What is the best macrolide for atypical pneumonia?

EVIDENCE-BASED ANSWER

Erythromycin, clarithromycin, and azithromycin are equally effective in treating pneumonia caused by *Mycoplasma pneumoniae* or *Chlamydophila* (formerly *Chlamydia*) *pneumoniae* (strength of recommendation [SOR]: **B**, small head-to-head trials). Macrolide choice can be based on other considerations—cost, side effects, and effectiveness against other suspected pathogens (SOR: **C**, expert opinion).

EVIDENCE SUMMARY

M pneumoniae and *C pneumoniae* account for about 30% of community-acquired pneumonia (CAP), making them the most common "atypicals." Clinically they are indistinguishable from other causes of pneumonia; most studies use cultures to identify cases among populations with CAP.

Azithromycin and erythromycin were compared in 3 studies of children with CAP.[1–3] Together, they identified 69 cases due to *M pneumoniae* or *C pneumoniae*. Only 3 patients did not respond to either antibiotic. In the largest of the 3 studies,[3] side effects were noted in 10% of CAP patients on azithromycin and 20% on erythromycin ($P<.05$).

Another study looked at patients aged 12 to 80 years with pneumonia due to *M pneumoniae* (75 cases) or *Chlamydophila psittaci* (formerly *Chlamydia psittaci*, 16 cases).[4] All patients responded to treatment. Clarithromycin and erythromycin were compared in children aged 3 to 12 years with CAP.[5] *M pneumoniae* or *C pneumoniae* was identified in 42 cases. Two of 18 patients did not respond to erythromycin; 3 of 27 patients did not respond to clarithromycin.

Another study compared these antibiotics for patients with CAP aged 12 to 93 years.[6] Subgroup analysis of those with *M pneumoniae* or *C pneumoniae* (n=27) showed similar efficacy. Pooling all 268 patients with CAP, side effects were seen in 31% of patients on clarithromycin and 59% on erythromycin ($P<.001$).

A comparison study of newer macrolides in 40 adults with CAP identified 13 with *M pneumoniae* or *C pneumoniae* (**Table**).[7] One patient did not respond of the 8 treated with clarithromycin; none among the 5 treated with azithromycin. There was 1 adverse event (from clarithromycin).

RECOMMENDATIONS FROM OTHERS

The Infectious Diseases Society of America[8] recommends a macrolide for adults with pneumonia caused by *M pneumoniae* or *C pneumoniae*, and does not promote one over another. The British Thoracic Society[9] recommends any of the macrolides for pneumonia caused by these pathogens in children.

Since CAP is often caused by "atypical organisms," macrolides are sometimes recommended as empiric outpatient therapy. In this setting, the American Thoracic Society[10] discourages using erythromycin, citing a higher side-effect rate and poorer effectiveness against *Haemophilus influenza*. However, the Canadian Infectious Disease Society[11] supports the use of any of the 3 macrolides in mild CAP except for patients with chronic obstructive pulmonary disease, who are more likely to harbor *H influenza*.

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TABLE

Macrolides: comparison studies

Antibiotic	Response rates* (%)	Side-effect rates† (%)	Cost for course of therapy in adult‡
Erythromycin[1–4]	77–100	10–59	$11 (500 mg #40)
Clarithromycin[5–7]	88–94	5–31	$76 (250 mg #20)
Azithromycin[1–4,7]	87–100	0–14	$57 (250 mg #6)

*Response rates of pneumonia due to *M pneumoniae* and *C pneumoniae*.
† In community-acquired pneumonia treated with macrolide as single agent.
‡ Prices from www.drugstore.com.

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CLINICAL COMMENTARY

Lower respiratory infections—a number of problematic decisions

You face several problematic decisions when treating a patient with a lower respiratory infection. First, is this pneumonia or just bronchitis? Clinical findings can be confusing, and a chest film is helpful.[12] If pneumonia is likely, you consider hospitalization, and prescribe antibiotics, usually without knowing the pathogen.

Because they cover both typical and atypical pathogens, macrolides (or doxycycline) are generally recommended, with cephalosporins to be added for higher-risk patients. (Quinolones are an alternative to this combination.) Finally, if you choose a macrolide, you face yet another decision without a clear answer: which one to use? All macrolides appear to be equally effective, so the choice depends on cost balanced against convenience and side effects.

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Does warfarin prevent deep venous thrombosis in high-risk patients?

EVIDENCE-BASED ANSWER

Warfarin (Coumadin) is effective in preventing deep venous thrombosis (DVT) among patients with a history of DVT. Conventional dosing and longer durations are the most effective, but the ideal length of therapy is unknown (strength of recommendation [SOR]: **A**, based on large randomized controlled trials and meta-analysis).

Warfarin is useful in preventing DVT in patients with cancer, specifically those treated with chemotherapy (SOR: **B**, based on small randomized

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