continue their studies on elastin-derived peptides. We hope that Frette and coworkers (2) who showed that there was a significant correlation between increased elastin-derived peptide levels in plasma and the presence of chronic obstructive pulmonary disease (2, 3). However, as mentioned previously, we do not currently recommend the measurement of elastin-derived peptides in plasma as a screening or diagnostic test for chronic obstructive pulmonary disease until additional studies determine whether this assay offers an advantage over spirometry in the detection of early emphysema" (1, p. 1080).

Frette and colleagues state their epidemiologic results do not support the observations presented in the three clinical studies referenced above (1–3). Unfortunately, all of the work that they have performed has used serum from different subject populations as the starting material. However, as described in detail in Kucich and coworkers (5), serum is an extremely unreliable starting material that tends to give abnormally elevated levels of EDF. Thus, it is likely that the values obtained by Frette and coworkers 0.36–10.27 μg/ml (4) as compared to the ng/ml concentrations observed in the other studies (1–3) could be related to the use of serum instead of plasma. The high values may also be related to a different antibody, developed against aortic kappa elastin.

Neither nor Dillon and colleagues (2) found a correlation between EDP levels and FEV 1, or smoking history; however, the latter did find a good correlation between plasma EDP and K, a sensitive indicator of alveolar distensibility. In addition, none of the earlier studies found a relationship between EDP levels and age (2, 3, 5), and while the letter from Frette and colleagues states that a decrease of elastin peptide level was observed with age, their abstract (4) states that elastin peptide level was unrelated to age. If, indeed, there is a decrease in EDP with age, then the elevation of EDP in COPD patients (who tend to be older) observed in 4 studies (1–3, 5) becomes even more significant.

Since Frette and colleagues are concerned with an epidemiologic study of a population of middle-aged, predominantly healthy individuals, it may be of interest that both our study (1) and that of Dillon and coworkers (2) observed a significant fraction of normal smokers with elevations in EDP. It is possible that those individuals may be a population at risk for the development of emphysema.

Finally, Frette and colleagues suggest a study with the use of CT scans as the method of choice to define a specific clinical group and propose that EDP be analyzed in relation to CT scan changes. Such a study has already been performed by Dillon and coworkers (2) who showed that there was a significant correlation between plasma EDP levels and CT scan percent emphysema score, suggesting that plasma EDP levels are indicators of mild to moderate pulmonary emphysema and may, therefore, be useful in epidemiologic studies. We hope that Frette and coworkers continue their studies on elastin-derived peptides with the goal of making such an assay feasible for the early diagnosis of emphysema as well as a useful technique for monitoring therapeutic efficacy in that disease.

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ERYTHROMYCIN REDUCES NEUTROPHILS AND NEUTROPHIL-DERIVED ELASTOLYTIC-LIKE ACTIVITY IN THE LOWER RESPIRATORY TRACT OF BRONCHIOLITIS PATIENTS

To the Editor:

Having previously demonstrated the clinical effectiveness of oral erythromycin in the treatment of bronchiolitis patients, Ichikawa and coworkers (1) report that erythromycin reduces neutrophils and neutrophil-derived elastolytic activity in the lower respiratory tract of bronchiolitis patients. They argue that this effect is probably due to a non-antimicrobial effect of erythromycin.

Their report did not include cell culture, direct fluorescent staining, or serologic testing for either Chlamydia trachomatis or Chlamydia pneumoniae. Serologic evidence for recent C. trachomatis infection has been detected in 28 of 166 (16.9%) children aged 12 to 18 months with bronchiolitis, and three additional children with bronchiolitis had C. pneumoniae-specific antibody (2). A case of multifocal bronchiolitis and pneumonia in an adult caused by culture- and serologically-proven C. pneumoniae infection, has also been reported (3). This adult bronchiolitis patient responded satisfactorily after an appropriate anti-chlamydial antibiotic (doxycycline) was added to his therapeutic regimen.

These observations raise the possibility that the cellular responses observed by Ichikawa and coworkers (1) might have been due to an anti-chlamydial effect of erythromycin. The authors have any additional information relating to this possibility?

Incidentally, erythromycin has also been reported to decrease bronchial hyper-responsiveness in asthma patients (4), and the authors speculated that the effect of erythromycin was related to a non-antimicrobial mechanism. C. pneumoniae infection has been associated with asthma (5) and anti-chlamydial antibiotic treatment has resulted in prolonged complete remission in one patient.
This raises the possibility that the effect of erythromycin on bronchial hyperresponsiveness could have been due to an antibiotic therapeutic effect. Future studies on mechanisms of antibiotic effects in chronic idiopathic pulmonary diseases should include tests for chlamydial infections.

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From the Authors:
We thank Dr. Hahn for his letter in regard to our article entitled "Erythromycin reduces neutrophils and neutrophil derived elastolytic-like activity in the lower respiratory tract of bronchiolitis patients" published in the Review. He suggested that the clinical efficacy of erythromycin in the bronchiolitis patients may be due to a simple bactericidal effect for organisms such as Chlamydiae that are sensitive to erythromycin. This possibility also raised as a major point by both reviewers of the manuscript. Certainly, Chlamydiae are important pathogens of respiratory infections in human being (1), and there are three species within the genus: Chlamydia trachomatis, C. psittaci, and C. pneumoniae (1, 2). C. trachomatis strains generally causes urogenital and conjunctival disease, but it has caused pneumonia in infants in whom the immune system is not fully competent (1). The incidence of C. trachomatis-associated respiratory disease in adult is unknown (1). Of the three species, only C. trachomatis has been particularly associated with disease in immunosuppressed patients (2). In a recent report (3) from Argentina, C. trachomatis infection was detected in relatively high incidence in children with bronchiolitis between the ages of 1 and 18 months of age. However, this report was concerned with infants and not adults such as our patients. We are not aware of a reported case of adult bronchiolitis associated with C. trachomatis infection. Also, we performed a serological test for C. trachomatis in all our reported bronchiolitis patients using a commercially available assay Kit using ELISA (Savoy Diagnostics, Israel), but had no positive cases. Infection with C. psittaci was also excluded by the fact that no patient had a history of direct exposure to infected birds and serologic testing (complement fixation test).

C. pneumoniae, the new third species of Chlamydiae, has recently been identified and is a common cause of community-acquired pneumonia and other acute respiratory tract infections (4—8). Dr. Hahn and coworkers reported that C. pneumoniae infection has been associated with wheezing, asthmatic bronchitis, and adult-onset asthma in a clinical population (9). It has been reported that about 10% of pneumonia cases were associated with C. pneumoniae infection (4), and the clinical findings of patients with C. pneumoniae infection were similar to those with Mycoplasma pneumoniae (1). Since C. pneumoniae is difficult to culture and is recently recognized as a pathogen of pneumonia, the clinical features and the histopathological findings of infection with C. pneumoniae are not well known (1, 2). H. influenzae, S. pneumoniae, or P. aeruginosa have been reported as a common pathogen in patients with diffuse panbronchiolitis (DPB), but Chlamydiae has not been reported in Japanese literature. Infection with C. pneumoniae, coinfection with other bacterial respiratory tract pathogen have been reported (7), and patterns of infection ranged from acute pneumonia to an apparent chronic asymptomatic carrier state. There was no characteristic clinical presentation (7). Accordingly, we cannot exclude the possibility of infection with C. pneumoniae in DPB patients. Further studies including serological testing or detection of C. pneumoniae antigen using polymerase chain reaction (10) are necessary to search for the possibility of infection with C. pneumoniae in DPB patients.

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