Acute Prostatitis

Aetiology
Acute prostatitis is caused by urinary tract pathogens [1,2]. These include:
• Gram negative organisms, most commonly *Escherichia coli*, *Proteus* spp, *Klebsiella* spp and *Pseudomonas* spp
• Enterococci
• *Staphylococcus aureus*
• Rarely anaerobes such as *Bacteroides* spp

Clinical features
Symptoms [1,3-5]
Acute prostatitis is an acute severe systemic illness. Symptoms include:
• symptoms of a urinary tract infection: dysuria, frequency and urgency
• symptoms of prostatitis: low back pain, perineal, penile and sometimes rectal pain
• symptoms of bacteraemia: fever and rigors; arthralgia and myalgia may occur

Signs [1,3-5]
Signs include:
• signs localised to the prostate: an extremely tender, swollen and tense, smooth textured prostate gland which is warm to the touch
• signs of the bacteraemia: pyrexia and tachycardia

Complications
Patients with acute prostatitis may present with acute retention secondary to prostatic oedema

Diagnosis
• Mid-stream urine sample for dipstick testing, culture for bacteria and antibiotic sensitivity
• Blood cultures for bacteria and antibiotic sensitivity
• Prostatic massage should not be performed on patients with acute bacterial prostatitis. This would be extremely painful, could precipitate bacteraemia, and is likely to be of little benefit as pathogens are almost always isolated from urine

Management
General Advice
Adequate hydration should be maintained, rest encouraged and analgesics such as non-steroidal anti-inflammatory drugs used

Treatment
• As acute prostatitis is a serious and severe illness empirical therapy should be started immediately.
• Parenteral or oral treatment should be selected according to the clinical condition of the patient. If there is deterioration or failure to respond to oral therapy urgent admission and parenteral therapy should be arranged.
• Good antibiotic penetration into all areas of the prostate gland is achieved because of the intense inflammation.
• Antibiotics should be continued or changed according to sensitivity results.
• If acute retention occurs suprapubic catheterisation should be performed to avoid damage to the prostate [1,3].

Recommended Regimens
For patients requiring parenteral therapy antibiotics covering the likely organisms should be used [6]:
• A high dose broad spectrum cephalosporin – for example, cefuroxime, cefotaxime or ceftriaxone plus gentamycin (level of evidence IV, grade of recommendation C)
• When clinically improved the therapy can be switched to oral treatment according to sensitivities.
For patients suitable for oral therapy, quinolones can be used [7,8]:
• Ciprofloxacin 500mg twice daily for 28 days (IV, C) [8,9]
  or
• Ofloxacin 200mg twice daily for 28 days (IV, C) [10,11].

Allergy
For patients intolerant of, or allergic to, quinolones an alternative is:
• Cotrimoxazole (TMP-SMX) 960mg twice daily for 28 days [3]
  or
• Trimethoprim 200mg twice daily for 28 days (IV, C).

Sexual partners
Treatment of sexual partners is not required as caused by uropathogens

Follow-up
• If the patient fails to respond fully to therapy the diagnosis of a prostatic abscess should be considered [12]. This can be confirmed by transrectal ultrasound scan or computed tomography scan of the prostate gland. If present perineal or transurethral drainage will be necessary [3].
• If acute prostatitis is managed correctly the prognosis is good and cure likely. At least 4 weeks of antibiotic therapy is recommended in all patients to try to prevent chronic bacterial prostatitis [3].
• When the patient has recovered his urinary tract should be investigated to exclude a structural cause for urinary tract infection [1].

Chronic Prostatitis

Aetiology
By use of the lower urinary tract quantitative localisation procedure [13] (see investigations) chronic prostatitis can be differentiated into [14,15]:
• chronic bacterial prostatitis (CBP)
• chronic abacterial prostatitis /chronic pelvic pain syndrome-inflammatorv (CAP/CPPS). This was previously called chronic non-bacterial prostatitis
• chronic abacterial prostatitis /chronic pelvic pain syndrome- non-inflammatory (CAP/CPPS). This was previously called prostatodynia

Many experts believe that CAP/CPPS inflammatory and non-inflammatory are variables of one condition [16,18]. This area is currently being extensively researched. At present the National Institutes of Health classification includes the two conditions both separately and grouped together.

Bacterial prostatitis (acute or chronic) is uncommon compared with CAP [19-21].

**Chronic bacterial prostatitis**
CBP is characterised by the recovery of pathogenic bacteria, in significant numbers, from prostatic fluid in the absence of concomitant urinary infection [15].

Usual causative bacteria are those causing acute bacterial prostatitis, most commonly *E coli* [22].

Some Gram positive organisms such as *Staphylococcus aureus, Streptococcus faecalis* and enterococci cause CBP. The role of other Gram positive organisms such as coagulase negative staphylococci, non-group D streptococci and diptheroids remains controversial and subject to much debate [23-30].

**Chronic abacterial prostatitis - inflammatory and non-inflammatory**
The aetiology of these conditions is unknown.

Although pathogenic bacteria are rarely found a significant number of patients appear to respond to antibiotics [19,31-34]. This does not prove the condition is caused by bacteria as most of the studies had no control group [19,32-34] and some antibiotics have anti-inflammatory effects.

Most evidence suggests that *Chlamydia trachomatis* is not a significant cause of CAP/CPPS [35-38]. Studies supporting its role have used non-specific chlamydia serology [37], or have not eliminated contamination [39,40].

*Ureaplasma urealyticum* and *Mycoplasma hominis* are common in healthy asymptomatic individuals [41]. Evidence that they are a major cause of CAP/CPPS is lacking. A biopsy based study failed to find any role for these organisms [36].

There is evidence that CAP/CPPS is caused by some form of persistent antigen within the prostate gland [42,43]. This antigen may be an organism/remnant or could be a constituent of urine [43,44] which has refluxed into the gland [45].

Urodynamic and cystoscopic examinations on patients with CAP/CPPS - non-inflammatory, have led to suggestions that symptoms may be caused by functional urethral obstruction [46,47], pelvic sympathetic nervous system dysfunction [48] and interstitial cystitis [49]. These remain unproved.
Whatever the aetiology of chronic prostatitis it undoubtedly has a very significant physical and psychological impact [50,51].

**Clinical features**

**Symptoms**

Chronic prostatitis has no standardised clinical definition despite being well recognised in clinical practice. It is characterised by a variety of symptoms most of which involve genital pain. These include:

- perineal pain
- lower abdominal pain
- penile pain (especially penile tip)
- testicular pain
- ejaculatory discomfort or pain
- rectal and lower back pain
- dysuria.

Attempts have been made to evaluate the symptoms of chronic prostatitis and reports suggest the first five symptoms listed above more discriminatory [52,53].

Strictly, symptoms should have been present for at least 6 months to diagnose chronic prostatitis although in practice the diagnosis is made after a shorter duration of symptoms.

Non-specific genital infection can cause many of these symptoms and this diagnosis should be considered and excluded.

**Signs**

There are few objective clinical signs and the prostate gland may, or may not, be locally or diffusely tender to palpation.

There is no evidence that the different types of chronic prostatitis can be differentiated on the basis of symptoms and signs.

**Diagnosis**

The investigation of chronic prostatitis which has been the standard for evidence based research is the lower urinary tract localisation procedure [13]. Although time consuming this is the most accurate method for differentiating CBP, CAP/CPPS-inflammatory and CAP/CPPS-non-inflammatory [14,15].

Some authors argue that the lower urinary tract localisation procedure should be confined to research [35]. It is useful in diagnosing CBP but it is often not used in clinical practice and may not alter patient management [54].

When the patient attends for prostatic massage:

- No antibiotics should have been taken for one month [55].
- The patient should not have ejaculated for two days.
- The patient should have a full but not distended bladder [1,56].

Prostatic massage should not be performed if there is evidence of urethritis or urinary tract infection. If either of these are present they should first be treated to prevent prostatic secretion contamination [57-59].
Prostatic massage

- The foreskin should be fully retracted and the penis well cleaned to prevent contamination.
- A 5-10 ml sample of first-void urethral urine (VB1) should be collected.
- The patient should urinate a further 100-200 ml urine and then a further 5-10 ml sample of mid-stream bladder urine (VB2) should be collected.
- By digital rectal examination a vigorous massage of the prostate gland should be performed for 1 minute, from periphery towards the midline with a sterile container held over the glans to collect any expressed prostatic secretions (EPS).
- A wet preparation microscopic examination of a sample of expressed prostatic secretions should be made to determine the number of polymorphonuclear leucocytes (PMNL) per high power field (x 400) [55,58].
- Immediately after the massage another 5-10 ml post-massage urine (VB3) should be collected.
- All three urine samples should have microscopy and quantitative culture.

A dry prostatic massage is reasonably common

Other possible investigations

- The presence of clumps of PMNL (5+) and oval fat bodies (macrophages containing fat droplets) can be noted on wet preparation examination [60,61].
- The pH of EPS increases with prostatitis and a pH ≥8 indicates likely prostatitis, but this should only be used in conjunction with other tests detailed above [61].
- Transrectal ultrasound in chronic prostatitis may detect those who have cysts or abscesses suitable for aspiration and likely relief of symptoms [57]. Transrectal ultrasound should not be used to differentiate the different forms of chronic prostatitis [62].
- A serum prostate-specific antigen should be measured in men over 45 years [1] although it will probably be above normal in men with prostatic inflammation [63].

Interpretation of results

- To assign an organism to the prostate the colony count in the EPS and VB3 is required to be at least 10 times greater than in VB1-2.
- For prostatic inflammation ≥10 PMNL/high power field (hpf) is considered diagnostic [17,42,64,65]. In cases of a dry expressate a PMNL count of 10/hpf greater in VB3 than VB1 and VB2 is diagnostic of prostatitis.
- If there is significant bacteruria in both VB2 and VB3 3 days of nitrofurantoin 50mg four times daily, which is not prostate penetrating, should be given and the procedure then repeated.
- An EPS pH ≥8 suggests prostatitis although it is not diagnostic.
- Clumping of PMNL and presence of lipid laden macrophages suggests prostatitis, although not diagnostic.

Management

General advice

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

**Chronic Bacterial Prostatitis**

Many antimicrobials penetrate the prostate gland poorly. In CBP the gland is either subacutely inflamed or non-inflamed. Treatment should be chosen according to antimicrobial sensitivities.

**Recommended Regimes**

For patients with CBP first-line treatment is with a quinolone such as [66,67]:

- Ciprofloxacin 500mg twice daily for 28 days (III, B) [68-70]
  
  or
  
- Ofloxacin 200mg twice daily for 28 days (III, B) [71,72]
  
  or
  
- Norfloxacin 400mg twice daily for 28 days (III, B) [73,74].

**Allergy**

For those allergic to quinolones:

- Minocycline 100mg twice daily for 28 days [75] (III, B) (In practice most experts would use doxycycline 100mg twice daily for 28 days because of more toxicity with minocycline.)
  
  or
  
- Trimethoprim 200mg twice daily for 28 days
  
  or
  
- Co-trimoxazole (TMP-SMX) 960mg twice daily for 28 days (III, B) [67].

If minocycline is used antibiotic sensitivity testing is essential as many urinary pathogens are tetracycline resistant. Many studies using trimethoprim or co-trimoxazole have used 90 days treatment [67].

Some studies have looked at longer treatment periods of 90 days or more, [66,67,69,75,76] but there is no evidence that this is superior to 28 days.

- It is difficult to make evidence based recommendations about treatment because most studies have small patient numbers, are non-comparative, define CBP in different ways, have no placebo group, use different doses of the drug studied for different lengths of time, use different treatment outcomes and have different periods of follow-up. These recommendations are based on the studies available plus expert opinion.

Prostatic calculi have been suggested as a source for recurrent infection [3]. They are extremely common radiographically [62,77]. Radical transurethral prostatectomy or total prostatectomy is effective in some patients if they are selected carefully [78,79].

**Chronic abacterial prostatitis/chronic pelvic pain syndrome**

There are no universally effective treatments for CAP/CPPS. The lack of knowledge of the aetiology of these conditions means that no specific recommendations can be made and treatment choice is usually trial and error. There is currently a systematic review of therapies for CAP/CPPS taking place [80].

Despite negative cultures most clinicians try antibiotics initially to cover occult infection. This may be effective in a number of patients [19,31-34,81] although this does not mean that the problem was genuinely infective. Treat as for CBP with a quinolone or tetracycline.
Other treatments include:

- **Transurethral microwave thermatherapy (CAP/CPPS-inflammatory)** (Ib, A) [82].
- **α blockers:**
  - Terazosin 2-10 mg for 28 days The dose should be increased gradually according to symptomatic response (CAP/CPPS-inflammatory and non-inflammatory) (Ib, A) [53,83].
  - Alfuzosin 2.5mg three times daily for 42 days in patients with confirmed urodynamic abnormalities (Ib, A) [84].
- **Non-steroidal anti-inflammatory drugs (CAP/CPPS-inflammatory)** No specific non-steroidal anti-inflammatory drug can be recommended as the evidence base uses a drug not licensed in the United Kingdom (III, B) [85].
- **Cernilton (pollen extract)** probably acts as an anti-inflammatory. One tablet three times daily for 6 months (CAP/CPPS) (III, B) [86,87].
- **The bioflavonoid, quercetin** 500mg twice daily for 28 days (CAP/CPPS-inflammatory and non-inflammatory) (Ib, A) [88]
- **Stress management** [89]. No specific therapy has been tested or advocated although referral for psychological assessment may be appropriate in some (IV, C). Diazepam 5mg twice daily for 90 days has produced symptomatic benefit [33] although benzodiazepines are not recommended in clinical practice because of dependency.
- **The role of allopurinal (CAP/CPPS)** remains controversial [90,91]. A Cochrane Systematic Review, published in 1999, recommended that further studies are needed [92].

**Sexual partners**
Partner notification and empirical treatment is not required unless a specific sexually transmitted pathogen is found at initial screening. Management should be according to the guidelines for that specific infection.

**Follow-up**
Chronic prostatitis is a difficult to manage, relapsing condition and patients are typically followed up for long periods of time. No specific follow-up recommendations can be made. The National Institutes of Health has produced a chronic prostatitis symptom index which can be used as a robust outcome measure [93].

**Auditable Outcome Measures**

- Treatment of acute prostatitis with an appropriate antibiotic for 28 days: target 90%
- Investigation of urinary tract following acute prostatitis: target 90%
- Treatment of chronic bacterial prostatitis with 28 days of an appropriate antibiotic: target 90%

**Acknowledgements**
We thank Graz Luzzi for his valuable contribution to this guideline.

**Authors and Centre**
Paul Walker, Janet Wilson, Department of Genitourinary Medicine, The General Infirmary at Leeds.
Membership of the CEG
Clinical Effectiveness Group: chairman, Keith Radcliffe (MSSVD); Imtyaz Ahmed-Jushuf (AGUM); Ian Welch (MSSVD); Mark FitzGerald (AGUM); Janet Wilson (Royal College of Physicians GU Medicine Committee).

Conflicts of Interest
None

Evidence Base
Medline Search 1966-2000 using keyword “prostatitis.” Cochrane Database of Systematic Reviews and the Cochrane Controlled Trials Register up to 2000 using keyword “prostatitis.” Further references from articles identified by Medline were included.

References