

Sexually transmitted diseases: from the clinician's perspective

Sexually transmitted diseases (STDs) with different clinical settings: urinary tract infections (= cervicitis) with or without discharge and genital ulceration are investigated below.

Urinary tract infection (= cervicitis in women)

Urinary tract infections can present with a burning sensation, particularly when urinating and at the urethral tip (differential diagnosis with non-infectious urinary tract infections) No associated pollakiuria (differential diagnosis with urinary infection) no back pain (acute pyelonephritis, lithiasic pathology). The discharge is not constant; more than half of all urinary tract infections are asymptomatic.

Cervicitis is seen through abundant leucorrhoea of varied colours, and often with urinary symptoms (including pollakiuria) by contiguity.

Diagnosis of urinary tract infections with discharge (or mucopurulent cervicitis)

The causative pathogenic agents are *Neisseria gonorrhoeae* (Ng), *Chlamydia trachomatis* (Ct) and *Mycoplasma genitalium* (Mg) (these 3 species are responsible for almost 50% of urinary tract infections), but also *Haemophilus influenzae* or *parainfluenzae*, (4% of cases), *Neisseria meningitis* in cases of oral sex), *enterobacteria* (in cases of anal sex) or *Trichomonas vaginalis* (Tv, rarer).

The visible appearance of the discharge is variable and is of no significant predictive value: white to green, mucous to purulent, more or less abundant, constant or in the morning. All types are seen, including gonococcal urinary tract infections without discharge (if the patient is seen at a later stage of infection or treats himself/herself through hyperhydration).

Samples

- **Urethral samples (US):** with a plastic tip (less painful in comparison to dacron or cotton which scrape); enter no more than 1 cm into the urethra (into the navicular fossa) if necessary. However, sampling is also possible using a drop of freshly obtained pus following cleaning of older pus with saline solution;
- **Cervical samples:** pus samples from the endocervix using a speculum with a swab;
- Testing is then completed with a first morning urine sample (urine samples from women include vaginal cells).

Diagnosis

- Prepare a Gram stain or blue stain smear sample: the urinary tract infection is defined through the presence of more than 5 polynuclear neutrophils (PN) on the urethral smear sample at approximately x100 or more than 10 PN upon examination of a pellet sample from the first morning urine sample at x400; screen for the presence of Gram negative intracellular cocci;
- Spread the sample on Columbia agar for culturing and identification of everyday bacteria and then on chocolate and/or VCAT agar for identification of *N. gonorrhoeae*.
- Screening through the amplification of nuclear acids (NAAT) using the first morning urine sample (preferred sample for male patients) or a vulvo-vaginal sample in women, Ct, Ng +/- Tv and Mg;
- Analyse while still fresh if *T. vaginalis* is suspected (culturing on Roiron medium is an almost obsolete practice).

Diagnosis of urinary tract infections or cervicitis without discharge

Do not collect a urethral sample; in cases of urinary tract infection, collect a first morning urine sample for cytological analysis and NAAT for Ct, Ng +/- tv and Mg In cases of cervicitis, collect a first morning urine sample or collect a vaginal sample (unless menstruating) for NAAT.

Test of almost no clinical significance:

- Serology testing for *C. trachomatis* (of significant clinical interest only in cases of venereal lymphogranuloma (VLG) or high infection),
- Mycoplasma culturing (*M. hominis*, *U. urealyticum*): outside of the scope of medically assisted procreation, Uu or Mh infections are not considered as true STDs. They only indicate another infection (*M. hominis* combined with bacterial vaginosis),
- Urine culture (2nd stream),
- Urine sample without discharge.

Genital ulceration

This is a loss of substance in the epidermal - dermal anal-genital area and, by extension, in the oral zone if the context indicates this (same reasoning when faced with oral or genital ulceration). In 50% of cases, no aetiology is found; in the other

half of cases, it is a STD (in descending order of frequency: herpes, syphilis, VLG, primary infection with HIV) or for non-infectious causes (trauma, corrosive, aphtha, fistula skin cyst, scabious nodule etc.). And chancroid? "It no-longer exists" (no cases have been identified outside of Saint Louis hospital for 20 years).

Diagnosis

Clinically, it lies in the depth, appearance and number of chancroids; the pain indication is rather suggestive of herpes, the size > 1 cm leads toward syphilis, but is not clinically reliable.

In the laboratory, we recommend:

- Carry out a smear on a slide for microscopic examination on a black background (the only examination that can rapidly confirm syphilis; PCR will soon replace this) and a Gram stain (Gram negative bacilli "school of fish" arrangement of *Haemophilus ducreyi*);
- It is also recommended to carry out swab samples for HSV by NAAT (more sensitive and specific than culturing, but not covered by the French health system) and Ct (VLG).
- Undertake treponemic testing (TPHA, TPLA, FTA, CMIA etc.) and a cardiolipid test (VDRL or RPR) as well as HIV serology testing +/- viral load if unprotected sex has been indicated within a set time-frame.

Test of almost no clinical significance:

- Herpes serology testing (to indicate who contaminated who?)
- FTA abs, FTA IgM: it is better to perform a test 15 days later to follow the TPHA/VDRL progression.

Interpretation of syphilis serology

1/ "Treatment-naive" patients:

- VDRL+ TPHA+: syphilis
- VDRL+ TPHA-: likely false +; test again in 15 days
If TPHA is still - = confirmation of false +
If TPHA += atypical chronology (normally the TPHA turns positive before the VDRL, however, this is not always the case);
- VDRL- TPHA+: very early stage syphilis is likely; test again in 15 days
If VDRL + = syphilis is confirmed
If VDRL is still - = false positive or patient not as naive as assumed (treated syphilis, ask the patient if they have taken ceftriaxone for another reason) or yaws (endemic treponematoses, can be seen in patients of African origin, especially if they grew up in the villages).

2/ "Treatment experienced" patients:

- **Request a copy of previous result in order to compare them.**
If the VDRL has increase by ≥ 2 dilutions = syphilis (reinfection)
If the VDRL has not increase or if the increase is < 2 dilutions = no recontamination.
- **No previous results available:**
In a HIV - patient, a VDRL of ≥ 8 is highly suspicious, except if syphilis was treated less than 1 year ago (use the clinical context to help) or if the patient had several syphilis infections.

Monitoring of syphilis serology in a treated patient is done via VDRL at 6 and 12 months: the titre normally decreases by 2 dilutions at 6 months and becomes negative at 12 months (naive patients or early stage syphilis). Patients who have had several syphilis infections and HIV+ patients should be followed-up twice per year with TPHA and VDRL (over the long-term).

Clinical case

A homosexual patient aged 35 having protected sexual intercourse except for oral-genital relations experienced primary syphilis infection (chancroid) that was treated by an Extencilline® injection in 2008. In October 2013, he presented with ulceration of the brim, worsening over the week. His last check up was performed in March 2013, which revealed TPHA at 1/1024 and VDRL at 1/2. He, therefore, did not receive treatment.

In relation to this last check-up (several answers are possible):

- The TPHA was raised, he should have been treated due to this highly likely recontamination
- The VDRL was greater than 0, he should have been treated due to this highly likely recontamination.
- This positive serology result can be explained by insufficient treatment in 2008, he should have received 3 injections 1-week apart.
- This positive serology result is likely to be a serological scar: comparison with a previous result would show this.
- This positive serology result is likely to be a serological scar: control testing in 15 days would show this.

Correct answers: d and e.

In regards to the ulceration, what test(s) would you request?

- An exudate examination of the ulceration by microscopy on a black background: it is the only test today that can absolutely confirm syphilis.
- A Nelson test: it is the only test today that can absolutely confirm syphilis.
- FTA IgM: this chancroid has only been developing for a week and there is a history of treated syphilis, only this test can be both positive at this early stage and specific for a developing infection.
- VDRL (or RPR) and TPHA (or TPLA, or any other treponemic test).
- PCR for *C. trachomatis* on the ulceration (VLG screening).

Correct answers: a, d and e.

The black background, Nelson test and FTA couldn't be performed, either because of the ad hoc material or because pathologists accustomed to this technique were not available (and the Nelson test is no-longer performed). The VDRL comes back as 1/128, TPHA 1/4096. What conclusion would you draw from this (several answers are possible)?

- TPHA has only increased by 2 dilutions, no developing syphilis.
- The VDRL titre has "increased" by 6 dilutions: developing syphilis, the patient should be treated with 3 injections of Extencilline® because, in light of his previous history, this would be more prudent.
- The VDRL "increased" by 6 dilutions: developing syphilis, treat with 1 injection of Extencilline®
- Repeat the serology test in 15 days in the same laboratory because in March 2013 it was performed in a different laboratory and the reproducibility from one operator to another is poor.
- Repeat the serology testing in 15 days because without the FTA IgM result, this result could correspond to an old syphilis infection.

Correct answer: c. The repeat test in March was reassuring; one must consider that it was an early-stage syphilis infection (treated by 1 injection of Extencilline®).

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