Diagnostic tests for sexually transmitted infections

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Abstract

The laboratory plays an essential role in the diagnosis of sexually transmitted infections (STIs). The ability to make an accurate diagnosis is essential because of the individual and public health implications associated with an STI diagnosis. This is achieved through a combination of direct microscopy, bacterial culture, molecular detection and serological testing. The choice of test is guided by the method with the highest sensitivity and specificity; in most cases, this is nucleic acid amplification testing. With antimicrobial resistance a significant global concern, monitoring resistance trends is crucial in guiding antimicrobial prescribing. STI testing must be both accessible and acceptable to patients, with testing now available in a variety of community and healthcare settings. Self-sampling for STIs offers a suitable alternative to clinician-taken swabs for those who do not want or need an examination. This paper summarizes the current methods available in the diagnosis of STIs and genital infections.

Keywords *Chlamydia trachomatis*; diagnostic testing; *Haemophilus ducreyi*; herpes simplex virus; human immunodeficiency virus; *Klebsiella granulomatis*; MRCP; *Neisseria gonorrhoeae*; sexually transmitted infections; *Treponema pallidum*; *Trichomonas vaginalis*

Key points

- All patients presenting with symptoms consistent with a sexually transmitted infection (STI) should be offered screening for chlamydia, gonorrhoea, HIV and syphilis
- A combination of laboratory techniques including direct microscopy, culture, molecular detection and serology is used in the diagnosis of STIs
- Self-sampling for bacterial STIs is acceptable to patients and has comparable sensitivity to a clinician-taken swab. This is a popular alternative for individuals not requiring examination
- Development and availability of near-patient and rapid diagnostics will allow for quicker detection of infection and treatment of patients to reduce morbidity and onward transmission

Introduction

The laboratory plays an essential role in the diagnosis of sexually transmitted infections (STIs) and other genital infections. A combination of direct microscopy, often available within the sexual health clinic, bacterial culture, molecular detection and serological testing is used.[1] Owing to the individual and public health implications of an STI diagnosis, choice of test is guided by the method with the highest sensitivity and specificity; in most cases, this is nucleic acid amplification testing (NAAT). Antimicrobial resistance, particularly with *Neisseria gonorrhoeae* and *Mycoplasma genitalium*, is now of significant global concern, and laboratory surveillance is essential in monitoring resistance to guide antimicrobial prescribing.

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In 2016, Public Health England recorded 280,622 new diagnoses of STIs in the over-25s alone, in addition to 128,098 cases of chlamydia in those aged 15–24 years. Recent reports showing a steep rise in rates of syphilis and gonorrhoea infection, highest among men who have sex with men (MSM), are worrying. Although the rate of new human immunodeficiency virus (HIV) diagnoses is decreasing, the rate of late diagnosis, with its associated increased morbidity and mortality, remains static.[2]

STI testing is now available in a variety of community and healthcare settings, making access easier. Wherever patients choose to test, they should be offered screening for chlamydia, gonorrhoea, HIV and syphilis as a minimum. Self-sampling for STIs is acceptable to many patients who do not wish to or do not require clinical examination.[3]

What tests to offer?

The choice of tests will be influenced by the history and examination, as well as by the setting in which the patient is seen, particularly regarding the availability of microscopy (Table 1). Where patients present to primary care with recurrent, refractory or unusual symptoms presentations, clinicians should have a low threshold for referral to level three sexual health services to access a broader range of investigations.

Chlamydia

Chlamydia trachomatis is an obligate intracellular bacterium. Serovars D–K cause urogenital infection, while serovars L1–L3 cause lymphogranuloma venereum (LGV). Asymptomatic urogenital infection is seen in up to 70% of women and 50% of men. A low threshold for screening is essential.

Molecular detection: NAAT is the gold standard for detection of *C. trachomatis* as it is highly sensitive and specific. For female patients, a vulvovaginal specimen is optimal; this can be taken by either the patient or the clinician. An endocervical swab can be used as an alternative but is slightly less sensitive and requires a speculum examination. First-void urine has lower sensitivity

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Sampling for the diagnosis of STIs[1]

	Female patients[a]	Male patients[a]
Asymptomatic	Vulvovaginal[b] NAAT for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* + HIV and syphilis serology ± serology for hepatitis B	First-pass urine NAAT for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* + HIV and syphilis serology ± rectal NAAT for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* ± pharyngeal NAAT for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* ± serology for hepatitis A, B and C
Symptomatic	As for asymptomatic women + lateral vaginal wall sample for pH, Gram stain and microscopy, *Candida* ± routine culture ± gonorrhoea culture + posterior fornix wet slide for microscopy + endocervical sample for Gram stain and microscopy ± midstream urine ± pregnancy test	As for asymptomatic men + urethral sample for Gram stain and microscopy, culture for *Neisseria gonorrhoeae* ± rectal wall sample for Gram stain and microscopy, culture for *Neisseria gonorrhoeae* ± pharyngeal sample for culture for *Neisseria gonorrhoeae* ± midstream urine
Genital ulcer present	As per symptomatic male/female patient + HSV PCR + syphilis PCR + repeat syphilis serology at 6 and 12 weeks after high-risk exposure ± swab of ulcer base for culture, Gram stain and ± PCR for *Haemophilus ducreyi* (chancroid) ± biopsy, scraping, swab or impression smear for microscopy + culture for *Klebsiella granulomatis* (Donovanosis)	
Proctitis present	As per symptomatic male/female patient + LGV serovar testing on rectal chlamydia NAAT + rectal HSV and syphilis PCR + repeat syphilis serology at 6 and 12 weeks after high-risk exposure	

HSV, herpes simplex virus; LGV, lymphogranuloma venereum; NAAT, nucleic acid amplification testing; PCR, polymerase chain reaction.
[a] Transgender patients should have a sensitive history taken to establish the type of sexual contact they are having, which will guide testing.
[b] Rectal ± pharyngeal NAATs for chlamydia and gonorrhoea can also be considered depending on the type of sexual activity reported.

Table 1

and specificity in women and is not the optimal specimen for detection. In men, a first-pass urine sample has an equivalent or higher sensitivity than a urethral swab and is therefore favoured because of patient tolerability. Although not licensed to be used at non-genital sites, NAATs have demonstrated good performance for pharyngeal and rectal samples. MSM presenting with proctitis should have serovar testing for LGV as a longer course of antibiotics may be needed.

Bacterial culture: *Chlamydia trachomatis* can be identified from cell culture; however, because this is slow and labour-intensive, and suffers from poor sensitivity, it is no longer widely used.

Gonorrhoea

Neisseria gonorrhoeae is a Gram-negative diplococcus that infects mucus membranes via direct inoculation. The presence of symptoms is variable depending on the infected site(s). Male urethral infection causes symptoms in >80% of patients and female endocervical infection symptoms in approximately 50%, but only 10% of patients with pharyngeal infection report symptoms.

Direct microscopy: *N. gonorrhoeae* can be identified by light microscopy of Gram-stained samples, with the organism seen as Gram-negative diplococci inside polymorphonuclear leucocytes. This method is most sensitive when urethral discharge is present. It is helpful for early diagnosis and treatment but must be confirmed by culture. Gram stain microscopy can also be used to make provisional diagnoses of gonorrohoea in rectal samples in symptomatic men and in endocervical samples in symptomatic women; however, sensitivity and specificity are lower with these sample types.

Bacterial culture: *N. gonorrhoeae* is a fastidious organism so requires culture medium with nutrient supplementation such as chocolate agar with carbon dioxide. Culture of *N. gonorrhoeae* is necessary to undertake antimicrobial sensitivity testing and should be performed where a diagnosis has been made or the index of suspicion is high. As treatment options for gonorrhoea are very limited, positive cultures allow for resistance testing to guide therapy. This is vital to safeguard first-line antibiotic treatment.

Molecular detection: NAAT for *N. gonorrhoeae* is more sensitive and easier to perform than culture in both symptomatic and asymptomatic patients. A vulvovaginal or endocervical swab can be used in women. In men, a first-pass urine sample can be used. NAAT testing for *N. gonorrhoeae* also has high sensitivity with rectal and pharyngeal samples, although clinicians should be aware of the potential for cross-reactivity with commensal *Neisseria* spp., particularly in the pharynx. A positive result at extragenital sites should always be confirmed using a NAAT with a different target.

Mycoplasma genitalium

M. genitalium is an established sexually transmitted pathogen in the aetiology of urethritis, cervicitis and pelvic inflammatory disease. It is extremely small and not visible by light microscopy; furthermore, it has no cell wall so cannot be Gram-stained. As in gonorrhoea, treatment options for this organism are severely limited because of high rates of circulating antimicrobial resistance, particularly to tetracyclines and macrolides.

Molecular detection: NAATs offer the best method of detection but laboratories have so far relied on in-house assays, few of

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