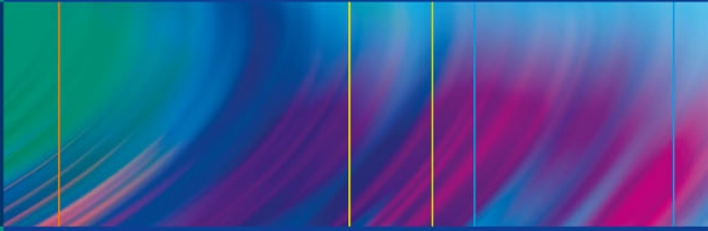


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Sexually Transmissible Infections in Clinical Practice

A Problem-Based
Approach

 Springer

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A problem-based approach



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Foreword

Patient care and training in the management of sexually transmitted infections has in recent years seen tremendous changes. A wider range of pathogens has been identified, tests streamlined with the introduction of newer technologies, evidence-based behavioural interventions introduced, and new therapeutic agents and vaccines developed. At the same time there has been a push to widen access to sexual health services and the development of protocol-based management where patients are often led through standardized histories and management guided by flow charts all performed by members of a mixed skilled and variously expert multidisciplinary team. Observing this process as an outsider either as a student or postgraduate trainee can be quite bewildering and much of the subtlety guiding management built into the processes can be lost unless one is working with expert clinicians who understand the theory and science underlying these strategies and are able to convey this to the trainee.

Book Title, *Sexually Transmissible Diseases in Clinical Practice*, provides a valuable resource to trainees in Sexual Health Medicine. It mimics the consultation process and although not an authoritative textbook on the subject provides the theoretical underpinning for management explained in an accessible way very much akin to sitting in on expert consultations in both common and some rarer conditions. It will also help trainees to prepare for Case Based Assessments (CBD) such as those required for training progression towards CCT in Genitourinary Medicine and guide preparation for the clinical OSCE component of the Diploma Examination in Genitourinary Medicine.

Raj Pat

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Preface

This book is aimed at several groups of health-care professionals who are involved in the care of individuals with or at risk of sexually transmissible infections.

With the relentless increase in the prevalence of the sexually transmissible infections in industrialized countries, and greater patients' expectations, most specialist clinics are under considerable pressure to provide a first-class service. One means of improving the performance of such clinics, particularly in the United Kingdom, has been to extend the role of the nurse practitioner. This has proved a most satisfactory solution in many clinics. It is hoped that this book will prove useful in the early training of the nurse practitioner through the presentation of a series of common clinical scenarios.

Problem-based learning has become the preferred teaching method in most universities, and it is hoped that undergraduate students will find the material presented here to be more than adequate to complement their clinical training in the management of sexually transmitted infections.

Postgraduate training in the specialty in the United Kingdom has undergone great changes over the past few years. By the end of the second year of specialist training, it is expected most trainees will have passed the examinations for the Diploma in Genitourinary Medicine, Society of Apothecaries, London. It is hoped that this book will give some assistance in the preparation for these examinations. In the United Kingdom, integration of Sexual Health services is the ultimate goal. Colleagues in disciplines related to Genitourinary Medicine, for example, Family Planning, should find the material presented a useful means of updating their knowledge of the sexually transmitted infections that they will be increasingly expected to manage. Clinical assistants who commence work in specialist clinics should also find the material presented here useful.

As access to specialist clinics may be difficult, many patients seek assistance from their general practitioner or practice nurse. It is hoped that this book will also prove useful to such health-care professionals.

The book is divided into two sections: Section A deals with the more common clinical scenarios that a competent practitioner should be able to manage, and Section B concerns more difficult cases and is more suited to those who have deeper knowledge about the infections. This book is not intended to be all-inclusive, but to focus on the practical aspects of patient care. A list of books and web sites from which detailed information on the epidemiology of the infections, the nature of the organisms involved, and their pathogenesis is found at the end of the book.

Alexander McMillan

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Part 1

SECTION - A

1. A Man Requesting a Sexual Health Screen

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Abstract

A specific history should be taken to elicit any symptoms that the individual may not have recognize as being those of a sexually transmissible infection (STI). (It is usually helpful to elicit this history before enquiring about sexual activity: it helps to establish rapport with the patient before questioning about intimate activities). For example

Robert, a 23-year-old student, attends a Sexual Health clinic and requests testing for sexually transmissible infections (STIs).

1.1 What History Would You Obtain from Robert?

A specific history should be taken to elicit any symptoms that the individual may not have recognize as being those of a sexually transmissible infection (STI). (It is usually helpful to elicit this history before enquiring about sexual activity: it helps to establish rapport with the patient before questioning about intimate activities). For example,

- Has he had discomfort on passing urine?
 - If so, consider urethritis.
- Has he noticed “growths” on the genitalia?
 - If so, consider genital warts, molluscum contagiosum, or normal anatomical variants, such as coronal papillae.
- Has he had an itch in the skin of the pubic area, genitocrural folds, shaft of the penis, scrotum, buttocks, or perianal region?
 - If so, consider phthiriasis and scabies, in addition to non-STI causes such as tinea cruris.
- Has he noticed swollen lymph glands in the groin (Fig. 1.1) or elsewhere in his body?
 - For example, painless inguinal lymph node enlargement may be a feature of primary syphilis and generalized lymphadenopathy may be associated with secondary syphilis or HIV infection.
- Has he had testicular pain or discomfort? Some men with urethral chlamydial infection complain of testicular discomfort in the absence of frank epididymo-orchitis.



Figure 1.1. Bilateral inguinal lymph node enlargement in primary syphilis.

The taking of an accurate sexual history is important so that the most appropriate microbiological tests can be undertaken and the need for any subsequent investigations. The following information should be obtained:

- The date of his most recent sexual contact, and, if penetrative sex had been performed, were condoms used? (Remember the pre-patent periods of the STIs, e.g., gonococcal urethritis between 1 and 10 days and chlamydial urethritis 7–21 days. *Note:* Testing for STIs in the symptomless patient is generally deferred until 7–10 days after the most recent sexual risk.)
- Does he have a regular sexual partner, and, if so, for how long have they been in the relationship and when did he last have sex with his partner? (Remember that one person’s definition of “regular” may differ significantly from that of another!)
- If he has had sexual contact within the preceding 3 months:
 - How many different partners has he had?
 - What were the approximate dates of these sexual contacts? Again this is a relevant question with respect to the pre-patent periods of the infections.
 - What was the gender of these partners? Remember that a sizeable proportion of men who are predominantly heterosexual have had homosexual contact. If he has had homosexual contact, it is helpful to enquire about what sexual activities had occurred (see [Case 4](#)). This will inform on possible risks of infection with, for example, HIV and syphilis.
- How many lifetime sexual partners has he had:
 - What was the gender of his partners?
 - Has he always used condoms for vaginal, anal, or oral–genital sex? Consistent use of condoms reduces the risk of infection with some, but not all, STIs. Examples of the former include gonorrhoea, chlamydia, and syphilis, and an example of the latter, human papillomavirus.
 - What was the country (countries) of origin of his sexual partner(s)? This is particularly

important when considering the risk of infection with HIV, hepatitis B virus, and syphilis, conditions that are more prevalent in geographical areas outwith Western Europe, Australasia, and the United States of America.

- Has he had any STI in the past, and if so what, and when? This history is particularly important for the interpretation of positive serological tests for syphilis (see [Cases 18, 19, and 33](#)).
- Has he ever been tested for HIV, and if so when, and what was the result?
- Has he or any of his sexual partners ever injected recreational drugs? If so, it is important to note when that (these) risk(s) occurred because of the often long pre-patent period before serological tests for the blood-borne viruses become positive.
- Has he had any serious medical conditions in the past, and what is the current state of his general health?
- Is he currently receiving medication, and if so what? This is important to know because of possible drug interactions with any drugs used for the treatment of STIs.
- Has he taken any antimicrobial drugs within the preceding month? Such therapy may have inadvertently treated an STI.
- Has he ever had a hypersensitivity reaction to drugs, particularly to antimicrobial agents?

Robert has no symptoms suggestive of the presence of an STI. The reason for his clinic attendance is that he has met a young woman with whom he wishes to form a relationship, and does not wish to infect her with an STI of which he is unaware. His most recent sexual contact had been 3 weeks previously with an ex-girlfriend, with whom he had been in a relationship for 3 months. He used a condom for vaginal intercourse but not for oro-genital sex. He has had no other sexual contacts in the preceding 3 months. Each of his six lifetime sexual partners was female, and there is no history of homosexual contact. Each partner was from the United Kingdom. Although he is aware of the risk of acquisition of STI from unprotected sex, he has not used condoms consistently. He has smoked cannabis in the past, but has never injected recreational drugs. He is not aware of injecting drug use by any of his sexual partners. His general health is good, and he is not currently receiving any medication. There is no history of antimicrobial drug use in the preceding month. He has no known drug allergies. He has not been vaccinated against either hepatitis A or B.

1.2 Outline the Physical Examination You Would Perform and Indicate Which Microbiological Tests You Would Undertake in This Case

The extent of the physical examination will be determined by the history. As Robert has no history of a rash or swollen lymph nodes, it is reasonable to confine the physical examination to the anogenital area. This examination is best performed with the patient lying on a couch in a warm and well-lit room. He should be offered a chaperone with whose gender he feels comfortable.

As up to 90% of men with uncomplicated chlamydial infection are symptomless, it is imperative that at least this infection is specifically looked for when a patient requests an STI screen. As gonococcal infection of the urethra is symptomless in up to 5% of cases, tests for *Neisseria gonorrhoeae* should be undertaken. Untreated, both infections have serious sequelae (see [Cases 13 and 24](#)).

1. Inspect the pubic area for, for example, *Phthirus pubis*, warts, and molluscum contagiosum.

2. Examine the genitocrural folds for tinea cruris or warts.
3. Palpate the inguinal lymph nodes. Non-tender inguinal lymph node enlargement may be a feature of primary syphilis (Fig. 1.1).
4. Palpate the testes and epididymes. Epididymo-orchitis may complicate untreated urethral chlamydial or gonococcal infections.
5. Examine the shaft of the penis. Identify lesions such as warts, molluscum contagiosum, and scabetic papules.
6. Retract the prepuce, if present, and look for warts or ulceration.
7. Examine the urethral meatus for urethral discharge. Evert the lips of the meatus to identify warts in the distal urethra.
8. In men with signs of urethritis (muroid or mucopurulent urethral discharge with or without inflammation of the meatus), take material for Gram-smear microscopy as follows:
 - a) Insert a plastic disposable inoculating loop (10 μ L) into the urethra to a distance of about 3 cm, gently scrape the walls of the urethra, and withdraw the loop.
 - b) Prepare a smear on a microscope slide.
 - c) Stain the smear by Gram's method and examine microscopically (see Cases 5 and 7).
9. Urethral gonorrhoea is diagnosed or excluded as follows, depending on local clinic and laboratory practices:
 - Obtain material for culture for *N. gonorrhoeae* by gently inserting a disposable plastic inoculating loop (10 μ L) into the distal 3 cm of the urethra, withdrawing, and inoculating a plate of selective culture medium, or
 - Obtain material using a cotton wool-tipped applicator stick and send to the laboratory in appropriate transport medium for culture, or
 - Send a first-voided specimen of urine to the laboratory for testing for *N. gonorrhoeae* by a nucleic acid amplification test.¹ (Combined assays for the dual detection of infection with *N. gonorrhoeae* and *C. trachomatis* are now available, and some laboratories can test for both infections on one urine sample), or
 - If the man is unable to provide a urine sample, urethral material for testing for *N. gonorrhoeae* by NAATs can be obtained by passing a swab, provided by the manufacturer of the test collection kit, about 3–5 cm into the urethra, withdrawing, and breaking off the end into a buffer solution. The dual detection NAATs are particularly helpful under these circumstances, as the need for two swabs is obviated.
 - (Some clinicians prepare a Gram-stained smear of urethral material collected as above for microscopy. The sensitivity of direct microscopy is low in symptomless individuals

10. Test for chlamydial infection, if not already done (see comments above on detection of gonococcal infection):

- Send an aliquot (about 20 mL) of first-voided urine for the detection of *Chlamydia trachomatis* DNA by a NAAT.
- If he is unable to provide a urine sample, urethral material for testing by a NAAT can be obtained as described above for gonorrhoea.

11. Offer serological testing for

- Syphilis (for example, an enzyme immunoassay).
- HIV infection.

Physical examination has failed to identify features of any STI; a urine sample is sent for the detection of N. gonorrhoeae and C. trachomatis. Robert accepts the offer of serological tests for syphilis and HIV. He is asked to contact the clinic for the results of the laboratory tests 1 week later.

At this time he contacts a Health Adviser. He is told that the test results are negative and that there was no evidence on infection. Robert, however, is uncertain as to the accuracy of the tests. What information would you provide?

Robert is assured that the tests for gonorrhoea and chlamydial infection are reliable. The sensitivity of NAATs is superior to culture for the diagnosis of urethral gonorrhoea in men. Although the sensitivity and specificity^{2 2} of polymerase chain reactions (PCRs) for *N. gonorrhoeae* are reported to be about 90 and 99.5%, respectively, for urine samples, the sensitivity is somewhat lower in symptomless than in symptomatic men. Slightly higher sensitivity (about 96%) is reported when urethral swabs are used as specimens.

The sensitivity and specificity of PCRs for *C. trachomatis* are about 84 and 99%, respectively, for urine samples. The sensitivity compares well with that of about 88% for urethral swabs.

As the sensitivity, specificity, positive-predictive, and negative-predictive values of NAATs for the diagnosis of infection using a first-voided specimen of urine are similar to those using directly obtained urethral material and does not involve invasive sampling, this specimen is preferred for screening.

As his most recent sexual contact had been only 3 weeks before testing, and the pre-patent period of syphilis varies between 10 and 90 days, Robert should be offered repeat testing in about 8 weeks time if he is concerned. In this case the risk of syphilis is low (most cases of syphilis in the United Kingdom have been acquired through homosexual contact or from individuals who have traveled from geographical areas where the infection is prevalent), and it is probably unnecessary to insist on repeat testing.

As HIV antibodies may take up to 3 months from infection to become detectable, a negative test at this time cannot exclude infection. Robert should be offered re-testing in about 8 weeks time, although, as in the case of syphilis, the risk of HIV infection is low (most cases of HIV infection in the United Kingdom have been acquired through homosexual contact, from unprotected vaginal or anal sex with a person from a geographical area where HIV is prevalent, or from sharing contaminated equipment used for injecting recreational drugs).

Robert has read about inapparent genital herpes and asks why he has not been tested for this viral infection. He has never been aware of any genital or oral lesions suggestive of genital or oral herpes

and none of his sexual partners is known to have genital herpes. What would you tell Robert?

Robert is correct in his understanding that many cases of genital herpes are symptomless. Only between 10 and 25% of individuals with serological evidence of herpes simplex virus (HSV) type 2 infection are aware that they have genital herpes (worldwide, HSV type 2 is the most common type associated with genital infection). In the absence of clinical lesions that can be sampled for virologic testing (see **Case 16**), serology remains the only means for detecting infection. Type-specific glycoprotein G (gG)-based assays are available that have sensitivities for the detection of HSV-2 antibodies of between 80 and 98% and specificities greater than 96%. The positive-predictive value (see Note 2), however, is poor in low prevalence populations. There is a good correlation between the seroprevalence of HSV type 2 and increasing age, the number of years of sexual activity, and the number of sexual partners. As Robert is young, has been sexually active for a short period of time, and has had few sexual partners, a positive result from his serum does not necessarily reflect true infection.

In some industrialized countries, including the United Kingdom, almost 50 and 70% of new genital herpes infections are associated with HSV type 1, the viral type classically associated with orolabial herpes. As in the case of genital infection with HSV type 2, more than one-third of orolabial infections are symptomless. In the absence of a history of oral or genital lesions it is therefore impossible to tell whether the detection of HSV type 1 antibodies reflects orolabial or genital herpes.

Opinion is divided as to whether or not HSV type-specific serology should be part of a sexual health screen. On the one hand, infection is lifelong, there is no curative treatment, and the psychological morbidity associated with a diagnosis of HSV type 2 infection can be profound. On the other hand, however, seropositive individuals can be taught to recognize minor recurrences and avoid intercourse at that time, thereby reducing, but not eliminating, the risk of transmission to a partner. With adequate support, the psychological impact is usually short lived. Persons with HSV type 1 antibodies should be advised to avoid oral–genital sex with a partner who has no history of orolabial herpes, or who is not known to be seropositive for that viral infection.

After this discussion, Robert does not wish to be tested for type-specific HSV antibodies.

Footnotes

1 A positive result in a nucleic acid amplification assay should preferably be confirmed by culture or an alternative NAAT.

2

True Positive w	False Positive x
False negative y	True negative z

Sensitivity = $w/(w+y)$. Specificity = $z/(x+z)$

Positive predictive value = $w/(w+x)$. Negative predictive value = $z/(y+z)$

2. A Woman Requesting a Sexual Health Screen

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Abstract

A specific history should be taken to elicit any symptoms that the individual may not have recognized. For example

Mary, a 28-year-old dental receptionist, attends a Sexual Health clinic requesting testing for sexually transmissible infections (STIs). She has just discovered that her ex-partner had had other sexual contacts during the time they were in the relationship.

2.1 What History Would You Obtain from Mary?

A specific history should be taken to elicit any symptoms that the individual may not have recognized. For example,

- Has she noticed increased vaginal discharge?
 - This may be physiological or associated with an STI such as *Trichomonas vaginalis*.
- Has she noticed “growths” on the genitalia?
 - If so, consider genital warts, molluscum contagiosum, or normal anatomical variants, such as pilosebaceous glands.
- Does she have itch in the skin of the pubic area, genitocrural folds, labia majora, introitus, perineum, buttocks, or perianal region?
 - If so, consider phthiriasis, scabies, candidiasis, or a non-STI such as a genital dermatosis (Fig. 2.1).
- Has she noticed post-coital bleeding or inter-menstrual bleeding?
 - If so, consider chlamydial infection.
- Has she had lower abdominal pain and/or deep dyspareunia?
 - These may be features of pelvic inflammatory disease (PID) that may be caused by chlamydial or gonococcal infections. Irregular menstrual bleeding may be an additional feature of PID.
- Has she had frequency of micturition with or without dysuria?

- Chlamydial and gonococcal infections can be associated with these symptoms, as may a urinary tract infection.
- Has she noticed swollen lymph glands in the groin or elsewhere in her body?
 - Painless inguinal lymph node enlargement may be a feature of primary syphilis, and generalized lymphadenopathy may be associated with secondary syphilis or HIV infection.



Figure 2.1 Lichen simplex of labium minus

The details in the sexual history do not differ significantly from those described in **Case 1** for the heterosexual man. Early in the consultation it should be established if her partners are male or female. Note should be made of the date of her last menstrual period, and the menstrual cycle should be recorded. The method of contraception used, if any, and an obstetric history should be noted. It is also helpful to know the date of her most recent cervical smear and the result.

Mary has no symptoms suggestive of the presence of an STI. Her most recent menstrual period has been 2 years previously – she had been fitted with a progestogen-only implant (Implanon[®]) for contraception. Her most recent sexual contact had been 4 months previously with her ex-partner with whom she had been for 3 years. As she thought that her partner was faithful, condoms were not used during sexual intercourse. She has had no other sexual partners during that time, and she has had only one other lifetime partner with whom she had separated 6 years previously. Both partners were British, neither they nor she has injected recreational drugs, and neither man is known to have had homosexual contact. She has had no female sexual partners. Her general health is good, and she is not currently receiving any medication other than Implanon[®], and she has not been treated with antimicrobial drugs within the preceding month. Since the age of 20 years, Mary has had 3-yearly cervical cytology examinations, the most recent having been 6 months previously, and no abnormalities have ever been reported. She has had one pregnancy that was terminated 3 years previously.

2.2 Outline the Physical Examination You Would Perform and Indicate Which Microbiological Tests You Would Undertake in This Case

The extent of the physical examination will be determined by the history (see **Case 1**). As Mary has r

history of a rash or swollen lymph nodes, it is reasonable to confine the physical examination to the anogenital area. The examination should be performed with the woman in the semi-lithotomy position on a couch in a warm and well-lit room. A presence of a chaperone should be offered and one must be present when a male doctor undertakes the examination.

As the majority of women with uncomplicated gonococcal and chlamydial infections are symptomless, it is imperative that at least these infections are specifically looked for when a patient requests an STI screen. Untreated, both infections have serious sequelae (see [Cases 14, 24, 27](#)).

1. Inspect the abdomen, and palpate for tenderness, guarding, and masses; note should be made of enlargement of the liver or spleen.
2. Inspect the pubic area for, for example, *Phthirus pubis*, warts, and molluscum contagiosum.
3. Palpate the inguinal lymph nodes, and note enlargement such as may occur in primary syphilis.
4. Inspect the labia majora for lesions such as warts or ulcers, or for a genital dermatosis (Fig. [2.1](#)).
5. Gently separate the labia minora from the labia majora. Examine the labia minora and, after wiping with a cotton wool ball, inspect the introitus. Look particularly for warts and lesions of herpes simplex virus.
6. Urethral gonorrhoea is diagnosed or excluded as follows, depending on local clinic and laboratory practices:
 - Obtain material for culture for *N. gonorrhoeae* by gently inserting a disposable plastic inoculating loop (10 µL) into the distal 1 cm of the urethra, withdrawing, and inoculating a plate of selective culture medium. Or,
 - Obtain material using a cotton wool-tipped applicator stick and send to the laboratory in appropriate transport medium for culture. Or,
 - If a nucleic acid amplification test (NAAT) ¹ is used for the detection of *N. gonorrhoeae*, obtain urethral material using the swab provided by the manufacturers of the test kit, break it into the buffer solution, and send it to the laboratory. (This test may be omitted if a NAAT is used for testing cervical material)
 - Some clinicians prepare a Gram-stained smear of urethral material collected as above for microscopy. The sensitivity of direct microscopy is low in populations where the prevalence of gonorrhoea is low, such as in Mary's case.

Note:

In many clinics serving populations with a low prevalence of gonorrhoea, testing for urethral infection has been abandoned.

7. Pass a plastic bivalve vaginal speculum and examine the character of any vaginal discharge. For example, typically in bacterial vaginosis, there is a homogeneous milky-white discharge that coats the vaginal walls. Note inflammation of the vaginal walls, as may occur in trichomoniasis.

8. ~~Collect a sample of material using a 10 µL plastic inoculating loop from the posterior vaginal fornix (or lateral fornices if candidiasis is suspected).~~

- Prepare a smear on a microscope slide for subsequent Gram staining, and then suspend some of the material in a drop of isotonic saline on another slide.
- Examine (oil immersion lens, magnification ×1,000) the Gram-stained smear, noting the presence or absence of lactobacilli (see [Case 9](#)).
- Examine (magnification ×400) the saline-mount preparation for the motile trophozoites of *T. vaginalis*, fungal hyphae or “pseudohyphae,” and “clue cells” (see [Cases 9, 10, 25](#) and [26](#)).

Note:

Facilities are available in some clinics for the detection of trichomonal infection by culture or NAAT. Vaginal specimens should be processed according to the instructions from the local laboratory.

9. Note the appearance of the ectocervix and the character of any discharge from the endocervical canal; in chlamydial and gonococcal infections, for example, there *may* be a mucopurulent discharge.

- In the majority of women with chlamydial infection the cervix appears normal.
- The cervix may appear normal in women with gonococcal infection, but sometimes a mucopurulent discharge may be observed.

10. Cervical gonococcal is diagnosed or excluded as follows, depending on local clinic and laboratory practices:

- Obtain material for culture for *N. gonorrhoeae* by gently inserting a disposable plastic inoculating loop (10 µL) into the distal 1 cm of the endocervical canal, withdrawing, and inoculating a plate of selective culture medium. Or,
- Obtain material using a cotton wool-tipped applicator stick and send to the laboratory in appropriate transport medium for culture. Or,
- If a nucleic acid amplification test (NAAT) (see Note 1) is used for the detection of *N. gonorrhoeae*, obtain endocervical material using the swab provided by the manufacturers of the test kit, break it into the buffer solution, and send it to the laboratory.
- Some clinicians prepare a Gram-stained smear of endocervical material collected as above for microscopy. Although the sensitivity is low in low prevalence populations, microscopy may be useful if mucopus exudes from the endocervical canal. If Gram-negative diplococci are seen, a *presumptive* diagnosis of gonorrhoea can be made and treatment given without delay.

11. Collect endocervical material for the detection of *Chlamydia trachomatis*-specific DNA sequences (by a NAAT), using the swab provided by the manufacturers of the test collection kit. The swab is inserted into the endocervical canal to a distance of about 1 cm. After rotating the swab once in the canal, it is withdrawn and the end broken off into the buffer

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