Weigh Antibiotic Options for Skin Infections

When selecting a drug, consider safety, efficacy, compliance, cost, and managed care formularies.

BY DAMIAN McNAMARA
Miami Bureau

MIAMI BEACH — There are many options for antibiotic treatment of uncomplicated and complicated skin infections, each with its own advantages and disadvantages, according to a presentation by Richard K. Scher, M.D., at a symposium sponsored by the Florida Society of Dermatology and Dermatologic Surgery.

Major goals of therapy include prompt eradication of the infection, reduction of potential antibiotic resistance, and lower risk of recurrence. Safety, efficacy, cost, compliance, managed care formularies, and community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) are important considerations when individualizing therapy, according to Dr. Scher, professor of clinical dermatology at Columbia University, New York.

Uncomplicated infections affect superficial skin tissue and include furuncles, cellulites, folliculitis, simple abscesses, and impetiginous lesions. Complicated infections affect deeper soft tissue or require significant surgery, such as infected ulcers, burns, or major abscesses. Infections are also complicated in the presence of significant underlying disease or if the affected site carries a higher risk for anaerobic or gram-negative infection, such as the rectal area.

Severe atopic dermatitis, poorly controlled diabetes, and patients with kidney failure may be predisposed to skin infections. Other risk factors are leukemia or lymphoma; malnutrition and low serum iron; alcohol abuse; intravenous drug use; and medications including systemic steroids, retinoids, cytotoxic agents, and immunosuppressants.

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Dr. Scher discussed these options for treating skin structure infections:

► **Cephalosporins.** These drugs have good tolerability and good sensitivity. The risk of hypersensitivity is low, probably less than 2%, for a patient with a history of nonanaphylactic penicillin allergy.

First-generation drugs in this class include cephalexin and cefadroxil. They have good activity against *S. pyogenes* and MRSA. Dosing is t.i.d. to q.i.d.

Second-generation cephalosporins include cefaclor and cefuroxime,which have expanded activity against gram-negative bacteria and a longer half-life than the first-generation drugs. Dosing is b.i.d.

Third-generation agents include cefixime and ceftibuten. They are good for gram-negative organisms but not as good for gram-positive bacteria, Dr. Scher noted. Dosing is once daily or b.i.d.

Extended-spectrum cephalosporins include cefdinir and cefpodoxime, which are active against gram-negative and gram-positive bacteria. Cefdinir is administered b.i.d.

► **Penicillins.** *S. pyogenes* is always sensitive to treatment with penicillins, but because of cross resistance from MRSA, *S. aureus* is no longer sensitive. Drugs in this class that are β-lactamase stable exhibit good antistaphylococcal activity. Most dosing is t.i.d. or q.i.d.

► **Macrolides.** These drugs include erythromycin, clarithromycin, and azithromycin. They are less likely to be used because of concerns about resistance, Dr. Scher said. Increasing resistance to *S. pyogenes* and *S. aureus* have been reported.

► **Tetracyclines.** The tetracyclines have some coverage for community-acquired MRSA. However, there are some resistance issues, and these agents can discolor childrens' teeth and cause photosensitivity.

► **Fluoroquinolones.** These drugs have a long half-life, and early studies suggest they are as efficacious as β-lactams for erysipelas, cellulitis, impetigo, surgical wounds, and diabetic foot infections. However, resistance is increasing. Possible adverse effects include tendonitis and tendon rupture in adults. They are contraindicated in pediatric patients.

► **Lincosamides.** Clindamycin has good activity against *S. pyogenes* and methicillin-susceptible strains of *S. aureus*. It is also active against some MRSA strains. Resistance to erythromycin could signal inducible resistance to clindamycin, Dr. Scher said. A higher risk of pseudomembranous colitis is associated with *Clostridium difficile*. Dosing is t.i.d.

► **Trimethoprim-sulfamethoxazole.** This combination covers some community-acquired MRSA infections. There is some resistance among staphylococci and no coverage for streptococci. Possible adverse reactions include rash and photosensitivity.

Factors that may alter antimicrobial decision making include emerging macrolide resistance among the β-hemolytic or viridans-group streptococci, Dr. Scher noted. Community-acquired MRSA might also be resistant to β-lactams, macrolides, and quinolones, further limiting choices. ■

Combination Drug Therapy Is Best for Crusted Scabies

BY SHERRY BOSCHERT
San Francisco Bureau

KOHALA COAST, HAWAII — Attack hyperkeratotic scabies both topically and systemically or your treatment will fail, Timothy G. Berger, M.D., said at a conference on clinical dermatology sponsored by the Center for Bio-Medical Communications Inc.

He divides patients with scabies into two categories to guide management—those with a low burden or a high burden of disease. For the typical patient with a low burden, two applications of permethrin 5% cream a week apart will cure 95% of cases.

But a double whammy usually is needed for patients with a high burden of disease—those with crusted or hyperkeratotic scabies, AIDS and scabies, or scabies acquired while in a long-term care facility or prison, said Dr. Berger of the University of California, San Francisco.

He prefers to use these two categories because patients with a high burden of disease may present with multiple papules instead of crusts, but need the combination therapy used for crusted scabies.

The combination treatment consists of weekly applications of permethrin 5% cream for 3-6 weeks plus ivermectin 200 mcg/kg every 2 weeks for two (or occasionally three) doses. The patient should show improvement by 3 weeks into treatment and continue to gradually improve.

Don't try to save a buck by skimping on the ivermectin, he warned. Don't round down the dose but, rather, give the full dose of ivermectin (usually 12-18 mg), and allow plenty of time to treat. "Every time it has failed, I've undertreated," Dr. Berger said. In appropriate doses, the combination therapy has never failed him.

Don't be dissuaded from suspecting scabies just because a patient has failed permethrin treatment or family members seem unaffected, Dr. Berger advised.

Treat the whole family, but not necessarily immediately. Family members who are affected get immediate treatment, but otherwise Dr. Berger waits to treat the family until the primary patient has been treated, so that the patient is no longer infectious.

High-burden cases often involve the scalp, so instruct patients to apply permethrin to the scalp too, he advised. Ivermectin won't help scabies involving the nail plate, so consider more aggressive treatments for nail scabies.

Ivermectin is secreted in sebum, he noted, which is one reason monotherapy may not work in the elderly, children, malnourished patients, or people with Down syndrome, all of whom make less sebum.

Immunosuppression plus neural disease puts patients at risk for crusted scabies, one reason that people with AIDS or Down syndrome are at higher risk for crusted scabies, he said. ■

High-Dose Valacyclovir Reduces Shedding of Oral Herpes Virus

BY PATRICE WENDLING
Chicago Bureau

NEW ORLEANS — Treatment with once-daily, high-dose valacyclovir caplets significantly decreases the duration and quantity of oral herpes simplex virus-1 shedding associated with recurrent herpes labialis, according to data from a randomized study.

Oral shedding, either associated with known outbreaks of herpes labialis or, perhaps more importantly, during asymptomatic periods, is the presumed mechanism for transmission of herpes simplex virus-1 (HSV-1), Stan C. Gilbert, M.D., said in a poster presentation at the annual meeting of the American Academy of Dermatology.

Patients receiving valacyclovir shed HSV-1 virus for fewer days than did the placebo group (1.8 vs. 4 days).

DR. GILBERT

HSV-1 causes gingivostomatitis in infants and children and recurrent cold sores in most people. It also has become the primary cause of most genital herpes cases in young adults. Recurrent herpes labialis (RHL) is seen in up to 40% of HSV-1–seropositive adults.

Research has shown oral shedding associated with episodes of RHL lasting from 1 to 8 days. But the studies are rare and have relied mostly on viral cultures, according to Dr. Gilbert, of the University of Washington, Seattle.

Dr. Gilbert's study randomized 64 adults with a history of three or more RHL episodes a year to four 500-mg valacyclovir (Valtrex) caplets taken at the first sign of an outbreak or placebo. The dosing was repeated 12 hours later. PCR swabs were collected every 12 hours starting at the first sign of outbreak and continuing for 10 days.

Both groups had a history of cold sores for an average of 28 years and an average of four cold sores in the previous 12 months.

Patients receiving valacyclovir experienced fewer days on which shedding occurred than the placebo group (1.8 vs. 4 days). A comparison of the log HSV-1 DNA copies detected by PCR over time, using the average area under the curve (AUC), showed significantly less shedding from the treatment group than from the placebo group (mean AUC 1.1 vs. 2.2).

Dr. Gilbert is a member of the speakers' bureau for GlaxoSmithKline, which manufactures Valtrex and provided 50% of the funding for the study. ■