Lymphogranuloma venereum: biopsy, serology,
and molecular biology

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A 21 year old woman presented with painful groin lymphadenopathy and malaise. Lymph node biopsy, to exclude atypical infection and malignancy, suggested the diagnosis of lymphogranuloma venereum. This diagnosis was confirmed by serology and polymerase chain reaction, with the patient subsequently admitting to a casual sexual contact within the United Kingdom. Alternative methods of investigation of this disease are discussed. (Genitourin Med 1997;73:399–401)

Keywords: lymphogranuloma venereum; histology; polymerase chain reaction

Introduction
Lymphogranuloma venereum (LGV) is a sexually transmitted disease endemic in East and West Africa, India, South East Asia, and South America. It is uncommon in the United Kingdom, with a combined total of only 91 reports of chancreoid, granuloma inguinale, or LGV from genitourinary medicine (GUM) clinics in 1995. These cases usually occur following sexual contact abroad, with indigenous transmission being rare. We report a case of LGV, supported by histology, serology, and polymerase chain reaction (PCR) technology, following sexual intercourse within the United Kingdom.

Case report
A 21 year old white heterosexual woman presented with a 3 day history of lower abdominal discomfort, a painful right groin mass, frequency of micturition, and a 4 week history of general malaise, anorexia, and weight loss. Her past medical history consisted of a non-toxic goitre and a cholecystectomy. She was unemployed, and had no pets. She denied recreational drug use, and was not on any medication. She was known to be allergic to penicillin.

On examination she was pale, apyrexial, and distressed with pain. There was a small smooth goitre. The cardiovascular and respiratory systems were unremarkable. Examination of the abdomen revealed a cholecystectomy scar, but no guarding or organomegaly. A 2 cm lymph node was identified in the right groin. A number of smaller non-tender nodes were present in the left groin, and there was a single palpable node in the left axilla. There was no other lymphadenopathy.

Full blood count, serum biochemistry, liver, and thyroid function tests on admission were all normal. The Monospot test for infectious mononucleosis was negative. Her plain abdominal x ray demonstrated “bowel loaded with faeces”, but “no radiological evidence of bowel obstruction or perforation”.

The following day, the patient described a 2 month history of offensive vaginal discharge and offensive menstrual loss. Her last unprotected vaginal intercourse had been 4 weeks earlier with her regular partner of 6 weeks. Speculum examination showed a small cervical ectropion with closed external os, and no obvious infection. Bimanual examination was normal. It was felt the symptoms were not of gynaecological origin, but that infection (including HIV) should be excluded. Urinary β HCG was negative. Swabs for Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis were negative, although β haemolytic group B streptococci and Candida albicans were isolated. The patient was seen by a counsellor who deemed the patient to be of “low risk” for HIV, and was consequently not tested.

In order to exclude atypical infection and neoplasia, the right groin was explored with an excisional lymph node biopsy. Two days postoperatively, the patient developed a wound haematoma requiring drainage. There was no demonstrable growth. Three days postoperatively, a urine sample taken at the time of the biopsy grew Escherichia coli which was sensitive to trimethoprim. In view of the histology report, the patient was transferred to the care of the Communicable Diseases Directorate.

The groin biopsy had demonstrated a reactive lymph node with marked paracortical and follicular hyperplasia, and many mononuclear B cells in the subcapsular sinus. Scattered geographic microabscesses containing polymorph neutrophils and polymorph debris were seen through the nodal parenchyma with a surrounding rim of histiocytes (fig 1). Stains for infective agents (Gram/PAS/Giemsia) failed to identify an infective agent. Extranodal inflammation with fibrosis was also present. The differential diagnosis included LGV, yersinial infection, cat scratch disease, and systemic lupus erythematosus, although LGV was favoured given the site and clinical details.

On further questioning by a genitourinary physician, the patient admitted to having had three sexual partners within the past 12 months. The most recent of these was her current partner as above. Before this relationship, she had engaged in unprotected vaginal inter-
Serial chlamydial serology

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<th>Day</th>
<th>19</th>
<th>1</th>
<th>2</th>
<th>15</th>
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<td>—</td>
<td>&lt;16</td>
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<td>—</td>
<td>96</td>
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<tr>
<td>WIF (Bristol PHLS)</td>
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<td>128</td>
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<td>512</td>
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<tr>
<td>MIF (Manchester PHLS)</td>
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<td>32</td>
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<td>LGV (Sheffield PHLS)</td>
<td>10</td>
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LGV = lymphogranuloma venereum; CFT = complement fixation tests; WIF = whole inclusion immunofluorescence test; MIF = microimmunofluorescence titres.

Barr virus reactivation (IgM seroconversion in the presence of existing IgG), elevated liver transaminases, and elevated antinuclear antibody/smooth muscle antibody titres suggestive of a possible underlying connective tissue disorder. Blood counts and serum biochemistry remained normal throughout the clinical course, and serology for syphilis, HIV, hepatitis A, B, and C, Toxoplasma, cytomegalovirus, and Yersinia were all negative. Chest x ray and abdominal/pelvic ultrasound scans were unremarkable. A 4 cm diameter cystic mass was noted in the right groin, although aspiration was unsuccessful.

Given the clinical signs, the abnormal liver function tests, and the histology the presumptive diagnosis was of LGV with Fitz-Hugh-Curtis syndrome. The patient was commenced on minocycline 300 mg immediately, followed by 200 mg twice daily. The health advisers initiated contact tracing.

Over the following 2 weeks, the patient’s genital lesions gradually healed, but around the posterior fourchette a crop of viral warts (DGI negative) were noted. These were...
In the past, the diagnostic gold standard for LGV has been the culture of *C. trachomatis* serovar L1–3 node from either the primary lesion or from a lymph aspiration. The specificity of cell culture is excellent, however its sensitivity is only about 50%.

Histology of the lymph nodes in LGV show follicular hyperplasia and geographic abscesses. These changes are supportive of LGV within the clinical background, but are not pathognomonic. The differential diagnosis includes yersinial infection, systemic lupus erythematosus, cat scratch disease, and tularemia.

Serology provides a useful tool in the diagnosis of LGV. Documented seroconversion, however, is rarely seen since patients usually present after the acute stage. Micro-immunofluorescence (MIF) titres are usually high (>1/512), but this test has broad cross reaction with other *C. trachomatis* serovars. The whole inclusion immunofluorescence test (WIF) is more specific for LGV strains of *C. trachomatis*. PCR is therefore used to confirm infection, rather than the previously used E serovar. A rise of 1/64 or greater with LGV complement fixation tests (CFT) is seen in 50% of patients. This response, in conjunction with the elevated WIF, is indicative of LGV.

By using PCR primers selected from the nucleotide sequence of the endogenous plasmid of *C. trachomatis*, the presence of *C. trachomatis* can be specifically differentiated from other species. The diagnosis in our patient was confirmed by serovar typing the major outer membrane protein gene of *C. trachomatis* by PCR and restriction fragment length polymorphism analysis.

The polymerase chain reaction may provide an accurate laboratory diagnosis of LGV in low prevalence areas, without the need for cell culture. However, it should be remembered that inhibitors of the PCR can be present in human material, including body fluids, and give rise to false negative reactions. Although PCR is rapid and sensitive, it cannot therefore totally replace current conventional laboratory methods, and should be viewed as a useful additional test to complement those that already exist. In conclusion, PCR is an exciting new test which should improve the diagnostic efficiency in cases of lymphogranuloma venereum.