

Community-Acquired MRSA Spread Detailed

BY TIMOTHY F. KIRN
Sacramento Bureau

ASPEN, COLO. — In Dallas, by the time the infectious disease specialists found out they had a problem with community-acquired methicillin-resistant *Staphylococcus aureus*, it already comprised one-third of staphylococcal infections, Dr. Sheldon L. Kaplan said at a conference on pediatric infectious diseases sponsored by Children's Hospital, Denver.

In a round-up talk about the present situation with community-acquired methicillin-resistant *S. aureus* (MRSA), Dr. Kaplan, the chief of infectious diseases service at Texas Children's Hospital, Dallas, described how extremely quickly it has spread—in this country and worldwide.

"I don't think we are really going to control [MRSA] unless we have a vaccine," Dr. Kaplan said.

At Texas Children's Hospital, the infectious disease specialists didn't pay much at-

tention to community-acquired MRSA until 2000 when they started noticing more cases.

By that time—in February of that year—MRSA already made up about one-third of community-acquired staphylococcal infections seen at the hospital's emergency center. By November, it represented 50%. Currently, it is about 77%, Dr. Kaplan said.

About 15% of the cases annually are in children less than 1 year of age, 15% are children in the second year of life, and about 20% are in patients 10 years or older.

Ninety-six percent of the cases at the hospital are associated with skin and soft tissue infections.

Nonetheless, 62% of all community-acquired MRSA cases seen are then hospitalized. That compares with 52% of the community-acquired methicillin-susceptible infections seen.

The average duration of hospitalization is 4 days.

Dr. Kaplan also noted that they are seeing increasing numbers of staphylococcal infections in normal, healthy infants in the first 30 days of life, and almost all of these cases are MRSA.

In the United States, the most common strain is one known as USA300. In 2003, 96% of MRSA isolates at Texas Children's were USA300. "This USA300 [strain], once it comes into a community, appears to take over," Dr. Kaplan said.

The genetic sequence of USA300 recently has been published, and that sequence has shown that USA300 has incorporated certain genetic elements of *S. epidermidis*. Those elements, which could confer a better ability to colonize skin, may explain why this USA300 clone has been able to spread through communities so quickly.

Fortunately, the USA300 strain has not

been found to produce the toxins associated with toxic shock syndrome, Dr. Kaplan added.

There is little good guidance on best antibiotic treatment of these community-acquired MRSA infections, Dr. Kaplan said.

One study found that long-acting tetracyclines are 90%-100% effective in treating skin and soft tissue infections, although they may not be for more serious infections.

Moreover, virtually all community-acquired MRSA associated with skin and soft tissue infection is susceptible to trimethoprim-sulfamethoxazole.

Therefore, at Texas Children's, the recommendation is to use trimethoprim-sulfamethoxazole as the first-line treatment for these infections.

That said, a survey of practice at the hospital found it was never used first line by any of the doctors, Dr. Kaplan said.

Several other studies have shown that the effective treatment for skin and soft tissue infection is surgical drainage and that the choice of antibiotic therapy makes little difference.

One study in particular showed that when an abscess was 5 cm or less in diameter, antibiotic choice made no difference in outcome, although it is not known whether ineffective or less-effective antibiotic treatment is associated with recurrence, Dr. Kaplan said.

Clindamycin resistance among community-acquired MRSA is not yet a big problem at Texas Children's, because the rate appears to be about 7% presently. However, clindamycin resistance there, and everywhere, is increasing, and in some places in this country may run as high as a rate of 30%.

"You have to know what is going on in your area," Dr. Kaplan said. ■



'I don't think we are really going to control [MRSA] unless we have a vaccine.'

DR. KAPLAN

Vigamox®

(moxifloxacin hydrochloride ophthalmic solution) 0.5% as base

DESCRIPTION: VIGAMOX® (moxifloxacin HCl ophthalmic solution) 0.5% is a sterile ophthalmic solution. It is an 8-methoxy fluoroquinolone anti-infective for topical ophthalmic use.

Clinical Studies: In two randomized, double-masked, multicenter, controlled clinical trials in which patients were dosed 3 times a day for 4 days, VIGAMOX® solution produced clinical cures on day 5-6 in 66% to 69% of patients treated for bacterial conjunctivitis. Microbiological success rates for the eradication of the baseline pathogens ranged from 84% to 94%. Please note that microbiologic eradication does not always correlate with clinical outcome in anti-infective trials.

INDICATIONS AND USAGE: VIGAMOX® solution is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:

Aerobic Gram-positive microorganisms:

*Corynebacterium species**, *Micrococcus luteus**, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Staphylococcus hominis*, *Staphylococcus warneri**, *Streptococcus pneumoniae*, *Streptococcus viridans* group

Aerobic Gram-negative microorganisms:

*Acinetobacter lwoffii**, *Haemophilus influenzae*, *Haemophilus parainfluenzae**

Other microorganisms:

Chlamydia trachomatis

*Efficacy for this organism was studied in fewer than 10 infections.

CONTRAINDICATIONS: VIGAMOX® (moxifloxacin HCl ophthalmic solution) is contraindicated in patients with a history of hypersensitivity to moxifloxacin, to other quinolones, or to any of the components in this medication.

WARNINGS: NOT FOR INJECTION.

VIGAMOX® solution should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye. In patients receiving systemically administered quinolones, including moxifloxacin, serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported, some following the first dose. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial edema), airway obstruction, dyspnea, urticaria, and itching. If an allergic reaction to moxifloxacin occurs, discontinue use of the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

PRECAUTIONS: General: As with other anti-infectives, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue use and institute alternative therapy. Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit-lamp biomicroscopy, and, where appropriate, fluorescein staining. Patients should be advised not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis.

Information for Patients: Avoid contaminating the applicator tip with material from the eye, fingers or other source.

Systemically administered quinolones including moxifloxacin have been associated with hypersensitivity reactions, even following a single dose. Discontinue use immediately and contact your physician at the first sign of a rash or allergic reaction.

Drug Interactions: Drug-drug interaction studies have not been conducted with VIGAMOX® solution. *In vitro* studies indicate that moxifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19, or CYP1A2 indicating that moxifloxacin is unlikely to alter the pharmacokinetics of drugs metabolized by these cytochrome P450 isozymes.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals to determine the carcinogenic potential of moxifloxacin have not been performed. However, in an accelerated study with initiators and promoters, moxifloxacin was not carcinogenic in rats following up to 38 weeks of oral dosing at 500 mg/kg/day (approximately 21,700 times the highest recommended total daily human ophthalmic dose for a 50 kg person, on a mg/kg basis). Moxifloxacin was not mutagenic in four bacterial strains used in the Ames *Salmonella* reversion assay. As with other quinolones, the positive response observed with moxifloxacin in strain TA 102 using the same assay may be due to the inhibition of DNA gyrase. Moxifloxacin was not mutagenic in the CHO/HGPRT mammalian cell gene mutation assay. An equivocal result was obtained in the same assay when v79 cells were used. Moxifloxacin was clastogenic in the v79 chromosome aberration assay, but it did not induce unscheduled DNA synthesis in cultured rat hepatocytes. There was no evidence of genotoxicity *in vivo* in a micronucleus test or a dominant lethal test in mice.

Moxifloxacin had no effect on fertility in male and female rats at oral doses as high as 500 mg/kg/day, approximately 21,700 times the highest recommended total daily human ophthalmic dose. At 500 mg/kg orally, there were slight effects on sperm morphology (head-tail separation) in male rats and on the estrous cycle in female rats.

Pregnancy:

Teratogenic Effects. Pregnancy Category C: Moxifloxacin was not teratogenic when administered to pregnant rats during organogenesis at oral doses as high as 500 mg/kg/day (approximately 21,700 times the highest recommended total daily human ophthalmic dose); however, decreased fetal body weights and slightly delayed fetal skeletal development were observed. There was no evidence of teratogenicity when pregnant Cynomolgus monkeys were given oral doses as high as 100 mg/kg/day (approximately 4,300 times the highest recommended total daily human ophthalmic dose). An increased incidence of smaller fetuses was observed at 100 mg/kg/day.

Since there are no adequate and well-controlled studies in pregnant women, VIGAMOX® solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Moxifloxacin has not been measured in human milk, although it can be presumed to be excreted in human milk. Caution should be exercised when VIGAMOX® solution is administered to a nursing mother.

Pediatric Use: The safety and effectiveness of VIGAMOX® solution in infants below 1 year of age have not been established.

There is no evidence that the ophthalmic administration of VIGAMOX® has any effect on weight bearing joints, even though oral administration of some quinolones has been shown to cause arthropathy in immature animals.

Geriatric Use: No overall differences in safety and effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS: The most frequently reported ocular adverse events were conjunctivitis, decreased visual acuity, dry eye, keratitis, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, subconjunctival hemorrhage, and tearing. These events occurred in approximately 1-6% of patients. Nonocular adverse events reported at a rate of 1-4% were fever, increased cough, infection, otitis media, pharyngitis, rash, and rhinitis.

Reference:

1. Data on file. Alcon Laboratories, Inc. 2005.

Rx Only
Manufactured by
Alcon Laboratories, Inc.
Fort Worth, Texas 76134 USA
Licensed from Bayer AG to Alcon, Inc.
U.S. PAT. NO. 4,990,517; 5,607,942; 6,716,830
©2003 Alcon, Inc.

Suspect Chronic Varicella Zoster in Immunocompromised Children

SAN FRANCISCO — Suspect chronic varicella zoster in all immunocompromised children, not just those with HIV, Dr. Christopher Bohyer said at the annual meeting of the American Academy of Dermatology.

Test zosterlike lesions in immunocompromised children for drug resistance, because chronic varicella typically implies antibiotic resistance, said Dr. Bohyer of Indiana University, Bloomington.

He presented what may be the first case of chronic varicella zoster in a child after bone marrow transplant. Other cases have been reported in children who have undergone chemotherapy or who have HIV. Dr. Bohyer's patient was an 11-year-old boy who was diagnosed in 2003 with acute myelogenous leukemia and was treated with chemotherapy. He relapsed in April

2004, who underwent donor stem cell transplant as treatment for acute myelogenous leukemia, and developed acute graft-versus-host disease. After the boy left the hospital, in September 2004 he developed abdominal pain. An eruption on his head and neck was identified as varicella zoster infection, and he was treated with high-dose IV acyclovir.

The patient went home but was readmitted with another unusual cutaneous eruption on his whole body. The vesicles and papules housed varicella zoster, culture showed. Another round of high-dose acyclovir stemmed the eruption of any new lesions, but the chronic lesions did not resolve. At this time the patient's condition deteriorated so much that support was withdrawn, and he died.

—Sherry Boschert