Prévention en pratique médicale

LA PRÉVENTION EN ACTIONS

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Lymphogranuloma venereum - "LGV"

A "new" sexually transmitted infection

Lymphogranuloma venereum (LGV) is a sexually transmitted infection (STI) caused by *Chlamydia trachomatis* serotypes L1, L2 and L3. Unlike serotypes A-K, LGV serotypes are invasive.

Epidemiological situation

LGV was formally described for the first time in 1900. LGV is endemic in some parts of Africa, Asia, South America and the Caribbean. **In January 2003**, an outbreak of LGV among men who have sex with men (MSM) was reported, first in Europe (Amsterdam, Paris, London) then in the United States.

In Canada, as of 3 November 2005, 36 cases of lymphogranuloma venereum (LGV) had been reported to the Public Health Agency of Canada since January 2004. In Quebec, a case of LGV was reported in 2004, and 24 cases in 2005 (23 in Montréal and 1 in the Eastern Townshipse). **Up to 83% of these cases were observed in the latter half of 2005. All cases were in men who have sex with men (MSM)** aged 21 to 55 years (average age: 38 years).

The principal clinical manifestations were the following: genital or anal papule or ulcer (4 people); anal symptoms: pain, tenesmus, discharge (19 people, 2 of whom had bloody stools), and inguinal lymphadenopathy (4 people); joint inflammation was also observed in 1 individual. Based on the nosologic definition currently in effect in Quebec and Canada, 9 of these cases were confirmed and 15 were probable cases.

A large majority of MSM for whom LGV was reported in 2005 had had sexual relations in gay saunas during the incubation period; up to 70% knew they had human immunodeficiency virus infection; about one third had used at least once during the past year, one of the following drugs: marijuana, poppers, ecstasy or smoked cocaine; and just over one out of five had had sex with a partner who usually lives outside Québec, either during a trip a patient had taken or when a partner was visiting Québec; partner living in Belgium (1), France (1), Latin America (1), and the United States (2). Fisting (a sexual practice that consists in inserting a finger, fingers, or the fist into the anus) and sharing sex toys were very rarely reported.

Transmission

LGV is transmitted through sexual relations (oral, anal or vaginal) involving contact with:

- a mucous membrane (anus, rectum, glans, vagina, mouth or throat) infected with LGV, with or without visible lesions
- infected discharge or secretions from the penis, anus or vagina.

A pregnant woman infected with LGV can transmit the infection to her newborn during childbirth, when the baby passes through the vagina.

A person who has infected but is not treated can transmit LGV for several weeks or even months after contracting it.

Epidemiological characteristics of lymphogranuloma venereum cases reported in Montréal in 2005

	(n = 23) %
Man who has sex with men	100
Man who has sex with men and women	0
French-Canadian or English-Canadian	88
Knows he has human immunodeficiency virus infection	70[1]
During the incubation period	
Had sexual relations in gay saunas in Montréal	83
Had sex with a partner who usually lives outside Quebec (when travelling or with a partner visiting Quebec)	22[1]
During the past year	
Received or gave money in exchange for sex in Québec	0
Consumed "illicit" drugs (including ecstasy)	31[1]
Injected drugs	0

1. This proportion is difficult to assess since information on this subject was often missing. Cases for whom data was missing were included in the denominator to calculate this proportion.

Clinical picture

LGV is commonly divided into three stages:

Primary LGV

- The incubation period is **3 to 30 days**.
- One or several small painless papules at site of inoculation (vagina, penis, rectum, sometimes cervix, but also in the mouth and pharynx following exposure through fellatio or cunnilingus); they may ulcerate.
- Primary lesions resolve spontaneously and can easily go unnoticed.

Secondary LGV

- Secondary LGV begins within two to six weeks (sometimes 4 to 6 months) of primary lesion.
- Often accompanied by **systemic symptoms** such as low-grade fever, chills, malaise, myalgias, arthralgias; occasionally by arthritis, pneumonitis or hepatitis/perihepatitis; rarely cardiac lesions, asepctic meningitis or ocular inflammatory lesions .
- Abcesses and draining fistula are possible (fewer than one out of three patients).
- Involves lymph nodes or the anus and rectum:

  - **Inguinal secondary LGV** is characterised by painful inguinal and/or femoral lymphadenopathy (usually unilateral); painful lymph nodes are referred to as buboes. The groove sign (inguinal nodes above and femoral nodes below the inguinal ligament) was once considered pathognomonic for LGV. Cervical lymphadenopathy has been described in cases where patient had had oral sex. LGV particularly affects lymph tissues.

  - **Anorectal secondary LGV** is characterized by acute proctitis with bloody, purulent or mucous discharge from the anus, sometimes accompanied by constipation or tenesmus.

Tertiary LGV (chronic, untreated)

Most patients recover spontaneously with no lasting effects following the secondary stages. However, some patients develop the following complications one, two or several years after disease onset:

- chronic inflammatory lesions leading to scarring and fibrosis:
  - lymphatic obstruction causing genital elephantiasis;
  - rectal strictures and fistulae;
- significant destruction of genitalia (esthiomene).

Disease duration may be prolonged in people with human immunodeficiency virus (HIV).

Having LGV can increase the risk of acquiring or transmitting HIV, other STI and other bloodborne pathogens such as hepatitis B or C virus.

Diagnosis

The symptoms and signs of LGV are very similar to those of other STI, other infections, drug reactions, malignancies or inflammatory bowel diseases.

Laboratory testing should be used for diagnosis. Generally, testing is not indicated for screening purposes.

Nosologic definition

❖ ***Confirmed case***

Presence of the three following conditions:

1. **one of the three following clinical manifestations:**
   - proctitis; or
   - inguinal or femoral lymphadenopathy; or
   - sexual contact with a confirmed case of lymphogranuloma venereum (LGV);

   AND
2. **test result positive for at least one of the following non-specific tests:**
   - *Chlamydia trachomatis* isolated in an appropriate clinical specimen; or
   - detection of *Chlamydia trachomatis* using nucleic acide amplification technique; or
   - serological dectection with a microimmunofluorescence test or complement fixation test of a significant increase in specific *Chlamydia trachomatis* antibodies between a serum sample taken during the acute phase and one collected during convalescence; or
   - serological detection with a microimmunofluorescence test of a single specific antibody titre for *Chlamydia trachomatis* $\geq$ 1:256; or
   - serological detection with a complement fixation test of a single specific antibody titre for *Chlamydia trachomatis* $\geq$ 1:64;

   AND
3. samples that have tested positive with culture or nucleic acid amplification testing, confirmation of one of the serotypes of LGV (L1, L2 AND L3) with DNA sequencing or RFLP.

❖ ***Probable case***

Presence of the two following conditions:

1. **one of the following three clinical manifestations:**
   - proctitis; or
   - inguinal or femoral lymphadenopathy; or
   - sexual contact with a confirmed case of LGV;

   AND
2. **test result positive for at least one of the followning non-specific tests:**
   - *Chlamydia trachomatis* isolated in an appropriate clinical specimen; or
   - detection of *Chlamydia trachomatis* using nucleic acide amplification technique; or
   - serological dectection with a microimmunofluorescence test or complement fixation test of a significant increase in specific *Chlamydia trachomatis* antibodies between a serum sample taken during the acute phase and one collected during convalescence; or
   - serological detection with a microimmunofluorescence test of a single specific antibody titre for *Chlamydia trachomatis* $\geq$ 1:256; or
   - serological detection with a complement fixation test of a single specific antibody titre for *Chlamydia trachomatis* $\geq$ 1:64.

Tests

(The availability of LGV tests varies by laboratory)

❖ ***Culture and nucleic acid amplification testing (NAAT)***

Bubo aspiration, swab of a lesion, or rectal, vaginal or urethral swab should be performed (or urine sample, if NAAT is to be performed, since a urine sample is not appropriate for culture).

- *C. trachomatis* culture testing is not readily available in Quebec.
- Nucleic acid amplification testing (NAAT) includes polymerase chain reaction (PCR), ligase chain reaction, transcription mediated amplification, and strand displacement amplification. NAAT have only been approved in Canada for urine samples and endocervical and urethral swabs. They have not been approved for use with rectal or oropharyngeal swabs or for lymph node biopsy or bubo aspiration. In these circumstances, a negative test result does not exclude LGV, and any positive test must be confirmed with a specific test.
- Neither culture nor commercial NAAT tests can differentiate LGV and non-LGV serotypes. Samples that test positive with culture or NAAT testing should be sent for testing to specifically identify LGV serotypes: **DNA sequencing** or restriction fragment length polymorphism (RFLP). Font-line laboratories send samples that are positive with culture or NAAT tests to the Laboratoire de santé publique du Québec (LSPQ); the LSPQ then sends the samples to the **National Microbiology Laboratory in Winnipeg**, where samples are tested specifically for LGV. It takes about 7 to 10 days between the time the sample is sent to Winnipeg and the LSPQ receives the result.

❖ ***Serology***

Serological tests do not distinguish the different *Chlamydia trachomatis* serotypes. However, because of the invasive nature of LGV, serology titres are in general significantly higher in LGV than in non-LGV *C. trachomatis* infections. Thus, a microimmunofluorescence titre $\geq$ 1:256 or **complement fixation** titre $\geq$ 1:64 (or seroconversion with a 4-time increase in titre) suggests an LGV serotype.

Treatment

Bubo aspiration can relieve symptoms. However incision/drainage or excision of nodes is not helpful and may delay healing.

The following treatments are recommended:

First line: Doxycycline, 100 mg, per os, twice a day X 21 days.
Alternative: Erythromycin[1], 500 mg, per os, 4 times a day X 21 days.
Possible: Azithromycin[2], 1 g, per os, once a week for 3 weeks.

[1] Erythromycin dosage refers to the use of erythromycin base. Equivalent dosages of other preparations can be substituted (with the EXCEPTION of the estolate formulation, which is contraindicated in pregnancy). During pregnancy, use erythromycin, but NOT the estolate formulation.
Erythromycin can interact with two classes of HIV medications: protease inhibitors and reverse transcriptase inhibitors.

[2] While some experts believe azithromycin to be effective in the treatment of LGV, there is not enough clinical data to confirm this belief.

Patients with LGV should be followed until tests are negative (test of cure). Surgery may be required to repair genital/rectal lesions caused by tertiary LGV.

Treatment of sexual partners

Sex partners from the last 60 days preceding onset of symptoms should be contacted so they can be informed of their exposure, and be evaluated and treated. Partners must be treated even if they do not have symptoms. Asymptomatic partners are treated as follows:

- Azithromycin, 1 g, per os, single dose **OR**
- Doxycycline, 100 mg, per os, twice a day X 7 days.

Informing one's partners can be difficult. In most regions of Quebec, a public health professional specialising in STI can help a patient find ways to talk with partners. The professional can also contact partners and give them confidential advice, without revealing the identity of the person who is infected.

In Quebec, LGV treatment is free for people who have been diagnosed with the infection and their sex partners.

Suggestions for intervention

- Pay attention to signs and symptoms consistent with lymphogranuloma venereum, particularly in men who have sex with men.
- Check for *C. trachomatis* on a sample (NAAT or culture) and with serological testing (complement fixation or immunofluorescence). **Specify on the lab requisition that LGV is suspected.**
- Eliminate other causes of genital ulcers (syphilis, herpes…) and check for concomitant STBI by proceeding with appropriate tests.
- **Treat suspected cases without waiting for definitive test results.**
- Report the case to the Montréal Public Health Department. LGV is on the list of reportable diseases in Quebec and is currently under increased surveillance; an epidemiological investigation will be undertaken.
- **Provide counselling to the patient**

  The following precautions help reduce the risk of contracting LGV:
  - use a condom everytime the penis or a sex toy penetrates the anus, vagina or mouth; use a new condom with each partner;
  - use a latex glove when inserting fingers or the fist into the anus; use a new glove with each partner;
  - reducing the number of sex partners decreases the possibility of having sex with a person who is infected.

  Thicker and well-lubricated condoms are recommended for anal relations, while thinner, unlubricated or flavoured condoms are suggested for oral sex (sucking). A dental dam can also be used for oral sexual relations.

It is important to recognise the symptoms of LGV and to consult a physician, who will make a diagnosis.
People can get LGV more than once in their life.

Provincial information campaign "It's about LGV"

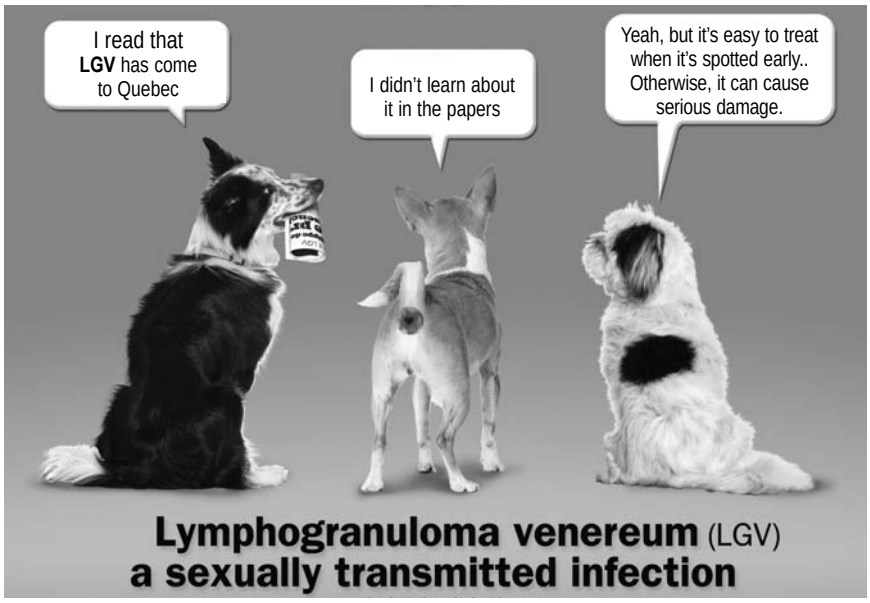
The provincial campaign "*It's about LGV"* **is designed for gay and bisexual men**. Its main objective is to inform them that a "new" sexually transmitted infection (STI) is now in Quebec. Another goal is to make gay and bisexual men aware of the signs and symptoms of LGV so that they can recognise them and consult a physician rapidly. Finally, the campaign aims to promote the adoption of safe behaviours.

The following elements are part of the campaign:

- a **poster**,
- an information **flyer**,
- a **leaflet**,

as well as:

- an **Internet site**: **www.infoITS.qc.ca** This address opens up the STBI page on the Montréal Public Health Department Web site. By clicking on "***LGV"***, the user can then access:
  - the campaign tools (poster, flyer, tract, etc.),
  - articles on LGV (statistics, evolution of the epidemic, etc.),
  - a quiz to test one's knowledge of LGV,
  - resources



- an **information letter** for health professionals, to encourage information sharing on syphilis and LGV, and to mobilise health professinals to participate in STI prevention among gay and bisexual men. Health professionals can register by sending an e-mail containing their name, title, organisation and e-mail address to: **infolettre-syphilis@santepub-mtl.qc.ca**.

The campaign tools will be widely distributed to various associations and places where people from the gay community meet to socialise, to community groups and medical clinics, and to the written and electronic media that serve this community.

Ressources and references

Direction de santé publique de Montréal
Partner notification service: tel.: (514) 528-2400 ext.: 3840
To order educational or promotional material: tel.: (514) 528-2400 ext.: 3817
Fax: (514) 528-2441

The clinical presentation, diagnostic procedure and treatment sections are adapted from the following documents:
"*Interim Statement on the Diagnosis, Treatment and Reporting of Lymphogranuloma venereum (LGV) in Canada"*; Public Health Agency of Canada, March 2005 and
"*Énoncé provisoire sur le diagnostic, le traitement et la déclaration du lymphogranulome vénérien (LGV) au Québec*"; Direction générale de santé publique du Québec, June 2005.

Ministère de la Santé et des services sociaux
Définitions nosologiques, Maladies d'origine infectieuses - Maladie à déclaration obligatoire au Québec. 5th Edition June 2005
http://publications.msss.gouv.qc.ca/acrobat/f/documentation/preventioncontrole/05-268-01W.pdf

Health Canada
Canadian STD Guidelines (1998)
www.phac-aspc.gc.ca/publicat/std-mts98/index.html
(the 2006 edition of the Guidelines will be available in winter 2006)

Lymphogranuloma venerium (LGV) Epi Update
www.phac-aspc.gc.ca/publicat/epiu-aepi/std-mts/lgv_e.html.

Lymphogranuloma venereum (LGV) in Canada: Recommendations for Diagnosis and Treatment and Protocol for National Enhanced Surveillance
www.phac-aspc.gc.ca/publicat/lgv/lgv-rdt_e.html.

Centers for Disease Control (United States)
Sexually Transmitted Diseases - Treatment Guidelines 2002
www.cdc.gov/STD/treatment/

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