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SYNAGIS REVISITED

Palivizumab (*Synagis* – MedImmune), an injectable monoclonal antibody, has been marketed in the USA since 1999 for prevention of respiratory syncytial virus (RSV) disease in high-risk infants and children (Medical Letter 1999; 41:3). "RSV awareness" ads sponsored by the manufacturer and directed at the parents of premature infants are now appearing on television (M Peterson, New York Times, January 31, 2001).

RSV DISEASE — RSV is the most common cause of bronchiolitis and pneumonia in young children. In the northern hemisphere, most infections occur between November and April; almost all infants have been infected at least once by the age of two (MMWR Morb Mortal Wkly Rep, Dec 8, 2000; 49:1091). In otherwise healthy children, RSV typically causes a mild upper respiratory infection, but premature infants and children with chronic lung disease (formerly called bronchopulmonary dysplasia), congenital heart disease or immune deficiency have an increased risk of hospitalization due to RSV lower respiratory tract disease.

CLINICAL TRIALS — A multicenter, randomized trial in about 1,500 children compared palivizumab (15 mg/kg), given as an intramuscular injection once a month for five months starting at the beginning of the RSV season, with placebo. Participating children were infants who were premature (≤ 35 weeks' gestation) and less than six months old at the time of enrollment and children ≤ 24 months old with chronic lung disease who required continuing medical therapy. Children with congenital heart disease were excluded. Hospitalization for RSV infection occurred in 4.8% of children treated with palivizumab and 10.6% of children who received placebo, a statistically significant difference. The rate of hospitalization was lower with the drug in both healthy premature infants (1.8% vs 8.1%) and in children with chronic lung disease (7.9% vs 12.8%). Four deaths (0.4%) occurred among the 1002 palivizumab recipients, and five (1%) among the 500 patients in the placebo group; this difference was not statistically significant (IMPACT-RSV Study Group, Pediatrics, 102:531, 1998). Serum antibody concentrations have reached levels thought to be protective in 66% of infants after one injection, and in 86% after the second (X Sáez-Llorens et al, Pediatr Infect Dis J 1998; 17:787).

ADVERSE EFFECTS — Increases in aminotransferase activity were more common with palivizumab than with placebo in the controlled trial. No other increases in local or systemic adverse events occurred in children treated with palivizumab.

DOSAGE AND COST — *Synagis* is supplied in 50-mg and 100-mg vials. The formulation must be used within six hours after reconstitution. It can be given at the same time as

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the usual recommended vaccines. The dosage of palivizumab is 15 mg/kg once a month intramuscularly, preferably in the anterolateral thigh. It should be started at the usual beginning of the RSV season, which varies from one region to another, and stopped at the end, generally four or five months later; local health departments can usually provide the dates. The cost of one vial containing 100 mg is about \$900 to \$1000, according to Medical Letter consultants; the cost of five injections for a 3-kg infant would be more than \$2000. Some pediatricians inject several infants at the same time to make full use of each vial.

INDICATIONS — The American Academy of Pediatrics has recommended RSV prophylaxis, based on age at the start of the RSV season, for children less than 2 years old with chronic lung disease who have required medical therapy during the previous six months, infants less than one year old born at ≤ 28 weeks' gestation, infants less than six months old born at 29 to 32 weeks, and infants less than six months old born at 32 to 35 weeks who have additional risk factors for RSV infection such as day-care attendance or three or more siblings (American Academy of Pediatrics Committee, Pediatrics 1998; 102:1211; HC Meissner et al, Pediatr Infect Dis J 1999; 18:223). Use of the antibody in children with congenital heart disease or cystic fibrosis is being evaluated.

CONCLUSION — Palivizumab, an injectable monoclonal antibody, given once a month from November to April can decrease the incidence of hospitalization for respiratory syncytial virus (RSV) disease in premature infants (≤ 35 weeks' gestation) and children with chronic lung disease less than 2 years old. The drug appears to be safe, but it is expensive. Antibody levels suggest that even one or two monthly injections near the end of the RSV season could be helpful, but clinical data are lacking.

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