Lymphogranuloma Venereum Among Men Who Have Sex with Men --- Netherlands, 2003--2004

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Lymphogranuloma venereum (LGV) is a systemic, sexually transmitted disease (STD) caused by a variety of the bacterium *Chlamydia trachomatis* that rarely occurs in the United States and other industrialized countries; the prevalence of LGV is greatest in Africa, Southeast Asia, Central and South America, and Caribbean countries (*1*). However, in the Netherlands, which typically has fewer than five cases a year, as of September 2004, a total of 92 cases of LGV had been

confirmed during the preceding 17 months among men who have sex with men (MSM). The first 13 cases, diagnosed during April–November 2003, were reported by local health authorities in Rotterdam in December 2003 (*2,3*). An alert was sent to the Early Warning and Reporting System of the European Union and to the European Surveillance of Sexually Transmitted Infections Network (ESSTI) (*4*). In April 2004, a report was made to CDC, and state and local health departments were alerted. Of the 92 cases confirmed in the Netherlands, 30 occurred during 2003 and 62 during 2004. This report describes the ongoing investigation of the LGV outbreak. Health-care providers should be vigilant for LGV, especially among MSM exposed to persons from Europe, and prepared to diagnose the disease and provide appropriate treatment to patients and their exposed sex partners (Box).

The cases in the Netherlands were investigated by staff members of public health services, academic medical centers, and the National Institute of Public Health and Environment. After the initial 13 cases were reported, efforts were implemented to increase awareness of the outbreak among health-care providers, staff at human immunodeficiency virus (HIV)–treatment centers and STD clinics, and members of the MSM community. As a result, an additional 17 confirmed cases and 40 probable cases that occurred in 2003 were identified retrospectively.

LGV was diagnosed by conducting polymerase chain reaction (PCR) tests on rectal swab specimens and performing subsequent restriction endonuclease pattern analysis of the amplified outer membrane protein A gene to determine the genotype. Confirmed cases were those in patients with 1) proctitis or contact with a patient confirmed with LGV; 2) a positive PCR test for *C. trachomatis* on a urine or rectal specimen; and 3) L1, L2, or L3 genotype determined by PCR. Probable cases were those in patients whose illness was consistent with the first two criteria and who also had a positive serologic test for *C. trachomatis*, but did not meet the third criterion because specimens were not available for genotyping. Possible cases were in patients who met only the first criterion and had a positive serologic test.

Increased awareness of the LGV outbreak resulted in retrospective reporting of 2003 cases and reporting of 62 confirmed cases in 2004, as of September 1. Additional epidemiologic information was obtained on these 62 patients. Preliminary evaluation determined that all the patients were white and that, among the 30 MSM whose HIV status was known, 23 (77%) were HIV positive. Other preliminary findings suggested that concurrent sexually transmitted infections were prevalent and that the majority had participated in casual sex gatherings (e.g., "leather scene" parties) and unprotected anal intercourse or other unprotected anal penetration (e.g., fisting) during the 12 months before onset of symptoms.

BOX. Etiology, clinical manifestations, diagnosis, and treatment of lymphogranuloma venereum (LGV)

Etiology

- LGV is caused by *Chlamydia trachomatis* serovars L1 to L3. (*C. trachomatis* serovars B and D–K are responsible for the syndromes of non-gonococcal urethritis and cervicitis.)

Clinical manifestations

- The primary lesion produced by LGV is a small, nonpainful genital papule, which can ulcerate at the site of inoculation after an incubation period of 3–30 days. This lesion can remain undetected within the urethra, vaginal vault, or rectum.
- Common clinical manifestations include 1) tender, unilateral, or bilateral inguinal and/or femoral adenopathy, which can become fluctuant; and 2) hemorrhagic proctitis or proctocolitis, which is associated with receptive anal intercourse (*1*). The clinical and histologic presentation of LGV protocolitis can be similar to the initial manifestations of inflammatory bowel disease (*2*).

Diagnosis

- Diagnosis is based primarily on clinical findings; routine laboratory confirmation might not be possible.
- Serologic tests for *C. trachomatis* (i.e., microimmunofluorescence or complement fixation) can support diagnosis.
- Direct identification of *C. trachomatis* from a lesion (i.e., bubo) or site of the infection (e.g., rectum) can be made by using culture or by using nonculture nucleic acid testing; however, neither method is specific for LGV, and use of rectal swabs for nucleic acid testing is not cleared by the Food and Drug Administration.

Treatment

- The recommended treatment is administration of 100 mg of doxycycline, twice a day for 21 days. Alternative treatment is 500 mg of erythromcyin base orally, four times a day for 21 days. Some specialists in sexually transmitted diseases believe 1 g of azithromycin, administered orally once weekly for 3 weeks, is effective; however, clinical data are lacking.
- Sex partners who had contact with the patient within 30 days of the patient's onset of symptoms should be evaluated; in the absence of symptoms, they should be treated with either 1 g of azithromycin in a single dose, or 100 mg of doxycycline, twice a day for 7 days.

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Only one patient, with onset of illness in April 2003, had symptoms usually associated with LGV (i.e., inguinal adenopathy [buboes] and a painful genital ulcer) (*3*); all other patients had gastrointestinal symptoms (e.g., bloody proctitis with a purulent or mucous anal discharge and constipation) (*2*). In all of the cases in Rotterdam, LGV was associated with high-titer antibodies to *C. trachomatis* in sera, as determined by peptide enzyme immunoassay. When urethral swab samples were obtained, they did not contain *C. trachomatis* DNA. LGV was temporally associated with HIV seroconversion in two patients and with recent acquisition of hepatitis C infection in five others.

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Editorial Note: Although some of the patients in this LGV outbreak reported having multiple sex partners in cities in Europe and the United States (*2*), limited information has been reported regarding LGV occurrence outside the Netherlands. However, recent reports from Belgium, France, and Sweden confirm that LGV is occurring elsewhere in Europe (*5,6*). Additional reports might follow increased awareness of the outbreak (*7*). In July 2004, CDC identified an L2 LGV strain on a rectal swab specimen from a patient in the United States who had signs and symptoms similar to those of the patients in the Netherlands. In this case, no known exposure to European MSM was reported; U.S. contacts of the patient were evaluated and treated.

Health-care providers and MSM in the United States and Europe should be aware of this LGV outbreak, which is similar to STD increases (e.g., in syphilis, rectal gonorrhea, and quinolone-resistant *Neisseria gonorrhoeae* and including coinfections with HIV) that have been reported in recent years among MSM (*8,9*). The ulcerative character of LGV can facilitate transmission and acquisition of HIV and other STDs or bloodborne diseases.

The number of cases reported in the Netherlands is likely a minimum estimate of disease occurrence; clinicians in industrialized countries diagnose LGV rarely and would usually not consider LGV as a likely cause of gastrointestinal illness. Estimates of the incidence and prevalence of LGV in the United States are difficult to obtain; the disease is not nationally reportable, and the diagnosis is not straightforward. The clinical presentation of LGV might easily be missed, as evidenced by the large number of retrospective cases identified in the Netherlands.

The laboratory criteria consistent with a diagnosis of LGV include a positive result (i.e., titer ≥1:64) on a complement fixation test for chlamydiae or a high titer (i.e., typically >1:128, but can vary by laboratory) on a microimmunofluorescence serologic test for *C. trachomatis*. However, most available serologic tests in the United States are based on enzyme immunoassays and might not provide a quantitative "titer-based" result. A list of laboratories that perform serologic tests for *C. trachomatis* and might provide a titered result is available at http://www.cdc.gov/std/lgv-labs.htm.

CDC and other laboratories are evaluating molecular approaches compliant with Clinical Laboratory Improvement Amendment regulations that will permit specific diagnoses of LGV. CDC advises clinicians who care for MSM to consider LGV in the diagnosis of compatible syndromes (e.g., proctitis and proctocolitis) and perform tests to diagnose *C. trachomatis* infections, without regard to the specific LGV serovars. Recommended treatment regimens for those suspected of having LGV and their sex partners are offered (Box).

Evaluation of gastrointestinal syndromes that might have been sexually transmitted should include appropriate diagnostic procedures (e.g., anoscopy or sigmoidoscopy) and microbiologic testing for *C. trachomatis*, syphilis, herpes, *N. gonorrhoeae*, and common enteric pathogens that can be sexually transmitted. Clinicians who identify cases compatible with LGV (e.g., proctitis associated with serologic or microbiologic evidence of chlamydial infection) should contact CDC at 404-639-2059 and local health departments.

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