Mycoplasmas are unique forms of life that lack the ability to produce cell walls. Recognition of Mycoplasma as a bacterial pathogen took many years of intense clinical and research work. The first Mycoplasma to be isolated in culture was the bovine pleuropneumonia (now known as Mycoplasma mycoides subsp. Mycoides) was described initially by Nocard and Roux in 1898. No reports on Mycoplasma in humans appeared until 1942, when Eaton et al. described the isolation of a filterable agent recovered from the sputum of a patient with primary atypical pneumonia. This agent later named as Eaton agent, was believed to be a virus particle rather than a bacterium. The ability to pass through viral filters, as well as difficulty of growing this organism in cell-free culture conditions, supported its hypothesis to be a viral agent. However, isolation of the Eaton agent from cell-free cultures and its susceptibility to antibiotics led to the postulation by Marmion and Goodburn in 1961 that the Eaton agent was a pleuropneumonia like-organism and not a virus. Chanock et al subsequently proposed the taxonomic designation of Eaton agent as Mycoplasma pneumoniae in 1963. Among human mycoplasma, M. pneumoniae is by far the best known and most carefully studied. The genome of M. pneumoniae was completely sequenced in 1996 and shown to consist of 816,394 bp with 687 genes.

M. pneumoniae is now known to be a frequent respiratory pathogen in children as well as in adults. It infects the upper and lower respiratory tracts, leading to upper respiratory tract infection, bronchiolitis, tracheobronchitis, bronchitis and community-acquired pneumonia (CAP). Although M. pneumoniae infections are usually mild, and many are asymptomatic, they are not always self limiting. Moreover, subsequent infections may be more common following initial mild infections as opposed to infection in which pneumonia develops, perhaps due to lesser stimulation of the immune response.

M. pneumoniae is also associated with asthma exacerbations. Interestingly, Mycoplasma respiratory tract infections are associated with non-respiratory symptoms in many cases, manifesting in the skin, mucous, central nervous system and other tissues. The first clues to differentiate pneumonia eventually proven to be due to Mycoplasma from classical pneumococcal pneumonia came from the observations that some cases failed to respond to treatment with sulphonamides or penicillin. The lack of response to antimicrobial therapy was deemed “atypical”, and the condition was thought likely to be a primary form of lung disease of uncertain aetiology; hence the term “primary atypical pneumonia” was coined.

M. pneumoniae causes up to 40 per cent or more of cases of CAP and as many as 18 per cent of cases requiring hospitalization in children. Older studies reported M. pneumoniae pneumonia to be somewhat uncommon in children aged less than 5 yr and greatest among school-aged children 5 to 15 yr of age, with a decline after adolescence and on into adulthood. However, latter studies have documented that M. pneumoniae may occur endemically and occasionally epidemically in older persons, as well as in children under 5 yr of age. These findings may also reflect improved detection abilities that were unavailable in the 1960s and 1970s, when the first descriptions of M. pneumoniae epidemiology and age distribution were published.

Whereas pneumonia may be the most severe type of M. pneumoniae infection, the most typical syndrome, especially in children, is tracheobronchitis often accompanied by a variety of upper respiratory tract manifestations. Esposito et al. demonstrated acute M. pneumoniae infection in 23 per cent of children with non streptococcal pharyngitis, using the criteria of elevated IgM antibody titre or a four-fold increase in IgG antibody titre and/or a positive PCR assay on the nasopharyngeal aspirate. Since the testing of
M. pneumoniae was performed only on specimens that were negative for Streptococcus pyogenes, it is possible that an even greater proportion of infections due to M. pneumoniae might have been detected, since some cases may be mixed.

Although most mycoplasm infections occur among outpatients (hence the colloquial term “walking pneumonia”), M. pneumoniae is a significant cause of bacterial pneumonia in adults requiring hospitalization in the United States. Marston et al reported that M. pneumoniae was definitely responsible for 5.4 per cent and possibly responsible for 32.5 per cent of 2,776 cases of CAP in hospitalized adults using complement fixing (CF) antibody determinations for detection. An additional striking finding of this was their observation that the incidence of pneumonia due to M. pneumoniae in hospitalized adults increased with age, and it was second only to S. pneumoniae in elder persons. Another study of hospitalized adults with CAP performed in Israel, which used commercial serological kits to detect antibodies, showed M. pneumoniae to be second only to S. pneumoniae, and it was responsible for 29.2 per cent of pneumonias overall.

The clinical presentation of M. pneumoniae respiratory disease is often similar to what is also seen with other atypical pathogens, particularly Chlamydia pneumoniae, various respiratory viruses and bacteria. M. pneumoniae may also be present in the respiratory tract concomitantly with other pathogens, and there is some evidence from humans and animal models indicating that infection with M. pneumoniae may precede and somehow intensify subsequent infections with various respiratory viruses and bacteria, including S. pyogenes and of Neisseria meningitides. Potential explanation for such a synergistic effect include immunosuppression or alteration in respiratory tract flora due to the presence of M. pneumoniae. Children with functional asplenia and immune system impairment are at a risk of developing more fulminant pneumonia due to M. pneumoniae.

Although M. pneumoniae is a well recognized pulmonary pathogen in the West, little information exists on disease prevalence in developing countries due to non-availability of reliable, rapid diagnostic techniques as well as the lack of clinical awareness. Kashyap et al in this issue demonstrated M. pneumoniae infection in 18 (24%) of 75 children with CAP, using the criteria of culture and/or serology and/or a positive PCR assay on nasopharyngeal aspirates. Previous studies relying upon serology have reported M. pneumoniae in 27.4 per cent of CAP in children and in 15 per cent of CAP in adults. Shenoy et al reported that M. pneumoniae was responsible for 24 per cent cases of pneumonia in hospitalized children.

M. pneumoniae infections cannot be diagnosed by clinical findings alone. Before the availability of new technologies, cold agglutinins were used to confirm a diagnosis of M. pneumoniae infection. However, lack of sensitivity and specificity rendered cold agglutination irrelevant for diagnosis. While culture is considered to be the reference standard for diagnosis, it is expensive, time consuming and only available in reference laboratories or large medical centres. Diagnosis of M. pneumoniae infection is usually performed by serological methods, such as passive agglutination, complement fixation and ELISA. ELISA is more sensitive than culture for detecting acute infection, has sensitivity comparable to PCR, but may be less sensitive than passive agglutination. Passive agglutination serology using paired sera shows good agreement with PCR results. Complement fixation tests, indirect immunofluorescent assays and particle agglutination assays have low sensitivity and specificity. A combination of PCR and serology is recommended for reliable diagnosis.

The advantages of PCR include high sensitivity and specificity, rapid results and no requirement for viable microorganism. The various targets that have been used include primarily the ATPase gene, Pl adhesin and conserved regions of 16s rRNA. The use of two different targets can maximize the ability to detect the organism. However, PCR assays may overestimate the incidence of Mycoplasma infections. Recent development of quantitative PCR assays will be beneficial in facilitating better understanding of the carrier state associated with M. pneumoniae.

Generally, antimicrobials for treatment of pneumonia are unable to cure patients of pneumonia caused by M. pneumoniae. Thus, there is a need to consider M. pneumoniae in the differential diagnosis of all pneumonia and to plan the initial antimicrobial therapy accordingly. Macrolides, tetracyclines and fluoroquinolones eliminate Mycoplasma efficiently both in vivo and in vitro. Macrolides are the antibiotics of choice for treating M. pneumoniae infections in both adults and children.

Advances in detection and characterization of M. pneumoniae by using PCR, serology, and culture augmented by knowledge obtained from the complete genome sequence of this organism, has led to the
appreciation of its role as a human pathogen. Despite these many advances, much is still unknown about this tiny bacterium, which is among the smallest of all free-living forms. A reliable and user-friendly amplified or none amplified method for detection of the mycoplasma or its nucleic acid in clinical specimens would be of immense importance for patients’ diagnosis and management.

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References