REVIEWS

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Characteristics of the *Chlamydia trachomatis* species – Immunopathology and Infections

Charakterystyka gatunku *Chlamydia trachomatis* – immunopatologia i zakażenia

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article; **G** – other

Abstract

Chlamydiae are microorganisms exhibiting characteristics intermediate between bacteria and viruses. Chlamydia is widespread in the natural world, intracellular parasites of people and animals. They are capable of independent reproduction, because they do not synthesize ATP, in its development cycle using the host cell metabolic pathways. The life cycle of these microorganisms is original, unique among bacteria and lasts from 24 to 48 hours. Chlamydia antigens consist of 4 groups: group-specific, species-specific, type-specific and subspecies-specific. The group of species-specific antigens consists of MOMP and heat shock proteins. *C. trachomatis* is a potent immunogen, stimulating the immune processes of microorganisms. In the course of *C. trachomatis* infection, the response mechanisms involved are: non-specific, specific, humoral and cellular. Chronic infection is characterized by maintenance of microorganisms in the host cell. Inflammation is formed in less time and with increased intensity and has a rapid immune response on the part of previously sensitized lymphocytes. *C. trachomatis* infections are the most common bacterial sexually-transmitted infections. It represents an important clinical problem for doctors in many areas of medicine such as dermatology, venereology, ophthalmology, gynecology and obstetrics, rheumatology and others. Chlamydial infections are important pathogens in medical practice, not only because they cause disease in various fields of medicine, but also because of the large proportion of the population suffering and exposed to these microbial infections. Chlamydial infections are characterized by multifocality and polymorphism changes. Chlamydia causes inflammation in the adult urethra and cervix with the possibility of serious complications, and can cause perinatal infections in infants (**Adv Clin Exp Med 2012, 21, 6, 799–808**).

Key words: *Chlamydia trachomatis*, immunopathology, infections.

Streszczenie

Chlamydie są drobnoustrojami wykazującymi cechy pośrednie między bakteriami a wirusami. Chlamydie to szeroko rozpowszechnione w świecie przyrody wewnątrzkomórkowe pasożyty ludzi i zwierząt. Są niezdolne do samodzielnego rozmnażania, ponieważ nie syntezują ATP. W swoim cyklu rozwojowym wykorzystują szlaki metaboliczne komórek gospodarza. Cykl rozwojowy tych drobnoustrojów jest oryginalny, niespotykany wśród bakterii i trwa 24–48 godz. Chlamydie mają 4 grupy antygenów: swoiste grupowo, gatunkowo, typowo oraz podgatunkowo. Do grupy antygenów swoistych gatunkowo należą: MOMP i białka szoku termicznego. *C. trachomatis* jest silnym immunogenem stymulującym procesy odpornościowe mikroorganizmów. W przebiegu zakażenia *C. trachomatis* biorą udział mechanizmy odpowiedzi nieswoistej, swoistej, humoralnej oraz komórkowej. Zakażenie przewlekłe charakteryzuje się utrzymaniem drobnoustroju w komórce żywiciela. Stan zapalny powstaje w krótszym czasie i ze zwiększonym nasileniem oraz szybką reakcją immunologiczną ze strony uczulonych wcześniej limfocytów. Zakażenia *C. trachomatis* są najbardziej rozpowszechnionymi infekcjami bakteryjnymi przenoszonymi drogą płciową. Stanowią istotny problem kliniczny dla lekarzy wielu dziedzin medycyny, takich jak: dermatologia, wenerologia, okulistyka, ginekologia i położnictwo, reumatologia i inne. Zakażenia chlamydialne są niezwykle ważnymi patogenami w praktyce lekarskiej, nie tylko dlatego, że wywołują choroby z zakresu różnych dziedzin medycyny, ale także z uwagi na duży odsetek populacji cierpiącej i narażonej na zakażenia tymi drobnoustrojami. Zakażenia

chlamydiami charakteryzuje wieloogniskowość i wielopostaciowość zmian. Chlamydie powodują u dorosłych stany zapalne cewki moczowej i szyjki macicy z możliwością groźnych powikłań, a u noworodków mogą być przyczyną zakażeń okołoporodowych (**Adv Clin Exp Med 2012, 21, 6, 799–808**).

Słowa kluczowe: *Chlamydia trachomatis*, immunopatologia, zakażenia.

On the basis of classification according to Bergey's manual, chlamydia belongs to the order Chlamydiales, represented by the family Chlamydiaceae and Chlamydia type. The type includes four species of bacteria pathogenic to humans: *C. trachomatis*, *C. pneumoniae*, *C. psitaci*, *C. pecorum*. They are characterized by a common antigen group and developmental cycle, but they have different phenotypes and pathogenicity. Differences and common features are shown in Table 1.

The new taxonomy of microorganisms of the family *Chlamydiaceae* in the research of Everetti et al. [1] is as follows: Order: Chlamydiales, Family: *Chlamydiaceae*, Type: Chlamydia, Species: *Chlamydia trachomatis*, *Chlamydia muridarum* sp nov., *Chlamydia suis* sp nov. Biotype: trachoma and LGV, type: Chlamydophila, Species: *Chlamydophila psittaci comb nov*., *Chlamydophila abortus* sp nov., *Chlamydophila felis* sp nov., Sp nov *Chlamydophila caviae*, *Chlamydophila pecorum* comb nov., *Chlamydophila pneumoniae comb nov*., biotype: TWAR, Koala, Equine [1].

In this taxonomy, the two lines and a new species of the family Chlamydiaceae were identified.

The term Chlamydia trachomatis derives from the Greek words chlamydos and trachoma. "Chlamys" – a coat, which are inclusions of intracellular bacteria flattening the host cell nucleus. "Trachoma" – an eye disease that leads to cicatricial changes, known since antiquity as a "rough eye" [3–5]. Currently, the *C. trachomatis* species consists of two biotypes: trachoma – a typical C/PK-2 strain, and LGV – venereal granuloma with a specific L2/434/BU strain. A mouse biotype previously belonging to this species has now been called *C. muridarum* and it causes pneumonia in mice [1]. Human pathogenic strains are divided into 18 serotypes (Fig. 1). The trachoma biotype includes A, B, Ba, and C serotypes. They are transmitted by indirect contact and cause trachoma. D, Da, E, F, G, H, I, Ia, J and K serotypes are responsible for so-called oculogenital infections (infections of the urogenital system in adults, conjunctivitis in adults and children, and pneumonia in children). L1, L2, L2A and L3 – the LGV biotype causes inguinal lymphogranuloma venereum, inflammation of the rectum, genital ulcers, and infections of the lymphatic tissue [1, 4–7]. Chlamydiae are microorganisms exhibiting common features of bacteria and viruses. Nevertheless, since 1966 they have been classified as bacteria [1, 4, 8–10].

The bacterial features are as follows: cell wall structure is similar to Gram (–), except that there is not a sufficient amount of peptidoglycan in the periplasmic space, the cell is lancet-shaped, the presence of two acids in the cell (DNA, RNA) and some organelles, different active metabolic enzymes (e.g. disintegrating glucose and producing CO2), reproduction by division and antibiotic sensitivity.

Viral features are as follows: cell size of 0.2–1.3 microns, the lack of some of their own mechanisms of metabolic energy production, only intracellular life cycle, using the ATP energy stored in the host cell (so-called energy parasitism), formation of cytoplasmic inclusions and they do not grow on synthetic bacterial media.

Other features of chlamydia: sensitivity to external environment (temperature, light, drying), at 45°C they are killed in 15 min and at 80°C in 1 min, sensitivity to commonly used disinfectants, such as 1% solution of chloramine [4].

Chlamydia Developmental Cycle

Chlamydia is widespread in the environment, an intracellular parasite of humans and animals. They are capable of independent reproduction, because they do not synthesize ATP. In its development cycle it uses the host cell metabolic pathways. The life cycle of these microorganisms is original and unique among bacteria. It lasts from 24 to 48 hours. Its uniqueness is associated with the occurrence of two morphologically different forms of microorganism: an elementary body (EB) and a reticulate body (RB). The differences between the EB and RB are described in Table 2. EB is an infectious form, metabolically inactive and can be transferred from person to person. It has a lancet shape, high electron density and a size of 0.4 microns. It also has a cell membrane that allows cells to survive for some time outside the host cell. RB is a non-infectious and metabolically active form. It has a reduced shell, is formed after cell infection, and is capable of intracellular multiplication (inclusion bodies are created). It has an oval shape, size of 0.8–1.3 microns and a low electron density. RB is surrounded by a thin cell membrane with high permeability, it does not contain haemagglutinin. The chlamydia cell wall does not contain pepti-

Table 1. Comparison of species of the family *Chlamydiaceae* according to [1, 2]

Tabela 1. Porównanie gatunków z rodziny *Chlamydiaceae* wg [1, 2]

Species (Gatunek)	*C. trachomatis*			*C. pneumoniae*	*C. psittaci*	*C. pecorum*
Biotype Biotyp Serotype Serotyp	Trachoma A, B, Ba, C, D, Da, E, F, G, H, I, Ia, J, K	LGV L1, L2, L2a L3	mouse lack	TWAR TW-183, AR-37, AR-277, AR-388, AR-427, AR-231, LR-65	1, 2, 3–9 probably 1 i 2	no data no data
Natural host (Gospodarz naturalny)	human			human	animals	animals
Infection route (Droga zakażenia)	contact			inhalation	inhalation	inhalation
Place of infection (Miejsce infekcji)	conjunctival and genitourinary epithelial cells			respiratory epithelium	respiratory epithelium	respiratory epithelium
Diseases (Choroby)	trachoma, venereal granuloma, infection of the urogenital system, inclusion conjunctivitis, reactive arthritis, conjunctivitis and pneumonia in children			pneumonia	zoonoses	zoonoses
Number of serotypes (Liczba serotyp)	18			1	numerous	3
LPS antigen (Antigen LPS)	(+)			(+)	(+)	(+)
EB shape (Kształt EB)	round			round	pear-shaped	pear-shaped
Antibiotic sensitivity (Wrażliwość na antybiotyki)	(+)			(–)	(–)	(–)

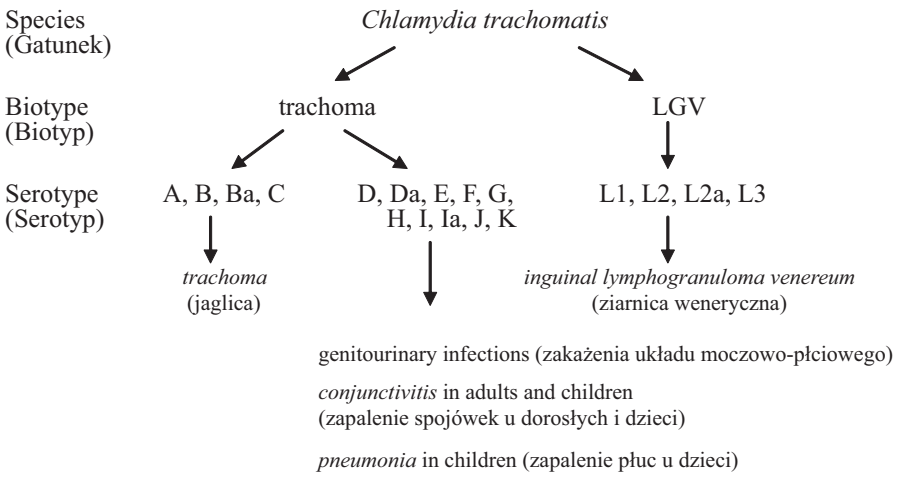

Fig. 1. Serological types of *C. trachomatis* and diseases caused by them [7]

Ryc. 1. Typy serologiczne *C. trachomatis* i choroby przez nie wywołane [7]

Table 2. The main differences between elementary and reticulate body [7]

Tabela 2. Główne różnice między ciałkiem elementarnym a siateczkowatym [7]

Property (Cechy)	EB	RB
Size (Rozmiar)	0.2–0.4 μm	0.8–1.3 μm
Morphology (Morfologia)	– lancet-shaped, – high electron density, – the presence of a thick, rigid cell wall with large amounts of cysteine protein, – the presence of cytoplasmic membrane	– oval-shaped, – low electron density, – the presence of a thin membrane with high permeability
Haemaglutinin in the cell wall (Hemaglutynina w ścianie komórkowej)	present	lack
Infectivity (Zakaźność)	high	lack
Place of development Miejsce rozwoju	extracellular (mainly) and intracellular	intracellular
Sensitivity to: – digestion by trypsin, – mechanical stress, – oxidative stress (Wrażliwość na: – trawienie trypsyną – stres mechaniczny – stres)	resistant	sensitive
Metabolic activity (Czynność metaboliczna)	lack	active
The ability to reproduce (Zdolność do rozmnażania)	lack	able

doglycan, which is characteristic for this group of microorganisms. It is thick, stiff, and similar to the wall of Gram-negative bacteria. It has two layers: internal and external which contain a high amount of proteins rich in cysteine. Disulfide bridges affect the resistance of EB to mechanical and oxidative stress, and provide wall rigidity. The presence of hemagglutinin facilitates its adhesion and penetration into host cells, which probably also affects the infectivity against the host cell [1, 4, 9, 10, 12, 13].

The Chlamydial developmental cycle lasts 48–72 hours and several stages can be distinguished: the binding of EB to the host cell, endocytosis of EB into the host cell and the creation of cytoplasmic inclusion, transition of RB into EB, the multiplication of RB transition of RB into EB, phagosomal rupture and release of EB. The stages of the developmental cycle of chlamydia are presented in Figure 2.

An infection occurs when EB cells bind with sensitive cells (usually the columnar epithelial cells of the conjunctiva and genital organs) and a reversible and then irreversible connections are produced. The next stage is the transition of EB into

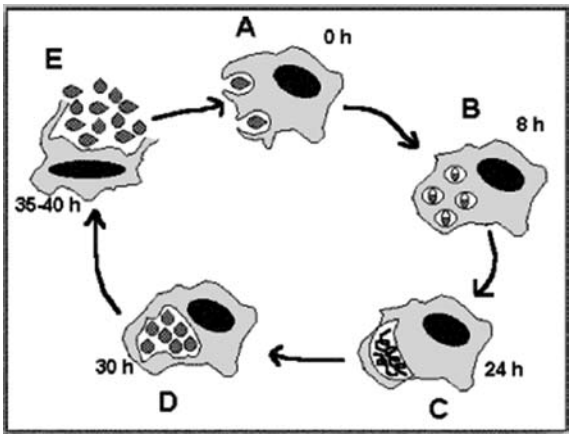

Fig. 2. The intracellular developmental cycle of *C. trachomatis*: A) EB cell penetration through endocytosis, B) phagosome formation and transformation of EB into RB, C) RB divisions, D) RB into EB transformation, E) lysis of infected cells

Ryc. 2. Wewnątrzkomórkowy cykl rozwojowy *C. trachomatis*. A) wnikanie ciałek EB na drodze endocytozy, B) powstawanie fagosomu i transformacja EB w RB, C) podziały RB, D) przeobrażenie RB w EB, E) liza komórki zakażone

the cell through endocytosis and producing a common phagosome together with other elementary bodies which are called cytoplasmic inclusions [6, 9, 12, 14]. EB differentiates into RB, while a reduction of the disulfide bridges occurs, leading to modification of the structure of outer membrane proteins, chromosome decondensation, an increase in the size and number of ribosomes as well as changes in the RNA to DNA proportion from 1 : 1 to 3 : 1 [7]. Within the phagosome, RB replication occurs (several divisions), which is associated with a significant enlargement of the cytoplasmic inclusion. It fills the cytoplasm, therefore the cell nucleus is pushed to the cell perimeter. After about 36 hours following infection, RB are surrounded by a plasma membrane and undergo transformation to EB. After 48 hours following cell infection, EB is released through lysis or cytoplasmic inclusion rupture without damaging the host cell. The 50–1000 mature bodies that exist outside the cell are the source of infection for other host cells. Chlamydiae have the ability to survive within the host cell without undergoing the developmental cycle.

The cycle may vary under the influence of various factors delaying the maturation of EB and EB transformation into invasive RB. These factors include: antibiotics – penicillin inhibits the RB transformation into EB, INF-γ, which inhibits the intracellular multiplication of Chlamydia and dietary factors – which reduce the level of exogenous tryptophan. These factors cause the loss of "pathogenicity" of the endospore form [12, 16].

Characteristics of *Chlamydia trachomatis* Antigens

Chlamydia have 4 groups of antigens: group-specific, species-specific, type-specific and subspecies-specific. The group-specific antigen (genus) is a multisaccharide-lipid complex which consists of two components:

LPS – the lipopolysaccharide component composed of several long-chain fatty acids, phosphate, D-galactosamine and deoxy-D-manno-2-octulosonic acid. LPS is present on the surface of EB and RB during the developmental cycle of Chlamydia.

GLXA – the glycolipid component composed of glucose, mannose, possibly galactose, and two fatty acids containing 17 and 18 carbon atoms. It is located on the surface of EB and RB within the cell membrane of cytoplasmic inclusions, the host cell membrane and surrounded by infected cells. In terms of chemical structure, the weight of the molecules and genus-specific antigen features are similar to the lipopolysaccharide antigen of Gram-negative bacteria.

MOMP and heat shock proteins belong to the species-specific antigens. MOMP is a protein whose molecular weight is approximately 40 kDa and it is 60% of the weight of outer membrane proteins. It is built of four variable hydrophilic domains exposed outside the cell membrane surrounded by five hydrophobic domains occurring on the inner surface. MOMP acts as a structural protein and is involved in the differentiation of the chlamydial development cycle. It is a protein with highly immunogenic properties, containing epitopes specific to the genus, species, subspecies and serotype. The c-HSP60 antigen, or heat shock protein, whose molecular weight is 60 kDa is moderately immunogenic in comparison to the poorly immunogenic smaller protein of 12 kDa molecular weight. They are invisibly present on the surface of the membrane, and antibodies specific to these proteins do not bind to live EB.

Type-specific antigens are probably polypeptides, whose molecular weight is 30 kDa, placed on the surface of EB and RB. They are used to differentiate serotypes using the MFI test. Polypeptides are subspecies-specific antigens. Based on the reactivity measured using the MIF test, C. trachomatis serovars were classified into three subspecies: B, Ba, D, Da, E, L1, L2 and L2A serotypes belong to the so-called group B, serotypes A, C, I, Ia, J and H belong to group C, and K and L3 serotypes that undergo cross-reaction, and the group C, F and G serotypes and B subspecies belong to the so-called intermediate group [7, 8, 11, 12, 17, 18].

Immunopathology and Infection Caused by *Chlamydia trachomatis*

C. trachomatis is a potent immunogen, stimulating the immune processes of microorganisms. In the course of *C. trachomatis* infection, non-specific, specific, humoral and cellular response mechanisms are involved.

In primary infection, non-specific immunity plays a special role, which includes local inflammation and the mechanisms associated with the anatomic barrier. In 24–48 hours after the infection, phagocyte infiltration of infection site occurs, mainly by polymorphonuclear leukocytes and monocytes. The presence of exudative fluid containing anti-microbial substances facilitates the destruction of microorganisms. Polymorphonuclear leukocytes form a so-called phagolysosome which is a result of binding with a lysosome. The bactericidal activity of neutrophils is dependent on oxygen. Hydrogen peroxide is produced from

which, in the presence of chlorine and other halogens, MPO enzyme chloric acid is formed, and then chloramine which is toxic to bacteria [1, 7].

In the initial phase, 20–24 hours after infection, the infected epithelial cells produce IL-1α, IL-6, IL-8 and IL-10 cytokines. The secreted cytokines which have chemotactic and activating neutrophils, monocytes and T cells properties also increase the adhesive properties of epithelial cells and stimulate secretion of other proinflammatory cytokines by macrophages and acute phase proteins.

In a further phase, macrophages and T leukocytes migrate to the infection site. B lymphocytes play a minor role here. The immune response from the host cells to primary chlamydial infection in most patients is temporary and is not associated with tissue damage. Mainly IgA show neutralizing action, which limit the spread of infection but do not eliminate the microorganisms from the body [7, 13].

Chronic infection is characterized by the maintenance of a microorganism in the host cell. The inflammation is induced in less time and with increased intensity and a rapid immune response by previously sensitized lymphocytes occurs. In the process of chronic infection, delayed-type hypersensitivity (DTH) and the Arthus reaction arise. DTH develops within 24–48 hours, and results from the interaction of antigen with specifically sensitized Th1 lymphocytes. In type III hypersensitivity (Arthus reaction), immune complexes lead to epithelial cell damage and the development of fibrosis and scarring within the infected organs.

In the pathogenesis of chlamydial infections, the following compounds are involved:

IFN-γ – completely inhibits the developmental cycle of chlamydia in high concentrations, in medium and low concentrations it causes the development of non-infected forms. The mechanism involves the secretion of an enzyme catalyzing the degradation of tryptophan, whose deficiency inhibits the growth of Chlamydia.

IL-1 – has immunostimulatory properties, inducing maturation of pre-B cells, it proliferates and differentiates B cells stimulated by antigens, it induces release of IL-2, IL-3, interferons, it stimulates the phase response and triggers fever. It also affects the chemotaxis of neutrophils, lymphocytes and monocytes. It is involved in scar formation and fibrosis.

IL-1α – intensifies the inflammatory response by stimulating those yet uninfected to secrete other cytokines.

IL-5 – influences the differentiation, activation and degradation of eosinophils. Together with antigen it induces growth and differentiation of B cells in combination with IL-2 and it is cytotoxic to T cells. It is secreted in a later phase of infection and may affect the protraction of the inflammation process and the formation of dangerous complications.

c-HSP60 – causes delayed-type hypersensitivity reaction which contributes to irreversible consequences in the course of infection with *C. trachomatis* [7, 13].

Infections and Complications Caused by *C. trachomatis*

C. trachomatis infections are the most common bacterial sexually transmitted diseases. They are a major clinical problem for physicians in many areas of medicine such as dermatology, venereology, ophthalmology, gynecology and obstetrics, rheumatology and others. Chlamydia infections are important pathogens in medical practice, not only because they induce diseases belonging to various fields of medicine, but also because of the large proportion of the population suffering from and exposed to infection by these pathogens [6, 10, 19–24]. The incidence of chlamydia diseases according to the WHO are 90 million people per year [6, 17].

Asymptomatic infections spread among sexual partners that lead to long-term complications. One infection does not give immunity and does not prevent further recurrences.

Risk factors for *C. trachomatis* infection include: low level of intimate hygiene, young woman's age (20–25 years old), having sexual intercourse with multiple partners, a partner with symptoms of non-gonococcal urethritis, blennorrheal infection, pregnancy, cervical ectopy, invasive diagnostic procedures within the reproductive tract, invasive diagnostic tests, intrauterine contraception, artificial insemination, previous or concomitant genitourinary infection of a different etiology, alcohol and drug abuse, low socio-economic status [7, 20, 25]. *C. trachomatis* infection may be the result of indirect contact, such as by objects or dirty hands. This applies mainly to A-C serotypes. Oculogenital infections with D-K and L1-L3 serotypes are mainly spread by sexual contact, and in newborns D-K serotypes are transmitted via perinatal route. The serotypes most commonly isolated from patients are E (50%), F (20%) and D (10%) of *C. trachomatis*. According to recent research, serotype F causes more severe infections, and E serotype causes asymptomatic infections [7, 20].

Chlamydial infections are characterized by multifocal and polymorphism changes. Serotypes A, B, Ba and C are the etiologic agents of tracho-

ma, i.e. chronic inflammation of the cornea and conjunctiva, the main cause of blindness. Infection occurs through direct contact with secretions of people infected with conjunctivitis or with contaminated clothing, towels. The disease is characterized by the occurrence of lesions within the epithelium of the eye and nasopharynx. There are cytoplasmic inclusions in the epithelial cells of the eye [2, 18, 26].

C. trachomatis is the most common cause of diseases transmitted by sexual contact [27–29]. L1, L2, L2A and L3 serotypes cause lymphogranuloma venereum, which occurs mainly in developing countries. In Poland, LGV is intermittent. The initial symptom is erosion or pimple in the groin, which in 1–4 weeks adopts a secondary form [30].

D, Da, E, F, G, H, I, Ia, J and K serotypes cause urogenital tract infections which are transmitted through genital sexual contact and through perinatal route in infants. C. trachomatis has a tissue tropism for columnar and transitional epithelium. Primary infection occurs in the cervical canal and the urethra [2]. The clinical picture of oculogenital infections with D–K serotypes depends on gender.

Infections of the urogenital system in men are non-gonococcal urethritis (NGU) and postgonococcal urethritis (PGU). If left untreated, they lead to serious complications such as epididymitis, prostatitis, reactive arthritis, and complete or incomplete Reiter's syndrome and infertility [8, 26, 29, 31, 32, 34].

NGU is a sexually transmitted disease. 50% of cases of NGU are caused by chlamydia [34, 35]. The incubation period is 2–3 weeks after infection. The clinical course is usually subacute and poorly symptomatic, the bacteria are rarely detected in patients without clinical signs of infection. The symptoms are: severe difficulties in urination (burning, itching, pain in the urethra during urination, urinary frequency and urgency), the presence of abnormal secretions in the mouth of the urethra, which appears in the morning (morning dew drops symptom), are watery, mucous, mucous-purulent or rarely purulent and pain in the lower abdomen and/or testicles [2, 18, 27].

Although the symptoms are varied and may go unnoticed by the patient, in rare cases hematuria and low-grade fever may occur [20, 29].

20–30% of men with gonococcal urethritis (GU) are also infected with *C. trachomatis*. In PGU, chlamydia is detected at a higher percentage than in NGU. The WHO has introduced new GU treatment regimens, as co-infection with C. trachomatis and N. gonorrhoeae is common [7, 18].

Urethral structure in men with NGU is a consequence of a long course of chronic and recurrent or late and inadequate treatment of NGU. The main symptoms include slowing or stopping the urine flow, which may cause difficulty in starting micturition. Additional symptoms are: urinary frequency, nocturia, urinary urgency and painful urination. Exacerbated local inflammation can lead to complete closure of the lumen of the urethra [29].

A complication of chlamydial infection of the urethra in men may be epididymitis, which can be accompanied by the following symptoms: severe pain in the epididymis which prevents walking, pain in the abdomen, fever, chills and general malaise. Within the scrotum the following symptoms may be observed: swelling, soreness, redness and warmth. Inflammation of the epididymis may be accompanied by inflammation of the testicles and obstruction of the seminiferous tubules, leading to infertility [20, 27, 29].

C. trachomatis is also involved in the pathogenesis of inflammation of the prostate (prostatitis), which is a urological disorder found in 50% of men under 50 years of age. Prostatitis caused by *C. trachomatis* is characterized by a triad of symptoms: acute, dull pain located within the perineum, lower abdomen and near the sacrolumbar spine radiating to the genital area, discomfort in the urinary tract (frequency, tenesmus, pain when urinating, decreased urination) and genital dysfunction (erectile dysfunction, pain during ejaculation or premature ejaculation). The disorders may be accompanied by hematospermia and hematuria [7, 18]. Chlamydia's effect on fertility in men raises a lot of controversy. It was found that epididymitis may lead to partial or complete obstruction of the tubules, and thus to reduce the amount of semen. Reduced sperm count and poor sperm construction may be observed. Chlamydia-infected seminal vesicles and prostate secrete more mucus, which weakens the movement of spermatozoa; leukospermia may also negatively affect fertility in men [27].

A potential source of infection for *C. trachomatis* in women is an infected sexual partner. Microorganisms can attach to sperm, which facilitates the spread of infection by ascending route in the female genital tract. However, the woman also may be a reservoir of the microorganism and a threat not only to her sexual partner, but also to her offspring [7]. In women, *C. trachomatis* has an affinity for columnar epithelium cells, resulting in a higher incidence of infection by this pathogen. Genitourinary tract infections in women are usually manifested by inflammation of the cervix, which spreads by ascending route into the uterus and fallopian tubes. The following factors are conducive to infection: permeable cervical canal, menstrual bleeding and other bleeding from the endo-

Fig. 3. The disintegration of the epithelial cells of the host and the release of elementary bodies

Ryc. 3. Rozpad komórki nabłonkowej gospodarza z uwolnieniem ciałek elementarnych

metrium, intrauterine procedures and remains after a miscarriage. The characteristic symptoms of inflammation of the cervix include: congestion and swelling of the mucous membrane and purulent-mucous discharge with polymorphonuclear leukocytes [20, 27, 29].

In the course of *C. trachomatis* infection the following symptoms can occur: a set of symptoms from the urethra (urinary syndrome), inflammation of the vagina (vaginitis), inflammation of the Bartholin's gland (bartholinitis), pelvic inflammatory disease (PID) and inflammation of the hepatic tissues and appendages (Fitz-Hugh-Curtis syndrome) [2, 29, 34, 35].

Chlamydial urethritis in women may be in the form of so-called urethral syndrome, which is characterized by: dysuria, frequency, leukocyturia, pain in the lumbar region and perineum, and negative results of routine bacteriological examination of urine. Redness and swelling of the external urethral orifice and the presence of mucous-purulent or mucous discharge are found under physical examination. 30% of patients who are sexual partners of men with NGU had urethritis [20, 29].

Vaginosis is often asymptomatic, it is characterized only by abnormal bacterial flora, although 4% of infected women have symptoms. This applies to patients after hysterectomy undergoing hormonal treatment and girls before puberty. One of the first and most common symptoms of inflammation is vaginal discharge [7].

A complication of chlamydial cervicitis is inflammation of the greater vestibular gland (Bartholin). In the course of infection, an abscess is formed and the duct is closed. Inflammation is associated with swelling and soreness around the labia [20, 30].

Pelvic inflammatory disease (PID) in women occurs in the course of inflammation of the cervix. Infection of the mucosa of the endometrium manifests with low-grade fever, atypical pelvic pain, uterine bleeding and heavy and painful periods. Histologically, it is considered the presence of inflammatory infiltrates composed of plasma cells and polymorphonuclear leukocytes. Physical examination shows tenderness of the uterus. Endometritis is associated with inflammation of the fallopian tubes caused by *C. trachomatis*, which is characterized by: a dull lower abdominal pain, low-grade fever, intermittent vaginal discharge, abnormal menstrual periods or bleeding after intercourse.

In the course of PID, inflammation of the ovaries, which is accompanied by secondary amenorrhea, may develop. *C. trachomatis* is the most common mechanical cause of infertility in women with a history of PID. During chronic infection, the fallopian tubes can be damaged and ectopic pregnancy may occur [20, 26, 29]. Rare complications in women include: inflammation of the liver tissue, Skene gland's inflammation, inflammation of the anus and throat, a syndrome of interstitial inflammation of renal tubules and uvea [7, 20].

In pregnant women, infection with *C. trachomatis* infects the urogenital system, which contributes to the pathological course of pregnancy and may pose a risk to the fetus, newborn and mother. Infection is facilitated by long-term congestion and looseness of cervical epithelium resulting from the estrogen activity. Microorganisms from the cervix of a pregnant woman infect amniotic epithelial cells, causing inflammation of the membranes and therefore may induce miscarriages. Complications of pregnancy also include: premature births, blighted pregnancy, premature rupture of membranes, low birth weight and perinatal infant infection [7, 26, 27].

Neonatal infection occurs during childbirth when the child contacts the birth canal of the cervix of infected women. The risk of perinatal infection is 30%. Cases have also been found of chlamydial infection in children born by caesarean section. *C. trachomatis* infection in children causes: conjunctivitis, pharyngitis, pneumonia, vaginitis, endocarditis and myocarditis, otitis media and gastroenteritis [20, 23, 27, 34].

The most common form of infection in newborns is conjunctivitis, which is 18–50% of cases. It occurs approximately 2 weeks after birth and is characterized by the following symptoms: mucous

secretion which changes into purulent secretion, swollen eyelids, redness of the conjunctiva, and then the whole eye. Inclusion conjunctivitis may be accompanied by rhinitis and/or otitis media. The untreated clinical form can lead to scarring within the conjunctival and corneal vacuolization [29].

Interstitial pneumonia caused by *C. trachomatis* is the second most common perinatal infection in neonates. This shows up between 2 and 16 weeks of age. It is characterized by good general condition and usually feverless course, dry cough, gradually growing shortness of breath and the associated conjunctivitis. The radiographic findings observed are interstitial or patchy inflammatory infiltration and hyperinflation [7, 29].

In the course of chlamydial infection of the genitourinary tract, conjunctivitis, joint pain and discharge and anorectal discomfort may occur in sexual partners [2, 21, 26, 30].

Infection of the urogenital system can be transferred to the conjunctiva of the eye (autoinfection) and cause inflammation. In adults, it is usually conjuctivitis, has subacute onset and one eye is involved. The infection lasts from several days to several weeks. Predominant symptoms include: watery eyes, congestion, conjunctivitis, photophobia, very severe swelling of the eyelid and the presence of mucous-purulent secretions [18, 19, 26, 27, 29].

Urogenital *C. trachomatis* infection may be a cause of reactive arthritis (SARA), acquired by sexual contact. SARA is manifested by inflammation of synovial membranes, tendons and fascia, mainly in the knee and ankle joints, usually unilaterally. If articular symptoms are accompanied by symptoms from the urogenital system and conjunctivitis is found then Reiter's syndrome is diagnosed [20, 30, 31, 35].

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