



CLINICAL SIGNIFICANCE OF UREAPLASMA IN UROGENITAL PATHOLOGY

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Ureaplasmosis is a sexually transmitted disease of the genitourinary system . It is caused by a specific bacterium, ureaplasma , which lives on the mucous membranes of the genitourinary organs. Ureaplasmas are present in every organism and do not become active until favorable conditions arise. Ureaplasmas belong to the class Mollicutes . Asymptomatic infection is common . carriage of bacteria , in which most individuals do not develop any disease. Ureaplasma urealyticum and Ureaplasma Parvum bacteria are sexually transmitted and are implicated in a number of diseases, including non-gonococcal urethritis, chorioamnionitis , and bronchopulmonary diseases in newborns, including adverse pregnancy outcomes. U. urealyticum is associated with urethritis in men and is detected in high concentrations, confirming its etiologic role in the disease. Men with high U. urealyticum levels are treated, although data on effective therapy are currently insufficient. Women with symptoms of discharge are tested for bacterial vaginosis, and if positive, appropriate therapy is prescribed.

Key words: ureaplasma , non-gonococcal urethritis, bacterial vaginosis, serotype, treatment .

Ureaplasmas are opportunistic pathogens that are often found on the mucous membranes of the genitourinary organs, upper respiratory tract, and oropharynx , including in healthy individuals.

Ureaplasma infection is a group of inflammatory and dysbiotic diseases associated with ureaplasmas (Ureaplasma species). There are two types of ureaplasma - Ureaplasma urealyticum and Ureaplasma parvum . The genome of U. urealyticum is slightly larger than that of U. parvum —0.84–0.95 versus 0.75–0.78 Mb, respectively. Currently, a link has been established between U. urealyticum and acute urethritis in men. In women, both ureaplasma species are associated with bacterial vaginosis. There are 10 serotypes of U. urealyticum and 4 serotypes of U. parvum .

Currently, the data obtained cast doubt on the absolute role of ureaplasmas in urogenital pathology. Their widespread carriage in various populations of healthy men and women and the lack of association with inflammatory diseases necessitate a balanced approach to the need for their treatment.

Contemporary views on the role of Ureaplasma spp . Ureaplasmas are often part of the normal microflora of the urethra and vagina. The detection rate of ureaplasmas in the urogenital tract averages 40–60% in women and 10–30% in men. U. parvum is detected significantly more frequently than U. urealyticum [8].

The frequency of detection of ureaplasma in newborns can reach 30% or more, decreasing to several percent by the first year of life [9].

Subsequently, the incidence of ureaplasma colonization increases with the onset of sexual activity (at ages 14–18) and declines after age 40. The first infection of U. urealyticum in the male urethra typically causes non-gonococcal urethritis—an inflammation of the urethra. This is



typically a subacute or sluggish disease with a clinical picture of mucous or mucopurulent discharge.

Thus, further, more detailed studies are needed on the role of *U. parvum* in the development of non-gonococcal urethritis. Male infertility has been the subject of long-standing research into the role of opportunistic mycoplasmas. A meta-analysis by Chinese scientists has demonstrated the causal role of *U. urealyticum* and *Mycoplasma. hominis* [13].

However, the study did not take into account the presence of STIs and bacterial vaginosis in sexual partners, with which these microorganisms are closely associated, which prevented experts from the International Union Against Sexually Transmitted Infections from taking the meta-analysis' findings into account. In women, potential ureaplasma- associated diseases included urethritis, vaginitis, cervicitis, pelvic inflammatory disease, and infertility; however, to date, convincing evidence of a correlation is lacking [4].

However, ureaplasmas in women are associated with bacterial vaginosis. Ureaplasmas have been shown to play a role in the development of bronchopulmonary diseases in newborns (bronchitis, pneumonia) and postpartum chorioamnionitis [5].

Thus, the role of ureaplasmas in human pathology has not yet been fully established. Research continues into the pathogenic links between these microorganisms and a wide range of diseases, including:

- 1) with diseases of the genitourinary organs in men (infertility, prostatitis, vesiculitis, epididymoorchitis) [4];
- 2) urogenital pathology in women (inflammatory diseases of the pelvic organs, infertility, inflammation of the large vestibular glands);
- 3) pathology of newborns (there is evidence that the presence of ureaplasma leads to low birth weight and a decrease in the Apgar score);
- 4) pathology of women in labor (premature birth, premature rupture of the amniotic sac, habitual miscarriage, frozen pregnancy, etc.);
- 5) urolithiasis, cystitis (ureaplasmas were detected in stones removed from the kidneys, bladder biopsies , and experiments on infecting mice resulted in the development of urate stones in the kidneys).

Ureaplasmas are spread through sexual contact: the more sexual partners a person has over a lifetime, the more frequently the vagina or urethra is colonized by ureaplasmas . Ureaplasmas are transmitted to newborns during passage through the birth canal, colonizing the mucous membranes of the vulva and vagina in girls and the nasopharynx in both sexes. Symptoms of the disease: Symptoms vary depending on the specific disease.

Urethritis may present with scanty discharge, a burning sensation in the urethra, and frequent urination. Without treatment, urethritis tends to resolve spontaneously ; however, a previous illness increases the likelihood of future inflammation of the prostate gland (prostatitis). Urethritis can also be complicated by epididymo -orchitis (inflammation of the testicle and its



epididymis), vesiculitis (inflammation of the seminal vesicle), and, rarely , couperitis (inflammation of the bulbourethral gland). Bacterial vaginosis is typically accompanied by a foul-smelling discharge, which intensifies during intercourse. The disease predisposes to obstetric and gynecological complications, including premature birth, low birth weight, pelvic inflammatory disease, and infertility [7].

The authors of the article share the views of world experts in the field of urogenital pathology [6, 8, 12] on the lack of connection between ureaplasmas and the occurrence of cervicitis and vaginitis, however, Russian clinical guidelines for the management of such patients call for the treatment of cervicitis and vaginitis based on the etiological role of ureaplasmas , which, of course, is a mistake [2].

Pathogenesis. Ureaplasmas are opportunistic pathogens, meaning their pathogenic properties are only realized in high concentrations on the mucous membrane, during immunosuppression , etc. Ureaplasmas attach to the mucous membrane surface via cytoadhesin proteins. In addition to the urethral epithelium, ureaplasmas are capable of attaching to erythrocytes and sperm. One of the main pathogenic factors is the enzymes phospholipases A and C, which induce the production of prostaglandins E2 and F2a in the body. These factors trigger smooth muscle contractions and can lead to premature labor in pregnant women. The inflammatory response is accompanied by the production of proinflammatory cytokines—interleukins 6, 8, and 10. Ureaplasmas possess IgA protease activity, destroying immunoglobulin A, a local protective factor of the mucous membrane [1].

A high concentration of ureaplasmas causes an inflammatory process in the urethra: thus, it has been shown that the density of pathogenic bacteria $\geq 10^3$ CFU/ml is associated with an increased content of leukocytes in the urethral contents [2].

Specific pathogenesis factors are realized during the development of bacterial vaginosis. At the same time, local immunity factors of the mucous membrane are weakened, due to which such patients are more susceptible to STIs, including the human immunodeficiency virus. The acidity of the vaginal secretions (normal pH 3.5-4.5) decreases to a neutral environment ($\geq 6.5-7$), and the natural protective barrier against pathogenic microorganisms is thus weakened. Classification and stages of disease development . Depending on the duration of the disease, a distinction is made between acute (up to 2 months) and chronic (more than 2 months) urethritis, with the latter having recurrent and persistent forms. Chronic recurrent urethritis is a disease in which the level of leukocytes in the urethra normalizes by the end of treatment, and after 3 months begins to increase again (>5 in the field of view at $\times 1000$). In chronic persistent urethritis, an increased leukocyte count is observed towards the end of treatment and 3 months after therapeutic measures [3].

To assess bacterial vaginosis in clinical cases, the Amsel criteria are used :

- vaginal pH above 4.5;
- presence of creamy vaginal discharge;
- the appearance of “clue cells” (desquamative vaginal epithelial cells dotted with anaerobic bacteria);



- a positive amine test with 10% potassium hydroxide (a characteristic "fishy" odor occurs when the reagent is added to a drop of vaginal secretion). The most sensitive criteria are vaginal pH > 4.5 and homogeneous milky adhesive discharge (89%), however, the presence of discharge has low specificity (19%) and positive predictive value (22%). The criterion with the highest specificity can be considered the detection of "clue cells" (80%). The presence of at least three criteria significantly increases the likelihood of an accurate diagnosis of bacterial vaginosis, which gives a sensitivity and specificity of 97 and 90%, respectively [4].

In men, complications of urethritis include balanoposthitis (inflammation of the glans and foreskin of the penis), prostatitis, and, less commonly , epididymo-orchitis and cervical cystitis. However , ureaplasmas are not considered an independent agent causing inflammation of the prostate gland. This chain of complications likely arises from posterior urethritis and is mediated by urethroprostatic reflux, i.e., the reflux of posterior urethral contents into the prostatic acini and vas deferens [5].

Bacterial vaginosis in women greatly increases the risk of pelvic inflammatory disease, infertility, and obstetric and perinatal complications. Pelvic inflammatory disease, in turn, can be complicated by tubo-ovarian abscess, peritonitis, and sepsis. Long-term complications can lead to serious social consequences, including chronic pelvic pain, ectopic pregnancy, and infertility.

It is unlikely that the mere presence of ureaplasmas in the vaginal biocenosis will lead to such complications: they realize their pathogenic potential together with other microorganisms, leading to dysbiotic changes – bacterial vaginosis [6].

Diagnostics Indications for testing for ureaplasma include clinical and/or laboratory signs of an inflammatory process, such as urethritis or pelvic inflammatory disease. Routine testing should not be performed on all patients, including those without signs of any disease. Only direct detection methods, such as bacteriological and molecular genetic, are used to detect ureaplasma . Determination of IgG , IgA , and IgM antibodies is uninformative. Samples for testing may include urogenital secretions, urine, vaginal secretions, and other biological material. Bacteriological testing allows for the determination of the concentration of microorganisms but does not differentiate between *U. urealyticum* and *U. parvum* . If the result is positive, the conclusion is formulated as " Ureaplasma growth was detected ." *urealyticum* at a concentration of 10x CFU/ml," which may indicate the presence of both *U. urealyticum* and *U. parvum* . Molecular genetic testing identifies ureaplasmas with species-specific accuracy. A more modern quantitative test, real-time polymerase chain reaction (real-time PCR), determines the concentration of microorganisms in the "genome equivalent per milliliter" format, which is one logarithm higher than traditional CFU/ml [7].

There are commercial panels of research based on quantitative molecular genetic methods (FlorocenoZ , Inbioflor , Femoflor) that are used to diagnose bacterial vaginosis [28]. Treatment Treatment is indicated only in cases where the examination reveals a clear connection between ureaplasmas and the inflammatory process. In the case of healthy *Ureaplasma* carriage, treatment is not indicated. The practice of prescribing therapy to all individuals diagnosed with ureaplasmas is flawed. Treatment is indicated for sperm donors, as well as in cases of infertility when no other causes have been identified. Recent bacteriological studies have confirmed high



activity against ureaplasmas. doxycycline , josamycin and a number of other antimicrobial drugs [10].

Treatment of urethritis associated with ureaplasmas and bacterial vaginosis is carried out according to the recommendations of the Russian Society of Dermatovenerologists [29, 30]. It is important to note that the goal of treatment is to relieve the symptoms of urethritis, bacterial vaginosis, and pelvic inflammatory diseases, while complete eradication of microorganisms is not required. In most cases, there is no need to treat the sexual partner. Prognosis and prevention: Limiting the number of sexual partners and using barrier methods of contraception reduce ureaplasma colonization. In cases where Ureaplasma is already present , preventive examination and consultation with specialized specialists are necessary before planning a pregnancy, upcoming surgical interventions on the genitourinary organs, and sperm donation [11].

CONCLUSION Thus , the modern view of Ureaplasma bacteria spp . is that they are opportunistic pathogens that, when present in high concentrations and in association with other microflora, can exert their pathogenic potential. The main diseases associated with ureaplasmas are non-gonococcal urethritis in men and bacterial vaginosis in women. Proper verification of these conditions is the basis for antibiotic therapy according to clinical guidelines.

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