

CLINICAL CONSULTATION

Answer to a reader's question on:

■ Asthma linked to *Chlamydia pneumoniae*

Defining the relationship between *C pneumoniae* and chronic asthma

What evidence is there that *Chlamydia pneumoniae* can cause chronic asthma?

■ The evidence linking *C pneumoniae* with asthma is based on case reports and case series, and on epidemiologic studies.¹ Proof of causality based on randomized, controlled trials and elucidation of mechanisms of pathogenesis are required before definitive treatment recommendations can be made.

Chlamydia pneumoniae is an obligate intracellular human pathogen that causes asymptomatic infections (70% of instances) via the respiratory route and also causes acute upper and lower respiratory tract illnesses, including bronchitis and pneumonia. These acute respiratory illnesses can sometimes develop into chronic asthma or chronic bronchitis.

Case reports and case series have documented that prolonged (4 to 6 weeks or longer, if necessary) antibiotic treatment of serologic- or culture-proven infections can sometimes result in improvement or even remission of asthma symptoms. Treatment later in the course of asthma when it is very severe, or when irreversible fixed obstruction has developed, may not be as successful. Antibiotics reported to improve asthma symptoms include doxycycline (100 mg bid), clarithromycin (500 mg bid), and azithromycin (1 g once weekly).

Since most human populations worldwide have been exposed to *C pneumoniae*, it is very difficult to determine from epidemiologic studies alone how many cases of asthma may be attributable to this

pathogen. A crude estimate of the attributable risk of adult asthma, however, includes the possibility that more than 50% of cases of adult-onset asthma could be related to *C pneumoniae* infection. Polymerase chain reaction (PCR)-based studies suggest a similar picture in children. It is important to refine these estimates through further research because of the possibility that worldwide increases in asthma in all age groups might be related to this infection.

Unfortunately, detection of *C pneumoniae* infection can be very difficult for the clinician. Most clinical laboratories do not have capabilities to detect *C pneumoniae*. Culture requires cell systems that are technically demanding and insensitive in most settings. PCR is more sensitive but has not been standardized.

Furthermore, upper respiratory tract secretions may be PCR-negative in patients with persistent lung infection. Serologic techniques have been very useful in describing *C pneumoniae* epidemiology and diagnosing acute infections but are not capable of diagnosing chronic infection. There are also no reliable clinical characteristics that distinguish acute *C pneumoniae* infection from acute respiratory viral or *Mycoplasma pneu-*

moniae infections.

I tend to treat acute respiratory illnesses that persist beyond 6 weeks as if they were caused by *C pneumoniae*, since this organism is known to produce chronic, persistent infections. Perhaps this represents inappropriate antibiotic prescribing. However, I do not usually prescribe antibiotics for acute, viral-type illnesses, such as acute bronchitis and acute sinusitis, in otherwise healthy adults, so I prescribe fewer antibiotics for respiratory illness than most primary care physicians.

I believe that major advances in the understanding and treatment of "chlamydial asthma" will come as a result of randomized, controlled trials of antibiotic treatment in well-defined groups of patients with asthma. These trials will collect detailed clinical, epidemiologic, microbiologic, and serologic data to determine which variables, if any, best predict a therapeutic response. This may be used to guide antibiotic prescribing that, if it is ever justified, will probably be based on risk factor analysis as it is for chronic disease, rather than on microbiologic detection alone as it is for acute infections.

In the meantime, until such research has been published, my advice to clinicians is to reserve empiric antichlamydial antibiotic treatment for severe asthma cases in which all conventional treatments have failed, so as to minimize any inappropriate antibiotic prescribing.

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1. Hahn DL. *Chlamydia pneumoniae*, asthma, and COPD: what is the evidence? *Ann Allergy Asthma Immunol.* 1999;83:271-292.

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