Chronic Prostatitis Syndrome: A Common, but Poorly Understood Condition. Part II

Michele Pavone-Macaluso

Chair of Urology, Paolo Giaccone Polyclinic Hospital, University of Palermo, via del Vespro 129, 90127, Palermo, Italy

1. Introduction

In a previous review [1] attention has been devoted to recent concepts and advances regarding the elusive condition called “chronic prostatitis syndrome” (CPS). It has been emphasised that a uniformly accepted definition is yet to be agreed on, although the National Institutes of Health (NIH) classification “chronic prostatitis/chronic pelvic pain syndrome” (CP/CPPS) has focused our attention on a few facts. (1) The condition is characterised by symptoms, although they are not specific and may be lacking completely in category IV CP/CPPS. (2) There is no pathognomonic pathology. (3) The symptoms may arise in the prostate itself but can also find their origin in adjacent structures, including the pelvic floor. Pain was considered to be the most typical manifestation but may be lacking in cases where micturition disorders are prevalent. This led to the conclusion that CPS is not a well-structured disease with uniform features, making definitions and epidemiologic studies difficult and ambiguous. In particular, considerable debate still exists regarding the causative role of gram-positive bacteria, Chlamydia and Ureaplasma. If these bacteria are accepted as causative agents, the percentage of patients considered affected by bacterial prostatitis would become much higher. A great impact on these...
concepts is generated by the different diagnostic work-ups adopted in various centres, which may include or exclude sperm culture, sperm analysis, and search for Chlamydia and Ureaplasma organisms and bacterial products.

2. Treatment

The problems encountered in obtaining a satisfactory definition and classification of CPS, its obscure pathophysiology, and the lack of agreement regarding an optimal diagnostic algorithm have produced even more unsolved controversies with regard to treatment.

An important question involves the need of stratifying patients into the various classification categories, assuming that they will require differential treatments. The need to better define outcomes and cures is of paramount importance, and uniform guidelines for future clinical trials should be adopted [2].

Many forms of therapy have been implemented, with results that are often presented as encouraging, but unfortunately most reports are empirical and based on very low number of patients, with undefined populations and unvalidated outcome measures. Very few are randomised, double-blinded studies with a placebo control arm and an adequate statistical power. The value of the vast majority of these reports remains open to question. Despite these limitations and the variety of possible remedies, the recommendations for treatment are more or less similar in different countries: Italy [3], France [4], Germany [5], Europe [6], and North America [7–9], as shown in Table 1. In addition to drug therapy, complementary measures have been proposed, as shown in Table 2. Some of these measures, such as pain medications, are prescribed with a palliative purpose, selected on the basis of symptom severity [10]; others are designed to interfere with aetiologic or pathogenetic factors.

2.1. Drugs

2.1.1. Antibacterial agents

An important observation regarding drug therapy for CPS is that penetration of many substances into the prostate is limited by a blood barrier. It is common knowledge that such barriers exist for the brain, testis, and epididymis. Recent findings have demonstrated a blood–prostate barrier in the rat ventral prostate with characteristics similar to the blood–testis barrier [11]. This has been shown for radiolabelled dextran, urea, and water. The existence of such a barrier had been suspected for several years but was mainly applied to poor penetration of antibiotics from plasma into the prostatic secretion. This was attributed to particular pharmacokinetics of antibiotics, depending on degree of ionisation, pK, protein binding, and lipid solubility [12]. For this reason, the choice of the antibacterial agent for the treatment of CPS depended much more on the knowledge of its pharmacokinetics than on in vitro sensitivity tests. Clinical experience had shown that trimethoprim has the most favourable pharmacokinetics, followed by the quinolones and some macrolides and tetracyclines, whereas β-lactams and aminoglycosides show poor penetration in the prostatic tissue. It is unknown to what an extent such penetration restrictions apply also to drug categories other than antibiotics.

For these reasons, the pharmacokinetics of various antibacterial agents have been thoroughly investigated, by measuring their concentration in prostatic fluid and in prostatic tissue in dogs and in benign prostatic hyperplasia (BPH) specimens in men. However, drug pharmacokinetics may vary

| Table 1 – A list of proposed drugs for treatment of chronic prostatitis syndrome |
| Treatment | Examples |
| Antibiotics | Quinolones, trimethoprim, macrolides |
| α-Blockers | Tamsulosin, alfuzosin, doxazosin |
| Anti-inflammatory agents | Nimesulide, celecoxib |
| 5α-reductase inhibitors | Finasteride, dutasteride |
| Plant extracts | Quercetin, Serenoa repens, pollen extracts |
| Pain control measures | Trazodone, aspirin, paracetamol |
| Antidepressants | Sertraline |
| Muscle relaxants | Diazepam, baclofen |
| Antimuscarinics | Tolterodine, trospium, solifenacin |
| Heparinoids + antihistamines | Pentosan polysulphate + hydroxyzine |
| Allopurinol | Zyloric |

| Table 2 – Complementary measures for treatment of chronic prostatitis syndrome |
| Prostatic massage | Meditation |
| Biofeedback | Diet |
| Thermotherapy | Surgery |
| Myofascial trigger point release | Intraprostatic injection of antibiotics |
| Psychotherapy | Botulinum toxin injection |
| Hot sitz baths | Electromagnetic therapy |
| Acupuncture | High-frequency electrostimulation |
considerably between dogs and humans because of the different pH conditions.

Furthermore, the distribution of drugs between adenomatous and normal human prostatic tissue may not be identical. The results from these experiments should therefore be interpreted with caution. Concentration in seminal fluid in men may provide useful information for this issue. There is consensus among different authors that antibiotic treatment of CPS should be prolonged, because, according to several reports, the best cures have been obtained using long-term treatment. Pfau [13] reported on a limited number of cases treated with cotrimoxazole in which none of the patients responded to a short-term treatment of 10–30 d, whereas 50% of patients were cured if treated for 4–8 mo. The optimal duration of treatment is still unknown, but it seems logical to give preference to oral rather than parenteral administration for such prolonged treatment. Therefore, aztreonam, which reaches relatively high concentrations in the seminal fluid, is seldom used because of its obligatory intramuscular administration [14]. It has been suggested that a relatively shorter treatment (1–2 mo) can be envisaged for fluoroquinolones, whereas 3 mo is the standard duration of treatment for trimethoprim-based therapy.

There is also consensus on the fact that, whenever Chlamydia, Ureaplasma, Gonococcus, or Candida organisms or other sexually transmitted germs are isolated from patients with CPS, whether or not they are considered as the main aetiologic agent, antibiotic treatment should be given simultaneously also to the sexual partners.

Before engaging ourselves in a revision of the current knowledge about antibiotic treatment of CPS, we should consider the following issues: (1) indications for antibiotic treatment and (2) choice of the drug.

2.1.1.1. Indications for antibiotic treatment. There is agreement on the indications for the use of antibacterial agents in cases of acute and chronic bacterial prostatitis. However, many clinicians still treat with antibiotics, at least as the initial therapy, practically all patients with CPS in the belief that an infections aetiolo gy may still be responsible for most cases, despite our failure to demonstrate the presence of the aetiologic factor. This may be due to several factors, such as presence of antibacterial factors in prostatic fluid or semen, blockade of prostatic ducts by inflammatory oedema or fibrosis or calculi, lack of elaborate investigations to detect particular bacterial species, positivity of bacterial products, isolation of bacteria in biopsy specimens, and knowledge that some patients with CPS category III do respond to treatment. This issue will be discussed further.

2.1.1.2. Choice of the antibacterial drug. For common germs, a combination of trimethoprim with a sulphonamide, co-trimoxazole, or kelfiprim [15] has been the treatment of choice for many years, due to the high penetration of trimethoprim in prostatic fluids. However, the sulpho moiety shows little activity and may cause an allergic reaction and trimethoprim alone is not commercially available in several countries. In recent years, the fluoroquinolones have become the standard of care for the treatment of bacterial prostatitis. Norfloxacin shows limited penetration [16], ofloxacin has some activity against chlamydiae [17], and ciprofloxacin and levofloxacin have shown good pharmacokinetic properties and a broad spectrum of activity. Bundrick et al [18] have shown that levofloxacin 500 mg once daily is as effective as ciprofloxacin 500 mg twice daily. Levofloxacin may be preferred, having the advantage of single daily administration. For an extensive bibliography on this topic the reader is referred to the reviews by Bjerklund Johansen et al [6] and Nickel and Moon [19]. Not all treated patients show a full response. Schaeffer et al [20] showed that of 337 men treated with either ciprofloxacin or levofloxacin for 28 d, those who failed to show a reduction of prostate-specific antigen (PSA) after treatment had a lower incidence of bacteriologic cure (eradication rate was slightly >60%). Similar results were obtained by Botto [21] who described bacteriologic cure in 75% and 73% of patients treated, respectively, with levofloxacin and ciprofloxacin.

However, response rates are much lower in pretreated patients. Alexander et al [22] described that ciprofloxacin, even with the addition of the α-blocker tamsulosin, did not reduce symptoms in men with long-standing CPS, but treatment >6 wk was not tested. Some workers have proposed direct injection of antibiotics directly into the prostate [23]. After the original report by Baert et al [23], the most recent advocates of this approach are Guercini et al [24]. They use a cocktail of antibiotics and betamethasone, repeated at weekly intervals. They claim satisfactory results, but we have never been convinced that a uniform distribution of the drugs can be obtained with this invasive manoeuvre and agree with Nickel [25] that some results reported in the literature are provocative but require further evaluation. Nickel’s comments are that “many prostatitis experts tried direct antibiotic injections in a few patients with no significant clinical results.
This approach has never been thoroughly evaluated in a well designed clinical trial.”

If Chlamydia or Ureaplasma species are present, different antibiotics should be used. Among quinolones, the greatest activity against chlamydiae is shown by ofloxacin. Tetracyclines, such as minocycline or doxycycline, are active against both chlamydiae and mycoplasma. Among macrolides, clarithromycin and azithromycin have also shown good activity. Azithromycin is used in a single dose in the treatment of acute urethritis caused by chlamydiae, but the usual long-term regimen should be recommended for the treatment of chlamydiae-associated CPS. Smelov et al [26] have shown that azithromycin and ofloxacin were the most effective drugs in vitro, but recommend ofloxacin as the primary drug in the treatment of chlamydiae-infected patients with CPS.

2.1.2. α-Blockers

Therapy with α-blockers has been reported by several authors to improve the voiding symptoms and the discomfort associated with CPS. An improvement in uroflow is to be expected in patients with reduced flow, but improvement of other symptoms was also observed even in patients who had a nonobstructed voiding pattern.

De la Rosette et al [27] used alfuzosin versus placebo, whereas Neal and Moon [28] used terazosin. Three fourths of the patients, belonging to NIH categories IIIa and IIIb, showed a symptomatic improvement if treated for 1 mo. Fifty percent of responders remained asymptomatic after discontinuation of the treatment. Tamsulosin has been used by other workers [29].

Barbalias [30] makes a plea for the combined use of antibiotics and α-blockers, especially in patients suffering from "painful male urethral syndrome," which is roughly equivalent to prostatodynia. He believes that α-blockers act primarily by abolishing intraprostatic urethral reflux and urethral hypertonia secondary to increased adrenergic stimulation [31].

2.1.3. Anti-inflammatory agents and analgesics

Enzymatic anti-inflammatory agents, such as chymotrypsin, have been occasionally used, but most reports deal with nonsteroidal drugs such as nimesulide [32] or the new cyclooxygenase 2 (COX-2) inhibitors (rofecoxib and celecoxib). They act not only with an anti-inflammatory mechanism but have intrinsic analgesic properties and can be efficacious in alleviating pain and discomfort even in patients without a demonstrable inflammatory component. Long-term administration is not encouraged because of gastrointestinal and cardiovascular side-effects, the latter being not exclusively produced by the COX-2 inhibitors. If pain is severe, the common pain killers (trazodone, paracetamol) may be of significant benefit.

2.1.4. 5α-Reductase inhibitors and hormones

Finasteride has been submitted to randomised studies versus placebo, but the first trial was underpowered and the apparent benefit was equivocal [33]. Three clinical studies suggest potential efficacy of finasteride in ameliorating symptoms due to CPS [34]. A more recent placebo-controlled multicentre study confirmed that finasteride may be of some benefit (75% of patients of the finasteride and 54% of the placebo group reported at least a mild improvement), but the authors concluded that the results do not justify recommending finasteride as monotherapy in patients with CPS. No experience with dutasteride has been hitherto reported, to our knowledge.

Various hormones, including paradoxically either androgens or oestrogens, have been used in the past with conflicting results.

2.1.5. Plant extracts

Pollen extracts (Cernilton, prostat/polit) have been claimed to have anti-inflammatory properties and to offer symptomatic relief in patients with either CPS or BPH [35,36].

Serenoa repens, also called saw palmetto, has been extensively used for BPH, but there is only one prospective study for CPS. Serenoa was less effective than finasteride [37]. A bioflavonoid, quercetin, produced a reduction of symptom score in 67% of patients versus 20% in patients receiving placebo [38].

2.1.6. Antidepressants

A placebo-controlled trial [39] showed a trend in favour of sertraline after 13 wk of treatment. Patients treated with the antidepressant showed not only an improvement in depression score but also a reduction of prostatic symptom severity. Unfortunately, the number was not sufficient to achieve statistical significance.

2.1.7. Drugs used for treatment of interstitial cystitis

The similarities and the possible relationship between CPS and interstitial cystitis (IC) in men have already been discussed in a previous review [1]. It was then a logical step to try using in patients with CPS category III the same treatments that can offer relief of symptoms in IC. Pentosan polysulphate (PPS) alone [40–43] or in combination with hydro-
xyzine hydrochloride (an antihistamine provided with anxiolytic properties) have been tested in recent years [42]. Pentosan polysulphate, a glycosaminoglycan, was used at the dose of 100 mg 3 times daily for 6 mo in a first study [40], but the dose was increased to 900 mg daily for 16 wk in a subsequent randomised study versus placebo [41]. The PPS group showed a significantly greater improvement in quality-of-life domain score than the placebo group, but some patients suffered from nausea and diarrhoea. Even better results were obtained by the addition of hydroxyzine hydrochloride (Atarax) to PPS [42], but some patients had a relapse after an excellent initial response and others complained of sleepiness and dizziness, so that Atarax was discontinued [43].

2.1.8. Other drugs
2.1.8.1. Administration. Gabapentin, colchicine, cyclosporine, thalidomide, cytokine inhibitors, antifungal agents (ketoconazole), meparinic [44], muscle relaxants (diazepam, baclofen), cannabinoids, capsacain, and antimuscarinic drugs have been used with variable success. Allopurinol has been tested on the grounds that penetration of uric acid in the prostate and crystal formation may play a pathogenetic role in CPS [45]. Ingenuity or despair from patients or clinicians have also led to attempts at cure using an endless variety of “natural therapies” such as plant products, from Echinacea to flowers of prickly pears (Opuntia ficus indica) or the so-called homeopathic remedies.

2.1.8.2. Local administration. Apart from the intraprostatic injection of antibiotics, other attempts have been made to reduce symptoms in CPS patients by administering drugs by perisphincteric or intraprostatic injection.

Botulinum toxin type A was used by perisphincteric injection in 11 patients by a group of workers from the United States, Germany, and Japan [46]. They concluded that weakening of the urethral sphincter is followed by pain relief, increase of uroflow, and symptom improvement.

A different approach has been adopted by Korean workers, who state that “many investigators have found that chronic prostatitis is associated with a drop in zinc content.” Accordingly, they injected zinc into the prostate of normal rats, observed that prostatic zinc level was maintained for at least 4 wk without any toxicity, and suggested that this method can be applied in the treatment of CPS [47].

Finally, intrarectal administration of tablets containing proteolytic enzymes (papain, trypsin), hydrolysate of calf thymus, and plant extracts daily for 20 d was quoted with favourable clinical response in 75% of patients, whereas the remaining 25% showed only moderate improvement of symptoms [48].

2.2. Physical and instrumental methods and surgery
2.2.1. Massage
Repetitive prostatic massage is an old tool in treating patients with CPS, but has been almost universally abandoned in recent years at least as a primary treatment. Then, via the Internet, the information reached many frustrated patients that physicians in Manila had a great success in treating CPS patients with massage and antibiotics [4]. Many patients flew from the United States to the Philippines, were treated, and were re-evaluated on their return home [49,50]. The conclusion was that this approach may be promising but its ultimate value needs to be confirmed. In a recent study from Egypt [51], prostatic massage did not improve the response of patients treated with antibiotics for CPS NIH categories II and IIIa.

No controlled study allows the evaluation of the effects of prostatic massage alone. The mechanism whereby prostatic massage may help patients with CPS is open to a number of interpretations; it could assist in the drainage of material obstructing the prostatic acini and may improve blood flow and antibiotic delivery to the prostate. It may also trigger a relaxation of pelvic muscle spasm. It deserves further investigations.

2.2.2. Hot sitz baths
This is another old-fashioned treatment, which is still adopted and may be useful in relieving symptoms but has never been tested in a proper study.

2.2.3. Pelvic electromagnetic therapy
Satisfactory results were reported by Rowe et al [52]. The authors believe that the chronic pelvic pain syndrome is due to muscular neural dysfunction of the urinary tract rather than to infection or inflammation. Therefore, they assume that interference with this dysfunction is the only logical way to treat CPS and advise electromagnetic therapy for this purpose. Sacral magnetic stimulation [53] and high-frequency electrostimulation have also been used following the same rationale.

2.2.4. Microwave thermotherapy
Hyperthermia and thermotherapy have been used for treatment of CPS since 1991 [54,55]. More recently [56], transurethral microwave thermotherapy (TUMT) with urethral cooling was evaluated in
39 patients with “intractable chronic prostatitis.” Improvement of total symptom score from baseline values was 51% and improvement in pain score was 60%. Side-effects were minimal and transient and the treatment “appears to be promising.”

2.2.5. Acupuncture
Acupuncture has been claimed to ameliorate symptoms of CPS with satisfactory results [57].

2.2.6. Other manipulative methods
Caudal anaesthetic block; myofascial trigger point release; pressure on soft tissue, joints, and bones; and chiropractic and osteopathic manipulations have been purported as useful methods in treating CPS.

2.2.7. Surgery
Surgery is frequently advocated by frustrated patients who hope that some form of surgical intervention may give them a hope of final resolution and permanent cure. Even total prostatectomy has been proposed in extreme cases, but the inherent risks of impotence and incontinence seem out of proportion for what is, after all, a benign disease.

Less invasive procedures, such as limited or extensive transurethral resection of the prostate, aimed at removing the affected parts of the prostate, especially those containing calculi [58], are advocated by some [59], but there is little evidence to confirm its durable efficacy. Furthermore, there is the risk of introducing an additional inflammatory condition and to make things become worse.

2.2.8. Alternative therapies
A list of non-conventional therapies can be added to various attempts to treat refractory CPS, including biofeedback, traditional Chinese medicine, Ayurveda, meditations, prayer, “creative therapy,” including art, music, and dance.

2.2.9. Psychological support and psychotherapy
These methods appear to be of primary importance in the frequent case of patients who develop severe anxiety and depression. In our experience, many patients do not accept being interviewed and treated by a psychologist or a psychiatrist. Some patients even resent such a suggestion because as they do not want to be considered neurotic or hysterical, but they want to be treated for a real organic disease. Those who accept do usually experience a real benefit, but there is a lack of exhaustive reports on the long-term results of psychological treatment for these patients. A careful analysis of the occurrence of mental distress related to CPS was carried out in Finland [60] in a population-based survey of 2500 men. The authors reported that 17% of patients with CPS presented fear of undetected cancer. Fear of having a sexually transmitted disease and suicidal thinking were even more common and 43% had decreased libido, erectile dysfunction, or marital problems. They concluded that “urologists and general practitioners should consider that a consultation with a psychiatrist may be appropriate for selected men with prostatitis,” but they give no information about frequency and results of such consultations.

In any case, it is fundamental for every clinician who takes responsibility for treating these patients to offer them a warm sympathetic approach and to be ready to listen to them with patience and dedication.

2.2.10. Changes in lifestyle
Patients are usually advised to avoid beer, strong alcoholics, pepper, and paprika and to have regular sexual activity, refraining from abstention, excess, and coitus interruptus. They are also encouraged to foster physical exercise; to avoid prolonged sitting, bicycle riding, and perineal microtraumas; and to correct any abnormalities in intestinal function. Such measures are frequently of some help. Stress reduction is often recommended but is seldom applicable.

2.2.11. Combination therapy
Antibiotics are frequently administered together with α-blockers or anti-inflammatory agents. Workers from Taiwan [61] have described their experience with a combination regimen including ciprofloxacin, doxazosin, allopurinol, biofeedback, and perineal massage. They claim that in NIH category IIIa patients they obtained a very high response rate.

3. Concluding remarks on therapy of CPS
As pointed out by Nickel et al [62], many forms of therapy have been used for bacterial and nonbacterial CPS and most of them have been credited with some degree of success, but the overwhelming number of these attempts were based on relatively few and nonhomogeneous patients, often without controls and with variable response criteria. The placebo effect in prostatic disease cannot be neglected, especially in a condition such as CPS in which psychogenic factors play an important role. Even for BPH, a significant improvement not only in
symptoms but also in objective parameters, including uroflow and postvoid residual urine, has been observed in placebo-treated controls in trials devoted to test the efficacy of finasteride or α-blockers. The same caveat should be considered for the evaluation of the effects of invasive treatment, in view of the placebo-like action of sham operations. In fact, some of the published studies on treatment of CPS are randomised and placebo-controlled [18,29,33,36,38,41,44,45,52,55] but, as Nickel (author of some of such publications) honestly admits [62] practically all of them are underpowered and cannot be attributed the rank of grade I evidence.

In conclusion, our choice of treatment cannot rely on the principles of “evidence-based medicine” and no universally applicable algorithm or guidelines can be put forward.

The most cogent question is the following: Can all patients with demonstrated or suspected CPS be treated in the same way, starting with a 30-d course of quinolones and shifting to α-blockers or anti-inflammatory agents in case of failure or recurrence? This may represent a reasonable solution if we believe that many cases targeted as nonbacterial (adopting the conventional diagnostic criteria) do harbour occult microorganisms. This approach would save us a considerable amount of time and money. Alexander [22], a well-known and respected authority in this field, reaches the conclusion that “data from recent studies do not support the tenets upon which the diagnosis and treatment of prostatitis have been based for the past three decades. The four-glass test should be abandoned and it is time for the urologist to accept the findings of careful clinical trials rather than outdated untested dogma when deciding how best to help their patients.” This is specially true for patients with long-standing CPS in whom repeated courses of antimicrobial drugs appear to be useless and the treatment should be directed towards palliation of symptoms, psychological support, and encouragement. For each patients the clinician’s judgement and skill may select one of the different therapeutic weapons resulting from the current literature, starting with the less invasive with the most favourable cost–benefit criteria. We do not favour the first-line simultaneous use of various drugs that leads to the impossibility of finding out which is effective, if any.

We would agree with Alexander’s suggestion that we should humbly start again from the very beginning and implement multicentre well-designed comparative trials with an adequate statistical power. In the meantime, we still believe that we should not abandon our current diagnostic work-up and try to sort out the cases in which an aetiolologic agent can be identified. The percentage of cases falling in the category of chronic bacterial prostatitis can vary according to the more or less extensive diagnostic work-up. Chronic bacterial prostatitis remains an “evolving clinical enigma” [19], but it seems logical to continue to treat these patients with antimicrobial agents, although bacteriologic cures in patients with bacterial prostatitis treated with various quinolones were, on average, only between 60% and 70%. Whether or not the addition of α-blockers or prostatic massage will improve the results cannot be substantiated with certainty at the present time.

The treatment of prostalgia, chronic pelvic pain syndrome, or NIH categories IIIa and IIIb rests on even more empirical grounds. According to Nickel [63], some clinical benefits can be obtained with antibacterial therapy in patients with antibiotic-naïve early-onset CPS. The α-blockers can be tried as first-line therapy in patients with moderately severe symptoms never treated before with drugs. Anti-inflammatory therapy is not recommended as a primary treatment, but it may be helpful in an adjunctive role in a multimodal therapeutic regimen. Similarly, finasteride, herbs, pollen, neuromodulation, immunotherapy, cognitive behavioural intervention, and a few other measures still under study may help in selected cases and improve quality of life. Do we need a multidisciplinary approach to diagnosis and treatment? It may well be the best management strategy for our future developments. The sympathetic approach to the patient and an optimal doctor–patient relationship remains of paramount importance. We agree with Nickel’s concluding remarks that “the management of chronic prostatitis will always be an art but it is rapidly becoming more as a science as well.” At least, we hope so.

References


CME questions

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1. The chronic prostatitis syndrome:
   A. Is a well-defined disease with uniform features
   B. Comprises a variety of symptoms
   C. Is genetically transmitted
   D. Prognosis and treatment are identical in all cases

2. The treatment with α-blockers in CPS:
   A. Brings about a symptomatic improvement in all NIH categories of patients
   B. Is useful only in improving urinary flow
   C. May reduce intraprostatic reflux
   D. Stimulates apoptosis

3. Intraprostatic injection of antibiotics:
   A. Is a good therapeutic measure only if cortisone is added
B. Reaches uniform concentration in the whole prostate gland  
C. Has not been conclusively proven to be effective  
D. Is safe, painless, and devoid of side-effects

4. The choice of an antibacterial agents for the treatment of chronic bacterial prostatitis is made according to:
A. In vitro sensitivity test  
B. Knowledge that aminoglycosides are active on gram-negative bacteria  
C. Knowledge of pharmacokinetics of drugs and capability to cross a blood–prostate barrier  
D. Knowledge of side-effects of the different drugs

5. Neurotic manifestations, anxiety, and depression are frequent among patients with refractory CPS. What is the best solution?
A. Advise psychotherapy  
B. Advise psychoanalysis  
C. Administer antidepressants  
D. Try to improve doctor–patient relationship and gain confidence

6. Prostatic massage has been proposed as a therapeutic method for treatment of CPS. Which is the most likely explanation?
A. It “unplugs” prostatic ducts from inflammatory debris  
B. It increases blood supply  
C. It facilitates penetration of antibiotics in the prostate  
D. It has a placebo-like effect