

ORIGINAL ARTICLE

Lymphogranuloma venereum in men who have sex with men: evidence of local transmission in New Zealand

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Abstract

Lymphogranuloma venereum (LGV) is a sexually transmitted infection caused by *Chlamydia trachomatis*. Five laboratory confirmed cases of LGV were detected in MSM (men who have sex with men) in the upper North Island; four in Auckland between September and December 2013 and a fifth case was detected in Waikato in June 2014. The absence of a recent travel history for four cases supports the likelihood of local transmission of this uncommon infection.

Chlamydia trachomatis is the most common bacterial sexually transmitted infection in New Zealand. In 2013 it was estimated that the national incidence was 633/100,000 population.¹ It commonly causes urogenital infections but less commonly can cause lymphogranuloma venereum (LGV). Urogenital infections are caused by serovars D through to K and LGV is caused by serovars L1, L2 and L3. LGV is endemic in developing countries but was uncommon until the early 2000's in most developed countries. It is infrequently diagnosed in New Zealand with the last cases being reported in 2008². Infection is usually acquired outside of New Zealand.

We report four cases of LGV occurring in late 2013 and a fifth case occurring in June 2014 and hypothesise that locally-acquired infection may have occurred.

Case 1—A 59-year-old male presented to a sexual health clinic in September 2013 with a painless bloody rectal discharge and clinical proctitis on rectal examination. He had returned from a trip to Europe and reported having casual unprotected sexual contact in Germany, France and UK. He was co-infected with *Neisseria gonorrhoeae* and human immunodeficiency virus (HIV). He was treated with 3 weeks of doxycycline.

Case 2—A 46-year-old male presented to a sexual health clinic in October 2013 with anal itch and discomfort for 3 days along with anal ulceration and rectal mucus. He reported having casual unprotected sexual contact but no recent unprotected anal sex or overseas travel. He was co-infected with *N. gonorrhoeae* and HIV and was treated with 3 weeks of doxycycline.

Case 3—A 51-year-old male presented in December 2013 to a sexual health clinic with rectal discharge on defaecation. He reported having casual sexual contact, but no recent unprotected anal sex or receptive “fingering,” nor overseas travel. He was co-infected with HIV and was treated with 3 weeks of doxycycline.

Case 4—A 46-year-old male presented in December 2013 to a general physician with signs consistent with proctitis. He was co-infected with *N. gonorrhoeae*. He reported no recent overseas travel. He was treated with 3 weeks of doxycycline.

Case 5—A 26-year-old male presented to the surgical service at Waikato Hospital in June 2014 with rectal bleeding. He reported casual male sexual partners. He was co-infected with *N. gonorrhoeae*. He denied recent overseas travel. He was treated with 3 weeks of doxycycline.

Diagnosis—The initial detection of *Chlamydia trachomatis* for cases 1–3 was by nucleic acid amplification using the strand displacement method on Viper XTR (Becton Dickenson and Company, Franklin Lakes, NJ, USA). Case 4 was tested on the Cobas 4800 CT/NG (Roche Molecular Diagnostics, Branchburg, NJ, USA) and case 5 on the Abbott Realtime CT/NG assay (Abbott Laboratories, Abbott Park, IL, USA).

The clinical specimens were then referred for confirmation of LGV serotype using an in-house real-time assay based on Morr ³ with modification to allow it to be run on the LightCycler 480 instrument. This assay uses a Taqman probe which targets the section of the polymorphic membrane protein H (*pmpH*) gene containing a deletion present only in the L serovars, thus allowing differentiation between serovars D-K and those serovars causing LGV.

DNA was extracted for this using MagNA Pure LC RNA HP extraction following the manufacturer's protocol (Roche Molecular Diagnostics, Branchburg, NJ, USA) protocol. Further sequencing of the *omp1* gene was performed using method described by Jurstrand⁴ on ABI3130x1 automated sequencer (Applied Biosystems Life Technologies, NY, USA). Briefly, sequencing was performed using both the forward and the reverse primers⁴ which ensured that there was sufficient overlap of sequence and fidelity on the ABI3130x1 automated sequencing run.

The consensus sequence for each specimen was obtained using Seqman (DNASTar software) and then the entire *omp1* gene was aligned against each other and also against those available in the GeneBank database and analysed using the BLASTN programme to get the specific serovars. The L2 serovar can be separated into L2, L2', L2a, or L2b according to amino acid differences. This confirmed that the isolates from case 1 and case 4 belonged to L2 serovar and cases 2, 3 and 5 belonged to the L2b serovar.

Discussion

The diagnosis of LGV was made in four MSM in Auckland over a 3-month period in 2013 and more recently in one MSM in the Waikato in 2014. All of the five cases presented with signs and symptoms consistent with rectal LGV infection including pruritus, anal discomfort or bloody rectal discharge. Four of the cases did not have a history of recent overseas travel and were likely to have acquired their infection locally.

Whilst the epidemiological link between these five cases was not established, they all reported casual sexual contact with other MSM before the onset of symptoms and three of the four were infected with the same LGV serotype. Prior to these five cases, no cases had been reported in New Zealand since 2008 when two HIV-positive MSM, who had travelled to Australia within the preceding 6 months, presented to sexual health clinics and were diagnosed with LGV. It was presumed that they had acquired the infection in Australia.² LGV is caused by serovars L1–L3 of *C. trachomatis*.

After an incubation period of 3–30 days a primary lesion develops at the site of inoculation. The small, painless papule may ulcerate, heal spontaneously and leave no residual scar. If the primary infection involves the rectum the mucosa becomes hyperaemic and friable. Multiple discrete superficial ulcers with irregular borders develop and the mucosa can be replaced with granulomas and crypt abscesses form.⁵ The secondary stage of the infection is characterised by involvement of the lymph nodes draining the primary lesion. This stage may be associated with systemic features such as malaise, fever and headaches.⁶

Since 2003 different outbreaks or clusters of LGV have occurred in Europe, North America and Australia among MSM.^{6,7} Serovar L2b has been identified as the main causative agent of

the epidemic and serovar L2 has been associated with recent clusters in Austria in 2008⁸ and in Northern Italy in 2012-2013.⁹

In our series, cases 2, 3, and 5 reported no recent overseas travel and were infected with serovar L2b. Case 1 with reported overseas travel was infected with serovar L2, the same serovar as case 4 with no overseas travel. This suggests that both epidemic serovars have been introduced locally, presumably by New Zealand residents infected overseas or potentially by visitors to New Zealand.

The majority of cases in these outbreaks were MSM co-infected with HIV with high risk sexual behaviour and a high rate of concomitant sexually transmitted infections¹⁰. All cases in our series reported high-risk sexual behaviour and concomitant sexually-transmitted infections were noted with case 1, 2, 4, and 5 were co-infected with *N. gonorrhoeae* and cases 1-3 co-infected with HIV. A recent multi-centre case-control study from the United Kingdom reported that 89% of all cases were co-infected with HIV and identified unprotected receptive anal intercourse as the key factor for rectal LGV (Adjusted OR 10.7, 95%CI 3.5-32.8).¹¹

The prevalence of anogenital *C. trachomatis* in MSM in New Zealand is unknown but in Australia is estimated at 5.6% (95% CI: 4.8-6.3);¹² serovars D, G and J predominate¹³ and infections tend to be asymptomatic. LGV remains uncommon but is more likely to be associated with anal symptoms.¹⁴ Therefore, LGV should be considered in MSM presenting with rectal pain, mucopurulent or bloody discharge, cramping abdominal pain, constipation and tenesmus regardless of whether they have a history of recent overseas travel or not.

In New Zealand, as in other countries, additional testing for LGV serovars on rectal swabs that are positive by a molecular assay for *C. trachomatis*, is currently only done on request by the clinician and specialist advice may be required regarding local laboratory requirements. The absence of clinical symptoms should not distract from additional testing if the clinical index of suspicion is high as in one series 40% of LGV cases were pauci-symptomatic or asymptomatic.⁶ However, in general anal symptoms are present and for this reason there is limited evidence to support routine screening of asymptomatic MSM for LGV.¹³

LGV is curable with antibiotics but if left untreated it can have serious and permanent adverse sequelae.¹⁵ Longer treatment courses with either doxycycline or a macrolide are required for LGV compared to urogenital *C. trachomatis* infections. Newer antimicrobial agents may have a role but clinical data is lacking.¹⁵ Test of cure is not considered necessary if the recommended 21-day treatment course is followed. The assessment of sexual contacts of a patient with LGV within the 4 weeks before onset of symptoms or the last 3 months if asymptomatic LGV is detected is recommended.¹⁵

LGV is not a notifiable disease in New Zealand and surveillance is limited to voluntary reporting from sentinel clinics. Routine STI testing for at-risk groups including anorectal specimen collection in MSM is recommended in national guidelines but implementation is not monitored.¹⁶ Accurate diagnosis, and awareness of the need for specific LGV testing in high risk patients who test positive for *C. trachomatis* infection is essential for accurate diagnosis. Public health strategies including targeted health promotion to raise awareness and enhanced surveillance may need to be developed to reduce ongoing local transmission of LGV infection in New Zealand.

Competing interests: Nil.

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References

1. The Institute of Environmental Science and research Ltd. Sexually Transmitted Infections in New Zealand: Annual Surveillance Report. Porirua, Wellington; 2013.
2. Robertson A, Azariah S, Bromhead C, et al. Case report: LGV in NZ. *Sexual Health*. 2008;5:369–370.
3. Morr  SA, Spaaregaren J, Fennema JS, et al. Real-time polymerase chain reaction to diagnose Lymphogranuloma venereum. *Emerg Infect Dis*. 2005;11:1311–2.
4. Jurstrand M, Falk L, Fredlund H, et al. Characterization of Chlamydia trachomatis omp1 genotypes among sexually transmitted disease patients in Sweden. *J Clin Microbiol*. 2001;39:3915–3919.
5. Richardson D, Goldmeier D. Lymphogranuloma venereum: an emerging cause of proctitis in men who have sex with men. *Int J STD & AIDS*. 2007;18:11–15.
6. Martin-Iguacel R, Llibre JM, Nielsen H, et al. Lymphogranuloma venereum proctocolitis: a silent endemic disease in men who have sex with men in industrialised countries. *Eur J Clin Microbiol Infect Dis*. 2010;29:917–25.
7. Stark D, van Hal S, Hillman R, et al. Lymphogranuloma venereum in Australia: anorectal Chlamydia trachomatis serovar L2b in men who have sex with men. *J Clin Microbiol*. 2007;45:1029–1031.
8. Sary G, Meyer T, Bangert C. New Chlamydia trachomatis L2 strains identified in a recent outbreak of Lymphogranuloma Venereum in Vienna, Austria. *Sex Trans Dis*. 2008;35:377–82.
9. Foschi C, Marangoni A, D’Antuono A, et al. Prevalence and predictors of Lymphogranuloma venereum in a high risk population attending a STD outpatients clinic in Italy. *BMC Research Notes* 2014;7:225.
10. deVries HJC, Van Der Bij AK, Fennema JSA, et al. Lymphogranuloma venereum proctitis in men who have sex with men is associated with anal enema use and high-risk behaviour. *Sex Trans Dis* 2008;35:203–208.
11. Macdonald N, Sullivan AK, French P, et al. Risk factors for rectal lymphogranuloma venereum in gay men: results of a multicentre case-control study in the UK. *Sex Trans Infect*. 2014;90:262–268.
12. Lewis D, Newton DC, Guy RJ, et al. The prevalence of Chlamydia trachomatis infection in Australia: a systematic review and meta-analysis. *BMC Infect Dis*. 2012;12:113.
13. Twin J, Moore EE, Garland S, et al. Chlamydia trachomatis genotypes among men who have sex with men in Australia. 2011;38:279–85.
14. Templeton DJ, Sharp N, Gryllis S, et al. Prevalence and predictors of lymphogranuloma venereum among men who sex with men at a Sydney metropolitan sexual health clinic. *Sexual Health* 2013;10:190–1.

<http://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2015/vol-128-no-1410/6456>

15. White J, O'Farrell, Daniels D. UK National Guidelines for the management of lymphogranuloma venereum. *Int J STD & AIDS*. 2013;24:593–601.
16. The New Zealand Sexual Health Society. Sexually Transmitted Infections; Summary of Guidelines, 2013. http://www.nzshs.org/guidelines/STI_Summary_of_Guidelines_2013.pdf (Accessed 28 November 2014)