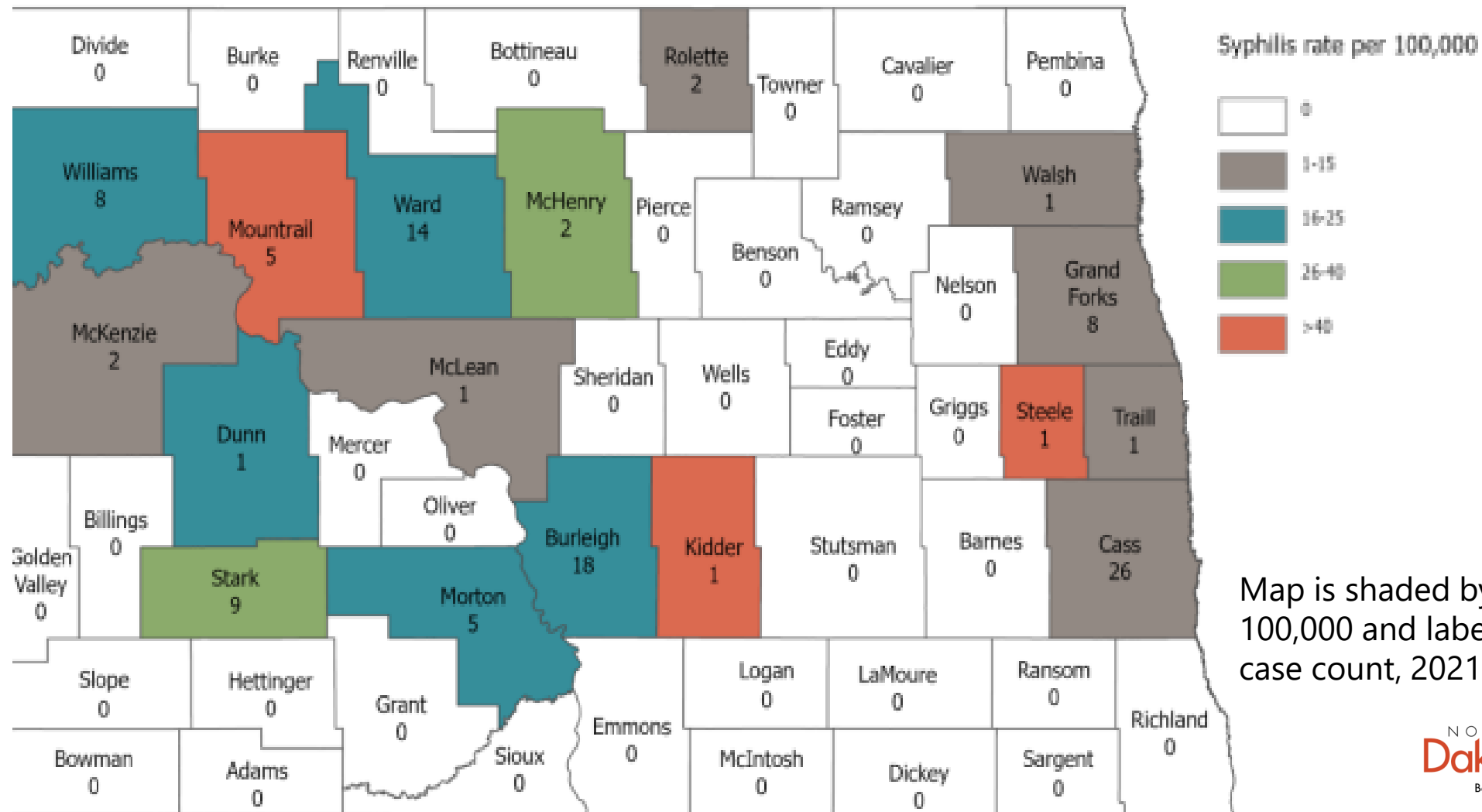


Black/African Americans Report a Disparity in Syphilis Rates in ND.

ND Syphilis Morbidity by Race, 2017 - 2021



In 2021, Syphilis was Reported in 17 Counties.



Map is shaded by rate per 100,000 and labeled by case count, 2021.

Syphilis, The Great Imitator

- Chronic sexually transmitted infection caused by *Treponema pallidum*
- Classified into stages
- Infection through small breaks in skin or mucous membranes
- Risk of developing syphilis after sexual contact 10-60% (average about 30%)
- Highest risk with contact to early syphilis; Lesions with many treponemes transmit most effectively



Syphilis Screening Recommendations.

Pregnant Women

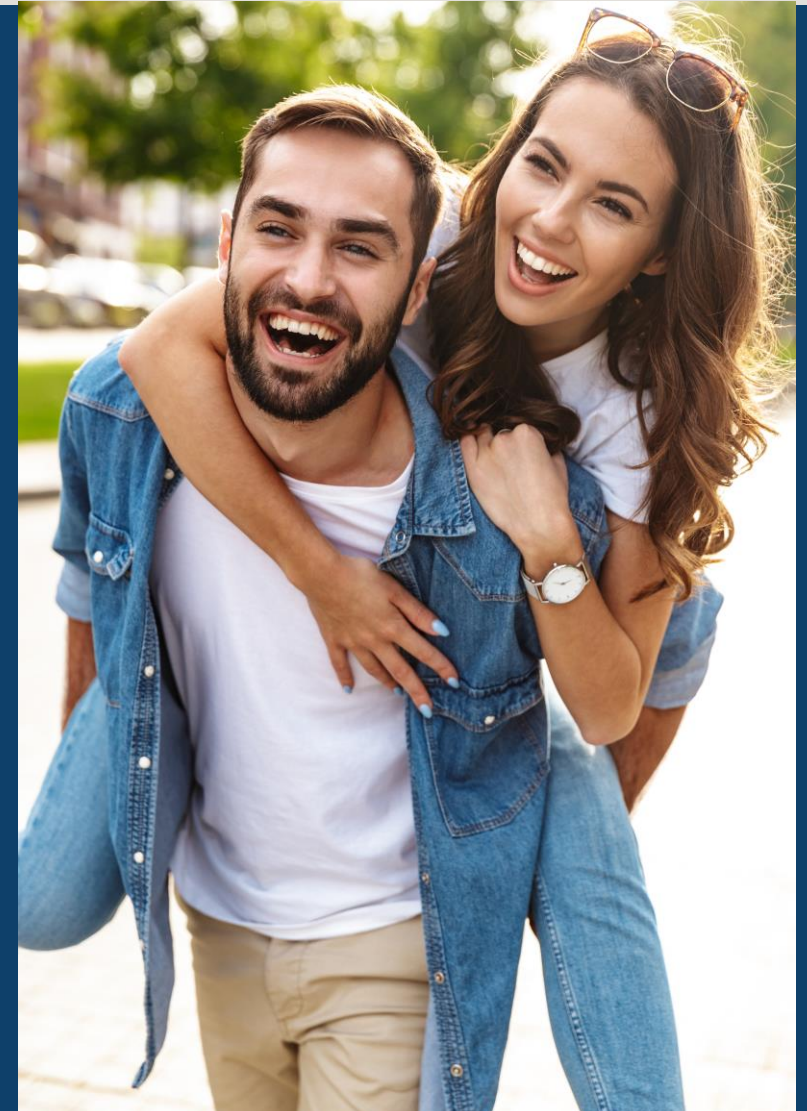
- All pregnant women at the first prenatal visit
- Retest at 28 weeks and at delivery

Men Who Have Sex with Men (MSM)

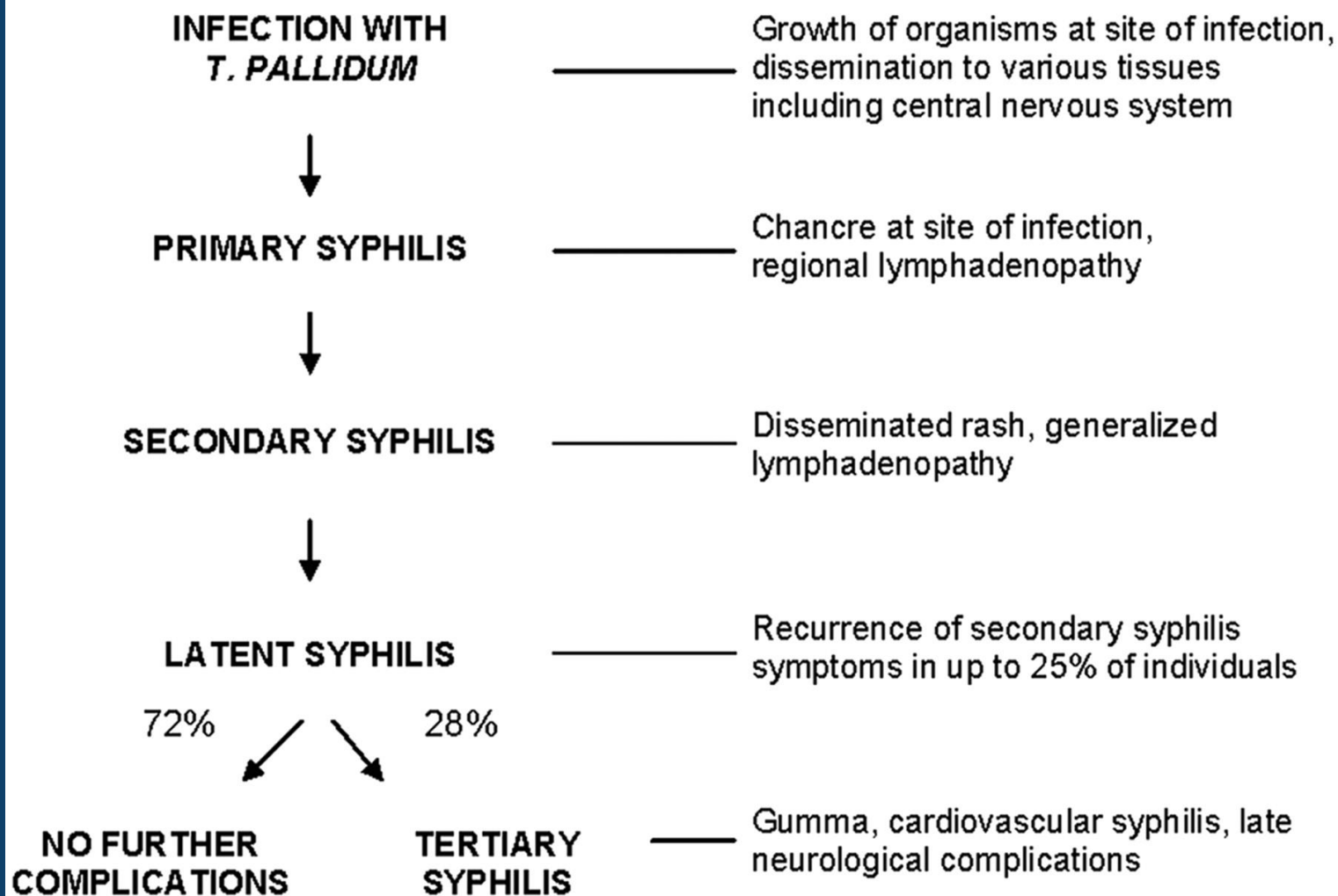
- At least annually for sexually active MSM
- Every 3 to 6 months if at increased risk

Persons with HIV

- For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter
- More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology

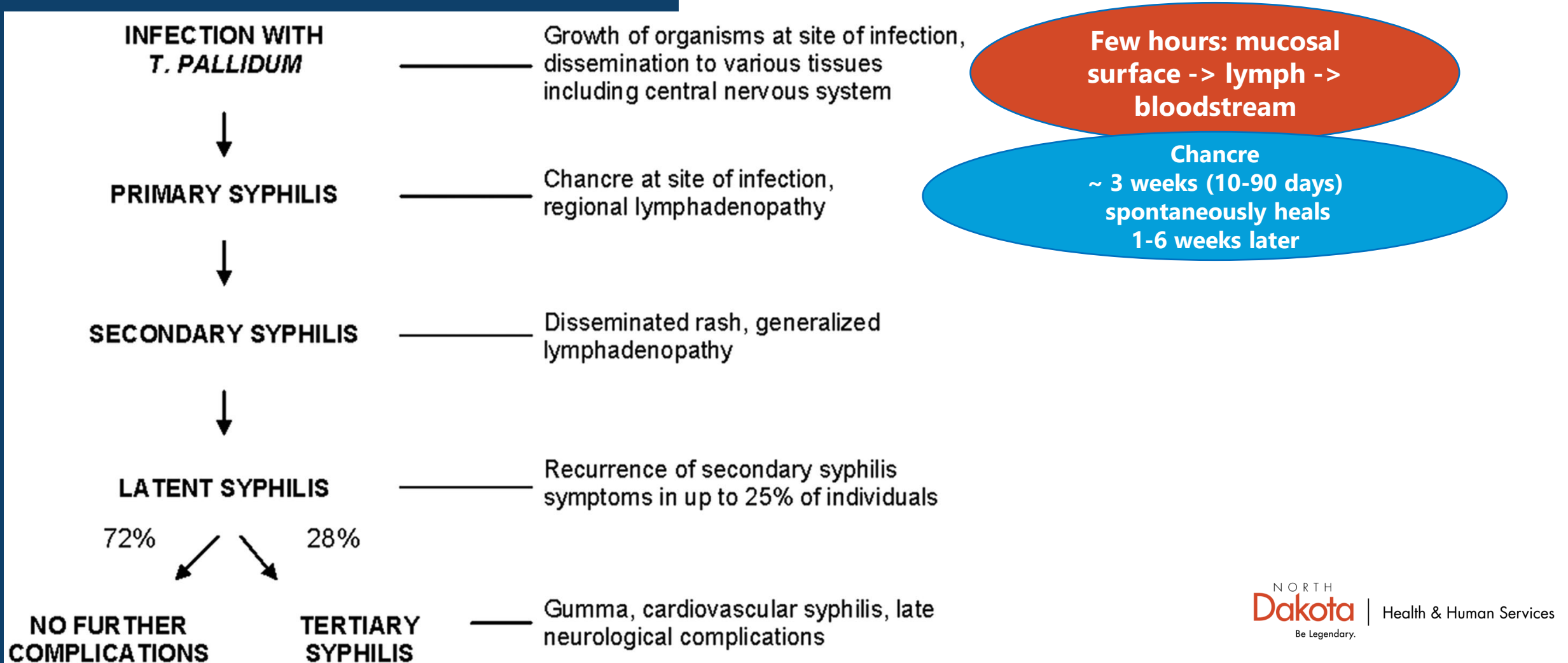


Clinical Manifestations and Staging



Few hours: mucosal surface -> lymph -> bloodstream

Primary Syphilis

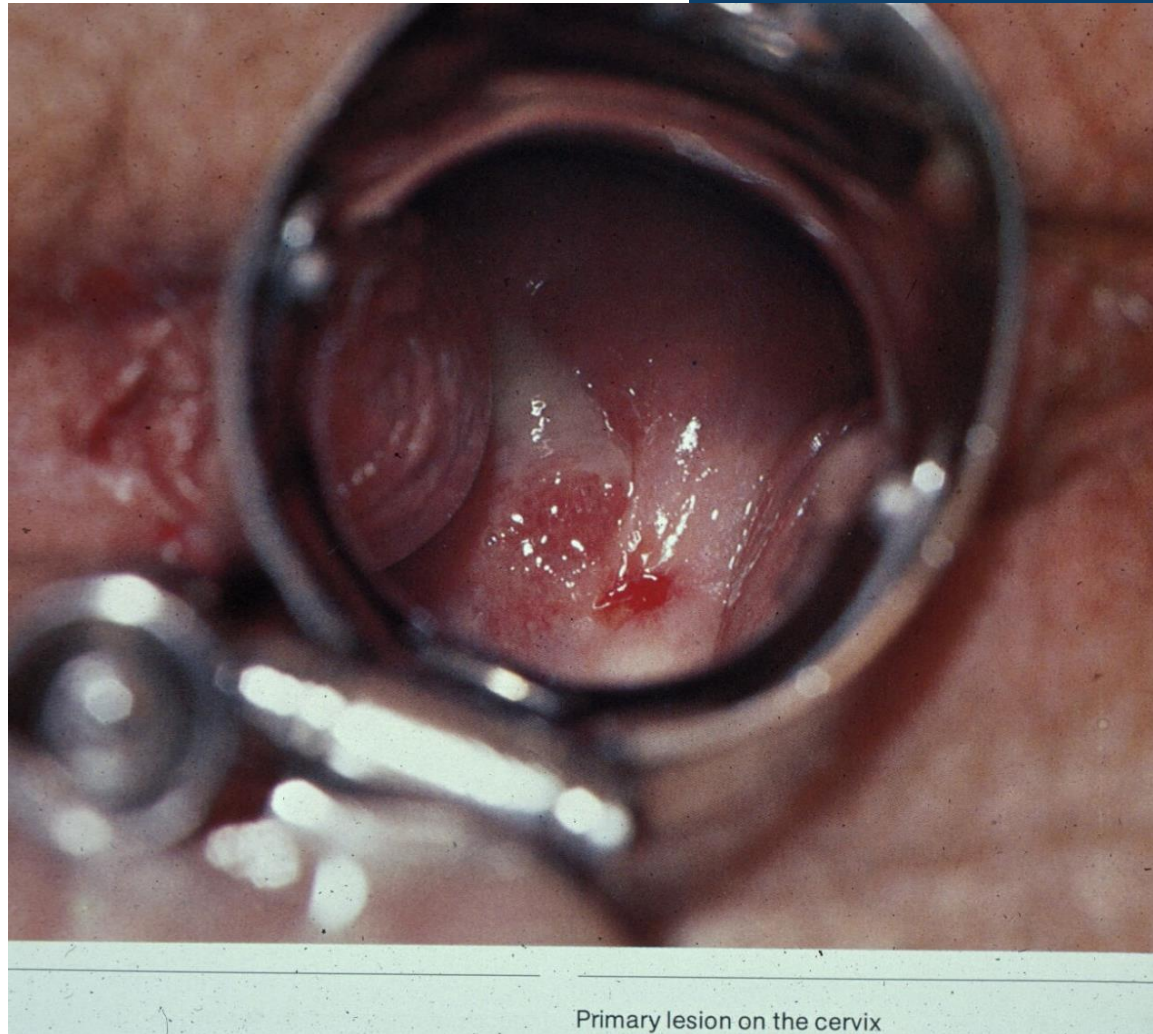


Primary Syphilis

- Chancres can occur anywhere inoculated by direct contact (fingers, mouth, anus)
- Nontreponemal tests (RPR, VDRL) negative in 15 -25% cases of primary syphilis
- Push to treat if any suspicion of early syphilis! Loss to follow up and spread of infection can be high

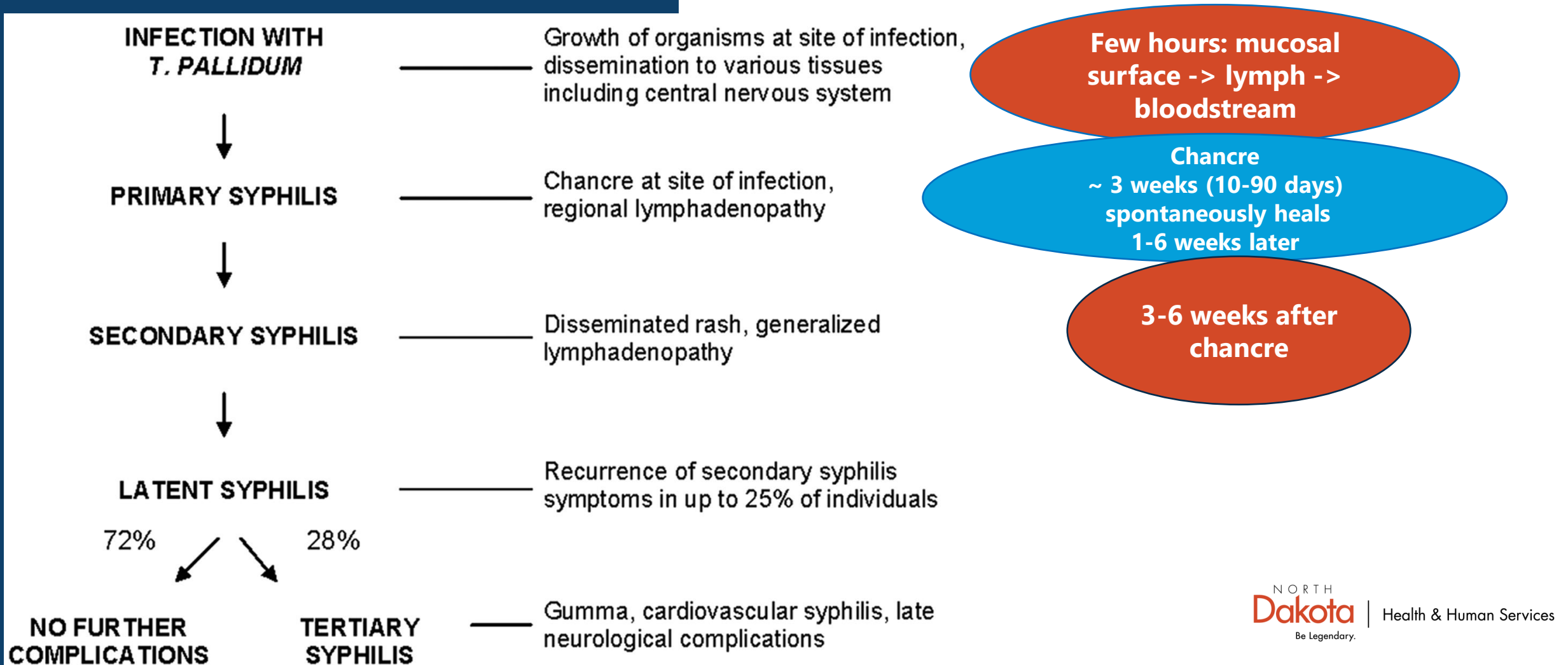


Cervical Chancre



Primary lesion on the cervix

Secondary Syphilis



Secondary Syphilis

- Generalized rash: evanescent, copper color, macular – reddish, popular, palms/sores
- Condyloma lata
- Mucous patches
- Fever, malaise, generalized lymphadenopathy, alopecia, liver/kidney involvement
- Lasts 2 – 6 weeks



Condyloma lata, Mucous Patches, Other Symptoms

- High numbers of treponemes – highly contagious!
- May occur at any moist body site
- Fleshy, flat-topped lesions that may be mistaken for anogenital warts
- Patchy, “moth-eaten” alopecia, loss of lateral eyebrows
- May affect any organ: kidney, stomach, spleen, liver, etc.



Latent Syphilis

- Defined by positive test in the absence of clinical manifestations
- **Early Latent: infected within the past year**
 - Negative syphilis serology in past year
 - Known contact to early case of syphilis
- **Late Latent: infected >1 year ago or unknown duration**
 - No syphilis serology in past year
 - No contact to syphilis case or history of symptoms in past year



There are Many Other Manifestations of Syphilis.



Neurosyphilis

- Cognitive Dysfunction
- Motor or Sensory Deficits
- Ophthalmic or Auditory Symptoms
- Cranial Nerve Palsies
- Specimen Source: CSF



Ocular Syphilis

- Can involve almost any eye structure.
- Ocular syphilis may lead to decreased visual acuity including permanent blindness.
- Eye redness, blurry vision, and vision loss.



Otosyphilis

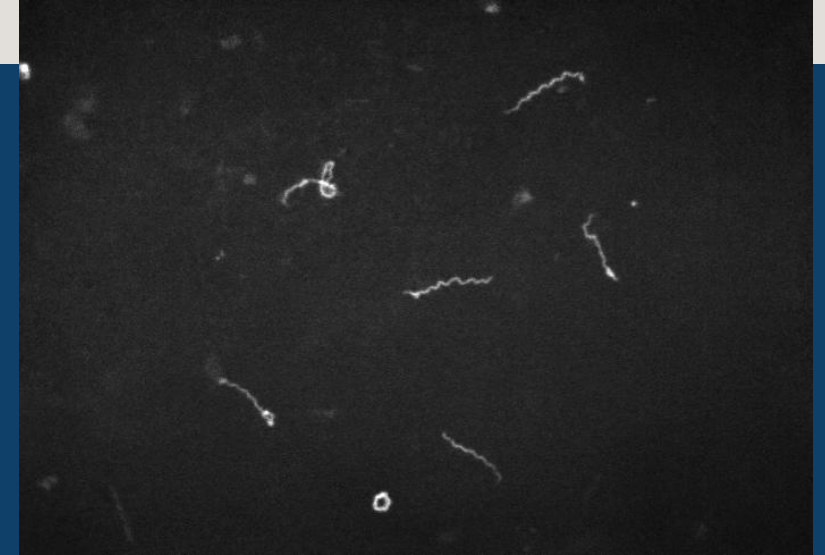
- Sensorineural Hearing Loss
- Tinnitus
- Vertigo

Late Manifestations

- 15-30 yrs. after untreated infection
- Inflammatory lesions:
 - Cardiovascular System
 - Skin
 - Bone
 - Other Tissue

Diagnostics for Syphilis.

- Definitive: dark field microscopy, molecular testing (PCR)
- Highly suggestive: histopathology
- POC Testing: Syphilis Health Check™



Serologic Testing for Syphilis.

Nontreponemal



RPR, VDRL

Quantitative = titers decrease
with treatment

Treponemal



FTA-ABS, TP-PA, EIA/CIA

Qualitative = Good for screening
but once positive, positive for life

RPR: Rapid plasma reagin; VDRL: Venereal Research Disease Laboratory: T. pallidum particle agglutination assay; EIA: Enzyme immunoassay/CIA: Chemiluminescence immunoassay; FTA-ABS: Fluorescent treponemal antibody absorption

Understanding the Difference in Types of Syphilis Testing.

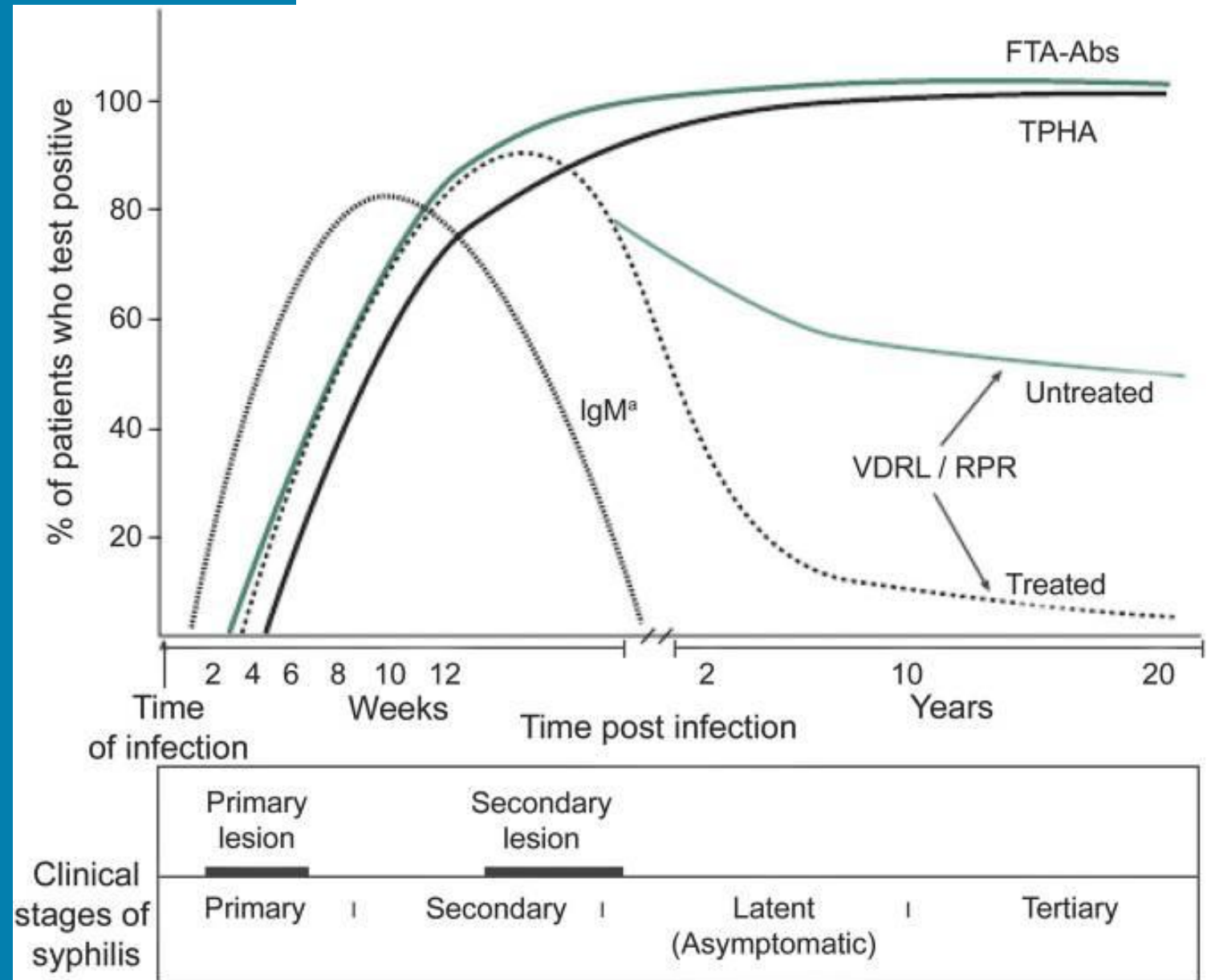
Nontreponemal Tests (RPR or VDRL)

- Detect antibodies to cardiolipin, lecithin, cholesterol antigens – non-specific marker of tissue damage
- Results expressed as a titer
 - Higher titers reflect greater disease activity
 - Titer should decline with successful therapy
 - Even without treatment, titers will decline over time
- May result in biologic false positive (1-2% in US)

Treponemal Tests (EIA/CIA)

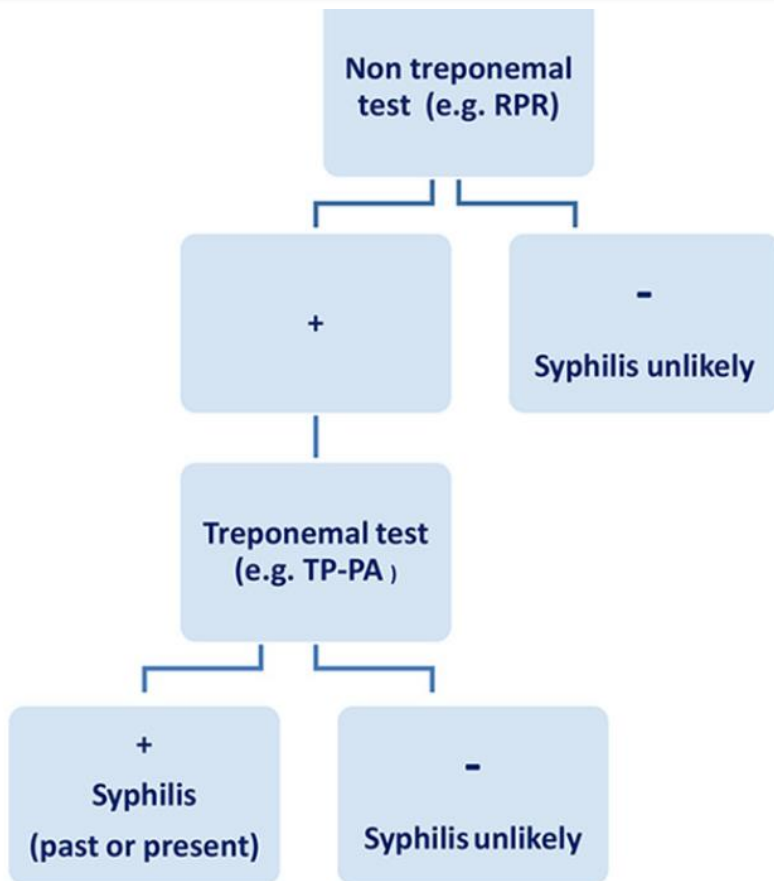
- FTA-ABS and TP-PA: measure antibody response to whole organism
- EIAs/CIAs: measure antibodies to recombinant *T. pallidum* proteins
- Results are expressed qualitatively (reactive or nonreactive)
- Once positive, stay positive for many years ("for life")
- False positives may occur; etiology not well-defined

Natural History of Syphilis

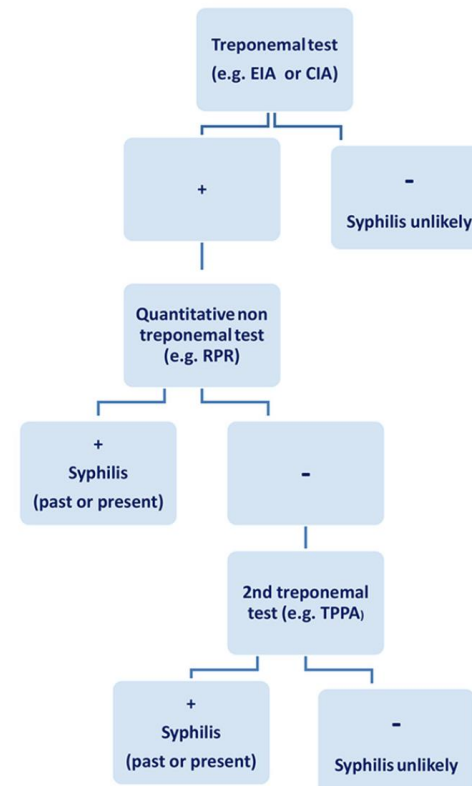


Two Algorithms for Syphilis Testing.

Traditional Screening



Reverse Sequence Algorithm



Sensitivity of Serologic Test Options.

Test	Sensitivity in untreated syphilis		
	Primary	Secondary	Latent
RPR	86	100	98
VDRL	78	100	96
TP-PA TP-HA	95 (88)	100	97-100
EIA/CIA	95	100	93-100
FTA-ABS	78 (84)	93 (100)	93-100

Park IU, Fakile YF, et al. CID, 2019;68(6).
Cantor AG, Pappas M, et al. JAMA, 2016;315(21).

Understanding Syphilis Titers.

- A **fourfold change or two dilutions** represents a clinically significant difference
 - 1:32 → 1:4 (decreased 8-fold or 3 dilutions 1:16, 1:8, 1:4)
 - 1:2 → 1:16 (increased 8-fold or 3 dilutions 1:4, 1:8, 1:16)
- **Persistent NTT positivity despite adequate treatment**
 - Mechanism not well-understood
 - Does not mean new infection
 - More likely and commonly seen in HIV+ patients
 - For HIV- patients, risk factors include: age >30, female sex, prior h/o syphilis, non-early stage, baseline RPR titer ≤1:32, non-PCN therapy
- **False Positive:** Other infections: HIV, HSV, malaria, leprosy, other spirochetal infections; older age, autoimmune disorders, cardiovascular disease, pregnancy, IVDU, recent immunizations (COVID, flu)



The Treatment for Syphilis Has Been Available Since 1943.

Penicillin still works and is the only treatment option for pregnant women. Dosage depends on stage.

Stage of Syphilis	Dosage
Primary	Benzathine penicillin G 2.4 million units
Secondary	Benzathine penicillin G 2.4 million units IM
Early latent	Benzathine penicillin G 2.4 million units
Late Latent	Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

ND Health Alert: April 20th, 2023

- Challenges Accessing Bicillin
- The manufacturer anticipates the issue will be resolved in the next two (2) months
- Notify HHS with treatment challenges
 - 701.327.2378

Potential Access Challenges to Bicillin L-A®

North Dakota Health & Human Services (HHS) is sharing information that the Centers for Disease Control and Prevention (CDC) has received reports of providers being currently unable to procure enough penicillin G benzathine (Bicillin L-A®) – the first-line recommended treatment for syphilis. The manufacturer anticipates the issue will be resolved in the next two (2) months. In the meantime, they are working closely with CDC and the U.S. Food and Drug Administration (FDA) to address urgent requests.

During this time, providers should:

- Continue to follow [CDC's treatment recommendations](#). Penicillin G benzathine (Bicillin L-A®) is the **only recommended treatment** for pregnant people infected or exposed to syphilis.
- Doxycycline 100mg PO BID for two (2) weeks (for early syphilis) or four (4) weeks (for late latent or syphilis of unknown duration) is an alternative for the treatment of non-pregnant people with a penicillin allergy.
- Prioritize the use of Bicillin L-A® to treat pregnant people and babies with congenital syphilis.
- Notify HHS (disease@nd.gov) of any shortage or low inventories of Bicillin L-A® in your practice so we can continue to monitor this situation and provide situational awareness to CDC, FDA and Pfizer.

CDC will update its [Drug Notices](#) webpage as updates are available.

Screening & Treatment in Pregnancy.

All pregnant individuals in North Dakota should be screened 3 times during pregnancy.

- At initiation of antenatal care and/or if stillbirth at >20 wks gestation
- At beginning of 3rd trimester, i.e. 28 weeks
- At delivery

PCN is appropriate for every stage of infection. Treat as appropriate for stage as if non-pregnant.

- If allergic to PCN - desensitize



Ongoing Follow-Up of Those Diagnosed.

- Quantitative nontreponemal titers used to follow response. Fourfold change (two dilutions) is an appropriate response within 6-12 months.
 - Factors associated with adequate serologic response: age, early state, initial titer

Stage	2015 Recommendations	2021 Recommendations
P&S, early latent	Retest at 6, 12 mo	Retest at 12 mo
Late latent/unk duration	Retest at 6, 12, 24 mo	Retest at 24 mo

- Local jurisdictions may choose to retest at 3 months (or sooner), reinfection risk is high
 - Assure continued engagement with care
 - Rescreen for all STIs, including HIV!

Partner Services for Syphilis.

- Individuals exposed to early syphilis <90 days before diagnosis
 - Presumptive treatment
- Partner Notification:
 - Primary: 3 Months + Duration of Symptoms
 - Secondary: 6 Months + Duration of Symptoms
 - Early Latent: 1 Year
- NDHHS: Registry of Syphilis Cases, Verify Treatment History in Other Jurisdictions



Case Study 1

30 year old male with a painless penile chancre tests positive for syphilis in the clinic on December 1, 2017. He reports having 3 male partners and 1 female partner in the last year. What partner (s) should be presumptively treated regardless of the test results?

John – last exposure was 7 weeks ago

Robert – unsure of exact date, but says it was in early summer

Lisa – on and off for the last 6 months, last time was last week

Steve – last exposure was August 2, 2017

John & Lisa

Persons who have had sexual contact with a person who receives a diagnosis of primary, secondary, or early latent syphilis within 90 days preceding the diagnosis should be treated presumptively for early syphilis, even if serologic test results are negative.

Case Study 2

A 46-year-old male presents to his local public health unit for STI screening as he recently heard on the news that STI rates have been increasing. He can't remember the last time he was tested but says he has never tested positive for a STI. He reports being in a monogamous relationship for the last 18 months with his boyfriend. He has no current symptoms or complaints. His syphilis results come back as TPPA positive and a RPR titer of 1:4. He states he has a penicillin allergy. How do you stage and treat?

Late Latent – Doxy 100mg BID 28 Days

Because the patient has no symptoms, no prior history of syphilis and the infection would have occurred more than 12 months ago, he would be staged as having late latent syphilis.

With a penicillin allergy, he can be treated with doxycycline
100 mg orally twice daily for 28 days

STI Educational Resources

ND Health & Human Services

- www.hhs.nd.gov/STI

University of WA STD Prevention Training Center

- www.uwptc.org

National Network of STD/HIV Prevention Training Centers

- www.nnptc.org

CDC 2021 STI Treatment Guidelines

- www.cdc.gov/std/treatment

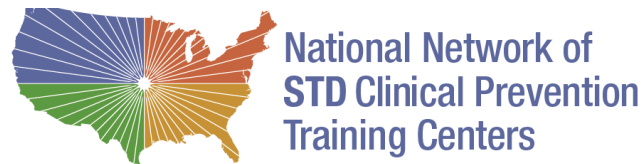
American Sexual Health Association (ASHA) booklets, books, handouts,

- www.ashastd.org

Sexually Transmitted Infections Treatment Guidelines, 2021

STD Clinical Consultation Network (STDCCCN)

- Provides STD clinical consultation services within 1-3 business days, depending on urgency, to healthcare providers nationally
- Your consultation request is linked to your regional PTC's expert faculty
- We are just a click away! www.STDCCCN.org



STD Clinical Consultation Network

Important for Requestors to Consider


The Clinical Consultation Service is intended for licensed healthcare professionals and STD program staff. We do not provide direct medical care, treatment planning, or medical treatment services to individuals.

The information provided through the Clinical Consultation Service is not a replacement for local expertise or your state STD program protocols. Information is offered as clinical decision support, is advisory in nature and is not intended to replace local healthcare decision-making or provision. Requestors are free to disregard any advice offered. Final clinical decisions are the sole responsibility of the healthcare provider.

CONTINUE

National STD Curriculum

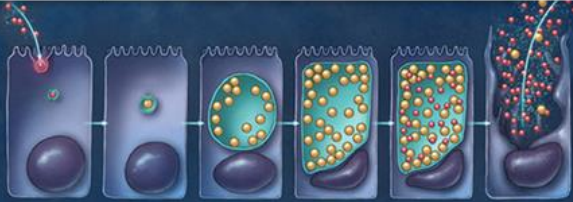
std.uw.edu

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National STD Curriculum

Funded by a grant from the
Centers for Disease Control and Prevention



STD Modules

 Chlamydia	Chlamydia Self-Study CNE/CME Tracking progress and receiving CE credit	Content View > Quick viewing of Chlamydia STD Module	Question Bank > Interactive board- review style questions
 Gonorrhea	Gonorrhea Self-Study CNE/CME Tracking progress and receiving CE credit	Content View > Quick viewing of Gonorrhea STD Module	Question Bank > Interactive board- review style questions
 HSV Herpes Simplex Virus (HSV)	HSV Self-Study CNE/CME Tracking progress and receiving CE credit	Content View > Quick viewing of HSV STD Module	Question Bank > Interactive board- review style questions
 HPV Human Papillomavirus (HPV)	HPV Self-Study CNE/CME Tracking progress and receiving CE credit	Content View > Quick viewing of HPV STD Module	
 PID Pelvic Inflammatory Disease (PID)	PID Self-Study CNE/CME Tracking progress and receiving CE credit	Content View > Quick viewing of PID STD Module	
 Syphilis	Syphilis Self-Study CNE/CME Tracking progress and receiving CE credit	Content View > Quick viewing of Syphilis STD Module	
 Vaginitis	Vaginitis Self-Study CNE/CME Tracking progress and receiving CE credit	Content View > Quick viewing of Vaginitis STD Module	

Sexually Transmitted and Bloodborne Diseases Unit.

Sarah Weninger

- HIV.STD.Hepatitis Prevention Coordinator
- 701.328.2366
- sweninger@nd.gov

CEU

www.hhs.nd.gov/HIV/Education



The United States will be a place where sexually transmitted infections are prevented and where every person has high-quality STI prevention, care, and treatment while living free from stigma and discrimination.

This vision includes all people, regardless of age, sex, gender identity, sexual orientation, race, ethnicity, religion, disability, geographic location, or socioeconomic circumstance.

National STI Strategic Plan, 2021 - 2025