Non-specific Urethritis and Non-specific Cervicitis
Clinical Guidelines – Sweden

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Background and clinical picture

Urethritis, inflammation of the urethra, causes pain upon micturition (dysuria), itch in the urethra, and sometimes a vague sensation of discomfort in the penis, which may be accompanied by a more or less evident outflow from the urethra.

An increase in the number of white blood cells is observed in a stained smear of the secretion. Symptoms may be absent or discrete and sometimes intermittent. The discharge may be minimal.

In women the picture is often more complex than in men; however, isolated urethritis can be treated in the same way as in men. Cervicitis, inflammation of the cervical canal, may cause lower abdominal pain and increased vaginal discharge. At examination purulent flour from the cervical os is observed and the cervix may be tender. In a stained smear from the cervix there is a pronounced increase in white blood cells, as well as in a wet smear of the vaginal secretion. An isolated finding of increased white blood cells from the cervix is unspecific, as the level of white blood cells may vary during the menstrual cycle or be dependent on other factors (e.g. an intrauterine device).

Known causes of urethritis/cervicitis, such as infections with *Neisseria gonorrhoeae, Chlamydia trachomatis* and *Mycoplasma genitalium*, are described in respective sections. Other causes of urethritis are infections with *Trichomonas vaginalis,* herpes simplex virus (HSV), *Neisseria meningitidis* and possibly *Ureaplasma urealyticum* and adenovirus. Urethritis may be seen concomitantly with condylomas and balanitis. Foreign bodies or strictures in the urethra also cause urethritis. Another cause of cervicitis is HSV. It is possible that hitherto unknown microorganisms may cause urethritis and/or cervicitis.

In the following paragraphs non-specific urethritis/cervicitis is defined as a situation in which tests for gonorrhoea, chlamydia and *M. genitalium* are negative and which fulfils the criteria given below. In Swedish sexually transmitted infections (STI) clinics these cases usually comprise 30–40% of all urethritis. Trichomoniasis occurs very rarely at present, and is thus almost never an alternative. Genital herpes may sometimes be expressed as an isolated urethritis and is characterized by pronounced dysuria. In the stained smear mononuclear cells are often present.

Diagnostics

Urethritis

Subjective symptoms, such as dysuria, urethral itch and, in men, discomfort in the penis. Objectively, there is a discharge from the urethra, which can be clear, mucous-like or purulent. A stained smear without the presence of gonococci with >4 polymorphonuclear neutrophilic leucocytes (PMNL)/high-power field (magnification 1000×) in >4 fields where the concentration of PMNL is highest. The technique is not standardized, e.g. different types of instrument are used when taking the smears, such as plastic loops, metal spatulas or cotton-tipped swabs. A representative sample should contain epithelial cells. An interval of 2 h since the last passing of urine is desired, or alternatively that the patient is examined in the morning before the first micturition. Careful massage of the urethra will contribute to obtaining a representative smear. For diagnosis, a urethral discharge and/or a positive smear is required. Only subjective complaints may require new validation at a later occasion and are not an indication for treatment.

Cervicitis

There is a lack of well-recognized and strict criteria. Pain in the lower bowel, post-coital bleeding and spotting are symptoms that may occur, as is perceived increased vaginal discharge. A mucopurulent fluor in the cervical os, which may also show easy bleeding upon sampling and tenderness are findings that may occur. Microscopically more white blood cells than epithelial cells are seen in a wet smear. In a stained smear from the cervix a pronounced increase in PMNLs without gonococci may be observed. The limit for a positive sample has arbitrarily been set to 30/high-power field.

Treatment

Motives for treatment

Alleviate/cure symptoms and reduce the risk of transmission. Despite a negative test for chlamydia, chlamydial infection cannot be 100% ruled out. To prevent complications such as reactive arthritis or epididymitis and, in women, upper genital infections such as salpingitis that hitherto unidentified microbial agents may give rise to. Reduce the risk of HIV transmission, which is increased concomitant with inflammation of the urethra/cervix, at epidemiological suspicion of STI before the test results are known. When there is a lack of subjective symptoms and discharge and findings of "low-grade" urethritis (5–10 PMNL/high-power field) active treatment should be awaited. Partner control may be undertaken.

Uncomplicated infection

Doxycycline 200 mg p.o. day 1, thereafter 100 mg p.o. for 8 days. Or: azitromycin 1 g immediate dose (only when there is

a negative test for *M. genitalium*). Alternatively: erythromycin 500 mg p.o. ×2 for 14 days.

Information about the nature of the disease and the importance of complying with the prescribed treatment. Abstain from intercourse even with condoms during the treatment period.

Pregnancy

See chlamydial infection.

Partner

Present sexual partner should be offered examination and epidemiological treatment, preferably with the same type of drug as the patient.

Follow-up

In general there is no need for a control.

Persistent or recurrent symptoms

Verify that urethritis/cervicitis is still present as defined above. Check compliance with the prescribed treatment. Exclude re-infection. New partner – new infection? Consider new tests for *Neisseria gonorrhoeae, Chlamydia trachomatis* and *Mycoplasma genitalium*. Non-infectious cause possible?

Treatment of persistent or recurrent non-specific urethritis/cervicitis

Azithromycin 500 mg p.o. day 1 followed by 250 mg p.o. days 2–5.
Alternatively: Erythromycin 500 mg p.o. ×4 for 21 days, or a prolonged course with doxycycline up to 3 weeks, especially if the patient reported a transient improvement with this drug earlier.

If the patient has been treated with a macrolide in the first place: doxycycline 200 mg p.o. day 1 followed by 100 mg p.o. for 8 days.

Note: Combination with metronidazole 400 mg p.o. ×2 for 1 week is only recommended in areas where *Trichomonas vaginalis* is prevalent according to the International Union against Sexually Transmitted Infections (IUSTI) guidelines.

If the patient has a positive test for *Ureaplasma urealyticum* and did not respond to doxycycline it is suggested to give clarithromycin 250 mg p.o. ×2 for 10 days.

If the patient is not cured after this treatment, consider referral to a urologist for urethroscopy and at negative findings individual actions – primarily reassuring support. Re-treatment of the partner is not considered necessary. At remaining cervicitis consider referral to a gynaecologist for evaluation.

Comments on the Guidelines – Edited by Tomas Norman Dam

General comments were submitted from Harald Moi and Olle Larko, they both found this guideline up-to-date and well written. Detailed comments to this guideline were given by Helle Kielberg Larsen (Bispebjerg Hospital, Denmark) and will be presented below in interview format. Further comments to the guidelines from Forum readers can be mailed to cme@medicaljournals.se and will be presented open for discussion in the next issue of the CME section.

General comments and comments on the recommended treatments

"I find the guideline "Non-specific urethritis and non-specific cervictitis" fine, and it covers all the aspects that you need in your daily work with this type of patients."

Do you have similar guideline in you country? "Yes, we have a national guideline, but it has not been renewed since 1999. We have a local guideline at our venereology clinic at Bispebjerg Hospital, Copenhagen that is more or less similar."

Do you find that this guideline is essentially similar to the corresponding guideline in your country? "I think the above answer is also the answer to this question, but less detailed, we should make it more like yours".

Regarding diagnostics: " I prefer to write: A stained smear without the presence of gonocci with ≥5 polymorphonuclear neutrophilic leucocytes....instead of >4, all though it is basically the same.

We do not examine for ureaplasma urealyticum as it can be isolated from at high percentage of healthy sexually young women (50–70%), so if a person is tested negative for gonorrhoea, chlamydia and mycoplasma genitaltium, we treat as non-specific urethritis, and that is, as I read your guideline, consistent with your recommendation".

Regarding treatments: "We follow IUSTI international guideline that recommend first line treatment for uncomplicated infection: Doxycyline 100 mg × 2 for 7 days (we say 10 days)".