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Molecular diagnosis of Lymphogranuloma venereum (LGV) infection

Chlamydia trachomatis is a gram-negative, non-motile, obligate intracellular bacterium which exists outside host cells as inactive elementary bodies but can infect host cells via endocytosis and reside as membrane-protected inclusion bodies intracellularly.

There are 19 known serovars and three biovars which cause distinct clinical syndromes:

- Serovars Ab, B1, B2 and C cause chronic follicular keratoconjunctivitis or 'trachoma' which may lead to chronic scarring and the most common cause of preventable blindness worldwide.
- Serovars D-K cause both common STI infections resulting in urethritis, pelvic inflammatory disease, ectopic pregnancy and infertility, but can also affect neonates born to positive mothers causing pneumonia and conjunctivitis.
- Lymphogranuloma venereum: **LGV** (serovars L1, L2 and L3) causing an endemic sexually transmitted infection (STI) in Africa, India, South-East Asia, South America and the Caribbean. It is most frequently detected in the UK in MSM (men who have sex with men) rectal swabs.

LGV was historically very rare in Western Europe and North America, but since 2003 a series of outbreaks have occurred, mostly among HIV-positive MSM. LGV is becoming increasingly common in the UK; in 2023 there were 1,360 cases, an increase of 15.9% from 2022 and 425% from 2012. Of these cases in 2023, 1246 (92%) were in MSM, with 24 in MSW and 16 in women. Two thirds of these cases were in London, with the remaining third spread around the country (UKHSA 2024 annual data, Ref: GOV-16764). Since 2017, changes in HIV prevention may have facilitated change in the epidemiology of LGV, with a significant rise in HIV-negative individuals testing positive for LGV (PHE, 2019).

Asymptomatic LGV infections are rare in the UK (~5% of cases). The clinical manifestations of symptomatic LGV infections are split into three stages, as detailed in the BASHH LGV guidelines:

1) Primary Lesion

Three to thirty days after exposure the patient develops a lesion in the form of a painless papule, a pustule, shallow erosion/sore, or an ulcer. The primary

manifestation in MSM is haemorrhagic proctitis, occurring in 96% of cases; symptoms of this include rectal pain, anorectal bleeding, rectal discharge, and constipation.

2) Secondary Lesions, lymphadenitis or lymphadenopathy

LGV is characterized by inflammation of the lymph nodes and tissue surrounding the infection. This causes tenderness and may result in buboes which then may ulcerate and discharge pus. This stage typically occurs 10-30 days following the development of the primary lesion.

3) Tertiary stage

The infection spreads in anogenital tissues and incites inflammation and destruction of tissue. Typically this presents as proctitis, proctocolitis mimicking Crohn's disease, fistulae and strictures. The infection very rarely proceeds to this stage, most patients recover after the second stage.

The 2023 BASHH guidelines for STI testing recommends testing all *C. trachomatis* positive rectal, pharyngeal, and ano-genital ulcer swabs from MSM for LGV (M-2753).

The recommended course of antibiotic treatment for LGV infection is significantly longer than that recommended for treatment against general *C. trachomatis* infection (CDC, 2015), therefore confirmation of the presence of an L serovar is clinically useful. Due to the fastidious nature of this intracellular organism nucleic acid amplification tests (NAATs) are exclusively the test of choice targeting the unique gap present in the DNA sequence of LGV strains compared to other of *Chlamydia trachomatis* serovars making this target a highly specific option.

At Micropathology Ltd we use a probe-based PCR to identify LGV serovars.

UKAS accredited sample types for this assay are swabs (endocervical, vaginal, rectal, throat, genital), first catch urine, and biopsies (rectal, lymph).

Other sample types, for example lymph node or buboe aspirate, may be tested and will be reported along with an appropriate caveat stating that the sample type is not accredited.

<u>References</u>

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