5.7 Lymphogranuloma Venereum REPORTABLE

ETIOLOGY

Lymphogranuloma venereum (LGV) is caused by *Chlamydia trachomatis;* serovars L1, L2, and L3. These strains invade and reproduce in regional lymph nodes.

CASE DEFINITIONS

Confirmed Case

Presence of *Chlamydia trachomatis* (*C. trachomatis*) serotype L1, L2, and L3 from genitourinary specimens confirmed by DNA sequencing or Restriction Fragment Length Polymorphism (RFLP)

Probable Case

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

CLINICAL FEATURES

There are three distinct stages of infection with LGV; primary, secondary and tertiary.

Primary LGV:

- Occurs 3 to 30 days after contact.
- Begins with a small (1 to 6 mm) painless papule, nodule or lesion at the site of inoculation (penis, vulva, vagina, rectum, oral cavity or cervix)
- Heals quickly and may go unnoticed in up to 50% of cases

Secondary LGV:

- Occurs within 2 to 6 weeks of the primary lesion
- Includes the development of lymphadenopathy and/or anorectal symptoms
- The first symptom of infection is painful enlargement of inguinal/femoral lymph nodes.
- Cervical lymph nodes may also be infected after oral sex.
- This lymphadenopathy is accompanied by significant systemic symptoms (low grade fever, chills, myalgias, arthralgias).
- Sinuses may drain and abscesses may occur in less than one third of cases.
- Involvement of the anorectum results in bloody, purulent or mucous discharge from the anus as well as constipation.

Tertiary LGV:

- Chronic inflammation leads to the destruction of tissue in the involved and contributes to lymphatic obstruction.
- Obstruction may cause genital elephantiasis, genital and rectal strictures and fistulae.
- This occurs in approximately 10 – 20% of untreated cases, and occurs more commonly in females.

Table 1: Clinical Features of LGV

Primary LGV	• Incubation period of 3 to 30 days • Small painless papule • Self-limited
Secondary LGV	• Within 2 to 6 weeks of primary lesion • Significant systemic symptoms • Lymphadenopathy and/or anorectal symptoms

Secondary LGV causing lymphadenopathy	• Buboes
	  ○ painful inguinal/femoral lymphadenopathy
	  ○ may be unilateral
	• Groove sign
	  ○ inguinal nodes above and femoral nodes below the inguinal ligament (once considered pathognomonic for LGV).
	• Lymphadenopathy depending on inoculation site

Secondary LGV causing anorectal symptoms	• Acute hemorrhagic proctitis • Bloody, purulent, or mucous discharge from anus • constipation
Tertiary LGV	• 10 to 20% of untreated cases • More common in females • Chronic inflammatory lesions lead to scarring • Possible extensive destruction of genitalia

Source: Canadian Guidelines on Sexually Transmitted Diseases, 2013

DIAGNOSIS

Laboratory Tests

Diagnosis may be difficult even in the presence of symptoms as the signs and symptoms of LGV may overlap with other STIs, infections, and malignancies.

Routine tests for *C. trachomatis* may be positive in patients with LGV, but generally do not include typing to distinguish LGV serovars from non-LGV serovars. Definitive diagnosis of LGV requires serovar-specific (confirmatory) testing using DNA sequencing or restriction fragment length polymorphism (RFLP). Clinicians will therefore need to request that testing be done for LGV specifically, as most laboratories will not automatically perform serovar typing.

Where possible, suspected cases of LGV should have both swab and sera samples submitted for laboratory testing. Serology and confirmatory testing (DNA sequencing and RFLP) are available at the NML.

For confirmation on laboratory specimens, contact the NL Public Health Laboratory at (709) 777-6583 or http://publichealthlab.ca/service/chlamydia-trachomatis-neisseria-gonorrhoeae-ctng-dna/

Specimen Collection

Female: Endocervical swab and vaginal swab

Container/Tube: Cobas® PCR Female Swab Collection Kit

Collection Instructions:

9. Remove excess mucus from exocervix with medium cleaning swab provided in Cobas PCR collection kit and discard. This step is important in removing mucus which may prohibit nucleic acid extraction.
10. Insert second medium swab into endocervix, rotate swab for 15 to 30 seconds to ensure adequate sampling.
11. Withdraw swab.
12. Holding tube upright, verify that all Cobas PCR collection medium is at bottom of transport tube. Unscrew cap of transport tube, fully insert swab into tube, and break swab at score line. Screw cap on securely.

Note: 1. Specimen source is required.

2. Spermicidal agents and feminine powder sprays interfere with the assay and should not be used prior to collection.

Male and Female: First Void Urine

Container/Tube: Cobas® PCR Urine Sample Kit

Specimen Volume**:** 10 mL urine

Collection Instructions:

5. Patient should not have urinated for at least 1 hour prior to specimen collection.
6. Patient/ health care provider should collect first portion of a voided urine (first part of stream) into a sterile, plastic, preservative-free specimen collection container.

Note: Specimen source is required.

Other specimen sources

Nasopharyngeal, rectal and conjunctival specimens collected in Cobas® PCR Female Swab Collection Kit have not been validated at the Newfoundland & Labrador Public Health Laboratory.

Interpretation of Results

EPIDEMIOLOGY

Occurrence

- LGV is a relatively rare infection in industrialized countries.
- Typically acquired in endemic areas such as Africa, Asia, South America and the Caribbean where it accounts for an estimated 2–10% of genital ulcer disease.
- Since 2003, there have been cases reported among MSM populations in Belgium, France, Germany, Sweden, the United Kingdom, the United States and Canada.
- LGV is not nationally notifiable and is still considered uncommon.
- It is reportable in NL but to date there has been no reported case.

Reservoir

The only known reservoir is humans.

Incubation

The period of communicability is variable with a range of 3-30 days for a primary lesion; if a bubo lesion is the first manifestation the period of communicability is 10 to 30 days to several months.

Transmission

- LGV may enhance the transmission and acquisition of HIV, other STIs and blood-borne pathogens.
- Direct contact with open lesions of infected people during vaginal, anal or oral sexual activity.

Communicability

The period of communicability is variable from weeks to years during presence of active lesions and relapses are known to occur.

CONTROL MEASURES

Management of Cases

Investigations

- Test symptomatic or asymptomatic clients who identify risk behavior through
- unprotected sexual intercourse and/or known contacts of chlamydia, gonorrhea, epididymitis/orchitis or pelvic inflammatory disease.
- If there is a history of the client performing unprotected fellatio or being the receptive partner in unprotected sex, the rectum and pharyngeal area should be tested (i.e. swabbed).
- Cooperation of the index case is essential to successful contact tracing; enhance cooperation of the index case by obtaining trust and providing an explanation of the reasons for contact tracing.
- Counsel and identify partners for follow up.

Consideration for other STIs

- Obtain specimen(s) to test for HIV, syphilis, gonorrhea, HSV, and hepatitis B and C.
- Consider testing for chancroid and granuloma inguinale, if there is a history of travel to endemic regions
- Immunization against hepatitis B is recommended in non-immune individuals
- Discuss HPV vaccine with women and men

Treatment

- Antibiotics are indicated and suggested regimens are listed in Table 2.
- Incision and drainage or excision of nodes is not helpful and may delay healing
- Cases should be interviewed for history of exposure, risk assessment and sexual partner(s) identification.
- Testing for chancroid and granuloma inguinale should also be considered in individuals with lesions; that have traveled; or have a sexual partner(s) from areas endemic for these infections.
- All cases should be educated regarding infection transmission.
- Patients should be counseled about the importance of abstaining from sex until appropriate diagnosis and treatment is completed.

Table 2: Antibiotic Treatment of LGV

First Line	**Doxycycline** 100mg PO bid for 21 days
Alternative	**Erythromycin** 500mg PO qid for 21 days
Possible	**Azithromycin** 1g PO once a week for 3 weeks

Source: Canadian Guidelines on Sexually Transmitted Infections, 2013

Pediatric Cases

- Perinatal transmission is rare.
- In the event the case is in an infant, the mother and her sexual partner(s) should be examined and tested.
- Beyond the neonatal period sexual abuse must be considered and reported to CYFS as per the Children and Youth Care and Protection Act.

Management of Contacts

Definition of a Contact

- A person who has had sex and /or has had significant exposure to the case.
- All contacts during the past six months should be screened and treated.

Notification

- Partner notification will identify those at risk, reduce disease transmission/reinfection and ultimately prevent disease sequelae.
- All sexual contacts during the last 60 days, regardless of signs or symptoms, must be located, examined, tested and treated empirically.
    - Empiric treatment regimens are presented below in **Treatment of Contacts** section.
    - If tests confirm an LGV infection, re-treat as recommended for cases above.

    - Contacts should abstain from unprotected intercourse until the treatment of the case is complete.
- Notification of partners and contacts is done in a confidential manner that protects the identity of the index case, is done in collaboration with the case or may be done by the index case or by the HCP. (See guidelines around contact tracing)
- All contacts should be screened for HIV and other STIs as detailed in the **Consideration of Other STIs** section above.
- All contacts should be educated regarding infection transmission.
- All contacts should be provided with individualized STI prevention education, targeted at developing knowledge, skills, attitudes and behaviors to reduce the risk and prevent recurrences of STIs.
- Follow-up is required for all out of province/country referrals for cases and partner(s).

Treatment of Contacts

- Sexual partners from the last 60 days prior to symptom onset or date of diagnosis if asymptomatic should be contacted, tested and treated empirically (regardless of whether signs/symptoms are present) as follows:

    - **Azithromycin** 1g PO in a single dose
      OR
    - **Doxycycline** 100 mg PO bid for 7 days

Management of Outbreaks

An outbreak management team should be established to address infection prevention and control measures.

PREVENTION

Follow-up Testing

- Patients should be followed until chlamydial tests are negative (test of cure) and the patient has clinically recovered. Serology should not be used to monitor treatment response, as the duration of antibody response has not been defined.
- Test of cure should be performed at 3–4 weeks after the completion of effective treatment to avoid false-positive results due to the presence of non-viable organisms (especially if using NAAT).
- Surgery may be required to repair genital/rectal damage of tertiary LGV.

Education and Preventive Measures

- Ensure appropriate treatment of LGV for cases.
- Make STI services culturally appropriate, readily accessible acceptable, regardless of economic status
- Educate the case, sexual partners, and the public on methods of personal protective measures, in particular the correct and consistent use of condoms.
- Discuss safer sex options which include:
    - delaying onset of sexual activity,
    - developing mutually monogamous relationships,
    - reducing the numbers of sexual partners,
    - minimize anonymous or casual sexual activity,
    - sound decision making,
    - transmission and prevention of infection
    - provide information about the risk of STIs when travelling.

Reporting Requirements and Procedures

- The laboratory (hospital or public health laboratories) will report case/s to the attending physician, the Chief Medical Officer of Health(CMOH) and the Regional Medical Officers of Health (RMOH).
- The RMOH office will notify, as required, local physicians, nurse practitioners, environmental health officers, community health nurses, communicable disease control nurses (CDCNs) and Infection Control Practitioners (ICP), in the particular region as required for case investigation and contact tracing.
- CDCN will collect case details in collaboration with the ICP (if necessary).
- CDCN enters the case details into the CDSS electronic reporting system and uses the CNPHI tool (if indicated) for alerts and/or outbreak summaries.

Provincial Disease Control

- Reports the aggregate case data to Public Health Agency of Canada (PHAC)
- Provides an analysis of the case/s with reports in the Quarterly Communicable
- Disease Report (CDR), which is also posted on the provincial public health website.
- Coordinates the response in cases where outbreaks across RHAs

DOCUMENTS