TAKE-HOME POINTS FROM LECTURES BY CLEVELAND CLINIC AND VISITING FACULTY

The four categories of prostatitis: A practical approach to treatment

JEANNETTE M. POTTS, MD

Department of Urology, Cleveland Clinic

ABSTRACT

To diagnose prostatitis correctly and select appropriate therapy, one should use the Meares-Stamey technique for culturing urine and prostatic secretions and apply the classification system for prostatitis devised by the National Institutes of Health. The continuing search for an effective therapy for the most common type, chronic abacterial prostatitis, has led to adoption of treatments from other specialties and reevaluation of standard treatments.

P ROSTATITIS ACCOUNTS FOR almost 2 million office visits per year in the United States,¹ but in 90% of cases no cause can be found, and management entails uncertainty and frustration for physician and patient alike. Moreover, quality of life for patients with chronic abacterial prostatitis (the most common type) is comparable to that of patients with myocardial infarction, angina, or active Crohn disease.²

Continuing controversy about the etiology and treatment of chronic abacterial prostatitis is leading some to reevaluate standard treatments, try some innovative treatments, and borrow treatments from other specialities, such as physical therapy, biofeedback, progressive relaxation, massage, and myofascial release.

This paper focuses on diagnosis and management of chronic abacterial prostatitis, but it also covers the other three categories of pro-



statitis in the four-category classification system developed by the National Institutes of Health (NIH).

CATEGORY I ACUTE PROSTATITIS: CLEAR DIAGNOSIS AND TREATMENT

Diagnosis. Acute prostatitis is usually easy to diagnose. More common in younger men, it presents as acute illness with fever and chills and pain in the rectum, lower back, and perineum. Physical examination reveals an enlarged, tender gland. Prostatic massage is contraindicated because of the danger of bacteremia. The diagnosis is based on clinical findings, urinalysis, and a positive urine culture.

Treatment. Acute prostatitis is very responsive to antibiotics. Initially, an aminoglycoside and penicillin or a quinolone should be given parenterally until sensitivities are known, followed by a 4-week course of oral agents. Quinolones remain the drugs of choice, especially as empiric therapy.

Because urine retention may occur with acute prostatitis, therapy may include temporary placement of an indwelling urethral or suprapubic catheter; however, urethral catheters may increase the risk of prostatic abscess and septicemia.³

CATEGORY II CHRONIC BACTERIAL PROSTATITIS: A TRICKIER DIAGNOSIS

Chronic prostatitis occurs most frequently in older men, some of whom have a history of acute prostatitis.

Diagnosis. Recurrent bacterial prostatitis may be the presenting feature for some men

Management entails uncertainty and frustration for patients and physicians

TABLE 1

Urethritis or prostatitis? The Meares-Stamey technique for locating the source of bacteriuria

Method for collecting specimens

- 1 Collect two urine specimens:
 - The first 10 cc of urine. Collect in voiding bottle 1 (VB1)
 Midstream. Collect in VB2
 - Instruct the patient to stop voiding with some urine remaining in his bladder
- 2 Perform prostate massage and collect any expressed **prostatic secretions**
- 3 Collect a third urine specimen:
 - 10 cc of urine, the first voided urine after prostatic massage. Collect in VB3

Interpreting the culture results

- A negative midstream culture (VB2) does not necessarily rule out prostatitis
- A 10-fold higher number of colony-forming units in cultures grown from VB3 compared with VB1 and VB2 indicates bacteria are localized to the prostate
- A positive culture on VB1 and negative cultures on VB2 and VB3 may indicate urethritis
- Equal growth of organisms on VB1 and VB3 may indicate contamination from urethral flora.

BASED ON MEARES EM, STAMEY TA. BACTERIOLOGIC LOCALIZATION PATTERNS IN BACTERIAL PROSTATITIS AND URETHRITIS. INVEST UROL 1968; 5:492–518.

with urethral strictures, because when a patient voids against a stricture, the resulting pressure dilates the prostatic ductules and forces any bacteria present into the prostate.⁴

Signs and symptoms include frequency, dysuria, and recurrent urinary tract infection. Symptoms usually occur intermittently when the urine becomes infected, although the culpable organism can be isolated in prostatic secretions between symptomatic events. Digital rectal examination frequently reveals a normal prostate. Urinalysis and culture of urine and prostatic secretions are done using the Meares-Stamey (three-bottle) technique for locating the source of the bacteria (TABLE 1).⁵ Typically, the same single organism is identified each time the symptoms recur, and the organism usually remains pan-susceptible to antimicrobial agents.⁶

Treatment. Quinolone antibiotics are the mainstay of treatment. *Escherichia coli*, the most common organism, can be eradicated in 70% to 80% of patients, as can *Klebsiella* and

Pseudomonas aeruginosa. Enterococci are more of a challenge because they call for nitrofurantoin (Macrodantin) or amoxicillin, which do not penetrate the prostate to the same extent that other antibiotics do.⁷

Ureaplasma urealyticum: The underdiagnosed pathogen

In a prospective study at the Cleveland Clinic, 42 men age 20 to 70 years sought second and third opinions for chronic prostatitis, genital pain, orchialgia, or postvasectomy syndrome. Of these, 24 (57%) tested positive for *Ureaplasma urealyticum* and were given a 1gram dose of azithromycin. The drug was effective, as assessed by repeat cultures and improved quality of life scores, in all but two patients; one became reinfected and the other had no response to the therapy.⁸

U urealyticum is also implicated in nongonococcal urethritis (which is manifested by dysuria, abnormal semen measures, and mucous threads in the urine) and in infertility resulting from abnormal sperm function and seminal oxidative stress.⁸

CATEGORY III CHRONIC ABACTERIAL PROSTATITIS: UROLOGY'S FUNCTIONAL PAIN SYNDROME?

The third category, chronic abacterial prostatitis or chronic pelvic pain syndrome, accounts for 90% of cases of prostatitis and is the most frustrating for physicians and patients alike.

Part of the problem, as with many chronic disorders, is the paucity of good, evidencebased research. Different studies used different criteria for patient selection and classification, and some studies lumped together categories II and III, further confounding the problem.

Cause is unknown

But the biggest source of frustration is that the cause of chronic abacterial prostatitis is unknown. Etiologic theories include:

Infection, perhaps with an atypical organism (although the search for a bacterial cause remains inconclusive).⁶

Urinary reflux into prostatic ductules, leading to chemically induced inflammation.⁹ Misdiagnosis of a voiding dysfunction as

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prostatitis¹⁰; examples include pseudodyssynergia, bladder neck dyssynergia, and benign prostatic hyperplasia.

A functional somatic syndrome. Chronic pelvic pain syndrome meets the criteria for a functional somatic syndrome: a constellation of persistent symptoms associated with stress and disability that cannot be explained after a thorough evaluation.

Many specialties have something analogous to prostatitis, such as inflammatory bowel disease, premenstrual syndrome, fibromyalgia, hyperventilation syndrome, and temporomandibular joint pain. These conditions may account for 20% to 35% of patients in each specialty. Some observers even suggest that all these conditions are in fact the *same* condition, and that the existence of specific somatic syndromes is largely an artifact of medical specialization.¹¹

Increasing scientific evidence supports a "mind-body connection." In 1988, Miller¹² pointed out that a form of stress prostatitis can be precipitated or exacerbated by stressful life events. Other studies found significant psychologic factors among men with genital pain¹³ and depression and difficulty with interpersonal relationships in patients with chronic prostatitis.¹⁴

Many experts who subscribe to the theory that chronic abacterial prostatitis is a functional somatic syndrome recommend limiting the amount of testing, not only because it is expensive and has a low yield, but also because testing increases symptoms and creates further anxiety for the patient.

Other possible causes include unidentified noninfective inflammatory agents, an autoimmune response, a viral infection,⁶ and pelvic floor tension myalgia.¹⁵

Symptoms greatly reduce quality of life

Patients are described as distressed and disabled. The impact of chronic abacterial prostatitis on quality of life is comparable to that of myocardial infarction, angina, or active Crohn disease.²

Symptoms include genital or pelvic pain with voiding, and sexual dysfunction in the absence of neurologic, colorectal, and other urologic disorders such as benign prostatic hyperplasia or kidney stone disease.¹⁶

Specific evaluation strategy helps patients understand therapy

Urine culture is done using the Meares-Stamey technique (TABLE 1) to be certain there are no bacteria in the prostate. Patients need to understand this information to wean them from antibiotics.

Physical examination is performed with the patient in the lithotomy position. During assessment of the internal and external muscles, patients have a characteristic pain referral pattern. Special attention is paid to the anal sphincter muscles, levator ani muscle group, and obturators. The hip adductors, for example, refer pain to the groin, anterior medial thigh, testicular area, and scrotum.

This pain can be reproduced. For instance, during the internal examination of the obturator muscles, the patient externally rotates the hip and pushes against the nonexamining hand. Likewise, trigger points can be identified over these and the levator ani, which also can cause sharp pain and muscle spasm. This evaluation is not only diagnostic, but also aids the patient therapeutically in understanding the source of his symptoms, and therefore, the rationale of therapy (see the patient information page, "Managing prostatitis", on page 398).

In effect, in these patients, a voluntary muscle seems to have turned into an involuntary guarding muscle that may cause obstructive voiding symptoms, a condition called pseudodyssynergia. (True detrusor-sphincter dyssynergia occurs with neurologic diseases such as multiple sclerosis.) A 1997 study found that 53% of patients diagnosed with prostatitis had voiding symptoms and 68% had pseudodyssynergia proven urodynamically (Potts and Fynn, unpublished data). In 1999, Zermann et al¹⁷ found evidence of pseudodyssynergia in 86% of prostatitis patients.

Traditional drug treatment

Even though fewer than 10% of patients have positive bacterial cultures, **antibiotics** have been the treatment of choice. However, since 1983, studies have shown **diazepam** to have the same efficacy. A retrospective study of 409 men with prostatitis syndromes showed that clinical outcomes after antibiotics or no antibiotic treatment were comparable.¹⁸

The evaluation helps the patient understand the rationale for therapy Alpha-blockers may have some utility, as demonstrated by Neal and Moon¹⁹ and Barbalias et al²⁰ (who used alpha-blockers in combination with antibiotics). These drugs probably have a neurosensory effect on the neck of the bladder, assuaging many of the symptoms.

Anecdotal evidence supports the use of **nonsteroidal anti-inflammatory drugs** when the pelvic floor is inflamed or when treating other noninflammatory causes such as autoimmune disorders.

New treatments show promise

Biofeedback and progressive muscle relaxation, strengthening, and stretching of the back and pelvic floor show much promise.²¹ In a 1997 study, a survey was sent to patients asking them to rate symptoms before and after treatment (Potts and Fynn, unpublished data). The respondents were also asked what treatments they had tried or were prescribed, and which ones actually worked. The response rate was 38%.

Patients were most satisfied with physical therapy and exercise compared with antibiotics, antidepressants, alpha-blockers, counseling, nonsteroidal anti-inflammatory drugs, sitz baths, and prostate massage.

CATEGORY IV ASYMPTOMATIC PROSTATITIS CAN CAUSE ELEVATED PSA LEVELS

This form of prostatitis is usually identified retrospectively among men without symptoms with demonstrated evidence of inflammation histologically via prostate biopsy or prostatecto-

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my,^{22,23} and men evaluated for infertility who had abnormal elevations of white blood cells in the semen. The high number of negative biopsies indicates that screening for NIH category IV prostatitis would increase the specificity of PSA screening, and thereby reduce unnecessary biopsies, as well as expense and anxiety. Although patients are asymptomatic, anxiety due to fear of prostate cancer and diagnostic procedures contributes to the clinical significance of this category of prostatis.

Studies indicate that we ought to look prospectively for asymptomatic prostatitis in men with elevated PSA levels before we look for prostate cancer.

In a recent study,²⁴ we recruited 122 men with elevated PSA levels but no symptoms. After we performed prostatic massage and then collected prostatic secretions and urine samples, we found that 51 (42%) of the patients had more than 10 white blood cells per high-powered field in their expressed prostatic secretions or postmassage urine, indicating they had asymptomatic prostatitis. They were treated with a 4-week regimen of antibiotics. PSA levels returned to normal in 22 of these 51 patients and remained normal after 24 months.

We performed biopsies in the 71 men who did not have laboratory signs of prostatitis, and found that 36 (51%) had cancer. In the 29 men with laboratory signs of prostatitis whose PSA levels remained elevated despite antibiotic treatment, biopsies detected cancer in 9 (31%). The positive predictive value of PSA testing for detecting biopsy-proven cancer improved with screening for prostatitis: 37% vs 51%.

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ADDRESS: Jeannette M. Potts, MD, Department of Urology, A100, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail pottsj@ccf.org.