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Takako Hirota1, Yuji Yoshida1, Yasuhiko Kitasato, Michihiro Yoshimi, Takaomi Koga, Nobuko Tsuruta, Masato Minami, Taishi Harada1, Hiroshi Ishii1, Masaki Fujita1, Kazuki Nabeshima, Nobuhiko Nagata and Kentaro Watanabe	Historogical evolution of pleuroparenchymal fibroelastosis	*Histopathology*	66(4)	545-554	2014
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中田光	LAM の分子標的療法	呼吸	32(3)	233-237	2013
井上義一	特発性間質性肺炎診断と治療の手引き（改訂第 2 版）：改訂の経緯と概要	呼吸と循環	61(2)	105-11	2013
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橘和延，井上康，井上義一	【コラム】特発性肺線維症の急性増悪に対するPMX—DHP療法：有用性，安全性，そして今後の展望	*INTENSIVIST*	5(4)	815-20	2013
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海老名雅仁，福岡正博，工藤翔二，安藤昌彦，大江裕一郎，中川和彦，山崎直也，荒川浩明，井上義一，楠本昌彦，桑野和善，弦間昭彦，酒井史和，上甲剛，谷口博之，福田悠，関顕洋	間質性肺疾患予後不良(転帰死亡)因子の検討-タルセバ錠非小細胞肺癌特定使用成績調査(全例調査)より-	肺癌　第56回肺癌学会総会号	53(6)	469	2013
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井上義一	呼吸器内科学 リンパ脈管筋腫症関連疾患に対するmTOR阻害剤を用いた新たな分子標的治療	週刊 医学のあゆみ 血液凝固異常研究の進歩	242(2)	200-1	2012
井上義一	特発性非特異性間質性肺炎と特発性器質化肺炎 -類似点と相違点-	*THE LUNG perspectives*	20(3)	249-54	2012
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新井徹，井上義一	今月の主題・間質性肺炎と臨床検査 - 各論「血清マーカー」	臨床検査	56(9)	972-8	2012
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Novel aspects on the pathogenesis of Mycoplasma pneumoniae pneumonia and therapeutic implications

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Mycoplasma pneumoniae (Mp) is a leading cause of community acquired pneumonia. Knowledge regarding Mp pneumonia obtained from animal models or human subjects has been discussed in many different reports. Accumulated expertise concerning this critical issue has been hard to apply clinically, and potential problems may remain undiscovered. Therefore, our multidisciplinary team extensively reviewed the literature regarding Mp pneumonia, and compared findings from animal models with those from human subjects. In human beings, the characteristic pathological features of Mp pneumonia have been reported as alveolar infiltration with neutrophils and lymphocytes and lymphocyte/plasma cell infiltrates in the peri-bronchovascular area. Herein, we demonstrated the novel aspects of Mp pneumonia that the severity of the Mp pneumonia seemed to depend on the host innate immunity to the Mp, which might be accelerated by antecedent Mp exposure (re-exposure or latent respiratory infection) through up-regulation of Toll-like receptor 2 expression on bronchial epithelial cells and alveolar macrophages. The macrolides therapy might be beneficial for the patients with macrolide-resistant Mp pneumonia via not bacteriological but immunomodulative effects. This exhaustive review focuses on pathogenesis and extends to some therapeutic implications such as clarithromycin, and discusses the various diverse aspects of Mp pneumonia. It is our hope that this might lead to new insights into this common respiratory disease.

Keywords: Mycoplasma pneumoniae pneumonia, animal models, epidemiology, pathology, pathogenesis

INTRODUCTION

Mycoplasma pneumoniae (Mp) was first isolated in tissue culture from the sputum of a patient with primary atypical pneumonia by Eaton et al. (1944). This "Eaton's agent" was shown to be a Mycoplasma species in 1961. Chanock et al. succeeded in culturing Eaton's agent in mammalian cell-free medium and proposed the taxonomic designation Mp in 1963 (Chanock et al., 1962; Chanock, 1963). Mp is a unique organism that lacks a cell wall in any circumstances, and does not need a host cell for replication. This organism causes a variety of clinical presentations, from self-limiting to life-threatening. The disease severity seems to depend on the degree of host's defenses. In this review, we focused on the pathogenesis of Mp pneumonia from the perspective of host defenses, based on findings from our mouse models.

EPIDEMIOLOGY

Mp is one of the most common pathogens of community-acquired pneumonia (CAP) in adults (Table 1). In general, both regional differences and varying periods of surveillance may influence the results of etiological studies of infectious diseases. Table 1 summarizes the proportions of adult Mp pneumonia among CAP populations enrolled in several large-scale studies conducted in various countries (Marston et al., 1997; Ngeow et al., 2005; Arnold et al., 2007; Von Baum et al., 2009; Gilloniz et al., 2011). Mp pneumonia accounted for 10.6–17.0 and 3.0–20.8% of CAP in out- or in-patients settings, respectively, and the frequency of ICU admission was relatively low (2–3.6%). Arnold et al. showed that Mp is the most common atypical pneumonia pathogen, accounting for 11–13% of CAP throughout the world (Arnold et al., 2007). Serological studies in Denmark over a 50-year period showed that Mp infections exhibit epidemic periodicity every 3–5 years, but this trend now seems to be getting obscured (Lind et al., 1997). Mp pneumonia occurs at any age, but the incidence is less common in elderly, as compared with young, adults (Lim et al., 2009), and is highest among school-aged children (Fovet et al., 1979).

Macrolides were recommended for treatment of microbiologically defined Mp pneumonia. However, macrolide-resistant