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Lymphogranuloma venereum in British Columbia, 2011 to 2015: Epidemiology and risk factors

A study comparing reports of lymphogranuloma venereum in two periods (2011 to 2014 and 2015) found that the characteristics of cases were similar, except for a decrease in patients self-identifying as Caucasian in 2015.

ABSTRACT

Background: **Lymphogranuloma venereum (LGV) is a sexually transmitted infection with potentially serious sequelae. We sought to describe the epidemiology of this infection in BC and explore reasons for the doubling of cases seen when data from 2015 were compared with data from 2011 to 2014.**

Methods: **All cases of LGV reported in BC from 2011 to 2015 were identified through surveillance and laboratory databases. The characteristics of cases, including patient risk factors, and the positivity rate for LGV test results in 2011 to 2014 and 2015 were assessed using descriptive statistics.**

Results: **From 2011 to 2015, 125 cases of LGV were reported in BC. The characteristics of cases reported in 2011 to 2014 and in 2015 were not significantly different, except for a decrease in cases involving patients self-identifying as Caucasian (62% in 2015 versus 76% in 2011 to 2014). There was a trend toward an increase in the proportion of cases with asymptomatic presentation (*P* = .20) and patients residing outside Vancouver Coastal Health (*P* = .06). The positivity rate for LGV test results in 2011 to 2014 was similar to that of 2015 (*P* = .78).**

Conclusions: **Lymphogranuloma venereum cases continue to increase in BC, likely in part because of increased awareness and testing. Primary care providers should consider this infection in the differential diagnosis and screen for LGV in high-risk subpopulations.**

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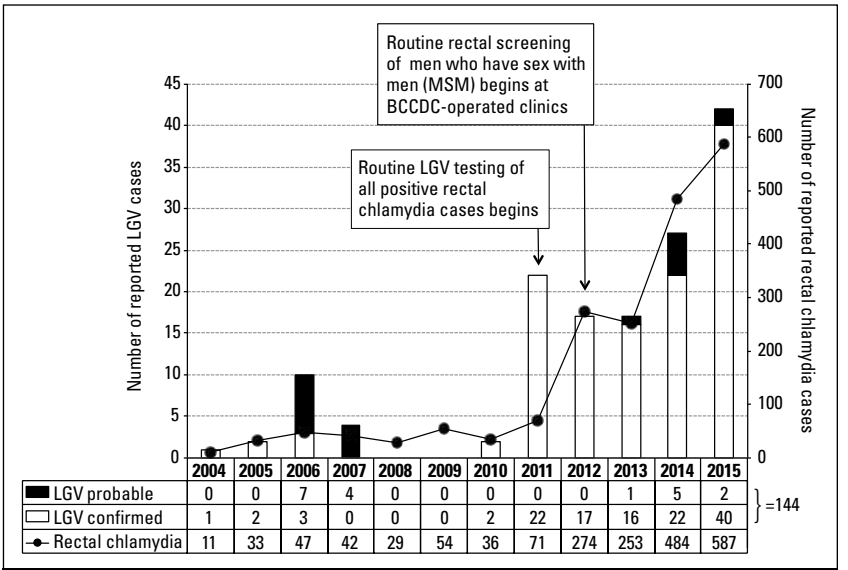
Background

Lymphogranuloma venereum (LGV) is a sexually transmitted infection (STI) caused by *Chlamydia trachomatis* serovars L1, L2, L2b, and L3. These serovars preferentially target lymph tissues, often leading to symptoms more severe than those presented by non-LGV chlamydia. Clinical presentation of LGV may include genital ulcers, inguinal lymphadenopathy, and hemorrhagic proctitis. Left untreated, LGV may lead to serious sequelae such as lymphatic obstruction, chronic ulcerations, abscesses, or colorectal strictures and fistulae.

LGV is endemic in many tropical and subtropical countries, but generally rare in Canada. Local transmission of LGV was first reported in Canada in 2003 and in BC in 2004. Over the past decade, LGV has become increasingly common in North America[1-3] and Europe[4-7] among gay, bisexual, and other men who have sex with men (MSM). These epidemics were caused almost exclusively by the L2b serovar.[8,9]

Since 2004, there have been 144 LGV cases (probable and confirmed) reported in BC (**Figure**). From 2004 to 2010, 2.7 LGV cases, on average, were reported each year. During this time, LGV serovar testing was performed only at the request of a clinician. Since July 2011, rectal specimens positive for chlamydia were routinely forwarded to the National Microbiology Laboratory (NML) for LGV serovar testing in an effort to increase detection of LGV. In addition, since 2012, clinics operated by the BC Centre for Disease Control (BCCDC), some of which serve MSM patients predominantly, have been routinely screening for chlamydia from pharyngeal and rectal sites when patients report behaviors that may put them at risk for infections at these sites. From 2011 to 2014, there were 83 cases of LGV reported (mean, 21 cases per year). However, in 2015, reports of LGV doubled to 42 cases.



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
LGV probable	0	0	7	4	0	0	0	0	0	1	5	2
LGV confirmed	1	2	3	0	0	0	2	22	17	16	22	40
Rectal chlamydia	11	33	47	42	29	54	36	71	274	253	484	587

=144

Figure. Reported cases of lymphogranuloma venereum (LGV) and rectal chlamydia in British Columbia, 2004 to 2015.

Given the substantial increase in LGV cases reported, we sought to characterize LGV cases in BC since 2011 when the current LGV serovar testing process was implemented, and explore possible reasons for the increase in LGV observed.

Methods

A confirmed case of LGV is defined as one with a specimen testing positive by DNA sequencing for *C. trachomatis* serovars L1, L2, L2b, or L3. In Canada, all LGV serovar testing is performed by the NML.[10,11] A probable case of LGV is defined as one with a positive nucleic acid amplification test (NAAT) or culture for *C. trachomatis* and either proctitis, inguinal or femoral lymphadenopathy, a suspicious lesion, or reports of a sexual partner confirmed or likely to have LGV or with clinical symptoms consistent with LGV and reports of a sexual partner confirmed or likely to have LGV.

Case-finding and data collection

All genital chlamydia diagnoses, including LGV, are reportable under the BC Public Health Act and recorded in the provincial STI Information System (STI-IS). Since July 2011, rectal specimens that test positive for chlamydia in BC are routinely forwarded to the NML for LGV serovar testing via the BCCDC Public Health Laboratory (PHL), regardless of which laboratory performed the chlamydia testing.

All LGV cases diagnosed in BC are followed up by public health nurses located at the BCCDC. These nurses notify the patient and/or the testing clinician and collect demographic and behavioral information using an enhanced case report form and document findings in the STI-IS.

All confirmed and probable cases of LGV recorded in the STI-IS from 1 January 2011 to 31 December 2015 were included in the study. Laboratory data from the BCCDC PHL during this period were also reviewed for cases that may have been missed.

Data analysis

Descriptive statistics were used to summarize demographic, clinical, and behavioral characteristics of LGV cases in two reporting periods: 2011 to 2014 and 2015. Changes in characteristics of LGV cases were assessed using the chi-square test or Fisher exact test for categorical variables and the Wilcoxon rank sum test for continuous variables.

LGV positivity rate was calculated as the number of LGV cases (probable and confirmed) over the LGV test volume each year. LGV test volumes were defined as the number of specimens sent to NML for LGV testing in the BCCDC PHL database. Differences in positivity rates were assessed using a two-sided proportion *z* test.

Data were analyzed using R-Studio 3.2.1 (RStudio Inc, Boston MA). A P value of $< .05$ was considered statistically significant.

This study was undertaken to understand the provincial epidemiology of LGV, which falls under the BCCDC public health mandate. Thus, institutional ethics review was not required. Data for this study are under the stewardship of the BCCDC and BCCDC PHL.

Results

All 125 cases of LGV identified from 2011 to 2015 involved men who have sex with men. **Table 1** describes the characteristics of 83 LGV cases reported in 2011 to 2014 and 42 cases reported in 2015.

Characteristics and risk factors of LGV cases diagnosed in both periods were similar, with the exception of ethnicity. When comparing the two periods, 76% of patients (63 of 83) self-identified as Caucasian in 2011 to 2014, while only 62% of patients (26 of 42) self-identified as Caucasian in 2015 ($P = .004$). An increas-

Table 1. Characteristics of 83 lymphogranuloma venereum (LGV) cases reported in British Columbia in 2011 to 2014 and 42 cases reported in 2015.

Characteristics		2011–2014 n (%)	2015 n (%)	*P*-value
Laboratory results	LGV confirmed	77 (93)	40 (95)	.72
	LGV probable	6 (7)	2 (5)	
Gender	Male	83 (100)	42 (100)	
	Female	0 (0)	0 (0)	
Gender of sexual partners	Male only	78 (94)	40 (95)	1
	Male and female	5 (6)	2 (5)	
Age group (in years)	20–24	6 (7)	2 (5)	.42
	25–29	7 (8)	6 (14)	
	30–39	11 (13)	10 (24)	
	40–59	54 (65)	22 (52)	
	60+	5 (6)	2 (5)	
	Median age (interquartile range)	46 years (36–51)	44 years (31–48)	.18
Ethnicity (self-identified)	Caucasian	63 (76)	26 (62)	.004
	Aboriginal	6 (7)	0 (0)	
	Hispanic	2 (2)	8 (19)	
	Asian	8 (10)	3 (7)	
	Other (a)	3 (4)	4 (10)	
	Unknown	1 (1)	1 (2)	
Residence by health authority	Interior	0 (0)	3 (7)	.06
	Fraser	7 (8)	5 (12)	
	Vancouver Coastal	69 (83)	29 (69)	
	Vancouver Island	7 (8)	5 (12)	
Signs and symptoms (b)	Proctitis (c)	57 (69)	24 (57)	.2
	Asymptomatic (d)	7 (8)	8 (19)	
	Inguinal lymphadenopathy	10 (12)	6 (14)	
	Lesion	3 (4)	1 (2)	
	Other	1 (1)	0 (0)	
	Unknown	5 (6)	3 (7)	
HIV status	Positive	54 (65)	25 (60)	.61
	Negative	25 (30)	16 (38)	
	Unknown	4 (5)	1 (2)	
HIV viral load (e) in LGV cases co-infected with HIV	Undetectable (< 40 copies/mL)	34 (63)	18 (72)	.38
	Low (40–1000 copies/mL)	11 (20)	2 (8)	
	High (> 1000 copies/mL)	2 (4)	3 (12)	
	Unknown	7 (13)	2 (8)	
Co-infection (f)	Genital gonorrhea only	12 (14)	8 (19)	.74
	Infectious syphilis only	7 (8)	4 (10)	
	Genital gonorrhea and infectious syphilis	2 (2)	2 (5)	
	None	62 (75)	28 (67)	
Recreational drug use	By rectal route	Data not available	11 (26)	
	Not by rectal route		20 (48)	
	Unknown		11 (26)	

(a) Other ethnicity refers to Arab, Black, South Asian, and other/mixed ethnicity.
(b) Signs and symptoms categorized in accordance with the hierarchy: (1) inguinal lymphadenopathy, (2) lesion, (3) proctitis, and (4) other
(c) Proctitis includes the clinical diagnosis of proctitis and/or ≥ 1 of the following anal/rectal symptoms: mucous discharge, bleeding, frequent bowel movements, persistent diarrhea, constipation, bloody stools, burning or itchiness, pain, lesions, or discomfort.
(d) Phrase "asymptomatic" or "no symptoms" was documented in case chart.
(e) Viral load collection date was 3 months prior or after rectal specimen collection date for initial *Chlamydia trachomatis*.
(f) Co-infection defined as genital gonorrhea and/or infectious syphilis reported into the provincial STI Information System at time of LGV diagnosis or ± 7 days of LGV specimen collection date.

ing proportion of LGV cases involved asymptomatic patients and patients residing outside of Vancouver Coastal Health, although these increases were not statistically significant. Over one-third of cases involving recreational drug use in 2015 (11 of 31 cases) reported administration by rectal route. Data for this were not collected previously, however, so a comparison with past years was not possible.

The positivity rate for LGV was highest at 51.2% in 2011, the same year routine LGV testing of positive rectal chlamydia samples was implemented, then fell to 6.4% in 2012 to 2014 (**Table 2**). Overall, the positivity rate for LGV in 2011 to 2014 was similar to that of 2015 ($P = .78$), and the difference between rates for 2012 to 2014 and 2015 was not statistically significant ($P = .27$).

Conclusions

In 2015, the number of LGV cases reported in BC reached an all-time high of 42. The *C. trachomatis* serovar identified in all LGV cases was L2b, consistent with LGV cases reported for MSM in other jurisdictions.[1,2,4-7] Characteristics and risk factors for LGV cases reported in 2011 to 2014 were similar when compared to those of cases reported in 2015, with the exception of ethnicity. The proportion of cases reporting an ethnic identity other than Caucasian was higher in 2015 than in 2011 to 2014. This pattern mirrors the epidemiology data of both infectious syphilis[12] and HIV[13] in BC, which may be the result of increased testing in non-Caucasian populations, a greater proportion of ethnic minorities engaging in higher-risk sexual behaviors,[14,15] or tightly interconnected sexual networks of same-ethnicity partners among non-Caucasians.[16]

The positivity rate for LGV was highest in 2011 when routine LGV testing of rectal chlamydia samples was implemented, but fell in 2012 when routine screening for rectal STIs commenced. Since 2012, the increase in LGV diagnoses has generally followed the increase in LGV testing, suggesting that increased screening for rectal STIs may be the reason for the greater number of cases reported. This is consistent with a lack of change in the characteristics of LGV cases in recent years, and an increase in the proportion of asymptomatic cases.

The increase in LGV cases among MSM mirrors increases in other STIs in BC. While the reason for these increases is not definitively known, increased awareness and regular screening may be increasing detection of STIs. Changes in sexual practices in response to reduced anxiety about HIV transmission and acquisition with the availability of highly effective antiretroviral therapy (i.e., HIV treatment optimism) may also be increasing STI transmission.[17,18]

A substantial proportion of cases in 2015 involved rectal use of recreational drugs. Other jurisdictions have reported similar findings.[19,20] This practice may have a synergistic effect on STI transmission, with the presence of drugs in the rectum causing trauma to the rectal mucosae or condom breakage that can lead to an increased risk of transmitting or acquiring LGV. Sexual practices such as anal enema use, anoreceptive sharing of sex toys, and being fisted may also cause damage to the rectal mucosae.[21,22]

Almost two-thirds of patients in LGV cases were co-infected with HIV. This may be due to higher screening rates for LGV (and other STIs), but given the fact that most LGV infections are symptomatic, it is more likely that people living with HIV have a higher risk of acquiring LGV. HIV infection has been shown to affect the innate immune response.[23] Also, the practice of serosorting (choosing sexual partners with the same HIV status) may lead to reduced condom use,[24] thus increasing the transmission of other STIs.[25] While there is concern that LGV may increase the transmission of HIV, the vast majority of LGV patients co-infected with HIV in our study population had undetectable viral loads, likely making the risk of HIV transmission low. Nevertheless, the presence of mucosal inflammation from concomitant STIs such as LGV may alter the risk of HIV transmission, even with virologic suppression.[26] Further study is needed to understand LGV trends among HIV-positive MSM, who are disproportionately affected by LGV.

Table 2. Positivity rate for lymphogranuloma venereum (LVG) tests requested in British Columbia in 2011 to 2014 and in 2015.

Year	LGV tests requested	LGV cases identified	Positivity rate
2011–2014 totals	994	83	8.4%
2011	43	22	51.2%
2012	257	17	6.4%
2013	217	17	7.8%
2014	477	27	5.7%
2015 totals	529	42	7.9%

In 2015, the number of LGV cases reported in BC reached an all-time high of 42.

Study limitations

Although our findings are consistent with those reported in other LGV studies, they are subject to limitations. One limitation is that only individuals diagnosed with LGV were included in the study, which may mean that populations more likely to be screened (e.g., MSM who are "out" to their health care providers or people living with HIV) are overrepresented in the LGV case counts. Another limitation is that only rectal chlamydia specimens were routinely sent for LGV serovar testing, which may mean that LGV infections from other body sites have been missed. Lastly, the risk factor information collected was subject to recall or social desirability bias and may be inaccurate.

Summary

As in other jurisdictions, reports of LGV have been increasing in BC over the past decade. In 2015 there were 42 cases reported, twice the mean number of cases in the previous 4 years. However, the characteristics of LGV cases have generally been consistent from 2011 to 2015. The positivity rate has also been stable during this period, suggesting that the increase observed in 2015 is likely due to increased awareness and case-finding.

While the majority of cases are symptomatic, the proportion of asymptomatic cases has increased recently. Primary care providers should offer routine STI screening for sexually active patients and consider LGV in the differential diagnosis for patients in a high-risk group, such as MSM living with HIV. More study of recreational drug use, particularly around the time of sex or to enhance sex, is warranted to better understand the potentially synergistic effect of this practice on STI transmission.

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Competing interests

None declared.

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