

MANAGEMENT OF SYNDROMES

European guideline for the management of epididymo-orchitis and syndromic management of acute scrotal swelling

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INTRODUCTION

- In men younger than 35 years-of-age epididymo-orchitis is most often caused by sexually transmitted pathogens such as *Chlamydia trachomatis* and *Neisseria gonorrhoeae*^{1–14}
- In men older than 35 years-of-age epididymo-orchitis is most often caused by non-sexually transmitted Gram-negative enteric organisms causing urinary tract infections^{1–14}. This may be associated with a history suggestive of bladder outflow obstruction
- There is cross-over between these groups and complete sexual history-taking is imperative^{1,5,9–11,13–14}
- Epididymo-orchitis caused by sexually transmitted enteric organisms also occurs in homosexual men who engage in insertive anal intercourse^{1,15–16}
- Gram-negative enteric organisms are more commonly the cause of epididymo-orchitis if recent instrumentation or catheterization has occurred^{1,17–20}
- Anatomical abnormalities of the urinary tract are common in the group infected with Gram-negative enteric organisms and further investigation of the urinary tract should be considered in all such patients but especially in those older than 50 years^{1,21}.

DIAGNOSIS

General

The presence of a sexually transmitted pathogen is frequently associated with a new sexual partner or more than one sexual partner in the recent past.

Clinical

Symptoms (these are usually unilateral)

- Testicular pain
- Scrotal swelling.

Symptoms of urethritis (this is often asymptomatic^{10,11,14}):

- Urethral discharge
- Dysuria
- Penile irritation.

Symptoms of bladder outflow obstruction may also be present.

Signs—on examination patients are usually found to have:

- Tenderness to palpation on the affected side
- Palpable swelling of the epididymis.

They may also have:

- Urethral discharge (this may only be present on urethral massage)
- Hydrocoele
- Erythema and/or oedema of the scrotum on the affected side
- Pyrexia.

Laboratory

The following investigations should be undertaken¹:

- Standard sexually transmitted disease (STD) examination as in guideline on non-gonococcal urethritis (NGU) to look for presence of urethritis and/or *N. gonorrhoeae* and/or *C. trachomatis*²²
- Either a urethral smear or a first-pass urine specimen can be used to detect urethritis by confirming an excess of polymorphonuclear leucocytes (PMNLs)
- In patients with urethritis, gram-negative intracellular diplococci should be looked for to exclude the diagnosis of gonorrhoea. This has a sensitivity of >90% for detecting gonococcal infection, in experienced hands
- A Gram-stained urethral smear containing ≥ 5 PMNL per high-power ($\times 1000$) microscopic field (averaged over 5 fields with greatest concentration of PMNLs), and/or
- The identification of ≥ 10 PMNL per high-power ($\times 1000$) microscopic field (averaged over 5 fields with greatest concentration of PMNLs) on a Gram-stained preparation from a first-passed urine (FPU) specimen

- The presence of an observable mucopurulent/purulent urethral discharge is also indicative of urethritis². However, this cannot reliably differentiate between gonococcal and NGU and the absence of such a discharge does not exclude urethritis
- A urethral culture for *N. gonorrhoeae*
- *C. trachomatis* should also be sought
- Urinalysis of the mid-stream urine (MSU) specimen, using a dipstick which contains leucocyte esterase and nitrites, in addition to blood protein and glucose. These dipsticks are an established screening test for bacterial urinary tract infections (UTI). However, they have not been assessed specifically in a STD clinic²³. The presence of blood in the MSU is usually the result of taking a urethral smear, and positive leucocyte esterase activity may reflect urethritis and not a UTI, indeed a positive leucocyte esterase test in the FPU specimen is indicative of urethritis, although this has a poor sensitivity^{2,24–26}). Thus the results of these for diagnosing a UTI should be viewed with scepticism. Nevertheless, a positive nitrite test is very specific although its sensitivity is only 40–80%²⁷
- MSU for microscopy and bacterial culture.

Consideration should be given to:

- Colour Doppler ultrasound is useful to help differentiate between epididymo-orchitis and torsion of the spermatic cord^{28–31}.

Differential diagnosis

- Torsion of the testis
- Epididymo-orchitis secondary to *N. gonorrhoeae* or NGU including *C. trachomatis*
- Epididymo-orchitis secondary to enteric organisms
- Testicular or epididymal tumour.

Torsion of the spermatic cord (testicular torsion) is the main differential diagnosis. It is a surgical emergency. It should be considered in all patients and should be excluded first as testicular salvage becomes decreasingly likely with time^{32,33}. Torsion is more likely if:

- The onset of pain is sudden
- The pain is severe
- Tests performed during the initial visit show neither the presence of a urethritis nor likely UTI
- The patient is younger than 20 years-of-age (the peak incidence is in adolescents), but it can occur at any age^{32,33}.

MANAGEMENT

General

- Empirical therapy should be given to all patients with epididymo-orchitis before micro-

biological results are available¹¹. The antibiotic regimen chosen should be determined in the light of the immediate tests as well as the age of the patient, the sexual history, any recent instrumentation or catheterization and any known urinary tract abnormalities in the patient

- Bed rest, scrotal elevation and support, and analgesics are recommended. Non-steroidal anti-inflammatory drugs may be helpful^{34,35}
- **If torsion is suspected an urgent urological opinion must be sought.**

Epididymo-orchitis secondary to *N. gonorrhoeae* or NGU including *C. trachomatis*

General advice

- See guideline on management of urethritis²².

Indications for therapy

- Symptoms and signs of epididymo-orchitis
- Urethritis detected
- UTI not suspected.

Recommended regimens

- Doxycycline 100 mg twice daily for 14 days^{7,15}
- Ofloxacin 200 mg twice daily for 14 days^{9,36,37}.

For epididymo-orchitis where gonococcal infection is suspected, either of the following in addition to doxycycline should be given:

- Ciprofloxacin 500 mg stat or ceftriaxone 250 mg intramuscularly.

Antibiotics used for gonorrhoea may need to be varied according to local knowledge of antibiotic sensitivities. If tetracycline resistance is common ofloxacin may be preferable.

Epididymo-orchitis secondary to enteric organism

General advice

The following should be discussed and clear written information provided:

- A detailed explanation of what epididymo-orchitis is and what causes it
- Side-effects of treatment and importance of complying fully with it and what to do if a dose is missed.

Indications for therapy

- symptoms and signs of epididymo-orchitis
- UTI strongly suspected.

Recommended regimens

- Ofloxacin 200 mg twice daily for 14 days
- Trimethoprim 200 mg twice daily for 14 days
- Antibiotics used may need to be varied according to local knowledge of antibiotic sensitivities.

Epididymo-orchitis of indeterminate aetiology

General advice

The following should be discussed and clear written information provided:

- A detailed explanation of what epididymo-orchitis is and what causes it and the difficulty in initially establishing the exact cause
- Side-effects of treatment and importance of complying fully with it and what to do if a dose is missed
- Advised to abstain from sexual intercourse until the microbiological results from the MSU specimen are available.

Indications for therapy

- Symptoms and signs of epididymo-orchitis
- Unable to differentiate between sexually transmitted pathogen or non-sexually transmitted enteric organism as the aetiological agent.

Recommended regimens

- Ofloxacin 200 mg twice daily for 14 days.

MANAGEMENT OF PARTNERS

All sexual partners at risk should be assessed and offered epidemiological treatment if:

- Epididymo-orchitis secondary to *N. gonorrhoeae* or NGU including *C. trachomatis* is diagnosed
- Epididymo-orchitis of indeterminate aetiology is diagnosed and the subsequent MSU specimen is negative
- This needs to be handled sensitively and the confidentiality of the index patient maintained. The duration of look-back is arbitrary as the incubation period of epididymo-orchitis is unknown; 3 months is suggested
- The treatment regimen used should be as detailed for uncomplicated *C. trachomatis* infection³⁸ and include treatment for uncomplicated gonorrhoea³⁹ if this is isolated from the index case
- If *C. trachomatis* or *N. gonorrhoeae* are detected it is particularly important to ensure that all sex partner(s) potentially at risk have been notified
- Details of all contacts should be obtained at the first visit. Consent should also be obtained to contact either the patient or his partners if tests for *C. trachomatis* or *N. gonorrhoeae* are found to be positive. This ensures that if the index patient does not reattend, he can be contacted and/or provider referral can be initiated for sexual contacts
- Contact(s) of men with chlamydial or gonococcal epididymo-orchitis should be treated regardless of results of microbiological investigations

- Concurrent treatment of the sexual partners of men with chlamydia-negative and/or gonococcal-negative epididymo-orchitis is recommended as it may result in improved response in some patients, and a possible reduction in female morbidity, since:

- No test is 100% sensitive for detecting *C. trachomatis* in men
- There is evidence that at least some men with 'chlamydia-negative' NGU have partners who are chlamydia-positive⁴⁰.

FOLLOW UP

If there is no improvement in the patient's condition after 3 days then the diagnosis should be reassessed and therapy re-evaluated. Reassessment is required if signs of swelling and tenderness persist after antimicrobial therapy is completed, although in some cases symptoms take longer than this to settle. Surgical assessment may be appropriate in these cases^{41,42}.

Differential diagnoses to consider in these circumstances include¹:

- Testicular ischaemia/infarction
- Initial diagnosis of infective aetiology, i.e. enteric organism versus STI, was wrong and patient was therefore treated incorrectly
- Enteric organism resistant to therapy with trimethoprim or ofloxacin
- Abscess formation and/or scrotal fixation
- Testicular or epididymal tumour
- Mumps epididymo-orchitis
- Tuberculous epididymitis
- Fungal epididymitis
- Gonococcal infection resistant to fluoroquinolones and tetracycline.

If epididymo-orchitis secondary to *N. gonorrhoeae* or NGU including *C. trachomatis* is diagnosed, the patient's follow-up in addition should include that as detailed in the guideline for urethritis, with a repeat examination for urethritis at 2 weeks²².

SYNDROMIC MANAGEMENT OF ACUTE SCROTAL SWELLING

The principal diagnoses are epididymo-orchitis, torsion, trauma and a testicular or epididymal tumour. Without recourse to diagnostic facilities it may be difficult to differentiate between these. Torsion of the spermatic cord (testicular torsion) is the main differential diagnosis. It is a surgical emergency. It should be considered in all patients and should be excluded first as testicular salvage becomes decreasingly likely with time. The flow-chart (Figure 1) details the syndromic management of this condition.

Of importance in the management is the syndromic detection of urethritis. If urethritis is detected the most likely aetiology is epididymo-orchitis secondary to *N. gonorrhoeae* or NGU including *C. trachomatis*.

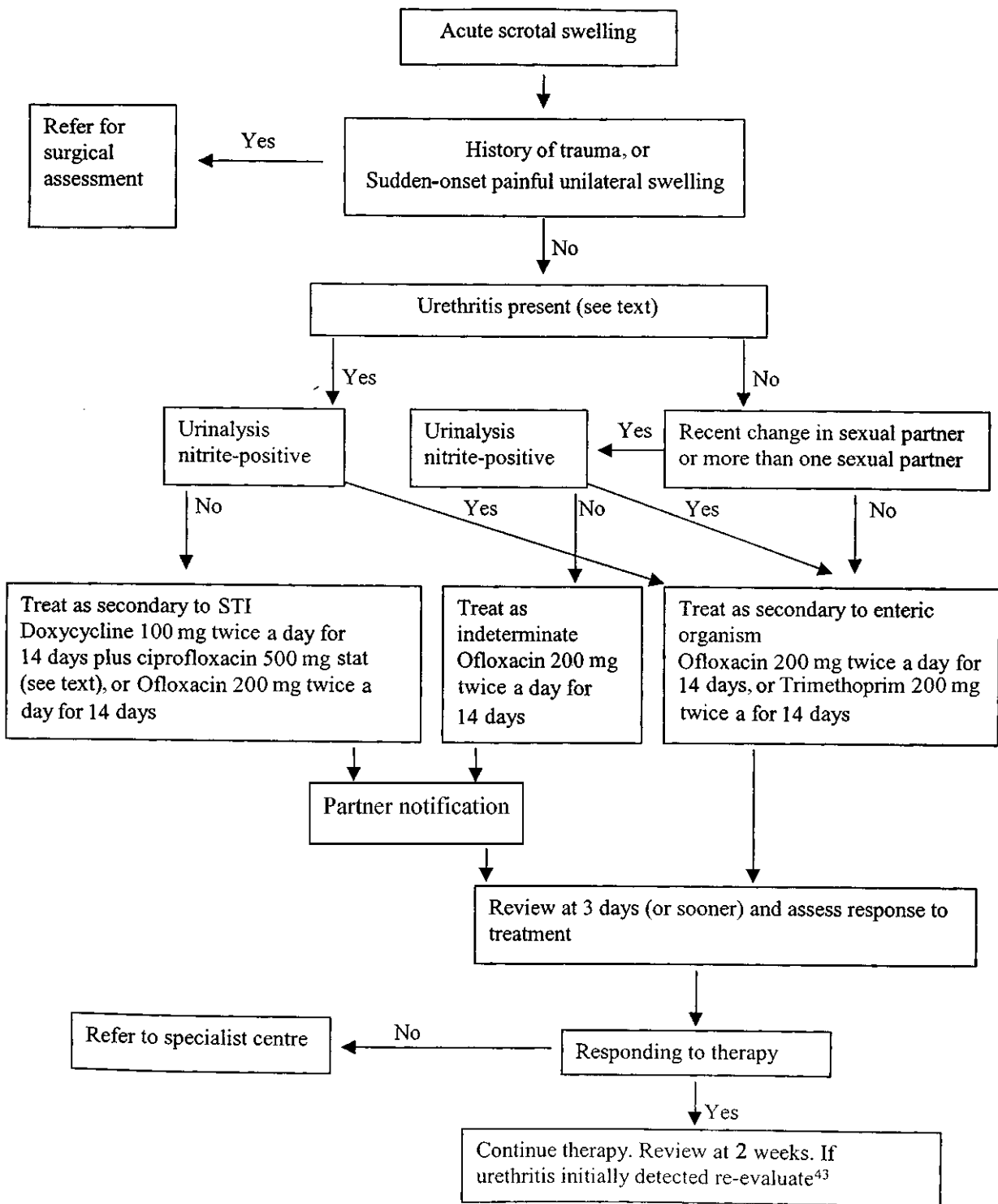


Figure 1. Syndromic management of acute scrotal swelling (see text)

How to do this is detailed in the guideline on the management of urethritis²² and summarized below. The use of urinary dipsticks containing nitrites, because of their specificity for detecting UTIs, would also be of clinical benefit (see above).

Diagnosis of urethritis—clinical

- Men should be examined for evidence of a urethral discharge. If none is seen, the urethra should be gently massaged from the ventral

part of the penis towards the meatus. This can be undertaken by the patient

- The absence of urethral discharge does not exclude urethritis
- In gonococcal infection the discharge is usually more evident and purulent than that in NGU. Nevertheless, the severity of urethritis cannot differentiate reliably between gonococcal and NGU.

Investigations

Microscope present:

- See guideline on urethritis²²
- Gram stain for Gram-negative diplococci to exclude gonorrhoea. This has a sensitivity of >90% in experienced hands.

Microscope absent:

- Mucopurulent or purulent discharge observable on examination, or
- Positive leucocyte esterase dipstick test on FPU specimen, or
- Positive two-glass urine test. The foreskin should be retracted fully and the patient asked to urinate into two clean specimen glasses, the first 10–20 ml into one glass, the rest into the second. If the urine is hazy, add sufficient 5% acetic acid to dissolve the phosphate crystals which are responsible for the haze. When there is infection of the anterior urethra, the haze will persist in the first glass of urine due to the presence of pus cells, threads or flecks, but the second will be clear. If both glasses are abnormal, the infection also involves the posterior urethra, bladder or kidneys. This is most likely to indicate a bacterial urinary tract infection but may also represent severe urethritis often due to gonorrhoea or may simply be due to the patient forgetting to void into two glasses and dividing the first glass into two.

Both the leucocyte esterase dipstick test and the two-glass urine test have reduced sensitivities compared to microscopy for detecting urethritis and are not recommended for the confirmation of NGU if microscopy is available.

Management

This is set out in the flow-chart (Figure 1). If microscopy has been used to diagnose urethritis, and this has been undertaken by an experienced operator, ciprofloxacin 500 mg can be omitted from the regimen: 'doxycycline 100 mg twice daily (BD) for 14 days plus ciprofloxacin 500 mg stat', as detailed for treatment of epididymo-orchitis as secondary to STI. Resistant gonococcal infection is likely to be more of a problem in countries where syndromic STI management guidelines are widely

used⁴³. Alternatives to ciprofloxacin 500 mg are detailed elsewhere^{22,39}.

Follow-up should take place after 3 days or sooner if there is no improvement. It is an essential part of management. The differential diagnoses for patients who fail to respond to therapy is as detailed previously. However, resistant gonococcal infection may be more common as a cause of failure, for the reason detailed above.

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