2012 European guideline on the management of epididymo-orchitis

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Appendix 1 is the authors' declarations of interests
Appendix 2 lists the full membership of the IUSTI Guidelines Editorial Board (2012)
Appendix 3 details levels and grading of evidence
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 caused by either sexually transmitted pathogens ascending from the urethra or non-sexually transmitted uropathogens spreading from the urinary tract.

**Sexually transmitted infections**

*Chlamydia trachomatis*- predominantly in the young\(^2\)

*Neisseria gonorrhoeae*- predominantly in the young\(^2\)

Gram negative enteric organisms – in men engaging in insertive anal intercourse\(^2\)

**Non- sexually transmitted infections**

Gram negative enteric organisms- risk factors include obstructive urinary disease, urinary tract surgery or instrumentation\(^3\).

Mumps (commonest cause of isolated orchitis) - may occur as part of an epidemic, more frequently in an area with insufficient vaccination programme\(^4\)

Tuberculosis - commonly associated with renal TB, but can also be an isolated finding\(^5\)

Brucellosis\(^6\)

Candida

**Non-infectious**

Amiodarone - symptoms usually resolve on cessation of treatment\(^7\)

Behcet's disease - associated with more severe disease, occurring in 12-19% of men with Behcet’s disease.\(^8\)

CLINICAL FEATURES

- **Symptoms:** acute onset, usually unilateral scrotal pain +/- swelling\(^9\)
  - symptoms of urethritis- urethral discharge, dysuria, penile irritation but patients can be asymptomatic\(^10,11,12\)
  - 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
• hydrocoele
• erythema +/- oedema of scrotum
• pyrexia

Disease specific symptoms and signs:
Mumps: headache and fever followed by uni/bilateral parotid swelling followed 7-10 days later by unilateral testicular swelling. Atypically, those affected can present with bilateral testicular swelling, epididymitis alone or without systemic symptoms\textsuperscript{13,14}

Tuberculosis: subacute/more chronic onset of painless/ painful scrotal swelling +/- systemic symptoms +/- scrotal sinus +/- thickened scrotal skin \textsuperscript{15,16}

Brucellosis: fever, sweats, headache, back pain, and weakness in acute infection. \textsuperscript{17}

Complications:
These tend to be more frequently seen with uropathogen-associated infection \textsuperscript{18}.
• hydrocoele
• abscess and infarction of the testicle
• infertility - It is not known if epididymo-orchitis increases the risk of 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.

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 \textsuperscript{19}. The patient should be promptly referred to urologist. Testicular salvage is required within six hours and the likelihood of a good outcome decreases with time \textsuperscript{20,21}. Empiric antibiotics should also be issued in these circumstances.
Torsion is more likely if
- 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 (UTI)²⁰,²¹.

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.²²,²³ Arranging an ultrasound should not delay surgical exploration.

Preliminary investigations should include
- diagnosis of urethritis with microscopy of a Gram stained²⁴/ methylene blue stained²⁵,²⁶ urethral smear showing > 5 polymorphonuclear leucocyte (PMNL) per High Power Field (HPF) (1000x) OR a spun down sample from first pass urine Gram stained showing >10 PMNLs per HPF (1000x).
- urine dipstick – useful only as an adjunct to mid-stream specimen of urine (MSU)²⁷. A negative dipstick test in men should not exclude the diagnosis of UTI.²⁸,²⁹ The presence of nitrite and leukocyte-esterase suggests UTI in men with urinary symptoms.²⁸,²⁹

Laboratory investigations
- Urethral swab for *N. gonorrhoeae* culture
- First pass urine (FPU)/ urethral swab for nucleic acid amplification test (NAAT) for *N. gonorrhoeae* and *C. trachomatis*
- Mid-stream specimen of urine for microscopy and culture
- C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) can aid the diagnosis of epididymitis if raised, but surgical referral or antibiotic treatment should not be delayed on the basis of these tests³⁰,³¹

All patients with sexually transmitted epididymo-orchitis should be screened for other sexually transmitted infections including blood borne viruses.
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 (if sexually transmitted cause).

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 settled.

Therapy- empiric antibiotics according to the likelihood of a sexually transmitted or uropathogen.

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

Sexually transmitted epididymo-orchitis –

First line choice
Ceftriaxone 500mg intramuscular injection $^{32}$ IIIB PLUS
Doxycycline 100mg bd for 10 to 14 days $^{33,34}$ IIIB

OR

Second line choice
Ofloxacin 200mg bd for 14 days $^{33,34}$ IIB or levofloxacin 500mg od for 10 days IIIB $^{35}$

Epididymo-orchitis most likely secondary to enteric organisms

Ofloxacin 200mg bd for 14 days $^{36,37,38}$ IIB OR
Ciprofloxacin 500mg bd for 10 days $^{39}$ IA

Points to note and consider

1. Where gonorrhoea is considered unlikely; i.e. urethral /FPU microscopy negative for gram negative intracellular diplococci (GNID), no risk factors for gonorrhoea identified (absence of all of the following - a purulent urethral discharge, known contact of GC, MSM, black ethnicity) $^{32}$ and in countries/ populations where there is
known to be a very low gonorrhoea prevalence, omitting ceftriaxone or using ofloxacin could be considered\textsuperscript{40}. Ofloxacin treats \textit{N. gonorrhoeae, C. trachomatis} and most uropathogens with good penetration into the prostate. However, it is not first line treatment for \textit{N. gonorrhoeae} due to increasing bacterial resistance to quinolones \textsuperscript{41}

2. Ciprofloxacin does not effectively treat chlamydia\textsuperscript{42}

3. If epididymitis secondary to gonorrhoea is confirmed, a test of cure is required 2 weeks after completing gonorrhoea treatment using a NAAT or after 3 days following completion of gonorrhoea treatment with a positive gonorrhoea culture, particularly if treatment has been with a quinolone \textsuperscript{41}.

**Partner notification**

For patients with confirmed or suspected sexually transmitted epididymo-orchitis (\textit{N gonorrhoeae} or \textit{C. trachomatis}) all partners potentially at risk should be notified and evaluated. They should be tested for other STIs and given treatment with antibiotics to cover \textit{C. trachomatis} (and \textit{N. gonorrhoeae} if confirmed in the index patient). The duration of look back is arbitrary, as the incubation period for epididymo-orchitis is unknown. Sixty days is suggested on the basis of current gonorrhoea and chlamydia guidelines \textsuperscript{43,44}.

**Follow up**

- At 3 days if no improvement in symptoms, the patient should be seen for clinical review and the diagnosis should be re-assessed.
- At 2 weeks for compliance check, assessment of symptoms, repeat NAAT and partner notification. This could be done by telephone but if the patient has persisting symptoms, arrangements should be made for clinical review.

**Further investigations**

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

All patients with uropathogen confirmed epididymo-orchitis should be referred to a urology specialist for further investigations looking for structural abnormalities / urinary tract obstruction \textsuperscript{45}.

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\textsuperscript{46}, testicular ischaemia/ infarct\textsuperscript{47} and testicular/ epididymal tumour\textsuperscript{48}. Further referral onto urology should also be considered.

**Prevention/health promotion**

Patients should be advised that consistent condom use will reduce the risk of acquiring sexually transmitted infections including epididymo-orchitis\textsuperscript{49}.

**SEARCH STRATEGY**

The guideline for 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. Current major European National and CDC guidelines were also reviewed.

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Appendix 1.

Declarations of interest: None of the authors or editors had any conflicts of interest for the content of this guideline.
Appendix 2.
European STI Guidelines Editorial Board

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Appendix 3.

Levels of Evidence.
Ia Evidence obtained from meta-analysis of randomised controlled trials.
Ib Evidence obtained from at least one randomised controlled trial.
IIa Evidence obtained from at least one well designed study without randomisation.
IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.
III Evidence obtained from well-designed non-experimental descriptive studies such as comparative studies, correlation studies, and case control studies.
IV Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

Grading of Evidence.
A (Evidence levels Ia, Ib) Requires at least one randomised control trial as part of the body of literature of overall good quality and consistently addressing the specific recommendation.
B (Evidence IIa, IIb, III) Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.
C (Evidence IV) Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality.