Leprosy (Hansen's Disease)

Manitoba
Public Health Branch

1. Case Definition

1.1 Laboratory Confirmed Case: Clinical evidence of illness* with laboratory confirmation in an appropriate clinical specimen (e.g., biopsy of tissue affected, usually skin nodes, nasal scrapings):

- Positive acid-fast stain with typical morphology for *Mycobacterium leprae*

OR

- Histopathological report from skin or nerve biopsy compatible with leprosy (1)

OR

- *M. leprae*-positive PCR in any specimen.

1.2 Probable Case: Clinical illness* in a person who is epidemiologically linked to a confirmed case (1).

***Tuberculoid or paucibacillary disease:** one of a few well demarcated, hypopigmented and anesthetic skin lesions, frequently with active, spreading edges and a clearing centre; peripheral nerve swelling or thickening may also occur.

Lepromatous or multibacillary disease: erythematous papules and nodules or an infiltration of the face, hands and feet with lesions in a bilateral and symmetrical distribution that progresses to thickening of the skin and loss of normal hair distribution, particularly on the face (madarosis).

Borderline (dimorphous): skin lesions characteristic of both the tuberculoid and lepromatous forms.

Indeterminate: early lesions, usually hypopigmented macules, without developed tuberculoid or lepromatous features (1).

2. Reporting Requirements

Laboratory:

- All positive laboratory results for *M. leprae* are reportable to the Public Health Surveillance Unit by secure fax: (204-948-3044).

Health Care Professional:

- Probable (clinical) cases of leprosy are reportable to the Public Health Surveillance Unit by secure fax: (204-948-3044) within 5 business days of being identified. The *Clinical Notification of Reportable Diseases and Conditions* form http://www.gov.mb.ca/health/publichealth/cdc/protocol/mhsu_0013.pdf should be used.

Regional Public Health or First Nations Inuit Health Branch (FNIHB):

- Once the case has been referred to Regional Public Health or FNIHB, the *Communicable Disease Control Investigation Form* http://www.gov.mb.ca/health/publichealth/cdc/protocol/mhsu_0002.pdf should be completed and returned to the Public Health Surveillance Unit by secure fax (204-948-3044).

3. Clinical Presentation/Natural History

Leprosy (Hansen's disease) is a disease that mainly affects the skin and peripheral nerves, resulting in neuropathy and associated long-term consequences, including deformities and disabilities (2). Leprosy has a long latency

period that may last up to 20 years (4). The clinical range from tuberculoid (paucibacillary) (PB) to lepromatous (multibacillary (MB) leprosy is a result of a variation in the host cellular immune response to the bacteria (3). *Mycobacterium leprae* is capable of direct peripheral nerve damage, even in the absence of inflammation or a cellular immune response (4). Signs of leprosy include pale reddish skin patches with loss of sensation; numbness or tingling of the hands or feet; weakness of the hands, feet or eyelids; painful or tender nerves; swellings or lumps in the face or earlobes; painless wounds or burns on the hands or feet (5). Leprosy lesions usually do not itch or hurt; they lack sensation to heat, touch, and pain (4). Eye involvement can occur, and patients should be examined by an ophthalmologist (4). The longer the delay between the appearance of the first symptoms of leprosy and the start of treatment, the more likely nerve damage will occur (5). Untreated leprosy can cause progressive and permanent damage to the skin, nerves, limbs and eyes (6). Differential diagnosis of leprosy includes psoriasis, vitiligo, tinea versicolor, pityriasis alba, sarcoidosis, syphilis, mycosis fungoides, mililaria profunda, and streptocerciasis, as well as other mycobacterial infections and infiltrative skin diseases (7).

The long-term consequences of leprosy (e.g., disfigurement of the face) are mostly due to nerve damage resulting directly from infection, or as a consequence of leprosy reactions (5). A leprosy reaction is the sudden appearance of signs and symptoms of inflammation in the skin lesions of a person with leprosy and can occur before, during or after multidrug therapy (MDT) (5). There are two types of reaction: reversal reaction (or Type 1) associated with an increase in the cellular immune response, and erythema nodosum leprosum (ENL) (or Type 2) characterized by a systemic inflammatory response secondary to immune complex deposition (5, 8). In a reversal reaction, the existing skin lesions become inflamed, red and swollen; in an ENL reaction, new red nodules (about 1-2 cm across) appear under the skin of the limbs or trunk, while the original leprosy skin patches remain as they were (5). ENL reactions also cause a general feeling of fever and malaise, while reversal reactions cause few or no systemic signs and symptoms (5).

4. Etiology

Leprosy is caused by *Mycobacterium leprae*, an obligate intracellular, acid-fast bacillus (4). A new species of mycobacteria, known as *Mycobacterium lepromatosis,* was isolated from two deceased patients who presented with diffuse lepromatous leprosy (9, 10). This new bacillus is a component of the *M. leprae* complex.

5. Epidemiology

5.1 Reservoir and Source

Humans and armadillos are the only proven reservoirs (7). Studies have confirmed a high frequency of *M. leprae* infection in asymptomatic household contacts of individuals with clinically apparent leprosy (11). Armadillos are a large natural reservoir for *M. leprae* in the United States such as Louisiana and Texas (12).

5.2 Transmission

The predominant mode of transmission is likely through respiratory droplets or nasal secretions, although transmission may also occur through skin contact, transplacentally,

via breast milk and after zoonotic (e.g., armadillo) exposure (13). There is little shedding of *M. leprae* from involved intact skin (4). Patients with polymerase chain reaction (PCR) positive nasal swabs, suggesting nasal excretion of *M. leprae*, probably have the highest transmission potential (14). The most contagious presentation of leprosy is lepromatous leprosy as these patients usually carry a very large number of leprosy bacilli (9). Asymptomatic infection among blood donors may be an unapparent mode of leprosy transmission via transfusion in leprosy endemic regions (15). Indirect transmission is unlikely, even though the organism can survive up to seven days in dried nasal secretions (7).

5.3 Occurrence

General: The global case detection rate, defined as the notification rate per 100,000 population, seems to be declining slowly (5). Changes in detection rate happen slowly, over decades, due to the long incubation period of the disease (5). Global initiatives have resulted in a reduction of prevalence rates from > 5 million cases in the mid-1980s to < 200,000 cases at the end of 2016 (16). More than 65% of the world's leprosy patients reside in South and Southeast Asia; the majority of these patients reside in India (4). High endemicity remains in some areas of Angola, Brazil, Central African Republic, Democratic Republic of Congo, India, Madagascar, Mozambique, Nepal, Republic of the Marshall Islands, the Federated States of Micronesia, and the United Republic of Tanzania (4). Brazil is among the top-five countries with the highest prevalence of leprosy (17), and accounts for almost all new cases of leprosy detected in the Americas (16). Approximately 150 cases of leprosy are reported in the United States each year, with about one-third of the cases believed to have been acquired locally (12). Most cases of leprosy reported in the US were in native-born citizens of Texas and Louisiana, and among immigrants in California, Florida, New York, and Massachusetts (4).

Canada: Eight cases of leprosy were reported to the Canadian Notifiable Diseases Surveillance System (CNDSS) in 2015 and five cases reported in 2016 (18).

Manitoba: As of June 4, 2019, four cases of leprosy have been reported in Manitoba since 2000. Cases were reported in 2004, 2012, 2014 and 2019. The first three cases were in males and the last in a female. Two of these cases were believed to be acquired from South Asia. No additional information is available on the other two cases.

5.4 Incubation Period

The incubation period ranges from one to many years but is usually three to five years (4). The incubation period for the tuberculoid form appears to be shorter than for the lepromatous form (4). Symptoms can take up to 20 years to develop (4).

5.5 Host Susceptibility and Resistance

The majority of people appear to be naturally immune to *M. leprae* (12). Several genes have been identified that are associated with susceptibility to *Mycobacterium leprae*; approximately 5% of people are genetically more susceptible to infection with *M. leprae* (4). Therefore, spouses of leprosy patients are not likely to develop leprosy, but biological parents, children and siblings who are household contacts of untreated patients with leprosy are at increased risk (4).

5.6 Risk Factors

Contacts of patients with leprosy have a higher risk of developing leprosy than does the general population, especially blood-related children, parents and siblings (19). Clinical disease has a bimodal distribution: adolescents aged 10 to 19 are the most susceptible, followed by a second peak at 30 years or older (13). Contacts of patients with paucibacillary (PB) leprosy with 2-5 lesions (PB2-5) and those with multibacillary (MB) leprosy had a higher risk than did contacts of patients with single-lesion PB leprosy (19). Persons seropositive for *M. leprae* are at increased risk of developing leprosy (14).

5.7 Period of Communicability

The most contagious presentation of the disease is the presentation of lepromatous leprosy as patients carry a very large number of leprosy bacilli (9). The infectivity of lepromatous patients ceases within 24 hours of the first administration of multidrug therapy for leprosy (4).

6. Diagnosis

The diagnosis of leprosy should be considered in cases of chronic dermatitis with peripheral nerve involvement in foreign-born individuals from leprosy endemic areas, as well as those who have lived or traveled to endemic areas for prolonged periods (20). Diagnosis is essentially a pathologic or clinical one, supported by demonstration of acid-fast bacilli in the specimen. *Mycobacterium leprae* cannot usually be cultured *in vitro*. Clinical diagnosis is based on complete skin examination and signs of peripheral nerve involvement (hypoesthesia, anesthesia, paralysis muscle wasting or trophic ulcers, or enlargement and tenderness with bilateral palpation of the ulnar nerve at the elbow, peroneal nerve at the head of the fibula or the great auricular nerve). Skin lesions are tested for sensation (light touch, pinprick, and temperature discrimination). Whenever possible, a skin biopsy confined to the affected area should be sent to the Health Sciences Centre Tuberculosis Laboratory. Please call the lab at 204-787-7652 for more information prior to submitting samples. Biopsies of the affected area should also be submitted to the National Microbiology Laboratory for *M. leprae* PCR as this is increasingly recognized as the gold-standard for diagnosis. Alternatively, skin slit smears may be referred to the National Hansen's Disease Program (Louisiana, USA). If performing skin slits as part of the investigation into leprosy, it is recommended that initial skin smears be taken from six "routine sites" (both ear lobes, elbows and knees) and several typical lesions from the patient. When leprosy is considered, patients should be referred to a physician with expertise in leprosy to obtain skin smears or biopsies and initiate therapy. In order to evaluate progress, repeat smears may be obtained from three to four of the most active sites, based on the initial testing, annually or at another time period determined by the clinician. The procedure for obtaining skin-slits for smears is detailed at https://www.hrsa.gov/hansens-disease/diagnosis/skin-smears.html . A chart for the documentation of the sites of the sample collection is available at https://www.hrsa.gov/sites/default/files/hansensdisease/pdfs/biopsychart.pdf .

7. Key Investigations for Public Health Response

- History of immigration from leprosy endemic area.

- Past history of leprosy.
- History of exposure to armadillos or to environments frequented by armadillos.

Contacts of infectious cases should be referred to a dermatologist or infectious diseases specialist for physical examination.

8. Control

8.1 Management of Cases

- Referral to an infectious diseases specialist is strongly recommended for the treatment of leprosy cases.
- Evaluation for any evidence of tuberculosis to avoid monotherapy of active tuberculosis with rifampin while treating active leprosy (4).
- Patient education about the nature of disease and the need for adherence to the treatment.
- No restrictions in employment or attendance at school are indicated for persons whose disease is regarded as non-infectious (7).
- Detecting and treating any nerve damage, including referral to appropriate specialists.
- Monitoring for any immunological reactions and sequelae from anesthesia. MB patients are more at risk of reactions compared to PB patients (5).

Infection Prevention and Control: Routine Practices. Refer to the Manitoba Health, Seniors and Active Living document *Routine Practices and Additional Precautions: Preventing the Transmission of Infection in Health Care* http://www.gov.mb.ca/health/publichealth/cdc/docs/ipc/rpap.pdf .

Treatment:

Two methods have been developed to classify leprosy as tuberculoid (paucibacillary) or lepromatous (multibacillary). The Ridley-Jopling system is based on histopathology and is used where histopathology is available (13, 21). The World Health Organization later developed another system based on the number of lesions present (if ≤ 5 lesions, classified as tuberculoid or paucibacillary, if > 5, classified as lepromatous or multibacillary) (13, 21).

- The primary goal of therapy is the prevention of permanent nerve damage (4).
- Refer to multidrug therapy (MDT) recommendations in Tables 1 and 2 below, which are based on the US National Hansen's Disease Program recommendations.
- "Standard regimen" MDT is safe during pregnancy and breastfeeding (5). Regimens containing fluoroquinolones and tetracyclines are contraindicated in pregnancy and breastfeeding.
- MDT can be given to HIV-positive patients, including those taking anti-retroviral treatment and patients on treatment for tuberculosis (5). Dosing adjustments may be required and treatment of concurrent tuberculosis is complex.

Provision of Multidrug Therapy:
Medications for hospitalized patients will fall under the usual hospital pharmacy budgets that are managed by the respective clinical programs. For outpatient treatments, patients would be subject to meeting their Pharmacare deductible before having any costs fully paid by Pharmacare.

Table 1: Multidrug Therapy for Leprosy (Standard regimen based on the Hansen Institute recommendations; https://www.hrsa.gov/hansens-disease/diagnosis/recommended-treatment.html

Indication	Adults	Pediatric
Tuberculoid (Paucibacillary)	• Dapsone, 100 mg/day, orally for 12 months and • Rifampin, 600 mg/day, orally, for 12 months	• Dapsone, 1 mg/kg, orally, every 24 hours. Maximum dose: 100 mg/day for 12 months; and • Rifampin, 10-20 mg/kg per day, not to exceed 600 mg orally for 12 months
Lepromatous (Multibacillary)	• Dapsone, 100 mg/day, orally for 24 months and • Rifampin, 600 mg/day, orally, for 24 months; and • *Clofazimine, 50 mg/day, orally, for 24 months	• Dapsone, 1 mg/kg, orally, every 24 hours. Maximum dose: 100 mg/day for 24 months; and • Rifampin, 10 mg/kg per day, orally for 24 months; and • Clarithromycin, 7.5 mg/kg per day, orally for 24 months

*****Clofazimine is a Special Access drug in Canada https://www.canada.ca/en/health-canada/services/drugs-health-products/special-access/drugs.html .

Table 2: ROM (Rifampicin, ofloxacin, minocycline) Therapy for Leprosy. Based on substitution recommendations of the Hansen Institute (https://www.hrsa.gov/hansens-disease/diagnosis/recommended-treatment.html**).**

Indication	Adults	Pediatric
Tuberculoid (Paucibacillary)	• Rifampicin 600 mg daily oral dose for 12 months plus one of either • †Ofloxacin 400 mg, daily oral dose for 12 months or Minocycline 100 mg, daily oral dose for 12 months.	Fluoroquinolone- and tetracycline-containing regimens are not generally recommended in pediatric patients. Consultation with pediatric infectious diseases is strongly recommended.
Lepromatous (Multibacillary)	• Rifampicin 600 mg daily oral dose for 24 months and • †Ofloxacin 400 mg daily oral dose for 24 months and • Minocycline 100 mg daily oral dose for 24 months	Fluoroquinolone- and tetracycline-containing regimens are not generally recommended in pediatric patients. Consultation with pediatric infectious diseases is strongly recommended.

†Ofloxacin 400 mg may be substituted for either levofloxacin 500 mg or moxifloxacin 400 mg.

Other regimens including reduced-frequency (monthly) dosing and other alternative agents (e.g. clarithromycin 500 mg daily as a substitute for any of the other drugs in a multiple drug regimen) may be appropriate in some situations for both tuberculoid and lepromatous leprosy. Referral to an infectious diseases specialist is strongly recommended.

Follow-up and Treatment of Leprosy Reactions:

- Patients with leprosy reactions should be followed up by an appropriate expert.
- Leprosy reactions should be treated aggressively to prevent peripheral nerve damage (4).
- All patients with leprosy should be educated about signs and symptoms of neuritis and cautioned to report signs and symptoms of neuritis immediately so that corticosteroid therapy can be instituted when appropriate (4).
- Rehabilitative measures, including surgery and physical therapy, may be necessary for some patients (4).

8.2 Management of Contacts

Due to the long incubation of the disease, secondary cases might occur long after the treatment of the "index case" (5).

- Household contacts, particularly contacts of patients with multibacillary disease or those who are blood-related to the case, should be examined initially and then annually for 5 years (4, 13). Contacts found to be infected should be treated (7).
- Postnatal transmission can occur during breastfeeding (4).
- Chemoprophylaxis is not routinely recommended for contacts (4). Referral to an infectious diseases specialist is recommended to assess the role of chemoprophylaxis in contacts.

8.3 Preventive Measures

- Early diagnosis and treatment of cases.
- A single bacilli Calmette-Guérin (BCG) immunization is reported to be from 28% to 60% protective against leprosy (4).
- Direct contact with armadillos and cooking and consumption of armadillo meat is discouraged (12).

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