

## When are antibiotics indicated for acute COPD exacerbations?

### EVIDENCE-BASED ANSWER

Antibiotics (including those given orally) reduce mortality and treatment failures for hospitalized patients with acute exacerbations of chronic obstructive pulmonary disease (COPD) (strength of

recommendation [SOR]: **A**, based on systematic reviews). Antibiotics may be prescribed in the outpatient setting for those with severe exacerbations (SOR: **C**, based on expert opinion).

### CLINICAL COMMENTARY

#### Antibiotics are indicated in COPD exacerbations requiring hospitalization

In an era when physicians aim to use antibiotics judiciously, this article clarifies that antibiotics are indicated in COPD exacerbations requiring hospitalization. In the outpatient setting, the correct action is less clear. Available guidelines, which

recommend antibiotics for severe exacerbations, do not generally differentiate between the inpatient and outpatient setting. Antibiotics clearly have no role in mild exacerbations and so should be avoided in many outpatient cases.

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### Evidence summary

A recent Cochrane review identified 11 randomized controlled trials (RCTs) (with a total of 917 patients) addressing antibiotic therapy for COPD exacerbations characterized by 1 or more of the following: an increase in sputum purulence or volume, dyspnea, wheezing, chest tightness, or fluid retention.<sup>1</sup> Eight trials were conducted on hospital wards, 1 was in a medical intensive care unit, and 2 trials were in the outpatient setting. Antibiotics were given orally in 9 of the 11 studies.

Overall, antibiotics reduced risk of short-term mortality by 77% (relative risk [RR]=0.23; 95% confidence interval [CI], 0.10–0.52; number needed to treat [NNT]=8), treatment failure by 53% (RR=0.47; 95% CI, 0.36–0.62; NNT=3),

and sputum purulence by 44% (RR=0.56; 95% CI, 0.41–0.77; NNT=8). A subgroup analysis that excluded the outpatient and intensive-care unit studies did not change the result. Another subgroup analysis of the 2 outpatient studies failed to find a significant effect, although the studies had very different designs.

These findings are more robust than those of an earlier, lower-quality meta-analysis of 9 randomized controlled trials (RCTs) with 1101 patients with presumed COPD, which also compared antibiotic therapy with placebo for acute exacerbations.<sup>2</sup> Specific diagnostic criteria were not stated for the diagnosis of either COPD or an acute exacerbation. No single outcome measure was common to all studies. The authors found a summary beneficial effect

**FAST TRACK**

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size of antibiotic therapy of 0.22 (95% CI, 0.10–0.34), which is generally interpreted as small. One clinical parameter, peak expiratory flow rate (PEFR), was reported in 6 of the studies. Antibiotic therapy resulted in an average 10.75 L/min improvement in PEFR compared with placebo (95% CI, 4.96–16.54 L/min).

Two RCTs addressing antibiotic use in the outpatient setting were identified in the Cochrane review. One double-blind cross-over trial performed in Canada compared antibiotic with placebo therapy for 173 outpatients with 362 exacerbations classified according to severity.<sup>3</sup> The protocol used oral trimethoprim-sulfamethoxazole, amoxicillin, or doxycycline (according to the attending physician's preference) or a look-alike placebo. Symptom resolution was seen by 21 days in 68% of antibiotic users vs 55% of those on placebo ( $P < .01$ , NNT=8). Ten percent of patients taking antibiotics deteriorated to the point where hospitalization or unblinding of the therapy was necessary, compared with 19% in the placebo group ( $P < .05$ , NNT=11).

For patients with all 3 cardinal COPD symptoms (increased dyspnea, sputum production, and sputum purulence) at enrollment, there was resolution at 21 days in 63% with antibiotics vs 43% for placebo ( $P$  value not given). Antibiotics did not benefit patients with 1 cardinal symptom (74% success with antibiotics vs 70% on placebo;  $P$  value not given).

The Cochrane review also identified a Danish RCT that studied 278 patients presenting to their general practitioners with subjective acute worsening of their COPD. Patients were randomized to 7 days of oral amoxicillin or placebo. There was no difference between the groups in terms of symptom resolution at 1 week (odds ratio=1.03, favoring placebo; 95% CI, 0.75–1.41) or in changes in PEFR (weighted mean difference = -0.89, favoring placebo; 95% CI, -29 to 27 L/min).

**Recommendations from others**

The Veterans Health Administration recommends antibiotics if a patient with

COPD has changes in sputum volume or quality as well as increased dyspnea, cough, or fever; infiltrate on x-ray suggesting pneumonia should be treated as such.<sup>4</sup>

The American College of Chest Physicians recommends that with severe COPD exacerbations, narrow spectrum antibiotics are reasonable first-line agents.<sup>5</sup> They also note that the superiority of newer, more broad-spectrum antibiotics has not been established.

**REFERENCES**

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