

2010 United Kingdom national guideline for the management of epididymo-orchitis

Clinical Effectiveness Group, British Association for Sexual Health and HIV

Authors and centre

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Scope and purpose

The main objective of these guidelines is to offer recommendations on the diagnostic tests, treatment and health promotion principles in the effective management of epididymo-orchitis. It is aimed primarily at people aged 16 years or older presenting to health care professionals, working in departments offering level 3 care in STI management within the United Kingdom. However, the principles of the recommendations could be adopted at all levels.

Rigour of development

The guideline has been updated by reviewing the previous guideline (2001) and medical literature since its publication. A medline search was performed for 2001-2009 using the keywords "epididymitis", "orchitis" and epididymo-orchitis". The Cochrane Database of Systematic Reviews and the Cochrane Controlled Trials Register up to 2009 were reviewed using the same keywords. Further references from articles identified were included.

New in the 2010 Guideline

Aetiology

Consider mumps in view of the epidemic in 2005

Consider tuberculous epididymo-orchitis in patients from high prevalence countries or with a previous history of tuberculosis and particularly in patients with immunodeficiency

Treatment

For epididymo-orchitis most probably due to any sexually transmitted pathogen:

Ceftriaxone 500mg intramuscularly single dose, **plus**
Doxycycline 100mg by mouth twice daily for 10-14 days
(in view of the high levels of quinolone resistant gonorrhoea)

The dose of ceftriaxone has been increased to 500mg stat to reflect the reduced sensitivity of *Neisseria gonorrhoeae* to cephalosporins and the current UK treatment guidelines for uncomplicated gonorrhoea.

If most probably due to chlamydia or other non-gonococcal organisms (i.e. where gonorrhoea considered unlikely as microscopy is negative for Gram negative intracellular diplococci and no risk factors for gonorrhoea identified) could consider:

Doxycycline 100mg by mouth twice daily for 10-14 days, **or**

Ofloxacin 200mg by mouth twice daily for 14 days

Introduction

Acute epididymo-orchitis is a clinical syndrome consisting of pain, swelling and inflammation of the epididymis +/- testes. The most common route of infection is local extension and is mainly due to infections spreading from the urethra (sexually transmitted pathogens) or the bladder (urinary pathogens).

Aetiology

- Under 35 years - most often a sexually transmitted pathogen such as *Chlamydia trachomatis* and *Neisseria gonorrhoeae* [1-12].
- Over 35 years - most often non-sexually transmitted Gram negative enteric organisms causing urinary tract infections [1-12]. Particular risks include recent instrumentation or catheterisation [13-16].
- There is crossover between these groups and complete sexual history taking is imperative [3, 7-9, 11, 12].
- Men who engage in insertive anal intercourse are at risk of epididymitis secondary to sexually transmitted enteric organisms [1, 17, 18].
- Abnormalities of the urinary tract such as anatomical or functional abnormalities are common in the group infected with Gram negative enteric organisms.
- All patients with urinary tract pathogen confirmed epididymo-orchitis should have further investigations of the urinary tract [19, 20].
- Mumps should be considered as an aetiology since the recent epidemic in 2005 [21]. This epidemic mainly affected non-immunised adults born between 1982 and 1986. This complication of mumps can occur in up to 40% of post-pubertal males [22-24].
- Extrapulmonary tuberculosis represents 40-45% of TB cases in the UK [25], but tuberculous epididymo-orchitis is a rare presentation. It is likely to present in patients from high prevalence countries or with a previous history of tuberculosis and particularly in patients with immunodeficiency [26]. It is usually as a result of disseminated infection and commonly associated with renal TB but can be an isolated finding.[26, 27]. Tuberculous epididymitis has also been noted as a complication of BCG instillation for treatment of bladder carcinoma [28].
- *Ureaplasma urealyticum* is found in men with epididymo-orchitis, often in association with *N. gonorrhoeae* or *C trachomatis* infection. Evidence supporting it as a common cause of epididymo-orchitis is lacking [5, 12].
- It has been suggested that *Mycoplasma genitalium* might cause some cases of epididymo-orchitis but evidence for this is so far lacking [29].
- 12-19% of men with Behcet's disease develop epididymo-orchitis. This is non-infective and thought to be part of the disease process. It is associated with more severe disease [30].
- Unilateral and bilateral epididymo-orchitis has also been reported as an adverse effect of amiodarone treatment and will resolve once treatment is ceased [31].
- Other rare infective causes include brucella and fungi such as candida [32].

Clinical Features

Symptoms

- Patients with epididymo-orchitis present characteristically with unilateral scrotal pain and swelling of relatively acute onset [33].
- In sexually transmitted epididymo-orchitis there may be symptoms of urethritis or a urethral discharge; however the urethritis is often asymptomatic [8, 9, 12, 34].
- In patients with uropathogen related epididymo-orchitis symptoms suggestive of UTI or a history of bacteriuria may be present.

- Torsion of the spermatic cord (testicular torsion) is the most important differential diagnosis. It is a surgical emergency. It should be considered in all patients and should be excluded first as testicular salvage IS REQUIRED WITHIN 6 HOURS and becomes decreasingly likely with time [35, 36].
- Torsion is more common in men who are younger than 20 years but it is important to recognise it can occur at any age [35, 36].
- A painful swollen testicle in an adolescent boy or a young man should be managed as torsion until proven otherwise [37] but if an infective cause cannot be excluded, antibiotics should be prescribed in addition to the surgical referral.
- Torsion is more likely if the onset of pain is acute (typically around four hours at presentation) and the pain is severe [38].
- Symptoms of mumps typically begin with a headache and fever before characteristic unilateral or bilateral parotid swelling followed 7-10 days later by unilateral testicular swelling. It may also present with epididymitis [39]. Scrotal involvement can occur without systemic symptoms [40].
- Symptoms suggestive of tuberculous infection include subacute/chronic onset of painless or painful scrotal swelling (epididymal first) +/- associated with systemic symptoms of tuberculosis +/- scrotal sinus +/-thickened scrotal skin [26, 27].

Signs

- Tenderness to palpation on the affected side
- Palpable swelling of the epididymis starting with the tail at the lower pole of the testis and spreading towards the head at the upper pole of the testis +/- involvement of the testicle.
- There may also be:
 - urethral discharge
 - secondary hydrocoele
 - erythema and/or oedema of the scrotum on the affected side
 - pyrexia
- Differentiation between epididymo-orchitis and testicular torsion on clinical examination may be difficult and if any doubt exists then urgent surgical exploration is advocated.

Complications

Complications are more often seen in patients with uropathogen related epididymo-orchitis than sexually transmitted infection associated epididymo-orchitis [41].

- Reactive hydrocoele
- Abscess formation and infarction of the testicle – these are rare complications [5, 42, 43].
- Infertility- there is a poorly understood relationship between epididymo-orchitis and infertility. The general consensus is that men who present with obstructive azoospermia are usually found to have epididymal obstruction when explored for sperm retrieval, which may be a consequence of previous infection. Mumps epididymo-orchitis can lead to testicular atrophy. Of those with bilateral orchitis, 13% will have reduced fertility [21].

Diagnosis

A sexually transmitted cause should always be excluded.

The following should be performed:

- Gram stained urethral smear – even if urethral symptoms are absent - examined microscopically for the diagnosis of urethritis, (≥ 5 polymorphonuclear leucocytes [PMNLs] per high power field x1000) and presumptive diagnosis of gonorrhoea (Gram negative intracellular diplococci) **or** Gram stained preparation from a centrifuged sample of first passed urine (FPU) for microscopy is an alternative method of diagnosing urethritis (≥ 10 PMNLs per high power field x1000).
- Urethral swab for *N. gonorrhoeae* culture and/or FPU or urethral swab for nucleic acid amplification test (NAAT) for *N.gonorrhoeae*.
- First pass urine or urethral swab for *C.trachomatis* NAAT.
- Microscopy and culture of mid-stream urine for bacteria.

A urine dipstick incorporating nitrite and/or a leucocyte esterase test is helpful, particularly at excluding a urinary tract infection but is not diagnostic and its results should not preclude the other microbiological investigations above [44]. In one study a urine dipstick for nitrites and leucocytes showed a sensitivity and specificity for a urinary tract infection of 83% and 90% respectively in the setting of NGU [45].

In testicular torsion, the above tests would show neither the presence of urethritis nor probable urinary tract infection.

If it can be arranged without delay colour Doppler ultrasound, to assess arterial blood flow, may be useful to help differentiate between epididymo-orchitis and torsion of the spermatic cord [46]. However the sensitivity for detecting torsion may not be 100% and this should not delay surgical exploration of the scrotum [47].

Further Investigations

Other investigations which could be considered include:

- All patients with sexually transmitted epididymo-orchitis should be screened for other sexually transmitted infections.
- All patients with urinary tract pathogen confirmed epididymo-orchitis should be investigated for structural abnormalities and urinary tract obstruction by a urologist [19, 20].
- When investigating for tuberculous infection, three early morning urines should be obtained but these are not always positive for AAFB in the setting of TB epididymitis. Other investigations recommended include intravenous urography, renal tract USS and biopsy of the site as well as a CXR to exclude or confirm co-existing respiratory involvement [48].
- When considering mumps as a possible diagnosis, mumps IgM/IgG serology should be checked.

There is no role for epididymal aspiration/fine needle aspiration cytology in routine clinical practice. It may be useful in recurrent infection which fails to respond to therapy and if epididymo-orchitis is found at operation [14] and in the case of suspected tuberculous epididymitis [48, 49].

Management

General Advice

Appropriate rest, analgesia and scrotal support are recommended. Non-steroidal anti-inflammatory drugs may be helpful [50, 51] (level of evidence III, grade of recommendation B).

Patients should be advised to abstain from sexual intercourse until they and their partner(s) have completed treatment and follow-up in those with confirmed or suspected sexually transmitted epididymo-orchitis [1].

Patients should be given a detailed explanation of their condition with particular emphasis on the long-term implications for the health of themselves and their partner(s). This should be reinforced by giving them clear and accurate written information.

Treatment

Empirical therapy should be given to all patients with epididymo-orchitis before culture/NAAT results are available. The antibiotic regimen chosen should be determined in light of the immediate tests (urethral or FPU smear, urinalysis) as well as age, sexual history including insertive anal intercourse, any recent instrumentation or catheterisation and any known urinary tract abnormalities in the patient.

Antibiotics used for sexually transmitted pathogens may need to be varied according to local knowledge of antibiotic sensitivities.

Recommended Regimens

- For epididymo-orchitis most probably due to any sexually transmitted pathogen:

Ceftriaxone 500mg intramuscularly single dose [12] (III, B), **plus**
Doxycycline 100mg by mouth twice daily for 10-14 days [3, 12] (III, B)

If most probably due to chlamydia or other non-gonococcal organisms (i.e. where gonorrhoea considered unlikely as microscopy is negative for Gram negative intracellular diplococci and no risk factors for gonorrhoea identified*) could consider:

* Common risk factors for gonorrhoea are: previous *N. gonorrhoeae* infection; known contact of gonorrhoea; presence of purulent urethral discharge, men who have sex with men and black ethnicity

Doxycycline 100mg by mouth twice daily for 10-14 days [3, 12] (III, B) **or**

Ofloxacin 200mg by mouth twice daily for 14 days [7, 52-53] (Ib, B)

- For epididymo-orchitis most probably due to enteric organisms:

Ofloxacin 200mg by mouth twice daily for 14 days [7, 52-53] (Ib, B) **or**

Ciprofloxacin 500mg by mouth twice daily for 10 days [54] (Ib, A)

Corticosteroids have been used in the treatment of acute epididymo-orchitis but have not been shown to be of benefit [55, 56] (Ib, B)

In those with severe epididymo-orchitis or features suggestive of bacteraemia in-patient management of fluid and electrolyte balance is required. Intravenous broad-spectrum therapy directed towards coliforms and *Pseudomonas aeruginosa* should be considered –

cefuroxime 1.5g tds +/- gentamicin for 3-5 days until fever subsides and in those with severe allergy to penicillin – ciprofloxacin 500mg bd [33, 57, 58].

Allergy

- For epididymo-orchitis of all causes where the patient is allergic to cephalosporins and/or tetracyclines:

Ofloxacin 200mg by mouth twice daily for 14 days [7, 52-53] (lib, B)

Sexual partners

Partner notification and treatment is recommended for all patients with epididymo-orchitis secondary to gonorrhoea, chlamydia and NGU or of indeterminate aetiology and subsequent MSU negative [2]. Please refer to appropriate sections of these guidelines for approach to partner notification. All partners should be treated epidemiologically [IV B]. This will prevent illness and complications in the contact and will also prevent reinfection of the index patient [59].

Follow-up

If there is no improvement in the patient's condition after 3 days, the diagnosis should be reassessed and therapy re-evaluated. Further follow-up is recommended at 2 weeks to assess compliance with treatment, partner notification and improvement of symptoms.

If the patient was gonorrhoea positive, a test of cure should be performed. If the test of cure is by culture this should be performed at least 72 hours after completion of antimicrobial therapy. Although there is currently insufficient evidence to determine the best time to conduct a test of cure with a NAAT, 3 weeks after completion of treatment seems reasonable.

The swelling and tenderness can persist after antimicrobial therapy is completed but should be significantly improved. Where there is little improvement further investigations such as an ultrasound scan or surgical assessment should be considered.

Differential diagnoses to consider in these circumstances include testicular ischaemia/infarction [42, 43], testicular/epididymal tumour [33], alternative infectious aetiologies such as tuberculosis, mumps or rarer infective/non-infective causes [32] or progression to an abscess [42, 43].

Auditable Outcomes

- The four basic microbiological investigations, as recommended in the guidelines, should be performed. Target 90%
- An appropriate antibiotic regimen, as recommended in the guidelines, should be prescribed. Target 100%
- Sexual partners of men with sexually transmitted epididymo-orchitis should be seen and treated epidemiologically. The targets achieved should be as set in the gonorrhoea and chlamydia national guidelines.
- A written action plan should be recorded for men who have not responded clinically to the initial course of antibiotics. Target 80%

Editorial independence

This guideline was commissioned and edited by the CEG of the BASHH, without external funding being sought or obtained.

Declarations of Interest

All authors have declared no conflict of interest.

Membership of the CEG

David Daniels, Mark Fitzgerald, Margaret Kingston, Neil Lazaro, Gill McCarthy, Keith Radcliffe (Chair), Ann Sullivan.

Acknowledgements

David Daniels, Chris Bignell, Chris Carne, Mark Fitzgerald, Phillip Hay, Paddy Horner, Francis Keane, Margaret Kingston, Gill McCarthy, Hugo McClean, Rudiger Pittrof, Jonathan Ross and Ann Sullivan.

Stakeholder involvement

Consultation with the entire specialty and the public via the BASHH website for three months as well urology input via the authors.

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Appendix 1: Clinical care pathway for management of epididymo-orchitis