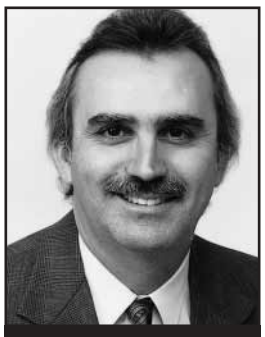

BY MICHAEL E. PICHICHERO, M.D.

ID CONSULT

Cephalosporins OK in Penicillin Allergic

Recent guidelines for the treatment of acute bacterial sinusitis and otitis media advise physicians to do something that most of us were taught never to do: Use a cephalosporin in a penicillin-allergic patient. Unfortunately, those documents neglected to explain why this once-taboo practice is now the standard of care.

The American Academy of Pediatrics' clinical practice guidelines for the management of sinusitis endorse the use of cefuroxime, cefpodoxime, ceftriaxone, and cefdinir for penicillin-allergic patients in whom the previous penicillin reaction was not severe (Pediatrics 2001;108:798-808), while the guidelines for the diagnosis and management of acute otitis media support the use of the same three oral cephalosporins in patients with "non–type-1 allergy" and ceftriaxone for type 1 allergy (Pediatrics 2004;113:1451-65).

Although the two documents are evidence based and have been endorsed by several other professional groups including the American Academy of Family Physicians, many clinicians have not embraced the recommendation because of the often-cited yet inaccurate statistic that there is a 10% rate of cross-sensitivity to cephalosporins among penicillin-allergic patients.

In fact, the risk that a patient with a history of penicillin allergy will experience a reaction to a first-generation cephalosporin is not more than 0.5%, to a second-generation cephalosporin, not more than 0.2%, and to a third-generation cephalosporin, practically nil. In at least 25 studies, cephalosporins were actually given to penicillin-allergic patients with reaction rates not greater than in non-allergic patients. I have reviewed this literature in the April issue of Pediatrics (2005;115:1048-57).

The misconception arose out of the belief that the cross-reactivity is to the shared β-lactam ring.

Now, however, we know that the β-lactam ring of cephalosporins—unlike that of penicillin and ampicillin—becomes rapidly degraded, so that antibodies are instead targeted to side chain structures. Therefore, cross-reactivity is only possible with the cephalosporins that share penicillin side chains. (See chart.) And even then, the likelihood of a reaction is still far less than 10%.

Many of the older studies suggesting greater rates of cross-reactivity were conducted with penicillin and/or amoxicillin that had been made with *Cephalosporium* mold, which of course would have caused cross-contamination. Yet, the caution remains in the package label for most cephalosporins.

Patients and physicians alike tend to use the term "allergy" very loosely. But unless the patient experienced a generalized pruritic skin reaction, hives, or anaphylaxis, it was not an IgE-mediated (type 1) reaction.

For patients who do report a true allergic history—or who have had a positive skin test—it would be prudent to avoid the four cephalosporins with side chains similar to amoxicillin—namely cefaclor, cefprozil, cephalexin, and cefadroxil. All other cephalosporins are acceptable, including the four endorsed in the sinusitis/otitis guidelines.

Consider that a major reason for the new guidelines is the increasing rates of macrolide-resistant *Streptococcus pneumoniae*. The rate was 35% in 2002, and it has been rising since. Therefore, the old paradigm of simply putting a penicillin-allergic patient on azithromycin or clarithromycin is no longer good medicine—in doing so, you are substantially compromising the anticipated efficacy of the drug.

There has never been a case of fatal anaphylaxis with a cephalosporin reported in a child. From a medicolegal standpoint, if the AAP/AAFP guideline says you can use a cephalosporin in a penicillin-allergic patient—as does my evidence-based peer reviewed article in AAP's journal, Pediatrics—rest assured you can do it. ■

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Cross-Reactivity Between Penicillins and Cephalosporins

Contrary to long-held belief, the risk of cross-reactivity between penicillins and cephalosporins is based on the similarities of their side-chain structures, not of the β-lactam ring they all share. The three lists below are grouped by side-chain similarity (or lack thereof in the third group). However, even within groups with related side chains, the risk that a patient with a history of sensitivity to one drug will have a reaction to another is still no more than 0.5%.

Group 1 (Related side chains)	Group 2 (Related side chains)	Group 3 (Unique side chains)
Amoxicillin	Cefepime	Cefazolin
Ampicillin	Cefotaxime	Cefdinir
Cefaclor	Cefpodoxime	Cefixime
Cefadroxil	Ceftriaxone	Cefotetan
Cefprozil		Ceftazidime
Cephalexin		Ceftibuten
Penicillin		Cefuroxime

Source: Dr. Pichichero

Candida *Resistance Is Rare in High-Risk Nurseries in the U.S.*

BY DAMIAN McNAMARA
Miami Bureau

MIAMI — Resistance to *Candida* species is rare in high-risk nurseries in the United States, according to a study from the Centers for Disease Control and Prevention presented in a poster at a meeting on fungal infections sponsored by Imedex.

Scott Fridkin, M.D., and colleagues also found the overall rate of invasive candidiasis in very-low-birth-weight infants has decreased since 2000—although they are unsure why.

Candida bloodstream infections are the third most common cause of late-onset sepsis in the neonatal intensive care unit. Infection incidence and resistance information could help target azole antifungal prophylaxis in this population.

The CDC investigators reviewed all cases of invasive candidiasis in neonates registered in the high-risk nursery section of the National Nosocomial Infections Surveillance System from January 1995 to December 2004. A total of 129 high-risk nurseries contributed information on 130,523 patients.

Dr. Fridkin, medical officer in the Division of Bacterial and Mycotic Diseases at the CDC's National Center for Infectious Diseases in Atlanta, and his associates assessed the incidence of invasive candidiasis among infants admitted to intensive care by birth weight, as well as the incidence of *Candida* blood stream infections associated with central venous catheter use.

They also looked for rates of resistance to different *Candida* species.

"The big take-home message is the [low] number of invasive candidiasis infections," Dr. Fridkin said in an interview at the meeting.

The rate of disease in very-low-birth-weight infants decreased considerably since 2000. (See chart.)

Although the decrease could be a result of antifungal prophylaxis or improved use of catheters, "why it went down is pure conjecture," said Dr. Fridkin.

Dr. Fridkin and his colleagues identified 1,997 neonates (1.5%) with invasive candidiasis. Most of these cases of invasive candidiasis (1,472 [74%]) occurred in infants with a birth weight less than 1,000 g.

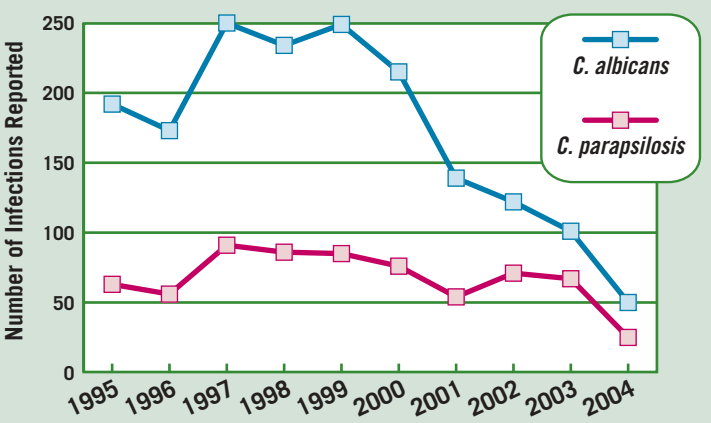
The incidence of invasive candidiasis varied by species, with 58% attributed to *C. albicans*, 34% to *C. parapsilosis*, 4% to *C. glabrata*, 2% to *C. tropicalis*, 2% to *C. lusitaniae*, and 0.2% to *C. krusei*.

Incidence of invasive candidiasis among infants with birth weight less than 1,000 g varied greatly between individual high-risk nurseries, the researchers noted—as did incidence density (the number of *Candida* blood stream infections per 1,000 central venous catheter days).

The researchers looked for resistance in *C. glabrata* and *C. krusei*, species commonly resistant to azole treatment. They wrote, "Although invasive candidiasis is a serious problem among neonates less than 1,000 g, invasive candidiasis due to species commonly resistant to azoles were extremely rare."

Dr. Fridkin said, "Despite all the fear about antifungal resistance in the NICU, these data say, right now in the U.S., there is almost no resistance to yeast. It's a real solid finding." ■

Invasive Candidiasis Cases Among High-Risk Neonates



Note: Of the 1,997 neonates with invasive candidiasis, 4% were infected by *C. glabrata*, 2% by *C. tropicalis*, 2% by *C. lusitaniae*, and 0.2% by *C. kruseii*.
Source: Dr. Fridkin

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