



The 2016 European guideline on the management of epididymo-orchitis

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Abstract

Epididymo-orchitis is a commonly encountered condition with a reported incidence of 2.45 cases per 1000 men in the United Kingdom. This 2016 International Union against Sexually Transmitted Infections guideline provides up-to-date advice on the management of this condition. It describes the aetiology, clinical features and potential complications, as well as presenting diagnostic considerations and clear recommendations for management and follow-up. Early diagnosis and management are essential, as serious complications can include abscess formation, testicular infarction and infertility. Recent epidemiological evidence suggests that selection of fluoroquinolone antibiotics with anti-Chlamydial activity is more appropriate in the management of sexually active men in the over 35 years age group.

Keywords

Epididymitis, epididymo-orchitis, Europe, treatment, antibiotic

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Principle changes in the 2016 Guideline

The guideline includes the management of epididymitis when *Mycoplasma genitalium* is identified: to treat with a 14-day course of moxifloxacin, with a need for test of cure at four weeks along with a three-month look-back period for partner notification.

The use of ciprofloxacin is no longer advised in treating epididymitis and levofloxacin/ofloxacin are recommended instead.

Aetiology and transmission

Epididymo-orchitis is an inflammatory process of the epididymis ± testes.¹ This clinical syndrome most often presents with acute onset of pain and swelling. It is usually caused by either sexually transmitted pathogens ascending from the urethra or non-sexually transmitted uropathogens spreading from the urinary tract.

Sexually transmitted infections (STIs)

- *Chlamydia trachomatis*: especially in younger patients;
- *Neisseria gonorrhoeae*: especially in younger patients;

- *M. genitalium*: limited data on epidemiology;
- Gram-negative enteric organisms: in men engaging in insertive anal intercourse.²

Non-sexually transmitted infections

- Gram-negative enteric organism risk factors include obstructive urinary disease, urinary tract surgery or instrumentation;³

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- Mumps (commonest cause of isolated orchitis) may occur as part of an epidemic, more frequently in an area with an insufficient vaccination programme;⁴
- Tuberculosis (TB): commonly associated with renal TB but can also be an isolated finding;⁵
- Brucellosis: in endemic areas;^{6,7}
- Candida.⁸

Non-infectious

- Amiodarone: symptoms usually resolve on cessation of treatment;⁹
- Behçet's disease: associated with more severe disease, occurring in 12–19% of men with Behçet's disease.¹⁰

Clinical features

- Symptoms: acute onset, usually unilateral scrotal pain ± swelling;¹¹
- Symptoms of urethritis: urethral discharge, dysuria, penile irritation; but patients can be asymptomatic;^{12–14}
- Symptoms of urinary tract infection: dysuria, frequency, urgency;
- Physical signs: typically unilateral swelling and tenderness of epididymis ± testes, usually beginning in the tail of the epididymis and spreading to involve the whole of the epididymis and testes.

Other signs

- Urethral discharge;
- Hydrocele;
- Erythema ± oedema of scrotum;
- Pyrexia.

Disease-specific symptoms and signs

Mumps: headache and fever followed by unilateral/bilateral parotid swelling. This is followed 7–10 days later by unilateral testicular swelling. Atypically, those affected can present with bilateral testicular swelling, epididymitis alone or without systemic symptoms.^{15,16}

TB: subacute/more chronic onset of painless/painful scrotal swelling ± systemic symptoms ± scrotal sinus ± thickened scrotal skin.^{5,17}

Brucellosis: fever, sweats, headache, back pain and weakness in acute infection.¹⁸

Complications

These tend to be more frequently seen with uropathogen-associated infection.¹⁹

- Hydrocele;
- Abscess and infarction of the testicle;
- Infertility – there is a poorly understood relationship between epididymo-orchitis and infertility.

Diagnosis

Epididymo-orchitis is a clinical diagnosis based on symptoms and signs. The history, eliciting genitourinary symptoms and the risk of STIs (including anal intercourse), alongside examination findings and preliminary investigations will suggest the most likely aetiology and guide empiric antibiotics.

Historically, STIs have been attributed as the predominant cause for epididymitis in the < 35 age group and enteric pathogens in the > 35 age group. Evidence to support this approach is limited, and age and sexual history taking are not sufficient for guiding antibiotic therapy alone.²⁰

Differential diagnosis

Testicular torsion is the main differential diagnosis. This is a surgical emergency. If a young man or adolescent presents with a painful swollen testicle of sudden onset then the diagnosis is testicular torsion until proven otherwise.²¹ The patient should be promptly referred to urologist. Testicular salvage is required within 6 h and the likelihood of a good outcome decreases with time.^{22,23} Empiric antibiotics should also be issued in these circumstances.

Torsion is more likely if:

- The patient is under 20 years (but can occur at any age);
- The pain is sudden (within hours);
- The pain is severe;
- Preliminary tests do not show urethritis or likely urinary tract infection.^{22,23}

A colour Doppler ultrasound (duplex) may be helpful in assessing the vascularity of the testes and therefore may aid in differentiating between epididymo-orchitis and testicular torsion.^{24,25} Although colour Doppler has high sensitivity for diagnosing epididymo-orchitis, it cannot be used to exclude the condition.^{26,27} If there is suspicion of testicular torsion, arranging an ultrasound should not delay surgical exploration.

Preliminary investigations should include

- Diagnosis of urethritis with microscopy of a Gram-stained²⁸/methylene blue-stained^{29,30} urethral smear showing > 5 polymorphonuclear leucocytes (PMNLs) per high power field (HPF) × 1000 OR a spun down sample from first pass urine (FPU) Gram stained showing > 10 PMNLs per HFP (1000×);
- Urine dipstick – useful only as an adjunct to mid-stream urine (MSU).³¹ A negative dipstick test in men should not exclude the diagnosis of urinary tract infection UTI.^{32,33} The presence of nitrite and leukocyte esterase suggests UTI in men with urinary symptoms.^{32,33}

Laboratory investigations

- Urethral swab for *N. gonorrhoeae* culture;
- FPU/urethral swab for nucleic acid amplification test (NAAT) for *N. gonorrhoeae*, *C. trachomatis* and *M. genitalium*;
- MSU for microscopy and culture;
- C-reactive protein and erythrocyte sedimentation rate can support the diagnosis of epididymitis if raised, but surgical referral or antibiotic treatment should not be delayed on the basis of these tests.^{34,35}

All patients with sexually transmitted epididymo-orchitis should be screened for other STIs including blood borne viruses (see International Union against Sexually Transmitted Infection Guideline on the organisation of a consultation for STIs).³⁶

Management

- Information, explanation and advice should be given to the patient: an explanation of the causes of epididymo-orchitis (both sexually transmitted and non-sexually transmitted), the short-term course of the infection and the long-term implications for themselves and their partner, including partner notification if a sexually transmitted cause is identified or suspected;
- General advice: analgesia, rest and scrotal support;
- Sexual abstinence should be advised for those with suspected sexually transmitted epididymo-orchitis until treatment is completed by both patient and partner and their symptoms have settled²;
- Therapy: empiric antibiotics according to the likelihood of a sexually transmitted or uropathogen;

- Choose regimen based on immediate tests – urethral/FPU smear, urinalysis and taking into account age, sexual history, recent surgery/catheterisation, any known urinary tract abnormalities and the local prevalence of gonorrhoea and antibiotic resistance patterns.

Sexually transmitted epididymo-orchitis

First line choice:

- Ceftriaxone 500 mg intramuscular injection³⁷ IIB PLUS
- Doxycycline 100 mg twice daily for 10–14 days^{38,39} IIB; OR

Second line choice:

- Ofloxacin 200 mg twice daily for 14 days^{38,39} IIB; OR
- Levofloxacin 500 mg once daily for 10 days⁴⁰ IIB

Epididymo-orchitis most likely secondary to enteric organisms

- Ofloxacin 200 mg twice daily for 14 days^{41–43} IIB; OR
- Levofloxacin 500 mg once daily for 10 days^{20,27,44} IIB.

Points to note and consider

1. Where *M. genitalium* testing has been performed, and the organism identified, treatment should be guided to include an appropriate antibiotic (e.g. moxifloxacin 400 mg once daily for 14 days)⁴⁵ IVC.
2. Where gonorrhoea is considered unlikely, urethral/FPU microscopy negative for Gram-negative intracellular diplococci, no risk factors for gonorrhoea identified (absence of all of the following – a purulent urethral discharge, known contact of a gonorrhoeal infection, men who have sex with men, black ethnicity)³⁷ and in countries/populations where there is known very low gonorrhoea prevalence, omitting ceftriaxone or using ofloxacin could be considered.⁴⁶ Ofloxacin treats *N. gonorrhoeae*, *C. trachomatis* and most uropathogens with good penetration into the prostate. However, it is not first line treatment for *N. gonorrhoeae* due to increasing bacterial resistance to quinolones.⁴⁷

3. In patients where gonorrhoea is considered likely (see risk factors above) azithromycin should be added to ceftriaxone and doxycycline to provide optimal antibiotic cover.⁴⁷

Partner notification

For patients with confirmed or suspected sexually transmitted epididymo-orchitis (*N. gonorrhoeae*, *C. trachomatis* or *M. genitalium*) all partners potentially at risk should be notified and evaluated. They should be tested for all STIs³⁶ and given treatment with antibiotics to cover *C. trachomatis* (and *N. gonorrhoeae* or *M. genitalium* if confirmed in the index patient). The duration of look-back for contact tracing would be six months for confirmed *C. trachomatis* epididymo-orchitis, 60 days for confirmed *N. gonorrhoeae* epididymo-orchitis and three months for confirmed *M. genitalium* epididymo-orchitis. In other cases thought to be STIs other than those specified above, the duration of look-back is arbitrary, although 60 days is suggested.^{45,48,49}

Follow-up

- At three days if there is no improvement in symptoms, the patient should be seen for clinical review and the diagnosis should be reassessed. For gonococcal epididymo-orchitis, a test of cure using culture can be done three days following completion of treatment.
- At two weeks to assess for treatment compliance, assessment of symptoms and partner notification. This could be done by telephone but if the patient has persisting symptoms, arrangements should be made for clinical review. For gonococcal epididymo-orchitis, a test of cure using NAAT should be done two weeks following completion of treatment.
- At four weeks after completing therapy, a test of cure is required if epididymo-orchitis is confirmed to be secondary to *C. trachomatis* or *M. genitalium*.

Further investigations

All patients with suspected/confirmed sexually transmitted epididymo-orchitis should be screened for all other STIs including blood borne viruses.³⁶

All patients with uropathogen-confirmed epididymo-orchitis should be referred to a urology specialist for further investigations looking for structural abnormalities/urinary tract obstruction.⁵⁰

In patients where there has not been significant improvement in symptoms/signs after completion of therapy, or there is diagnostic doubt, a scrotal ultrasound should be ordered. Differential diagnoses to consider in these circumstances include progression to abscess,⁵¹ testicular ischaemia/infarct,⁵² testicular/epididymal tumour.¹¹ Further referral to urology should also be considered.

Prevention/health promotion

Patients should be advised that consistent condom use will reduce the risk of acquiring sexually transmitted epididymo-orchitis.⁵³

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Composition of editorial board

Please refer to document at http://www.iusti.org/regions/Europe/pdf/2014/Editorial_Board2014.pdf

List of contributing organisations

Please refer to text at <http://www.iusti.org/regions/Europe/euroguidelines.htm>

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Appendix I

Search strategy

This guideline represents an updated and revised version of the '2012 European guideline on the management of epididymo-orchitis'.⁵⁴ This guideline on the management of epididymo-orchitis was written after a literature search in the Medline, Embase and Cochrane databases for English-language articles published between 2001 and March 2012. The guideline was updated following a further literature search in the Medline, Embase and Cochrane databases between March 2012 and February 2016. Current major European, national and CDC guidelines were also reviewed.

Grading of evidence

For details of the tables of levels of evidence and grading of recommendations please see: http://www.iusti.org/regions/Europe/pdf/2013/Levels_of_Evidence.pdf