Prostatitis – management in primary care

Content written by Dr Jon Rees, GP with a special interest in urology

What is prostatitis?

• Poorly understood
• Range of presentations and causes
• Prostatitis suggests inflammation of the prostate
  – Acute (acute prostatitis) – commonly due to infection
  – Persistent or relapsing chronic prostatitis
    (chronic pelvic pain syndrome)

Little is known about prostatitis than was reported by Hugh Hampton Young and associates in 1906.

Chronic prostatitis is a wastebasket of clinical ignorance.

Most urologists freely acknowledge that they would be happy never to see another patient with prostatitis in their office again; given ample access to see these patients, they ignore the real issue, delivering their antibiotics of the month and generally discharging the patients, hoping that, if they ignore them, they will not return. This approach has led to frustration and even anger on the part of the patients as they either shop around for a compassionate urologist or suffer without help from the established medical community.

What is prostatitis?

J. Curtis Nickel 1998

Chronic prostatitis – desperate measures…
Prostatitis Expert Reference Group (PERG)

- **Primary objective:**
  - Improve patient care

- **Supporting objectives:**
  - Provide guidance to clinicians treating prostatitis, both in primary and secondary care
  - Improve awareness of the signs and symptoms of prostatitis
  - To promote the efficient sharing of care between primary and secondary care

Prostatitis – a classification

US NIH classification:

- I: Acute bacterial prostatitis
- II: Chronic bacterial prostatitis
  (I & II account for <5% of all prostatitis diagnoses)
- III: Chronic prostatitis/chronic pelvic pain syndrome (CPPS)
  (>95% of prostatitis diagnoses)
- IV: Asymptomatic inflammatory prostatitis

Acute prostatitis - diagnosis

Rarely encountered in primary care

- Usually spread from bladder/urethra/inflammation
- Patient often significantly unwell
  - High fever
  - Urinary voiding symptoms (dysuria, frequency, urgency)
  - Intense local pain
  - Systemic features
  - Retention (secondary to prostatic oedema)

- Prostate tender++ on examination – 'boggy'
- Urine dip – leucocytes / blood positive

Acute prostatitis - management

- Oral antibiotics – e.g. Ciprofloxacin 500mg bd for 28 days, Trimethoprim 200mg bd for 28 days if quinolone intolerant
- Analgesia & hydration
- Stool softener if defecation painful
- Early review – admit if inadequate response
- If respond well will need routine urology referral
Chronic bacterial prostatitis

Definition: "chronic bacterial infection of the prostate (with or without symptoms of prostatitis) with a history of recurrent UTI."

Clinical features:
- Recurrent/relapsing UTI/urethritis/epididymitis
- GI/pelvic pain during flare up
- Asymptomatic/mild pelvic pain/storage symptoms between episodes
- Diffusely tender prostate during episode

CBP – diagnosis & management

- Urine dip/MSU
- Ultrasound to exclude urinary tract abnormality
- Consider flow/urodynamics
- Antibiotic – quinolone for 28 days first line
- Alpha blocker – may help alongside antibiotic
- High risk of recurrence – likely to need urological referral

Chronic Prostatitis or Chronic Pelvic Pain Syndrome (CPPS)

- Urological heart sink
- Difficult condition for patients and doctors alike
- Symptoms can persist or fluctuate for many years
- Common - 2-14% lifetime prevalence

Why ‘CPPS’?

While some of the symptoms experienced by men with CP/CPPS do originate from the prostate, it is increasingly understood that many of the symptoms do not, and are generated by other structures within the pelvis, or by neuropathic mechanisms within the sensory nervous system. It is for this reason that the term Chronic Pelvic Pain Syndrome (CPPS) is used, to emphasise that the prostate may not be to blame and that a more holistic approach to managing patients with these symptoms is required.
The more or less severe tickling and burning in the urethra or at the glans, either incessantly or at intervals, the often increased frequency of micturition, the aching and stabbing pains in the anus, sacrum or perineum, the pain in the suprapubic region as well as the radiating pain along the lumbar region and the legs are well-known manifestations of the chronic prostatitis. I hardly need mention the often…

H.R. Wossidlo M.D. 1898
Chronic prostatitis and its treatment. Presented to the Section on Surgery and Anatomy at the 49 Annual Meeting of the American Medical Association.

Chronic Prostatitis JAMA 1898

I mention the great frequency of nervous troubles as a sequel of chronic prostatitis. The more or less constant uneasy or painful sensations along the genito-urinary tract constantly close the patient’s thoughts to this region. Should he then in addition to these genito-urinary symptoms, develop a degree of sexual weakness, incomplete erection or premature seminal emission, or the patient’s spirit becomes depressed, he is constantly worrying over his illness and has all capacity for mental or physical work. In the worst cases physical nervousness leads to melancholic symptoms, frequently accompanied by tenderness of the abdomen, of the inguinal region, the perineum, or by delusions of hypochondriac. It would be impossible to go into the details...

H.R. Wossidlo M.D. 1898
Chronic prostatitis and its treatment. Presented to the Section on Surgery and Anatomy at the 49 Annual Meeting of the American Medical Association.

Chronic Prostatitis JAMA 1898

CP/CPPS - presentation

Suggested definition: ‘presence of typical symptoms of discomfort or pain in the genital or pelvic region for more than three months within the past six months’

- Urogenital Pain
- Lower Urinary Tract Symptoms
- Sexual Dysfunction
- Psychological issues

CP/CPPS: Symptoms

- Lower Urinary Tract Symptoms
  - Voiding and/or Storage LUTS
  - Urinary burning during, and independent of, micturition
  - Recurrent UTI (more applicable to CBP)

- Urogenital pain
  - Perineum
  - Suprapubic region
  - Testicles/Paras (especially penile tip pain)
  - Lower back
  - Abdominal/inguinal region/pain
  - Rectum
  - Pain on miction
  - Functional bowel symptoms (eg, IBS)
CP/CPPS: Symptoms (cont.)

- Sexual Dysfunction
  - Erectile dysfunction
  - Ejaculatory dysfunction/pain
  - Decreased libido
  - Haematospermia (blood in semen)

- Psychological Issues
  - Anxiety
  - Depression
  - QoL impact

Initial assessment

- Pain (four questions evaluating pain location, frequency and severity, 0 to 21)
- Voiding (two questions evaluating voiding and storage symptoms, 0 to 10)
- Impact on QoL (three questions, 0 to 10)

International Prostate Symptom Score (IPSS)
- Urinary symptoms (seven questions, 0 to 35)
- Impact on QoL (one question, 0 to 6)

International Index of Erectile Function (IIEF-5) or Sexual Health Inventory for Men (SHIM)
- Item questionnaire for screening/diagnosis of ED

Patient Health Questionnaire-9 (PHQ-9)
- Item questionnaire to assess the frequency of depressed mood

Generalised Anxiety Disorder-7 (GAD-7)
- Item questionnaire to assess the severity of anxiety

Summary of physical examination/investigations

<table>
<thead>
<tr>
<th>Examination/Investigation</th>
<th>Non-specialist</th>
<th>Specialist</th>
<th>Core</th>
<th>Optional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Examination of abdomen, external genitalia &amp; DRE</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Urine dip +/- MSU</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Uroflowmetry</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>PSA</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>STI Screen</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Ultrasound</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imaging (TRUS or MRI)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Prostate Biopsy</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinalysis &amp; Culture</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td>Diagnostic Cystoscopy</td>
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</tbody>
</table>

Psycho-social factors to consider when assessing men with CP/CPPS

Any pre-existing or current mental health problems?

Anxiety screening questions:
- In the last month have you often been bothered by:
  - feeling nervous, anxious, or on edge?
  - not been able to stop or control worrying?

Depression screening questions:
- In the last month have you often been bothered by:
  - feeling down, depressed, or hopeless?
  - having little interest or pleasure in doing things?

Screening for trauma and/or abuse:
- When growing up, or more recently, have any relationships been difficult or have situations happened that you have found yourself uncomfortable with?
- Life events:
  - Have you recently undergone any major life events e.g. moving house, divorce, bereavement, change of job/career?

If “yes” to any of the above questions further questioning is required from a practitioner who is competent in mental health assessment.
**CP/CPPS – treatment options**

- Antibiotics
- Alpha-blockers
- NSAID’s
- Finasteride
- Phytotherapy
  - Cernilton
  - Quercetin
- Antidepressants
- Gabapentin/Pregabalin
- Prostatic massage
- Pelvic floor physio
- Cognitive behavioural therapy
- Hyperthermia
- Acupuncture
- Thermotherapy
- Electromagnetic therapy
- ESWL

**Antibiotics for CP/CPPS**

- Antimicrobial therapy has a moderate effect on total, pain, voiding and QoL

**Antibiotic options**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Advantages</th>
<th>Considerations</th>
<th>PERG recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinolones: eg, CIPROFLOXACIN</td>
<td>Favourable pharmacokinetic profile</td>
<td>Depending on substance: ▪ Drug interactions ▪ Phototoxicity ▪ Central nervous system adverse events</td>
<td>Consider ▪ first-line ▪ Dose and duration should be sufficient to eradicate the infection, eg: CIPROFLOXACIN 500 mg bd 28/7</td>
</tr>
<tr>
<td>Tetracyclines: eg, DOXYCYCLINE</td>
<td>Good activity against Chlamydia and Mycoplasma</td>
<td>Contraindicated in renal and liver failure</td>
<td>Consider ▪ second-line ▪ Dose and duration should be sufficient to eradicate the infection, eg: DOXYCYCLINE 100 mg bd 28/7</td>
</tr>
<tr>
<td>Macrolides: eg, AZITHROMYCIN</td>
<td>Good penetration into prostate</td>
<td>Minimal supporting data from randomised controlled trials</td>
<td>Reserve for special indications, based on advice from microbiologist and microbiological findings</td>
</tr>
</tbody>
</table>

**Alpha blockers for CP/CPPS**

- Systematic review of eight trials (Cohen 2012):
  - Among 7/8 RCTs (n= 770) comparing alpha-blockers to placebo:
    - Average NIH-CPSI total reduction of 4.8 (95% CI: -7.1 to -2.6)
    - Average NIH-CPSI pain reduction of 2.1 (95% CI: -3.1 to -1.2)
    - Average NIH-CPSI voiding reduction of 1.1 (95% CI: -1.7 to -0.4) [7 RCTs]
    - Average NIH-CPSI QoL reduction of 1.4 (95% CI: -2.3 to -0.4) [7 RCTs]

- EAU guidelines for chronic pelvic pain (Feb 2012):
  - Alpha-blockers have moderate treatment effect regarding total, pain, voiding, and QoL scores in PPS (1a), and are recommended for patients with a duration of PPS < 1 year
**NSAID’s for CP/CPPS**

- Limited data for use of NSAIDs
- Moderate effect on symptoms, predominantly pain
- Most beneficial during early stages of CPPS (1st six months)
- Or for acute inflammatory flare
- Try to avoid long term use due to side effect profile

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**Central Sensitisation**

- Painful stimulus produces increased amount of pain
  - Hyperalgesia
- Non-noxious stimulus produces pain
  - Allodynia

**Use of neuropathic analgesics**

**NICE Neuropathic pain guidelines – CG173**

- Offer a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment for neuropathic pain.
- If the initial treatment is not effective or is not tolerated, offer one of the remaining three drugs, and consider switching again if the second and third drugs tried are also not effective or not tolerated.
- Titrate dose to achieve therapeutic effect.
Anti-neuropathic treatment options

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Drug name</th>
<th>Starting dose</th>
<th>Maintenance dose</th>
<th>Common adverse effects</th>
<th>PERG practical points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabapentinoids</td>
<td>GABAPENTIN</td>
<td>100 – 300mg at night</td>
<td>600mg tds</td>
<td>Dizziness, sedation, dyspepsia, dry mouth, ataxia, peripheral oedema, weight gain.</td>
<td>Few drug interactions. Safe in overdose. Gut transport mechanism can become saturated limiting absorption from GI tract.</td>
</tr>
<tr>
<td></td>
<td>PREGABALIN</td>
<td>50 – 75mg at night</td>
<td>300mg bd</td>
<td>Dizziness, sedation, dyspepsia, dry mouth, ataxia, peripheral oedema, weight gain.</td>
<td>Linear pharmacokinetics.</td>
</tr>
<tr>
<td>Tricyclic antidepressants/SNRIs</td>
<td>AMITRIPTYLINE</td>
<td>10mg in evening</td>
<td>50 – 75mg in evening</td>
<td>Sedation, dry mouth, blurred vision, urinary retention, constipation, postural hypotension, weight gain.</td>
<td>Many patients obtain pain relief at lower dose.</td>
</tr>
<tr>
<td></td>
<td>DULOXETINE</td>
<td>30mg in evening (or in morning, if insomnia)</td>
<td>60 – 120mg od</td>
<td>Nausea, sedation, insomnia, headache, dizziness, dry mouth, constipation.</td>
<td>Less sedating. May cause insomnia in some patients.</td>
</tr>
</tbody>
</table>

*Based on information from the British National Formulary and PERG expert consensus

Abbreviations: bd = twice-daily; GI = gastrointestinal; od = once-daily; SNRIs = serotonin-norepinephrine reuptake inhibitors; tds = three times daily

CP/CPPS - phytotherapy

- Pollen extract: Cernilton – 1 study suggesting 78% of men taking tds had benefit
- Flavonoids: Quercetin – 1 prospective double blind RCT – 30 men – Significant improvement vs placebo
- Saw palmetto – Poor evidence base for benefit in chronic prostatitis

Phytotherapy has a modest beneficial effect on symptom improvement in CP and CP/CPPS and may be considered as a therapeutic option in treatment-refractory patients (Level 2).

CP/CPPS - physiotherapy

- Pelvic floor re-education
- Local pelvic floor relaxation
- Biofeedback
- General relaxation
- Deep relaxation/mindfulness
- Trigger point release
- Myofascial release
- Daily exercise encouraged for pain management
- TENS
- Acupuncture for trigger point release and pain management
- Bladder retraining

There is insufficient evidence to warrant recommending surgical techniques, including radical prostatectomy, transurethral resection of the prostate, transrectal high-intensity focused ultrasound, or prostatic massage for the treatment of CBP or CP/CPPS, except in the context of a clinical trial setting (Level 3).
Priorities for implementation

- Patients with CBP or CP/CPPS should be managed according to their individual symptom pattern – no single management pathway is suitable for all patients with these conditions.

- Most patients with CP/CPPS do not have an infection, and repeated use of antibiotics such as quinolones should be avoided where no obvious benefit from infection control is evident or cultures do not support an infective aetiology.

- Early use of antineuropathic pain medication should be considered for all CBP and CP/CPPS patients refractory to initial treatments. If neuropathic pain is suspected, ensure a quick referral to the MDT, which includes pain specialists.

Treatment algorithm

- Patients present with symptoms
- Clinical assessment, including “red flag” physical examination and investigation
- Urgent referral if possible
- Clinical assessment if necessary
- Avoid antibiotics unless infection is confirmed
- Consider referral to MDT

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Priorities for implementation (2)

- Early referral to specialist services should be considered when patients fail to respond to initial measures. Referral should ideally be to a clinician with an interest in the management of CBP and/or CP/CPPS, but not necessarily a urologist.

- An MDT approach should be implemented and made available to CBP and CP/CPPS patients. The MDT should include urologists, pain specialists, nurse specialists, specialist physiotherapists, GPs, cognitive behavioural therapists/psychologists and sexual health specialists.

- Patients should be fully informed about the possible underlying causes and treatment options of CBP and CP/CPPS. The MDT responsible for the management of these patient groups should be able to explain the chronic pain cycle and other relevant information to improve patient understanding of the conditions.

Research Recommendations

In CP/CPPS patients who are refractory to initial mono-pharmacotherapy approaches, further research into multimodal pharmacotherapy is warranted. Randomised, placebo-controlled trials should be performed to establish pharmacotherapy treatment options for those who fail to show symptom responses to initial monotherapy treatment modalities.

Further research is required to establish the clinical benefit of 5-alpha-reductase inhibitors, specifically in the CP/CPPS population, especially older (>50 years) patients and/or those at increased risk of prostate cancer (PSA levels >3.5 ng/ml in a man aged 50–60 years or 3.0 ng/ml in a man aged over 60 years).

Further research is required to evaluate the cost impact and effectiveness of interventions to treat CBP and CPPS to help inform future cases for service redesign.

Further research is required to assess the effectiveness of a multidisciplinary approach and symptom-based management over ‘usual care’ for CBP and CP/CPPS patients.

Research Recommendations (2)

Further research is required to assess the use of daily phosphodiesterase type 5 (PDE5) inhibitors for those with CBP or CP/CPPS plus sexual symptoms such as ED.

Further research is required to assess the prevalence and impact of psychological factors in CBP and CP/CPPS patient. Research on the effectiveness of specific treatments, such as mindfulness/relaxation, would be useful in these patient groups.

Further research is required to investigate the possible association of CBP and CP/CPPS with other co-morbidities: for example, IBS.

Clinical studies and RCTs on any treatment modality for the management of CBP or CP/CPPS need to include long-term (at least five years) follow-up with annual assessments.

Chronic prostatitis

- Normal two year course
- 33% no symptoms at one year
- 33% moderate/marked improvement at two years
- Prognosis worse in those with:
  - Severe symptoms
  - Anxiety/depression
  - Ejaculatory pain
Resources

- PERG Guideline: available to download at: www.prostatecanceruk.org/prostatitisguideline
- BASHH UK National Guideline for the management of prostatitis (2008)
- EAU Guidelines on Chronic Pelvic Pain
- Map of Medicine
- Clinical Knowledge Summaries
- Prostate Cancer UK website & telephone support service www.prostatecanceruk.org