

The following abstracts, from medical journals containing literature on the management of respiratory infections, were selected for their relevance to this Special Report supplement.

Association Between Respiratory Virus Infections and Acute Otitis Media in Young Children

The frequencies of human rhinovirus (HRV), respiratory syncytial virus (RSV), and coronavirus (HCV) infection were determined in 92 children aged 3 months to 7 years with acute otitis media (AOM). Middle ear fluids (MEF) collected by tympanocentesis and nasopharyngeal aspirates (NPA) at the time of AOM diagnosis were examined using reverse transcriptase polymerase chain reaction for HRV, RSV, and HCV RNA. Viral RNA was found in a total of 69 children (75%) and in 44 MEF samples (48%) and 57 NPA samples (62%) at the time AOM was diagnosed. Human rhinovirus RNA was detected in both MEF and NPA in 18 (20%), in MEF alone in four (4%), and in NPA alone in 10 (11%). Respiratory syncytial virus was detected in both MEF and NPA in 12 (13%), in MEF alone in 5 (5%), and in NPA alone in 9 (10%). Coronavirus RNA was found in both MEF and NPA in 5 (5%), in MEF alone in 2 (2%), and in NPA alone in 9 (10%). Five percent of the children were found to have dual viral infections. Human rhinovirus and RSV were found at the same time in 2 MEF samples, as well as in 2 NPA samples; RSV and HCV were detected in one NPA sample. Bacterial pathogens were found in 56 (62%) MEF samples from 91 children. Viral RNA was found in 20 (57%) MEF samples from 35 bacteria-negative samples and in 25 (45%) of 56 bacteria-positive MEF samples. No marked differences existed in the risk of treatment failure, relapse, or the occurrence of late secretory otitis media between children with virus-positive and virus-negative MEF aspirates. The findings underscore the importance of common respiratory viruses, especially HRV and RSV, in predisposing to and causing AOM in young children.

Pitkaranta A, Virolainen A, Jero J, Arruda E, Hayden FG. Detection of respiratory syncytial virus and coronavirus infections in acute otitis media by reverse transcriptase polymerase chain reaction. *Pediatrics* 1998;102:291-295.

Choosing an Antibiotic for Drug-Resistant *Streptococcus Pneumoniae*

Streptococcus pneumoniae with reduced susceptibility to penicillin is becoming a growing problem, not only because of the high prevalence of infections but also because of the rate at which resistance has progressed. With the incidence of penicillin resistance approaching 40% in some areas of the United States, the occurrence of high-level resistance has expanded some 60-fold during the past decade. Except for meningitis and otitis media, no conclusive evidence exists that the resistance of S. pneumoniae to beta-lactam antibiotics carries any greater morbidity and mortality in infections caused by this pathogen. However, if current trends in resistance patterns persist, morbidity and mortality can be expected to increase. Beta-lactam resistance to S. pneumoniae involves genetic mutations that change penicillin-binding protein structure and result in a reduced affinity for all beta-lactam antibiotics. When treating infections caused by S. pneumoniae, no assumptions should be made that nonsusceptibility to beta-lactam antibiotics corresponds to the clinical efficacy of these agents. Instead, the recommended therapy for non-meningeal pneumococcal infections, such as pneumonia, sepsis, and acute otitis media, includes a beta-lactam antibiotic, such as penicillin G, cefuroxime, amoxicillin, amoxicillin/clavulanate, cefotaxime, or ceftriaxone. Cefotaxime or ceftriaxone are recommended therapy for meningitis, with the addition of vancomycin until susceptibility is known. Such agents are recommended because of their ability to achieve serum/tissue concentrations that exceed the minimum inhibitory concentrations of these agents against penicillin-susceptible, penicillin-intermediate, and most penicillin-resistant strains (eg, penicillin G, cefotaxime, and ceftriaxone) and their ability to provide adequate concentration in cerebrospinal fluid (eg, cefotaxime and ceftriaxone).

Jacobs MR. Drug-resistant *Streptococcus pneumoniae*: Rational antibiotic choices. *Am J Med* 1999;106:19S-25S.

Management of Acute Sinusitis in Adults

More than 14% of the population is affected by sinusitis, a prevalent and costly disease that accounts for more than \$2 billion in annual healthcare costs. Sinusitis is one of the most common conditions treated by primary care physicians. A multitude of host and environmental factors contribute to its pathogenesis, and the lack of clear guidelines for its diagnosis and treatment is a challenge to effective management of the problem. Diagnosis of uncomplicated cases is based primarily on the medical history and clinical examination. Attempts have been made to identify the most efficacious clinical predictors of acute bacterial sinusitis. Microbiological and imaging studies are seldom performed as part of the initial assessment, being reserved instead for recurrent or refractory disease. Treatment consists of drainage of the congested sinuses and eradication of the pathogenic organisms. Although antimicrobial therapy can speed the resolution of symptoms of acute sinusitis, the need for such therapy is questionable, and its proper use is challenged by the increase in antibiotic-resistant Haemophilus influenzae and Streptococcus pneumoniae, which are most often implicated in acute sinusitis. Failure to resolve sinusitis or its frequent recurrence warrants evaluation by a specialist.

Poole MD. A focus on acute sinusitis in adults: Changes in disease management. *Am J Med* 1999;106:38S-47S.

Heptavalent Pneumococcal Vaccine Conjugated to CRM₁₉₇ Evaluated for Safety and Immunogenicity in Infants

The safety and immunogenicity of heptavalent pneumococcal saccharide vaccine (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) that was individually conjugated to CRM₁₉₇ (PNCRM7) given at 2, 4, 6, and 12 to 15 months of age were determined in 200 healthy 2-month-old infants. The infants were randomly assigned to be given 4 consecutive doses of PNCRM7 or an investigational meningococcal group C conjugate vaccine, which served as a control. Routine vaccines administered at the same time included oral polio vaccine and combined diphtheria toxoid, tetanus toxoid, and whole cell pertussis vaccine/Haemophilus influenzae type b vaccine, consisting of capsular oligosaccharides conjugated to CRM₁₉₇ (DTP/HbOC) at 2, 4, and 6 months, and either measles-mumps-rubella vaccine or HbOC at 12 and 15 months. Active safety surveillance was carried on for 3 days after each dose. Concentrations of antibodies to each of the 7 pneumococcal serotypes were measured by enzyme-linked immunosorbent assay before vaccination, after doses 2 and 3, prebooster, and postbooster. Markedly fewer children experienced local reactions at the PNCRM7 injection site than at the DTP/HbOC injection site. No increase occurred in the incidence or severity of local reactions at the PNCRM7 site with increasing doses of vaccine. Mild to moderate postvaccination fever was common in both the PNCRM7 and control vaccine groups; however, DTP/HbOC was given concurrently. All 7 vaccine serotypes were immunogenic. The kinetics of the immune responses were specific to serotypes. After 3 doses of PNCRM7, between 92% and 100% of children had 0.15 µg/mL or more of antibody, and 51% to 90% achieved a level of 1 µg/mL or more against specific serotypes. A booster shot of PNCRM7 led to a brisk anamnestic response to all 7 vaccine serotypes, revealing the effective stimulation of T-cell memory by the primary series of vaccinations. Primary immunization that is followed by a booster dose of PNCRM7 appears to be acceptably safe and results in marked increases in antibody to all 7 serotypes.

Rennels MB, Edwards KM, Keyserling HL, et al. Safety and immunogenicity of heptavalent pneumococcal vaccine conjugated to CRM₁₉₇ in United States infants. *Pediatrics* 1998;101:604-611.

Five-Day Treatment With Dirithromycin Compared With 7-Day Treatment With Erythromycin for Acute Exacerbations of Chronic Bronchitis

Five days of treatment with dirithromycin were compared with 7 days of treatment with erythromycin for acute exacerbations of chronic bronchitis in a meta-analysis of 2 identically designed, well-controlled, randomized, double-blind clinical trials. Five hundred thirty-one patients were randomly assigned to receive dirithromycin 500 mg once a day for 5 days, and 526 patients were randomly assigned to receive erythromycin 250 mg 4 times a day for 7 days. Assessment was made of clinical and bacteriological responses 3 to 5 days after therapy and at the end of the study. Information on adverse events was collected from those in both groups and compared before and after treatment. Of 690 clinically assessable patients at the posttherapy visit, 298 (84.2%) patients treated with dirithromycin and 270 (80.4%) patients treated with erythromycin were found to have a favorable response. At the end of therapy, 273 (77.1%) of the patients treated with dirithromycin and 243 (72.3%) of the patients treated with erythromycin responded favorably. At 75% and 74.1%, the microbiological cure rate was equivalent in both groups. After therapy, dirithromycin was found to be as efficacious as erythromycin in eradicating *Streptococcus pneumoniae* (77.8% versus 90.9%), *Haemophilus influenzae* (71.7% versus 72.2%), *Moraxella catarrhalis* (93.3% versus 88.9%), and *Staphylococcus aureus* (81.8% versus 82.1%). A nonstatistically significant number of patients treated with dirithromycin reported adverse events compared with patients treated with erythromycin, with nausea (6.8% versus 7.8%), headache (7.3% versus 8.2%), and diarrhea (6.6% versus 9.5%) being the most frequent in both groups. In treating acute exacerbations of chronic bronchitis, 5 days of dirithromycin were found to be as effective as 7 days of erythromycin.

Wasilewski MM, Johns D, Sides GD. Five-day dirithromycin therapy is as effective as seven-day erythromycin therapy for acute exacerbations of chronic bronchitis. *J Antimicrob Chemother* 1999;43:541-548.

Once-Daily Levofloxacin Effective in Treatment of Acute Exacerbation of Chronic Bronchitis

Using a randomized, double-blind, 3-armed parallel design, a multicenter study was conducted among adult patients who had an acute exacerbation of chronic bronchitis (AECB) to compare the efficacy and safety of 2 different doses of levofloxacin with cefuroxime axetil. Eight hundred thirty-two patients were randomly assigned to be given oral levofloxacin 250 or 500 mg once a day or oral cefuroxime axetil 250 mg twice a day for 7 to 10 days. The primary analysis of efficacy was based on the clinical response of the patients with bacteriologically confirmed AECB, which was ascertained 5 to 14 days after the end of therapy (per-protocol population). Of the 839 patients who were enrolled at 71 centers in 14 countries, 7 were not treated, yielding an intention-to-treat (ITT) population of 832. In all, 281 patients received levofloxacin 250 mg, 280 received levofloxacin 500 mg, and 271 received cefuroxime axetil 250 mg. The cure rates in the ITT population were levofloxacin 250 mg, 70% (196/281); levofloxacin 500 mg, 70% (195/280); and cefuroxime axetil, 61% (166/271). Those in the per-protocol population were 78% (121/156), 79% (108/137), and 66% (88/134), respectively. Both levofloxacin 250 and 500 mg were at least as effective as cefuroxime axetil and were active against the principal clinically relevant pathogens: *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis*. All 3 regimens were equally well tolerated. The results showed that once-daily levofloxacin 250 and 500 mg are effective and well tolerated in the treatment of adult patients with AECB.

Shah PM, Maesen FPV, Dolmann A, Vetter N, Fiss E, Wesch R. Levofloxacin versus cefuroxime axetil in the treatment of acute exacerbation of chronic bronchitis: Results of a randomized, double-blind study. *J Antimicrob Chemother* 1999;43:529-539.

Curbs Needed to Prevent Overprescription of Antibiotics for Treatment of Colds, Upper Respiratory Tract Infections, and Bronchitis

The use of antibiotics leads to an increase in the rate of antibiotic organisms. An earlier study showed that colds, upper respiratory tract infections, and bronchitis account for almost one third of all antibiotic prescriptions written by ambulatory care physicians. Antibiotic prescription rates were measured and predictors of antibiotic use were identified for US adults diagnosed as having colds, upper respiratory tract infections, and bronchitis in a sample survey of practicing physicians who took part in the National Ambulatory Care Survey, 1992. Fifteen hundred twenty-nine practicing office-based physicians who completed patient record forms for 28,787 adult patients were surveyed, and it was found that about 12 million antibiotic prescriptions, or 21% of all antibiotics prescribed for adults in 1992, were written for patients who made office visits for colds, upper respiratory infections, and bronchitis. Fifty-one percent of the patients were diagnosed as having colds, 52% as having upper respiratory infections, and 66% as having bronchitis. Higher prescription rates of antibiotics were found for women (odds ratio [OR], 1.65; 95% confidence interval [CI], 1.05-2.62) and rural location (OR, 2.25; 95% CI, 1.33-3.80), whereas the black population (OR, 0.44; 95% CI, 0.21-0.93) was associated with lower antibiotic prescription rates. In a bivariate analysis, patient age, Hispanic origin, geographic region, physician specialty, and payment sources were found to be unrelated to antibiotic prescription rates. Only rural practice location (adjusted OR, 2.58; CI, 1.39-4.76) was independently associated with more frequent antibiotic prescriptions for colds, upper respiratory tract infections, and bronchitis. Although antibiotics afford minimal or no benefit for colds, upper respiratory tract infections, and bronchitis, such conditions account for a sizable proportion of total antibiotic prescriptions written for adults by office-based physicians. Because there is widespread overuse of antibiotics, effective, broad-based strategies are needed to change physicians' prescribing behavior.

Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. *JAMA* 1997;278:901-904.