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EDITORIAL

Relevance of *Chlamydia pneumoniae* in community-acquired respiratory infections

*A.Torres, M. El-Ebiary

Genus Chlamydiae is composed of small bacteria, presenting unique characteristics such as intracellular habitat and a specific replication cycle different from conventional bacteria. There are different species of Chlamydiae that can infect animals and men. The best known are *Chlamydia trachomatis* and *Chlamydia psittaci*. TWAR is a recently described bacterium of the genus Chlamydia, which was originally isolated in 1965 from the conjunctiva of a Taiwanese child. The organism was first assumed to be *Chlamydia trachomatis*, until its growth in cell culture suggested it to be *Chlamydia psittaci* [1]. However, on the basis of ultrastructure studies and deoxyribonucleic acid (DNA) homology, a new Chlamydia species named *Chlamydia pneumoniae* has been identified [2]. Until now, only two strains or serovars, the TWAR and the IOL-207 strain, have been found [2, 3]. The most well studied is Chlamydia TWAR. This microorganism, unlike *Chlamydia trachomatis*, cannot be sexually-transmitted nor be a cause of conjunctivitis [4]. Since *Chlamydia pneumoniae* strain TWAR was first reported to be the respiratory pathogen causing an unusual epidemic in northern Finland [5], several publications have confirmed the high prevalence (up to 60%) of antibodies to this organism in adults [6], and also its importance as a "new" respiratory pathogen in the spectrum of community-acquired pulmonary infections.

GRAYSTON and co-workers [1] were the first to point out the importance of *Chlamydia pneumoniae* strain TWAR as a respiratory pathogen. They demonstrated that it accounted for 12% of 76 episodes of pneumonia, 5% of bronchitis, and 1% of pharyngitis, in a population of university students. Studying hospitalized patients with community-acquired pneumonia in Nova Scotia, a 6% prevalence of this infection was found [7]. More recent reports [8, 9] investigating both the epidemiology and the aetiology of community-acquired pneumonia in patients requiring hospitalization, have shown that this "new" pathogen is a frequent cause of pneumonia, and may even be responsible for one third of the cases of pneumonia [9]. In older populations, the role of *Chlamydia pneumoniae* strain TWAR in community-acquired pneumonia has been also shown [10]. In the present issue of this journal, ALMIRALL *et al.* [11] report their results regarding a prospective study of 105 non-hospitalized patients from a Mediterranean area, suffering from community-acquired pneumonia. With an annual incidence rate of community-acquired pneumonia of 2.6 cases per 1,000 inhabitants, *Chlamydia pneumoniae* (strain IOL-207) was, surprisingly, the major cause of respiratory infection in those cases with proven aetiological diagnosis (50%).

Since all of the epidemiological studies reported have used a similar methodology to diagnose *Chlamydia pneumoniae* strain TWAR (microimmunofluorescence test) we must assume that respiratory infection caused by this organism varies, according to the population studied and in particular the geographic area investigated. Seasonal and annual variables may be risk factors for *Chlamydia pneumoniae* strain TWAR acquisition, but this still needs to be demonstrated. Furthermore, *Chlamydia pneumoniae* is probably more frequent in mild cases (non-hospitalized) than in patients requiring hospitalization; 35% of cases in the study of ALMIRALL *et al.* [11] *versus* 6% in the study in Nova Scotia [7]. The variability of the incidence of *Chlamydia pneumoniae* strain TWAR and other microorganisms (*Legionella pneumophila* and *Mycoplasma pneumoniae*) has implications for the empirical therapy of community-acquired pneumonia. Protocols for empirical treatment cannot be elaborated in a given geographic area until periodic and seasonal epidemiological studies have been performed.

From all reported epidemiological studies, it seems that *Chlamydia* TWAR pneumonia is a mild and probably self-limited disease. Severe cases have not been reported. The self-limited and benign characteristics of the disease were evident in the study of ALMIRALL *et al.* [11], since the majority of patients were cured without specific antibiotics against *Chlamydia pneumoniae* strain TWAR (tetracyclines or erythromycin), but were cured with other antibiotics (personal communication).

The clinical picture is variable, and may be indistinguishable from that of *Mycoplasma pneumoniae*, or very similar to that caused by pyogenic bacteria. However, in the first reported cases, GRAYSTON and co-workers [1] showed that sore throat was a typical symptom. Another remarkable finding is that *Chlamydia pneumoniae* strain TWAR can infect concomitantly with other respiratory pathogens [11]. Probably, this

* Correspondence: A. Torres, Servei de Pneumologia, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain.

organism is the first step, "setting up the way" for other bacterial infections.

The prevalence of antibodies against *Chlamydia pneumoniae* strain TWAR in a general population is high and varies from 25–77% [7, 12]. This finding along with the epidemiological studies mentioned above, leads us to conclude that the organism is a common pulmonary pathogen, which can cause a wide spectrum of respiratory diseases, such as pharyngitis, tracheitis, bronchitis, and pneumonia.

Chlamydia pneumoniae strain TWAR may, furthermore, be responsible for some of the exacerbations of chronic obstructive pulmonary disease (COPD) patients. Only two studies have addressed this issue extensively [12, 13]. The first was conducted by BEATY *et al.* [12], who demonstrated that acute *Chlamydia pneumoniae* strain TWAR infection occurred in 5% of COPD exacerbations. However, the prevalence of serological evidence of a past infection was similar in COPD patients and in controls. A similar study is also reported in the present issue of this Journal. BLASI *et al.* [13], studying 142 out-patients, affected by an acute purulent exacerbation of COPD, found 4% of cases with positive immunoglobulin M (IgM) titres (>1/16), high immunoglobulin G (IgG) titres (1/512) in 19 patients (14%), and one case presenting a fourfold increase of IgG titres. The prevalence of acute *Chlamydia pneumoniae* strain TWAR infection was at least 15%. As opposed to the study of BEATY *et al.* [12], the percentage of *Chlamydia pneumoniae* strain TWAR past infection was higher in COPD patients than in controls (63% *vs* 47%; p=0.007). Data regarding treatment against the organism were not given in both studies, but some proven cases of *Chlamydia pneumoniae* strain TWAR infection in the study BLASI *et al.* [13] resolved completely with erythromycin.

The diagnosis of *Chlamydia pneumoniae* strain TWAR infection can be performed by using monoclonal antibodies on throat washing samples. At present, this technique is not routinely used in the majority of laboratories. The microimmunofluorescence test is the most common diagnostic method used. A single IgM titre ≥1/32, or an IgG titre ≥1/512, or a fourfold increase in IgG or IgM titres are the criteria widely accepted for diagnosis of an acute *Chlamydia pneumoniae* strain TWAR infection [12]. A single IgG titre of 1/16 to 1/256 is demonstrative of a past infection by this organism.

It is now evident that *Chlamydia pneumoniae* has become a frequent respiratory pathogen, accounting for a variable percentage of community-acquired respiratory infections. However, there are two unresolved questions with important implications for the empirical treatment of these pulmonary infections. Firstly, how useful is it to include specific treatment against *Chlamydia pneumoniae* in our empirical therapeutic strategies in community-acquired pneumonias? Secondly, what percentage of severe community-acquired pneumonias is caused by this organism? If *Chlamydia pneumoniae* is responsible for some severe pneumonias, empirical treatment against this microorganism should always be considered when planning the best antibiotic strategy.

Through the last decade we have detected the emergence of "new" respiratory pathogens. Firstly, *Legionella pneumophila*, then *Branhamella catarrhalis*, and now *Chlamydia pneumoniae*, all being clear examples. The epidemiological studies of community-acquired pneumonia show that around 50% of cases are still of unknown aetiology. More respiratory pathogens will be identified in future years, giving us a better understanding of these frequent respiratory infections.

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