

Antibiotic Exit Strategy Can Reduce Resistance

BY BETSY BATES
Los Angeles Bureau

SANTA BARBARA, CALIF. — Tetracyclines may wind up being the safest, cheapest, easiest-to-tolerate nonintravenous drugs available to treat future cases of methicillin-resistant *Staphylococcus aureus* (MRSA), and that should be reason enough to get on the bandwagon to preserve tetracycline's potency through wise use, according to one dermatologist.

"I view the tetracyclines as the drugs I would like to save ... for the future," Dr. Hilary Baldwin said at the annual meeting of the California Society of Dermatology and Dermatologic Surgery.

Dermatologic prescribing of antibiotics for acne and rosacea, as well as for skin infections, may be driving resistance in unexpected ways, suggested



Dr. Baldwin of the State University of New York, Brooklyn.

"The message is getting out to dermatologists and nondermatologists that antibiotic resistance is here, it's now, and we have to worry about it," she said.

Her strategy has been to "utilize antibiotics when necessary, but devise an exit strategy on day 1."

For example, she may prescribe a topical retinoid, hormonal therapy, or an androgen receptor blocker alongside an antibiotic, so that the time clock will begin ticking right away for nonantibiotic workhorses that don't necessarily act quickly.

By the time a topical retinoid really is beginning to take hold—at about 12 weeks—the antibiotic will have produced quick, patient-pleasing results and can be discontinued.

"On the day you stop topical or oral antibiotics [while continuing the alternative medication], also start benzoyl peroxide," she advised.

Even though it is bactericidal, no resistance develops in response to benzoyl peroxide, she said.

"What I don't think people worry about are topical antibiotics," she said, noting that the timing of serious resistance problems coincides with the introduction of topical erythromycin and clindamycin.

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DR. BALDWIN

More specific evidence arrived in 2003 with a disturbing study showing tetracycline-resistant *Streptococcus pyogenes* in the throats of 85% of long-term users of topical or oral antibiotics, com-

pared with 20% of controls (Arch. Dermatol. 2003;139:467-71).

Another study looked retrospectively at the charts of 118,496 patients, finding that patients who had received 6 weeks or more of topical or systemic antibiotics were at more than a twofold risk of upper respiratory infections (Arch. Dermatol. 2005;141:1132-6).

"The issue is bigger than [*Propionibacterium acnes* resistance or upper respiratory infections," Dr. Baldwin said. "The whole thing ends up being a story of more severe organisms and MRSA."

Community-acquired MRSA is increasingly familiar to dermatologists,

Antibiotic Choices for MRSA Reviewed

Currently Available Antibiotics

Tetracyclines: Cover 80% of MRSA.

Penicillins/cephalosporins: Ineffective against MRSA.

Trimethoprim-sulfamethoxazole: Reasonable, cheap; sufficient to cover most MRSA but not *Streptococcus*.

Fluoroquinolones (ciprofloxacin, levofloxacin, etc.): Promote emergence of MRSA.

Lincosamides (clindamycin): Resistance is growing. Covers some MRSA, but resistance to erythromycin may signal resistance to clindamycin as well, even if culture suggests sensitivity.

Glycopeptides (vancomycin): Resistance is increasing. Requires intravenous dosing. Not effective for many serious infections.

Streptogramins: Effective, but require intravenous dosing. They are very expensive and have major adverse effects.

Oxazolidinones (linezolid, etc.): Oral, but very expensive, with significant adverse effects. Resistance is developing.

Daptomycin: Intravenous only, but very effective for skin/soft-tissue infections.

Tigecycline: The newest antibiotic is intravenous only, but very effective.

Drugs on the Horizon

Dalbavancin: Pfizer withdrew the application of this once-weekly injectable pending further study.

Telavancin: The application of this injectable has been delayed indefinitely by the Food and Drug Administration.

Ceftobiprole: The application of this new cephalosporin has been delayed indefinitely by the FDA.

Oral antibiotics in development for MRSA: none.

Sources: Dr. Baldwin, Dr. Paul Holtom

since it presents as skin and soft-tissue infections in 85% of cases. Abscesses often occur below the waist, and pain is more severe than the clinical appearance of lesions might suggest.

"The treatment is drainage, drainage, drainage," she said, adding that it most often works in the sentinel patient. Contacts at home, especially siblings, may develop severe necrotizing pneumonia and death.

When MRSA does get nasty, "tetracyclines are probably the easiest drugs that we have to treat it," she said. (See box.)

"Do we overprescribe antibiotics? Of course we do," Dr. Baldwin said. Dermatologists write 8-9 million prescriptions a

year for antibiotics and 40%-50% of all prescriptions for tetracyclines.

The reasons are many: not wanting to miss infections, avoiding medicolegal problems, and basically just wanting a quick response to inflammatory conditions such as acne and rosacea. "Sometimes patients just wear us the heck down," she admitted.

Dr. Baldwin disclosed ties with Allergan Inc., Coria Laboratories, Galderma S.A., GlaxoSmithKline, OrthoNeutrogena, Medicis Pharmaceutical Corp., Ranbaxy Pharmaceuticals Inc., Sanofi-Aventis, SkinMedica Inc., and Stiefel Laboratories Inc. ■

Rapid Test Flags *Staph. aureus* and Methicillin Susceptibility

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — A single-use bacteriophage amplification test kit was able to both accurately identify *Staphylococcus aureus* and determine whether it was methicillin sensitive or resistant within 5 hours in a study of clinical bacteremia isolates.

The findings suggest that it is possible not only to slash the diagnostic time for bacteremia—from 2-3 days to 5 hours—but also to obtain rapid results that will guide treatment and prevent overuse of broad-spectrum antibiotics, Dr. J. Drew Smith said in an interview during his poster presentation at the jointly held annual Inter-science Conference on Antimicrobial Agents and Chemotherapy (ICAAC) and the annual meeting of the Infectious Diseases Society of America (IDSA).

The test, made by MicroPhage Inc., uses bacteriophage amplification technology, which detects proteins produced by viruses that are selected to amplify in response to *S. aureus*. Blood culture samples are mixed in two separate tubes and placed in an incubator for 5 hours. The tubes are removed and six drops of each sample are applied to dipstick-type detectors similar to those used in home pregnancy tests.

One tube determines whether or not the sample contains *S. aureus*; the other determines whether the bacteria are antibiotic resistant or susceptible, explained Dr. Smith,

director of research and development at MicroPhage.

In a panel of 120 *S. aureus* clinical isolates and 120 closely related nonpathogenic coagulase-negative staphylococci, the identity test for *S. aureus* had a sensitivity of 93% and a specificity of 96%.

Among the strains identified as *S. aureus*, methicillin susceptibility was determined with 99% sensitivity and 99% specificity. Only 1.8% of samples were falsely identified as methicillin-resistant *S. aureus* (MRSA) and no samples were falsely identified as methicillin sensitive (MSSA), Dr. Smith and his associates reported.

Current polymerase chain reaction (PCR) technology allows for rapid detection of MRSA but doesn't accurately determine susceptibility. With the bacteriophage test, a result indicating MSSA allows for the patient to be safely switched from empiric vancomycin to nafcillin or another conventional β -lactam antibiotic, which are more effective against *S. aureus* than is vancomycin and can reduce mortality by 30%-50% if the organism is susceptible.

The PCR test gives too many false positives for MSSA in order to be used for this purpose, Dr. Smith explained in the interview.

Bacteriophage amplification technology also could be used to prospectively screen patients for MRSA carriage.

In a separate study presented in another poster, nasal swabs were collected from preoperative and ICU patients and were streaked on agar plates for MRSA detection. The swabs were then transferred to MicroPhage tubes, incu-

bated for 7-24 hours, and read in the same way as was done for the bacteremia test. This time, 32 samples were read at 7 and 24 hours and 77 were read at 12-18 hours and again at 18-24 hours. (More time is needed for nasal swabs than blood cultures because fewer bacteria are present, Dr. Smith explained.)

Sensitivity for detecting MRSA nasal carriage was just 33% at 7 hours, but improved to 92% at 12-18 hours and 100% by 18-24 hours. At the same time, there was little loss of specificity, which began at 100% at 7 hours and dropped to 98% only at 12-18 and 18-24 hours. Positive predictive value was 100% at 7 hours, dropping to 88% by 18-24 hours while negative predictive value rose from 94% at 7 hours to 100% at 18-24 hours.

Lab personnel were trained to use the test in less than half an hour, and it required no specialized or dedicated equipment.

Moreover, "the test is flexible with respect to read times, allowing it to be adapted to a variety of testing and reporting schedules," the investigators said.

MicroPhage is hoping to market both uses for the technology to community hospitals and to offer the nasal tests to outpatient settings such as nursing homes or surgical centers.

Clinical testing will begin in early 2009, and the company hopes to obtain licensure from the Food and Drug Administration by late 2009 or early 2010, Dr. Smith said. ■