

AAP modifies indications for use of palivizumab in high-risk infants, young children

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Based on additional data regarding the seasonality of respiratory syncytial virus (RSV) disease as well as risk factors for disease acuity, AAP guidelines for immunoprophylaxis with palivizumab have been updated in the 2009 Red Book.

Among the changes are new recommendations for infants born at 32 weeks' to less than 35 weeks' gestation (32 weeks, 0 days through 34 weeks, 6 days).

This article summarizes the recommendations and major changes present in the 2009 Red Book (pages 562-568) and in an AAP policy statement soon to be published in *Pediatrics*. The updated guidelines aim to ensure optimal balance of benefit and cost.

Disease burden

More than 125,000 hospitalizations due to RSV infection occur annually in the United States. Approximately 2% to 3% of all infants in the first 12 months of life will be hospitalized because of an RSV infection. Most of these infants will be previously healthy, term infants.

RSV-infected premature infants, infants with chronic lung disease (CLD) of prematurity and infants with hemodynamically significant congenital heart disease have hospitalization rates four to five times greater than those of healthy infants. Parents of infants at high risk for severe RSV infection are routinely educated on the importance of decreasing exposure to and transmission of RSV.

In the absence of a safe, effective vaccine or a broadly effective antiviral agent for chemoprophylaxis or treatment, passive immunoprophylaxis with the monoclonal antibody palivizumab remains the most important intervention for reducing the burden of RSV disease among high-risk infants and children. However, immunoprophylaxis is costly. The cost effectiveness of immunoprophylaxis can be maximized by restricting its use to infants at highest risk of hospitalization during times when RSV is most likely to be circulating.

Palivizumab was approved by the Food and Drug Administration (FDA) in 1998 for prevention of serious lower respiratory tract disease caused by RSV in pediatric patients at increased risk of severe disease. FDA approval was based on the results of a randomized clinical trial showing that prophylaxis with five monthly doses of palivizumab reduced RSV hospitalization rates by about 50% compared with placebo recipients. AAP guidelines for selection of infants for immunoprophylaxis first were published in November 1998 and revised in December 2003.

Initiation and termination of prophylaxis

For most areas of the United States, recommendations for initiation and termination of prophylaxis remain unchanged for infants with hemodynamically significant congenital heart

disease, chronic lung disease of prematurity and birth before 32 weeks' gestation. For children in these categories living in most areas of the United States, the first dose of palivizumab should be administered during the first week of November, and the fifth and last dose should be administered in March.

For the majority of areas in the United States, outbreaks of RSV disease begin in November or December, peak in January or February and end in March or April. Five monthly doses of palivizumab will provide more than 20 weeks of protective serum antibody concentration for most infants. If prophylaxis is initiated in October in a geographic area with an earlier onset of RSV season, the fifth and last dose of palivizumab should be administered in February.

Surveillance data from the Centers for Disease Control and Prevention have identified variations in the onset and offset of the RSV season in areas within Florida that should affect the timing of palivizumab administration. Infants and young children in Florida who qualify for prophylaxis for the season should receive palivizumab only during the five months following onset of RSV season (maximum of five doses). Detailed guidelines for specific areas of Florida are discussed in the 2009 Red Book and the AAP policy statement.

Eligibility criteria for prophylaxis of high-risk infants, young children

Infants with chronic lung disease of prematurity

No change is recommended for consideration of palivizumab prophylaxis for infants and children younger than 24 months of age who receive medical therapy (supplemental oxygen, bronchodilator, diuretic or chronic corticosteroid therapy) within six months before the start of the RSV season (a maximum of five monthly doses).

Infants born before 32 weeks' gestation (31 weeks, 6 days or less)

No change is recommended for consideration of prophylaxis for infants born at or before 28 weeks' gestation who may benefit from prophylaxis during the RSV season, whenever that occurs during the first 12 months of life. Infants born at 29 to 32 weeks of gestation may benefit from prophylaxis up to 6 months of age (a maximum of five monthly doses).

Infants born at 32 weeks' to less than 35 weeks' gestation (32 weeks, 0 days through 34 weeks, 6 days)

A change has been made in the recommendation for infants in this category so that these infants receive a maximum of three doses. Available data do not enable definition of a subgroup of infants in this gestational age group at risk of prolonged hospitalization or admission to the intensive care unit. Therefore, recommendations have been modified to reduce the risk of RSV hospitalization during the period of greatest risk (the first 3 months of life) among infants with consistently identified risk factors for hospitalization.

Palivizumab prophylaxis should be limited to infants in this age group who are at greatest risk of hospitalization due to RSV, namely infants younger than 3 months of age at the start of the RSV

season or born during the RSV season and who are likely to have an increased risk of exposure to RSV. Epidemiologic data suggest that RSV infection is more likely to occur and more likely to lead to hospitalization for infants in this gestational age group when either of the following two risk factors is present: infant attends child care or infant has a sibling younger than 5 years of age.

Prophylaxis may be considered for infants from 32 through less than 35 weeks' gestation (32 weeks, 0 days through 34 weeks, 6 days) who are born less than three months before the onset or during the RSV season and for whom at least one of the two risk factors is present. Infants in this gestational age category should receive prophylaxis only until they reach 3 months of age and should receive a maximum of three monthly doses; many will receive only one or two doses before they reach 3 months of age. Once an infant is older than 90 days of age, the risk of hospitalization attributable to RSV lower respiratory tract disease is reduced. Administration of palivizumab is not recommended for these infants after they reach 90 days of age.

The table provides a guide for use of palivizumab for RSV prophylaxis of preterm infants without CLD based on birth date, gestational age and presence of risk factors.

Table
Maximum number of palivizumab doses for RSV prophylaxis of preterm infants without CLD, based on birth date, gestational age and presence of risk factors (shown for areas beginning prophylaxis on Nov. 1)^a

Month of birth	Maximum number of doses		
	≤ 28 weeks, 6 days gestation and < 12 months of age at start of season	29 weeks, 0 days through 31 weeks, 6 days of gestation and < 6 months old at start of season	32 weeks, 0 days through 34 weeks, 6 days and with risk factor ^b
Nov. 1-March 31 of previous RSV season	5 ^c	0 ^d	0 ^d
April	5	0 ^d	0 ^e
May	5	0 ^d	0 ^e
June	5	5	0 ^e
July	5	5	0 ^e
August	5	5	1 ^f
September	5	5	2 ^f
October	5	5	3 ^f
November	5	5	3 ^f
December	4	4	3 ^f
January	3	3	3 ^f
February	2	2	2 ^f
March	1	1	1 ^f

2009 Red Book (Table 3.61, page 566)

^aIf infant is discharged from the hospital during RSV season, fewer doses may be required.

^bRisk factors: infant attends child care or has sibling younger than 5 years old

^cSome of these infants may have received one or more doses of palivizumab in the previous RSV season if discharged from the hospital during that season; if so, they still qualify for up to five doses during their second RSV season.

^dZero doses because infant will be older than 6 months of age at start of RSV season.

^eZero doses because infant will be older than 90 days of age at start of RSV season.

^fOn the basis of the age of patients at the time of discharge from the hospital, fewer doses may be required because these infants will receive one dose every 30 days until the infant is 90 days of age.

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