REVIEWS

Adv Clin Exp Med 2014, **23**, 1, 123–126
ISSN 1899–5276

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Infections Caused by *Chlamydophila pneumoniae*

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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

High affinity to the epithelial lining of the airways makes *Chlamydophila pneumoniae* a common etiological agent of respiratory tract infections (RTI). It causes among others: pharyngitis, tracheitis, sinusitis, otitis media, bronchitis and bronchiolitis, and pneumonia. It is estimated that *Chlamydophila pneumoniae* infection is responsible for about 20% of lower respiratory tract infections. *Chlamydophila pneumoniae* infection may play an important role in the pathogenesis and course of bronchial asthma. The recent results indicate that *Chlamydophila pneumoniae* infection may be a factor responsible for 4–16% of COPD (Chronic obstructive pulmonary disease) exacerbations. A relationship of chlamydial infection with atherosclerosis raises huge interest. A connection of *Chlamydophila pneumoniae* infection with other non-communicable diseases such as lung cancer, arthritis, Alzheimer's disease, multiple sclerosis, sarcoidosis and erythema nodosum is also recognized, although the role of these bacteria has not been fully understood in any of the listed diseases (**Adv Clin Exp Med 2014, 23, 1, 123–126**).

Key words: *Chlamydophila pneumoniae*, RTI, asthma, COPD.

Chlamydophila pneumoniae causes infections that are common throughout the world. Approximately in 40–70% of the population the presence of specific antibodies against these pathogens is found. It is characteristic that as a result of contact, a person does not acquire a permanent immunity to this microorganism [1].

The occurrence of infections caused by this pathogen is noted throughout the world and it demonstrates a lack of seasonality. Some researchers have suggested a higher infection rate in southern countries than in temperate climates and northern hemisphere countries [2].

The infection is spread by inhaling aerosols containing microorganisms. They are particularly easily spread in large groups of people [3–5].

High affinity to the epithelial lining of the airways causes *Chlamydophila pneumoniae* is a common etiological agent of respiratory tract infections. It causes among others: pharyngitis, tracheitis, sinusitis, otitis media, bronchitis and bronchiolitis, and pneumonia [6]. It is estimated that *Chlamydophila pneumoniae* infection causes about 20% of lower respiratory tract infections [1].

It is estimated that about 70% of respiratory tract infections caused by *Chlamydophila pneumoniae* are asymptomatic or with minimal symptoms, which do not lead patients to seek medical help. About 20% are symptomatic upper respiratory tract infections, and the remaining 10% are pneumonia cases [7].

Infection may take the following form:

1) acute infection – has a mild course, especially in young patients, in older patients, or burdened with chronic diseases or damaged immune systems it becomes a more severe form of infection that requires hospitalization;

2) recurrent infection (reinfection) – the course of subsequent infection is different and depends on the patient's immune system;

3) chronic infection (latent or intermittent) – the risk of such infection is associated with the development and exacerbation of chronic diseases such as bronchial asthma or COPD;

4) carrier-state – microorganisms are detected in the biological material from a patient, but there is a so-called serological window period in the serum.

Carriers who represent 2–5% of the population may be the source of the infection but they do not exhibit the symptoms of an acute infection. The infection can take a symptomatic form in immunocompromised conditions. Carrier-state does not require treatment, although it is important to distinguish the carrier-state from asymptomatic infection, in which there is a serological reaction resembling acute infection [5, 8].

Infections affect all age groups, although they are rarely found in children under 5 years of age [9, 10]. It is estimated that 50% of people under 20 years of age have serologic characteristics of prior infection. With age, the percentage of seropositive people increases, and in the elderly it even reaches 70–80%. This data suggests that during a lifetime almost everyone is infected at least once [9, 10].

Most infections caused by *Chlamydophila pneumoniae* are usually mild, with a characteristic subacute onset, difficult to diagnose in the first phase, because they resemble a viral infection. They rarely can have a severe course and lead to respiratory failure, ending in death. They involve a risk of upper respiratory tract infections in patients with concomitant pneumonia, myocarditis, meningitis, encephalitis and other systemic diseases [21]. Lower respiratory tract infections are very often, in 50–65% of cases they are accompanied by other bacterial or viral infections. Among all these community-acquired pneumonia there are 2.2–8.1% those caused by *Chl. pneumoniae* [2, 11].

Chlamydophila pneumoniae, to a large extent, is responsible for chronic pharyngitis, acute, chronic and recurrent middle ear infections (with effusion), sinusitis, and infections whose course is similar to sinobronchial syndrome [3].

Pneumonia is usually a two-phase process. In the beginning, there are flu-like symptoms (pharyngitis, laryngitis, sinusitis) and mild pneumonia follows. In the first phase the following symptoms are noted: hoarseness, sore throat, elevated temperature. After 1–4 weeks, pneumonia develops whose predominant symptom is cough that persists for several weeks. Body temperature is usually slightly elevated or normal [5, 9]. The characteristic features indicative of atypical pneumonia is a lack of purulent sputum, mild auscultatory changes in contrast to the significant changes on X-ray [5].

A typical form of infection is upper respiratory tract infection. It is estimated that 10% of infections caused by *Chlamydophila pneumoniae* proceed as pneumonia and 5% as bronchitis [2, 5, 9].

Most cases of pneumonia are so mild that they do not require hospitalization. Sometimes, even when mild, although antibiotic therapy is properly maintained, complete remission of the disease is slow, a cough and general weakness may persist for several weeks [9].

In laboratory studies there are no apparent abnormalities; inflammatory parameters may be slightly increased, leukocytosis is usually normal, a picture similar to a viral infection is often seen in the smear [12]. Radiological examination shows the presence of irregular or spotted segmented inflammatory infiltrates or interstitial densities. The predominant location is the middle or lower pulmonary lobes [2, 10].

Studies are carried out to determine the role of infection in other respiratory diseases such as bronchial asthma or chronic obstructive pulmonary disease (COPD).

Chlamydophila pneumoniae infection may play an important role in the pathogenesis and course of asthma. It can either be a causative factor resulting in the emerging of symptoms of asthma in previously healthy individuals or present infection may exacerbate the disease in people already diagnosed with asthma. The presence of this pathogen was showed in 12% of patients treated due to their first ever attack of bronchospastic shortness of breath or newly diagnosed asthma exacerbation [2, 13].

Chlamydophila pneumoniae has the ability to induce a chronic inflammatory response, paralyse the ciliary apparatus and damage epithelial cells, which leads to the unveiling of the subepithelial nerve endings, which may contribute to bronchial hyperresponsiveness to irritants and allergens, and thus, according to some authors, can exacerbate asthma and COPD [10, 14].

The chlamydial heat shock protein cHSP60 may play a role in this process. It, being a highly immunogenic material, induces a chronic inflammatory response, which may be important in the pathogenesis of diseases such as COPD and asthma [24]. Their role in both the initiation of asthma, and the pathogenesis of exacerbation has been confirmed. They cause, among others, an increased production of matrix metalloproteinases associated with the development of bronchial remodelling [15].

Around the world, *Chlamydophila pneumoniae* antibodies are detected in 50–80% of patients with asthma [14, 16].

In some patients, *Chlamydophila pneumoniae* is capable of stimulating the process of producing IgE antibodies. Their presence was detected in 85% of asthma patients and those with culture positive results [2]. The observations suggest that an infectious agent can induce an immune response whose course is similar to that of atopic reactions. It is possible that the presence of IgE antibodies against *Chlamydophila pneumoniae* can exacerbate asthma by the release of inflammatory mediators that

cause spasm and airway hyperresponsiveness as well as a chronic form of infection that leads to vascular remodelling [17].

Respiratory tract infections are recognized risk factors for COPD. They can also exacerbate symptoms. Chronic infection was found in 71% of those with severe, and in 46% of patients with moderate or mild COPD [16, 18].

The most important risk factor for COPD is considered tobacco smoking, and long-term smokers represent 90% of patients. Microbial agents are thought to participate in the exacerbation of the disease by synergistic effect of tobacco smoke resulting from chronic respiratory tract inflammation [16].

Association of *Chlamydophila* infection with the development of atherosclerotic lesions raises considerable interest. Clinical studies have confirmed a higher incidence of antibodies to *Chlamydophila pneumoniae* in patients with ischemic heart disease, prior myocardial infarction and atherosclerosis. The presence of bacteria was also found in atherosclerotic plaques [1, 2].

High levels of antibodies against this pathogen have been demonstrated in atherosclerotic plaque in nearly 80% of patients with coronary artery disease and in 50% of the "plaques" from aortic aneurysm in humans [19].

Pathomechanism of atherosclerotic lesions involving *Chlamydophila pneumoniae* is associated with the presence of living microorganism cells in macrophages which are transferred into the blood vessels and atherosclerotic lesions. At the same time they stimulate macrophages to produce proinflammatory cytokines such as TNF, IL-6, IL-1 and transform them into foam cells, which are produced in the early stages of the formation of atherosclerotic lesions. During the infection, the production of chlamydial heat shock protein cHSP60 is also increased, which shows among other things the ability to activate endothelial cells, smooth muscle cells and macrophages to produce cytokines and enzymes and it induces the expression of endothelial receptors for leukocytes. Lipopolysaccharide of these bacteria can affect the vascular permeability and coagulation. The components of bacterial cells may form immune complexes with antibodies, which initiates the process of destroying tissue. In the process of plaque formation, damage of the inner wall of the artery and an increase in the permeability of endothelial cells is important, which leads to the deposition of fibrinogen, plasma proteins and low-density lipoprotein [20–22].

Many researchers have noted the relationship of *Chlamydophila pneumoniae* infection with other non-communicable diseases such as lung cancer [23], arthritis, Alzheimer's disease, multiple sclerosis, sarcoidosis, erythema nodosum, although in any of these diseases, the role of these bacteria has not yet been fully understood [2, 4].

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Conflict of interest: None declared

Received: 11.06.2012
Revised: 10.10.2012
Accepted: 20.02.2014