Prostatitis – management in primary care
What is Prostatitis???

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What is Prostatitis???
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 more is known about prostatitis than was reported by Hugh Hampton Young and associates in 1906.  
Stamey 1981

Chronic prostatitis is a wastebasket of clinical ignorance.  
Stamey 1980
Most urologists freely acknowledge that they would be happy never to see another patient with prostatitis in their office again; others simply refuse to see these patients. Many ignore the real issue, dispensing their ‘antibiotic of the month’, and quickly discharge the patients, hoping that, if they ignore them, they will not return. This approach has resulted in 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…

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/epididymis

- 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
- GU/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 flows/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.
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 draw the patient’s thoughts to this region. Should he then, in addition to his disagreeable sensations, observe a degree of sexual weakness, incomplete erection or premature seminal emission, our patient’s spirit becomes depressed. He is constantly worrying over his illness and loses all capacity for mental or physical work. In the worst cases general nervous debility sets in, not infrequently increasing to more or less complete exhaustion. Our patients become more or less obstinate hypochondriacs. 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.
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

• Urogenital pain
  – Perineum
  – Suprapubic region
  – Testicles/Penis
    (especially penile tip pain)
  – Lower back
  – Abdomen/Inguinal region/groin
  – Rectum
  – Pain on urination
  – Functional bowel symptoms
    (eg, IBS)

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

NIH-CPSI
- 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 12)

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) 5-item questionnaire for screening/diagnosis of ED

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

Generalised Anxiety Disorder-7 (GAD-7) 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>X</td>
</tr>
<tr>
<td>Urine dip +/- MSU</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>4-glass or 2-glass test</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>PSA</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>STI Screen</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Uroflowmetry</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Imaging (TRUS or MRI)</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
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<tr>
<td>Prostate Biopsy</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Urethral Swab &amp; Culture</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

www.prostatecanceruk.org/prostatitisguideline
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
- Allopurinol
- Finasteride
- Phytotherapy
  - Cernilton
  - Quercetin
- Amitriptylline
- 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

• Single use of antimicrobial therapy (quinolones or tetracyclines) is recommended in treatment-naïve patients over a minimum of six weeks with a duration of CPPS < 1 year

• Need to move away from model that CP/CPPS is an infective process & decrease antibiotic use.
# Antibiotic options

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Advantages</th>
<th>Considerations</th>
<th>PERG recommendation</th>
</tr>
</thead>
</table>
| Quinolones: CIPROFLOXACIN | Favourable pharmacokinetic profile  
Excellent penetration into the prostate  
Good bioavailability  
Good activity against typical and atypical pathogens | Depending on substance:  
- Drug interactions  
- Phototoxicity  
- Central nervous system adverse events | Consider – first-line  
Dose and duration should be sufficient to eradicate the infection, eg:  
CIPROFLOXACIN  
500 mg bd 28/7 |
| TRIMETHOPRIM | Active against most relevant pathogens  
Monitoring unnecessary  
Good penetration into the prostate | No activity against Pseudomonas, some enterococci and some enterobacteriaceae | Consider – second-line  
Dose and duration should be sufficient to eradicate the infection, eg:  
TRIMETHOPRIM  
200 mg bd 28/7 |
| Tetracyclines: DOXYCYCLINE | Good activity against Chlamydia and Mycoplasma  
Contraindicated in renal and liver failure  
Unreliable activity against coagulase-negative staphylococci, E. coli, other enterobacteriaceae, and enterococci  
No activity against P. Aeruginosa  
Risk of skin sensitisation | | Consider – second-line  
Dose and duration should be sufficient to eradicate the infection, eg:  
DOXYCYCLINE  
100 mg bd 28/7 |
| Macrolides: AZITHROMYCIN | Good penetration into prostate  
Active against Chlamydia and Gram-positive bacteria  
Minimal supporting data from randomised controlled trials  
Unreliable activity against Gram-negative bacteria | Reserve for special indications, based on advice from microbiologist and microbiological findings |

*Based on information adapted from Grabe et al, 2013, the British National Formulary and PERG expert consensus. Abbreviations: bd = twice daily.*
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 NSAID’s

• Moderate effect on symptoms, predominantly pain

• Most beneficial during early stages of CPPS (? first six months)

• Or for acute inflammatory flare

• Try to avoid long term use due to side effect profile
Central Sensitisation

Painful stimulus produces increased amount of pain
- **Hyperalgesia**

Non-noxious stimulus produces pain
- **Allodynia**

Expansion of painful area beyond the site of injury
Use of neuropathic analgesics

**Guidelines for the use of neuropathic analgesics**

- **Antidepressants**
  - First-line drugs unless contraindicated
  - No contraindications (recent infarction, arrhythmias, severe hepatic/renal disease)

- **Amitriptyline**
  - First-line antidepressant
  - 10mg at night in first instance
  - 10mg increments every 5-7 days in the absence of affect or side-effects
  - Maximum 150mg/day

- **Relative contraindications**
  - Elderly, use of machinery/driving important, dry mouth undesirable (e.g., oral cancer)

- **CONSIDER:**
  - **Fluoxetine**
    - 20mg in the morning; may be increased to 40mg. Recommended for depressed patients and where sedation a disadvantage, may not help neuropathic pain.
  - **Dothiepin**
    - 25mg at night, up to 150mg. Consider for neuropathic pain associated with anxiety.
  - **Imipramine**
    - 10mg at night, up to 150mg. Consider for pain associated with unstable bladder.
  - **Nortriptyline**
    - Start 10mg at night and progressively increase through 30mg, 50mg, 75mg, up to 100mg.

- **Side-effects or no benefit from 150mg/day for 6 weeks**

- **Contradictions, side-effect or failure**
  - Consider antiepileptics
  - Guidelines for the use of neuropathic analgesics 2

**Simple nociceptive analgesics**

- **Trial of opiates**
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>Analgesic 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</td>
<td>Less sedating. May cause insomnia in some patients.</td>
</tr>
</tbody>
</table>
Specialist Physiotherapy

• Studies have shown that the symptoms of CP/CPPS may be the result of physical dysfunction, such as abnormal pelvic muscle spasm and muscle tenderness.

• Majority of evidence for treating CP/CPPS with specialist physiotherapy is derived from small proof-of-principle or pilot studies.

• Important to exclude underlying causes for symptoms e.g. infection, prostate cancer etc prior to physiotherapy referral.

• Multiple treatment options (Level 5 evidence):
  – 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
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 CBP and CP/CPPS and may be considered as a treatment option in treatment-refractory patients (Level 2).
Prostatic Massage

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).
Treatment algorithm

Patient presents with symptoms*

Clinical assessment, including history*, physical examination† and investigations‡

Empirical antibiotics (4–6 weeks), if antibiotic naïve for CP/CPPS

If voiding LUTS present, alpha blockers for 4–6 weeks

If pain present, simple analgesics ± NSAIDs

Follow up at 4–6 weeks
**Symptoms resolve**

No bacterial cause identified and no response to antibiotics:
- consider sexual abuse/trauma.

**Follow up at 4-6 weeks**

**Persistent symptoms**

If bacterial cause confirmed or partial response to antibiotics:
- consider one further course of antibiotics at sufficient dosage and duration for each instance of a confirmed bacterial cause or partial response to antibiotics
- consider sexual abuse/trauma, psychosocial factors and yellow flags.

**Persistent symptoms**

**Symptoms resolve**
Persistent symptoms

Pain
- Explain neuropathic pain to patient (refer to Box 1).
- Stop simple analgesics and NSAIDs, unless nociceptive/inflammatory route is suspected.
- Initiate neuropathic pain treatment.
- Refer to NICE CG173.

Psychosocial symptoms
- Full assessment in primary care and management along local pathways, including PHQ-9 and GAD-7 (refer to NICE CG90 and NICE CG91).
- Consider referral to local mental health services.

Urinary symptoms
- Full LUTS assessment.
- Management as per NICE CG97.
- Refer for specialist assessment if not responding, including involvement of MDT.

Sexual symptoms
- Assessment and management as per BSSM guidelines.
- Low threshold for referral for psychosexual counselling and/or specialist urology/andrology services.

Consider referral to the MDT, specialist pain service and/or a condition-specific service at any stage, including at initial presentation and at the regular clinical reviews, especially if the patient has severe pain or their pain significantly limits their lifestyle, or their underlying health condition has deteriorated.
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.
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.
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 benefits 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 >2.5 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.
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 patients 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
Thank you

- PERG Guideline: available to download at: www.prostatecanceruk.org/prostatitisguideline
- Prostate Cancer UK website & telephone support service www.prostatecanceruk.org
- Guideline endorsed by BASHH, BAUS, BAUN, NICE CKS
- Summary published in British Journal of Urology International 2015