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Review Article

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Recent Advancements in the Study of Chlamydia Pneumoniae Developing Pneumonia and Lung Cancer in Humans

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Abstract

Chlamydia pneumoniae is an intracellular, obligate pathogen causing diseases in humans, including pneumonia, chronic obstructive pulmonary disease (COPD), asthma, lung cancer, and other sclerotic cardiovascular diseases. Although various links have already been established documenting the role of C. pneumoniae in causing pneumonia and lung cancer, their role as a single causal factor in lung cancer is still paradoxical. Therefore, it requires further research to better understand the association of C. pneumoniae in developing lung cancer in humans. The present review is an attempt to establish the same link in the light of recent researches done so far in the field of medical microbiology and pathology in humans.

Keywords: Chlamydia Pneumoniae, TWAR, Atypical/walking pneumonia, Lung Cancer

Introduction

There are various types of lung pneumonia found in nature. The microbial origin of pneumonia is one of them. This is caused by various types of bacteria, viruses and fungi. The atypical pneumonia in humans is caused by Chlamydia pneumoniae, Mycoplasma pneumoniae and Legionella pneumophila. However, the atypical pneumonia's lung infections are mild, often associated with some extrapulmonary symptoms. While Mycoplasma pneumoniae infection is common in people under the age of 40 and in school-aged children, Chlamydia pneumoniae infection spreads throughout the year via respiratory droplets. Legionella pneumophila causes Legionnaires' disease or legionellosis in humans, often linked to water, causing severe pneumonia. The present paper deals with the study of Chlamydia pneumoniae in developing lung pneumonia and cancer in humans. [1].

There are three main Chlamydial species causing diseases in humans. They are C. pneumoniae, C. trachomatis and C. psittaci. They cause pneumonia and other associated diseases, including urogenital problems. C. pneumoniae has a tendency to persist in tissues, causing usually 10% of community-acquired pneumonia (CAP) and 5% of bronchitis, pharyngitis and sinusitis [1-3].

Chlamydia pneumoniae, formerly termed as Taiwan acute respiratory agent (TWAR) was identified as a respiratory pathogen in 1983. [2]. Chlamydia pneumoniae causes walking pneumonia / atypical pneumonia in humans, with mild lung infections associated with some extrapulmonary symptoms. Humans are the only known reservoir of Chlamydia pneumoniae, having a prolonged incubation period. Moreover, a majority of cases are resolved spontaneously. C. pneumoniae causes community-acquired pneumonia (CAP), associated with chronic obstructive pulmonary disease (COPD), asthma, bronchitis and lung cancer, if not treated well within time [4].

Further, there are also studies supporting the role of C. pneumoniae causing lung cancer in humans [5-8]. The present paper deals with the study of Chlamydia pneumoniae in developing lung pneumonia and cancer in humans.

Epidemiology and Spread of the Disease

Most of the people are exposed to the bacterium at least once in their lifetime. It has also been observed that nearly half of the entire world population has bacterial antibodies by the age

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of 20 years. Since the primary infection of C. pneumoniae is very common and mild in children and young adults without seeking any treatments, many cases are likely to go undetected. The same infection did not follow the seasonal variations and occurs year-round. Outbreaks are usually common in densely populated regions where people are living in close contact. The bacteria are transmitted via respiratory droplets [9,10].

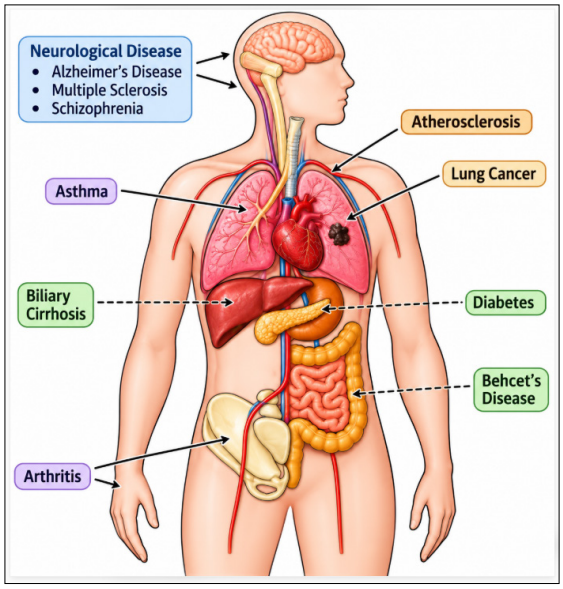


Figure 1: Some of the inflammatory diseases caused by the infection of Chlamydia pneumoniae [4].

A recent resurgence of Chlamydia pneumoniae respiratory infections was observed in France during 2024–2025 [11].

Symptoms of the Disease

The infection begins with the upper respiratory tract, although finally the infection spreads to the lower respiratory tract. The onset of the disease is gradual, persisting for weeks to months. The common symptoms of the disease are headache, rhinitis, cough, fever, sore throat, hoarseness and malaise. If the illness continues, it may progress to laryngitis, pharyngitis and pneumonia. Other possible symptoms may include tachypnea and pharyngeal congestion without exudate. Some of the extrapulmonary symptoms of C. pneumoniae are encephalitis, myocarditis, arthritis, thyroiditis, erythema nodosum, reactive arthritis, and Guillain–Barré syndrome [9,10]. Lastly, reactive infectious mucosal eruptions (RIME) are a rare and poorly understood clinical manifestation of C. pneumoniae infection [3].

Severity of the Disease

Chlamydia pneumoniae is a common bacterium causing respiratory infections like bronchitis and community-acquired pneumonia (CAP). It is linked to an increased risk of lung cancer. CAP causes approximately 7–10% of adults, accompanied by sore throat and laryngitis. The bacteria living inside human cells when transformed into an active form establish the disease. Similarly, long-term persistent and repeated infection of C. pneumoniae develops lung inflammation and cancer in humans [8,12-14].

Diagnosis and Differential Diagnosis of the Disease

Imaging studies including chest X-rays may confirm the cases of pleural effusion. Further, the bacteria is diagnosed with the help of culture, serology and molecular methods. The culture of C. pneumoniae is somehow possible but very difficult. Other possible diagnostic techniques are immunoassay (EIA), direct fluorescent antibody and polymerase chain reaction (PCR). PCR can be applied for sputum, nasopharyngeal swabs or bronchoalveolar lavage (BAL) fluid [7].

The differential diagnosis of the disease may include atypical pneumonia caused by Mycoplasma pneumoniae, Legionella, Chlamydia psittaci, Francisella tularensis and Coxiella burnetii. Other possible conditions may also include viral or fungal pneumonia, tuberculosis and influenza [10].

Prognosis and Complications of the Disease

The prognosis of the disease is good. While the majority of individuals are asymptomatic or experience mild infections, patients are usually recovered within 7 to 10 days of initial treatment.

Only a few of them can develop complications requiring hospitalization. Some of these complications , sometimes might prove to be fatal, if not taken seriously and handled properly.

Some of them are asthma, COPD, arthritis, multiple sclerosis, atherosclerosis, myocarditis, encephalitis, muscular degeneration, chronic fatigue syndrome (CFS), chronic skin wounds, Alzheimer's disease, schizophrenia and lung cancer [8-10].

Replication and Perpetuation of the Species

The perpetuation and persistence of C. pneumoniae depend on its ability to enter and survive reversibly, establishing long-term chronic infections in human cells. The replication and persistence of C. pneumoniae happen with the help of elementary and reticulate bodies [15,16].

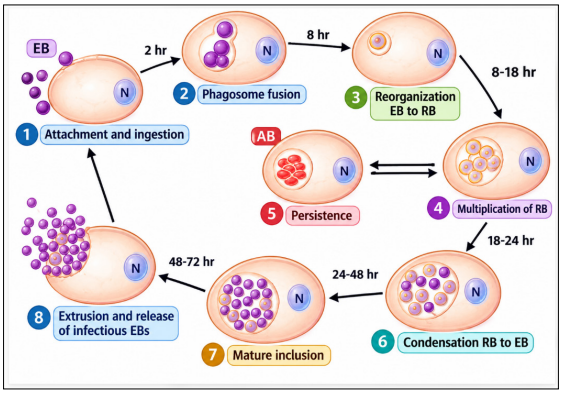


Figure 2: Life cycle of Chlamydia in epithelial cells [15]. (EB, Elementary body; AB, Aberrant body; RB, Reticulate body; N, Nucleus)

As an obligate intracellular bacteria, Chlamydia pneumoniae possesses a unique biphasic reproductive cycle, relying on the host nutrient facilities and dissemination. Although as usual, the host has already acquired multiple immune mechanisms, Chlamydia has also developed multiple strategies to counteract them by inducing host-cell death in due course. Therefore, this bacterium is very difficult to kill except by using antibiotics to alleviate the symptoms. Currently, there is no vaccine available for the same infection [17].

The Development of Lung Cancer by Chlamydia pneumoniae

Lung cancer is still a kind of disease-causing high morbidity and mortality in humans. About 4 out of 10 lung cancer patients hardly survive five years after diagnosis. According to an estimate, in 2018, 11.6% new cases and 18.4% lung cancer deaths have been reported [18]. There are mainly two types of lung cancer, namely non-small cell carcinoma (NSCC, 80%) and small cell lung carcinoma (SCLC, 20%). NSCC is further subdivided into adenocarcinoma (40 to 60%), squamous cell carcinoma and large cell carcinoma [19].

First postulated that C. pneumoniae was associated with lung cancer [20]. Since then, several studies have been put forward to explain the mechanism of lung cancer development by C. pneumoniae in humans [7,8].

The mechanism of development of lung cancer is yet to be fully solved. However, it has been hypothesized that the long-term persistence of Chlamydia pneumoniae in lung tissues causes active irritation and inflammation, leading to the development of lung cancer in future [8].

Several mechanisms have been put forward to explain the development of lung cancer by the infection of C. pneumoniae. One of them is via the mediators of inflammation. These mediators cause lung tissue and DNA damage, with an outcome of lung carcinogenesis. Superoxide oxygen free radicals, tumour necrosis factor, IL-1h and IL-8 are released by the activated monocytes.

Inflammation also gives rise to ROS damaging the DNA. Sometimes, smoking has also played a good role in lung cancer pathogenesis [4,7,8,13].

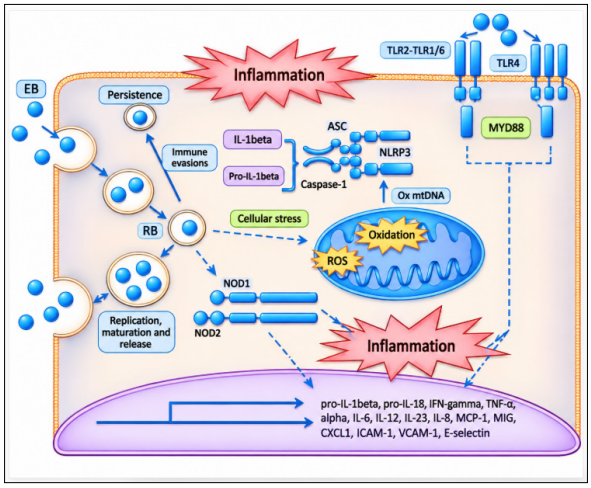


Figure 3: Inflammatory innate immune responses caused by the Chlamydia pneumoniae infection [4].

Though the incidence of lung cancer has been reported within the range of 2.3% to 10.3% following an episode of C. pneumoniae, a connection between C. pneumoniae and lung cancer is yet to be fully established. There is limited evidence about Chlamydia being a causal cofactor of LC [21].

Treatment of C. pneumoniae Infection

The C. pneumoniae infection is often mild; many patients do not require any treatment. Sometimes, when treatment is required, antibiotics are given for a longer period of time because the infection has a tendency to reverse. The recommended antibiotics according to CDC are macrolides, tetracyclines or fluoroquinolones. However, beta lactum penicillin, ampicillin and sulfa drugs are not prescribed as they are in vitro resistant [9]. Azithromycin is one of the macrolide antibiotics used to treat as a first-line drug therapy for the treatment of C. pneumoniae infection. Macrolide antibiotics usually inhibit the growth of bacteria by blocking bacterial protein biosynthesis [22,23].Tetracyclines and doxycycline are also sometimes prescribed for the treatment of C. pneumoniae infection. However, they are not usually prescribed during the course of pregnancy or to patients under the age of 8 years due to the potential and permanent discoloration of the teeth and enamel hypoplasia [24]. Similarly, fluoroquinolone antibiotics are also prescribed with some restrictions due to the risk of developing tendon rupture and tendinitis in patients. Fluoroquinolone antibiotics like levofloxacin and moxifloxacin are contraindicated for patients with myasthenia gravis. Both these antibiotics also have the potential for interacting with antacids, warfarin, antidiabetic agents and antiarrhythmics [25,26].

Lastly, as C. pneumoniae is an atypical bacterium having no cell wall, antibiotics working on cell wall degradation do not work and become in vitro resistant. Therefore, penicillin, ampicillin and sulfa drugs are never prescribed [27].

Conclusion

Chlamydia pneumoniae is an intracellular obligate pathogen which develops atypical/walking pneumonia in humans associated with COPD, asthma, arthritis, cardiovascular diseases and lung cancer. The bacteria, either persisting for a longer period of time in human cells, cause inflammation, diseases and lung cancer.In immunocompromised patients, the same bacteria found in human cells sometimes reactivate to cause pneumonia and lung cancer in humans. Further, the culture of C. pneumoniae is difficult. However, it can successfully be diagnosed with the help of PCR. The prognosis of the disease is good. The pneumonia caused by C. pneumoniae is often treated with the help of macrolide, tetracycline and fluoroquinolone antibiotics. The most preferred antibiotics are azithromycin, ciprofloxacin, tetracycline and doxycycline.

The present review also discusses the inflammation caused by pneumonia and the development of lung cancer. Although it has been proved to be a potential risk factor for lung carcinoma, C. pneumoniae as an individual risk factor is still debatable. Last but not least, recently, a major outbreak wave of C. pneumoniae was observed across Europe (2024–2025) for respiratory infections in humans.

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Ethical Clearance:

As this is purely a review article, therefore, it does not require any ethical clearance.

Conflict of Interest:
The authors have declared no conflicts of interest.

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