Careful assessment key in managing prostatitis


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**How** do patients with prostatitis present?

**How** should patients be investigated?

**What** are the treatment options?

**PROSTATITIS IS A COMMON CONDITION ESTIMATED TO AFFECT UP TO 30% OF MEN IN THEIR LIFETIME.** It is most prevalent in men aged between 35 and 50 years old and represents a significant health economic burden. The term prostatitis is commonly associated with inflammation and infection. The clinical reality is that prostatitis represents a spectrum of disease processes and symptoms, some of which involve neither infection nor inflammation. Prostatitis can be challenging to diagnose accurately and treat satisfactorily.

**CAUSES**

The aetiology of prostatitis may involve infectious, anatomical, endocrine, neuromuscular, immunological or psychological factors. Although the precise cause of prostatitis is poorly understood; it is thought likely that susceptible men may be exposed to one or more initiating factors which may be either isolated or repetitive events.

**NIH CLASSIFICATION**

The National Institutes of Health (NIH) classification of prostatitis forms the current basis for stratifying disease type and guiding treatment. Prostatitis is subclassified into one of four entities: acute bacterial prostatitis, chronic bacterial prostatitis, chronic pelvic pain and asymptomatic inflammatory prostatitis, see table 1, p16.

The key factor that differentiates prostatitis from other urinary tract infections or urinary tract differential diagnoses is the fact that the symptoms and cause are localised to the prostate gland. In the case of chronic pelvic pain this may be a diagnosis of exclusion.

**NIH categories I and II: Acute and chronic bacterial prostatitis**

In the presence of documented urinary tract infections the propagated flow of infected urine through the prostate is likely to be the primary aetiology. Common Gram-negative uropathogens are *E. coli*, proteus and enterococcus. Gram-positive causative organisms are rare although staphylococci and streptococci have been acknowledged in the literature.

Sexually transmitted infections such as chlamydia and gonorrhoea are less common but should be considered in patients with risk factors for sexually transmitted diseases (e.g. multiple partners).
NIH category II:

- Haematospermia
- Dysuria
- Voiding (hesitancy, poor stream, straining)

Patients may also report haematuria or pelvic region including specifically the prostate, perineum, urethra, penis, testes, groin and lower back.

NIH category IIIA and IIIB:

Chronic genitourinary pain in the absence of bacterial infection

IIA - Significant white blood cells (WBC) in expressed prostatic secretion (EPS)

IIIB - Insignificant WBC in EPS

NIH category IV:

Acute bacterial prostatitis

Chronic bacterial prostatitis

Chronic genitourinary pain in the absence of bacterial infection

Asymptomatic inflammatory prostatitis

Other risk factors for infective aetiology include:

- Indwelling catheters
- Instrumentation of the urinary tract
- Diabetes
- Immunosuppression

Recent reports suggest fungi may be causative in the latter group.11

NIH categories III and IV: Chronic pelvic pain syndrome and asymptomatic inflammatory prostatitis

The underlying aetiology in the absence of documented urinary tract infections includes infection but may be more complex. For this reason chronic prostatitis without a documented infective cause has more recently been appropriately redefined as inflammatory or non-inflammatory chronic pelvic pain syndrome.

Various theories have been proposed but the current paradigm is that chronic pelvic pain syndrome may be multifactorial and part of a more generalised pain disorder. Pelvic floor muscle abnormalities, altered neuroendocrine pathways, chemically induced inflammation, bacterial infection, autoimmune processes, dysfunctional voiding as well as intraprostatic ductal reflux mechanisms have all been identified in men with chronic pelvic pain syndrome.2,4,6,7,10

Psychological factors are also acknowledged to play a significant role in chronic pelvic pain syndrome: an increased incidence of the syndrome has been identified in patients with depression, hysteria, somatisation and maladaptive coping mechanisms.12

Patients with prostatitis may present with a variety of symptoms of differing severity. Common presenting symptoms are summarised in box 1, below, according to NIH classification subtype.

**Prostatitis symptoms**

NIH category I: Acute bacterial prostatitis

- Acute onset pain which may or may not be related to voiding. This pain may be located within the pelvic region including specifically the prostate, perineum, urethra, penis, testes, groin and lower back.
- Lower urinary tract symptoms which may be subclassified as storage (urgency, frequency, nocturia, dysuria) and voiding (hesitancy, poor stream, straining). Patients may also report haematuria or pelvic region including specifically the prostate, perineum, urethra, penis, testes, groin and lower back.
- Systemic symptoms: fever, rigors, nausea, vomiting and septicaemia.

NIH category II: Chronic bacterial prostatitis

- A documented history of recurrent urinary tract infections is the key feature.
- Previous acute prostatitis predisposes approximately 10% of men to chronic bacterial prostatitis.
- Patients may report acute or chronic episodes of pain (as described above).
- Patients may complain of systemic symptoms associated with the episodes of pain.
- Duration of symptoms > three months defines chronicity.

NIH category IIIA and IIIB: Chronic pelvic pain syndrome

- Clinically, inflammatory and non-inflammatory chronic pelvic pain syndrome symptoms may be identical. Duration of symptoms > three months defines chronicity.
- The key symptom is pain, as described above. Patients may describe pain during or after ejaculation as their predominant symptom.13
- Sexual dysfunction including erectile dysfunction, ejaculatory dysfunction and decreased libido may also be reported.
- These patients are likely to describe a significantly diminished quality of life at presentation. They may display features of psychological distress: stress, anxiety, depression, diminished quality of life.14

NIH category IV: Asymptomatic inflammatory prostatitis

- These patients by definition do not present with symptoms but have a pathological diagnosis of prostatitis made during investigation or management of other urological conditions (at transurethral resection of the prostate or prostate biopsy).

**Table 1**

<table>
<thead>
<tr>
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<th>Description</th>
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<tbody>
<tr>
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<td>Non-bacterial prostatitis</td>
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<tr>
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<td>Prostatodynia</td>
</tr>
<tr>
<td>IV Asymptomatic inflammatory prostatitis</td>
<td>WBC in EPS, post-prostatic massage, semen or histologic specimens of prostate gland</td>
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**Box 1**

**Prostatitis symptoms**

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secretions; VB3 = any EPS remaining in the prostatic urethra; WBC = white blood cells

Cat IIIB

Cat IIIA

Cat II

Table 2
Interpretation of the four glass test

<table>
<thead>
<tr>
<th>Classification</th>
<th>Specimen</th>
<th>VB1</th>
<th>VB2</th>
<th>EPS</th>
<th>VB3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat II</td>
<td>WBC</td>
<td>–</td>
<td>±</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Culture</td>
<td>–</td>
<td>±</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cat IIIA</td>
<td>WBC</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Culture</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Cat IIIB</td>
<td>WBC</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Culture</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

VB1 = urethral specimen; VB2 = bladder specimen; EPS = expressed prostatic secretions; VB3 = any EPS remaining in the prostatic urethra; WBC = white blood cells

Table 3
Interpretation of the two glass test

<table>
<thead>
<tr>
<th>Classification</th>
<th>Specimen</th>
<th>Pre-prostatic massage</th>
<th>Post-prostatic massage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat II</td>
<td>WBC</td>
<td>±</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Culture</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Cat IIIA</td>
<td>WBC</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Culture</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Cat IIIB</td>
<td>WBC</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Culture</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

TREATMENT

Only around 10% of patients with acute and chronic bacterial prostatitis will present with a proven urinary tract infection.22 Despite this infection may be the underlying pathology in a significantly higher percentage of patients presenting with prostatitis and for this reason empirical treatment with antibiotics is a reasonable option if prostatitis is suspected clinically and the culture results are negative.

In patients presenting with suspected chronic prostatitis it is imperative to explain that the cause of prostatitis is poorly understood, the treatment is chronic and as such improvements may not be seen till after six months. It is important to highlight that prostatitis is a benign condition and treatment may be about controlling and improving symptoms rather than effecting a cure. Self-help leaflets are available and patients should be encouraged to access them, see Useful information box, p19. The NIH Chronic Prostatitis Symptom Index is a useful method of monitoring patients’ response to treatment.21

NICE guidance recommends the following treatment in patients with acute bacterial prostatitis:

- Start antibiotic treatment immediately. Antibiotic options include: ciprofloxacin 500 mg bd, ofloxacin 200 mg bd, or trimethoprim 200 mg bd if quinolones are not tolerated or indicated
- Prescribe adequate analgesia: paracetamol and NSAIDs
- Reassess in 24-48 hours — if there is
Antibiotic regimen for acute and chronic bacterial prostatitis

<table>
<thead>
<tr>
<th>Antibiotic regimen</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-line therapy is oral quinolone antibiotics. If the patient is systemically unwell refer for admission to hospital. In hospital the initial management will include intravenous high dose ceftriaxone/penicillin + gentamicin. When clinically improved consider ciprofloxacin 500 mg bd for 28 days or ofloxacin 200 mg bd for 28 days.</td>
<td>Consider admission to hospital early. With quinolones, advise patients about tendon damage. For those with allergy to quinolones or prone to seizures, minocycline or trimethoprim can be considered but sensitivity testing is important. Duration 2 to 4 weeks depending on preference of clinician.</td>
</tr>
</tbody>
</table>

Consider adjunct use of alpha-blockers and adequate analgesia — anti-inflammatories. Duration can be 6 weeks depending on clinician preference.

Consider admission to hospital early. With quinolones, advise patients about tendon damage. For those with allergy to quinolones or prone to seizures, minocycline or trimethoprim can be considered but sensitivity testing is important. Duration 2 to 4 weeks depending on preference of clinician.

In patients presenting with symptoms consistent with acute bacterial prostatitis, failure of symptoms to improve despite antibiotic treatment may indicate the possibility of a prostatic abscess, see figure 1, p15. This can be confirmed on CT or TRUS scan. Radiological drainage using a perineal approach or transurethral resection are commonly used methods to treat such cases.

Infective and inflammatory processes causing prostatic swelling and oedema resulting in obstruction to urinary flow and patients may present with acute urinary retention and may need suprapubic catheterisation in this situation.

EMERGING CONCEPTS
Over the past decade there has been renewed interest in the management of prostatitis. The use of validated NIH-CPSI questionnaires in combination with appropriately designed randomised controlled trials continues to inform progress in this field.

The UPOINT classification, that categorises chronic pelvic pain syndrome patients into six domains (urinary, psychosocial, organ-specific, infection, neurogenic/systemic and tenderness), is helpful, see table 5, below.

Future management may shift from monotherapy to multimodal treatment options to achieve more successful outcomes. There is evidence in the literature suggestive that combination treatment with alpha-blockers and antibiotics helps to reduce high recurrence rates.26,31

Optional treatment strategies for refractory cases include intermittent antimicrobial treatment of acute symptomatic episodes, low-dose antimicrobial suppression. Prostatic massage along with antibiotics has also been used to achieve successful outcomes but evidence is limited. One study has also suggested that frequent ejaculation can achieve the same outcome as prostatic massage.31 Phytotherapeutic agents such as saw

### Table 5

<table>
<thead>
<tr>
<th>UPOINT domain</th>
<th>Features</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary</td>
<td>Bothersome lower urinary tract symptoms</td>
<td>Alpha-blockers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anticholinergics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dietary changes</td>
</tr>
<tr>
<td>Psychosocial</td>
<td>Stress, anxiety, depression</td>
<td>Cognitive behavioural therapy, counselling, antidepressants, referral to psychologist</td>
</tr>
<tr>
<td>Organ specific</td>
<td>Haematospermia, tender DRE</td>
<td>Alpha-blockers, prostate massage</td>
</tr>
<tr>
<td>Infection</td>
<td>Recurrent urinary tract infections</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Neurologic/systemic</td>
<td>Neuropathic pain, coexisting conditions - irritable bowel, fibromyalgia</td>
<td>Antidepressants, gabapentoids</td>
</tr>
<tr>
<td>Tenderness</td>
<td>Palpable tender points in pelvis or abdomen, painful spasm</td>
<td>Physiotherapy, muscle relaxants</td>
</tr>
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Prostatitis is a common condition estimated to affect up to 30% of men in their lifetime, it is most prevalent in men aged between 35 and 50. Prostatitis is subclassified into one of four entities: acute bacterial prostatitis, chronic bacterial prostatitis, chronic pelvic pain and asymptomatic inflammatory prostatitis.

In the presence of documented urinary tract infections the propagated flow of infected urine through the prostate is likely to be the primary aetiology. Common Gram-negative uropathogens are E. coli, proteus and enterococcus. Gram-positive causative organisms are rare.

Chronic pelvic pain syndrome may be multifactorial and part of a more generalised pain disorder. Pelvic floor muscle abnormalities, altered neuroendocrine pathways, chemically induced inflammation, bacterial infection, autoimmune processes, dysfunctional voiding as well intraprostatic ductal reflux mechanisms have all been identified in men with chronic pelvic pain syndrome.

Acute bacterial prostatitis presents with acute onset pelvic pain which may or may not be related to voiding, lower urinary tract symptoms, sometimes haematuria or haematospermia and systemic symptoms such as fever and rigors. A documented history of recurrent urinary tract infections is the key feature of chronic bacterial prostatitis. Duration of symptoms > 3 months defines chronicity. The key symptom of chronic pelvic pain syndrome is pain. Patients may describe pain during or after ejaculation as their predominant symptom.

Clinical assessment includes a thorough history and examination. A digital rectal examination (DRE) should be performed after a midstream urine (MSU) sample has been collected for urine dipstick, microscopy and culture. There is no evidence that DRE exacerbates clinical parameters. The prostate should be checked for nodules. In acute bacterial prostatitis the MSU is the only laboratory investigation required.

For acute prostatitis start antibiotic treatment immediately, antibiotic options include: ciprofloxacin 500 mg bd or ofloxacin 200 mg bd or trimethoprim 200 mg bd if quinolones are not tolerated or indicated, and prescribe adequate analgesia. Reasses in 24–48 hours – if there is no improvement or deterioration of symptoms refer the patient to urology for admission and further review. Once the patient has recovered, referral to urology for evaluation of the urinary tract is advisable.

Chronic pelvic pain requires adequate analgesia, a single 4-6 week course of antibiotics and a 4-6 week trial of an alpha-blocker if significant lower urinary tract symptoms are present. If symptoms have been present for less than six months do not prescribe an alpha-blocker and an antibiotic at the same time.

Palmetto, quercetin (bioflavonoid) and cnernilin (pollen extract) look promising but further larger scale randomised trials are required before their use can be promoted.32 The emerging link between chronic pelvic pain syndrome and psychosocial parameters may mean that screening for psychological problems is recommended in the future for this patient group, see table 5, p18,33,34

CONCLUSION
Prostatitis is made up of a continuum of four distinct diseases (acute bacterial prostatitis, chronic bacterial prostatitis, chronic pelvic pain syndrome and asymptomatic inflammatory prostatitis) that is poorly understood and challenging to manage.

Acute bacterial prostatitis is easier to identify and successfully treat whereas chronic prostatitis and chronic pelvic pain syndrome remain demanding: the multimodal therapy and UPOINT approach show promise.

Further larger scale clinical trials evaluating the efficacy of some options should help manage these conditions better in the near future.

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