

LYMPHOGRANULOMA VENEREUM (LGV)

I. INTRODUCTION

Lymphogranuloma venereum (LGV) is a sexually transmitted infection (STI) caused by unique serovars of *Chlamydia trachomatis* (L1, L2, L3) that are unlike those that typically cause urethritis, cervicitis, and proctitis (A-K). It occurs only sporadically in North America but is endemic in many parts of the developing world. A recent outbreak of LGV proctocolitis has been reported among men who have sex with men (MSM) in North America and Europe. Many of these individuals were co-infected with HIV.

HIV alters the natural history and response to therapy of many STIs; however, its impact on LGV remains unclear. No current evidence exists to support a difference in acquisition, natural history, or response to therapy of LGV in the setting of HIV co-infection.

II. PRESENTATION

RECOMMENDATION:

Clinicians should include LGV as part of the differential diagnosis of genital ulcer disease, inguinal lymphadenopathy, or proctocolitis, especially in men who have sex with men.

LGV progresses over several clinical stages. The incubation period is between 3 days and 1 month after exposure. Infection is initially characterized by a small and often innocuous non-tender papule, vesicle, or ulcer, which is often overlooked by the patient. This lesion occurs at the place of contact with an infected partner and thus may involve almost any aspect of the genital or rectal tissue. Lesions in the urethra or cervix can provoke symptoms of urethritis or cervicitis. Over time, these primary lesions resolve without therapy.

The hallmark of LGV is unilateral or bilateral tender lymphadenopathy that dramatically evolves 2 to 6 weeks after the primary lesion. Lymphadenopathy may or may not be associated with signs of lymphangitis. The involved lymph nodes increase rapidly in size, and pain and erythema are common. If adjacent to one another, several involved lymph nodes may coalesce. The central areas of such lymph nodes can then undergo necrosis. Fluctuant and suppurative lymph nodes then develop, causing the classic ‘bubo’ of LGV. The bubo may then rupture and drain purulent material, which is associated with relief from symptoms. The ‘groove sign’ characteristic of LGV is seen if both the inguinal and the femoral nodes are involved. Resolving buboes can result in significant scarring. In women, lymphatic drainage patterns result in potential involvement of deep pelvic lymph nodes with attendant pelvic, abdominal, and lower back pain.

In both men and women, infection occurring as a result of anal intercourse can cause proctocolitis. Symptoms include fever, pain, tenesmus, and bloody rectal discharge. Colonic mucosal ulcerations develop and may be replaced by progressively enlarging areas of granulation tissue, which, in time, lead to fistulas and strictures. For these reasons, LGV has been

occasionally misdiagnosed as Crohn's disease. Of note, non-LGV serovars also occasionally cause a less aggressive form of proctocolitis. Invasive LGV is characterized by constitutional symptoms such as fever, chills, and malaise. Superinfection with other bacterial species may also complicate the presentation.

III. DIAGNOSIS

RECOMMENDATION:

Clinicians should diagnose LGV through the presence of consistent clinical findings, such as inguinal lymphadenopathy and erosive proctocolitis, as well as the absence of other definable pathologies.

The diagnosis of LGV is made most commonly on the basis of consistent clinical findings. No reliable diagnostic tests are widely available that can consistently assist clinicians to make a diagnosis of LGV.

Although direct testing for *Chlamydia trachomatis* can be performed using nucleic acid amplification tests (NATs), cell culture, or immunofluorescence tests, these tests have limited applicability for LGV due to lack of sensitivity or specificity for these specific serovars. In addition, commercially available NATs for chlamydia are not FDA-approved for use on rectal specimens. Urine, urethral, and cervical specimens that test positive for *Chlamydia trachomatis* using FDA-approved tests do not provide the genotyping needed for LGV serovar determination. Such specimens, as well as those from rectal swabs and purulent material aspirated from buboes, may yield a useful diagnostic specimen upon which genotyping of LGV-specific serovars can be performed; however, genotyping can only be performed in select laboratories. Clinicians interested in such testing should contact their local health departments for instructions on proper specimen collection (see Appendix A for contact information for local health departments and Appendix B for testing and shipping instructions). Treatment, however, should not await LGV serovar determination.

Serologic testing for chlamydia, including complement fixation (CF) and microimmunofluorescence (MIF), has never been adequately standardized, and results from laboratory to laboratory may vary. Serologic tests do not differentiate between LGV and non-LGV serovars. When serologic testing is performed, higher serum antibody levels may be seen in the presence of LGV compared with non-LGV chlamydia infections due to the invasive nature of LGV. CF titers >1:64 and MIF titers >1:256 are strongly suggestive of LGV, particularly when accompanied by consistent clinical findings. Studies have not demonstrated altered LGV testing parameters in the presence of HIV; however, it is likely that serologic tests would be less specific.

IV. TREATMENT

RECOMMENDATIONS:

Doxycycline (100 mg PO bid) for 21 days is the preferred treatment regimen for LGV.

Treatment should not await LGV serovar determination, even in the context of clinicians electing to investigate LGV-specific genotyping.

The treatment of choice for LGV is doxycycline 100 mg PO bid for 21 days. Other tetracyclines can be used as alternatives. Data supporting the use of non-tetracycline alternatives are limited. Erythromycin 500 mg PO qid for 21 days is the standard alternative, although frequency of dosing and gastrointestinal upset limit its utility. Some experts have recommended azithromycin 1g PO once weekly for 3 weeks, but data to support this option are also lacking. There are no data to support the use of alternative regimens in HIV-infected patients.

In individuals with tender, swollen inguinal lymphadenopathy, relief can be achieved by prompt aspiration or incision and drainage.

V. MANAGEMENT OF PARTNERS

RECOMMENDATION:

Clinicians should consider both the HIV exposure and the STI exposure to partners when HIV-infected patients present with a new STI. Clinicians should also assess for the presence of other STIs.

A. Management of HIV Exposure in Partners

RECOMMENDATIONS:

When HIV-infected patients present with a new STI, clinicians should encourage their partner(s) to undergo HIV testing at baseline, 1, 3, and 6 months. In New York State, HIV diagnoses must be confirmed by a Western blot assay.

Clinicians should educate patients to be vigilant for any post-exposure acute HIV symptoms in their partners, such as febrile illness accompanied by rash, lymphadenopathy, myalgias, and/or sore throat. If the partner presents with signs or symptoms of acute HIV seroconversion, a quantitative RNA PCR should be obtained, and consultation with an HIV Specialist should be sought. Positive RNA tests should be confirmed with HIV antibody testing performed within 6 weeks of the RNA test (see [Antiretroviral Therapy: Acute HIV Infection](#), for more information about diagnosis and management of acute infection).

Clinicians should offer assistance with partner notification if needed, or refer patient to other sources for partner notification assistance (CNAP, PNAP).

Presentation of a new STI in HIV-infected patients suggests exposure of HIV to their partners. In this case, offering HIV nPEP to partners is usually not an option because the period prior to STI symptom onset is usually longer than the 36-hour window for initiating HIV nPEP. Therefore, sequential HIV testing of partners for early identification of potential HIV acquisition should be performed. However, if a patient with an HIV exposure does present within 36 hours, evaluation for nPEP should occur (see [HIV Prophylaxis Following Non-Occupational Exposure Including Sexual Assault](#)).

B. Management of LGV Exposure

RECOMMENDATION:

Clinicians should encourage partners of patients with LGV whose exposure occurred within 60 days prior to symptom onset to be examined and treated with a full 21-day course of doxycycline.

Partners of patients with LGV who had sexual contact with the patient within 60 days prior to symptom onset should be examined and treated. No data on which to base the optimal contact interval have been published; some clinicians may treat partners whose exposure occurred up to 6 months prior to the patient's symptom onset.

The appropriate length of LGV treatment in asymptomatic, sexual contacts remains under investigation. In New York State, in accordance with the treatment guidelines for contacts of other sexually transmitted diseases, a full 21-day course of doxycycline is recommended. The Centers for Disease Control and Prevention and the British Association for Sexual Health and HIV recommend that sex partners who had contact within 30 days of the patient's symptoms should be evaluated and treated with regimens for uncomplicated chlamydia infection (azithromycin 1g PO in a single dose, or doxycycline 100 mg PO bid for 7 days).^{1,2}

REFERENCES

1. Centers for Disease Control and Prevention. 2006 Sexually Transmitted Diseases Treatment Guidelines. *MMWR* 2006;55. Available at: www.cdc.gov/std/treatment/2006/genital-ulcers.htm#genulc5

2. British Association for Sexual Health and HIV. 2006 National Guideline for the Management of Lymphogranuloma Venereum (LGV). Available at: www.bashh.org/guidelines.asp#guides

APPENDIX A

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APPENDIX B

INSTRUCTIONS FOR OBTAINING CHLAMYDIA PCR TESTING

Currently, the Wadsworth Center of the New York State Department of Health can perform chlamydia PCR testing to identify *Chlamydia trachomatis* and the L2 serovar on anorectal specimens. Clinicians interested in such testing should first contact their local health departments for instructions on proper specimen collection. New York State Department of Health STD County Coordinator contact information is provided below.

Depending on the location of the clinician, samples for LGV testing should be sent to the following laboratories:

For those facilities located within New York City, dry rectal swabs or those samples in BD ProbeTec buffer may be sent to the New York City Department of Health and Mental Hygiene Public Health Laboratory for *Chlamydia trachomatis* NAT testing. Positive samples will then be forwarded to the Wadsworth Center for LGV serovar determination. Inquiries prior to shipment should be directed to 212-447-6887.

For those facilities located outside of New York City, dry swabs or those in BD ProbeTec buffer collected for *Chlamydia trachomatis* LGV testing should be sent as soon as possible directly to:

The Wadsworth Center Bacteriology Laboratories
New York State Department of Health
120 New Scotland Avenue
Albany, NY 12208

Overnight shipment on cold ice packs is preferred. Please do not use wet or dry ice. Please note that the Wadsworth Center does not accept samples for routine *Chlamydia trachomatis* testing. Inquiries prior to shipment should be directed to 518-474-4177.