

Gonorrhoea Clinical Guidelines, Sweden

PRESENTED BY ANN-KERSTIN RUDÉN

Department of Dermatology, Södersjukhuset, SE-118 83 Stockholm, Sweden. E-mail: ann-kerstin.ruden@sodersjukhuset.se

Background and clinical presentation

At present approximately 600–700 cases of gonorrhoea are reported each year in Sweden, of which approximately 80% occur in men, especially among men who have sex with men (MSM) who are mainly infected in Sweden, and heterosexual men who are infected abroad. Women are infected mainly in Sweden. The infection is caused by the bacterium *Neisseria gonorrhoeae*, a Gram-negative diplococcus. The usual incubation period is 2–10 days. Approximately 50% of women and a smaller proportion of men have an asymptomatic genital infection.

Gonorrhoea can be transmitted through sexual intercourse, oro-genital contact, from mother to child during delivery, and through transmission of infected genital secretions to the eye. Contagiousness is 60–70% in the case of repeated unprotected sex with an infected partner.

The uncomplicated infection in men is urethritis with symptoms such as discharge, often purulent, and dysuria. Urgency of urination and itching of the urethra can also occur. An ascending infection can result in epididymitis, usually localized in one epididymis, with pain, swelling and sometimes fever. Prostatitis can also be a complication.

The uncomplicated infection in women is cervicitis and urethritis, often with symptoms such as discharge, often purulent and sometimes sanguineous, dysuria and low-seated abdominal pain. Bartholinitis is a rare manifestation that may result in labial swelling. Ascending infection can lead to endometritis, salpingitis/pelvic inflammatory disease (PID), sometimes with perihepatitis and periappendicitis. Approximately 10–15% of women with uncomplicated gonorrhoea develop PID, often with symptoms of abdominal pain of varying intensity, fever and influence on the general condition, but the infection can also have few symptoms. Residual conditions after PID can be infertility, extra-uterine pregnancy and chronic abdominal pain.

Proctitis can develop due to infection through anal intercourse. In women proctitis also can result from direct spread from the urethra or cervix. Pharyngitis, usually asymptomatic, is spread to the throat via oro-genital contact. Conjunctivitis due to transmission from infected genital secretions is an often serious complication, which untreated can result in perforation of the cornea and scarring. This complication can also be seen

in newborns, who are infected during delivery by an infected mother. Disseminated gonococcal infection (DGI) is caused by haematogenous spread and is rare. Women are affected to a greater extent than men. The most common symptoms are low-grade fever and septic arthritis, particularly affecting the large joints, such as the knee and ankle. Skin lesions in the form of pustules are usually located on the extremities. It is essential to consider the diagnosis and to collect genital samples.

Immunological complications of gonorrhoea may occur, primarily in the form of reactive arthritis, isolated or as a part of Reiter's syndrome.

Diagnosis

Indications for testing

Epidemiological and clinical suspicion, sexual contacts abroad, MSM, persons who buy or sell sex.

Sampling

The patient should preferably not have urinated for 1–2 hours prior to sampling. Routine samples for culture are taken from the urethra in men and from the urethra and cervix in women. Tests for microscopy are taken from the urethra with a plastic loop, and from the cervix with a cotton swab or plastic loop. Microscopic examination of mucus, mounted on slides and stained with methylene blue, is almost always positive in men with symptoms and in 30–50% of women. Diplococci are seen lying with the long sides facing each other in the cytoplasm of polymorphonuclear leucocytes. Samples for culture are taken with an ear nose and throat (ENT) stick, which is placed in special transport medium. Samples are taken 1–2 cm into the urethra for both men and women. The stick is swirled gently, and then a few seconds allowed to elapse before the stick is pulled out, to allow time for secretions to be absorbed. Samples are taken 1–2 cm into the cervix after the portio is dried off. Only water is used on speculum, as lubricants can be toxic to gonococci. When samples can only be taken from the cervix and not from the urethra, approximately 6% of gonorrhoea cases are missed. The patient's history and clinical presentation may provide guidance as to whether further testing is current. Samples from the throat are taken with a stick, which passes over the posterior pharyngeal wall and both tonsils. Samples

from the rectum are taken 3–4 cm into the anal canal. For symptomatic infections, samples are taken through a proctoscope. Cultures from the throat and rectum have a sensitivity of < 60%. On suspicion of eye infection, samples are taken from inside the lower eyelid. If septic arthritis is suspected, samples are taken from the synovial fluid. On suspicion of spread into the blood (DGI) culture from the blood is carried out, but is usually negative due to varying bacteraemia.

Laboratory diagnostics

Culture is the reference method. Tests for antimicrobial susceptibility is always performed. Nucleic acid amplification tests (NAAT) are methods with high sensitivity and nowadays also with high specificity. These tests are particularly useful in screening asymptomatic patients but they are not validated for extra-genital sites and susceptibility testing cannot be carried out. These tests can be used on urine samples (first void urine) and on swabs from the vagina, urethra and cervix.

Treatment

In recent years gonococcal strains have increasingly shown reduced susceptibility or resistance to a variety of microbial agents, and the infection has become increasingly difficult to treat. In addition, up to 20–30% of gonococcus strains are penicillinase-producing (penicillinase-producing *Neisseria gonorrhoeae*; PPNG). Because of the above factors, patients with gonorrhoea should preferably be dealt with by, or in consultation with, a venereologist.

In addition, note that co-infection with *Chlamydia trachomatis* is common. Testing should be carried out for *Chlamydia trachomatis* and treatment given liberally on clinical or epidemiological suspicion.

Current sexual partners should be treated immediately the test is taken. Remaining sexual partners should be treated according to clinical picture and the test results.

Uncomplicated anogenital infection

Treatment in cases of clinical or epidemiological suspicion, or a positive direct test when results of the susceptibility testing is not ready:

Recommended alternatives

- Cefixime (Suprax®) 400 mg single dose (which is a licensed oral drug). The development of resistance to cefixime has been seen in recent years, and currently 5% of strains have reduced susceptibility or resistance.
- Inj ceftriaxone 250 mg i.m. single dose. Note: Use a preparation containing lidocaine.

- Inj spectinomycin (Trobicin®) 2 g i.m., single dose (which is a licensed drug). Spectinomycin is an aminocyclitol. The only indication is gonorrhoea. Spectinomycin may be given in cases of penicillin allergy.

Previously, ciprofloxacin was the recommended regimen for gonorrhoea therapy. The rapid development of resistance, especially in strains from Asia, has meant that this drug can now only be used when susceptibility testing shows that a strain is sensitive to ciprofloxacin.

Also, rapid development of resistance to azithromycin has been seen in recent years. Currently 14% of strains have reduced sensitivity or resistance. In addition, it should be noted that even if the strain is sensitive to azithromycin in vitro, treatment failure can occur at a dosage of 1 g. A higher dosage, of 2 g, must be given, but this often leads to gastrointestinal side-effects.

Treatment based on resistance patterns

Ampicillin-sensitive strain: amoxicillin 2 g, single dose + probenecid 1 g.

Ciprofloxacin-sensitive strain: ciprofloxacin 500 mg, single dose.

Treatment of pregnant women with uncomplicated infection

Inj ceftriaxone 250 mg i.m. single dose. Alternatively, inj spectinomycin (Trobicin®) 2 g i.m., single dose.

Pharyngeal infection

Usually treatment based on resistance patterns.

Inj ceftriaxone 250 mg, single dose. Few and small studies with cefixime 400 mg, single dose. Poor efficacy of spectinomycin.

Gonococcal conjunctivitis

Few good studies, small materials. Always co-operate with ophthalmologists. Inj ceftriaxone 1 g i.m., single dose if uncomplicated conjunctivitis. If cornea is engaged i.v. therapy for a longer period is necessary.

Treatment of complications

Epididymitis

Aetiology is often unclear when treatment is initiated. Inj ceftriaxone 250 mg i.m. single dose + doxycycline 100 mg × 2 for 10 days. Treatment often in consultation with the urologist.

Note that this is not an effective treatment for *Mycoplasma genitalium*.

PID

Aetiology is often unclear when treatment is initiated.

Outpatients: Inj ceftriaxone 250 mg i.m. single dose + doxycycline 100 mg × 2 and metronidazole 400 mg × 2 for 2 weeks.

Inpatients: Inj ceftriaxone 1 g i.v. or i.m. once daily for up to 1 day after clinical improvement + doxycycline 100 mg × 2 and metronidazole 400 mg × 2 for 2 weeks.

Treatment in collaboration with the gynaecologist.

Note that this treatment is not effective for *Mycoplasma genitalium*.

Disseminated gonococcal infection

Inj ceftriaxone 1 g i.m. or i.v. once a day or inj spectinomycin

(Trobicin®) 2 g i.m. twice a day. Parenteral treatment for up to 1–2 days after clinical improvement followed by oral treatment with cefixime (Suprax®) 400 mg × 2. Total treatment time 7 days.

Follow-up

After uncomplicated genital gonorrhoea with a strain sensitive to the antibiotics used, for patients without symptoms after completing treatment, and with no suspicion of reinfection, a check-up 1–2 weeks after completed treatment is recommended. After complicated gonorrhoea, pharyngeal infection or rectal infection, two check-ups are recommended at weekly intervals.

Notification and contact tracing

In Sweden gonorrhoea infection is notifiable under the Communicable Disease Act, and contact tracing must be carried out.

Comments on the Guidelines – Edited by Tomas Norman Dam

Specific comments on these guidelines were made by Bolli Bjarnason, Jon Hjaltalin Olafsson, Harald Moi, Sirkku Peltonen, Carsten Sand and Arne Wikström. These comments have been compiled into a summary, edited and commented on by CME editor Tomas Norman Dam. Further comments on the guidelines from Forum readers can be mailed to cme@medicaljournals.se. They will be presented for discussion in the next issue in the CME section.

General comments and comments on the recommended treatments

The guideline recommendations are problematic in Denmark, Finland and Norway as spectinomycin and cefixime are not registered in these countries. In contrast, they generally align with Icelandic practice in the Department of Venereology. In Denmark, ceftriaxon is the routine treatment, while in Norway, where the European IUSTI guidelines are followed, cefixime is indicated for uncomplicated urethral gonorrhoea.

According to the editors' responses, there are no published gonorrhoea guidelines in any of the countries. However, guidelines have just been published in Finland, and it is possible that the guidelines presented here can be assimilated in

Iceland with some modifications. It was commented that the presentation of the treatments for disseminated gonococcus infection was difficult to follow, especially when combinations of more than one therapy were recommended.

Comments on diagnostic approaches

In Finland, routine screening involves gene amplification using urine samples, while culture samples are only taken from patients with symptoms. It was recommended that culture samples be processed in the lab on the day that they are collected because decreased sensitivity has been observed if their processing is delayed until the next day.