

Anogenital *Chlamydia trachomatis* Infection Including Lymphogranuloma Venereum

Clinical Guidelines, Sweden

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Background and clinical features

Within the genus *Chlamydia* there are three species that cause disease in humans; one of these is *Chlamydia trachomatis*. This species contains three biovars. The bacterium has different serovars (genotypes). Genotypes A–C cause trachoma, whereas genotypes Ba and D–K cause sexually transmitted anogenital chlamydial infection. Lymphogranuloma venereum, a rare disease in industrialized countries, is caused by the genotypes L1–L3.

C. trachomatis is the dominant pathogen causing urethritis, cervicitis and salpingitis. Salpingitis is not uncommonly a subclinical asymptomatic infection, which nevertheless causes tubal factor infertility. Male infertility due to *C. trachomatis* infection is thought to be rare. *C. trachomatis* is the most common known bacterial sexually transmitted infection worldwide. In Sweden more than 40,000 cases are reported annually to the Swedish Institute for Infectious Disease Control. Approximately 90% of infected individuals are between 15 and 30 years of age, with a median age of 20 years. The transmission rate of *C. trachomatis* infection is very high; there is an estimated chance of transmission of 50% each time unprotected sexual intercourse takes place.

More than half of cases of male urethritis are asymptomatic. When symptoms do occur, the main ones are a mucus discharge from the urethra and a slight to moderate dysuria (pain during micturition) that is unrelenting or intermittent. An epididymitis, often unilateral, is the most common and serious complication. In women, if there are any symptoms (two-thirds of infected women are asymptomatic), the most common is vaginal discharge, often foul smelling and caused by concurrent bacterial vaginosis, which occurs in almost half of cases. Other common symptoms are intermenstrual or post-coital bleeding. An endometritis or salpingitis often causes lower abdominal pain, not uncommonly slight or moderate.

Conjunctivitis due to passive transmission by a finger from the genitalia to the eye usually starts unilaterally. Infection in the throat is uncommon and probably of minor importance. Anal chlamydial infection may lead to symptoms of proctitis.

Sexually acquired reactive arthritis appears occasionally and a chlamydial infection can trigger Reiter's syndrome in genetically predisposed individuals.

Lymphogranuloma venereum

The primary lesion of lymphogranuloma venereum (LGV) usually takes the form of an ulcer or erosion, which develops after an incubation period of 3–12 days or longer. Lymph nodes, usually the inguinal nodes, enlarge after an incubation period of 1–6 months, causing pain and eventually erupting as an abscess. Fistulas may appear. In Western countries there is an epidemic of LGV among men who have sex with men (MSM). Among MSM the signs and symptoms of LGV are less prominent, although signs and symptoms of proctitis are common.

Clinical diagnosis

Indications for testing

Testing for *C. trachomatis* should be offered to all individuals who have had unprotected sexual intercourse with a new partner within the last 12 months and to those with symptoms of infection, regardless of whether or not they have changed partners. Individuals attending sexually transmitted infection (STI) clinics, seeking termination of pregnancy, first-time pregnant women, and women pregnant and with a new partner within the last year, should all be tested for *C. trachomatis*. In addition, no-one requesting a *C. trachomatis* test should be denied testing.

Men

First-catch urine (FCU), of maximum volume 10 ml, with a urinary bladder incubation time of at least 1 hour, should be sampled. In MSM with a history of fellatio, a swab sample should be taken from the wall of the throat or, alternatively, a gargle specimen. When passive anal intercourse or fisting has occurred a rectal specimen should be taken, preferably via a proctoscope.

Women

Swab sampling from the endocervix, and preferably also from the lateral vaginal wall, is recommended. Patients' self-sampling from the vagina has a similar sensitivity and is recommended in a screening context. FCU testing is less

sensitive, and a combination of a vaginal sampled swab placed into a tube of FCU is probably not more sensitive than a vaginal swab, and is less easy to obtain. The highest sensitivity is achieved by samples from all described sites being analysed separately, but this procedure is prohibitively expensive. Women with symptoms of infection should always be referred for a gynaecological and clinical evaluation and microscopic examination of smears.

A positive *C. trachomatis* test could be expected to appear one week after sexual intercourse at the earliest.

Lymphogranuloma venereum

Samples should be taken as described above with a firm sampling. In the case of an ulcer or erosion, then that site should be used for sampling, otherwise samples should be collected from the relevant site, such as the rectal mucus or the urethra.

Laboratory diagnosis

The clinician should be knowledgeable about which method of analysis is used at the laboratory. In 2006, a deletion of a DNA-segment of *C. trachomatis*, which was used as a target for some nucleic acid amplification tests (NAATs), was detected in Sweden, and it is estimated that 7,000 individuals had an undetected chlamydial infection. The strain was termed the new variant of *C. trachomatis*, and NAATs have since been adjusted and, as a consequence, many methods use two or more target DNA sequences for detection. It is still possible to perform tissue culture for isolation of *C. trachomatis* at some laboratories, but this method is not used routinely. NAATs, as polymerase chain reactions (PCRs), are the methods of choice. At certified laboratories control of inhibition is performed and positive samples are always re-analysed using the original specimen. Hence, the specificity of the tests is close to 100% and the sensitivity is acceptably high.

In cases of alleged sexual assault the initial *C. trachomatis* tests of the victim and suspect should be genotyped, in addition to *C. trachomatis* positive specimens sampled at least 2 weeks later. The genotyping can be performed at the Department of Microbiology at Akademiska Hospital in Uppsala (phone +4618-611 3916).

Lymphogranuloma venereum

NAAT and, for specific diagnosis, genotyping is required. If an LGV infection is suspected the examining doctor may contact the Department of Microbiology at Akademiska Hospital in Uppsala (+4618-611 3916). For epidemiological reasons the choice of treatment is very important to confirm an LGV infection. If genotyping was overlooked initially the sampled specimen can be genotyped later.

Treatment

Indications for treatment

C. trachomatis is susceptible to the relevant antibiotics, and antibiotic resistance is extremely rare. Current sexual partners of an infected individual should always be tested before being treated, but should also always be treated as soon as possible. Previous partners should be treated on the basis of signs, symptoms and the result of *C. trachomatis* tests.

Uncomplicated infection

Doxycycline 100 mg, two tablets on the first day and one tablet daily for a further 8 days¹. At high levels of ultraviolet (UV) radiation, as occur in June and July in Sweden, lymecycline 300 mg twice a day for 10 days, oxytetracycline 500 mg twice a day for 10 days, azithromycin 1 g in a single dose, or erythromycin 500 mg twice a day for 10 days can be prescribed.

Pregnancy

Amoxicillin 500 mg three times a day for 7 days during pregnancy. Doxycycline, which is a more reliable treatment, can be prescribed up to gestation week 15 and azithromycin 1 g as a single dose after gestation week 12. All treated women should be given a test of cure 4–5 weeks after commencement of treatment.

Severe infection

Salpingitis: Out-patients: Ceftriaxone 250 mg as a single dose intramuscularly (contains lidocaine) followed by a 2-week treatment with doxycycline 100 mg twice a day and concurrent 10-day treatment with metronidazole 400 twice a day. This treatment should be prescribed if testing has been done but no results are available. Ceftriaxone is effective against gonorrhoea, but other possible pathogens should also be considered, such as *Mycoplasma genitalium* (which is less susceptible to many antibiotics and for which azithromycin is the treatment of first choice).

Epididymitis: If a concurrent infection with *Neisseria gonorrhoeae* cannot be ruled out ceftriaxone 250 mg as a single dose intramuscularly (contains lidocaine) followed by doxycycline twice a day for 10 days should be prescribed. Concurrent infection with *Mycoplasma genitalium* should also be considered (which is less susceptible to many antibiotics and for which azithromycin is the treatment of first choice).

¹In most European countries and in North America there is a recommendation in the guidelines to prescribe doxycycline 100 mg twice a day for 7 days. Several Swedish studies have shown the above-mentioned 9-day treatment to be as effective (1–3).

Asymptomatic current partners are treated as described above (under the heading “uncomplicated infection”).

Lymphogranuloma venereum: Individuals with suspected LGV should never be treated without a previous consultation with an STI clinic.

Doxycycline 100 mg twice a day for 3 weeks.

Follow-up

Individuals, if not pregnant, with a treated uncomplicated chlamydial infection need no test of cure. It is of great importance, however, to emphasize that all sexual relationships should be avoided up to 10 days after commencement of treatment, both for patients and their current partners.

Patients should also be given written governing rules (The Communicable Diseases Act (SmL) 2004: 168 and SOSFS 2005: 23 (Guidelines from The National Board of Health and Welfare)).

In cases of alleged sexual assault repeat testing for *C. trachomatis* should be performed after 2–3 weeks if initial testing for the bacterium was negative and no antibiotic treatment was prescribed. All patients with severe infections, such as LGV,

should always be given an appointment for a follow-up visit 5–6 weeks after commencement of treatment.

Reporting to authorities and contact tracing

Physicians in Sweden are obliged to report *C. trachomatis* infection under legislation passed in 1988 (The Communicable Diseases Act (SmL 2004: 168)), which also includes mandatory partner notification (contact tracing). How these procedures should be carried out is documented clearly in publications from The National Board of Health and Welfare (SOSFS 2005: 23 and “Smittspårning vid sexuellt överförbara infektioner” (2007)) (available from: www.socialstyrelsen.se).

References

1. Ripa KT, Mårdh PA, Thelin I. Chlamydia trachomatis urethritis in men attending a venereal disease clinic: a culture and therapeutic study. *Acta Derm Venereol* 1978; 58: 175–179.
2. Jeskanen L, Karppinen L, Ingervo L, Reitamo S, Happonen HP, Lassus A. Ciprofloxacin versus doxycycline in the treatment of uncomplicated urogenital Chlamydia trachomatis infections. A double-blind comparative study. *Scand J Infect Dis Suppl* 1989; 60: 62–65.
3. Falk L, Lindberg M, Jurstrand M, Bäckman A, Olcén P, Fredlund H. Genotyping of Chlamydia trachomatis would improve contact tracing. *Sex Transm Dis* 2003; 30: 205–210.