

# A SLOW EPIDEMIC OF LGV IN THE NETHERLANDS IN 2004 AND 2005

MJW van de Laar<sup>1</sup>, FDH Koedijk<sup>1</sup>, HM Gotz<sup>2</sup>, HJC de Vries<sup>3</sup>

In 2004, an outbreak of LGV was detected in MSM in the Netherlands. By January 2006, 179 confirmed cases of LGV had been reported; 65 (retrospectively) in 2002/2003, 76 in 2004 and 38 in 2005. The evolution of the LGV outbreak appears to have slowed down and only a few cases were found in the first months of 2006.

Euro Surveill. 2006;11(9): 150-2 Published online September 2006

**Key words:** Lymphogranuloma venereum, outbreak, The Netherlands

## Introduction

LGV was very rarely reported in Western Europe until January 2004, when a cluster of LGV cases in men who have sex with men (MSM) who were predominantly HIV positive was reported by the Health Service Rotterdam area [1]. Laboratory results confirmed infection with *Chlamydia trachomatis* serovar L2 [2]. The majority of the men reported unprotected sexual contact with numerous partners from several European countries. Immediate alerts with information about the clinical signs and symptoms of LGV were sent to STI and HIV clinics, gastroenterologists, public health services across the country and *Nederlands tijdschrift voor geneeskunde* (the Dutch Medical Journal). The gay community was informed via peer group oriented websites, periodicals for gay men and via the Schorer Foundation (a national foundation promoting sexual health of gay men and lesbians). International alerts were sent out through the European Surveillance of Sexually Transmitted Infections network (ESSTI), the European Early Warning and Response System (EWRS), and the United States Centers for Disease Control and Prevention's Epidemic Information Exchange (EPI-X) and Morbidity and Mortality Weekly Report (MMWR) [1,3]. A national investigation team was established in January 2004 to discuss the current outbreak and decide future actions.

## Methods

Between 2003 and 2005, surveillance of sexually transmitted infections (STIs) in the Netherlands consisted of a sentinel surveillance network of five low threshold STI clinics that were free of charge, and nine STI services at Public Health Services throughout the country. A standardised questionnaire was used to collect anonymous demographic and epidemiological key parameters, including date of consultation, sex, year of birth, 4 digits of the postal code, sexual preference, previous HIV testing, previous STIs,

injecting drug use, concurrent STIs and commercial sex work, for every new consultation. Laboratory tests for gonorrhoea, chlamydial infection, syphilis, hepatitis B, HIV and other infections were also registered together with the test results and site of infection (if applicable). Data were entered into a web based surveillance application called SOAP.

Enhanced surveillance of LGV was begun shortly after the first report, in January 2004. An additional questionnaire was developed which addressed clinical signs and symptoms, microbiology and diagnostics, sexual behaviour (meeting places, number of partners, the kind of sexual intercourse and condom use). The two questionnaires were matched using a unique number generated by SOAP. Data on LGV cases diagnosed at the STI clinic in Amsterdam were sent to RIVM in a Microsoft Excel worksheet that included date of consultation (or diagnosis), information on the site of infection (proctum, inguinal), sexual preference, HIV status, and current co-infections. No additional information was obtained on clinical aspects, microbiological tests or sexual behaviour.

Cases in this outbreak were managed as follows: Cases were further investigated if (a) a patient presented with clinical signs of inguinal syndrome, anorectal syndrome (proctitis), oropharyngeal syndrome or (b) a patient was known to be a sexual contact of a confirmed LGV case. Further classification followed the results of laboratory testing as detailed below. The case definition was deliberately broad, so as to include highly suspect clinical cases reported retrospectively by physicians shortly after the initial alert. A broad case definition enabled the investigating team to get a rapid idea of the size of the outbreak [TABLE].

The sentinel STI clinics were asked to report on suspected LGV cases voluntarily using both the routine STI and the enhanced LGV questionnaires. The alerts and the *Nederlands Tijdschrift voor Geneeskunde* [4] gave information on clinical signs and symptoms of LGV, e.g. for example this specific rectal syndrome, to increase awareness among medical professionals nationwide. They were invited to report any suspect case of LGV either to local MHS or to RIVM. If cases were reported directly to RIVM, additional information was requested using the questionnaires. RIVM notified the local MHS to contact the physician for contact tracing and interviewing.

Genotyping was performed in two microbiological laboratories, the Erasmus University Medical Centre in Rotterdam, and the Public Health Laboratory in Amsterdam.

## Results

By January 2006, 179 confirmed cases had been reported with additional epidemiological information, although this is not yet complete. In 2004-2005, 114 cases were seen in patients and reported: 76 in 2004 and 38 in 2005. Of these, 78 (68%) were reported from the STI outpatient clinic in Amsterdam. Several cases were reported with dates of consultation in 2003 and 2004, but some could not be confirmed as L2 because specimens were not available. In 2002-2003, 65 confirmed cases were reported retrospectively. The epidemic curve

1. Centre for Infectious Disease Control, National Institute of Public Health and the Environment, Bilthoven, the Netherlands
2. Municipal Health Service Rotterdam and environments, Rotterdam, the Netherlands
3. Department of Dermatology, Academic Medical Centre, University of Amsterdam, and STI outpatient clinic, Health Service Amsterdam, Amsterdam, the Netherlands

TABLE

## LGV outbreak in the Netherlands 2004-2006: LGV case definition

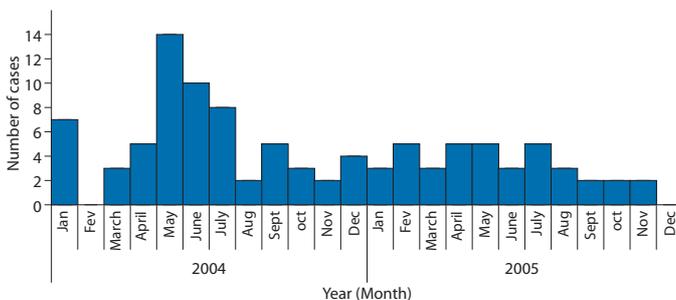
Case definition	Genotype	PCR urine or PCR rectum	<i>C. trachomatis</i> serology	Histology*
Confirmed	L1 or L2 or L3	Positive	High positive Unknown	-
Probable	Unknown	Positive	High positive	-
Possible	Unknown	Positive	Unknown	-
Possible	Unknown	Unknown or Negative	High positive	-
Possible	Unknown	Positive / Unknown	Unknown	Chronic inflammation
Rejected	Other genotype	Negative or Unknown	Low or negative or Unknown	Unknown or Other description

\* Histology is mainly used for retrospective diagnosis of cases reported by gastroenterologists

of cases, by date of consultation from January 2004, shows a slowly increasing outbreak with the highest number reported in May 2004 [FIGURE]. Genotyping demonstrated that all positive L2 samples in Amsterdam contained a new variant, L2b [5]. This genotype was identified in both symptomatic and asymptomatic patients in a study in Amsterdam that retrieved 87 cases retrospectively [5,12]. In the first few months of 2006 only a few cases were reported.

FIGURE

## Number of LGV cases by date of consultation, The Netherlands, January 2004 – December 2005



Source: RIVM – enhanced surveillance of LGV

## Epidemiology

Routine STI surveillance data are available for 92% (104/114) of the confirmed LGV cases in 2004 and 2005. Additional data from the enhanced surveillance is available for 33% (34/104). Preliminary evaluation reveals the following characteristics: 101/104 (97%) were MSM (1 heterosexual, 2 missing), at least 70/104 (67%) were HIV positive (HIV status was unknown in 16 cases); 86% were of Dutch origin, and the mean age was 40 years (range 26-58). Concurrent STIs were frequently diagnosed: 24% (25/104) had gonorrhoea, 21% (16/104) had early syphilis, 10% (10/104) had hepatitis C, 6% (8/104) had genital chlamydial infection and 21% (16/104) were diagnosed with another STI (such as herpes or genital warts).

## Clinical manifestation

The majority of the cases attended because of clinical signs, 82% (74/90; 14 cases missing). The majority (n = 95) were diagnosed with LGV proctitis and 6 with the inguinal syndrome. Most cases presented with proctitis symptoms: rectal discharge (85%; 29/34), rectal pain (74%; 25/34) and bloody rectal discharge (65%; 22/34). Genital symptoms were reported less frequently: swollen lymph nodes (24%; 8/34) or systemic symptoms, including general malaise (41%; 14/34). Most cases (91%; 23/26) were treated with a 21 day course of doxycycline.

## Sexual behaviour

Detailed information on sexual behaviour was only obtained for 24 cases. The mean lifetime number of partners was 275 (range: 6-1000), the mean number of new partners in the last 12 months was 18 (range: 0-100), and the mean number of partners in the last 6 months was 11 (range: 0-50). Only one case reported always having used a condom with a steady partner, and five cases reported always having used a condom

with a casual partner. Half (11/24) reported unprotected anal intercourse (both insertive and receptive), 18/24 reported oral sex without the use of a condom; 29% reported having shared sex toys without using protection or cleaning the toys while sharing. Another 55% (12/22) reported having taken part in group sex; most of them did not change condoms between partners. Of the 18 HIV infected MSM, 10 reported that they had never disclosed their HIV status before having sex.

## Discussion

This LGV epidemic is occurring in a group of MSM in the Netherlands, a large proportion of whom were infected with HIV and other STIs. We report what is undoubtedly a minimum estimate of disease occurrence: the majority of the cases in MSM presented with gastrointestinal problems such as bleeding and inflammation of the colon and rectum, which are not symptoms commonly associated with STIs. Clinicians in industrialised countries rarely make the diagnosis of LGV, and would not be expected to consider LGV as a likely cause of gastrointestinal illness [6-9]. The clinical presentation of LGV might therefore easily be missed, as evidenced by the large number of retrospective cases identified in Amsterdam [5,10]. Furthermore, before 2003 no additional testing was performed routinely when chlamydia proctitis was diagnosed based on positive anal swabs [11]. Further investigation of stored samples of MSM who attended the Amsterdam STI outpatient clinic demonstrated that LGV was circulating already in Amsterdam in 2000 [10]. Also, L2b was identified in patients who had no symptoms at all, suggesting that physical examination alone may not exclude LGV [5,12]. We believe that the actual number of cases is much higher than we have reported, due to underdiagnosis, lack of adequate diagnostics, misclassification and underreporting.

This current epidemic may reflect an increase in unsafe sexual behaviour, as has also been suggested by recent increases in several other STIs in MSM, such as syphilis, rectal gonorrhoea, and quinolone-resistant *N. gonorrhoeae*. [13-16]. It is important from a public health perspective because consequences for HIV transmission are as yet unclear. Behavioural data from the enhanced LGV surveillance is limited due to the small number, however preliminary results suggest that this group of MSM had multiple sex partners, practised 'rough' insertive techniques, and used condoms infrequently. This behaviour, together with their positive HIV status, can result in increased transmission of HIV. In a retrospective case-control study a positive HIV status was identified as the strongest risk factor for LGV [12]. If both partners are HIV positive, the risk of causing a new infection is reduced, but the effects of super-infection are yet unclear. In the here presented group, 10 HIV positive individuals reported that they never disclosed their HIV status to their sex partners.

The ulcerative character of LGV may facilitate transmission and acquisition of HIV, other STIs and bloodborne diseases, particularly in combination with specific sexual techniques that may lead to mucosal damage [6,7]. In Rotterdam, at least two cases with seroconversion for HIV were confirmed and five cases of recent hepatitis C virus (HCV) infection were found [17]. Hepatitis C is not normally considered as an STI, but ulcerative lesions in one of the partners together with high-risk behaviour

may enable the transmission of HCV during sex [7]. Furthermore, a rise was observed in the number of notified cases of HCV in 2004 in the Netherlands [18]. The increase coincided with the LGV outbreak in time and in most cases sexual contact between men was the most likely route of transmission reported for these new HCV infections [18].

The enhanced surveillance of LGV is currently being evaluated in the Netherlands. Our results so far suggest that non-response increases with the sensitivity of the topics. The response to the routinely collected attributes on STI surveillance was 92%. However, the basic dataset lacks the sensitivity to identify the risk factors for this outbreak in this specific group of MSM. In the enhanced surveillance questionnaire, specific questions were included, based upon the investigation of the first cluster of cases in Rotterdam, and yet, detailed information on sexual behaviour was available for only a few individuals. This may reflect not only the reluctance of the patients to disclose the information, but other reasons as well, such as low levels of staffing at MHS or clinic, no extra time available, patient could not be reached, etc. Obtaining reliable information on sexual behaviour requires professional and time-consuming interviewing. Furthermore, detailed information on the patients attending the Amsterdam STI outpatient clinic is not yet available. As 68% of the cases were diagnosed in this STI clinic, this affects our current insight into the epidemiological features.

The number of recently reported cases in the Netherlands is relatively low, suggesting that the epidemic may have already peaked. The rapid dissemination of information to healthcare providers may have facilitated the recognition of clinical signs. Also, adequate diagnostics (e.g. real time PCR) and treatment may have contributed to have prevented further spread of cases. However, LGV cases may still be missed if appropriate diagnostics are not available or if the diagnosis of LGV is not considered. LGV has occurred in a network of MSM in several different countries, and clinicians and health authorities in Europe and the US should remain alert to the occurrence of LGV and associated infections.

#### Acknowledgements

The authors thank clinicians and public health services for the reporting of cases.

#### References

- Götz H, Nieuwenhuis R, Ossewaarde T, Thio B, van der Meijden W, Dees J, de Zwart O. Preliminary report of an outbreak of lymphogranuloma venereum in homosexual men in the Netherlands, with implications for other countries in Western Europe. *Eurosurveillance Weekly*. 2004;1(4) 040122. Available from: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=122>
- Nieuwenhuis RF, Ossewaarde JM, van der Meijden WI, Neumann HAM. Unusual presentation of early lymphogranuloma venereum in an HIV-1 infected patient: effective treatment with 1 g azithromycin. *Sex Transm Infect*. 2003;79(6):453-5.
- Laar MJW van de, et al. Lymphogranuloma Venereum Among Men who have Sex with Men -- The Netherlands; 2003-2004. *MMWR Morb Mortal Wkly Rep*. 2004;53(42):985-8.
- Götz HM, JM Ossewaarde, RF Nieuwenhuis, WI van der Meijden, J Dees, B Thio, O de Zwart, MJW van de Laar. Cluster van Lymphogranuloma venereum onder homoseksuele mannen in Rotterdam - Gevolgen voor de volksgezondheid. *Ned Tijdschr Geneesk*. 2004;148(9):441-2. [in Dutch]
- Spaargaren J, Fennema HS, Morre SA, de Vries HJ, Coutinho RA. New Lymphogranuloma venereum Chlamydia trachomatis variant, Amsterdam. *Emerg Infect Dis*. 2005;11(7):1090-2. <http://www.cdc.gov/ncidod/EID/vol11no07/04-0883.htm#cit>
- Peerenboom RM. Lymphogranuloma venereum proctitis: An emerging sexually transmitted disease in HIV-positive men in the Netherlands. *Drugs Today (Barc)*. 2006;42 Suppl A:43-5.
- Agtmael MA van, Perenboom RM. [Two HIV-positive men with anorectal lymphogranuloma venereum and hepatitis C: emerging sexually transmitted diseases]. *Ned Tijdschr Geneesk*. 2004;148(148): 2544-6. [in Dutch]
- Nieuwkoop C van, J. Gooskens, V.T.H.B.M. Smit, et al. Lymphogranuloma venereum proctocolitis: tweejarig beoog als M.Crohn. *Samenvattingen wetenschappelijke najaarsvergadering VIZ/NVMM*, 2006. *Infectieziekten Bulletin*. 2006;17(8): 259-62 [in Dutch]
- Tinmouth J, Rachlis A, Wesson T, Hsieh E. Lymphogranuloma venereum in North America: case reports and an update for gastroenterologists. *Clin Gastroenterol Hepatol*. 2006;4(4):469-73.
- Spaargaren J, Schachter J, Moncada J, et. al. Slow epidemic of Lymphogranuloma Venereum L2b strain. *Emerg Infect Dis*. 2005 Nov;11(11):1787-8. Available from: <http://www.cdc.gov/ncidod/EID/vol11no11/05-0821.htm>
- Vries HJC de, Fennema JS, Morre SA. Lymphogranuloma venereum among men having sex with men; what have we learned so far? *Sex Transm Infect*. 2006;82(4):344
- Van der Bij AK, Spaargaren J, Morre SA, Fennema HS, Mindel A, Coutinho RA, de Vries HJ. Diagnostics and clinical implications of anorectal lymphogranuloma venereum in men who have sex with men: a retrospective case-control study. *Clin Infect Dis*. 2006;42(2):186-94.
- Rudd E, Fenton KA, Ison C. Ciprofloxacin resistant gonorrhoea in England and Wales - a changing epidemiology. *Eurosurveillance Weekly*. 2004;8(33) 040812. Available from: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=122>
- Centers for Disease Control and Prevention (CDC). Increases in fluoroquinolone-resistant *Neisseria gonorrhoeae* among men who have sex with men -- United States, 2003, and revised recommendations for gonorrhea treatment. *MMWR Morb Mortal Wkly Rep*. 2004;53(16):335-8
- Rietmeijer CA, Patnaik JL, Judson FN, Douglas JM Jr. Increases in gonorrhea and sexual risk behaviors among men who have sex with men: a 12-year trend analysis at the Denver Metro Health Clinic. *Sexually Transm Dis* 2003; 30:562-7.
- Fenton KA, Nicoll A, Kinghorn G. Resurgence of syphilis in England: time for more radical and nationally coordinated approaches. *Sex Transm Infect*. 2001;77(5):309-10.
- Götz HM, Doornum GJJ van, Niesters HGM, et al. A cluster of acute hepatitis C virus infection among men who have sex with men -- results from contact tracing and public health implications. *AIDS*. 2005;19(9):969-74
- Op de Coul ELM, Laar MJW van de. Aangifte acute hepatitis C in 2005. *Infectieziekten Bulletin*. 2006;17(2):77. [in Dutch]

## ORIGINAL ARTICLES

### Surveillance report

# LYMPHOGRANULOMA VENEREUM EMERGING IN MEN WHO HAVE SEX WITH MEN IN GERMANY

V Bremer<sup>1</sup>, T Meyer<sup>2</sup>, U Marcus<sup>1</sup>, O Hamouda<sup>1</sup>

A resurgence of lymphogranuloma venereum (LGV) has been observed in several European countries. LGV is not a mandatorily

notifiable disease in Germany. Reports of LGV cases have actively been collected by the Robert Koch-Institut since 2004 to describe the outbreak and estimate the extent of the LGV problem in Germany. Updates on the LGV outbreak were published in the German national epidemiological bulletin. Physicians were asked to send

- Robert Koch-Institut, Dept. for Infectious Disease Epidemiology, Germany
- Laboratory Prof. Arndt und Partner, Hamburg, Germany