

ered for patients in whom the involvement of iron deficiency remains uncertain.

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C PNEUMONIAE IN ADULT ASTHMA

TITLE: Treatment of *Chlamydia pneumoniae* infection in adult asthma: a before-after trial

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JOURNAL: *The Journal of Family Practice*

DATE: October 1995; Volume 41:345-351

Clinical question. Is antibiotic therapy for *Chlamydia pneumoniae* an effective treatment for adult-onset asthma?

Background. Recently, it has become clear that several chronic illnesses may be caused in part by chronic bacterial infection. For example, infection with *Helicobacter pylori* has been implicated in gastric and duodenal ulcer disease. Some physicians have anecdotally reported the onset of asthma in patients who have had a *Chlamydia pneumoniae* infection, as well as an improvement in asthma symptoms in adults and children treated with antibiotics for this infection.

Population studied. The author studied adult outpatients with moderate asthma (two or more symptomatic episodes per week) or moderately severe asthma (previous oral steroid use or hospitalization) who presented to his suburban family practice. The population was described as "mostly white and middle-class," with a mean age of 48 years (range 17 to 78 years) and a mean age of onset of asthma symptoms of 42 years. Almost one half of the study population were smokers. This group appears typical of patients cared for by family physicians.

Study design and validity. The study design used is called "pretest/posttest without a control group." That is, the FEV₁ level and subjective symptoms were measured antibiotics that are used to treat *Chlamydia pneumoniae* were given, and the FEV₁ level and subjective symptoms were reassessed after the antibiotic intervention. Patients were followed for an average of 6 months (range 1.5 to 36 months) after treatment, and the last recorded test results were used for the analysis.

This design has a number of possible biases. For example, patients are likely to present to the physician

when their symptoms are worse than average. By simply waiting a few months, the symptoms are more likely to improve than worsen, a phenomenon known as "regression to the mean." (The same phenomenon is responsible for the so-called sophomore jinx in sports, in which an outstanding rookie season is followed by a less successful second year.) Patients who experienced improvement may have been more likely to take other medications, make lifestyle changes, mitigate environmental exposures, experience improvement due to seasonal change, or differ in some other way, than nonresponders. The variable follow-up period is also troubling, as is the lack of information on patients who were not asked to participate. The design could have been strengthened by enrolling all patients, adding a comparison group of patients who were randomized to receive a placebo, having a standard follow-up period, and using a previously validated symptom score.

Outcomes measured. The primary measures were the percent change in the FEV₁ level and the score on the Patient Global Improvement (PGI) scale. The latter is a Likert-type scale ranging from -4 (complete worsening) to 0 (no change) to +4 (complete improvement). It has not been previously validated, but did correlate with the changes in FEV₁ levels.

Results. The FEV₁ improved an average of 12.5% with treatment (95% confidence interval [CI], 4.6 to 20.3). Twenty-five patients were classified as "responders" with a posttreatment PGI score of +3 or +4, whereas 21 had little or no response to treatment and a posttreatment PGI of less than 3. Responders tended to have a shorter duration of asthma symptoms before treatment (3.1 years vs. 8.3 years, $P=.01$) and were less likely to have used inhaled steroids (24% vs 62%, $P=.015$).

Recommendations for clinical practice. The results of this innovative practice-based trial are intriguing, and certainly warrant further study. It is tempting to respond by giving all one's newly diagnosed adult, nonatopic asthma patients a round of erythromycin, considering the possible benefit and short duration of therapy in this chronic illness. However, moving too quickly to advocate a new treatment has several disadvantages: if further study does not support the efficacy of this treatment, physicians will have to "unlearn" this behavior; using ineffective treatments drives up costs, including those of side effects; and widespread adoption may have the effect of stifling further research, as in the rapid adoption of bypass

surgery for carotid disease. Given the limitations of the current study's design, I agree with the author that it is premature for physicians to change the way they manage asthma based on the results of this study.

Paul M. Fischer, MD, has recently written of the "tyranny of the randomized controlled trial,"¹ and our unwillingness to change the way we practice without evidence from such a study, as exemplified by the Cochrane Collaboration and the Evidence Based Medicine Working Group.^{2,3} An approach that would avoid some of the complexities of the randomized controlled trial and still be quite convincing, would be to include patients with *Chlamydia*-negative

asthma in the study and compare their response to that of patients with *Chlamydia*-positive asthma.

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