

Antibiotics Still Key to Survival in Cystic Fibrosis

BY TIMOTHY F. KIRN
Sacramento Bureau

RANCHO MIRAGE, CALIF. — Antibiotic use needs to be aggressive in cystic fibrosis, even if it is not exactly clear which antibiotics to use and when to use them in any particular case, Peggy Radford, M.D., said at a pediatric pulmonology meeting sponsored by the American College of Chest Physicians.

The median survival of cystic fibrosis patients has increased dramatically since the 1940s, and the increase is related to the development of more antibiotic drugs.

With penicillin and streptomycin, median survival rose to about 10 years in 1960. It rose to about 15 years in 1970, following the introduction of carbenicillin and gentamicin. With ceftazidime and ciprofloxacin in the 1980s, median survival rose to almost 30 years. It is now known to be at least 33 years and may ac-

tually be about 40 years, said Dr. Radford, director of the cystic fibrosis center at Phoenix Children's Hospital.

Clinical trials are often lacking the nuances of antibiotic treatment, which makes prescribing antibiotics something of an intellectual challenge, she said.

However, there is clinical evidence to guide current practice in some areas:

► **Prophylaxis.** In younger children, *Staphylococcus aureus* is the organism that most often colonizes the lungs of cystic fi-

brosis patients. It is not until age 4-5 years that *Pseudomonas aeruginosa* colonization becomes more prevalent.

One placebo-controlled study looked at 119 children younger than 2 years who were treated prophylactically with cephalexin for 5-7 years. Treated children were less likely to have a positive culture for staphylococcus than were those treated with placebo (6% vs. 30%) but were more likely to have a positive culture for *P. aeruginosa* (26% vs. 14%). The re-

searchers concluded, therefore, that long-term antistaphylococcus prophylaxis should not be recommended.

► **Eradication of asymptomatic colonization.** *P. aeruginosa* is the organism most highly associated with lung function decline in cystic fibrosis, and it has become clear that when *P. aeruginosa* infection becomes chronic, the colonizing organism develops a mucoid phenotype that makes eradication problematic. So it would appear early detection is advantageous.

Child Transmits MSSA Infection To Doctor

A 4-month-old boy with fatal pneumonia transmitted Pantone-Valentine leukocidin-producing *Staphylococcus aureus* to a physician who had attempted to resuscitate him.

This case represents the first reported incident of Pantone-Valentine leukocidin-producing *S. aureus* transmission during resuscitation, said Martin Chalumeau, M.D., of the Hôpital Saint-Vincent de Paul, Paris, and his colleagues (Clin. Infect. Dis. 2005;41:e29-30).

The resuscitation occurred in the general pediatric ward, when the child went into cardiac arrest while being examined by a physician. None of the health care personnel involved in the resuscitation efforts was wearing a face mask or gloves.

Necropsy results revealed right lobar pneumonia, a necrotizing hemorrhage of the right lung and half of the left lung, and a tracheal aspirate culture that yielded methicillin-susceptible *S. aureus* (MSSA). The child had presented with 3 days of coughing and 1 day of fever, and had a normal chest radiogram. He developed progressive respiratory failure within 12 hours of hospital admission.

Five days after the incident, the physician who performed the oral intubation on the child had developed furuncles on the fingers and face, and MSSA was found in cultures from the skin lesions. In addition, MSSA was found in cultures collected from 5 of the 15 health care workers who were involved in the resuscitation. The presence of Pantone-Valentine leukocidin, a cytotoxin associated with tissue necrosis and leukocyte destruction, was confirmed in the child and the infected physician, but not in the other health care workers.

This incident emphasizes the importance of protecting health care workers against infection, even in general care wards.

—Heidi Splete

25,827 Cases

of Pertussis Reported in 2004—a 40-Year High¹⁻³

Prevent Them

Safety Information

There are risks associated with all vaccines. Local and systemic adverse reactions to DAPTACEL vaccine may include redness, swelling, or tenderness at the injection site, fever, irritability, and drowsiness. Other local and systemic adverse reactions may occur.

DAPTACEL vaccine is contraindicated in persons with a hypersensitivity to any component of the vaccine. In addition, it is contraindicated in persons with any immediate anaphylactic reaction or encephalopathy not attributable to another identifiable cause after a previous dose of DAPTACEL vaccine.

Indications and Usage

DAPTACEL vaccine is indicated for the active immunization of infants and children 6 weeks through 6 years of age (prior to 7th birthday) for the prevention of diphtheria, tetanus, and pertussis (whooping cough). DAPTACEL vaccine is recommended for administration as a 4-dose series at 2, 4, 6, and 17 to 20 months of age. The interval between the 3rd and 4th dose should be at least 6 months. It is recommended that DAPTACEL vaccine be given for all doses in the series because no data on the interchangeability of DAPTACEL vaccine with other DTaP* vaccines exist. As with any vaccine, vaccination with DAPTACEL vaccine may not protect 100% of individuals. Please see brief summary of Prescribing Information for DAPTACEL vaccine on adjacent page.

References: 1. Centers for Disease Control and Prevention (CDC). Notice to readers: final 2004 reports of notifiable diseases. *MMWR*. 2005;54:770-792. 2. CDC. Summary of notifiable diseases—United States, 2002. *MMWR*. 2004;51:69-84. 3. CDC. Summary of notifiable diseases, United States—1994. *MMWR*. 1995;43:69-80. 4. Gustafsson L, Hallander HO, Olin P, et al. A controlled trial of a two-component acellular, a five-component acellular, and a whole-cell pertussis vaccine. *N Engl J Med*. 1996;334:349-355. 5. Gustafsson L, Hallander H, Olin P, et al. Efficacy trial of acellular pertussis vaccines: technical report trial I with results of preplanned analysis of safety, efficacy and immunogenicity. Stockholm, Sweden: Swedish Institute for Infectious Disease Control; 1995. Contract N01-AI-15125. 6. WHO meeting on case definition of pertussis: Geneva, 10-11 January 1991; Geneva, Switzerland: 4-5. Issue MIM/EPI/PERT/91.1. 7. Edwards KM, Decker MD. Pertussis vaccine. In: Plotkin SA, Orenstein WA, eds. *Vaccines*. 4th ed. Philadelphia, Pa: Elsevier Inc; 2004:471-528.

Two studies have investigated early eradication with tobramycin, Dr. Radford said at the meeting, which was also sponsored by the American Academy of Pediatrics.

In one study, 15 patients in whom *P. aeruginosa* infection was detected for the first time were treated with inhaled tobramycin (80 mg twice daily) for 1 year. At the end of the year, 14 had negative cultures and negative pseudomonal serum antibody titers. The negative status was maintained for a year following treatment. Pulmonary function was at the same level that it was prior to intervention, and remained at that level for the 2-year trial and follow-up.

A second, placebo-controlled, early-treat-

ment trial was planned with an enrollment of 98 patients with *P. aeruginosa* colonization; all of those patients were less than 6 years of age. But the effect of treatment was so positive in the first 21 patients, the study was halted. All eight treated patients were free of *P. aeruginosa* infection with bronchoalveolar lavage, compared with only 1 of 13 placebo patients.

► **Acute exacerbations.** Depending on lung function, cystic fibrosis patients have a 30%-80% incidence of annual acute exacerbations, Dr. Radford said.

In most cystic fibrosis centers, these infections are treated empirically, assuming that the most likely pathogen is *P. aerugi-*

nosa, followed by staphylococcus.

There are very few clinical trials comparing treatment regimens, but one investigation recently looked at whether *P. aeruginosa* susceptibility made a clinically important difference in how successful treatment was with intravenous tobramycin and ceftazidime. Seventy-seven patients who were in a placebo arm of a tobramycin trial and had an exacerbation were treated. Fifty-four had an improvement in their spirometry measurements following treatment, 14 had no change, and 9 worsened. The investigators concluded that reduced susceptibility was probably not likely to be a clinical problem.

Some practitioners also add rifampin to a regimen of tobramycin and ceftazidime because, although rifampin itself has little activity against *P. aeruginosa*, laboratory studies suggest it may have synergy with the other two agents and therefore can help fight against mucoid colonization.

► **Chronic infection suppression.** In addition to inhaled tobramycin treatment, many centers now offer long-term macrolide therapy to suppress chronic infection. In a study of azithromycin at 250 mg or 500 mg, 3 days a week for 168 days, the treatment improved spirometry measures 6% and decreased hospital stays almost 50%. Patients also had a weight gain. ■

sanofi pasteur

The vaccines business of sanofi-aventis Group

CPT* Code: 90700



DAPTACEL®

Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed

Protects Against All Severities of Pertussis

Count on a broad range of protection

- **77.9%** efficacy against all severities of pertussis: ≥ 1 day of laboratory-confirmed pertussis^{4,5}
- **84.9%** efficacy against severe/WHO[†]-defined pertussis: ≥ 21 days of consecutive paroxysmal cough with culture or serologic confirmation or contact with a confirmed case^{4,6}
- Vaccines that are protective against mild pertussis may be more effective at interrupting disease transmission^{4,7}

To order DAPTACEL vaccine,
log on to
www.vaccineshoppe.com
or call **1-800-VACCINE**
(1-800-822-2463).

Please visit www.DAPTACEL.com

*DTaP = Diphtheria, tetanus, and acellular pertussis; †CPT is a registered trademark of the American Medical Association; †WHO = World Health Organization.
DAPTACEL vaccine is manufactured by Sanofi Pasteur Limited (formerly Aventis Pasteur Limited) and distributed by Sanofi Pasteur Inc. (formerly Aventis Pasteur Inc.).