

**TABLES OF EVIDENCE 2009-2013
LYMPHOGRANULOMA VENEREUM**

MEDLINE SEARCH STRATEGY:

- 1 lymphogranuloma venereum.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier] (402)
- 2 lgv.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier] (203)
- 3 1 or 2 (468)

ALSO SEARCHED:

ISSTDR 2009 (London), National STD Prevention Conf. 2010 (Atlanta), ISSTDR 2011 (Quebec), National STD Prevention Conf 2012 (Minneapolis)

Citation	Study Design	Study Population	Exposure / Intervention	Outcome Measures	Reported Findings	Design Analysis Quality / Biases
LGV Treatment						
deVries HJC et al. European guideline for the management of lymphogranuloma venereum, 2010. Int J STD AIDS 2010; 21:533-6.	Guideline	Meta-analysis	Review of literature on clinical management of LGV	Appropriate clinical management of LGV	First line therapy: doxycycline 100 mg twice daily x 21 days. Second line therapy: erythromycin 500 mg four times daily x 21 days	Azithromycin has been proposed, but evidence lacking to support this medication
Mechai F et al. Doxycycline failure in lymphogranuloma venereum. Sex Transm Infect 2010; 86: 278-9.	Case report	1 pt with LGV (France)	Treatment with doxycycline	Resolution of proctitis and lymphadenopathy	Anal pain, anal ulceration, and inguinal lymphadenopathy, not improving despite > 3 weeks of doxycycline. Recovered after treatment with moxifloxacin 400 mg daily x 10 days.	HIV-negative male. LGV diagnosis presumed from clinical presentation (but not confirmed L2 serovar)
Cunningham et al						All pts responded to 3

2012; Geisler et al. 2012, Vanousova et al. 2012; Peuchant et al. 2012, Hoie et al. 2012; Heras et al 2011; Singhraj et al. 2011; Kamarashev et al. 2010; Flexor et al. 2010; Vall-Mayans et al. 2009; Heras et al 2009; El Karoui et al 2009						weeks of doxycycline EXCEPT: -Geisler: pt improved after 3 wks, clinically cured after add'l 3 wks of doxy. -Kamarashev: 1 pt treated with azithromycin 1 gm; others received doxy for 10-20 days; - El Kouri: pts received doxy for 30 days.
LGV Clinical Manifestations						
Arnold CA et al. Syphilitic and lymphogranuloma venereum (LGV) proctocolitis: clues to a frequently missed diagnosis. Am J Surg Pathol 2013; 37:38-46.	Case series	7 syphilis pts, 2 LGV pts, 1 syphilis/LGV pt (USA)	Clinically-confirmed LGV or syphilis	Histologic core features of anocolonic biopsies	Biopsies showed intense lympho-histiocytic infiltrate w/prominent plasma cells & lymphoid aggregates, mild-to-moderate inflammation, rare granulomas.	None of the initial impressions included LGV. Clinical correlates of 10 pts were: HIV+ (10), MSM (9), bleeding (9), ulcerations (7), pain (6), tenesmus (4).
Gallegos M et al. Lymphogranuloma venereum proctosigmoiditis is a mimicker of inflammatory bowel disease. World J Gastroenterol 2012; 18	Case series	3 pts with rectal LGV (USA)	LGV procto-sigmoiditis	Clinical and endoscopic correlates of LGV	Cases characterized by incomplete/undisclosed history, and endoscopic/histologic findings suggesting inflammatory bowel disease (IBD)	Consider LGV after failure to respond to IBD therapy, further history is elicited (travel, MSM), positive Chlamydia test, or adequate response to antibiotics.
Verweij SP et al. The first case record of a female patient	Case report	1 pt with inguinal bubo (Netherlands)	C. trachomatis infection	Confirmation of L2b serovariant	Real-time PCR confirmation of C. trachomatis, serovariant	First case report of female with bubonic LGV caused by L2b serovariant

with bubonic lymphogranuloma venereum (LGV), serovariant L2b. Sex Transm Infect 2012; 88:346-7.					L2b	(probably from bisexual male partners)
Cunningham SE et al. Lymphogranuloma venereum proctitis. Gastrointestinal Endoscopy 2012; 75:1269-70.	Case report	1 pt with rectal LGV (USA)	LGV proctitis	Clinical and endoscopic correlates of LGV	Pt had 6 months of hematochezia, rectal pain. Colonoscopy showed multiple rectal ulcers with thick white exudate, erythema.	HIV+, CD4=429. CDC confirmed L2 serotype. Responded to 3 weeks of doxycycline.
Kennedy JE, Higgins SP. Complicated lymphogranuloma venereum infection mimicking deep vein thrombosis in an HIV-positive man. Intl J STD AIDS 2012; 23:219-20.	Case report	1 pt with LGV (UK)	LGV proctitis with reactive arthropathy	Clinical correlates of LGV infection	LGV proctitis was followed by reactive arthropathy which mimicked DVT (acute swelling of lower limb)	HIV+ MSM. Early treatment of LGV may have prevented reactive arthropathy.
Geisler WM et al. Chronic rectal bleeding due to lymphogranuloma venereum proctocolitis. Am J Gastroenterol 2012; 107:488-9.	Case report	1 pt with LGV (USA)	LGV proctocolitis (L2b variant confirmed by ompA sequencing)	Clinical correlates of LGV infection	Pt had chronic rectal bleeding x 3 months, with mucoid discharge, tenesmus. Colonoscopy revealed erythema, friability, shallow and deep ulcers, with active focal colitis in cecum, sigmoid, and rectum.	HIV+ MSM. 21 day course of doxy improved symptoms; repeat treatment led to clinical cure.
Vanousova D et al. First detection of Chlamydia trachomatis LGV biovar in the Czech Republic, 2010-2011. Euro	Case series	4 pts with LGV (Czech Republic)	LGV proctitis (LGV genotype confirmed by PCR amplification of pmpH gene)	Clinical correlates of LGV infection	Symptoms included intense rectal pain, blood in stool, mucus discharge, tenesmus, constipation. Endoscopy showed congested, irritated	All were HIV+ MSM. Lymph node abscess occurred in 1 pt. Treatment with oral doxycycline was curative.

Surveillance 2012; 17(2).					mucus membranes.	
Vargas-Leguas H et al. Lymphogranuloma venereum: a hidden emerging problem, Barcelona 2011. Euro Surveillance 2012; 17(2).	Case series	146 pts with LGV (Spain)	C. trachomatis infection with L serovar confirmed by rt-PCR	Epidemiological and clinical characteristics of LGV	Most cases were HIV+ MSM with proctitis. Median 35 days from symptom onset to diagnosis.	70 cases were reported in 2011 (compared with 69 reported from 2007-2010) – control measures ramped up.
Peuchant et al. First case of Chlamydia trachomatis L2b proctitis in a woman. Clin Microbiol Infect 2011; 17(12):E21-3.	Case report	1 pt with LGV (France)	LGV proctitis (L2b variant – confirmed by ompA genotype and sequencing)	Clinical correlates of LGV infection	Symptoms included anorectal pain, mucopurulent discharge, rectal bleeding, tenesmus. Colonoscopy showed ulcerative proctitis.	HIV-negative with multiple sex partners. Responded to 3 weeks of doxycycline.
Ronn MM, Ward H. The association between lymphogranuloma venereum and HIV among men who have sex with men: systematic review and meta-analysis. BMC Infect Dis 2011; 11:70.	Meta-analysis	Published studies of LGV among MSM (17 studies, 1145 pts)	LGV infection	HIV infection among MSM with LGV	O.R. 8.19 for HIV+ among LGV patients (95% CI 4.68-14.33)	Raw pooled HIV prevalence estimate of 77.9% among MSM with LGV
Quint KD et al. Anal infections with concomitant Chlamydia trachomatis genotypes among men who have sex with men in Amsterdam, the Netherlands. BMC Infect Dis 2011; 11:63.	Case series	201 Ct-positive rectal swabs from MSM (99 LGV, 102 non-LGV)	Rectal Ct infection	Detection of concomitant Ct genotypes in Ct+ specimens	Concomitant non-LGV genotype was detected in 6.1% of LGV samples. No concomitant LGV infections were identified in the non-LGV samples.	Concomitant non-LGV genotypes do not lead to missed LGV diagnoses.

Hoie S et al. Lymphogranuloma venereum proctitis: a differential diagnosis to inflammatory bowel disease. Scand J Gastroenterol 2011; 46:503-10.	Case series	4 pts with LGV (Denmark, Norway)	LGV proctitis	Clinical correlates of LGV infection	Gastrointestinal symptoms raised suspicion of inflammatory bowel disease.	All cases were MSM. ¾ were HIV+. All responded to doxycycline.
Heras E et al. Lymphogranuloma venereum proctocolitis in men with HIV-1 infection. Enfermedades Infecciosas y Microbiologia Clinica 2011; 29:124-6.	Case series	15 pts with LGV (Spain)	LGV proctocolitis (L2 serovar confirmed with reverse hybridization)	Clinical correlates of LGV infection	80% had clinical proctitis	All pts responded to 21 days of doxycycline, with negative follow-up test results.
Kober C et al. Acute seronegative polyarthritis associated with lymphogranuloma venereum infection in a patient with prevalent HIV infection. Intl J STD AIDS 2011; 22:59-60.	Case report	1 pt with LGV (UK)	LGV rectal infection	Clinical correlates of LGV infection	Asymmetrical polyarthropathy x 3 months, which resolved after successful treatment of LGV	HIV+ MSM.
Singhroo T et al. Lymphogranuloma venereum presenting as perianal ulceration: an emerging clinical presentation? Sex Transm Infect 2011; 87:123-4	Case report	2 pts with LGV (UK)	LGV rectal infection (confirmed LGV-associated serovar on rectal swab)	Clinical correlates of LGV infection	Both pts presented with isolated perianal ulcers.	Both pts responded to 3 weeks of doxycycline. High index of suspicion required for non-proctitis presentations.

Soni S et al. Lymphogranuloma venereum proctitis masquerading as inflammatory bowel disease in 12 homosexual men. <i>Alimentary Pharmacology & Therapeutics</i> 2010; 32:59-65.	Case series	15 pts with LGV (UK)	LGV proctitis (confirmed with LGV-specific DNA)	Clinical and endoscopic correlates of LGV infection	Retrospective analysis. Pts had mucosal ulcers, cryptitis, crypt abscesses and granulomas.	LGV proctitis closely resembles inflammatory bowel disease (IBD).
Castro R et al. Lymphogranuloma venereum serovar L2b in Portugal. <i>Int J STD AIDS</i> 2010; 21:265-6.	Case series	9 pts with chronic proctitis (Portugal)	LGV proctitis (confirmed by rtPCR / omp1 gene amplification)	Clinical correlates of LGV infection	Two patients confirmed infected with L2b serovar, with $\geq 10,000$ antibody titers	First 2 cases of LGV in Portugal.
Kamarashev J et al. Lymphogranuloma venereum in Zurich, Switzerland: Chlamydia trachomatis serovar L2 proctitis among men who have sex with men. <i>Swiss Medical Weekly</i> 2010; 140:209-12.	Case series	12 pts with proctitis (Switzerland)	LGV proctitis (confirmed serovar L2 by PCR)	Clinical correlates of LGV infection	12 confirmed cases since 2003: anorectal pain, discharge, tenesmus, change in stool frequency.	All pts were MSM, most were HIV+. 4 pts successfully treated with 1 gm azithromycin, 7 cases successfully treated with doxycycline 100 mg twice daily for 10-20 days.
Flexor G et al. Genital lymphogranuloma venereum in an HIV-1 infected patient. <i>Annales de Dermatologie et de Venereologie</i> 2010; 137:117-20.	Case report	1 pt with LGV (France)	Genital LGV infection (PCR-confirmed serovar L2)	Clinical correlates of LGV infection	Penile ulceration x 3 weeks with large swollen granulomatous lesion and inguinal lymph node, but no proctitis.	Genital bubo due to LGV. Responded to doxycycline 200 mg daily.
Savage EJ et al. Lymphogranuloma venereum in Europe	Case series	1693 cases of LGV (8 European)	LGV infection	Clinical correlates of LGV infection	Cases were predominantly MSM, most were HIV+.	Little evidence of spread to the wider population.

2003-2008. Euro Surveillance 2009; 14(48).		countries)			Anorectal symptoms were most common.	
Vall-Mayans M, Caballero E. Lymphogranuloma venereum: an emerging cause of proctitis in homosexual men in Barcelona. Revista Clinica Espanola 2009; 209:78-81.	Case series	7 pts with proctitis (Spain)	LGV infection (confirmed serovar L)	Clinical correlates of LGV infection	Mean duration of proctitis symptoms 28 days	All cases were MSM, HIV+.
Vall-Mayans M et al. The emergence of lymphogranuloma venereum in Europe. Lancet 2009; 374(9686):356.	Case report	1 pt with proctitis and arthropathy (Spain)	LGV infection (confirmed by rtPCR)	Clinical correlates of LGV infection	Proctitis, conjunctivitis, and arthritis affecting knees and R elbow.	LGV and sexually acquired reactive arthritis (SARA) - responded to doxycycline x 21 days
Heras E et al. Lymphogranuloma venereum proctitis in the setting of HIV: a case report and differential diagnosis. AIDS Patient Care & STDs 2009; 23:493-4.	Case report	1 pt with proctitis (Spain)	LGV infection (serotype L2a confirmed by PCR)	Clinical and endoscopic correlates of LGV infection	Rectal pain, tenesmus, mucopurulent discharge. Endoscopy revealed ulcerations, friability,	MSM, HIV+. Pt was initially misdiagnosed as lymphoma. Symptoms resolved completely with doxycycline.
El Karoui K et al. Reactive arthritis associated with L2b lymphogranuloma venereum proctitis. Sex Transm Infect 2009; 85:180-1.	Case report	1 pt with proctitis and reactive arthritis (France)	LGV infection (confirmed L2b serovar by PCR of omp1 gene)	Clinical correlates of LGV infection	Pt had fever, weight loss, purulent rectal discharge, tenesmus, followed by conjunctivitis and oligoarthritis (wrist, knee, ankles).	HIV+ MSM with sexually acquired reactive arthritis (SARA), responded to doxycycline x 30 days.
Ward H et al. The prevalence of	Multi-center cross-sectional	4825 urethral and 6778	Presence of LGV and non-LGV serovars	Clinical correlates of LGV and non-	Prevalence of non-LGV: 6.06% rectal, 3.21%	Did not identify a large reservoir of asymptomatic

lymphogranuloma venereum infection in men who have sex with men: results of a multicentre case finding study. Sex Transm Infect 2009; 85:173-5.	survey	rectal samples from MSM attending genitourinary clinics in UK		LGV chlamydial infection	urethral. Prevalence of LGV: 0.90% rectal, 0.04% urethral. 95% of rectal LGV was symptomatic.	LGV in rectum or urethra. Serovar typing not indicated in the absence of symptoms.
Annan NT et al. Rectal Chlamydia – a reservoir of undiagnosed infection in MSM. Sex Transm Infect 2009; 85:176-9.	Cross-sectional prevalence study	3076 MSM attending genitourinary clinics in UK	Presence of LGV and non-LGV serovars	Clinical correlates of LGV and non-LGV chlamydial infection	Ct prevalence (LGV and non-LGV) 8.2% in rectum, 5.4% in urethra. 69.2% of rectal infections were asymptomatic.	Most rectal infections would have been missed if routine screening had not been performed. 36 cases of LGV identified.
Cusini M et al. Lymphogranuloma venereum: the Italian experience. Sex Transm Infect 2009; 85:171-2.	Case series	13 pts with LGV (Italy)	LGV infection (confirmed by PCR or clinical/epi criteria)	Clinical correlates of LGV infection	Symptoms included anal discharge, rectal erosion, nodular erosive lesions, and inguinal abscess	All pts MSM, most HIV+.
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LGV Laboratory Diagnosis						
Almeida F et al. Polymorphisms in inc proteins and differential expression of inc genes among Chlamydia trachomatis strains. J Bacteriol 2012; 194:6574-85.	Laboratory analysis	51 Chlamydia strains (LGV, ocular, urogenital) (Portugal)	Analyses of polymorphisms and phylogeny of 48 inc proteins	Amino acid differences between LGV and ocular/urogenital isolates	LGV strains showed significant AA differences; 10 inc genes likely under positive selective pressure. Subtle nonsilent mutations contribute to tropism/ invasiveness of LGV strains.	Inhibition of phagolysosomal fusion is hypothesized to account for LGV invasiveness
Korhonen S. et al. Genotyping of	Cross-sectional study	140 C. trachomatis	Genotyping by pmpH and ompA	Detection of LGV and non-LGV C.	114/140 (81%) were successfully typed by	Genotyping by pmpH PCR is feasible in diagnostic

Chlamydia trachomatis in rectal and pharyngeal specimens: identification of LGV genotypes in Finland. Sex Transm Infect 2012; 88:465-9.		NAAT+ rectal and pharyngeal swabs	real-time PCR	trachomatis types	pmpH PCR (104 non-LGV, 9 LGV, 1 both). Of the L-types, 6 were L2b, and 2 were L2 by ompA PCR and sequencing. L types were mostly rectal.	labs which already perform NAATs to detect chlamydia.
Mobius N et al. Protocol for the rapid detection of the urogenital tract mollicutes and Chlamydia with concomitant LGV-(sub)typing. Methods Molec Biol 2012; 903:235-53.	Laboratory assay development	C. trachomatis L serovar primers	Development of real-time PCR protocol	Detection of LGV-associated L serovars	Step-by-step description of a protocol for using TaqMan multiplex real-time PCR (qPCR) to detect LGV-associated serovars	Allows subtyping of L1, L2, and L3 variants
Verweij SP et al. Lymphogranuloma venereum variant L2b-specific polymerase chain reaction: insertion used to close an epidemiological gap. Clin Microbiol Infect 2011; 17:1727-30.	Laboratory assay development	C. trachomatis L2b serovars	Development of rapid L2b-specific PCR	Detection of L2b-specific serovar	Description of an L2b-specific primer/probe set for rapid identification of L2b variant using rtPCR	Based on unique insertion in pmpH gene; avoids laborious ompA sequencing
deVries HJ et al. Anal lymphogranuloma venereum infection screening with IgA anti-Chlamydia trachomatis-specific major outer membrane protein	Laboratory assay development	61 pts with anal Ct infection (42 Ct+/LGV+ vs. 19 Ct+/LGV-)	Serologic assays for chlamydia: IgA anti-MOMP, IgG anti-MOMP, IgA anti-LPS, IgG anti-LPS	Differential LGV from non-LGV anal infections	IgA anti-MOMP performed best, even in asymptomatic pts: sensitivity 85.7%, specificity 84.2%.	Subsequent validation showed the test was most accurate when cut-off point was set to 2.0 (sens. and spec. both approx. 75%), could be useful screening tool.

serology. Sex Transm Dis 2010; 37(789-95).						
Quint KD et al. Comparison of three genotyping methods to identify Chlamydia trachomatis genotypes in positive men and women. Molecular & Cellular Probes 2010; 24: 266-70.	Laboratory assay development	50 Ct+ specimens (Aptima Combo 2)	Detection of Ct by Omp1 sequencing, Ct-DT assay, and pmpH rt-PCR	Differentiation of LGV and non-LGV infections	Ct-DT assay was best for distinguishing LGV from non-LGV infections.	pmpH rtPCR assay performed well for LGV, but missed substantial numbers of non-LGV infections.
Cai L. et al. Differentiation of Chlamydia trachomatis lymphogranuloma venereum-related serovars from other serovars using multiplex allele-specific polymerase chain reaction and high-resolution melting analysis. Int J STD AIDS 2010; 21:101-4.	Laboratory assay development	15 rectal specimens from patients with COBAS Amplicor PCR-confirmed C. trachomatis infection	Comparison of high resolution melting analysis (HRMA) and multiplex allele-specific PCR (MAS-PCR)	Detection of L2 serovars	Both methods identified 2/15 samples as serovar L2.	Both HRMA and MAS-PCR are inexpensive, rapid, and easy tools to identify LGV in clinical and research settings.