

# Antibiotics Cut Treatment Failure in Acute COPD

BY MIRIAM E. TUCKER  
Senior Writer

PITTSBURGH — The use of antibiotics was associated with a significantly reduced risk of treatment failure for acute exacerbations of chronic obstructive pulmonary disease in the largest-ever study of patients hospitalized for that condition.

Chronic obstructive pulmonary disease (COPD) affects 24 million Americans and is the fourth leading cause of death in the United States. Acute COPD exacerbations are among the top 10 causes of hospitalization of adults in this country. About 50%-60% of acute exacerbations are caused by infections, and current COPD guidelines recommend antibiotic treatment for patients who have severe exacerbations with purulent sputum, even though most of the evidence supporting that practice comes from small, heterogeneous trials that often combined hospitalized and non-hospitalized patients.

Although the routine use of antibiotics does appear beneficial for patients on mechanical ventilation, there is scant published literature that supports their use for other hospitalized patients, Dr. Michael B. Rothberg said at the annual meeting of the Society of General Internal Medicine.

To address the question using a large-enough sample size, Dr. Rothberg and his associates at Baystate Medical Center of Tufts University, Springfield, Mass., conducted a retrospective cohort study of patients hospitalized in 2001 for acute COPD exacerbations at 375 acute care facilities

that were part of a large database for measuring quality of care and resource utilization. Included were patients hospitalized for at least 2 days with either a primary diagnosis of COPD or a primary diagnosis of respiratory failure and a secondary diagnosis of COPD; to avoid confusion with asthma, only patients older than 39 years were included.

Patients with direct admission to the intensive care unit also were excluded, as were those who had other bacterial infections for which antibiotics would have been indicated. Antibiotic treatment was defined as at least 2 consecutive days of an appropriate antibiotic for COPD begun on the first or second day of hospitalization. Treatment failure was defined as either initiation of mechanical ventilation after hospital day 2, in-hospital mortality, or all-cause readmission within 30 days.

Of a total 35,053 patients who met the enrollment criteria, 79% (27,812) had received antibiotics (most commonly quinolones, cephalosporins, or macrolides) and 21% (7,241) had not. Those given antibiotics were significantly younger (median age 70 years vs. 71 years), more likely to be in managed care (20% vs. 19%) and to be white (78% vs. 73%), and less likely to have comorbidities including secondary pulmonary hypertension, sleep apnea, alcohol abuse, renal failure, and heart failure. The proportions with comorbid diabetes and solid tumors did not differ significantly. (Because the database was so large, even seemingly small differences often reached statistical significance, Dr. Rothberg noted.)

Patients who received antibiotics appeared to have more severe disease, based on the tests and other treatments they were given. Significantly more of the patients treated with antibiotics had been given steroids (87% vs. 74%), an arterial blood gas measurement (58% vs. 53%), sputum testing (13% vs. 5%), and short-acting bronchodilators (55% vs. 50%). They also received more methyxanthines, loop diuretics, and morphine. The two groups were equally likely to have been given nutritional supplements and to have been prescribed continuous positive airway pressure or bilevel positive airway pressure.

Unadjusted overall rates of treatment failure were significantly lower in the antibiotic-treated group (20% vs. 22%), mostly accounted for by the significantly lower rates of readmission within 30 days (17% vs. 19%). Although the rates of both mortality (1.5% vs. 1.7%) and mechanical ventilation after day 2 (1.2% vs. 1.4%) also were lower among those receiving antibiotics, those numbers were too small to reach significance, Dr. Rothberg said.

Adverse events, including allergic reactions, diarrhea, and treatment for *Clostridium difficile* infection after day 3, were not increased in the antibiotic-treated group. Length of stay was significantly greater for the antibiotic group (4.92 days vs. 4.65 days) as was total cost (\$4,361 vs. \$4,277).

The unadjusted odds of treatment failure were significantly lower for those treated with antibiotics, with an odds ratio (OR) of 0.88. However, because this was not a randomized trial, there was a need to control for selection bias—that is, patients who received antibiotics were likely to have been sicker than those who did not. To control for that, a propensity model was used to predict the likelihood of receiving antibiotics, based on patient factors such as

demographics, comorbidities, prior COPD admissions, diagnostic tests and treatments (e.g., arterial blood gas, steroids), physician specialty, and hospital factors such as size and teaching status.

Even after adjustment for the propensity score and covariates, receiving antibiotics still resulted in a lower risk for treatment failure (OR 0.87). The adjusted risk of mortality was also lower (OR 0.85), but the number of deaths was too small for that value to reach statistical significance.

“Having such a large data set allowed us to adjust for just about everything ... No matter how we looked at it, we were still left with a benefit for antibiotics,” said Dr. Rothberg, adding that future studies will address whether there are differences between the antibiotic classes.

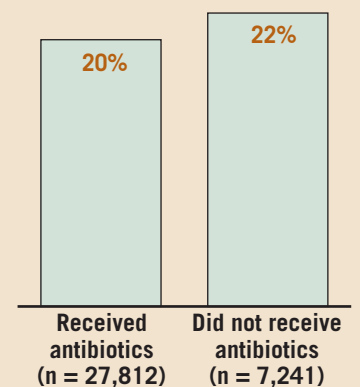
This study was funded internally by Baystate Medical Center’s Division of Healthcare Quality. ■



**‘No matter how we looked at it, we were still left with a benefit for antibiotics.’**

DR. ROTHBERG

## Lower Rates of COPD Treatment Failure With Antibiotics



Note: Based on data for patients aged 39 or older with a diagnosis of chronic obstructive pulmonary disease.  
Source: Dr. Rothberg

## Ask About Use of Unconventional Therapies for Lung Disorders

BY DAMIAN McNAMARA  
Miami Bureau

FORT LAUDERDALE, FLA. — Ask patients in an open-minded way about their use of unconventional therapies related to asthma, allergies, and other pulmonary conditions.

“The take-home message is ‘beware of being unaware,’” Dr. Cheryl Doyle said at a pediatric pulmonology meeting sponsored by the American College of Chest Physicians. Otherwise, drug or disease interactions, unnecessary testing or changes in therapy, and therapeutic failures can result.

“It’s a tremendous act of faith and [cooperation] to integrate complementary and conventional [therapies], when not contraindicated,” said Dr. Doyle, a pediatric pulmonologist in private practice in Brooklyn, N.Y. She had no relevant financial disclosures.

The term “complementary medicine” has evolved into “integrative holistic medicine,” because “complementary” assigns an adjunctive role to nonconventional medicine, she said. “Healing addresses the body, mind, and spirit, and we as healers—not providers—are part of that system.”

Integrative holistic medicine includes six systems: biomolecular therapies; botanical therapies; ethnic/cultural therapies; homeopathic remedies; manual therapies such as massage, yoga, and chiropractic treatment; and

energy therapies such as reflexology, the laying-on of hands, and manipulation of people’s auras.

Different cultures have different nonconventional therapies. In traditional Chinese medicine, asthma therapies include ma huang, ginkgo biloba, ginseng, magnolia, Minor Blue Dragon, *Scutellaria*, cinnamon, and licorice. Ma huang, for example, is an acrid herb believed to open pores, facilitate lung qi (energy), and control wheezing, Dr. Doyle said, adding that it controls wheezing because “about 80%-90% [of the herb] is L-ephedrine, a  $\beta$ -agonist that relaxes smooth muscle.” It also contains D-pseudoephedrine, L-methylephedrine, L-norepinephrine, and D-N-methyl pseudoephedrine.

Albuterol, for instance, could attenuate the ma huang side effects, which include increased heart rate, increased blood pressure, palpitations, nervousness, headache, insomnia, and dizziness.

Ginkgo biloba is commonly used in Europe for asthma, Dr. Doyle said. It is an expectorant and bronchodilator, and a treatment for coughing and wheezing when combined with *Ephedra*, apricot seed, and *Morus alba* root. The leaf extract contains ginkgetin, which inhibits histamine-induced bronchoconstriction.

Panax ginseng, also known as Korean ginseng, “tonifies the lungs” and is said to enhance qi; it is used to treat wheezing, shortness of breath, and dyspnea on exertion, Dr. Doyle said. The root is used for cough, and the leaves are used as emetics and expectorants. Animal studies

show ginseng is an anti-inflammatory that decreases IgE serum levels.

Although Hispanic people come from different countries and backgrounds, they share some common medical beliefs. Religion, faith, and spiritual healing are an integral part of their health and well-being, Dr. Doyle said. Opposing properties of illness and treatment are another common tenet so that a “cold” disease, such as asthma, is treated with “hot” remedies, she said.

Unconventional Hispanic treatments are sometimes administered in combination as “zumas” or syrup mixtures. For example, the Siete Jarabes (Seven Syrups) contain honey syrup, sweet almond oil, castor oil, wild cherry, licorice, honey, and cocillana (a bark used for bronchitis). Because of the honey components, Dr. Doyle asked, “Wouldn’t you want to know if a 3-year-old is getting sick on this?”

African/Caribbean therapies include the consumption of raw onion to treat asthma, chest colds, and persistent cough. Onion, or *Allium cepa*, contains quercetin, an anti-inflammatory used for allergic rhinitis.

The understanding and acceptance of nonconventional therapies can go a long way to help patients. “It would be nice for us to return to our mission as physicians,” Dr. Doyle said, quoting Dr. Harold S. Jenkins: “The truly competent physician is the one who sits down, senses the ‘mystery’ of another human being, and offers with an open hand the simple gifts of personal interest and understanding” (JAMA 2002;287:161-2). ■