# Genital-inguinal *Lymphogranuloma venereum* in men taking HIV Pre-Exposure Prophylaxis

## Making the diagnosis: a report of two cases

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# *Lymphogranuloma venereum*

- One of three invasive Chlamydia trachomatis serovars (L1, **L2**, L3)→ lymphatic infiltration

- **Endemic in countries in our region**: South East Asia and India (as well as in Sub-saharan Africa, Caribbean)
- In Australia-outbreaks in sexual networks of MSM with HIV

  LGV associated **proctitis in MSM with HIV** (symptomatic anorectal infection)

  **Genital (ulcerative) LGV exceedingly rare**

UK/European evidence:

- Asymptomatic rectal infection relatively common in MSM in Netherlands but not UK

In all groups: genital (ulcerative) LGV uncommon

Sethi G et al. Lymphogranuloma venereum presenting as genital ulceration and inguinal syndrome in men who have sex with men in London, UK. Sex Transm Infect. 2009 Jun;85(3):165-70.

Read PJ, McNulty AM. Lymphogranuloma venereum presenting as genital ulceration and inguinal syndrome. *Med J Aust* 2013; 199 (1): 27-28.

Davies SC et al. Lymphogranuloma venereum presenting as penile ulcer in two HIV-negative gay men. *Int J STD & AIDS* 2019;30(5): 095646241882157

# LGV: Clinical course

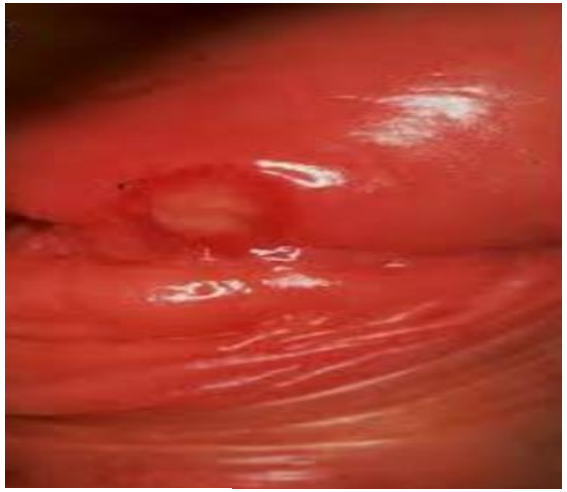
**Primary stage** (**Acute infection**: **incubation period 3-30 days**)

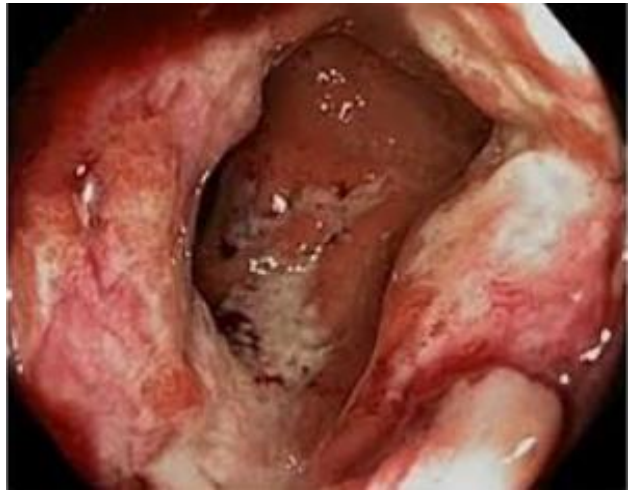
Clinically 2 forms:

1) Proctitis- rectal pain, bleeding, discharge, tenesmus, constipation +/- fever, malaise

2) Primary lesion: on coronal sulcus of penis, vulva, posterior fourchette, cervix

*Transient self-resolving papule →ulcer (+/-pain) +/- fissuring, lymphadenopathy*







White J, O'Farrell N, Daniels D. UK National Guideline for the management of Lymphogranuloma venereum. 2013. *Int J STD & AIDS,* 2013; 24(8) 593–601

# LGV: Clinical course

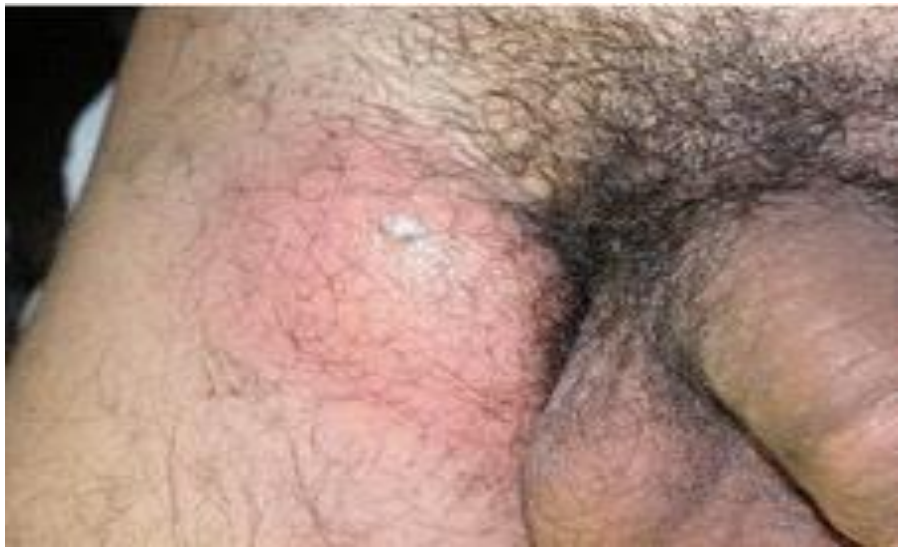
**Secondary stage** (**Lymphatic spread: 10-30 days after resolution of primary lesion**)

unilateral inguinal & femoral lymphadenopathy

+/- ‘buboe’ formation: ‘groove sign’

fever, malaise, arthralgia

sexually acquired reactive arthritis





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# LGV: Clinical course

**Tertiary advanced disease (Chronic tissue destruction, inflammation, fibrosis, scarring)**

persistent / relapsing proctocolitis

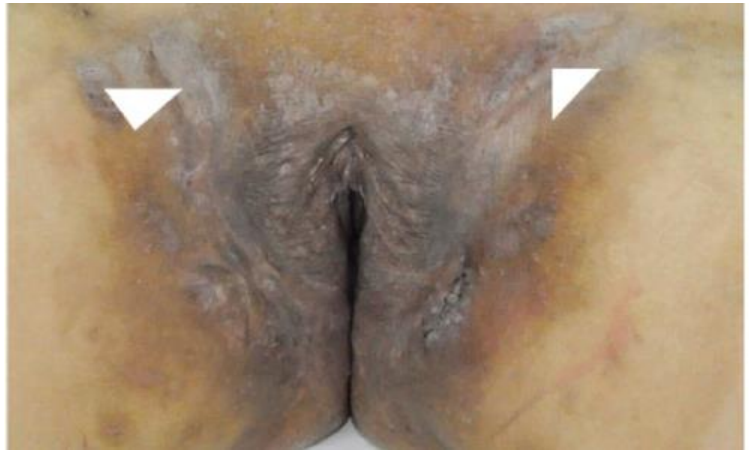
rectal fistulae

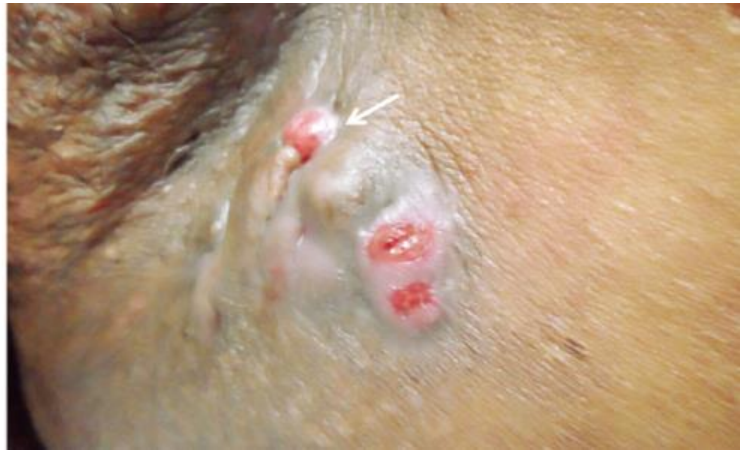
genital tract / rectal strictures

lymphoedema

vulval fibrosis, scarring

SCC risk







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# Case 1-History

35 year old man

Pre-Exposure Prophylaxis (PrEP)

10 day history of a painful penile ulcer and an enlarging left inguinal mass

Systemically well

condomless insertive penile-anal sex (casual male partner) 18 days earlier in Thailand.

6 male partners in the previous 3 months (Thailand, Australia)

Had early latent Syphilis treated 9 months previously

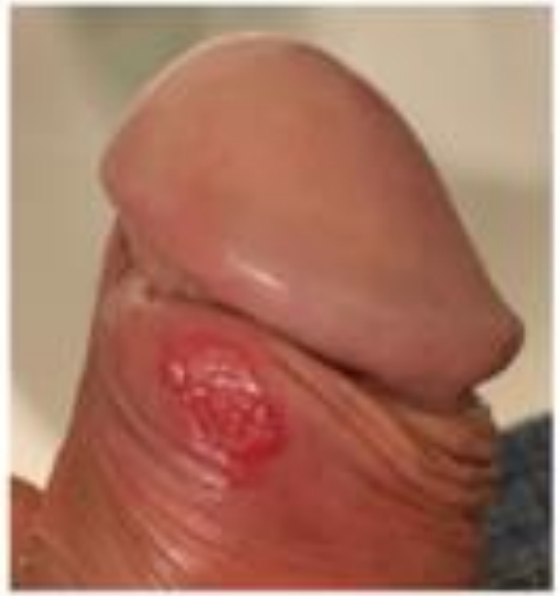
# Case 1- Examination

10mm non-indurated ulcer (left coronal sulcus-peripheral erythema, slough to ulcer base)

30x30mm tender, left inguinal mass (no erythema or fluctuance)

Normal vital signs

No other signs of active Syphilis elsewhere



# Case 1- Progress in consult

Tests sent:

*Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) Nucleic-Acid Amplification Tests (NAAT-throat, rectal, first-void urine)

HIV, Hepatitis C, Syphilis Rapid Plasma Reagin

Herpes (HSV) and Syphilis NAAT/PCR (ulcer base)

CT NAAT (ulcer base)

Management: intramuscular benzathine penicillin 1.8g statim

# Case 1- Progress 3 days later

Penile ulcer unchanged.

New, second ulcer-2x2mm, superficial-right coronal sulcus.

Inguinal mass larger (60x70mm)-remained non-fluctuant.

Test results:

*Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) Nucleic-Acid Amplification Tests (NAAT-throat, rectal, first-void urine) all non-reactive

HIV, Hepatitis C, Syphilis Rapid Plasma Reagin non-reactive

Herpes (HSV) and Syphilis NAAT (ulcer base) non-reactive.

**CT NAAT (ulcer base)=REACTIVE: referred for LGV PCR.**

Management: Oral doxycycline (100mg,12-hourly,21 days) commenced

# Case 1- Progress 7 days later

Ulcers receding, mass unchanged but now painful

**LGV PCR (ulcer case)=REACTIVE**

Inguinal mass aspiration (day 6 Doxycyline):

Granulomatous inflammation (histopathology)

CT NAAT non-reactive

Bacterial culture no growth

Followed to treatment completion

Symptoms resolved at treatment completion

# Case 2-History

37 year old man taking PrEP

4 day history of a painful, swollen penile shaft

Systemically well.

Multiple episodes of condom-less insertive penile-anal sex previous 4 weeks

5 male partners over the preceding month

No recent travel. No new or regular medications. No trauma. Otherwise well

# Case 2-Pre-consult

Penile ultrasound (with referring doctor) revealed soft tissue oedema (no collection or vascular/lymphatic changes)

First-void urine CT NAAT (with referring doctor)=REACTIVE

Had already commenced oral doxycycline (100mg, 12-hourly, 7 days) 2days prior to consult.

All else negative/non-reactive (CT & NG-rectal, pharyngeal NAAT, and Syphilis, Hepatitis C & HIV serology)

# Case 2- examination

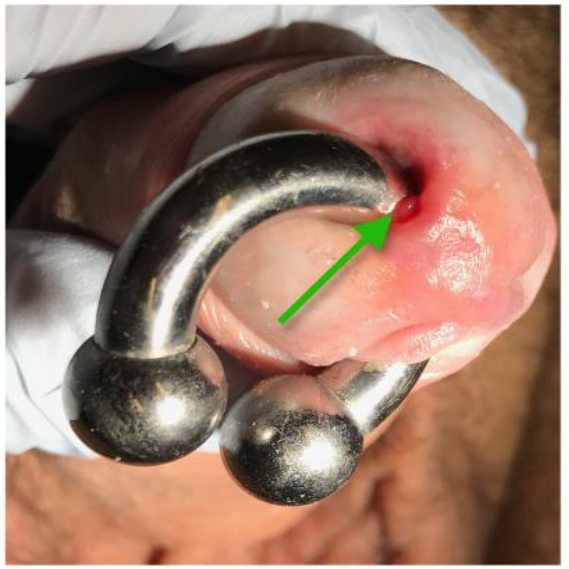
3mm superficial, non-indurated ulcer inside urethral meatus, adjacent to piercing (?potential entry)

Markedly swollen, red, tender, non-fluctuant penile tissue (dorsal mid-shaft extending to penile base)

No inguinal lymphadenopathy.

Vital signs normal.

No signs of active Syphilis elsewhere



Hounsfield V, Davies SC. Genital piercing in association with gonorrhoea, chlamydia and warts. International Journal of STD & AIDS 2008; 19: 499–500

# Case 2- Progress in consult

Tests sent:

Bacterial culture, HSV, Syphilis, NG and CT (ulcer base)

Management:

Transferred to Emergency Department for presumed cellulitis

2 day admission

Intravenous piperacillin/tazobactam4/0.5g 8-hourly then oral amoxicillin/clavulanate 875/125mg 12-hourly 5 days

Also continued on Doxycycline to 7 days.

# Progress 5 days later

Seen 5 days later (day 3 post-discharge, day 7 doxycycline)

Only reactive/positive microbiological investigation before or during hospital admission was **CT→reflex LGV reactive** (result available 3 days after post-discharge).

All changes had significantly receded.

Management:

Doxycycline was extended to 21 days with resolution of symptoms at completion of treatment

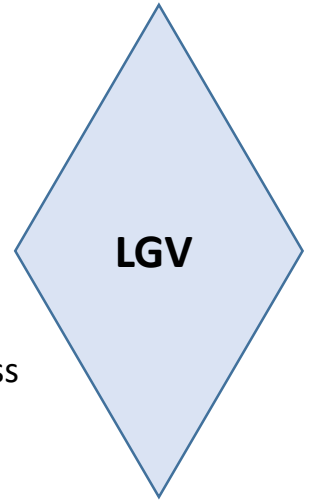
Partner notification completed

# LGV Diagnosis and Management

## Diagnosis

**Risk Factors for LGV:**
MSM, Bacterial, STIs, HIV, Contact,
?Travel, ?Behavioural, ?Immunological

**Symptoms**
-proctitis
-ulcer
-inguinal mass




**Chlamydia**
-esp Rectal

**Tissue / Specimens**
>10-20 x PMNLs / HPF
-NOT culture, serology
**-LGV DNA (PCR):**
*Rectal, FVU, throat ulcer, buboe material*
*Tissue biopsy*

## Management

***Presumptive VS Confirmed***

**Aspirate** fluctuant lesions/buboes

**Doxycycline**
PO 100mg 12 hrly for 21 days

Pregnancy / lactation
use macrolide
eg Azithromycin PO
1g wkly/3wk

Resolution: 2-6 wks (dep. stage)

**Abstain on Rx/ until TOC**

**Notify PHU**

**Contact tracing**:
-4 weeks if sympts
-3 months if A-Sx

**Test of cure** 2 weeks post Tx completion

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# LGV DNA (PCR)

- Limited testing sites
- In-house assays at reference laboratories. At ICPMR (Westmead): Roche Light Cycler 2.0
- Reflex/automatic referral (by request) of samples reactive for Chlamydia trachomatis **or** recollection of LGV PCR

- Clinicians with high sexual health & HIV caseloads should ensure there is a specimen referral pathway (reflex/automatic referral of samples reactive for Chlamydia trachomatis or recollection of LGV PCR)

***LGV PCR can take up to two weeks to return result but:***

***Chlamydia trachomatis NAAT (ulcer base) has a quicker turnaround->reflex LGV if positive***

***Syphilis serology can help rapidly rule out Syphilis- but use with caution***


# Genital-Inguinal LGV: Other approaches to Diagnosis from Australian Cases in Sexual Health Clinics

***Read P, McNulty AM ( MJA 2013)***

LGV test rationale: buboes after self-resolving genital ulcer (Dx & Rx as 'chancre'). Longstanding HIV infection

LGV test method: aspiration from buboes LGC DNA PCR

***Davies SC, Shapiro J, Comninos NB, Templeton DJ (Int J STD&AIDS 2019)***

Case 1:

LGV test rationale: large ulcer with concurrent inguinal mass. On PrEP

LGV test method: Ulcer base CT→LGV PCR

Case 2:

LGV test rationale: persisting genital ulcer and inguinal mass (Syphilis and HSV PCR negative, empirical Rx for both) + Chlamydia contact. On PrEP

LGV test method: Ulcer base LGV DNA PCR

Lymphogranuloma venereum presenting as genital ulceration and inguinal syndrome. *Med J Aust* 2013; 199 (1): 27-28.

Davies SC et al. Lymphogranu Read PJ, McNulty AM. loma venereum presenting as penile ulcer in two HIV-negative gay men. *Int J STD & AIDS* 2018

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# Conclusions

We may be missing LGV genital ulcers → risk of disease progression

Consider LGV in the differential diagnosis of genital ulcers in at-risk groups (consider testing at first presentation)

Carefully consider LGV in genital ulcers testing negative for Herpes and Syphilis

Surveillance of genital LGV is key- in the age of increasing STIs, 'sero-mixing' and PrEP

Travel histories alongside sexual histories- learning more about STIs in our region

Impact of changes in antimicrobial use (eg Doxycycline STI Prophylaxis)- watch this space

Read PJ, McNulty AM. Lymphogranuloma venereum presenting as genital ulceration and inguinal syndrome. *Med J Aust* 2013; 199 (1): 27-28.

Davies SC, Shapiro J, Comninos NB, Templeton DJ. Lymphogranuloma venereum presenting as penile ulcer in two HIV-negative gay men. *Int J STD & AIDS* 2019;30(5): 095646241882157

Australasian Society for HIV, Viral hepatitis and sexual health medicine. Australian STI management guidelines for use in primary care, www.sti.guidelines.org.au (accessed 14 July 2019).

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