Nitric oxide in preterm infants? Nitric oxide is not ready for widespread use.

Reducing the occurrence of bronchopulmonary dysplasia (BPD) in preterm infants will improve both morbidity and mortality rates, but to date few benefits of nitric oxide in reducing BPD have been demonstrated in preterm infants in clinical trials. In two multisite, double-blind, randomized trials, researchers evaluated the safety and efficacy of nitric oxide in preterm infants undergoing mechanical ventilation.

In the first trial, investigators randomized 582 infants (mean birth weight, 760 g) to receive either inhaled nitric oxide or placebo (beginning 7 to 21 days after birth for at least 24 days). Compared with infants in the placebo group, infants in the treatment group were significantly more likely to survive without BPD (36.8% vs. 43.9%) and to be discharged sooner. Death rates did not differ significantly between groups.

In the second study, 792 infants (mean birth weight, 792 g) received either low-dose, inhaled nitric oxide (5 ppm) or placebo for 21 days or until extubation. Overall, the incidence of BPD or death did not differ significantly between groups. However, among infants who weighed between 1000 and 1250 g at birth, the incidence of BPD was lower in treated infants compared with the placebo group (29.8% vs. 59.6%). Overall, rates of central nervous system findings, such as periventricular leukomalacia, were significantly lower in the treatment group (17.5% vs. 23.9%).

Comment Based on these and other studies, an editorialist comments that the data are sufficient to recommend against using nitric oxide in the treatment of most critically ill infants with extremely low birth weight. However, nitric oxide may benefit less critically ill infants, and she encourages additional clinical trials. Further, because of the high cost (US$3000 per day and as much as US$12,000 for 30 days) and lack of long-term follow-up data on associated rates of cerebral palsy and mental retardation, nitric oxide is not ready for widespread use.

Howard Bauchner, MD
Published in Journal Watch Pediatrics and Adolescent Medicine
September 13, 2006

Rescue therapy and secondary prevention of asthma Inhaled budesonide-formoterol was better than formoterol alone for rescue therapy, and early use of inhaled fluticasone did not prevent later development of asthma.

Findings from two industry-sponsored, randomized, double-blind studies add to our understanding of the role of inhaled steroids and l-agonists in asthma control.

In a multinational study, investigators compared three acute treatment strategies in more than 3,300 patients (age, 12 years and older) who had moderate-to-severe persistent asthma and who remained symptomatic on low-dose budesonide-formoterol (160 µg and 4.5 µg twice a day). Patients were randomized to receive terbutaline, formoterol alone, or additional combined budesonide-formoterol for as-needed relief therapy. At 1 year, combination budesonide-formoterol significantly had reduced the risk for severe exacerbations by 27% compared with formoterol alone and by 45% compared with terbutaline. The combination also reduced rates of exacerbations requiring emergency-room treatment compared with the other two treatments. After randomization, increases in FEV, were greater in the budesonide-formoterol group. The number of asthma-free days did not differ among the three groups, and adverse events were rare in all groups.

In a placebo-controlled trial, investigators in the U.K. examined whether early use of inhaled fluticasone (100 µg twice a day) would prevent later development of asthma in 200 young children (median age, 1.2 years) who had had one or two previous wheezing episodes. Compared with placebo, early use of fluticasone did not prevent future development of asthma or enhance lung function as measured at age 5 years.

Comment The struggle for better treatments for controlling asthma continues. The first study suggests that the combination of an inhaled corticosteroid and a long-acting l-agonist is helpful for rescue therapy in children with moderate-to-severe persistent asthma on maintenance therapy with low-dose, inhaled budesonide-formoterol. However, we still need to try and find ways to prevent the development of asthma and the need for treatment. Unfortunately, inhaled fluticasone isn’t such a remedy.

F. Bruder Stapleton, MD
Published in Journal Watch Pediatrics and Adolescent Medicine
October 4, 2006

Ear drops cure draining ears faster Acute otitis media in children with tympanostomy tubes resolved faster with topical, rather than with oral, antibiotics.

Otorrhea is common among children with tympanostomy tubes who develop acute otitis media (AOM). To compare topical and oral antibiotics for treatment of AOM, otolaryngologists randomly assigned 80 children (age range, 6 months to 12 years) who had tympanostomy tubes and acute onset of otorrhea to receive either topical ciprofloxacin/dexamethasone for 7 days or oral amoxicillin/clavulanic acid for 10 days. Parents recorded the time to resolution of otorrhea, and blinded investigators determined the presence or absence of otorrhea (clinical cure) after 18 days.

The topical antibiotic group experienced faster resolution of otorrhea than did the oral antibiotic group (median time, 4 vs. 7 days), and children in this group had a significantly higher clinical cure rate (85% vs. 59%). Microbiologic response was not significantly different between the two groups. Mild-to-moderate adverse events occurred more often in the oral antibiotic group than in the topical antibiotic group (29% vs. 13%).

Comment The findings of this manufacturer-supported study suggest that topical antibiotics plus steroid provide faster cessation of otorrhea and better cure rates for “acute tube otorrhea” than a commonly used systemic antibiotic. The authors note that topical antibiotics also might be less likely to cause antimicrobial resistance. An editorialist emphasizes that these findings may not apply to infants, who have a different set of bacterial pathogens that may respond
better to oral antibiotics. Finally, careful cleaning of the ear canal is necessary for ear drops to be effective in the middle ear.

Cornelius W. Van Niel, MD
Published in Journal Watch Pediatrics and Adolescent Medicine
October 4, 2006

Dohar J, et al. Topical ciprofloxacin/dexamethasone superior to oral amoxicillin/clavulanic acid in acute otitis media with otorrhea through tympanostomy tubes. Pediatrics 2006;118:551–9.

Isaacson G. Why don’t those ear drops work for my patients? Pediatrics 2006;118:1252–3.

Hyperpyrexia: do bacteria cause higher fevers?

In the post-Haemophilus influenzae type b vaccination era, most children with hyperpyrexia have proven or probable viral infection. Studies conducted before the Haemophilus influenzae type b vaccination era have shown mixed results about the risk for serious bacterial infection in children with extremely high fevers. In this observational study, researchers evaluated the risk in 103 children with temperatures of 106˚F or higher who presented to an emergency department in Texas during a 2-year period after the introduction of the HIB vaccine. Evaluations included complete blood cell counts, blood cultures, and nasopharyngeal viral cultures. Additional testing was performed as clinically indicated. Eighty-five percent of children were younger than 3 years old, and 19 children had pre-existing medical conditions. Twenty children (18%) had documented serious bacterial infections, and 22 (21%) had documented viral infections (including the one child with meningitis who also had a urinary tract infection [UTI] with bacteremia). Bacteremia and UTI were the most commonly diagnosed bacterial infections; only two children were given a diagnosis unrelated to infection. The remaining 60 children were presumed to have culture-negative febrile illnesses.

Comment
The authors conclude that all children with hyperpyrexia without a confirmed viral illness should be treated with antibiotics, but my interpretation of their data leads me to a different conclusion. Eighty percent of these children had proven or probable viral infection. Most children with bacterial infection had UTIs, infection of a central catheter from pre-existing medical conditions, or Streptococcus pneumoniae bacteremia (since this study was conducted before routine use of conjugated pneumococcal vaccine). Therefore, I would use the same criteria for prescribing antibiotics in children with hyperpyrexia as I use for other febrile patients. As with all children, careful evaluation is indicated for febrile children.

Peggy Sue Weintrub, MD
Published in Journal Watch Pediatrics and Adolescent Medicine
October 4, 2006

Trautner BW, et al. Prospective evaluation of the risk of serious bacterial infection in children who present to the emergency department with hyperpyrexia (temperature of 106˚F or higher). Pediatrics 2006;118:34–40.