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Respiratory tract infections by *Mycoplasma pneumoniae* in children:
a review of diagnostic and therapeutic measures

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Abstract This review discusses the current knowledge on laboratory tests and treatment
of respiratory tract infections caused by *Mycoplasma pneumoniae* (MP) in children. MP
infection is endemic in most areas of the world. The highest incidence is seen in children
aged between 3 and 14 years. Most infections are mild and non-pneumonic. Parapneumonic
complications of MP pneumonia are rare. Complications are described affecting
the skin, central nervous system, kidneys, heart, muscles and the eyes. To diagnose an
acute MP infection in children, a combination of PCR and IgM serology is sensitive and
convenient. In both tests it is possible to obtain a result in 1 to 2 days. As a consequence,
adequate antibiotic treatment can be prescribed to the child. Macrolides are the first
choice in treatment of MP infection in children.

Conclusion The most sensitive and rapid test to diagnose a *Mycoplasma pneumoniae*
infection in children is a combination of nasopharyngeal polymerase chain reaction and
IgM enzyme immunoassay. The treatment of choice in children is a macrolide.

Key words Laboratory diagnosis · *Mycoplasma pneumoniae* · Outcome · Review ·
Therapy

Abbreviations CFA complement fixation assay · EIA enzyme immunoassay ·
ELISA enzyme-linked immunosorbent assay · MP *Mycoplasma pneumoniae* ·
PCR polymerase chain reaction

Introduction

Some 16 *Mycoplasma* species are found in humans [126].
These species, belonging to the class of *Mollicutes*, may
colonise the oropharynx and genitourinary tract of
humans. Several *Mycoplasma* species including
*Mycoplasma salivarium*, *Mycoplasma orale*, *Mycoplasma
buccae*, *Mycoplasma faecium* and *Mycoplasma lipophilum*
are part of the normal flora of the human orophar-
ynx, but only *Mycoplasma pneumoniae* (MP) may be
encountered as a pathogen. Of the infections caused by
MP, roughly 20% are asymptomatic, the majority
(±75%) are minor respiratory illnesses (tracheobron-
chitis, pharyngitis etc.) and only a small proportion
(3–10%) are serious infections such as pneumonia
[16,29]. In children, MP accounts for 10–40% of all cases
of community-acquired pneumonia, which is influenced
by epidemics [26, 28, 29, 43, 45, 110].

Here an overview of respiratory tract infections
caused by MP in children is provided with a special
focus on laboratory tests and treatment.

Epidemiology

Infection due to MP is endemic in most areas of the
world, although it is more common in temperate zones.
Infection occurs during all months of the year, but is
slightly more frequent during late summer and early

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autumn [121]. The incidence of MP infections varies every year with an epidemic peak approximately once every 4 years [29, 55, 90]. Hauksdottir et al. [55] showed that outbreaks of MP were similar in timing and pattern in different countries in Europe.

The prevalence of infection of all clinical syndromes caused by MP varies from 2% during endemic years to 10–35% in epidemic periods [15, 42, 84]. The highest incidence is seen in children aged between 3 and 14 years. Another peak in the age distribution is found in adults between 25 and 40 years. In the youngest group, boys predominate and there is no explanation for this difference in gender distribution. In the second age peak, women predominate [88]. The rate of MP infections under endemic conditions in children aged 5–9 years was 4/1000 per year and in children between 10 and 14 years 3/1000 per year [15, 42]. Due to the long incubation period (2–3 weeks) and low transmission rate, the duration of the epidemic lasts approximately 1 year. Spread of infection from person to person is very slow, therefore one may deduce that very close contact is needed. MP is transmitted by direct contact or by contaminated respiratory droplets. Foy et al. [41] reported that it took several months before infection by MP was disseminated among four households. Spread among playmates in the neighbourhood seemed more important than that in the classroom.

MP has the propensity to cause very intensive outbreaks in facilities where people live in very close contact. In the late 1960s, outbreaks in military institutions, universities, homes for mentally disabled or homes for psychiatric patients were reported [14, 22, 36, 100, 113, 119]. More recently Feikin et al. [38] reported an outbreak of MP in combination with adenovirus at a Federal Service Training Academy. Of a group of 586 students, 54% reported respiratory illness during the outbreak period. The outbreak showed peaks of illness every 2–3 weeks.

MP infection is rarely diagnosed under the age of 6 months. Several explanations can be given: protection by maternal antibodies and/or immaturity of receptors for MP in the respiratory tract, or this agent is rarely considered in infants [15, 131]. MP may cause up to 35% of all cases of outpatient pneumonia and 3–18% of pneumonia cases necessitating hospitalisation [91]. Recurrent infection by MP is not uncommon. In people with pre-existing immunity against MP re-infection may occur after a lapse of 3 to 5 years [46]. Second episodes appear to be milder. Re-infection is less commonly seen after pneumonia than after infection with minor symptoms [43]. This might be explained by elevated complement-fixing antibodies measurable for 2 to 9 years after pneumonia. These antibodies, however, fall very rapidly after the 2nd year in persons with mild upper respiratory tract infections [43].

Clinical manifestations

In children younger than 5 years of age, MP infections are mostly mild and non-pneumonic. The major symptoms are coryza and wheezing without concurrent fever. In children between 5 and 15 years of age, the risk for MP-induced pneumonia is maximal. More than 30% of infections caused by MP in this age group result in pneumonia [121].

MP infection is a subacute and gradual process. Illness usually lasts for 1 month or longer, excluding the incubation period [29]. Clinical symptoms normally start in the upper respiratory tract and then spread to the lower respiratory tract. The initial manifestation is usually a sore throat followed by hoarseness or dysphonia [91]. When the infection reaches the trachea, bronchi and bronchioles, an intractable cough appears. It is a constant, relatively nonproductive cough that keeps the patient awake. When the disease progresses, fever becomes higher, the cough more troublesome and the patient may become dyspnoeic [91]. Table 1 summarises the symptoms and signs of lower respiratory MP infection from three studies. Stevens et al. [120] studied 44 children ranging from 16 months to 14 years. The other two investigators compiled their data from different studies in children and adults [24, 29]. Stevens et al. [120] reported that in their group coryza was more commonly seen in the younger children. Headache and production of sputum in association with MP pneumonia varies between studies [24]. This is probably caused by the difference in ages of the patients between the studies.

Severe illness may be seen in the presence of a concomitant infection [56, 91, 118]. Heiskanen et al. [56] reported that in 50% of the patients infected with MP, another aetiological agent was involved. Hers et al. [58] found co-infection with Haemophilus influenzae in 6% of the patients infected with MP. Block et al. [13] reported co-infection of MP and Chlamydia pneumoniae in 8% of community-acquired pneumonia. Severe manifestations can be seen in patients with sickle cell disease, Down syndrome, immunodeficiency syndromes, drug-induced immunosuppression and pre-existing cardiopulmonary dysfunction [15, 91].

Pneumonia

On physical examination rales and rhonchi are common, but signs of consolidation are seldom detected. On the chest radiograph MP pneumonia appears mostly diffuse and with reticular infiltrates, consolidation is infrequent. In 20% of cases, bilateral abnormalities are seen. Cough, abnormal chest signs, and radiographic changes may last several weeks. Pleuritic chest pain and pleural effusion are unusual [121].

Severe pneumonia may be due to an enhanced host cellular immune response [21]. This may lead to bronchiolitis obliterans, based on the obstruction of the terminal and respiratory bronchioles by polyoid/fibroblastic masses. Recently, bronchiolitis obliterans was described by Leong et al. [86] with involvement of the larger bronchi. Kim et al. [75] evaluated children who