SYPHILIS CLINICAL MANAGEMENT

2015

DEPARTMENT OF HEALTH & COMMUNITY SERVICES
DISEASE CONTROL DIVISION

ACKNOWLEDGEMENTS

The Department of Health and Community Services would like to acknowledge the work previously done by Eastern Health in developing this document.

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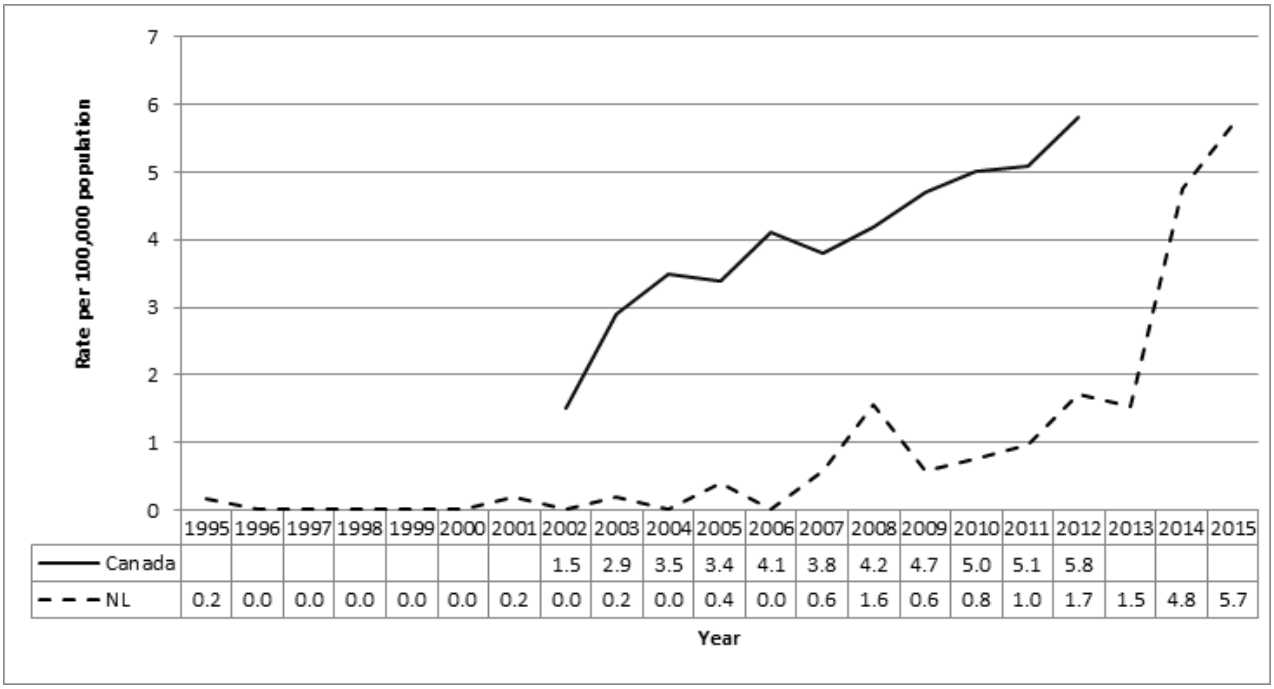
ETIOLOGY

Syphilis is a sexually transmitted infection (STI) caused by the spirochete (bacterium) *Treponema pallidum* (*T. pallidum*).

EPIDEMIOLOGY

Newfoundland and Labrador has been experiencing an outbreak of infectious syphilis since October 2014 (Figure 1). Cases have been mostly located in St. John's with sporadic cases in rural areas. The majority of cases have occurred among men who have sex with men (MSM). Contacts of cases may be in any part of the province, other provinces or territories, and other countries.



	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Canada								1.5	2.9	3.5	3.4	4.1	3.8	4.2	4.7	5.0	5.1	5.8			
NL	0.2	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.2	0.0	0.4	0.0	0.6	1.6	0.6	0.8	1.0	1.7	1.5	4.8	5.7

Figure 1: Infectious syphilis rates in Canada and in Newfoundland and Labrador, 1995-2015.
Note: 2015 includes cases reported up to July 9, 2015.

TRANSMISSION

- Syphilis is transmitted by direct contact with the lesions of an infected person
- If lesions are internal or unnoticed, transmission can occur without either partner being aware of the disease
- The primary mode of transmission is by anal, oral and vaginal sexual contact
- A pregnant woman can transmit syphilis infection to her unborn child, which can result in miscarriage, stillbirth or congenital syphilis infection
- Transmission can also occur through blood transfusion in the early stages of disease

WHO SHOULD BE SCREENED?

1. **Anyone with risk behaviours/potential exposures to infectious syphilis**
   - Contacts of known syphilis cases;
   - Men who have sex with men (MSM);
   - Street involved/homeless persons;
   - Injection drug users;
   - Those with multiple sexual partners;
   - Those with history of STIs;
   - Those originating from or having sex with an individual from a high prevalence country or a province where there is an outbreak;
   - Sexual partners of any of the above; and
   - All pregnant women ideally in their first trimester and those at high-risk should have screening repeated at 28-32 weeks and at delivery.

2. **Anyone with *clinical signs* suspicious for infectious syphilis**
   - Current or past history of characteristic lesions or rash (see Clinical Manifestations).

CLINICAL MANIFESTATIONS

Primary syphilis (infectious)

- Occurs 3 to 90 days after contact
- Chancre/lesion on genitals, anus or in the mouth (site of inoculation)
- Regional lymphadenopathy
- A high proportion of individuals fail to recall a primary chancre

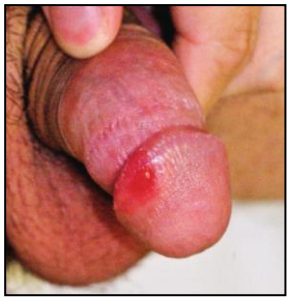
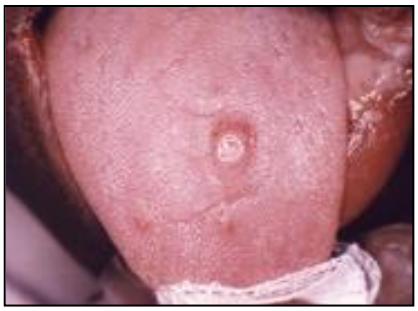
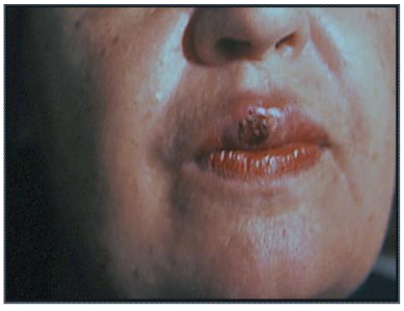


Photo Credit:
Dr. Richard Garceau



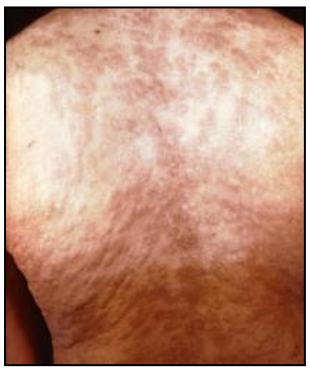
US Centers for Disease Control (CDC)



US Centers for Disease Control (CDC)

Secondary syphilis (infectious)

- Occurs 2 weeks to 6 months after contact
- Rash (often on palms of hands, soles of feet, and trunk/back area), fever, malaise, lymphadenopathy, mucosal lesions, condyloma lata, patchy or diffuse alopecia, meningitis, headaches, uveitis, retinitis



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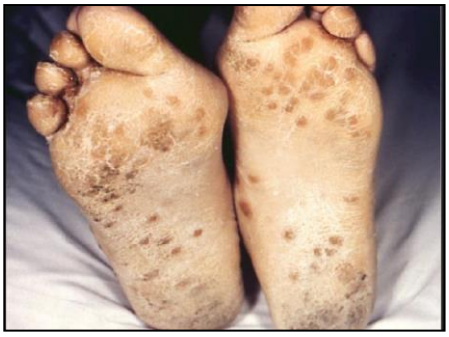

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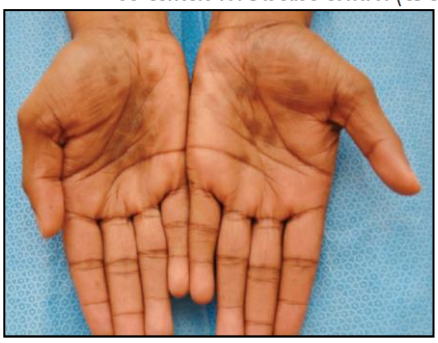

Photo Credit: Dr. Gabriel Girouard

Latent syphilis

- Early latent: < one year duration (infectious)
- Late latent: ≥ one year duration (non-infectious)
- Cases are asymptomatic
- Only evidence of infection is a positive serology test

Tertiary (late) syphilis

- Approximately 30% of untreated patients progress to this stage within 2-20 years of infection.
- Manifestations include cardiovascular syphilis and gumma.

Congenital syphilis

- Early onset: < two years of age (infectious)
    - 2/3 of patients may be asymptomatic
    - Infected infants may be seronegative if maternal infection occurred late in gestation
    - Symptoms include fulminant disseminated infection, mucocutaneous lesions, osteochondritis, anemia, hepatosplenomegaly, and neurosyphilis
- Late onset: > two years of age
    - Symptoms include hepatosplenomegaly, anemia, and neurosyphilis

Neurosyphilis

- Occurs at any stage of disease and is infectious if untreated
- <2 to 20 years after contact
- Ranges from asymptomatic to symptomatic with headaches, vertigo, loss of hearing, personality changes, dementia, ataxia, presence of Argyll Robertson pupil

Co-infection with Human Immunodeficiency Virus (HIV)

- Signs and symptoms may be modified in the presence of HIV
- Disease may progress faster when co-infected with HIV

DIAGNOSIS OF SYPHILIS INFECTION

A diagnosis of syphilis should be considered for people with compatible signs, symptoms and risk factors. Interpretation of clinical history, physical examination and laboratory finding should be made in consultation with the Medical Officer of Health (MOH) or other experienced health care providers.

Clinical history

- Typical signs/symptoms in the past 12 months
- Known contact of a confirmed case
- History of previous syphilis infection

Physical examination

- Lymph nodes
- Skin of torso
- Palms and soles
- Genital, perineal and oropharyngeal areas
- Abdomen
- Neurological exam

Laboratory diagnosis

Serological testing is performed to identify *Treponema pallidum* (*T. pallidum).* The serological diagnosis of syphilis is divided into treponemal tests (qualitative) and non-treponemal tests (qualitative and quantitative).

<u>Treponemal tests</u>

- Measures antibody directed against *T. pallidum* antigens
- Usually reactive for life
- Cannot be used to assess treatment response
- This is the first test in the series done by the Newfoundland and Labrador Public Health Laboratory (PHL) (refer to Figure 2)
- Includes
    - TP (*T. pallidum*)
    - TP-PA (*T. pallidum* particle agglutination*)*

<u>Non-treponemal tests</u>

- Measures antibody directed against a cardiolipin-lecithin cholesterol antigen
- Non-specific for *T. pallidum*
- Titres correlate with disease activity
- Used to follow response to treatment
- Include:
    - VDRL (venereal disease research laboratory)
    - RPR (rapid plasma reagin)

Testing considerations

- Serology can yield false negative results in the early stages, particularly in primary syphilis. It may take 2-3 weeks after development of chancre before a positive result which may be 6-8 weeks after sexual contact with case.
- A negative serology test should be repeated in 2 to 4 weeks in suspicious cases or known contacts of a positive syphilis case.
- Successful treatment reduces the amount of lipoidal antigen; this can be monitored by observing a decrease in RPR/VDRL titre.
- The diagnostic algorithm employed at the PHL, figure 2, is based on a "reverse sequence" screening whereby serum is screened for *T. pallidum*-specific antibodies (syphilis TP), and if reactive is confirmed with RPR (non-treponemal test). If the RPR is negative, the initial reactive *T. pallidum*-specific antibody result requires confirmation; this is performed employing the TP-PA test.

For details on testing see: http://publichealthlab.ca/service/syphilis-serology/

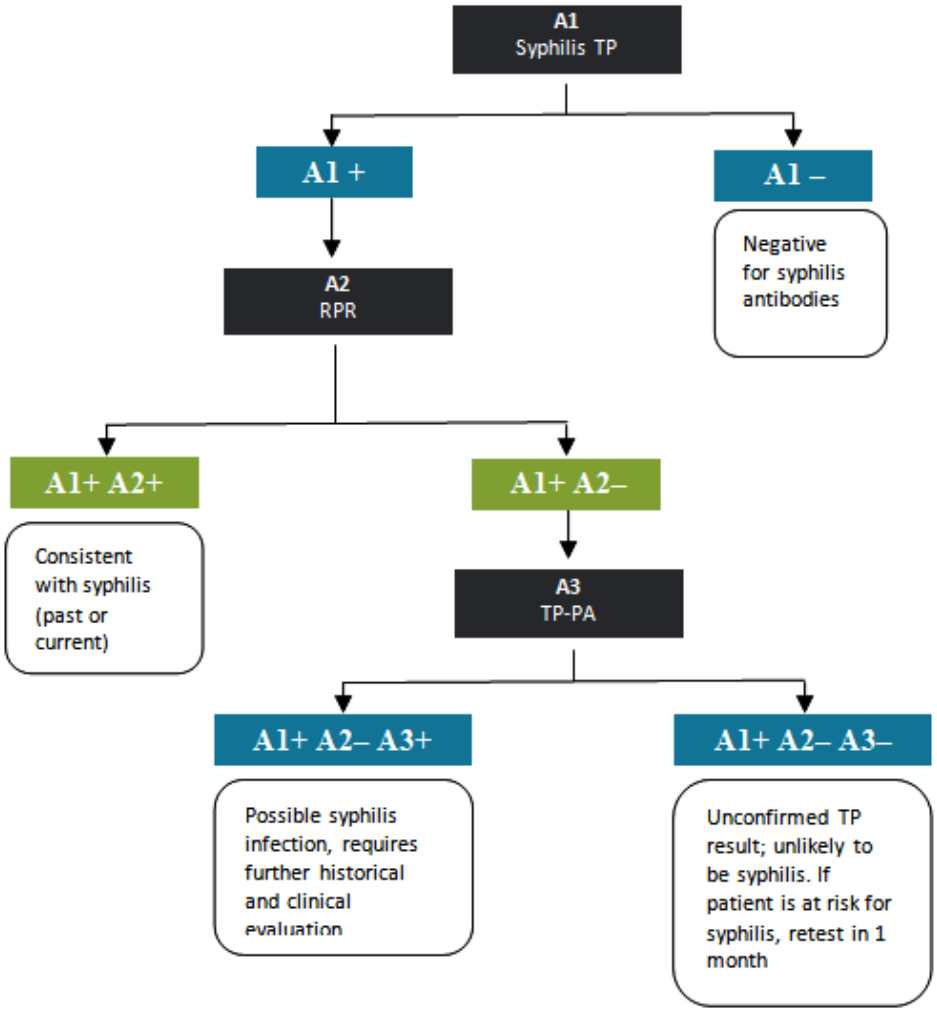

Figure 2: Syphilis Screening Algorithm
Source: Newfoundland and Labrador Public Health Laboratory website (www.publichealthlab.ca)

Interpretation of Results

Syphilis TP	RPR	TP-PA	Interpretation
Non-Reactive	NP*	NP*	Negative. No syphilis or incubating syphilis.
Reactive	Reactive	NP*	Confirmed positive. Syphilis yaws, or pinta or Lyme disease.
Reactive	Non-Reactive	Reactive	Confirmed positive. Primary or latent syphilis; previously treated or untreated syphilis; yaws or pinta or Lyme disease.
Reactive	Non-Reactive	Non-Reactive	Negative. Biological false positive TP result or Lyme disease.

***NP- Test Not Performed**

Indications for testing cerebrospinal fluid (CSF)

CSF examination is indicated in patients with suspected/confirmed syphilis with a presence of:

- Neurologic or ophthalmic signs and symptoms;
- Congenital syphilis
- Treatment failure

TREATMENT

- Long-acting benzathine penicillin G (Bicillin® L-A) as a single dose of 2.4 million units IM is the preferred treatment for non-pregnant adults with primary, secondary and early latent syphilis.
- Long-acting benzathine penicillin G (Bicillin® L-A) can be obtained through the regional pharmacy. This medication is not available in private pharmacies. To order this drug please complete the Request for *Syphilis Treatment –Benzathine Penicillin G* (Bicillin® L-A) found in Appendix A and fax as follows:

Regional Health Authority	Facility	Telephone	Fax	Switchboard (After hours/ weekends only)
Eastern Health	Health Science Centre Outpatient Pharmacy	777-6244	777-8120	777-6455
Central Health	JPMRHC Pharmacy	256-5414	256-5711	651-2500
	CNRHC Pharmacy	292-2134	292-2253	292-2500
Western Health	WMRH		637-5160	637-5000
Labrador-Grenfell Health	Labrador Health Centre (Happy Valley Goose Bay)	897-2117	896-4017	897-2000
	Labrador West Health Centre (Labrador City)	944-9284	944-9384	285-8100
	Charles S. Curtis Memorial Hospital (St. Anthony)	454-0113	454-3232	454-3333

Note: This drug is temperature sensitive and must be stored between 2- 8 ^{0}C. For this reason the medication will only be shipped from the pharmacy Monday – Wednesday**.**

Caution: Long-acting benzathine penicillin G (Bicillin® L-A) should not be confused with short-acting benzylpenicillin (Penicillin G).

Alternatives for penicillin-allergic patients:

- Doxycycline** 100 mg PO bid for 14 days for primary, secondary or early latent syphilis
- Doxycycline** 100 mg PO bid for 28 days for latent syphilis
- Ceftriaxone 1 g IV or IM daily for 10 days (exceptional circumstances only)

***Patients prescribed Doxycycline should be closely monitored for compliance due to possible gastrointestinal side effects*

Other treatment considerations

- Treatments for neurosyphilis, infections ≥1 year and congenital syphilis are listed in the Canadian Guidelines for STIs.[1]
- Every effort should be made to obtain and document prior history of treatment for syphilis and prior serologic results in order to avoid unnecessary re-treatment.
- Presumptive/empirical treatment regime is long-acting benzathine penicillin G (Bicillin® L-A) as a single dose of 2.4 million units IM. This should be considered for those who have had sexual contact with a positive case(s) in the last 90 days.
- All patients should be made aware of the possible Jarisch-Herxheimer reactions to treatment. This may occur within a few hours and up to 24 hours post treatment. Patients may experience fever, myalgia, rigors, and nausea.

MANAGEMENT

- Clinicians are encouraged to discuss clinical management of cases with the MOH or an ID specialist.
- The evaluation of all positive syphilis cases should include a history and physical examination and possibly referral to an ID specialist.
- All patients with reactive syphilis serology should be tested for other sexually transmitted and blood borne Infections (STBBI) including HIV, hepatitis B, hepatitis C, chlamydia and gonorrhea. Genital ulcers, if present, should be tested for herpes simplex virus.
- A referral to the appropriate specialist is required for patients with HIV infection and those with congenital and neurosyphilis.
- Persons co-infected with HIV must be referred to the Provincial HIV clinic 709-777-5041.
- Immunize with age appropriate vaccine including hepatitis B if not already immune. Immunization against hepatitis A may be indicated. Discuss HPV vaccination with high risk individuals.

[1]Canadian Guidelines on Sexually Transmitted Infections, 2010 Edition. Ottawa, ON: Public Health Agency of Canada. http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-10-eng.php

FOLLOW UP

To ensure adequate serological response after treatment it is recommended that the patients be assessed as follows:

Primary or secondary (early) syphilis cases

- Reexamine and test at 1, 3, 6 and 12 months post treatment

Late latent and tertiary syphilis cases

- Reexamine and test at 12 and 24 months

Co-infected with HIV and syphilis (at any stage)

- Follow-up in collaboration with the HIV Clinic and testing is required at 1, 3, 6, 12 and 24 months after treatment and yearly thereafter.

RPR initial titre (e.g. 1/128) → Repeat RPR according to stage

- **If satisfactory reduction in RPR consider cured**
- **Inadequate reduction in RPR titre consider neurosyphilis or re-infection → Consult ID Specialist**
- **Failure of treatment → Consult ID Specialist**

Stage	Adequate Serological Response
Primary	4-fold drop at 6 months 8-fold drop at 12 months 16-fold drop at 24 months
Secondary	8-fold drop at 6 months 16-fold drop at 12 months
Early latent	4-fold drop at 12 months

PREVENTION

All individuals who are identified as cases or contacts and others who present with concerns about syphilis should be provided with the following information:

- Facts about the disease and how it is transmitted
- Treatment and the follow-up required
- Discussion on risk reduction behaviors
    - These practices include properly and consistently using barrier methods such as condoms and dental dams, reducing the number of sexual partners, syphilis screening of individuals at risk and routine screening of pregnant women.
- Information on the importance of contact tracing

CONTACT NOTIFICATION

- At the initial interview with a case contact tracing should begin. For details on pre and post-test counselling see the Canadian STBBI Guidelines: http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-10-eng.php
- All sexual or perinatal contacts within the following time periods need to be located, assessed, tested and treated as indicated below:

Stage of syphilis	Trace-back periods
Primary syphilis	3 months prior to the onset of symptoms
Secondary syphilis	6 months prior to the onset of symptoms
Early latent	1 year prior to diagnosis
Late latent/tertiary	Assess marital or other long-term partners as appropriate
Congenital	Assess mother and sexual partner/s
Stage undetermined	Assess/consult with ID specialist

COMMUNICABLE DISEASE CONTROL SERVICES

Reporting

- Syphilis (infectious and non-infectious) is reportable in Newfoundland and Labrador.
- Cases are reported to the Medical Officer of Health or designate in the appropriate RHA.
- For details on notifiable diseases see: http://www.health.gov.nl.ca/health/publichealth/cdc/notifiable_disease_list.pdf

Testing, treatment and counseling

- Testing, treatment and counseling services are offered through family physicians.
- In St. John's, Eastern Health's Sexual Health Clinic can be reached at 752-4882.
- Clients can also call the Healthline at 811.

Contact tracing

All syphilis cases require contact tracing and empirical treatment of contacts. For assistance please contact the Communicable Disease Control Division of your Regional Health Authority.

- Eastern Health 752-3918
- Central Health 651-6234 or 292-8881
- Western Health 637-5417, 637-5000 ext. 5436 or 5917
- Labrador Grenfell Health 897-7354

REFERENCES AND OTHER RESOURCES

Canadian Guidelines on Sexually Transmitted Infections, 2010 Edition. Ottawa, ON: Public Health Agency of Canada. Retrieved July 9, 2015, from http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-10-eng.php

New Brunswick Clinician's Guide to Syphilis Diagnosis and Treatment 2013. Retrieved July 9, 2015, from http://www2.gnb.ca/content/dam/gnb/Departments/h-s/pdf/en/Publications/9246e-final.pdf

Syphilis Serology. Newfoundland and Labrador Public Health Laboratory Guide to Services. Retrieved July 9, 2015, from http://publichealthlab.ca/service/syphilis-serology/

APPENDIX A: Request for Syphilis Treatment - Benzathine Penicillin G

Patient Name: _____

MCP: _____ **DOB:**_____

Address:_____ **Phone:** _____

Physician:_____ **Licence #:**_____

Clinic Name: _____ **Phone:** _____

Complete Clinic Mailing Address: _____

Indication/Diagnosis	Drug/Dosage	Doses Ordered
Primary, secondary, and early latent stages of syphilis infection (infected less than 1 year) Sexual contact with a known positive syphilis case in last 90 days	**Benzathine Penicillin G (Bicillin® L-A) 2.4 Million Units IM x 1 dose (Supplied in 2 syringes)	
Late latent syphilis (infected more than 1 year or of unknown duration) Syphilis (at any stage) with HIV co-infection	**Benzathine Penicillin G (Bicillin® L-A) 2.4 Million Units IM x 3 doses (Supplied in 6 syringes)	

Long-Acting Benzathine Penicillin G (Bicillin® L-A) should not be confused with Short-Acting Benzylpenicillin (Penicillin G)

Benzathine Penicillin G (Bicillin® L-A) must be stored in a refrigerator that is temperature monitored and stored between 2-8^{0}C

Physician's Signature: _____ Date: _____