Atopic Patients May Not Have Higher *S. aureus* Risk

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Patients with atopic dermatitis are highly colonized with *Staphylococcus aureus* but do not appear to be preferentially infected with community-acquired methicillin-resistant *S. aureus*.

Up to 79% of patients with atopic dermatitis have *S. aureus* in their anterior nares, 64%-75% have it on their normal skin, and more than 90% have it on their lesional skin.

In contrast, up to 30% of atopic-free adults have *S. aureus* in their nasal carriage and 10% have it on their skin, Dr. Sheila Fallon Friedlander said at a conference sponsored by Rady Children's Hospital, San Diego.

A reason why patients with atopic dermatitis may have trouble with *S. aureus* is that they appear to lack an adequate number of cathelicidins, said Dr. Friedlander, director of pediatric dermatology at the University of California, San Francisco.

"The end result clinically is that they don't have as much antimicrobial peptide helping to ward off infection. Atopics also have an impaired skin barrier, sometimes as a result of abnormal or decreased filaggrin. With increasing dryness and lack of appropriate adhesion, there is also increased skin surface area for the *S. aureus* to adhere to," she said.

In addition, she said *S. aureus* can elaborate superantigens, "which have the ability to stimulate the production of alternative glucocorticoid receptors. These receptors are more resistant to the effects of steroids. So often when *S. aureus* is present in the skin, there is elaboration of a receptor [that] makes it more difficult for the patient to respond to topical corticosteroid treatment."

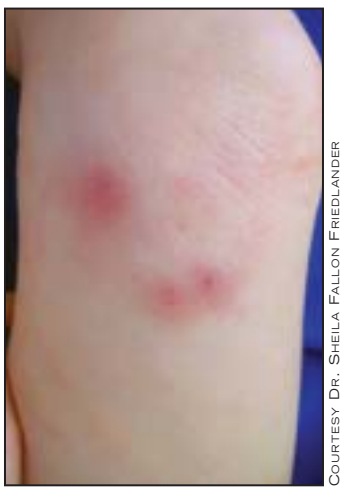
A recent study estimated that 40%-66% of patients with atopic dermatitis develop *S. aureus* skin infections (Pediatr. Derm. 2000;17:111-4). Another concluded that the condition is a risk factor for invasive *S. aureus* infection in this patient population, including bacteremia, osteomyelitis, and endocarditis (Am. J. Med. 2005;118:1048-51).

However, Dr. Friedlander described the link between atopic dermatitis and invasive disease as "a controversial issue" with data that remain unclear.

"In some papers, it appears that there are lower levels of invasive disease in patients with atopic dermatitis," she said. "Invasive disease does occur, but atopics don't seem to be at higher risk for invasive disease. Further studies are required to clarify this issue."

The good news is that patients with atopic dermatitis do not seem to be preferentially affected with community-acquired methicillin-resistant *S. aureus* (CA-MRSA). An estimated 6%-19% of children with atopic dermatitis were found to have the condition (Arch. Dermatol. 2002;138:939-41).

Another group of researchers concluded that the "observed incidence of cutaneous CA-MRSA lesions in patients with atopic dermatitis or other non–intact skin barrier is less than reported in other at-risk groups" (J. Clin. Dermatol. 2007;8:259-70).



COURTESY DR. SHEILA FALLON FRIEDLANDER

This patient's family mistook an MRSA infection for multiple spider bites.

Dr. Friedlander explained that, compared with the hospital-acquired form of MRSA, the community-acquired form is clonal, has many drug options, and has a predilection for skin disease. "It preferentially infects the skin; skin and soft tissue infections are what we see," she said. "But you must remember that you can have invasive disease from this organism."

Clinically, CA-MRSA presents as furuncles or folliculitis 65%-95% of the time. "Parents will say, 'my child keeps getting a spider bite,' " Dr. Friedlander said. Most patients look well, but 40%-50% will have fever.

Most often, CA-MRSA organisms possess Panton-Valentine leukocidin, a virulence factor that is a bicomponent cytotoxin. This virulent toxin "destroys our leukocytes by punching holes in the membrane," she said. "This leads to capillary dilation and significant necrosis."

CA-MRSA also may possess an aberrant fibronectin-binding protein gene, which enables the *S. aureus* "to adhere better to our tissue and therefore enhances invasion."

Incision and drainage alone appears to suffice in CA-MRSA skin and soft tissue lesions smaller than 5 cm. "If a lesion is bigger than that, you need to be aggressive," she said. "Please culture these lesions. In the old days, people used to drain these and throw the exudate away. Do not throw it away because the antibiotic susceptibility patterns differ from the hospital-acquired form, and you may need this information to determine the best therapy for your patient."

Dr. Friedlander often starts patients on clindamycin. However, some organisms may be resistant, and therefore you need to check for inducible resistance in these patients. "Sometimes you need to use trimethoprim/sulfamethoxazole," she said.

"In older children, you can use minocycline or doxycycline, but remember, these drugs can damage the teeth of young children, and I will not use tetracyclines in children less than 8 years of age."

Attempts to eradicate MRSA with various combinations of antibiotics have had mixed results, but recent studies have found the use of bleach baths in combination with nasal mupirocin to be useful.

Dr. Friedlander recommends adding one-quarter of a cup of Clorox to a regular bath and repeating this treatment two times a week. In addition, some experts apply mupirocin ointment twice a day to the nares for 1 week each month.

"If you don't repeat the mupirocin treatment for a week each month, the patient appears more likely to colonize," she said. "There is no absolutely clear superior, evidence-based regimen, but studies are ongoing and we may have some more information in the future."

Control of atopic dermatitis "is the first goal in preventing infection," she pointed out. "If you control the itching and maintain the skin barrier, you are less likely to have the patient self-inoculate with staph or any other organism."

Dr. Friedlander disclosed that she has received grant and research support, honoraria, and/or consulting fees from Barrier Therapeutics Inc., Medicis Pharmaceutical Corp., Sanofi-Aventis, and Stiefel Laboratories Inc. ■

Most Antihistamines Cause Some Cognitive Impairment

BY BRUCE JANCIN
Denver Bureau

KYOTO, JAPAN — Fexofenadine is the sole truly nonsedating antihistamine—and the only one that does not cause objectively measurable cognitive and psychomotor impairment at doses that are commonly used in clinical practice, said Dr. Kazuhiko Yanai.

Fexofenadine (Allegra) is the only antihistamine that doesn't permeate the blood-brain barrier and therefore cannot bind to CNS histamine$_1$ (H_1) receptors, explained Dr. Yanai, professor of pharmacology at Tohoku University, Sendai (Japan), at an international investigative dermatology meeting.

He is credited as a pioneer in utilizing PET scanning to measure brain H_1 occupancy by antihistamines and in demonstrating that this measurement correlates with the degree of cognitive and psychomotor impairment.

Dr. Yanai categorizes antihistamines into three classes: fexofenadine, which does not cross the blood-brain barrier even at supratherapeutic doses; the "less sedating" antihistamines, which occupy roughly 20% or less of available cortical H_1 receptors and are associated with little cognitive impairment at their approved doses; and "more sedating" antihistamines, which bind to 50% or more of brain H_1 receptors at recommended doses.

The first-generation antihistamines belong in the more sedating category. The prototype is ketotifen, which Dr. Yanai called "the most sedating antihistamine ever made." He has shown that a 1-mg oral dose of ketotifen results in a 72% brain H_1 occupancy rate (Br. J. Clin. Pharmacol. 2006;61:16-26).

Second-generation antihistamines, with the exception of fexofenadine, fall into the less sedating category, he continued.

Another speaker at the Sanofi-Aventis-sponsored symposium, Dr. Ian Hindmarch, took a harder-line stance. He argued that from a safety standpoint there is no such thing as mild cognitive/psychomotor impairment.

The often-cited distinction between first- and second-generation antihistamines is mostly marketing hype. Antihistamines ought properly to be categorized as either not binding to brain H_1 receptors—a category to date occupied solely by fexofenadine—and everything else, according to Dr. Hindmarch, professor emeritus of psychopharmacology at the University of Surrey (England).

Fexofenadine is the only antihistamine that doesn't permeate the blood-brain barrier.

DR. YANAI

"I like to make the analogy to pregnancy. Women are either pregnant or not pregnant. There is no such thing as being a little bit pregnant. Just the same, there's no such thing as being a little bit impaired. …Even a slight degree of impairment can cause an accident if the circumstances are present. All impairment is impairment, and it is only the circumstances—the child who runs into the street—that determine whether that impairment is going to damage you," he asserted.

It is well established that a person can experience quantifiable antihistamine-induced impairment of memory, attention, reaction time, decisiveness, and psychomotor coordination without feeling sleepy or drowsy, according to Dr. Hindmarch. And while such impairment may be less evident with many of the second-generation antihistamines when prescribed at the doses approved for seasonal allergic rhinitis, these agents are often used at far higher, even heroic, doses in treating a variety of pruritic dermatologic diseases.

For example, the standard dosing of cetirizine (Zyrtec) or loratidine (Claritin) for allergic rhinitis is 10 mg/day. But a dosage of 40-50 mg/day is often required to achieve clinical efficacy in patients with idiopathic urticaria or atopic dermatitis. And brain H_1 receptor occupancy as well as impairment of superior cognitive functions are antihistamine dose dependent, Dr. Hindmarch stressed at the meeting of the European Society for Dermatological Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

Dr. Yanai and Dr. Hindmarch are both on the speakers bureau for Sanofi-Aventis, the manufacturer of Allegra. ■