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Molecular diagnosis of Lymphogranuloma venereum infection

Lymphogranuloma venereum infection is caused by *Chlamydia trachomatis,* a dimorphic, non-motile, ovoid shaped bacteria. *C. trachomatis* consists of three biovars: serovars Ab, B, Ba and C which cause trachoma; serovars D-K which cause urethritis, pelvic inflammatory disease, ectopic pregnancy, neonatal pneumonia and neonatal conjunctivitis; and serovars L1, L2 and L3 causing lymphogranuloma venereum (LGV).

Chlamydia is the most commonly diagnosed STI in the UK. By comparison, LGV infection, caused by the L1, L2 and L3 *C. trachomatis* serovars, was rare in Western Europe and the USA for many years. Outbreaks of infection, however, have occurred amongst MSM more commonly in the UK since 2003, with most cases appearing in HIV positive individuals [1]. In the UK, the LGV positivity rate in *C. trachomatis* positive MSM is in the region of 15% [2]. Heterosexual transmission of the L-serovar remains extremely rare [3].

The health protection report for LGV infections published by Public Health England in July 2016 revealed how positive diagnoses in the UK had risen rapidly over the previous twelve years, with a sharper increase observed in the last three years recoded [4]. The UK's highest annual number of LGV diagnoses was reported in 2015 (946 cases). The number of diagnoses continued to rise in the first quarter of 2016 immediately before the report was published.

L-serovars of *C. trachomatis* are invasive and disseminate via connective tissue to regional lymph nodes [3]. Infection progresses in three stages following initial exposure: a primary ulcerative stage, a secondary stage where the patient may present with buboes and fistulae, and a tertiary, more complicated fibrotic stage with irreversible lymphedema [3]. Rectal exposure to these strains may also result in proctocolitis (inflammation of the rectum/colon) which can cause symptoms mimicking those caused by inflammatory bowel disease. Limited instances of cervical and oropharyngeal LGV infection have been described [5]. Due to the non-specific nature of some symptoms, clinicians should observe diligence when diagnosing patients and should always consider the individuals sexual history. Asymptomatic infection may also occur in around 25% of cases [3].

LGV diagnosis is typically based on clinical suspicion, epidemiological information and the exclusion of other aetiologies for proctocolitis. Indeed, persons presenting with clinical syndromes consistent with LGV should be presumptively treated for LGV at the initial visit. The recommended course of antibiotic treatment for LGV infection is 100mg of doxycycline orally twice a day for 21 days, which is significantly longer than the recommended treatment against general *C. trachomatis* infection [3]. In instances

of inguinal bubonic LGV, several clinical observations have suggested that this standard therapy could be insufficient [5]. Therefore, to prescribe the most appropriate and effective treatment plan, it is beneficial to the clinician to be able to confirm LGV infection via detection of *C. trachomatis* L1, L2 and L3 serovars.

Micropathology Ltd. uses a probe-based PCR assay for qualitative detection of *C. trachomatis* LGV strains. The polymorphic membrane protein H gene (*pmp* gene) is targeted during PCR DNA amplification. It is the unique gap present in this DNA sequence in LGV strains of *Chlamydia trachomatis* compared to other serovars which makes this assay highly specific to L-type serovars.

Validated sample types for this assay include swabs, urine and tissue. Appropriate swab sites will include the rectum, vagina, penis and lymph nodes dependent on clinical presentation. By extension, rectal and lymph node biopsies are considered the most clinically relevant tissue types for *C. trachomatis* detection in suspected cases of LGV. First-catch urine specimens can be used when urethritis and/or inguinal lymphadenopathy is present and LGV is suspected as the cause. Enlarged or fluctuant lymph node or buboe aspirate may also be useful to test where a patient presents with inguinal lymphadenopathy [1].

References

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