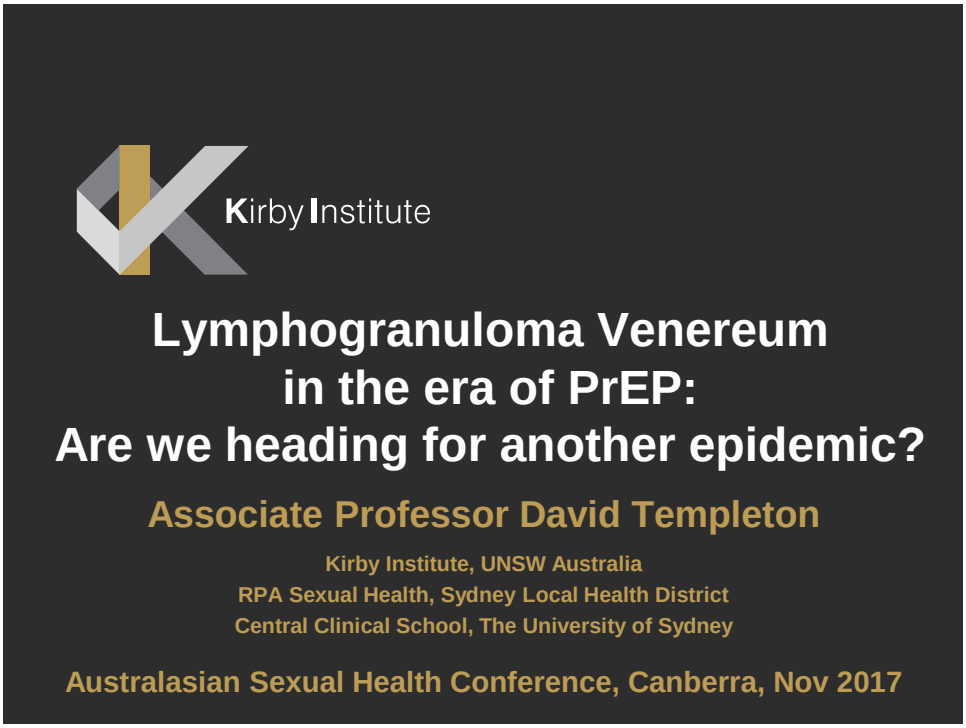
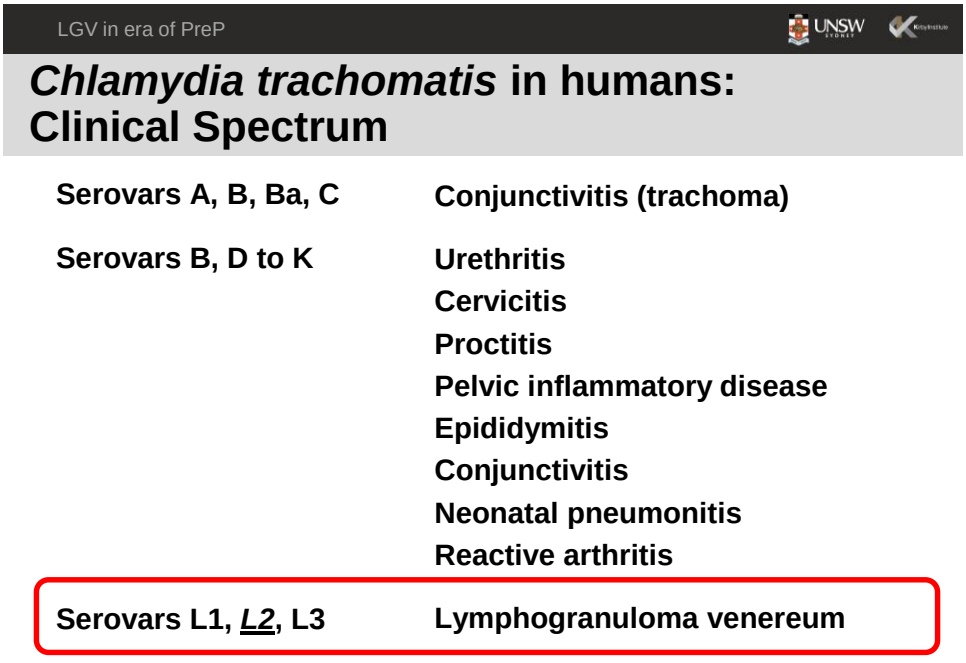

Kirby Institute
Lymphogranuloma Venereum
in the era of PrEP:
Are we heading for another epidemic?
Associate Professor David Templeton
Kirby Institute, UNSW Australia
RPA Sexual Health, Sydney Local Health District
Central Clinical School, The University of Sydney
Australasian Sexual Health Conference, Canberra, Nov 2017


LGV in era of PreP
UNSW
Chlamydia trachomatis in humans:
Clinical Spectrum
Serovars A, B, Ba, C
Conjunctivitis (trachoma)
Serovars B, D to K
Urethritis
Cervicitis
Proctitis
Pelvic inflammatory disease
Epididymitis
Conjunctivitis
Neonatal pneumonitis
Reactive arthritis
Serovars L1, L2, L3
Lymphogranuloma venereum
2

CASE REPORT

International Journal of STD & AIDS 2008; **19**: 563–564

Unusual transmission route of Lymphogranuloma venereum; following sexual contact with a female donkey

Farzin Khorvash MD*, **Ammar H Keshteli** MD†, **Hassan Salehi** MD*, **Levente Szeredi** DVM PhD‡ and **Servaas A Morré** PhD§**††

LGV in era of PreP

Historical perspective of LGV

- **"Genital ulcer-adenopathy syndrome"**
  - endemic in tropical regions and recognised worldwide for centuries
- **1980s**
  - Original descriptions of US men with LGV-proctitis
- **Then "outbreak" of LGV reported from 2003 onwards**
  - Retrospective analysis of GBM rectal specimens 2000-2003 – 126 cases Amsterdam, Paris and London
  - Subsequently cases of LGV proctitis in GBM reported worldwide

JULIUS SCHACHTER, PHD, AND JEANNE MONCADA, MT **Editorial**

Sexually Transmitted Diseases, June 2005, Vol. 32, No. 6, p.331–332

Lymphogranuloma Venereum: How to Turn an Endemic Disease Into an Outbreak of a New Disease? Start Looking

Sexually Transmitted Diseases • Volume 40, Number 10, October 2013

The Etiology of Infectious Proctitis in Men Who Have Sex With Men Differs According to HIV Status

Melanie Bissessor, FAChSHM,† Christopher K. Fairley, FRACP, PhD,*† Timothy Read, FAChSHM,*† Ian Denham, FRACP,† Catriona Bradshaw, FAChSHM, PhD,*†‡ and Marcus Chen, FRCP, PhD*†*

TABLE 1. Etiology of Infectious Proctitis Among HIV-Positive and HIV-Negative MSM

Clinical Presentation and Pathogens Detected	HIV Positive (n = 141)	HIV Negative (n = 138)	*P*
Anorectal pain	108 (76%)	109 (79%)	0.6
Anal discharge	29 (21%)	27 (20%)	0.8
≥1 of the above symptoms	137 (97%)	136 (99%)	0.4
Anal ulceration	18 (13%)	12 (9%)	0.3
Chlamydia	33 (23%)	30 (22%)	0.7
Gonorrhea	19 (13%)	15 (11%)	0.5
HSV	51 (36%)	26 (19%)	0.001
HSV-1	20 (14%)	9 (7%)	0.04
HSV-2	31 (22%)	17 (12%)	0.03
LGV	11 (8%)	1 (0.7%)	0.004
Syphilis*	2 (1%)	1 (0.7%)	0.6
≥2 concurrent pathogens	25 (18%)†	11 (9%)†	0.02
No pathogen detected	25 (18%)	65 (47%)	<0.001

LGV: why it's important

Several reports from Australia[1-5] & New Zealand[6] followed international reports

- majority anal infections in GBM & serovar L2b

All symptomatic (often severe proctitis)

- mainly HIV+, often HCV+

Why important to distinguish from non-LGV-CT?

- Serious sequelae
- prolonged Ab Rx
- ? ↑ risk of HIV & HCV transmission

Frequently misdiagnosed…

(1) Stark et al. J Clin Microbiol 2007;45:1029-31
(2) Morton et al. Sex Health 2006;3:189-90
(3) Lee et al. Aust NZ J Public Health 2009;33:94
(4) Templeton et al. Sex Transm Dis 2011;38:48-9
(5) Templeton et al. Sex Health 2013;10:190-1
(6) Robertson et al. Sex Health 2008;5:369-70

Misdiagnoses of LGV…

Case report

Delayed diagnosis of lymphogranuloma venereum-associated colitis in a man first suspected to have rectal cancer

Aaron S Bancil[1], Christopher Alexakis[2] and Richard Pollok[2]

Case Report

CMJ

www.cmj.ac.kr

Chlamydial Proctitis in a Young Man Who Has Sex with Men: Misdiagnosed as Inflammatory Bowel Disease

Kyung-Jin Lee, Jaeyeon Kim*, Dong Hwan Shin, Jun Oh Jung, Seokyoung Koh, Ka Young Kim and Jae Min Lee

Department of Internal Medicine, National Police Hospital, Seoul, Korea

CASE REPORT

Lymphogranuloma venereum proctosigmoiditis is a mimicker of inflammatory bowel disease

Marlene Gallegos, Dawn Bradly, Shriram Jakate, Ali Keshavarzian

CASE REPORT

The potential role of serology in diagnosing chronic lymphogranuloma venereum (LGV): a case of LGV mimicking Crohn's disease

B Forrester, J Pawade, P Horner

JEADV

EADV

Journal of the European Academy of Dermatology and Venereology

Letter to the Editor

Lymphogranuloma venereum with only proximal rectal involvement mimicking inflammatory bowel disease: a potential diagnostic pitfall

F. Rob, J. Kašpírková, K. Jůzlová, M. Pešta, J. Hercogová

JGH

Journal of Gastroenterology and Hepatology

JGHF

EDUCATION AND IMAGING

Gastrointestinal: Outbreak; proctocolitis mimicking inflammatory bowel disease

V Nguyen, EY Lee, D Couldwell, D Packham

AP&T

Alimentary Pharmacology and Therapeutics

Lymphogranuloma venereum proctitis masquerading as inflammatory bowel disease in 12 homosexual men

S. Soni, R. Srirajaskanthan S. B. Lucas, S. Alexander, T. Wong, J. A. White

BMJ Case Reports

Reminder of important clinical lesson

Lymphogranuloma venereum and HIV infection: misdiagnosed as Crohn's disease

Sheel Patel, Phillip Hay

Pathogenesis

Non-LGV CT

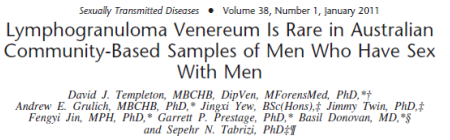
– mucosal columnar epithelial cells

LGV

– Predom. affects lymphatic tissue

– Regional LNs → thrombo/peri-lymphangitis

– Necrosis & inflammation



Sexually Transmitted Diseases • Volume 38, Number 1, January 2011

Lymphogranuloma Venereum Is Rare in Australian Community-Based Samples of Men Who Have Sex With Men

David J. Templeton, MBCHB, DipVen, MForensMed, PhD,† Andrew E. Grulich, MBCHB, PhD,* Jingxi Yew, BSc(Hons),‡ Jimmy Twin, PhD,‡ Fengyi Jin, MPH, PhD,* Garrett P. Prestage, PhD,* Basil Donovan, MD,*§ and Sepehr N. Tabrizi, PhD‡¶*

Sydney-based HIM & pH studies, 2005-7

- 2082 & 521 tests in HIV- & HIV +
- HIM: 34 anal, 9 urine, 3 pharyngeal CT+
  - **No LGV at any site in HIV- cohort**
- pH: 13 anal, 3 urine, 2 pharyngeal CT+
  - **One rectal LGV in HIV+ cohort**

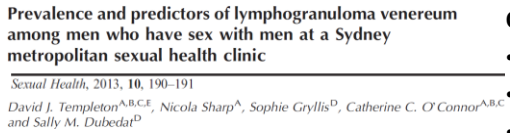
Journal of Clinical Microbiology, June 2004, p. 2596–2601 Vol. 42, No. 6
0095-1137/04/$08.00+0 DOI: 10.1128/JCM.42.6.2596–2601.2004
Copyright © 2004, American Society for Microbiology. All Rights Reserved.

Variability of the *Chlamydia trachomatis omp1* Gene Detected in Samples from Men Tested in Male-Only Saunas in Melbourne, Australia

Nichole A Lister,[1]* Sepehr N. Tabrizi,[2] Christopher K. Fairley,[1] Anthony Smith,[3] Peter H. Janssen,[4] and Suzanne Garland[2]

Melbourne SOPVs, 2001-2

- All (n=39) RCT+ isolates genotyped
- **No LGV**



Prevalence and predictors of lymphogranuloma venereum among men who have sex with men at a Sydney metropolitan sexual health clinic

Sexual Health, 2013, **10**, 190–191

David J. Templeton[A,B,C,E], Nicola Sharp[A], Sophie Gryllis[D], Catherine C. O'Connor[A,B,C] and Sally M. Dubedat[D]

Clinic-based study, Sydney 2011-12

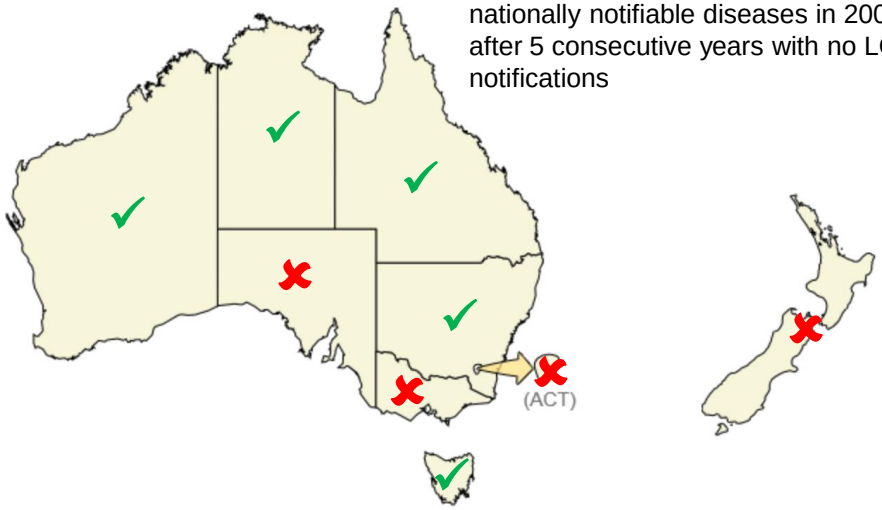
- 1732 RCT tests, 75 (4.3%) positive
- **3 LGV (L2b) - all sympt & HIV+**
- No LGV in any of 59 asymp RCT+

LGV in era of PreP

Public Health Surveillance

Australasian jurisdictions with current mandatory LGV notification to PHUs

LGV removed from list of Australian nationally notifiable diseases in 2001 after 5 consecutive years with no LGV notifications



LGV in era of PreP

COMMUNICABLE DISEASES

Enhanced surveillance of a lymphogranuloma venereum outbreak in Sydney 2010–2012

Aust NZ J Public Health. 2016; 40:368-70

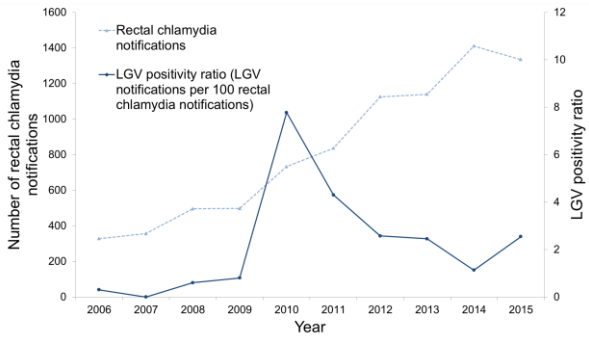
David J. Templeton,[1,2,3] Kelly-Anne Ressler,[4] Kirsty Hope,[5] Isobel M. Poynten[2]

37 doctors interviewed: diagnosed ≈75% of 88 anorectal LGV
- all inner-Sydney residents & L2b serovar
- almost 90% S100 prescribers working in high-caseload clinics
- symptoms in >95% for median 8 days (range 2–1825)
- almost one-third diagnosed with concurrent STI

22 patients interviewed:
- >80% HIV+
- reported other STIs in past year
- all reported condomless anal sex
- median no. CMPs 5 (range 0–100)

Likely huge testing bias in NSW LGV diagnoses

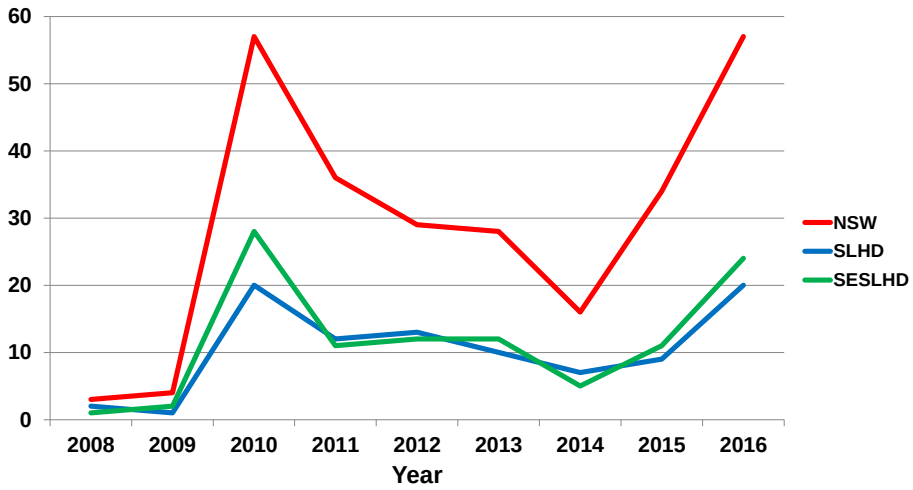
Kotevski D, Lam M, Selvey C, Templeton DJ, Donovan L, Sheppeard V. Epidemiology of LGV in New South Wales, 2006-2015
(submitted Nov 2017)



Anatomical sites of LGV infection in males, NSW, 2006-2015

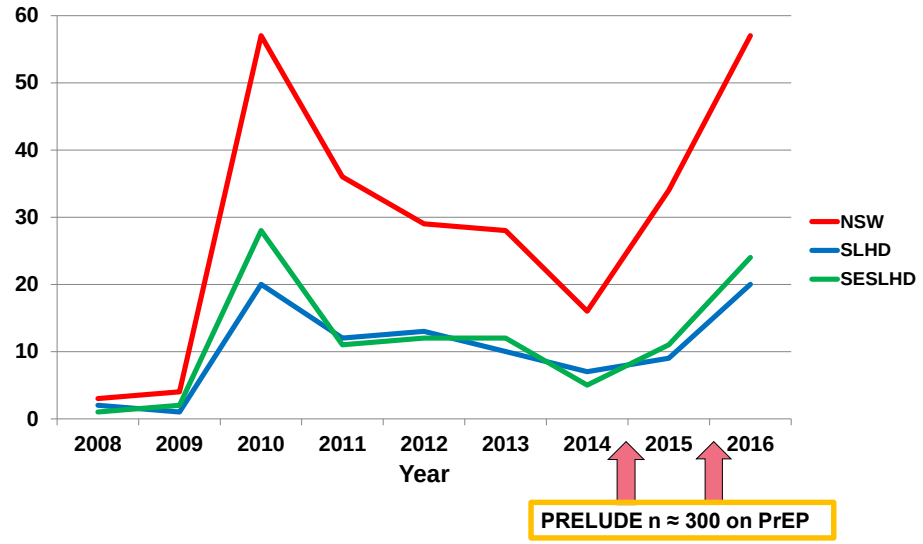
Site of infection	n	%
Anorectum	179	86.1%
Anorectum and throat	1	0.5%
Genitourinary tract	8	3.8%
Genitourinary tract and anorectum	9	4.3%
Genitourinary tract and other	1	0.5%
Other	1	0.5%
Unknown/missing site	9	4.3%
Total	**208**	**100%**

NSW LGV notifications, males, 2008-2016*



***Data courtesy of NSW Health Protection, SESLHD Public Health Unit and SLHD Public Health Unit**

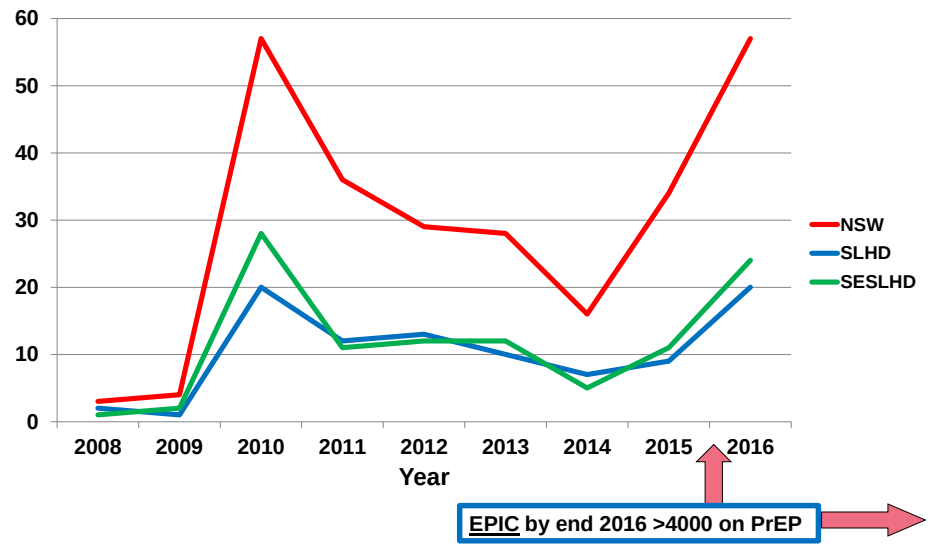
NSW LGV notifications, males, 2008-2016*



*Data courtesy of NSW Health Protection, SESLHD Public Health Unit and SLHD Public Health Unit

LGV in era of PreP

NSW LGV notifications, males, 2008-2016*



*Data courtesy of NSW Health Protection, SESLHD Public Health Unit and SLHD Public Health Unit

LGV - Clinical Features - 1° stage

- Incubation period 3-30 days
- Symptomatic disease M>>F
- 3 stages
- Primary Stage
  - Papule (site of inoculation)
  - May → painless ulcer
  - Mostly unnoticed
- Sites
  - Genital
  - anorectal
  - extragenital

LGV - Clinical Features - 2° stage

"Inguinal Syndrome"

- wks after 1° lesion
- Buboes – pain +/-, unilateral inguinal ± femoral LAN
- "Groove sign" in 10-20%
- 20% relapse; 30% rupture

Acute proctitis in GBM

- rectal pain
- tenesmus
- constipation
- lower abdo cramps
- rectal discharge/bleeding

LGV - Clinical Features - 3° stage

- F>M
- Chronic inflammatory lesions lead to anogenital scarring
- Rectal abscesses, strictures, stenoses, fistulae
- Lymphatic obstruction
  - Lymphorrhoids
  - Elephantiasis of genitalia

Diagnosis and management

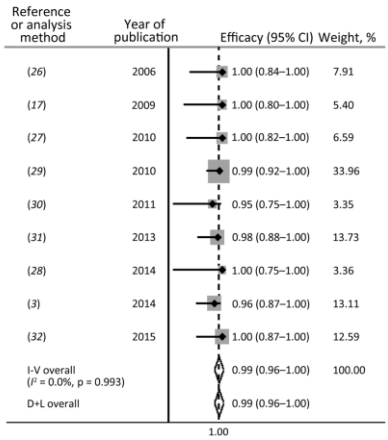
- NAAT diagnosis has largely superseded serological Dx
- Dramatic response of acute stage; bubonic stage slower
- Aspiration of fluctuant buboes
- Surgery for late complications

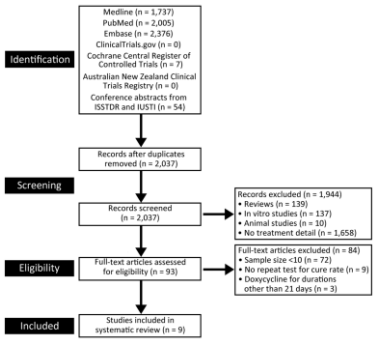
RESEARCH

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 22, No. 10, October 2016

Systematic Review and Meta-Analysis of Doxycycline Efficacy for Rectal Lymphogranuloma Venereum in Men Who Have Sex with Men

Charussri Leeyaphan, Jason J. Ong, Eric P.F. Chow, Fabian Y.S. Kong, Jane S. Hocking, Melanie Bissessor, Christopher K. Fairley, Marcus Chen





For Rx rectal LGV Rx in GBM
Pooled Rx efficacy of 100mg doxycycline BD x 21 days
= 98.5%
(95%CI 96.3%–100%)

Asymptomatic LGV – does it exist? **YES**

Studies performing LGV testing on consecutive GBM clinic attendees

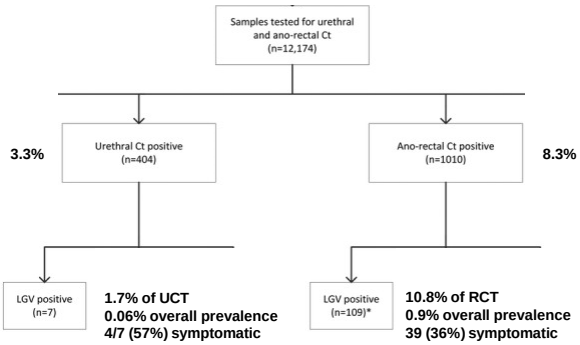
- **asymptomatic anorectal LGV**
  - UK STI clinics[1] 2009 (n≈7,000): **5%** of 61
  - German STI clinics 2010[2] (n≈1800): **53%** of 15
  - Spanish STI clinics 2009-11[3] (n>3,000): **11%** of 82
  - UK STI clinics[4] 2012 (n>10,000): **22%** of 54
  - Amsterdam STI clinic[5] 2014-15 (n>12,000): **36%** of 108
- **asymptomatic urethral LGV**
  - UK STI clinics[1] 2009 (n≈5000): **50%** of 2
  - Spanish STI clinics[3] 2009-11 (n≈2500): **0%** of 10
  - Amsterdam STI clinic[5] 2014-15: **57%** of 7
- **asymptomatic pharyngeal LGV**
  - Case reports only, rare, but occas. symptomatic

(1) Ward et al. STI 2009;85:173-5; (2) Haar et al Emerging Infect Dis 2013;19:488-92 (3) Rodriguez-Dominguez et al. Clin Microbiol Infect 2014;20:219-25; (4) Saxon et al. Emerg Infect Dis 2016; 22:112–116; (5) de Vrieze et al. STD 2017;44:547-550

Low Prevalence of Urethral Lymphogranuloma Venereum Infections Among Men Who Have Sex With Men: A Prospective Observational Study, Sexually Transmitted Infection Clinic in Amsterdam, the Netherlands

Sexually Transmitted Diseases • Volume 44, Number 9, September 2017

Nynke H.N. de Vrieze, Bart Versteeg,† Sylvia M. Bruisten,†‡ Martijn S. van Rooijen,† Jannie J. van der Helm,† and Henry J.C. de Vries†‡§*



- Ur v R: 15X lower prevalence
- Other modes of transmission likely
- GBM with anorectal (v. urethral) LGV sig more likely to be HIV+ (84 v. 43%, p= 0.02

Is it all behaviour or does immunodeficiency play a role???

Why the discrepancy in anorectal vs. urethral LGV?

- Although initially suggested[1] – sharing sex toys and fisting have subsequently been dismissed[2]
- No indication for tissue tropism between anatomic sites[3-5]

1. Nieuwenhuis et al. Clin Infect Dis 2004;39:996–1003.
2. Van der Bij et al. Clin Infect Dis 2006; 42:186–194.
3. Bax et al. Sex Transm Infect 2011;87:503–7.
4. Jeffrey et al. Infect Immun 2010;78:2544–53.
5. Versteeg et al. BMC Infect Dis 2014;14:464.

Could LGV acquired orally via rimming pass through the GI tract to cause anorectal LGV proctitis???

- Neonates infected perinatally with nasopharyngeal & conjunctival CT several wks later tested pos at anorectal sites

Schachter et al. J Infect Dis 1979;139:232–4

- Chlamydiae in almost all natural animal hosts are transmitted faecal-orally & reside naturally in GIT for long periods without causing disease/inflammation

Rank et al. Clin Infect Dis 2015;60:1585-6

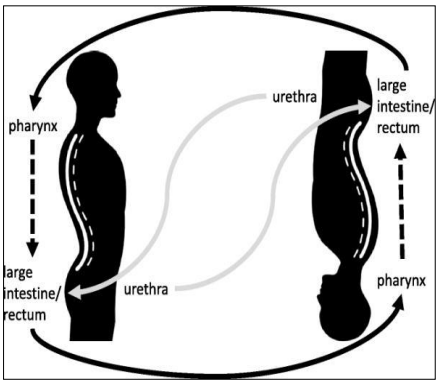
- Mice infected orally with the *C. muridarum* become infected in the lower GI tract & are unable to clear the infection

Igietseme et al. Infect Immun 2001;69:1832-40

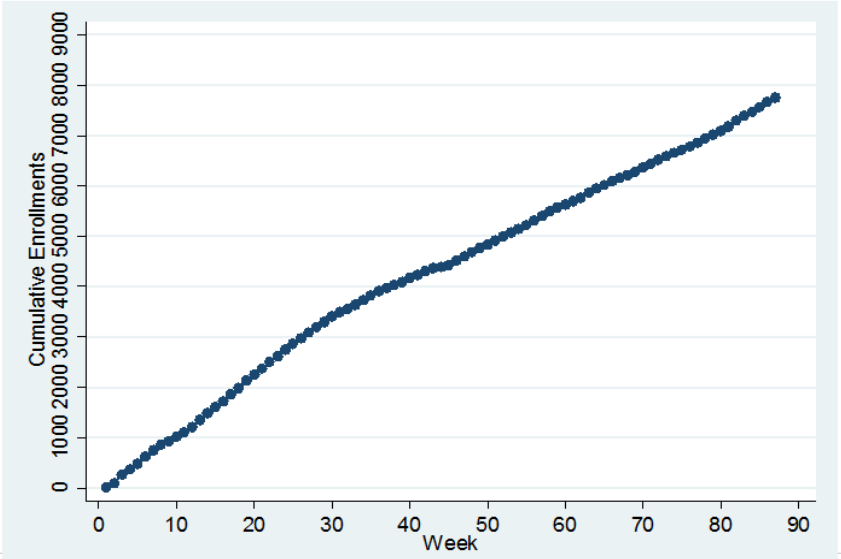
Could LGV acquired orally via rimming pass through the GI tract to cause anorectal LGV proctitis???

Oral infection could result in pharyngitis & organisms pass thro' GI tract to rectum where L2b strains could induce LGV proctitis or asympt infection contributing to ongoing transmission

de Vries HJ. Sex Transm Dis 2016; 43:420–2



EPIC-NSW enrolments by end Oct 2017



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Conclusions (1)

- Test all GBM with anal symptoms for LGV (if CT+)
- Case finding by intensive contact tracing
- Test for CT (then LGV if CT+) at all 3 sites in GBM contacts of LGV (and Rx with 3/52 doxy whilst awaiting result)
- Test all CT Rx failures for LGV
- Education of non-sexual-health clinicians on LGV risk factors, presentation, Ix & Mx

28

Conclusions (2)

- Urgent need for research on LGV typing of asymptomatic GBM with anorectal CT attending Australasian clinics to inform screening guidelines
  - Prevalence of asymptomatic LGV
  - Risk factors

- and…….

….don't fuck donkeys….

Photos: Man arrested with a hard-on after he was caught banging a donkey