

Modified Recommendations for the Use of Palivizumab for the Prevention of Respiratory Syncytial Virus (RSV) Infections from the 2009 AAP Committee on Infectious Diseases (COID)—Reasons for Concern from the Perspective of a Neonatologist/Pediatrician

Virtually all infants have been infected with RSV by age two and some infants will have serious lower respiratory tract infections. A monoclonal antibody, palivizumab, was licensed by the Food and Drug Administration in 1998.^{1,2} It is the only licensed product available for prevention of lower respiratory tract disease in infants and children with chronic lung disease, history of preterm birth < or = 35 weeks gestation, or hemodynamically significant congenital heart disease. The AAP published policy statements on palivizumab's use in 1998, 2003, 2006, and now in 2009.

Major changes in the 2009 policy statement from guidelines previously published include the following:³

1. Preterm infants 32-35 wks GA
 - Definition changed from 32 wk 1d - 35 wk 0d to 32 wk 0d - 34 wk 6d; **infants at 35 wk GA no longer qualify**
 - Maximum number of doses changed from 5 to 3; final dose administered by 3 mos (90 days of age)
 - Start of dosing chronologic age changed from <6mos at the beginning of RSV season to <3 mos at the start of RSV season or born during the RSV season
 - Risk factors changes to '1 of 2' risk factors; attendance at child care facility or siblings <5 yrs of age
2. Seasonality—stronger language for maximum of 5 doses regardless of length of RSV season including Florida
3. Dosing—stronger language for maximum of 5 doses: 3 doses maximum for 32 through <35 weeks GA infants

Following these guidelines may increase the risk of severe RSV disease for an estimated 145,000 infants born annually in the U.S. Areas of concern include:

1. Association between lower respiratory tract infection and future episodes of recurrent wheezing, reactive airway disease, and pulmonary function abnormalities later in childhood⁴
2. Increased burden on healthcare resources since RSV associated disease is the leading cause of infant hospitalizations in the U.S.—often requiring mechanical ventilation and admission to a critical care unit
3. Rate of prematurity continues to increase despite collaborative efforts to abate this incremental change; presently many states have rates of prematurity exceeding 15% with the majority of this increase being in the Late Preterm infant (34 wks 0d to 36 wks 6d)
4. Incomplete lung development in the Late Preterm infant (surface area, lung volume 52% lower in the 32-35 wk infant, and total number of alveoli)⁵
5. The number of infants with RSV respiratory failure who are rescued with Extracorporeal Membrane Oxygenation (ECMO) each year is approximately 35 infants according to the ELSO registry—many of these infants would have died without cardio-pulmonary bypass
6. Lack of adequate protection for the entire RSV season (decreased dosing may lead to decreased protection)⁶
7. GA dating is imprecise using the Ballard—accuracy is only ± 2 wks. Lack of prenatal care and universal obstetrical ultrasounds makes precision dating arbitrary—drawing a chronologic line for immunizations is quite different in an older child – there is no debate on the exact age of the infant
8. Risk factors are additive and not taken into account in the new recommendations⁷

The COID updated their recommendations to “ensure optimal balance of benefit and cost from this expensive intervention”. These changes were made without peer reviewed data and publication in respected journals, therefore, unsupported by evidence-based medicine. Speaking as a neonatologist, such dramatic changes in recommendations should have the endorsement of members of the Committee on Fetus and Newborn (COFN).

One would question if these recommendations would have been made if the costs of this monoclonal antibody could have been reduced. One wonders about the effect on R & D (research and development) of future generations of monoclonal antibodies. These recommendations put the neonatologist and PCP (primary care providers) into an abyss between the family and third party payers. Also, it creates an ethical conundrum of “what is

right for the patients". All clinicians want to do their best for their patients regardless of cost and do not want to be put in this position.

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