Syphilis in Manitoba

Office of the Chief Provincial Public Health Officer

Presented on the original lands of Anishinaabe, Cree, Oji-Cree, Dakota, and Dene peoples, and the homeland of the Métis Nation.

Manitoba

Conflicts of Interest

There are no conflicts of interest to declare.

Manitoba

Objectives

- Increase understanding of the epidemiology of syphilis in Manitoba
- Review diagnosis, treatment and follow-up of syphilis infections
- Improve prenatal screening rates
- Support public health reporting using simplified provider report form

Manitoba

Outline

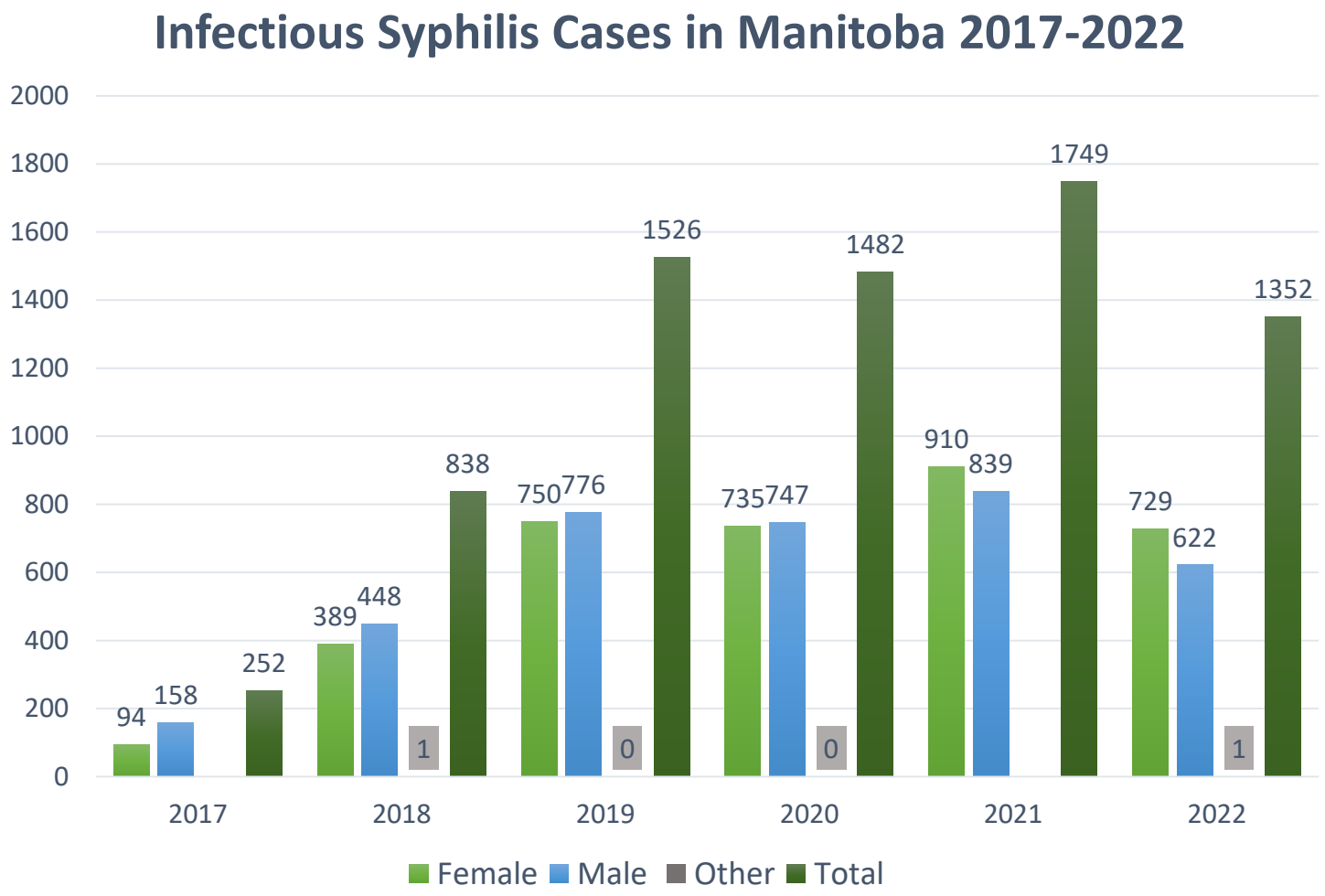
1. Epidemiology of syphilis in Manitoba
2. Screening
   - Who and when to test
3. Testing and serologic interpretation/diagnosis
4. Clinical overview
   - Staging and presentation
5. Congenital syphilis
   - Risk factors and testing
6. Treatment and follow-up
7. Reporting to public health

Manitoba

Epidemiology of syphilis in Manitoba

Manitoba

Epidemiology of Syphilis in Manitoba

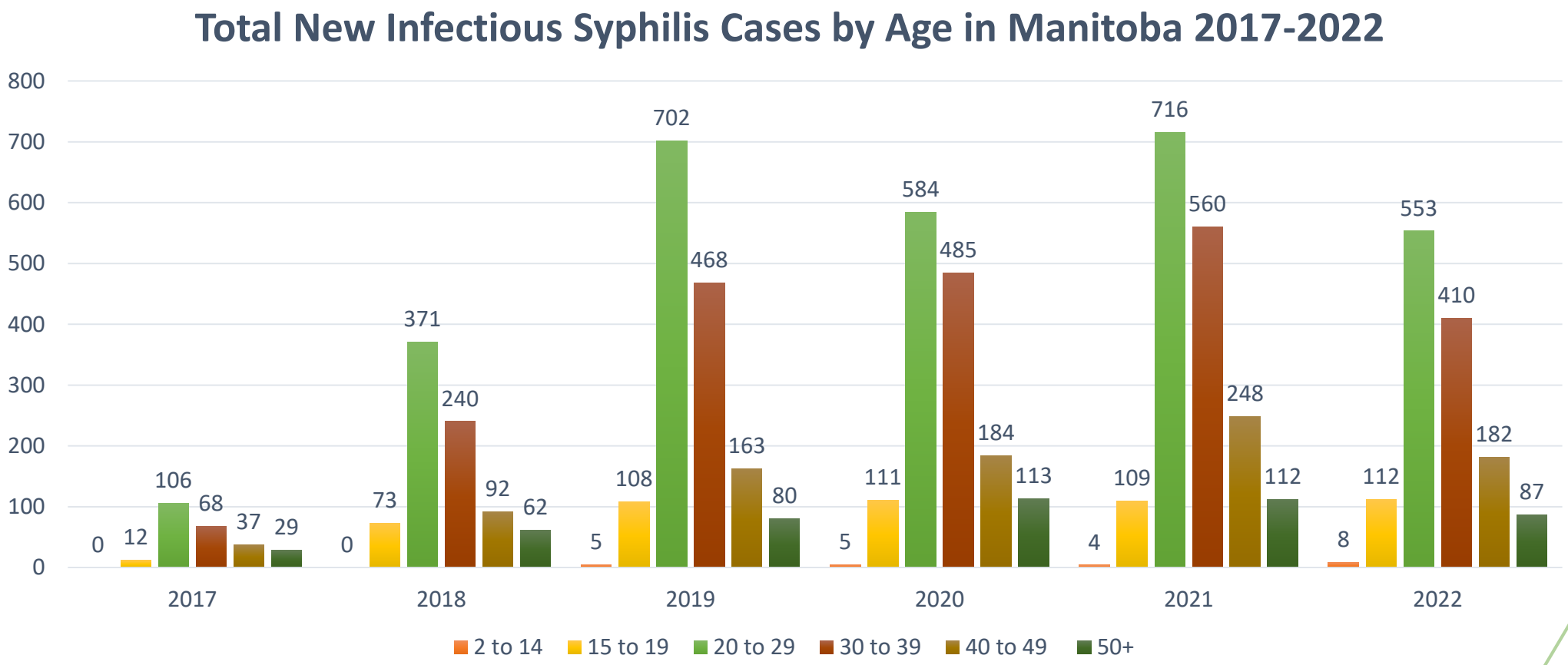


Manitoba had the **highest rate** of infectious syphilis diagnoses of all Canadian provinces, in 2019 (136.7 per 100,000).

Screening for infectious syphilis decreased in 2020 due to the COVID-19 pandemic but has returned to pre-pandemic levels.

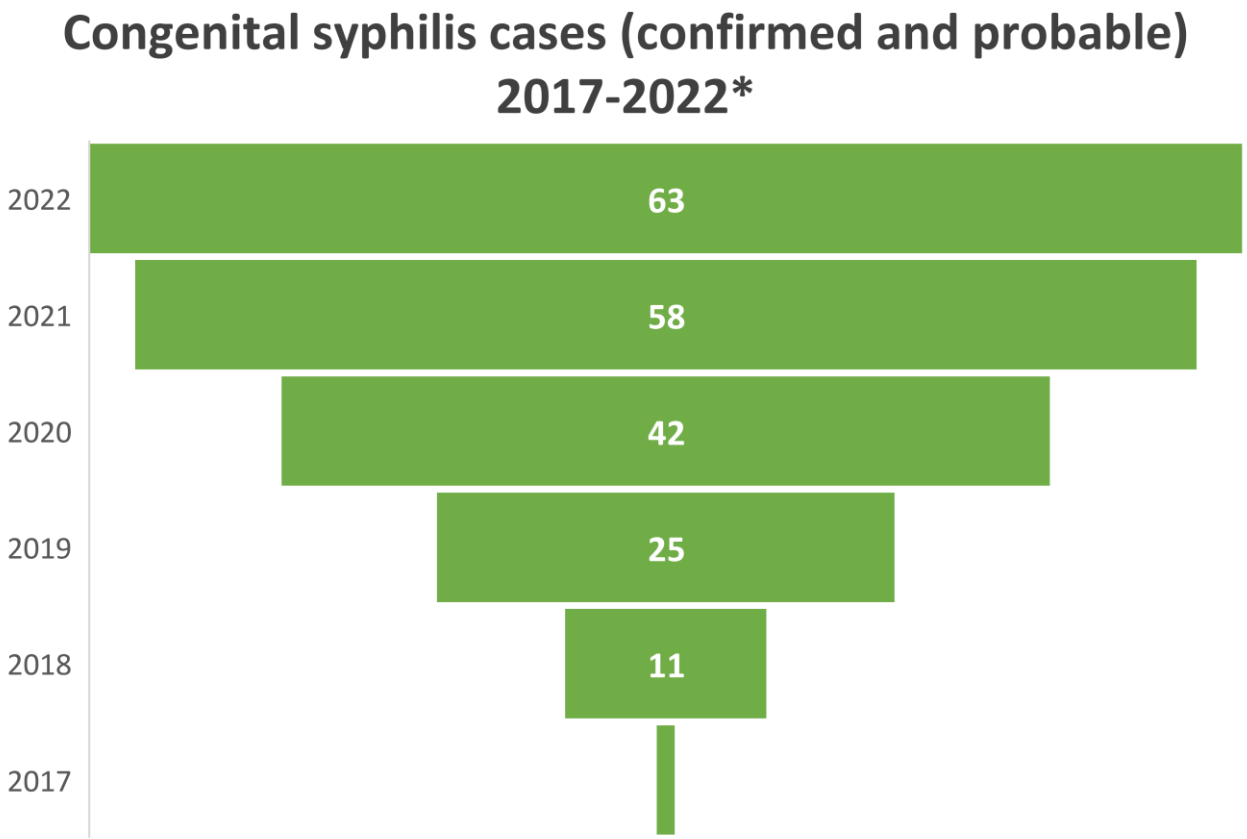
Manitoba

Epidemiology of Syphilis in Manitoba



Manitoba

Epidemiology: Congenital Syphilis



*2022 data is preliminary

2015: first case of congenital syphilis in 30+ years.
2017: Second case and start of significant rise.
2018-2019: case #'s double
2020: 86% of national cases occurred in AB, SK and MB
2019-2021: case #'s double again

High numbers of infectious syphilis cases continue to result in **perinatal transmission.**

Manitoba

Syphilis Screening

- Who and when to test

Manitoba

Screening: Who and when to test for syphilis

- All people who present with consistent symptoms
- All sexual contacts to syphilis cases
- All pregnant people **THREE** times during pregnancy
- All people with new, multiple, or anonymous sexual partners (**every 3 to 6 months**)
- All people requesting STI testing
- All people with any confirmed or suspected STI
- Infants born to mothers/birthing parents with reactive syphilis serology
- Stillborn infant ≥20 weeks gestation

Offer STBBI testing to all clients/patients as part of routine care

Manitoba

Screening: Which sexual contacts to test?

Contact Investigation: Trace back period	
Primary syphilis	3 months
Secondary syphilis	6 months
Early latent syphilis	1 year
Late latent/tertiary syphilis	Assess long term sex partner(s)/contacts and children (as appropriate). The estimated duration of infection of the case will determine who to test.
Congenital syphilis	Assess birthing parent and their sexual partner(s)/contacts.

*Trace-back period refers to the time period prior to case's symptom onset or date of specimen collection (if asymptomatic)

Manitoba

Screening: When to test during pregnancy?

Year of birth	% not tested for syphilis	% with 3 or more syphilis tests
2020	3%	17%
2021	1%	45%
2022 (up to June 30)	1%	62%

Screen ALL pregnant people for syphilis three times during pregnancy.

1. **First trimester**
2. **28-32 weeks**
3. **At delivery**

More frequent screening indicated if there are ongoing risk(s)

ALL pregnant people should be tested monthly and at delivery if:

- newly diagnosed with syphilis infection or reinfection
- previous syphilis infection, but received/receiving treatment during current pregnancy

Manitoba

Syphilis Testing

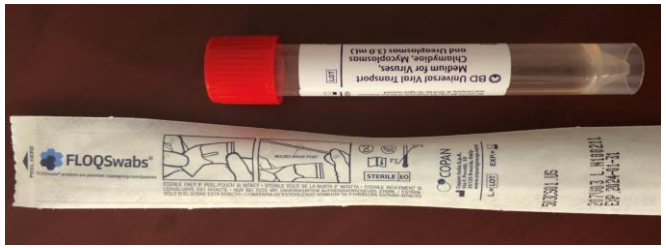
Serologic interpretation and diagnosis

Manitoba

Syphilis Testing: Swabs - Adjunct to serology

Cadham Provincial Lab (CPL): Nucleic Acid Amplification Test (NAAT)

Dacron swab in viral transport media (VTM)



Sites to sample:

- Mucocutaneous lesions - chancres, mucous patches, moistened condyloma latum
- Newborn nasal secretions
- Stillbirth nasopharynx or placenta

SPECIMEN INFORMATION			OTHER TESTS OR REQUESTS
Specimen Type:	Swab	Specimen Source: Nasopharyngeal	Syphilis PCR

Indicate the site and test requested (T. pallidum or syphilis PCR testing)

Manitoba

Syphilis Testing: Cerebral Spinal Fluid (CSF)
For suspected neurosyphilis

Cadham Provincial Lab (CPL): VDRL, FTA-ABS and syphilis PCR

Non-treponemal test: VDRL
- If reactive, i.e. 1 dilution or higher, then it is confirmatory for neurosyphilis

Treponemal test: fluorescent treponemal antibody absorption (FTA-ABS)
- Often reactive, but it is more sensitive and less specific than VDRL
- Automatically run after VDRL

Syphilis NAAT (PCR): can be requested in addition to the above
- If not detected, does not rule out the diagnosis

SPECIMEN INFORMATION			
Specimen Type:	CSF	Specimen Source:	Spine

OTHER TESTS OR REQUESTS
VDRL

OTHER TESTS OR REQUESTS
VDRL and Syphilis PCR

Manitoba

Syphilis Testing: Serology – Serum Sample

CPL performs the reverse sequence screening algorithm

1st treponemal screening test

Chemiluminescent microparticle immunoassay (CMIA)

- Qualitative result
- Once positive, usually stays positive

Non-treponemal (NTT) test

RPR

- Quantitative result (e.g. 1 dil)
- Rises with infection, decreases with treatment and over time → useful to monitor
- Change in **2 or more dilutions** (at least four fold) is significant, for example:
  - 1:1 → 1:2 dilution ✗
  - 1:1 → 1:4 dilution ✓

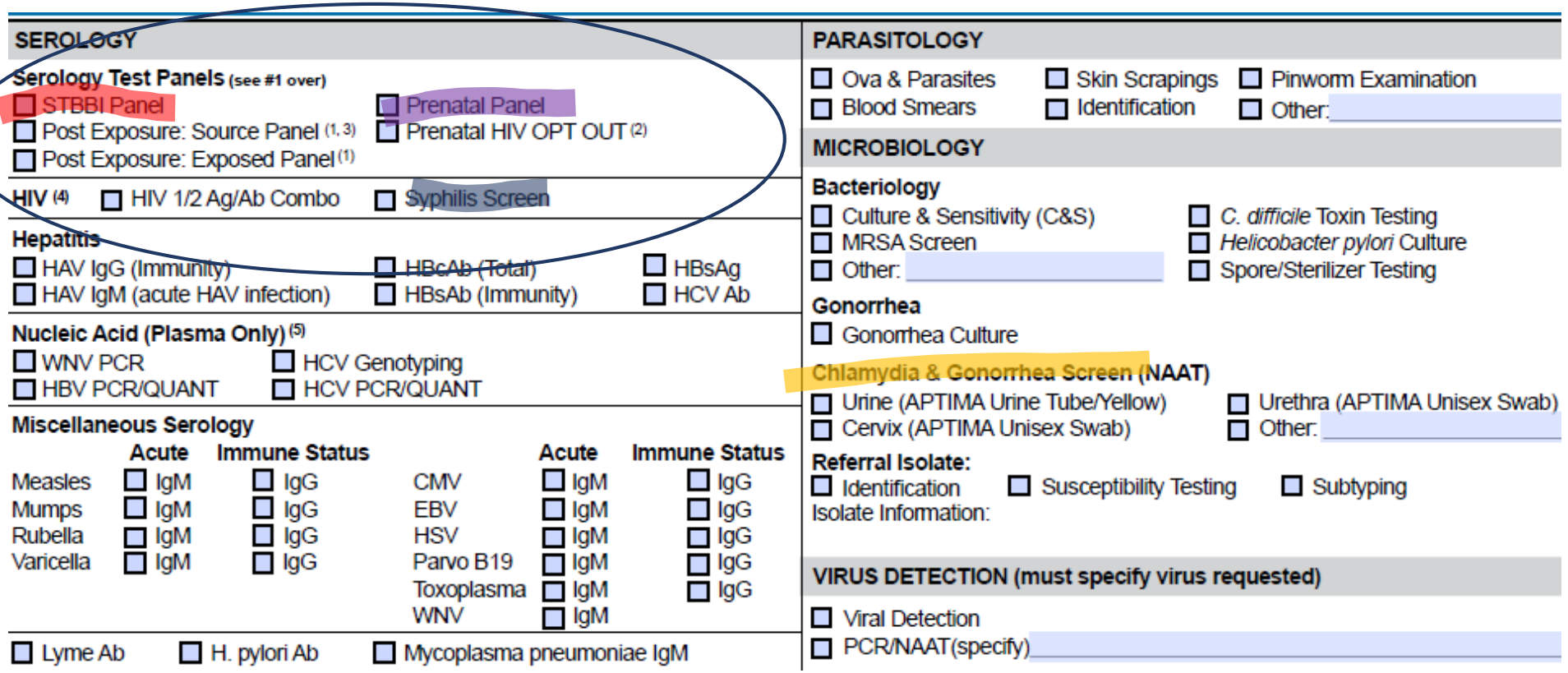
2nd confirmatory treponemal test

T. pallidum particle agglutination tests (TPPA)

- Qualitative result
- Completed on individuals for first positive test result in MB
- Helps to confirm syphilis

Manitoba

Syphilis Testing: Completing the lab requisition



SEROLOGY

Serology Test Panels (see #1 over)
- ☐ STBBI Panel
- ☐ Prenatal Panel
- ☐ Post Exposure: Source Panel (1, 3)
- ☐ Prenatal HIV OPT OUT (2)
- ☐ Post Exposure: Exposed Panel (1)

HIV (4) ☐ HIV 1/2 Ag/Ab Combo ☐ Syphilis Screen

Hepatitis
- ☐ HAV IgG (Immunity)
- ☐ HAV IgM (acute HAV infection)
- ☐ HBcAb (Total)
- ☐ HBsAb (Immunity)
- ☐ HBsAg
- ☐ HCV Ab

Nucleic Acid (Plasma Only) (5)
- ☐ WNV PCR
- ☐ HBV PCR/QUANT
- ☐ HCV Genotyping
- ☐ HCV PCR/QUANT

Miscellaneous Serology

	Acute	Immune Status		Acute	Immune Status
Measles	☐ IgM	☐ IgG	CMV	☐ IgM	☐ IgG
Mumps	☐ IgM	☐ IgG	EBV	☐ IgM	☐ IgG
Rubella	☐ IgM	☐ IgG	HSV	☐ IgM	☐ IgG
Varicella	☐ IgM	☐ IgG	Parvo B19	☐ IgM	☐ IgG
			Toxoplasma	☐ IgM	☐ IgG
			WNV	☐ IgM	

☐ Lyme Ab ☐ H. pylori Ab ☐ Mycoplasma pneumoniae IgM

PARASITOLOGY
- ☐ Ova & Parasites
- ☐ Blood Smears
- ☐ Skin Scrapings
- ☐ Identification
- ☐ Pinworm Examination
- ☐ Other:

MICROBIOLOGY

Bacteriology
- ☐ Culture & Sensitivity (C&S)
- ☐ MRSA Screen
- ☐ Other:
- ☐ *C. difficile* Toxin Testing
- ☐ *Helicobacter pylori* Culture
- ☐ Spore/Sterilizer Testing

Gonorrhea
- ☐ Gonorrhea Culture

Chlamydia & Gonorrhea Screen (NAAT)
- ☐ Urine (APTIMA Urine Tube/Yellow)
- ☐ Cervix (APTIMA Unisex Swab)
- ☐ Urethra (APTIMA Unisex Swab)
- ☐ Other:

Referral Isolate:
☐ Identification ☐ Susceptibility Testing ☐ Subtyping
Isolate Information:

VIRUS DETECTION (must specify virus requested)
- ☐ Viral Detection
- ☐ PCR/NAAT(specify)

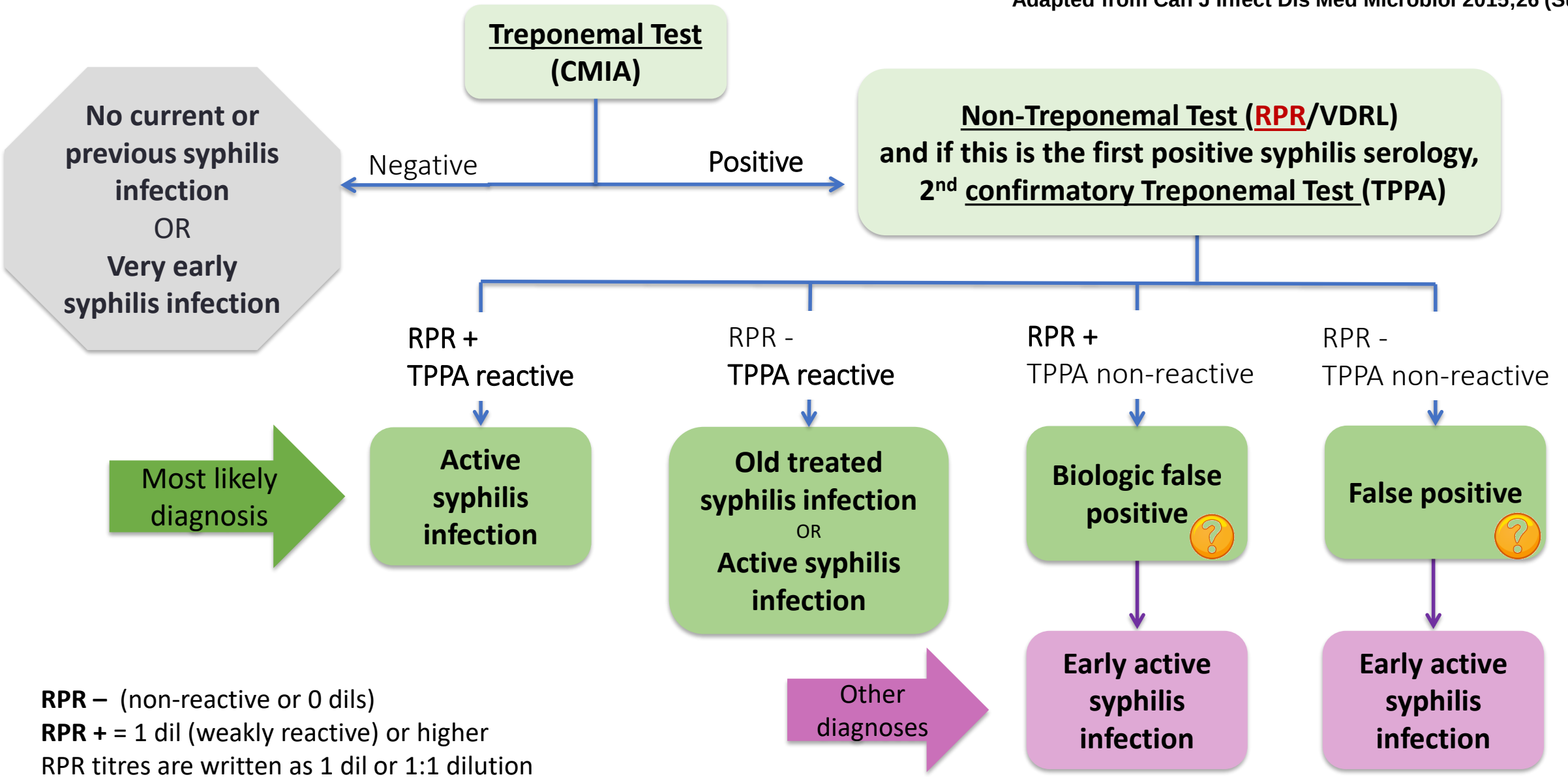
STBBI Panel includes: HBsAg, HCV Ab, Syphilis and HIV 1/2 Ag/Ab Combo

Prenatal Panel includes: HBsAg, Rubella IgG, Syphilis, HIV 1/2 Ag/Ab Combo

Manitoba

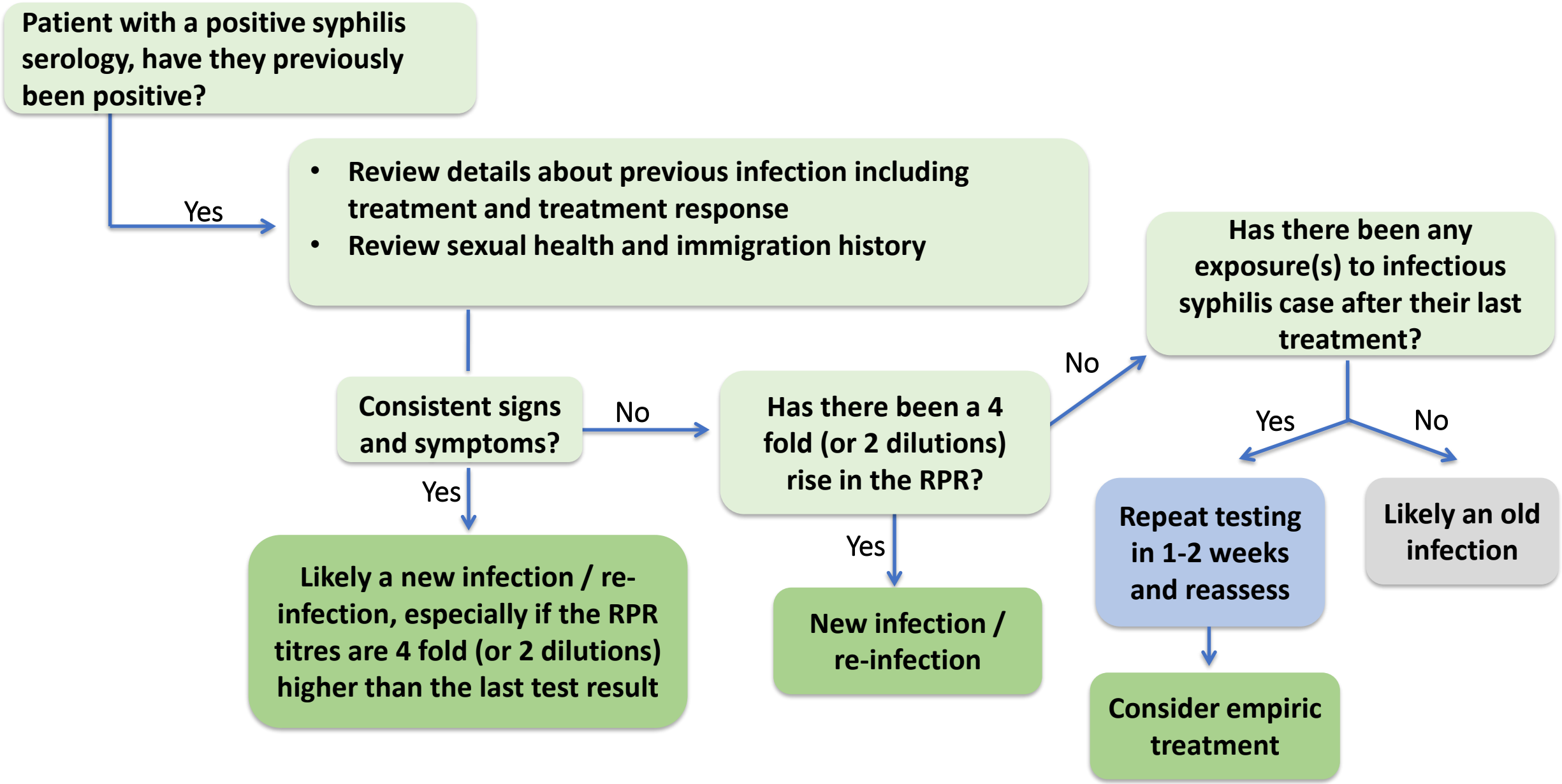
Syphilis Testing: Interpretation of results

Adapted from Can J Infect Dis Med Microbiol 2015;26 (Supp A)



RPR – (non-reactive or 0 dils)
RPR + = 1 dil (weakly reactive) or higher
RPR titres are written as 1 dil or 1:1 dilution

Syphilis Testing: Reinfection?



Syphilis Serology: Interpretation of Results

Example # 1	
Test Name	**Result**
Final syphilis interpretation	Cannot exclude recent infection if specimen collected within 2-3 weeks after appearance of suspected lesions.
Treponema pallidum antibody (CMIA)	Negative

Likely NO syphilis infection

If uncertainty, or high clinical suspicion, repeat test in 2-3 weeks.

Consider empiric treatment if high risk exposure.

Manitoba

Syphilis Serology: Interpretation of Results

Example # 2	
Test name	**Result**
Final syphilis interpretation	Indeterminate syphilis results. This results suggests very recent infection or a non-specific reaction. Repeat testing should be considered after 7 to 10 days if clinically indicated.
Treponema pallidum antibody (CMIA)	**Positive**
Reagin antibody (RPR)	Non-reactive
Treponema pallidum antibody (Aggl)	Non-reactive

Either NO syphilis infection or early syphilis infection

If uncertainty, or high clinical suspicion, repeat test in 1-2 weeks

Manitoba

Syphilis Serology: Interpretation of Results

Example # 3	
Test name	**Result**
Final syphilis interpretation	The results suggest either recent or previous Treponemal infection
Treponema pallidum antibody (CMIA)	**Positive**
Reagin antibody (RPR)	**Reactive** 1:128 dilution, 128 dils
Treponema pallidum antibody (Aggl)	**Reactive**

Active syphilis infection

This is the patient's first positive syphilis serology in MB so the 2nd confirmatory treponemal test (TPPA) was done.

Whether this is a new infection / re-infection, or previous infection with or without treatment depends on the patient's history.

Manitoba

Syphilis Serology: Interpretation of Results

Example # 4	Patient A	Patient B
Final syphilis interpretation	The results suggests either recent or previous Treponemal infection. This syphilis CMIA positive patient has a known history or reactive confirmatory syphilis serology. Clinical correlation is required.	The results suggests either recent or previous Treponemal infection.
Treponema pallidum antibody (CMIA)	**Positive**	**Positive**
Reagin Antibody (RPR)	Reactive 1:4 dilution, 4 dils	Non-reactive
Treponema pallidum antibody (Aggl)	⊖	Reactive

Syphilis infection

Patient A has previously had positive syphilis serology in MB, so CPL did not perform the 2nd treponemal test (i.e. no TPPA result).

- Whether this is an old infection (post treatment) or a re-infection depends on the patient's history.

Manitoba

Syphilis Serology: Interpretation of Results

Example # 5			
Date collected:	**January 2021**	**May 2021**	**December 2021**
Treponema pallidum antibody (CMIA)	Positive	Positive	Positive
Reagin antibody (RPR)	Reactive **1:64 dilution, 64 dils**	Reactive **1:8, 8 dils**	Reactive **1:128, 128 dils**
Treponema pallidum antibody (Aggl)	Reactive		

Appropriate treatment given in February 2021

Syphilis infection adequately treated, with re-infection

- greater than 4 fold rise (greater than 2 dilution rise)!

Manitoba

Syphilis Serology: Interpretation of Results

Example # 6			
Date collected:	**January 7, 2021**	**January 22, 2021**	**Case notes**
CMIA	Positive	Positive	*Staged as late latent syphilis *First 2 of 3 doses IM benzathine penicillin G doses given January 12 and 19th. *January 22nd test was done because the patient requested as they were curious, no change clinically.
RPR	**Reactive 1:32, 32 dils**	**Reactive 1:64, 64 dils**	
Aggl	Reactive		

Syphilis infection with patient in the process of completing treatment course. No evidence of re-infection at this time based on serology alone.

- 1:32 → 1:64 is an "increase" of 2 fold (1 dilution rise), not significant from a lab perspective.
- Finish the planned treatment course and planned serology follow-up. If concerned, do repeat serology sooner – in 1 month after last treatment dose.

Manitoba

Clinical Overview

Staging and presentation

Manitoba

Clinical Overview: Staging

Congenital syphilis:

- Early (diagnosed ≤ 2 years after birth)
- Late (diagnosed > 2 years after birth)

Infectious syphilis:

- Primary
- Secondary
- Early Latent

Non-infectious syphilis (sexual transmission unlikely):

- Late Latent
- Tertiary

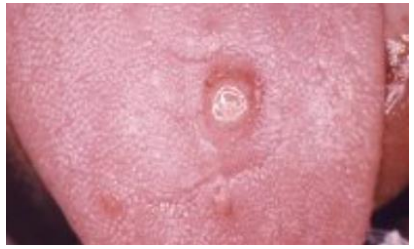
Accurate staging is essential to determine appropriate treatment, follow up, contact management and for surveillance purposes.

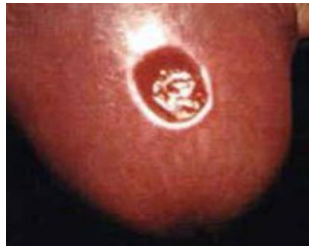
Manitoba

Clinical Presentation: Primary & secondary syphilis

Primary Syphilis

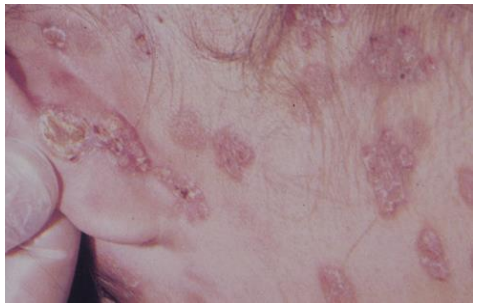
- Chancre at the site of infection (genitals, cervix, mouth, perianal area)
  - Painless papule → ulcerated lesion
- Regional lymphadenopathy

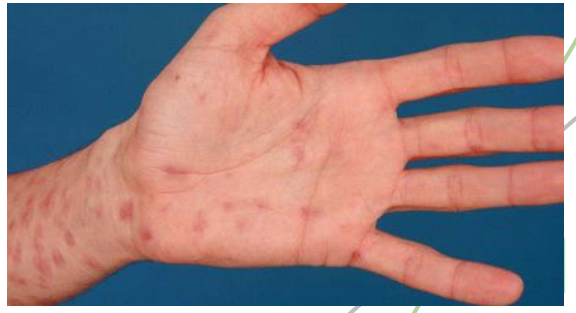


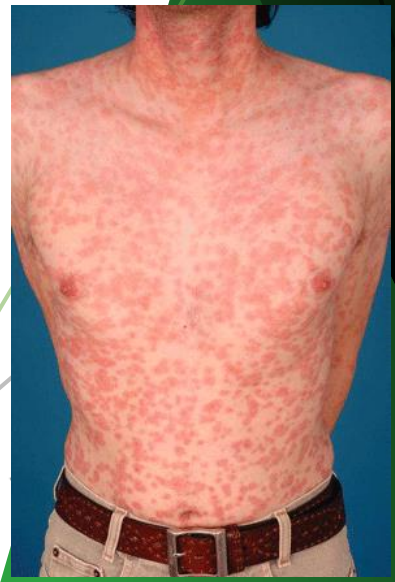


Secondary Syphilis

- Dissemination of spirochetes causes systemic symptoms
- Most commonly: skin (any kind of rash, palms/soles, condyloma lata), constitutional symptoms, musculoskeletal
- Less frequent: central nervous system, osteitis, etc.







Photos from CDC and CMAJ

Clinical Presentation: Latent Syphilis

Subclinical/asymptomatic period with serological evidence of infection

Early Latent: Asymptomatic and acquired in the last year

- 25% relapse to secondary syphilis
- Risk of sexual transmission

Late latent: Asymptomatic and acquired more than a year ago

- Relapse rare
- Sexual transmission unlikely
- Can be transmitted transplacentally or by direct blood transfer

When staging is uncertain in an asymptomatic person who, in the past year had an exposure to a sexual partner(s) with unknown syphilis status:

- **stage as early latent (reporting and contact tracing purposes)**
- **but treat as late latent (3 weekly doses of IM benzathine penicillin G)**

Manitoba

Clinical Presentation: Tertiary Syphilis

Slow, progressive, inflammatory disease, considered less infectious.

Clinical presentations divided into:

- **Late neurosyphilis**
  - general paresis, *tabes dorsalis*
  - ataxia, vertigo, dementia, headaches, personality changes, Argyll Robertson pupil, otic/ocular symptoms
- **Cardiovascular syphilis**
  - aortic aneurysms/regurgitation, coronary artery ostial stenosis
- **Gummatous syphilis**
  - any organ, but commonly skin or bone

Manitoba

Clinical Presentation: Neurosyphilis

Early neurosyphilis (within 12 months of infection):

- Meninges and vessels: Stroke, seizures, aphasia, meningitis
- Parenchyma: Personality, intellect, reflexes, speech, pupils, hallucinations, optic nerve damage
- Spinal cord: Tabes dorsalis, incontinence, ataxia
- Auditory abnormalities

Late neurosyphilis (more than 12 months after infection:

- General paresis
- Tabes dorsalis

- Neurosyphilis refers to a site of infection not a stage of infection
- Can occur during ANY stage of infection
- Asymptomatic OR symptomatic
- Diagnostic challenge – requires positive VDRL or syphilis PCR in CSF
- Only clue may be a persistent elevation of titres after appropriate treatment

Manitoba

Clinical Overview: When to assess for neurosyphilis?

Indications for CSF examination (via lumbar puncture) include:

- Previously treated patients who do not achieve adequate serologic response to treatment
- Patients with suspected/confirmed syphilis (any stage) **AND**
  - Presenting with neurologic, ophthalmic or otic involvement **OR**
  - Living with HIV with RPR ≥ 1:32 dilutions ***and*** CD4 ≤ 350 cells/µL
- Patients with confirmed/suspected tertiary syphilis
- Patients with confirmed/suspected congenital syphilis

Manitoba

Congenital Syphilis

Risk factors and testing

Manitoba

Clinical Overview: Congenital syphilis

If untreated, pregnant people can transmit syphilis to the fetus at all stages of pregnancy or during passage through the birth canal.

Rate of perinatal transmission in an untreated birth parent:

Primary	• 70 to 100%
Secondary	• 70 to 100%
Early latent	• 40%
Late latent	• Less than 10%

Manitoba

Clinical Overview: Risk factors for congenital syphilis

Lower Risk	High Risk
Diagnosed and treated in pregnancy with adequate drop in RPR titres	No prenatal care
Completed treatment at least 4 weeks before delivery	Re-infection with syphilis during pregnancy
Received penicillin treatment based on disease staging	Infection with other STBBI during pregnancy
Reassuring clinical exam of infant	Chancre or “HSV lesions” at delivery
Reassuring paired infant/maternal syphilis serology	

Risk Factors:

- Lack of prenatal care
- First prenatal visit late in pregnancy
- Lack of maternal screening
- Lack of treatment
- Injection drug use

Manitoba

Congenital Syphilis: Which infants should have syphilis serology requested?

Send paired maternal/birthing parent-infant syphilis serology for ALL infants born to mothers/birthing parents with reactive syphilis serology.

- Regardless if the infection was prior to or during the current pregnancy

- Do this in the immediate post-partum period
- Infant and birthing parent specimens should be drawn closely together (within a week)

Manitoba

Congenital Syphilis: Which infants should you be worried about or need follow-up testing?

Refer to pediatric ID if birthing parent was diagnosed or received treatment during the pregnancy.

- No need to refer if diagnosed & treated prior to pregnancy AND no concerns of reinfection during the pregnancy
- BUT if uncertain, can page on-call Peds ID to discuss

Manitoba

Treatment and Follow-Up

Manitoba

Treatment Principles: Non-pregnant adults

First Line Therapy

Penicillin G benzathine is the preferred drug for treatment of all stages of syphilis (not involving CNS).

2.4 M units IM = 2 injections of 1.2 M units each hip

Second Line Therapy

Ceftriaxone 1g IV or IM daily for 10 days

Third Line:

Doxycycline 100 mg PO BID for 14 days*

Primary, secondary and early latent treatment:

Benzathine penicillin G 2.4 M units weekly X1

Late latent treatment:

Benzathine penicillin G 2.4 M units weekly X3

Neurosyphilis:

usually IV antibiotics (consult ID)

Manitoba

Treatment Principles: Congenital syphilis prevention

Treatment in pregnancy:

Benzathine penicillin G 2.4 M units weekly **X2**

- except late latent = weekly X3
- neurosyphilis usually IV antibiotics

Penicillin allergy and treatment in pregnancy:

- do not use ceftriaxone and doxycycline
- allergy desensitization is the only treatment option

Treat all sexual partner(s) to prevent re-infection!

STI medications are provided free of charge by Manitoba Health

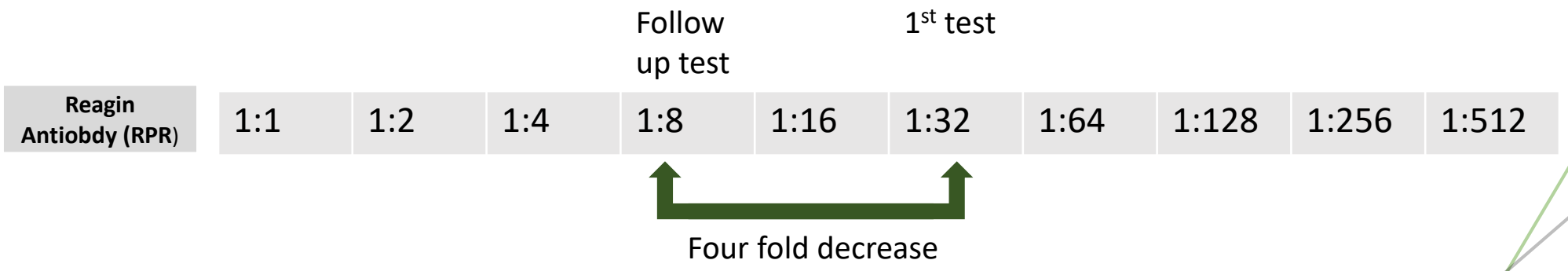
Call Materials Distribution Agency at 204-945-0570 or download form:
www.gov.mb.ca/health/publichealth/cdc/protocol/form11.pdf

Manitoba

Treatment Principles: Post-treatment follow up serology (excluding congenital syphilis)

<u>Following adequate treatment of syphilis:</u>

- NTT (RPR) usually become nonreactive (some remain serofast)
- **Adequate treatment** = fourfold or greater decline in titres after 1 year for infectious syphilis (primary, secondary and early latent)
- Primary syphilis: Titres should be nonreactive or weakly reactive (1 dil) within one year
- Secondary syphilis: Titres should be nonreactive or weakly reactive (1 dil) within two years
- Late latent syphilis: Titres are not as useful for monitoring treatment adequacy and take much longer to drop



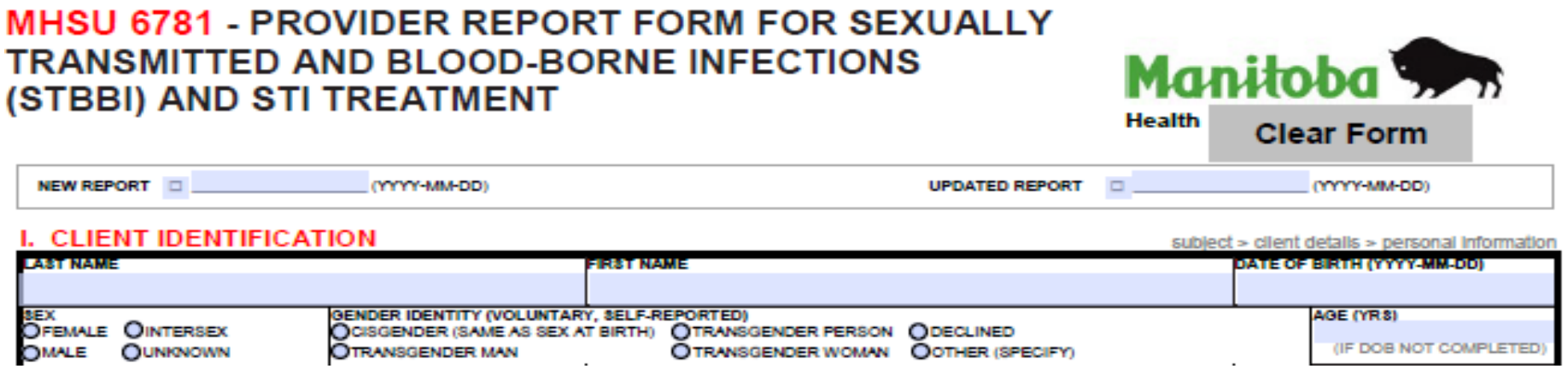
Manitoba

Reporting to Public Health

Manitoba

Reporting to Public Health: Provider Report Form for STBBI's and STI Treatment

- ✓ **STBBI's reportable to Manitoba Health per section B of the Public Health Act.**
- ✓ Simplified process for reporting treatment and contacts to Public Health with new *Provider Report Form for STBBI's and STI Treatment*



MHSU 6781 - PROVIDER REPORT FORM FOR SEXUALLY TRANSMITTED AND BLOOD-BORNE INFECTIONS (STBBI) AND STI TREATMENT

Manitoba Health

Clear Form

NEW REPORT ☐ _____ (YYYY-MM-DD) UPDATED REPORT ☐ _____ (YYYY-MM-DD)

I. CLIENT IDENTIFICATION

subject > client details > personal information

LAST NAME	FIRST NAME	DATE OF BIRTH (YYYY-MM-DD)

SEX: ○ FEMALE ○ INTERSEX ○ MALE ○ UNKNOWN

GENDER IDENTITY (VOLUNTARY, SELF-REPORTED): ○ CISGENDER (SAME AS SEX AT BIRTH) ○ TRANSGENDER PERSON ○ DECLINED ○ TRANSGENDER MAN ○ TRANSGENDER WOMAN ○ OTHER (SPECIFY)

AGE (YRS) (IF DOB NOT COMPLETED)

https://www.gov.mb.ca/health/publichealth/surveillance/docs/mhsu_6781.pdf

Manitoba

Treatment Details in eChart Manitoba

STI treatment information soon to be available in **eChart Manitoba**

Data source: PHIMS (Public Health Information Management System) via Provider Report Form and Medication Summary

Manitoba

Summary

- Syphilis case rates remain high and women represent an increased proportion of cases.
- Offer syphilis and other STBBI testing as part of routine care.
- Follow-up syphilis serology is important to monitor treatment adequacy.
- In situations of uncertainty (? early infection, ? re-infection):
  - close follow-up with repeat syphilis serology in 1 to 3 weeks
  - consider emipiric treatment
- Accurate staging is essential to determine treatment, follow up and management of contacts.
- Congenital syphilis is preventable through routine testing and appropriate treatment of the birthing parent and treatment of all sexual partner(s).
- Syphilis cases, treatment and contacts are reportable to public health, using the new *Provider Report Form for STBBI Infections and STI Treatment*.

Manitoba

For assistance with testing and interpretation of test results:

- Cadham physician on call (204-787-2071)

For assistance with diagnosis and management of complex cases:

- ID (204-787-2071)

For discussion or consultation re: congenital syphilis:

- Peds ID (204-787-2071)

Manitoba

Questions?

Health care provider questions/inquiries can be directed to: STBBI@gov.mb.ca

For vaccine specific questions/inquiries:

vaccines@gov.mb.ca

Public questions/inquiries can be directed to:

mgi@gov.mb.ca or by going to www.gov.mb.ca/contact/ for more information.

Manitoba