

Review

# Ethiopathogenetic Peculiarities of Diagnosis, Clinical Course and Treatment of Chronic Abacterial Prostatitis

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## Abstract

Chronic abacterial prostatitis or chronic pelvic pain syndrome remains an urgent problem due to its high prevalence among young men of reproductive age. Chronic abacterial prostatitis or chronic pelvic pain syndrome, especially its etiology, diagnosis and treatment, is the most discussible issue in the literature and among healthcare professionals. Many modern authors increasingly associate the etiology of this disease with viruses. However, viral etiology of chronic abacterial prostatitis has not been clearly confirmed yet.

## Keywords

chronic abacterial prostatitis; chronic pelvic pain syndrome; herpes virus; cytomegalovirus

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Nowadays, chronic prostatitis remains rather widespread, insufficiently studied and poorly treated condition. It ranks first among inflammatory diseases of the male genitalia and male diseases in general [6, 41]. Chronic prostatitis is called a "basket for clinically unclear conditions". Probably, therefore, this disease develops in about 1 in 10 urological patients in Ukraine [3, 4, 5, 6]. According to various authors, the prevalence of chronic prostatitis is 4.5 - 9%, and the frequency of seeking medical assistance in outpatient practice reaches 35-41% [1, 3, 4]. "Prostatic syndrome" or its newer synonym "chronic pelvic pain syndrome" (CPPS) is a condition in which an infectious agent can not be detected; it is considered as multifactorial pathology [1]. Prostatitis affects mainly young and middle-aged men, i.e. the most sexually active ones, and is often complicated copulatory and reproductive dysfunction [2]. Recently, prostatitis with co-existent benign prostatic hyperplasia has been diagnosed in older men as well [29]. There is an evidence that patients with chronic prostatitis develop secondary immunodeficiency [3]. Nowadays, many urologists associate the increase in the number of patients suffering from chronic prostatitis not only with the greater number of sexually transmitted infections, changes in sexual behavior, urbanization and other social, demographic and medical factors, but also with the emergence of more advanced diagnostic methods [30]. However, the diagnostics of chronic prostatitis may be difficult, since in most cases, even significant morphological changes in the prostate can occur without clinical symptoms. Thus, B. D. Bennet et al. who pathoanatomically studied 150 corpses of men who had no complaints of prostatitis during their lives and died at the

age of 16-42 years, revealed inflammatory infiltration in the glandular epithelium of the prostate in 110 cases (73%) [31]. K. Boston conducted similar study and revealed morphological changes typical for chronic prostatitis in the prostate of 80 out of 100 male corpses [30, 31].

The study of prostatitis has a long history. Herophilus first described the prostate gland as an organ in about 350 BC, and in 1815, Legneau published his observations on the inflammatory process in the prostate. Belfield was the first to isolate prostatitis as a separate nosological unit in 1800. At the present stage, to make a diagnosis of chronic prostatitis, a complete physical examination of men is required [31]. According to the theory proposed by G. Battalias (2000), prostatitis results from the disorder of urine passage, the condition which, in a number of cases, is aggravated by microorganism involvement. In chronic prostatitis, as well as in prostatodynia, pain is caused by urethral hypertension. Urethral sensitivity as well as tenderness or discomfort is the reflection of this hypertension. High maximal urethral pressure results from increased adrenergic stimulation, which, in turn, is due to local or general factors. All this causes the reflux of urethral content into the peripheral zone of the prostate gland and leads to chronic abacterial or bacterial (in case of infectious agent involvement) prostatitis [28]. Recently, global decline in male reproductive capacity has been noticed. In half of infertile marriages, prostate pathology is known to be the major cause [4]. Therefore, the problem of increasing the effectiveness of diagnosis and treatment of chronic prostatitis is of both medical and social significance. Today, chronic prostatitis ranks first among prostate diseases as an independent disease

(59%) or a disease co-existing with benign prostatic hyperplasia (85% of cases) [5]. At present, only in 5-10% of cases, chronic prostatitis has a bacterial nature, in about 60-65% of cases, abacterial prostatitis is found and in 30 - 35% of cases, prostatodynia is observed [6, 7, 8]. K. Nickel's classification being one of the major classifications adopted in Europe, distinguishes bacterial prostatitis (acute and chronic), chronic abacterial prostatitis (CAP), prostatodynia or CPPS [9]. All disadvantages of the traditional classification system gave grounds to develop and validate the classification system of chronic prostatitis by the National Institutes of Health (NIH) of the United States in December 1995.

Category I (acute bacterial prostatitis) and category II (chronic bacterial prostatitis) correspond to the traditional division into acute and chronic bacterial prostatitis. The addition of new categories, namely CPPS of inflammatory and noninflammatory prostatitis (category III) and asymptomatic inflammatory prostatitis (category IV) was aimed at solving problems and eliminating drawbacks of the traditional classification. Treatment of patients with category I or category II chronic prostatitis is described in detail in most manuals on inflammatory diseases of male genital organs. However, there are considerable difficulties when selecting medications for treating patients with CAP - category IIIA and category IIIB according to the NIH classification. This is due to the uncertainty of CAP definition, unclear etiology and pathogenesis of this disease. This pertains mostly to category IIIB (CAP/CPPS) [10]. Causes of CAP/CPPS are not fully identified. Currently, CAP/CPPS is considered as multifactorial disease associated with both non-infectious factors (inflammation, autoimmune processes, hormonal imbalance, hypertonia of pelvic floor muscles accompanied by myalgia, etc.) and agents undetectable by traditional methods: *C. Trachomatis*, *M. Hominis*, *U. urealyticum*, *M. genitalium*, *T. vaginalis* [11]. According to the literature data, the development of chronic prostatitis is necessarily preceded by hemodynamic disorder. Hyperemia or stasis in the prostate gland contributes to the development of inflammation being the cause of chronic prostatitis exacerbation [32, 33]. If clear picture concerning the etiology and pathogenesis of CPPS is absent, treatment of patients with this pathology has an empirical nature. Repeated and often ineffective treatment courses undergone by such patients reduce their capability to work, which also leads to economic losses [12]. In addition, therapeutic measures are traditionally aimed at eliminating or reducing the intensity of pain, improving urination and psycho-emotional state, and do not involve the management of co-existent disorders. Treatment of chronic prostatitis depends on the severity of the disease, its duration, co-occurrence of sexual dysfunction. However, the effectiveness of treatment is low. It is very difficult to restore the function of the prostate. Young patients diagnosed with chronic prostatitis may develop erectile dysfunction, their reproductive function may be disturbed as well [12]. Recent researches have proved the effect of both systemic and local immune mechanisms on the development of

chronic prostatitis. A significant role in the development of inflammatory reactions in patients with CPPS is played by cytokines, which are produced as a result of impaired immune response. Patients of this category have elevated levels of proinflammatory cytokines such as IL-1, IL-1b, IL-6, IL-8, TNF- $\alpha$  in their spermatic plasma, which indicate the inflammatory process in the prostate and spermatic ducts [25].

At the present stage, the etiology of CAP is more often associated with viruses. For the first time, the assumption concerning the presence of herpes simplex and cytomegalovirus in male ejaculate was published in the late 1970s [42]. The uncontrolled widespread increase in the incidence of genital herpes (GH) equates the problem of herpesvirus infection (HVI) with the most urgent socially significant health problems. HVI, particularly herpes infection (HI) and cytomegalovirus infection (CMVI) are common, and their incidence tends to increase annually in many countries of the world [14, 15, 16]. About 90% of the adult population are infected and have antibodies to several types of herpesviruses [17, 18, 19]. The reactivation of latent herpes virus occurs on the background of stress and endocrine disorders, in patients with primary and secondary immunodeficiency, as well as in those undergoing immunosuppressive therapy (after organ transplantation). Polytypism of herpes viruses causes a variety of clinical manifestations that come into the view of different specialists, e.g. dermatovenereologists, gynecologists, urologists, neurologists, ophthalmologists and dentists [20, 21]. The incidence of GH in Western Europe exceeds 80 cases per 100, 000 people. According to Halioua B, et al. (1999), 86 million people all over the world are infected with herpes simplex virus (HSV) type 2, which is traditionally associated with GH, although, it has been proved that GH can be caused by HSV type 1 [43]. HI is one of the most common human viral infections: 90% of adults develop antibodies to HSV-I in their serum and 73% - to HSV-II, which more often causes GH [23, 43]. According to various authors, prostatitis is caused or maintained by HSV in 29-30% of cases. Chronic prostatitis with herpetic urethritis manifests itself mostly in the catarrhal form, while its clinical course is characterized by frequent and persistently recurrent nature [3]. The effect of herpesvirus on the male reproductive system has been proved [22, 23]. The presence of herpesvirus markers in organs and tissues of the male reproductive system, as well as the data indicating an increased incidence of HSV manifestations in men's ejaculate, indicate the possible role of HVI as the etiology of chronic infection of the male reproductive system [22, 23]. There are insufficient data indicating the influence of CMVI on the male genital system, the reproductive system in particular, and they are quite contradictory. The effect of human HSV-I and HSV-II and CMV on the course of pregnancy in women has been proven [24].

CMVI is one of the most common diseases in the world. It is a sexually transmitted infection that is transferred through saliva, maternal milk, during pregnancy, from mother to her child. HSV and CMV are widespread among people, they can

be transmitted through sexual intercourse and cause a wide range of diseases: GH, viral and bacterial epididymitis, male infertility or erectile dysfunction [26].

At present, the problem of CAP is extremely relevant. There are many research works concerning the etiology of this disease, the role of the immune system and the effectiveness of immunomodulators in treatment of CAP [27].

Thus, high prevalence of HI and CMVI, the possibility of the persistence of herpesviruses in the human body for lifetime, their activation in immunosuppression, difficulties of clinical and laboratory diagnostics, lack of effective therapeutic and prophylactic measures serve as a reason for further complex study of these male infections being of significant importance to science and practice. The improvement of therapeutic, diagnostic and rehabilitative measures in men with HI and CMVI has an important medical and social significance.

The etiology and pathogenesis are not the only problem of chronic prostatitis. Treatment approaches to this disease are problematic as well. According to some authors, at present, there are no substantial approaches to treatment of chronic prostatitis: therapy should be aimed at eliminating the infectious agent, normalizing the immune status, regressing inflammatory changes and restoring the function of the prostate [6, 29]. The main principles of treatment should include the following: the effect on all the chains of the etiology and pathogenesis of the disease; analysis and consideration of the activity, categories and extent of the process, application of a complex of therapeutic measures [34].

Widespread use of non-steroidal anti-inflammatory drugs by patients with chronic prostatitis is quite justified and pathogenetically substantiated, with the rectal route of administration being particularly successful [34, 35]. The effectiveness of enzyme preparations in chronic prostatitis is highlighted in national literature.

An innovative approach to treating chronic prostatitis is the use of  $\alpha$ -adrenoblockers. Various drug therapies, prostate massage, hirudotherapy, physiotherapeutic procedures and other treatment methods are used to restore blood circulation in small pelvis and microcirculation in the prostate gland in patients with chronic prostatitis. In recent years, many research works concerning the use of preparations obtained from the prostate of cattle being purified from hormones and proteins (e.g. raveron, prostaveron, prostatilen) in combination treatment of patients with chronic prostatitis have been published. According to some experts, it is reasonable to use antisense drugs in combination therapy for prostatitis to neutralize the effect of histamine being a mediator of vascular reactions at the inflammation site. Several authors used to prescribe diphenhydramine in the form of rectal suppositories for this purpose [29, 36].

The literature data of the last decade indicate the presence of immunodeficiency in patients with chronic prostatitis, and moreover, both inflammatory and local immunity is suppressed. The necessity of mandatory consideration of these factors in the administration of combination therapy is emphasized

[36, 37, 38]. Medicinal herbs are used in various combinations for their diverse effects on the body. Modern phytotherapists often prefer various herbal combinations [39]. Some authors offer homeopathic remedies for treatment of patients with chronic prostatitis. To increase the resistance of human body to infection, a number of authors recommend administration of vitamins when treating patients with prostatitis. Other authors report the effectiveness of zinc in treatment of patients with chronic prostatitis. Prostate massage has been used in treatment of chronic prostatitis since the 19th century; however, there is still no unified view of its effect as compared to other methods used to treat this widespread disease. In most cases of chronic prostatitis, it is important to pay attention to the normalization of the mental status of the patient administering both medication therapy and rational psychotherapy [40]. Ukrainian and Russian urologists use a large variety of physiotherapeutic procedures to treat patients with chronic prostatitis more often than their foreign colleagues; however, pathogenetic practicability of their application is not well substantiated, and their effectiveness requires further study [36, 41].

A lot of representatives of pharmacological groups are used for treatment of CPPS. Their diversity is explained by the lack of a clear understanding of the etiology and pathogenesis of the disorder, as well as its resistance to treatment and high frequency of recurrence of pain syndrome.

Thus, modern views toward the development, etiology, pathogenesis, as well as treatment of chronic prostatitis are very ambiguous. There is a number of disputable questions that require further thorough study using the latest techniques. The provability of viral etiology of chronic CAP remains actual at the current stage. However, the role of HSV and CMV as the etiology of CAP in men has not been clearly proven yet.

Thus, today chronic prostatitis should be considered as a disease with complex pathogenesis and polymorphic clinical picture. Its clinical manifestations and the possibility of their adequate correction will acquire an additional content as soon as the range of verification methods of this pathology and introduction of new therapeutic technologies expand.

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