PROSTATITIS

Mr Ben Challacombe MS FRCS
Consultant Urological Surgeon
& Honorary Senior Lecturer
Guy’s Hospital and KCL, London, UK
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What is it?
- Acute vs Chronic
- How to treat-practical management for primary care
- When to refer and secondary care treatment options

INTRODUCTION

“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

DEFINITION: Infection or Inflammation of the prostate

PREVALENCE: 5–16%

ASSOCIATIONS:
- BPH (OR 7.7)
- STI (OR 1.8)
- Stress (OR 1.5)

WORST SYMPTOMS IN WINTER AND FEAR OF CANCER

ASSOCIATION WITH DEVELOPMENT PROSTATE CANCER (OR 1.6)

PROSTATITIS EPIDEMIOLOGY

Causes of Bacterial Prostatitis

- Trans-rectal biopsy of the Prostate
- Sexually Transmitted Disease
- Trauma
  - Post-surgical cystoscopy, TURP
  - Post-catheterisation, convene
- Epididymo-Orchitis
- Prostatic Stones
- Phimosis
- Anal intercourse

PRESENTATION and ASSESSMENT

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Type I - Acute bacterial prostatitis
Type II - Chronic bacterial prostatitis
Type III - Chronic pelvic pain syndrome (CPPS)
  IIIa/b - Inflammatory/Non-Inf
Type IV - Asymptomatic inflammatory (histological)

Krieger et al JAMA, 1999
**Acute prostatitis - diagnosis**

Rarely encountered in primary care

- Usually spread from bladder/urethra/epididymis
- Prostate tender++ on examination – ‘boggy’
- Patient often significantly unwell
  - high fever
  - urinary voiding symptoms (dysuria, frequency, urgency)
  - intense local pain
  - systemic features
  - retention (secondary to prostatic oedema)
- Urine dip – leucocytes / blood positive

**How to Treat: Acute Bacterial Prostatitis**

- Diagnosis on clinical criteria
- Levofoxacin, Ciprofloxacin for 2-4 weeks
  - + doxycycline if STD (TMP if allergic)
- Analgesia & hydration
- Stool softener if defecation painful
- Early review – admit if inadequate response
- If respond well will need routine urology referral

**Organisms in Bacterial Prostatitis**

- Organisms well defined
  - 90% Gram negative
    - Ecoli, Proteus, Klebsiella, Pseudomonas
  - 10% Enterococcus
- Type I – clinical features
- Type II – recurrent UTIs

**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

**Uncommon**

**Medical management**
- often unsuccessful.

**After TRUS/CT**
- Needs drainage if >1cm

**Transrectal or perineal aspiration of the abscess is preferred**

**TURP and drainage of the cavity**
- less desirable because of the potential haematogenic spread of bacteria.
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 is the commonest reason for a man less than 50 years to visit a urologist

(McNaughton Collins 1998, 2002)

The quality of life impact is equivalent to MI, Crohn’s disease and angina

(Wenninger 1996)

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.

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
  - Urethral burning during, and independent of, micturition
  - Recurrent UTI (more applicable to CBP)

- 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)
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)
- Voids (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

Psychosocial 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?

If “yes” to any of the above questions further questioning is required from a practitioner who is competent in mental health assessment.

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-naive 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.

Initial assessment

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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):
  - α-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

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.

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

Limited evidence/s. If sterile, consider antibiotic therapy. If infection, treat with appropriate antibiotics. If pain present, simple analgesics. If NSAID’s, pelvic floor re-education. If painful, consider trigger point release. If follow up within 4-6 weeks, repeat clinical assessment.
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.

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 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.

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 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

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

ASSESSMENT

- Time
- Keep an open mind
- Define most troublesome symptoms
- Define which symptoms affect QOL
- In absence of identifiable cause direct management to symptom amelioration
- Simple lifestyle changes
- Behavioural and coping strategies
- Multidisciplinary approach

Conclusions

- Prostatitis is common but not well understood
- Significant impact on quality of life
- Infection unusual but needs to be excluded
- Ciprofloxacin for 6 weeks seems to work
- Anti-inflammatory agents also helpful
- Psychological support paramount

TYPE IV PROSTATITIS

- Very much uncharted territory
- May have completely separate pathophysiology to clinical prostatitis
- Cause of elevated PSA
- Found at TRUS Biopsy or post TURP
- Pathophysiology unknown

PRESENTATION

- Past History
  - NSU/STIs common
  - Anxiety related illness
  - Irritable Bowel Syndrome
- Social History
  - Sexual relationships outside partnership
- Fears
  - STI and Cancer
ASSESSMENT

Examination
- Non-specific findings – abdomen, genitalia
- Allodynia: exaggerated response to stimuli
- Pelvic floor tenderness
- Prostate tenderness
- Trigger points and point tenderness

Need to exclude specific pathology – CaP, urolithiasis, stricture, scrotal pathology

ASSESSMENT

- Questionnaires – NIH-CPSI and IPSS
  - Pain, voiding, QOL
- Urinalysis, MSU
- Baseline bloods – FBC, CRP, E&C, LFTs, PSA
- Free urinary flow rate and residual volume
- Psychological assessment
- Prostatic U/S – not routinely
- Cross-sectional imaging or renal tract U/S only if symptoms indicate

CHRONIC PELVIC PAIN

Pragmatic pathway
- Exclude definite infective aetiology
- Exclude specific cause and reassure not cancer
- Quinolone – Ciprofloxacin or Ofloxacin 1 month
- Alpha-blockers
- NSAIDs
- Co-analgesics – Gabapentin or Amitriptyline, Diazepam plus behavioural and coping strategies
- Pain clinic referral/psychologist

TYPES II and III CHRONIC PROSTATITIS

- Is there a need for Stamey localisation?
- The detection rates in controls (8%) equivalent to prostatitis study group (8%) (Nickel 2002)
- An organism count x 10 greater in EPS and/or VB3 over and above that in VB1 and VB2 and leucocytes 10 per hpf in EPS (x 1000) and/or VB3 (x 400) in centrifuged urine (Ludwig 2000)

Pathophysiology: theories
- Infected urine refluxes into the ejaculatory and prostatic ducts that empty into the posterior urethra.
- Ascending urethral infection: following sexual intercourse.
- Meatal inoculation may occur during unprotected anal intercourse, instrumentation, and prolonged catheterization.
- Direct invasion or lymphogenous spread from rectum
- Direct haematogenous infection
**III\textsubscript{A} or III\textsubscript{B} by Stamey**

- VB1 first 10mls voided
- VB2 MSU
- VB3 first 10mls post prostatic massage (**ve = prostatitis**)
- EPS: **ve culture = prostatitis**

- IIIA
  - WBC in EPS, VB3, or semen
- IIIB
  - No WBC in EPS, VB3 or semen

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**Treatment Options: TYPE III PROSTATITIS**

- **Antibiotics**
- NSAIDs
- **Alpha-adrenoceptor blockers** (tamsulosin)
  - Alfoparilol
  - Finasteride
- **Phytotherapy**
  - Pentosan polysulphate
- **Amitriptyline and other co-analgesics**
- Microwave Therapy
- **Prostatic massage**
- Pelvic floor physiotherapy
- **Cognitive behavioural therapy**
  - Hyperthermia
  - Thermotherapy
  - Electromagnetic therapy
  - ESWL