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The Role of Antibiotics in the Treatment of Chronic Prostatitis: A Consensus Statement

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Abstract

Practical guidelines for the diagnosis and treatment of chronic prostatitis are presented. Chronic prostatitis is classified as chronic bacterial prostatitis (culture-positive) and chronic inflammatory prostatitis (culture-negative). If chronic bacterial prostatitis is suspected, based on relevant symptoms or recurrent UTIs, underlying urological conditions should be excluded by the following tests: rectal examination, midstream urine culture and residual urine. The diagnosis should be confirmed by the Meares and Stamey technique. Antibiotic therapy is recommended for acute exacerbations of chronic prostatitis, chronic bacterial prostatitis and chronic inflammatory prostatitis, if there is clinical, bacteriological or supporting immunological evidence of prostate infection. Unless a patient presents with fever, antibiotic treatment should not be initiated immediately except in cases of acute prostatitis or acute episodes in a patient with chronic bacterial prostatitis. The work-up, with the appropriate investigations should be done first, within a reasonable time period which, preferably, should not be longer than 1 week. During this period, nonspecific treatment, such as appropriate analgesia to relieve symptoms, should be given. The minimum duration of antibiotic treatment should be 2–4 weeks. If there is no improvement in symptoms, treatment should be stopped and reconsidered. However, if there is improvement, it should be continued for at least a further 2–4 weeks to achieve clinical cure and, hopefully, eradication of the causative pathogen. Antibiotic treatment should not be given for 6–8 weeks without an appraisal of its effectiveness. Currently used antibiotics are reviewed. Of these, the fluoroquinolones ofloxacin and ciprofloxacin are recommended because of their favourable antibacterial spectrum and pharmacokinetic profile. A number of clinical trials are recommended and a standard study design is proposed to help resolve some outstanding issues.

Key Words
Chronic prostatitis
Treatment
Antibiotics
Guidelines

Introduction

Although a number of papers have been published with the aim of clarifying the diagnostic and therapeutic problems associated with chronic prostatitis, there is still a need for a set of clear practical guidelines for use by all physicians involved in the diagnosis and treatment of chronic prostatitis, but particularly for use by the general practitioner and the general clinician to whom such patients are most likely to present first. This paper aims to

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Table 1. Classification of chronic prostatitis[1]

Chronic bacterial prostatitis	Significant prostatic inflammation Isolation of an aetiologically recognized organism from the prostatic fluid/urine
Chronic abacterial (nonbacterial) prostatitis	Significant prostatic inflammation Failure to isolate an organism from the prostatic fluid/urine, or isolation of an organism whose aetiological significance is debatable
Prostatodynia	No significant prostatic inflammation Failure to isolate an organism from the prostatic fluid/urine

[1] Classification using the Meares and Stamey localization technique adapted from Drach et al. [8].

fulfil this need, by presenting the results of a consensus meeting on the aetiology, diagnosis and therapy of chronic prostatitis. Issues relating to fungal and viral prostatitis will not be covered.

Prostatitis, which is associated with a number of signs and symptoms in the pelvic region, is a widespread condition in men with an estimated prevalence of 10% [1]. It has been estimated that approximately half the adult male population will experience symptoms of prostatitis at some point [2, 3] and that it results in about 25% of all visits to a urologist [4]. Although it is a common diagnosis, chronic prostatitis is poorly characterized and the aetiology is not always clear, with only 5–10% of cases having an identifiable microbial cause [5]. The most common pathogen is *Escherichia coli*, accounting for 80% of cases of chronic bacterial prostatitis. *Klebsiella* spp., *Proteus* spp., *Enterococcus faecalis* and *Pseudomonas aeruginosa* occur less frequently.

Antibiotic therapy is usually prescribed where there is good clinical, bacteriological or immunological evidence of infection, and the choice of antimicrobial agent is based upon its activity against the known or strongly suspected causative pathogen(s), and upon its ability to reach the site of infection in adequate concentrations.

In acute prostatitis, application of these principles is relatively easy, since the clinical presentation of this condition is generally well defined, the aetiology well established, bacteriological confirmation of infection almost always obtained [6], and most antibiotics achieve therapeutically significant levels in the acute inflamed prostatic tissue. However, in chronic prostatitis, the exact opposite is true.

The definition of chronic prostatitis is complicated for a number of reasons. Firstly, chronic prostatitis is not a single condition, but a term that is loosely used to describe a group of conditions causing genito-pelvic pain and urinary dysfunction in adult men [7]. The generally accepted classification of chronic prostatitis, introduced by Drach et al. [8] in 1978, divides cases into chronic bacterial prostatitis (CBP), abacterial chronic prostatitis (ACP) and prostatodynia, according to the degree of prostate inflammation, and the microbiological results of expressed prostatic secretions (EPS) and midstream urine samples (table 1).

Secondly, the differential diagnosis of these various forms is impossible on clinical grounds alone [9] since their clinical presentation varies widely, and is often similar to that of other diagnoses. It is also impossible to make a diagnosis by examining the EPS in isolation due to unavoidable contamination from the urethra [9]. Thirdly, the most accurate test currently available for the differential diagnosis of chronic prostatitis, the Meares and Stamey localization technique [10], is rarely used by clinicians because it has low sensitivity, its interpretation criteria are, as yet, not unambiguously defined, it is time-consuming, relatively expensive, and patient-invasive [6, 7, 11, 12]. However, despite these shortcomings, it remains a fundamental diagnostic tool in clinical trials of chronic prostatitis.

Fourthly, diagnosis is complicated by the fact that an aetiologically recognized pathogen, such as *E. coli*, *Klebsiella* spp., *Proteus* spp., *E. faecalis* or *P. aeruginosa*, is only isolated from 5 to 10% of patients with chronic prostatitis [5]. In the majority of patients, bacteriological evaluation of prostatic fluid either fails to identify a pathogen or identifies an organism of debatable significance, for example, *Chlamydia trachomatis, Ureaplasma urealyticum* and *Mycoplasma hominis*, even though in many of these patients (60%) significant prostatic inflammation can be demonstrated (leucocyte counts in EPS of >10/hpf or >1,000/μl) [7, 11].

In addition to the diagnostic difficulties associated with this condition, response rates obtained in clinical trials of CBP are frequently poor, even though the pathogens were shown to be highly sensitive in vitro to the antibiotic used, and remained so at the end of treatment [13]. This is thought to be primarily due to the inability of the antibiotic prescribed to achieve adequate concentrations in the prostatic site of infection.

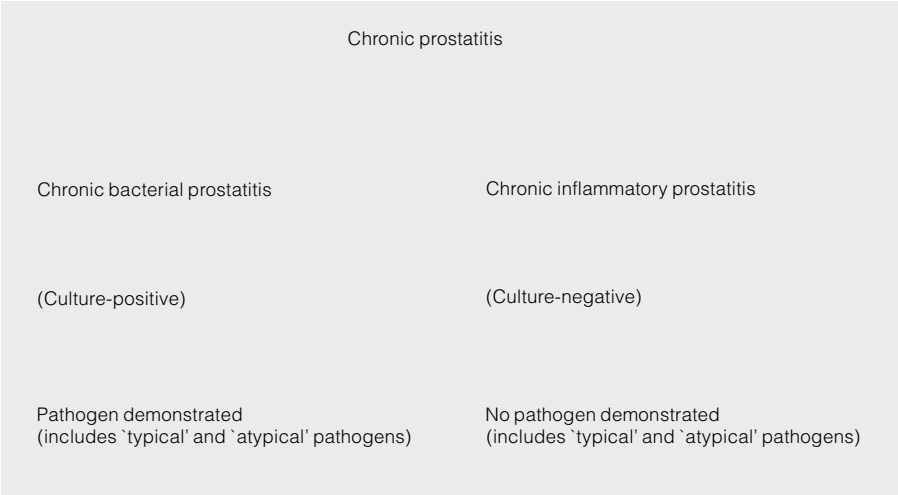

Fig. 1. Recommended classification of chronic prostatitis according to bacteriological results.

Definition of Chronic Prostatitis Suitable for Antibiotic Treatment

A diagnosis of chronic prostatitis should only be made if the appropriate investigations, such as the Meares and Stamey localization technique, and correct culture methods have been performed. Chronic prostatitis can then be divided into culture-positive (CBP) where a pathogen can be isolated, and culture-negative (chronic inflammatory prostatitis) where no pathogen can be demonstrated (fig. 1). It is important, however, to state that this definition of culture-negative prostatitis does not exclude the possibility of a bacterial cause, since it simply means that, with current methods and knowledge, a bacterial cause cannot be identified.

The so-called 'atypical' bacteria, *Mycoplasma, Ureaplasma* and *Chlamydia*, have a debatable role in this disease. That they are present is not in dispute but whether they are causative pathogens in this condition is not clear. However, we conclude that these 'atypical' bacteria should be included in the definition of CBP because they are, by definition, bacteria, but their significance, in relation to the disease, is open to question.

Another classification of prostatitis was introduced by a Workshop Committee of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) in 1995 [14] as the NIDDK reference standard for research studies. The NIDDK classification is as follows:

I. Acute bacterial prostatitis (acute infection of the prostate).

II. Chronic bacterial prostatitis (recurrent infection of the prostate).

III. Chronic abacterial prostatitis – chronic pelvic pain syndrome (CPPS) (no demonstrable infection). IIIA. Inflammatory CPPS (white cells in semen/EPS/voided bladder urine-3 (VB-3)). IIIB. Noninflammatory CPPS (no white cells in semen/EPS/VB-3).

IV. Asymptomatic inflammatory prostatitis (AIP) (no subjective symptoms, detected either by prostate biopsy or the presence of white blood cells in prostate secretions during evaluation for other disorders).

This classification uses the same principles (presence or absence of white blood cells and/or pathogens) as defined by the localization technique of Meares and Stamey [10] and histology. Category IIIA corresponds to abacterial prostatitis and IIIB to prostatodynia. Thus, the term 'prostatitis' is only used for patients with acute, chronic or recurrent bacterial prostatitis in whom causative pathogens can be identified. The term 'pelvic pain syndrome' indicates that it is not known whether or not the symptoms are related to the prostate. This reflects the present state of knowledge and the clinical situation. The main purpose for the NIDDK classification is to improve the study of CPPS, which is the most prevalent of the symptomatic diseases. The present paper, however, concentrates in more detail on the indication for and management of antimicrobial therapy if causative pathogens have been demonstrated or are reasonably suspected. The first two categories, acute and chronic (recurrent) bacterial prostatitis, are the same in both the NIDDK and our classification. We have used a classification based on that of Drach et al. [8] since this is widely accepted.

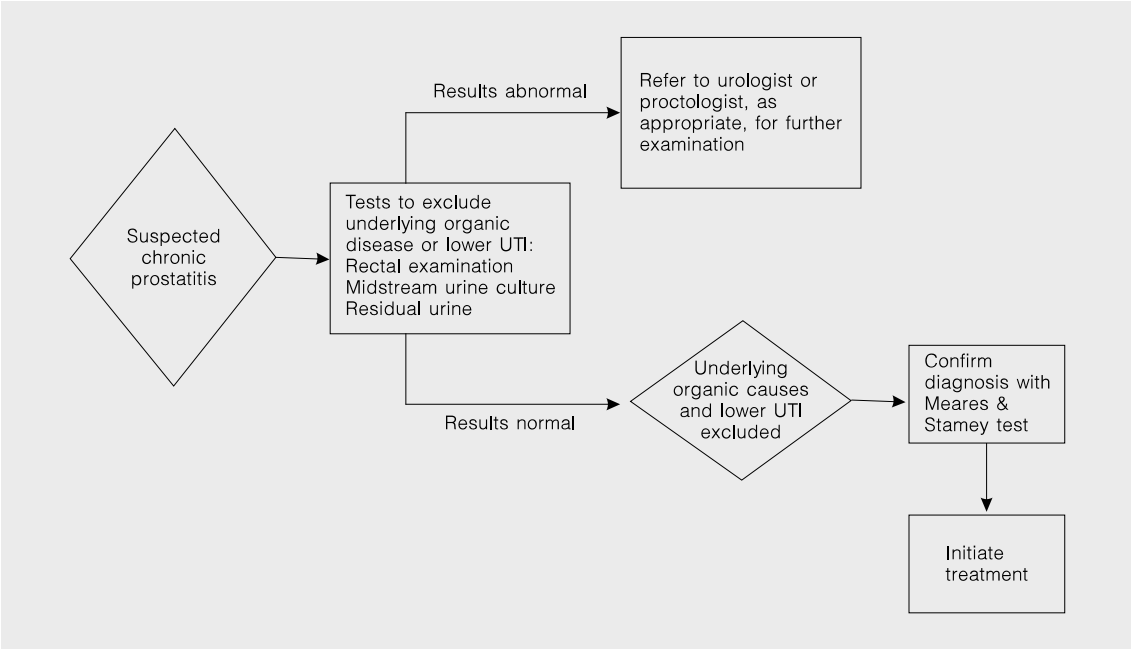

Fig. 2. Flow chart of recommended diagnostic procedures for a patient presenting with suspected chronic prostatitis.

Table 2. Clinical symptoms characterizing chronic prostatitis[1]

Frequent need to urinate
Difficulty urinating, e.g. weak stream and straining
Pain on urination, or that increases with urination
Fatigue
Pain (other than with urination) in the pelvic area
Pain in the lower back
Abdominal pain
Arthralgia
Myalgia
Pain at other location

[1] Adapted from Alexander and Trissel [15].

Clinical Presentation

CBP should be suspected if the patient presents with either relevant symptoms (table 2) [15], recurrent urinary tract infection or urinary tract infection that fails to respond to treatment. However, before antibiotic therapy is initiated, a number of investigations should be performed to confirm the diagnosis. For the diagnosis of prostatitis, there must be a correlation with inflammation, not just the symptoms. The main parameter for diagnosing inflammation in the male urogenital tract is increased leucocytes in the prostatic fluid and possible supporting parameters are complement C3, coeruloplasmin or PMN-elastase in the ejaculate [16].

An exception to this 'rule' applies to the patient whose presenting symptoms are indicative of an acute prostatitis or an acute, mainly febrile, episode against a background of chronic prostatitis, i.e. a sudden onset of fever and acute lower urinary tract symptoms and/or urinary retention. Such an acute exacerbation can be a serious illness and requires immediate antibiotic therapy. Digital rectal examination may be useful in acute or severe, febrile prostatitis since the prostate gland is often tender and swollen, whereas in chronic prostatitis it is usually normal [6].

Recommended Diagnostic Procedures

For the general clinician, it is important to distinguish between chronic prostatitis and other conditions which require a different treatment approach: other organic diseases, such as carcinoma in situ and bladder tumours, pelvic floor irritation or spasms, those patients with clinically acute prostatitis, as defined above, who then may develop

chronic prostatitis, and patients who have a lower UTI. Urine cytology screening should be performed to exclude malignancies [17]. Figure 2 shows a flow chart of the recommended procedures.

A patient suspected of having chronic prostatitis should have a urological and proctorectal examination, to rule out underlying urological or proctohaemorrhoidal diseases [18]. These basic clinical investigations should be a rectal examination, midstream urine culture and residual urine. If the results of these tests are normal, underlying urological conditions can be mostly excluded. However, if the results are abnormal, the patient should be referred to a urologist or proctologist, as appropriate, for further examination. Further tests would include urodynamics, ultrasound, radiography, cystoscopy, proctoscopy, etc. The possibility of prostate cancer should be excluded by serial prostate-specific antigen (PSA) measurements and/or biopsy in patients considered to be at risk or with a family history of cancer. If elevated PSA levels are found together with symptoms of prostatitis, the PSA should be controlled after a few weeks of antibiotic treatment. Culture-negative patients with macro- or microhaematuria, a sign of possible bladder carcinoma, should be referred to a urologist to rule out organic disease [19].

If no abnormalities are found and the segmented culture technique (Meares and Stamey [10]) can localize inflammation to the prostate, the diagnosis of chronic prostatitis can be confirmed. However, although the Meares and Stamey technique is currently the most accurate way of confirming the diagnosis of prostate infection, it is not used routinely by all physicians in clinical practice.

Patients Recommended for Antibiotic Therapy

Once the possibility of other underlying causes for the clinical presentation has been excluded, we recommend that all patients with chronic prostatitis, i.e. both culture-positive and culture-negative, should receive antibiotic therapy, although the choice of agent will vary according to the culture results. There can be little debate concerning the treatment of CBP where a 'typical' pathogen is isolated from the site of infection. However, the recommendation for antibiotic therapy in culture-negative cases (chronic inflammatory prostatitis) and cases where an 'atypical' organism is isolated, is contrary to that suggested by some authors [11, 20].

Whilst there is considerable evidence demonstrating that 'atypical' bacteria are present, their aetiological role in chronic prostatitis remains questionable. Diagnostic and culture techniques need to be refined so that the pathogenic role of these 'atypical' bacteria can be defined [9].

The justification for this is that failure to isolate a bacterium does not necessarily mean that one is not present and there is a reasonable possibility that a good clinical response can be achieved. A negative culture result may arise as a consequence of sampling errors, or poor culture or detection techniques [20]. This recommendation is supported by clinical evidence showing that culture-negative cases of chronic prostatitis do respond to antibiotic treatment [11, 21]. If there is clinical and immunological evidence of infection, we consider that antibiotic therapy should be tried in culture-negative cases.

In culture-negative prostatitis, antibiotics should not be given for more than 2 weeks unless the patient is improving. If there is no improvement, the antibiotic should be stopped and the treatment reconsidered. Caution should be exercised in treating these patients and they should be followed closely. If the assumption is that this is prostatitis, e.g. by the evidence of improvement after initiation of antibiotic therapy, but a bacterium cannot be grown, there is still a duty of care to that patient to treat them for the same length of time as a culture-positive prostatitis patient would be treated. It would be illogical to treat a culture-negative patient for a shorter period of time. Therefore, as stated below, if there is improvement, treatment should be continued for at least a further 2–4 weeks. However, it is important that antibiotic treatment should not be continued for 6–8 weeks without any appraisal of whether it is effective.

Principles of Antibiotic Treatment in Chronic Prostatitis

Antibacterial Activity

The choice of antibacterial therapy should be based upon the pathogen and its sensitivity together with the pharmacokinetics of the drug. In CBP, since bacteriological confirmation of the causative pathogen is obtained, the antibacterial cover required is apparent. However, in chronic inflammatory prostatitis, where no bacteria are identified, antibiotic therapy is prescribed on an empirical basis, and as such should provide cover against both 'typical' and 'atypical' pathogens. A logical choice of antibiotic for empirical therapy would therefore be one which has a broad spectrum of activity against the most probable pathogens. A further consideration is the low growth rate

of bacteria in chronic prostatitis. Some antibiotics, such as β-lactams, are only active when bacteria are multiplying rapidly.

Antibiotic Levels in Prostatic Tissue

A basic consideration in the choice of an antibiotic, in terms of its pharmacokinetics, is how well it penetrates to the site of prostatic infection. Most antibiotics that are active against urinary tract pathogens diffuse poorly into prostatic fluid and tissue. In order to diffuse into the site of prostatic infection, an antibiotic must be lipid-soluble, a weak base and have a dissociation coefficient (pKa) such that it is nonionized in plasma and able to ionize in the acidic environment of the prostatic fluid, thereby being preferentially concentrated in the prostatic fluid by ionic trapping. Unfortunately, few antibiotics have these necessary characteristics to be of use in the treatment of chronic prostatitis. In addition, some studies have indicated that the pH of prostatic fluid in CBP patients is alkaline rather than acidic [22–24]. The fluoroquinolones have an advantage in this respect because they are amphoteric drugs or zwitterions and thus have two pKa values, one at acid pH and one at alkaline pH.

The diffusion of an antibiotic into the prostatic site of infection is a critical factor in determining its effectiveness in treatment [25]. It is considered to be the major contributing factor explaining the poor response rates achieved with many antibiotics in clinical trials of CBP, since the pathogens in these studies had been shown to be highly sensitive in vitro to the antibiotic used, and remained so at the end of treatment [13]. In acute prostatitis, however, the situation is different and the intense inflammation which occurs allows many antibiotics to penetrate prostate gland readily.

Initiation of Treatment

Unless a patient presents with fever, with or without acute lower urinary tract symptoms, antibiotic treatment should not be initiated immediately at the first patient visit. Antibiotic treatment should only be started immediately in cases of acute prostatitis or an acute, mainly febrile, episode in a patient with CBP. The work-up, with the appropriate investigations, should be done first. If fever and acute urinary symptoms are absent, there is no requirement to give an antibiotic immediately. Generally, patients with chronic prostatitis have had the symptoms for a considerable time and therefore there is not the urgency to begin antibiotic treatment straight away. The work-up should be done within a reasonable time period which, preferably, should not be longer than 1–2 weeks. During this period, nonspecific treatment, such as appropriate analgesia to relieve symptoms, should be given while the diagnosis is confirmed. Initiating antibiotic treatment before the diagnosis is confirmed may produce false-negative test results.

Dosage

The dose will depend on which antibiotic is used and dose recommendations vary greatly from country to country. However, it is important to emphasize that the maximum dose available of the chosen antibiotic is required in order to ensure that adequate concentrations are achieved in the prostatic site of infection.

Length of Treatment

As with other chronic conditions, the duration of treatment required for chronic prostatitis is relatively long and an 'adequate' course of treatment should be given. This is because, in CBP, bacteria are found in small, isolated microcolonies deep within the acini and ducts of the prostate. In addition, some causative organisms, such as *Chlamydia*, are intracellular pathogens. It has been suggested that a significant factor contributing to the failure of antibiotic therapy in CBP is the difficulty of eradicating bacteria in protected microcolonies within an infection-induced altered microenvironment within the prostate gland [26]. There is great variation in the duration of treatment of chronic prostatitis which ranges in clinical studies from a few days to several months [27]. We recommend that the minimum duration of treatment should be 2–4 weeks. If there is no improvement in symptoms after this time, the treatment should be stopped and reconsidered. However, if there is improvement, treatment should be continued for at least a further 2–4 weeks to achieve clinical cure and, it is hoped, eradication of the causative pathogen. If the patient has not improved by this stage, expert advice from a urologist should be sought. If the patient is being treated by a general practitioner, the recommendation is that the patient should be referred to a urologist if there is a treatment failure after 2 weeks of therapy. Antibiotic treatment should not be continued for 6–8 weeks without any appraisal of whether the treatment is effective.

Cost

Most antibiotics will be given for a similar length of time to treat chronic prostatitis. Therefore, the cost of antibiotic treatment is a question of cost as an intrinsic characteristic of the drug, that is, the cost per day to give a drug, not just in drug acquisition terms, but also in terms

Table 3. The advantages and disadvantages of antibiotics currently prescribed in CBP

Antibiotic	Advantages	Disadvantages	Recommendation
Aminoglycosides	Good activity against Gram-negative bacteria	Parenteral formulation only Dose-related toxicity Need for monitoring (if >2 or 3 doses) Inadequate activity against Gram-positive bacteria	Not recommended
Oral β-lactams	Comparatively nontoxic Incidence of serious adverse events rare Monitoring unnecessary	Sensitivity to amoxycillin unreliable Resistance common among *Staphylococcus* spp. and Gram-negative bacteria Poor penetration into the prostate Little supporting clinical trial data Contraindicated in patients with allergy to β-lactams	Not recommended
Tetracyclines	Cheap Oral and parenteral forms available Good activity aginst *Chlamydia* and *Mycoplasma*	No activity against *P. aeruginosa* Unreliable activity against coagulase-negative staphylococci, *E. coli*, other Enterobacteriaceae, and enterococci Contraindicated in renal and liver failure Risk of skin sensitization	Reserve for special indications
Co-trimoxazole	None No advantage over trimethoprim	Risk of serious adverse events Incidence of adverse events increases with age	Not recommended
Trimethoprim	Good penetration into prostate Oral and parenteral forms available Relatively cheap Monitoring unnecessary Active against most relevant pathogens	No activity against *Pseudomonas*, some enterococci, and some Enterobacteriaceae	Consider
Macrolides	Reasonable activity against Gram-positive bacteria Active against *Chlamydia* Good penetration into prostate Relatively nontoxic	Little supporting clinical trial data Unreliable activity against Gram-negative bacteria	Reserve for special indications
Fluoroquinolones (ofloxacin, ciprofloxacin)	Favourable pharmacokinetics Excellent penetration into prostate Good bioavailability Equivalent oral and parenteral pharmacokinetics (ofloxacin) Good activity against 'typical' and 'atypical' pathogens and *P. aeruginosa* Good safety profile	Possibility of drug interactions with ciprofloxacin, especially at high doses	Recommended

of the cost of administration, the number of doses, the need for monitoring, etc. The element of flexibility between intravenous and oral formulations, and therefore the option for step-down therapy if this is required, should also be considered as some drugs can only be given parenterally or orally whilst others can be given by both routes. For long-term treatment, which is often required in chronic prostatitis, oral therapy is preferred.

Choice of Antibiotic Treatment

The advantages and disadvantages of the antibiotics currently used for the treatment of chronic prostatitis are shown in table 3. The aminoglycoside and β-lactam antibiotics are not recommended since, compared with the other antibiotic groups, they offer no therapeutic advantages. Tetracyclines and macrolides are also not recom-

mended for the treatment of CBP caused by 'typical' bacteria, due to their lack of, or unreliable, activity against these bacteria. However, their good antibacterial activity against *Chlamydia* (tetracyclines and macrolides) and *Mycoplasma* (tetracyclines) makes them useful for the treatment of infections caused by these bacteria. Co-trimoxazole can be excluded from the recommendations because the sulphamethoxazole component offers no therapeutic advantages over trimethoprim alone, it is associated with potentially serious adverse events and the incidence of adverse events associated with co-trimoxazole increases with age.

Thus, the antibiotics that should be considered for the treatment of chronic prostatitis are trimethoprim and the fluoroquinolones (table 3). A definitive comparison between these antibiotics is not possible due to the lack of comparative clinical studies, and the lack of consistency in the design of noncomparative clinical trials. However, there are good reasons for recommending a fluoroquinolone for antibiotic treatment.

Of the fluoroquinolones currently available, ofloxacin and ciprofloxacin can be recommended on the basis of their spectrum of activity, which includes the most likely pathogens, and pharmacokinetic profiles, which enable good concentrations to be obtained in the prostate [28]. The following information therefore relates to these two fluoroquinolones.

Firstly, they show good antibacterial activity against most of the causative bacteria. As such, they are appropriate for the first-line treatment of both CBP and chronic inflammatory prostatitis. This breadth of antibacterial spectrum is not obtained with trimethoprim, macrolides or tetracyclines. Secondly, the fluoroquinolones are amphoteric drugs or zwitterions with a pKa value at both acid and alkaline pH and achieve good penetration in the prostate with high concentrations in prostatic tissue, prostatic fluid and seminal fluid. Clinical studies have shown that ofloxacin and ciprofloxacin levels achieved in prostatic tissue, prostatic fluid, seminal fluid and ejaculate, following both oral and intravenous administration, exceed the MICs of most of the common prostatitis pathogens [25, 27, 29–31].

Whilst the safety profiles of these two antibiotics are generally similar, ofloxacin is associated with fewer drug interactions than ciprofloxacin particularly at the high doses recommended for the treatment of chronic prostatitis. In particular, it does not interact with xanthine drugs such as theophylline and caffeine, whereas such interactions do occur to a limited extent with ciprofloxacin [32–34].

A number of clinical studies have shown ofloxacin and ciprofloxacin to be of value in the treatment of CBP [21, 27, 29, 35–43]. However, it is difficult to make between-study comparisons as study designs vary so markedly, a common feature of trials of antibiotic efficacy in this area.

Recommendations for Future Clinical Studies

There are a number of unresolved issues concerning the diagnosis, therapeutic management and design of clinical studies of chronic prostatitis. A number of clinical trials are recommended to resolve or explain some of these issues (table 4). In addition, because of the problems encountered when trying to compare clinical trials with different study designs, we have proposed a standard design, based on that of Naber and Giamarellou [12], which could be adopted and would assist in the comparison of different studies (table 5). Also important for standardization is the assessment of symptoms using questionnaires or scoring instruments. Several authors have described the use of symptom scoring instruments for the assessment of prostatodynia and benign prostatic hyperplasia [44–46] and Nickel and Sorensen [47] have developed a symptom severity index and symptom frequency questionnaire for the assessment of chronic non-bacterial prostatitis patients. Similar symptom scoring techniques should also be developed for the assessment of CBP.

Conclusions

Summary of Recommendations

Chronic prostatitis is classified as CBP (culture-positive) and chronic inflammatory prostatitis (culture-negative). The diagnosis should be confirmed by the Meares and Stamey segmented localization technique and underlying urological conditions excluded by the following tests: rectal examination, midstream urine culture and residual urine.

Antibiotic therapy is recommended for acute, mainly febrile, episodes in patients with chronic prostatitis; CBP and chronic inflammatory prostatitis. Unless a patient presents with fever and acute lower urinary tract symptoms, antibiotic treatment should not be initiated immediately. The work-up, with the appropriate investigations, should be done first within a reasonable time period which, preferably, should not be longer than 1–2 weeks.

Table 4. Unresolved issues in the diagnosis and antibiotic management of chronic prostatitis

Issue	Action required
A To clarify whether a suspected pathogen is definitely related to the presenting symptoms and inflammation	Prospective randomized trial of a fluoroquinolone vs. placebo or nonspecific analgesic/inflammatory treatment
B To determine the optimum duration of antibiotic treatment once symptoms have resolved	A double-blind, randomized, comparative trial of 4 weeks' treatment with an antibiotic vs. nonspecific treatment, followed by similar trials using progressively shorter treatment periods
C Follow-up period in most published studies is too short for a chronic disease	All clinical trials of chronic prostatitis should include a follow-up period of at least 6 months and preferably 1 year
D To confirm that clinical results with the fluoroquinolones are better than those with trimethoprim	Prospective randomized, comparative trial in patients with moderate symptoms
E To improve the reproducibility and standardization of the Meares and Stamey technique	Improve the methodology of the Meares and Stamey technique, so that it is easier to standardize and the results are more reproducible Develop supporting investigations and correlate the results of the Meares and Stamey technique

Table 5. Proposed study design for trials in chronic prostatitis

Investigation	Study entry	During treatment	Follow-up		
			1 month	6 months	1 year
History	+		+	+	+
Physical examination	+				+
Meares and Stamey test	+		+	+	+
MSU		+[1]			
Transrectal ultrasonography	+				
Blood chemistry	+		+	(+)[2]	

[1] In case of treatment failure or relapse.
[2] Only in case of previous pathological findings.

During this period, nonspecific treatment, such as appropriate analgesia to relieve symptoms, should be given.

The minimum duration of treatment should be 2–4 weeks. If there is no improvement in symptoms after this time, the treatment should be stopped and reconsidered. However, if there is improvement, treatment should be continued for at least a further 2–4 weeks. Antibiotic treatment should not be continued for several weeks without any appraisal of whether it is effective. Of the antibiotics currently used for treatment, the fluoroquinolones ofloxacin and ciprofloxacin are recommended because of their favourable antibacterial spectrum and pharmacokinetic profile.

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