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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controlled trials). Warfarin may be effective in preventing DVT in immobilized patients such as those with trauma, spinal cord injury, or stroke (SOR: **B**, based on an underpowered randomized controlled trial and uncontrolled studies).

EVIDENCE SUMMARY

Warfarin, at both low and conventional doses, has been shown to be effective in preventing recurrence of DVT. A large, 4-year placebo-controlled randomized controlled trial showed that long-term low-dose warfarin (international normalized ratio [INR], 1.5–1.9) was more effective than placebo for prevention of DVT (hazard ratio=0.36; 95% confidence interval [CI], 0.19–0.67).[1]

A double-blind randomized controlled trial of 738 patients demonstrated that conventional-intensity warfarin therapy (INR=2.0–3.0) was more effective than low-intensity therapy (INR=1.5–1.9) in prevention of recurrent DVT. There were 1.9 vs 0.7 DVTs per 100 person-years in the low-intensity vs conventional-intensity therapy groups (hazard ratio=2.8; 95% CI, 1.1–7.0; number needed to treat [NNT]=37). No significant difference was seen in the frequency of bleeding complications between the groups.[2] This and other studies suggest that low-intensity warfarin therapy reduces the relative risk of thrombosis by about 75%, and conventional-intensity therapy reduces this risk by over 90%.[2]

Several studies have examined the duration of warfarin therapy. A meta-analysis found treatment with warfarin for 12 to 24 weeks decreased DVT recurrence compared with 2- to 6-week regimens (relative risk [RR]=0.60; 95% CI, 0.45–0.79; NNT=21).[3] A multicenter randomized controlled trial found extending warfarin treatment for 12 months vs 3 months resulted in a 95% relative risk reduction (RRR) in risk of DVT recurrence (95% CI, 63–99; NNT=5).[4] A multicenter randomized trial showed similar results, but risk for recurrence was the same after treatment was stopped, regardless of the length of treatment.[5]

In patients with cancer, warfarin was shown to be more effective than placebo in prevention of DVT. In a trial of 311 breast cancer patients receiving chemotherapy, treatment with very-low-dose warfarin (INR=1.3–1.9) decreased thrombotic events compared with placebo, with no increase in bleeding complications (RRR=85%; *P*=.031; NNT=27).[6] A later cost analysis showed that very-low-dose warfarin can be used in prevention of DVT in breast cancer patients on chemotherapy without an increase in health care costs.[7]

Although immobilized patients are at high risk for DVT, no randomized controlled trials exist for the use of warfarin in these patients. A few small studies suggest that warfarin reduces DVT rates in spinal-cord-injured patients.[8] A small trial randomized stroke patients undergoing rehabilitation to placebo or fixed 1- or 2-mg doses of warfarin. This underpowered study showed a nonsignificant decrease in the risk of development of DVT (RR=0.39; 95% CI, 0.13–1.37).[8]

RECOMMENDATIONS FROM OTHERS

The 6th American College of Chest Physicians Consensus Conference on Antithrombotic Therapy makes these recommendations:[9]

Prior DVT: Oral anticoagulation therapy (INR=2.0–3.0) is indicated for at least 3 months for patients with proximal DVT or for at least 6 months in those with idiopathic proximal vein thrombosis or recurrent venous thrombosis. Indefinite anticoagulation is indicated for patients with more than 1 episode of idiopathic proximal vein thrombosis or pulmonary embolus.

Malignancy: Indefinite anticoagulation (INR=2.0–3.0) is indicated for patients with thrombosis complicating malignancy. Prophylaxis with low-intensity warfarin in ambulatory patients with cancer to prevent initial DVT warrants further study.

Acute spinal cord injuries: Low-molecular-weight heparin or switch to full-dose oral anticoagulation (INR=2.0–3.0) for the duration of the rehabilitation phase.

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CLINICAL COMMENTARY

Routine prophylaxis dramatically reduces DVT cases

I can clearly recall the dramatic reduction in the number of our patients who developed DVT when our orthopedic colleagues embraced routine prophylaxis for the high-risk surgical patients with hip surgery and knee replacements. This answer indicates that we may also be able to reduce the risk of DVT in our high-risk nonsurgical patients with previous DVT or breast cancer. Note that much of the evidence is based on the use of low-dose and very-low-dose warfarin. This may help mitigate our fear of substituting bleeding complications for the prevention of clots.

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Do antibiotics improve outcomes in chronic rhinosinusitis?

EVIDENCE-BASED ANSWER

For children, antibiotics do not appear to improve short-term (3–6 weeks) or long-term (3 months) outcomes of chronic rhinosinusitis (strength of recommendation [SOR]: **A**, randomized controlled trials). No adequate placebo-controlled trials have been performed in adults. Two consensus statements report that 10 to 21 days of antibiotics active against organisms producing beta-lactamase might be beneficial in some cases (SOR: **C**).

EVIDENCE SUMMARY

The American Academy of Otolargynology–Head and Neck Surgery defines chronic rhinosinusitis as the persistence of 2 major or 1 major and 2 minor criteria lasting at least 12 weeks (**Table**).[1] The other categories of rhinosinusitis are acute (symptoms lasting <3 weeks) and subacute (symptoms lasting 3–12 weeks).

Two placebo-controlled trials have evaluated antibiotic treatment of chronic rhinosinusitis in children. In 1 study, 141 children with chronic rhinosinusitis were randomly assigned to 1 of 4 treatment arms: saline nose drops; xylometazoline (Otrivin) drops with oral amoxicillin 3 times daily; surgical drainage; or surgical drainage, amoxicillin 3 times daily and xylometazoline drops.[2] Outcomes were resolution of purulent rhinitis, no purulent drainage on exam, and no abnormalities of maxillary sinus on x-ray. The absence of all 3 findings constituted cure. At 6 weeks there was a non-statistically significant higher resolution in the fourth group, but by 26 weeks the groups were indistinguishable. At 6 weeks, 53%, 50%, 55%, and 79% of each group, respectively, were cured. These results increased to 69%, 74%, 69%, and 64% at 26 weeks.

Another study randomized 79 children with chronic sinusitis to treatment with cefaclor vs placebo following antral washout.[3] Measured

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