

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.

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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?pubId=2004/040122.asp#1>
- 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 beloop 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?pubId=2004/040812.asp#5>
- 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

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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

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their samples to a laboratory for genotyping. A possible case was defined as a person with symptoms of proctitis and/or inguinal lymph node swelling and a positive chlamydia serology. A probable case had in addition a positive chlamydia rectal or urinary PCR test. A case was confirmed if the genotype L1-L3 was identified based on sequence analysis of *omp1* gene sequences.

Since 2003, LGV has been reported in 78 male patients in Germany. Of these, 61 patients were confirmed as genotype L2. Fifty eight out of 78 patients (74%) are known to be men who have sex with men (MSM). Fifty five patients (71%) had rectal symptoms and 49 (63%) knew they were HIV positive. Sixty two (79%) of the patients were residents of Berlin or Hamburg.

LGV has emerged in MSM in Germany at the same time as in other European countries. It is thought that LGV may become endemic in the MSM community in German metropolitan areas, because the number of reported patients with LGV continues to increase. The increase in the number of LGV cases and the high HIV prevalence in LGV patients are of great public health concern. Clinicians and MSM may not be sufficiently aware of the disease, and existing efforts to promote awareness and prevention of sexually transmitted infections and HIV need to be strengthened.

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Introduction

Lymphogranuloma venereum (LGV) was a notifiable disease under the old venereal disease legislation (Bundesseuchengesetz) in Germany, which was in use until the end of 2000. No case definition was used and the system provided only aggregated case numbers, without information on patients' risk factors [1]. The number of reported LGV infections declined from a median of 35 infections per year between 1990 and 1995) to seven infections per year between 1996 and 2000. Under the new Infektionsschutzgesetz (Protection Against Infection Act) introduced in 2001, the only sexually transmitted infections (STIs) to remain notifiable were HIV and syphilis. At the end of 2002, a nationwide sentinel surveillance system for STIs was introduced by the Robert Koch-Institut to collect information on HIV, chlamydia, gonorrhoea, trichomonas, anogenital warts and genital herpes. LGV was not included, because it was considered a rare tropical disease. After the first alert from the Netherlands in 2004 [2] and the report of the first LGV cases in Germany [3, 4], we asked sentinel and all other physicians and laboratories performing L1-L3 genotyping to voluntarily report LGV cases to the Robert Koch-Institut in order to describe the outbreak and estimate its magnitude.

Methods

The German sentinel surveillance system for STIs collects data from 60 local health offices, 13 hospital-based STI clinics and 159 private practitioners. Private practitioners such as specialists in dermatovenerology, gynaecology, urology and HIV have been chosen at random in all federal states. Sentinel physicians are asked to report LGV cases to the Robert Koch-Institut using sentinel reporting forms.

Updates on LGV were published in the German national epidemiological bulletin [5, 6] which is read by local health authorities and private practitioners. All physicians were asked to send their samples to laboratories that perform chlamydia genotyping. Reports on cases were received from sentinel physicians, other physicians, hospitals and laboratories. We also provided information about LGV to magazines aimed at a gay readership.

A possible case was defined as a person with symptoms of proctitis

and/or inguinal lymph node swelling and a positive chlamydia serology. A probable case also had a positive chlamydia rectal or urinary polymerase chain reaction (PCR) test. A case was confirmed if the genotype L1-L3 was identified, even if the patient's symptoms were unknown.

Chlamydia trachomatis infections sent to the Arndt and Partner diagnostic laboratory were diagnosed by DNA amplification of lesional swabs or lymph node aspirates using PCR (Cobas TaqMan CT, Roche, Mannheim) or strand displacement amplification (ProbeTec ET, Becton-Dickinson, MD). *C. trachomatis* genotypes were identified by sequence analysis of variable *omp1* gene regions (VS1, VS2, and VS4), amplified by PCR using primer pairs MF21/MB22 and MF44/MB4 [6].

Additional patient information was obtained by asking physicians. We described confirmed, probable and possible LGV cases by demographic characteristics and symptoms.

Results

Between May 2004 and November 2005, 61 confirmed and 17 probable or possible cases were reported to the Robert Koch-Institut. All confirmed cases were genotype L2. Reports were received from two local health offices, seven hospital-based STI clinics and 17 private practitioners.

The epidemic curve is shown in figure 1. The median number of monthly reported cases has increased from two in 2004 to four in 2005. All cases were in men, and the mean age was 39 years. Main characteristics of LGV patients are shown in the table. All 58 patients from whom an information on sexual orientation was obtained were MSM. Twenty seven of all 78 cases (35%) had proctitis and 31 had unspecified rectal symptoms. Ten patients showed an inguinal lymph node swelling. Of those, one patient showed confluent lymph nodes with signs of extensive inflammation. Whether this patient was MSM is unknown.

TABLE

Demographic characteristics and clinical picture of possible, probable and laboratory confirmed cases of LGV in Germany, 2003-2005

	Confirmed n=61	Probable n=10	Possible n=7
Sexual orientation			
Men who have sex with men	50	4	4
Unknown sexual orientation	11	6	3
Symptoms*			
Proctitis	14	8	5
Unspecified rectal symptoms	31		
Inguinal lymph node swelling	5	3	2
Unspecified genital symptoms	1		
Unknown symptoms	10		
HIV positive serostatus			
HIV positive	42	3	5
HIV negative	2	0	0
Unknown serostatus	17	7	2

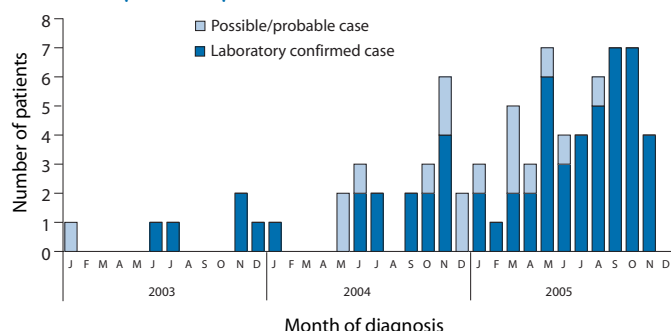
Note: All cases were male

* One patient had rectal and genital symptoms

Of the 52 patients with a known HIV status, 50 (96%) were known to be HIV-positive. Two patients were HIV-negative while the HIV status of 26 patients remains unknown. Patients originated from eight different federal states. Forty five patients (58%) were diagnosed in Hamburg, 17 (22%) in Berlin and 6 (8%) in Munich. The geographical distribution is shown in figure 2.

FIGURE 1

Number of possible, probable and laboratory confirmed cases of Lymphogranuloma venereum by month of diagnosis in Germany, January 2003 – November 2005, n=78



Of 24 patients for whom information on sexual contacts in other countries was available, three reported sexual contacts in the Netherlands and in Belgium. The other 21 patients did not report any contacts outside of Germany.

Discussion

In Germany, the first cases of LGV in MSM were observed at approximately the same time as the first cases in the Netherlands, France, Belgium and the United Kingdom [7-10]. It is possible that the outbreak began among MSM in the Netherlands and subsequently spread to Germany, but this remains unproven. Although information on sexual contacts in other countries was only available for a few German patients, the majority of these patients appear to have become infected in Germany. LGV may therefore have become endemic in the MSM community within two years of detection of the first cases in Germany. Furthermore, the number of reported patients with LGV has increased over the past few months and there are no signs that the epidemic is over. Over 80% of the reported cases have been diagnosed in large cities with a substantial MSM community such as Berlin, Hamburg and Munich. LGV may be more prevalent in these cities, but the difference could also reflect a diagnostic bias. Since the main diagnostic laboratory is situated in Hamburg, awareness among physicians may be higher in Hamburg than elsewhere.

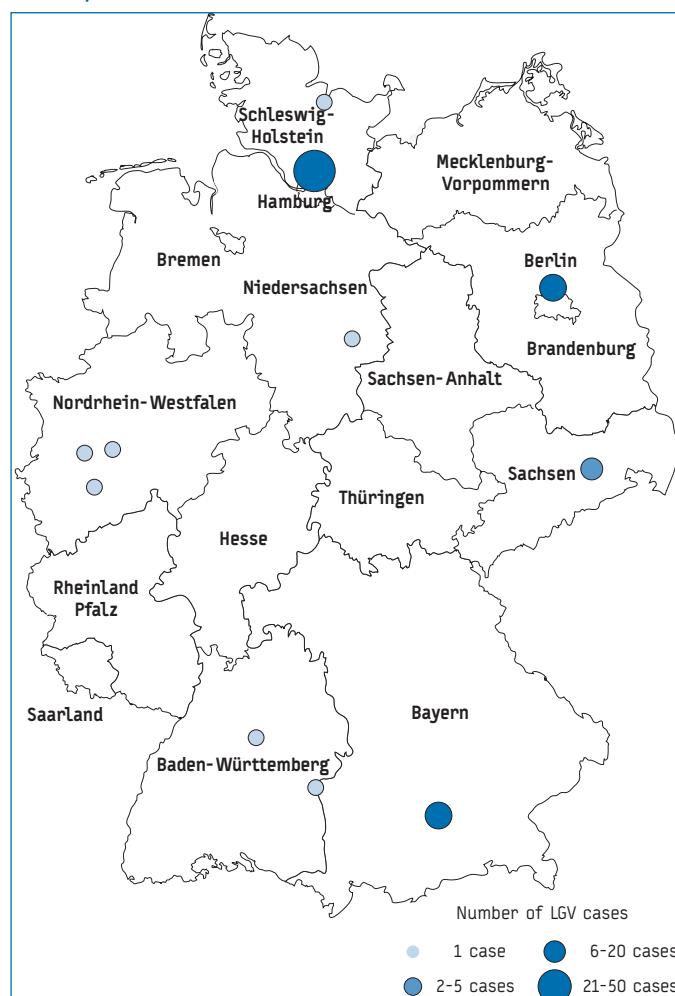
About two thirds of LGV patients knew they were HIV positive at the time of their LGV diagnosis, a feature which has been observed in other countries as well [7, 9]. Reported cases of HIV and syphilis among MSM have also increased over the past three years in Germany [11, 12]. Since LGV facilitates HIV transmission, the emergence of LGV in the MSM community in the context of increasing numbers of newly acquired HIV infections should not be ignored. Clinicians and MSM may not be sufficiently aware of the disease, and existing efforts to promote awareness and prevention of sexually transmitted infections and HIV need to be strengthened.

References

- Petzoldt D, Jappe U, Hartmann M, Hamouda O. Sexually transmitted diseases in Germany. *Int J STD AIDS*. 2002;13(4):246-53.
- Gotz HM, Nieuwenhuis RF, Ossewaarde JM, Thio B, Van der Meijden WI, Dees J, et al. 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;22;1(4) 040122. Available from: <http://www.eurosurveillance.org/ew/2004/040122.asp#1>.
- v Krosigk A, Meyer T, Jordan S, Graefe K, Plettenberg A, Stoehr A. [Dramatic increase in Lymphogranuloma venereum among homosexual men in Hamburg]. *J Dtsch Dermatol Ges*. 2004;2(8):676-80.

FIGURE 2

Geographical distribution of LGV cases in Germany (n=78), January 2003 – November 2005



- Rampf J, Essig A, Hinrichs R, Merkel M, Scharffetter-Kochanek K, Sunderkotter C. Lymphogranuloma venereum - a rare cause of genital ulcers in central Europe. *Dermatology*. 2004;209(3):230-2.
- Robert-Koch-Institut. Zum gehäuftem Auftreten von Lymphogranuloma venereum in Hamburg im Jahr 2003. *Epidemiologisches Bulletin*. 2004;2005(25):197-198. [in German].
- Robert-Koch-Institut. Lymphogranuloma venereum Ausbrüche bei homosexuellen Männern in Europa und Nordamerika - aktueller Stand. *Epidemiologisches Bulletin*. 2005;8(8):65-66. [in German].
- Herida M, Sednaoui P, Couturier E, Neau D, Clerc M, Scieux C, et al. Rectal lymphogranuloma venereum, France. *Emerg Infect Dis*. 2005;11(3):505-6.
- Vandenbruaene M, Ostyn B, Crucitti T, De Schrijver K, Sasse A, Sergeant M, et al. Lymphogranuloma venereum outbreak in men who have sex with men (MSM) in Belgium, January 2004 to July 2005. *Euro Surveill*. 2005;10(9):E050929.3. Available from: <http://www.eurosurveillance.org/ew/2005/050929.asp#3>.
- Nieuwenhuis RF, Ossewaarde JM, Gotz HM, Dees J, Thio HB, Thomeer MG, et al. Resurgence of lymphogranuloma venereum in Western Europe: an outbreak of Chlamydia trachomatis serovar L2 proctitis in The Netherlands among men who have sex with men. *Clin Infect Dis*. 2004;39(7):996-1003.
- Macdonald N, Ison C, Martin I, Alexander S, Lowndes CM, Simms I, et al. Initial results of enhanced surveillance for lymphogranuloma venereum (LGV) in England. *Euro Surveill*. 2005;10(1):E050127.5. Available from: <http://www.eurosurveillance.org/ew/2005/050127.asp#5>.
- Marcus U, Kollan C, Bremer V, Hamouda O. Relation between the HIV and the re-emerging syphilis epidemic among MSM in Germany: an analysis based on anonymous surveillance data. *Sex Transm Infect*. 2005;81(6):456-7.
- Marcus U, Bremer V, Hamouda O. Syphilis surveillance and trends of the syphilis epidemic in Germany since the mid-90s. *Euro Surveill*. 2004;9(12):11-4. Available from: <http://www.eurosurveillance.org/em/v09n12/0912-225.asp>