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*, 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 use 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 necessary 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, adding that even though it is bactericidal, no resistance develops in response to benzoyl peroxide.

"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.

More specific evidence emerged in 2003 with a study showing tetracycline-resistant *Streptococcus pyogenes* in the throats of 85% of long-term users of topical or oral antibiotics, compared with 20% of controls (Arch. Dermatol. 2003;139:467-71).

A retrospective study looked at the charts of 118,496 patients, and found 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, because 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.)

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. ■

Agents in Hand and on the Horizon

Currently Available Antibiotics

Tetracyclines: Cover 80% of MRSA.
Penicillins/cephalosporins: Ineffective.
Trimethoprim-sulfamethoxazole: Reasonable, cheap; sufficient to cover most MRSA but not *Streptococcus.*
Fluoroquinolones: Promote emergence of MRSA.
Lincosamides (clindamycin)**:** Resistance is growing. Covers some MRSA, but resistance to erythromycin may also signal resistance to clindamycin.
Glycopeptides: 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: Oral, but very expensive, with significant adverse effects. Resistance is developing.
Daptomycin: Intravenous only, but 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: FDA has indefinitely delayed the application of this injectable.
Ceftobiprole: The application of this new cephalosporin has been also been delayed indefinitely by the FDA.
Oral antibiotics: none.

Sources: Dr. Baldwin, Dr. Paul Holtom

Office Testing for Infectious Diseases Can Boost Clinical Care

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

BOSTON — Rapid in-office testing for infectious diseases can help physicians get the right drug on board as quickly as possible, and cut down on unnecessary testing and inappropriate antibiotics.

"Having the diagnosis in real time can affect clinical decision making," Dr. Leonard Krilov said at the annual meeting of the American Academy of Pediatrics. "For instance, with rapid influenza testing, it's been shown that doctors who have a confirmed diagnosis from a rapid flu test order fewer unnecessary tests, fewer radiographs, and give out fewer antibiotics and more antiviral drugs."

The only diagnostic tests approved for use in the office setting are those that have been waived by the Clinical Laboratory Improvement Amendments of 1988 (CLIA) law. Waived tests are defined as simple laboratory examinations and procedures that are cleared by the Food and Drug Administration for home use; employ methodologies that are so simple and accurate as to render the likelihood of erroneous results negligible; and pose no reasonable risk of harm to the patient if it's performed incorrectly.

The most common in-office tests for infectious diseases include those for group A streptococcus (GAS), influenza, respiratory syncytial virus (RSV), mononucleosis, and human immunodeficiency virus (HIV), said Dr. Krilov, chief of pediatric infectious diseases at Winthrop University Hospital, Mineola, N.Y.

There are 35 CLIA-waived tests for GAS, with varying ranges of sensitivity and specificity. "Overall, the tests are very specific, ranging from 85% to 100%, but the concern is that the sensitivity is quite variable and can be as low as 62%," Dr. Krilov said.

Because of this, a negative test always requires a backup throat culture for confirmation. On the other hand, "If you get a positive test, you can believe it. There's no need for a culture," he said.

However, even a positive test doesn't mean that the presenting symptoms are because of GAS pharyngitis. "Recovery of group A strep from the pharynx doesn't necessarily distinguish true infection from carriers who might happen to have a coincidental viral pharyngitis. You can't completely rely on the test—you have to be able to interpret the clinical picture as well."

Of the 15 rapid influenza tests available, 3 are waived for office use; they all give results in about 30 minutes. While they are highly specific (90%-95%), the sensitivity isn't great (70%-75%), Dr. Krilov said.

Because of this, "successfully using these is somewhat dependent on the time of year and the likelihood of influenza infection in your community. False positives and true negatives are more likely if prevalence is low, but false negatives and true positives are more likely in the midst of an epidemic. But in the right time of winter, with the right clinical picture, a positive test is both believable and important."

Accuracy also depends on when during the course of illness testing occurs. In children, most of the viral shedding occurs in the first 48 hours. The quality of the specimen is very important as well, Dr. Krilov noted. "The more secretions you get, the more cell material you get, so a nasal wash or aspirate is probably better than a nasopharyngeal swab."

In light of the continued emergence of antibiotic-resistant bacteria, an early, certain diagnosis of viral illness can significantly decrease inappropriate antibiotic prescribing, Dr. Krilov said.

A 2003 study enrolled 391 patients with symptoms of influenza; all had a rapid flu test done in the hospital. Half of the referring physicians were given the results; these doctors ordered significantly fewer lab tests and x-rays and prescribed significantly fewer antibiotics than physicians who didn't know the diagnosis. In addition, Dr. Krilov said, treatment costs and hospital length of stay were significantly lower for patients whose diagnosis was known; the rate of antiviral prescriptions given to these patients also was significantly higher than for those whose diagnosis was not known (Pediatrics 2003;112:363-7).

Most testing for RSV is done in the hospital, but one test is available for office use. It detects RSV fusion protein, and results are available in 15 minutes. The kit has a sensitivity of up to 88% and specificity of up to 100%. "Again, if it's winter and RSV is in the community, you can believe a positive result," he said. "It might be useful in how you monitor the patient, and it's very helpful in preventing unnecessary antibiotic use."

Monospot is the only CLIA-waived test for mononucleosis. Again, accuracy depends on timing, Dr. Krilov said. "A negative test in the first week of illness doesn't mean they don't have the disease. Typically, it isn't until the second week of illness that the heterophile antibodies are made, and they can persist for 6 months or more. So using this test to follow the course of disease, or as a way of determining when kids can go back to school, is not worthwhile."

Children younger than 6 years may not even make the heterophile antibodies, so a negative test on a young child shouldn't affect clinical decision-making, Dr. Krilov said. "The antibodies are detected in up to 85% of older kids and adolescents, but [in] 40% or less of those younger than 4 years. If you have a patient of the appropriate age and symptoms, and the test is negative, treat it as early disease and test again in 1-2 weeks. Or you have the option of sending to the lab for specific serology."

Dr. Krilov also spoke about in-office HIV testing. Two CLIA-waived kits are available and give results in 20 minutes. "It's useful in some clinical settings, since it allows more people to be tested … but they don't give a complete diagnostics, so a positive test must always be confirmed by the Western blot analysis. The other part of HIV testing is, if you do the test, it needs to be done in conjunction with counseling and hooking patients into appropriate follow-up." ■