Manitoba
Health, Healthy Living and Seniors

Public Health and Primary Health Care
Communicable Disease Control
4th Floor, 300 Carlton St, Winnipeg, MB R3B 3M9
T 204 788-6737 **F** 204 948-2040
www.manitoba.ca

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Re: Lymphogranuloma Venereum (LGV) Reporting and Case Investigation

Reporting of LGV (*Chlamydia trachomatis* L1, L2 and L3 serovars) is as follows:

Laboratory:

- All positive laboratory results for *Chlamydia trachomatis* L1, L2 and L3 serovars are reportable to the Public Health Surveillance Unit by secure fax (204-948-3044).

Health Care Professional:

- For Public Health investigation and to meet the requirement for contact notification under the Reporting of Diseases and Conditions Regulation in the *Public Health Act*, the *Notification of Sexually Transmitted Disease* (NSTD) form (http://www.gov.mb.ca/health/publichealth/cdc/protocol/form3.pdf) must be completed for all laboratory-confirmed cases of LGV.
- Please check with the public health office in your region with respect to procedures for return of NSTD forms for case and contact investigation.
- Cooperation with Public Health investigation is appreciated.

Regional Public Health or First Nations Inuit Health Branch:

- Return completed NSTD forms to the Public Health Surveillance Unit by mail (address on form) or secure fax (204-948-3044).

Sincerely,

"Original Signed By"

Richard Baydack, PhD
Director, Communicable Disease Control
Public Health and Primary Health Care
Manitoba Health, Healthy Living and Seniors
Seniors

"Original Signed By"

Carla Ens, PhD
Director, Epidemiology & Surveillance
Public Health and Primary Health Care
Manitoba Health, Healthy Living and

Lymphogranuloma Venereum (LGV)

Manitoba

Communicable Disease Control Unit

Etiology

LGV is caused by *Chlamydia trachomatis* (*C. trachomatis*), a non-motile gram-negative obligate intracellular bacterium (1). There are three known serovars that cause LGV, designated L1, L2 and L3 (2-4). LGV serovars are related to but distinct from the serovars that cause trachoma and oculogenital infections (5).

Case Definition (6)

Confirmed:

- Presence of *C. trachomatis* serovar L1, L2 or L3 confirmed by DNA sequencing or restriction fragment length polymorphism (RFLP).

Probable:

- Positive *C. trachomatis* testing (nucleic acid amplification or serology) **PLUS** the presence of proctitis **OR** inguinal/femoral lymphadenopathy **OR** a sexual partner with LGV.

Reporting Requirements

- All probable and laboratory confirmed cases of LGV are to be reported to the Director, Communicable Disease Control Unit, Manitoba Health by fax (204) 948-3044 using the *Notification of STI* form or by telephone (204) 788-6736.
- Manitoba Health will then forward the case information to regional health authorities for public health follow-up and to the Sexual Health and Sexually Transmitted Infections (STI) Section of the Public Health Agency of Canada (PHAC) (7).

Clinical Presentation/Natural History

The LGV serovars of *C. trachomatis* are more invasive than the more prevalent A-K serovars (8). Classic LGV infection can be divided into three distinct stages (2, 9). Primary infection appears three to 30 days after infection (2, 8) and presents as a small (1-6 mm) painless papule at the site of inoculation (vulva, vagina, penis, rectum, oral cavity, occasionally cervix) that may ulcerate (8, 10). The primary lesion is self-limiting and may go unnoticed (8, 10). The secondary stage occurs two to six weeks after the primary lesion (10) and is characterized by painful, unilateral lymph nodes (buboes) in the inguinal/femoral or anorectal region (10). Clinical symptoms associated with this stage include fever, headache and myalgias (2). Secondary LGV cannot be distinguished clinically from other causes of genital ulceration with bubo formation such as chancroid (8). If left untreated, infection may progress to the tertiary stage, resulting in lymphatic obstruction leading to genital elephantiasis, and rectal involvement leading to the formation of strictures and fistulae (6, 8, 10, 11). Systemic complications including hepatitis, pneumonia and arthritis have been described (1). **Although inguinal buboes are the typical classic presentation of LGV, proctitis may be the major or sole clinical finding (12), particularly among men who have sex with men (MSM) (13-15).** Misdiagnosis as non-infectious gastrointestinal illness (typically Crohn's disease) has been frequently reported among MSM presenting with anorectal disease (16). Anorectal LGV may mimic rectal carcinoma (13). Recent studies have documented a substantial proportion of asymptomatic LGV infections in MSM (15, 17). Active LGV may persist from weeks to many years (4). The LGV serovars of *C. trachomatis* are recovered mainly from MSM in industrialized countries (2, 10, 12, 16, 18). The LGV organism may be recovered from genital ulcers and may also be present in the cervix or urethra (1). LGV infection is often asymptomatic in women (4). The ulcerative character of LGV can facilitate transmission and acquisition of Human Immunodeficiency Virus (HIV) and other STI or bloodborne diseases (15, 18).

Epidemiology

Reservoir: Humans, particularly asymptomatic females (5).

Transmission: LGV can be transmitted through vaginal, anal or oral sexual contact (6, 10). Perinatal transmission of LGV serovars is rare (4).

Occurrence:

General: LGV occurs worldwide, particularly in tropical and subtropical areas (4, 5). LGV is endemic in Africa, India, Southeast Asia, South America and the Caribbean (2, 8). Gender differences are not pronounced in countries with high endemicity (5). Although LGV is believed to be a rare disease in industrialized countries (10), researchers in the United States have been isolating the LGV biovars of *C. trachomatis* for many years (12). In the past the lack of reporting may have been due to the inability of common diagnostic tests to discriminate between the biovars (12).

Canada: As of Nov. 1, 2006, 85 cases of LGV had been reported in Canada (19). Forty-two cases were confirmed cases and 43 were probable cases according to the national case definition (19). All reported cases involved males between the ages of 30 and 45 (19). The true incidence is likely higher than the reported incidence (12).

Manitoba: No cases of LGV have been reported in Manitoba (20) as of April 25, 2007.

Incubation Period: The incubation period for LGV ranges from three to 30 days after infection for a primary lesion and from 10 days up to several months if a bubo is the first manifestation (5).

Host Susceptibility and Resistance: For LGV, the status of natural or acquired resistance is unclear (5). Acquisition of LGV has been associated with unprotected anal intercourse (21), concurrent STI including HIV (19, 22) as well as hepatitis C, sex parties and other higher-risk sexual activities such as "fisting" (10, 19). A recent study found HIV seropositivity to be the strongest risk factor for LGV (15).

Period of Communicability: LGV serovars are communicable from weeks to years during the presence of active lesions (5).

Diagnosis

LGV Specimens (7): If a case of LGV is suspected, multiple specimens must be collected. A clinical specimen (outlined in Table 1) taken with a Dacron swab and a paired serological sample in addition to a standard cervical or urethral swab for chlamydial detection should be submitted to the Cadham Provincial Laboratory (CPL). **The clinical information on the requisition must indicate the possibility of LGV infection.** Standard chlamydial detection techniques are not able to confirm a case of LGV. Specimens taken from suspect LGV cases will be referred to the National Microbiology Laboratory (NML) for confirmation and serotyping.

Key Investigations

- Interview case for history of exposure, risk assessment, contacts, adequacy of treatment and promotion of safer sex practices.
- Interview contacts and provide epidemiological treatment, with risk assessment and promotion of safer sex practices.

Control

Management of Cases:

For suspected cases, empiric treatment (see Table 2) should be given for LGV (and for gonorrhea when clinically indicated) while the results are pending (7).

Table 1 – Collection of Specimens for LGV Testing

Specimen	Test Performed	Specimen Collection
ONE OF a) Swab (Dacron) of anogenital ulcer (rectal, vaginal or urethral) **OR** b) Bubo swab or fluid aspirate **OR** In the absence of a) and b), cervical, urethral and/or rectal specimen	Restriction Fragment Length Polymorphism (RFLP) **OR** DNA Sequencing	Dacron swabs or fluid should be placed in sterile, dry containers and transported frozen on ice. Dacron swabs can be ordered through CPL at (204) 945-6806. Needle aspiration of buboes should be approached through adjacent healthy skin/tissue using a large bore needle.
PLUS Serum samples (acute and convalescent)	Microimmunofluorescence (MIF) **OR** Complement Fixation (CF)	Specimens should be taken 14-21 days apart.
PLUS Standard urethral or cervical swab	NAAT (Nucleic acid amplification test) (Genprobe Aptima unisex swab specimen collection kit)	Collect urethral swab from males and cervical swab from females in Genprobe unisex swab transport system.
OR Male urine	RNA/DNA Amplification (RDA)	Genprobe Aptima urine specimen transport tube.

Note: Biopsy is contraindicated because sinus tracts may develop.

Special Considerations:

Pregnancy

Pregnant and lactating women should be treated with erythromycin. Azithromycin may prove useful for treatment of LGV in pregnancy, but no published data are available regarding its safety and efficacy.

HIV Infection

Persons with both LGV and HIV infection should receive the same regimens as those who are HIV-negative. Prolonged therapy may be required and delay in resolution of symptoms may occur (3).

Treatment Considerations:

- Aspiration of buboes through healthy adjacent skin may give symptomatic relief (8, 10, 23). However, incision/drainage or excision of nodes is not helpful and may delay healing (10, 23).
- Serology is not an effective method for monitoring treatment response as the duration of antibody response has not been defined (10).
- A test of cure is recommended. Patients should be followed until chlamydial tests such as nucleic acid amplification test (NAAT) are negative (10).
- The test of cure should be performed at least three to four weeks after the completion of effective treatment to avoid false positive results due to the presence of non-viable organisms (especially if using NAAT) (10).
- Surgery may be required to repair genital/rectal damage of tertiary LGV (10, 23).
- Having LGV can increase the chances of acquiring or transmitting HIV, other STI and other bloodborne pathogens, such as hepatitis C. **Counselling and testing for other STI** including HIV infection, other chlamydial serovars, gonorrhea, syphilis, hepatitis B and hepatitis C, are recommended (7).

- Testing for chanchroid and donovanosis (granuloma inguinale) should also be considered in patients with LGV, especially if there has been travel to regions where these infections are endemic (24).
- Hepatitis B immunization should be offered to non-immune patients (24).
- The opportunity to provide safer sex counselling should not be missed (24).

Table 2 – Recommended Regimen (3, 6, 10)

Antibiotic	Dose	Indication	Comments
Doxycycline	100 mg po BID for 21 days	Primary treatment	Doxycycline should be used with extreme caution; contraindicated in pregnant women.
Erythromycin base	500 mg po QID for 21 days	Alternate treatment	In pregnancy, erythromycin (non-estolate preparations) should be used for treatment of LGV.
Azithromycin	1 g po once weekly for 3 weeks	Alternate treatment	Although clinical data are lacking, some experts believe azithromycin (1 g orally once weekly for three weeks) to be effective (3, 6, 10).

Erythromycin dosage refers to the use of the erythromycin base. Equivalent doses of other formulations may be substituted except that the estolate formulation is contraindicated in pregnancy.

Management of Contacts (7):

Sexual partners (within the preceding 60 days) of probable or confirmed cases should be contacted, tested and treated. Contact tracing may be difficult as cases may report multiple anonymous sexual contacts in saunas, leather bars, at sex parties or through the Internet (21).

- Symptomatic and asymptomatic contacts should be treated empirically with doxycycline 100 mg orally twice daily for seven days while tests are performed and the diagnosis is confirmed; if *Chlamydia* and/or LGV are detected, the treatment should be continued for a further 14 days to complete a 21 day course. If *Chlamydia* and/or LGV are not detected, the treatment should be stopped after seven days.
- Specimen sites may differ according to sexual practices.

Preventive Measures:

- Early diagnosis and treatment of the patient and sexual partners (6).
- Ensuring that MSM are aware of LGV and able to recognize the symptoms and receive prompt treatment (16).
- Use of condoms or other barrier methods for vaginal, anal and oral sex (6, 8, 10, 24).

Additional Resources for Health Care Professionals

- More information on LGV can be found on the Public Health Agency of Canada website (www.phac-aspc.gc.ca/publicat/lgv/pdf/lgv-rdt_e.pdf) or the Canadian Medical Association Journal (www.cmaj.ca/cgi/rapidpdf/cmaj.050621v1.pdf)

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