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Policy Statement—Prevention of Varicella: Update of Recommendations for Use of Quadrivalent and Monovalent Varicella Vaccines in Children

abstract

FREE

Two varicella-containing vaccines are licensed for use in the United States: monovalent varicella vaccine (Varivax [Merck & Co, Inc, West Point, PA]) and quadrivalent measles-mumps-rubella-varicella vaccine (MMRV) (ProQuad [Merck & Co, Inc]). It is estimated from postlicensure data that after vaccination at 12 through 23 months of age, 7 to 9 febrile seizures occur per 10 000 children who receive the MMRV, and 3 to 4 febrile seizures occur per 10 000 children who receive the measles-mumps-rubella (MMR) and varicella vaccines administered concurrently but at separate sites. Thus, 1 additional febrile seizure is expected to occur per approximately 2300 to 2600 children 12 to 23 months old vaccinated with the MMRV, when compared with separate MMR and varicella vaccine administration. The period of risk for febrile seizures is from 5 through 12 days after receipt of the vaccine(s). No increased risk of febrile seizures is seen among patients 4 to 6 years of age receiving MMRV. Febrile seizures do not predispose to epilepsy or neurodevelopmental delays later in life and are not associated with long-term health impairment. The American Academy of Pediatrics recommends that either MMR and varicella vaccines separately or the MMRV be used for the first dose of measles, mumps, rubella, and varicella vaccines administered at 12 through 47 months of age. For the first dose of measles, mumps, rubella, and varicella vaccines administered at ages 48 months and older, and for dose 2 at any age (15 months to 12 years), use of MMRV generally is preferred over separate injections of MMR and varicella vaccines. *Pediatrics* 2011;128:630–632

COMMITTEE ON INFECTIOUS DISEASES

KEY WORDS

MMRV, measles-mumps-rubella-varicella, vaccine, MMR, immunization

ABBREVIATIONS

MMR—measles-mumps-rubella vaccine
MMRV—measles-mumps-rubella-varicella vaccine

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INTRODUCTION

Since implementation of routine varicella vaccination in 1995, disease and death from varicella-zoster virus has declined significantly.[1–3] Two varicella-containing vaccines currently are licensed for use in the United States: monovalent varicella vaccine (Varivax [Merck & Co, Inc, West Point, PA], licensed in 1995) and quadrivalent measles-mumps-rubella-varicella vaccine (MMRV) (ProQuad [Merck & Co, Inc], licensed in 2005).

The American Academy of Pediatrics updated its statement on the prevention of varicella[4] in 2007 and reaffirmed that statement in 2010. The purpose of this brief vaccine policy statement is to provide additional data to update these recommendations.

BACKGROUND AND RATIONALE

Prelicensure studies of the MMRV indicated that fever was more common after MMRV (22%) than after measles-mumps-rubella (MMR) and varicella vaccines administered concurrently but at separate sites (15%) during the 0 through 42 days after receipt of the vaccine. The reasons for this are not fully understood, but the increased occurrence of fever might suggest a more vigorous immune response as a reaction to an increase in measles virus replication, as reflected in measles antibody titers. The measles, mumps, and rubella viruses in the MMRV are identical and of equal potency to those in the MMR vaccine, but the potency of the varicella-zoster virus is at least 7 times higher than the potency in the monovalent varicella vaccine. However, measles geometric mean titers (GMTs) measured 6 weeks after vaccination were higher among children who received the first dose of MMRV than among children who received the first dose of MMR vaccine and varicella vaccine administered concurrently but at separate sites; varicella GMTs were similar. Statistical modeling indicated that the level of the measles antibody titer after receipt of MMRV was associated positively with the rate of fever.

It was postulated at the time of licensure that the increased frequency of fever after the MMRV might correlate with an increased likelihood of febrile seizures. Postlicensure studies were conducted in 2008 and 2009 by the Centers for Disease Control and Prevention Vaccine Safety Datalink and Merck to evaluate this possibility.[5]

EVIDENCE TO SUPPORT POLICY/ RECOMMENDATION

Results of the Vaccine Safety Datalink and Merck studies were remarkably similar. After vaccination at 12 through 23 months of age, 7 to 9 febrile seizures occur per 10 000 children who receive the MMRV, and 3 to 4 febrile seizures occur per 10 000 children who receive the MMR and varicella vaccines administered separately. Thus, 1 additional febrile seizure is expected to occur per approximately 2300 to 2600 children 12 through 23 months old vaccinated with the MMRV compared with separate MMR and varicella vaccines. The period of increased risk for febrile seizures is from 5 through 12 days after receipt of the vaccine.

Among older children 4 through 6 years of age receiving the second dose of the MMRV, there is no evidence to suggest an increased risk of febrile seizures after MMRV vaccination compared with those who receive separate MMR and varicella vaccine injections at the same visit.

Febrile seizures do not predispose to epilepsy or neurodevelopmental delays later in life. Although they are frightening for parents, febrile seizures are not associated with long-term health impairment for the affected child.

POLICY OR RECOMMENDATION

The routinely recommended ages for measles, mumps, rubella, and varicella vaccination continue to be 12 through 15 months for dose 1 and 4 through 6 years for dose 2. The American Academy of Pediatrics recommends for the first dose at ages 12 through 47 months that either MMR and varicella vaccines administered separately or MMRV can be used. Use of separate MMR and varicella vaccines averts the slight increase in risk of fever and febrile seizures after MMRV administration but at the cost of the pain associated with an extra injection and the risk of an infant falling behind schedule if all vaccines indicated at that visit are not given. Providers who are considering administering MMRV should discuss the benefits and risks of both vaccination options with the parents or caregivers. Because parents need to be fully aware of the slight increase in risk of febrile seizures with the combination MMRV compared with separate MMR and varicella injections at the same visit, providers who face barriers to clearly communicating these benefits and risks for any reason (eg, language barriers) should administer MMR and varicella vaccines separately.

The risk of febrile seizures is not increased in older children who receive the second dose of MMRV. Therefore, when the first dose of measles, mumps, rubella, and varicella vaccines is administered at ages 48 months and older, and for dose 2 at any age (15 months through 12 years), use of the MMRV generally is preferred over separate injections of its equivalent component vaccines (ie, MMR and varicella vaccines) because of the decreased number of injections required with the MMRV.

A personal or family (such as sibling or parent) history of seizures is now a precaution for MMRV vaccination. Children with a personal or family history of seizures generally should be vaccinated with MMR and varicella vaccines, because the risks of using the MMRV in this group of children generally outweigh the benefits.

IMPLEMENTATION ISSUES

Fact sheets have been developed (www.cdc.gov/vaccines/vpd-vac/combo-vaccines/mmrv/vacopt-factsheet-hcp.htm), and the Vaccine Information Statement (VIS) has been updated (www.cdc.gov/vaccines/pubs/vis/downloads/vis-mmrv.pdf). Current availability of

the MMRV can be accessed at www.cdc.gov/vaccines/vac-gen/shortages/default.htm#4 (as of June 28, 2010).

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